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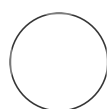
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# Aspirin for primary prevention of cardiovascular events in patients with chronic kidney disease: an updated meta-analysis

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bellosioan

## ABSTRACT

The present meta-analysis aims to evaluate the role of aspirin for the primary prevention of cardiovascular disease among patients with chronic kidney disease. A systematic literature search will be conducted and all studies (randomized controlled trials and cohorts) evaluating the efficacy and safety of aspirin will be evaluated. The quality of evidence will be critically assessed following the GRADE approach,

**Keywords:** aspirin, chronic kidney disease, cardiovascular, mace

- 1 Objective To determine the efficacy and safety of aspirin given for primary prevention of cardiovascular diseases in patients with chronic kidney disease.
- 2 Eligibility criteria The population of the study will consist of patients with diagnosed chronic kidney disease, without evidence of cardiovascular disease at baseline. The intervention of interest will be aspirin administration, given for primary cardiovascular prevention. The intervention will be compared to placebo. The primary outcome of interest will be the occurrence of major adverse cardiovascular events. Secondary outcomes will include: cardiovascular mortality, all-cause mortality, coronary heart disease, stroke, adverse renal outcomes (doubling of serum creatinine or progression to kidney failure) and bleeding (major, minor, gastrointestinal). Both randomized controlled trials and cohort studies will be held eligible. Case-control, cross-sectional and descriptive studies, as well as those examining exclusively dialysis patients be excluded. Studies evaluating the effects of aspirin for atrial fibrillation treatment were also not included in the present review.
- 3 Literature search Literature search will be performed by systematically searching from inception PubMed, Scopus, Web of Science and CENTRAL (Cochrane Central Register of Controlled Trials). In addition, Google Scholar will be screened to provide grey literature coverage, while the full reference lists of the included studies will be examined to recognize potential missing articles. No date/language restrictions will be applied.
- 4 Data extraction The following data will be extracted: year of publication, country, eligibility criteria, sample size, study design, type of population, aspirin dose, percentage of female sex, diabetes mellitus, hypertension, statin administration, mean age, systolic blood pressure, estimated glomerular filtration rate, as well as the definitions of chronic kidney disease and outcomes of interest.
- 5 Quality assessment The quality of randomized controlled trials will be assessed with the RoB-2 tool, which takes into account the following domains: randomization, deviations from intended interventions, missing outcome data, measurement of the outcome and selection of the reported results. The risk of bias of the included cohort studies will be evaluated with the ROBINS-I tool, which takes into account the following domains: confounding, selection of participants, classification of interventions, departures from intended interventions, missing data, measurement of outcomes and selection of the reported results.
- 6 Data analysis Confidence intervals will be set at 95%. Random-effects models will be fitted using the maximum likelihood method for between-study variance estimation. Pool estimates of hazard and risk ratios will be calculated. The inter-study heterogeneity will be quantified by the inconsistency index (I<sup>2</sup>), while the 95% predictive intervals will be calculated to assess the effects to be expected by future studies. Subgroup analysis is planned based on the following

parameters: study design, location, chronic kidney disease stage and presence of hypertension/diabetes mellitus. Funnel plots will be constructed and the Egger's test will be performed to assess their asymmetry, if appropriate (>10 studies).

- 7 Quality of evidence The quality of the existing evidence will be appraised following the GRADE approach. Specifically, evidence will be classified as very low, low, moderate or high by judging the following domains: study limitations, consistency, directness, imprecision and publication bias.