Screening for Chronic Kidney Disease (CKD): A Systematic Review and Meta-Analysis of Trials

EPH209

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INTRODUCTION

- CKD is progressive decline in kidney function that could lead to end stage kidney disease (ESKD), which are debilitating and costly to treat, imposing huge economic burden on health systems[1,2].
- While CKD is symptomless at early stages, it can be detected using biomarkers (e.g., creatinine, urine albumin, albumin-creatinine ratio, etc)[3].
- Screening for undiagnosed CKD in asymptomatic individuals followed by appropriate treatment may increase early detection and delay ESRD[2,4].
- The case for screening is further strengthened by a recent meta-analysis[5] that found SGLT2 inhibitors to be effective in slowing CKD progression in both diabetic and non-diabetic patients.

OBJECTIVES

- To examine the efficacy of CKD screening in detecting undiagnosed CKD among asymptomatic individuals, compared to no screening.
- To examine the uptake of CKD screening in screening arms of interventional studies.

METHODS

- We searched six databases (CENTRAL, EMBASE (via Ovid), MEDLINE (via Ovid), Web of Science, ClinicalTrials.gov, ICTRP) Jan 2011 – June 2024.
- Two independent researchers screened the titles / abstracts and full-text articles, with differences resolved through discussions.
- Two independent researchers assessed risk-of-bias using the Joanna Briggs' Institute (JBI) Critical Appraisal Checklist for RCT, with differences resolved through discussions.
- We meta-analysed risk ratios (RR) of CKD detection (comparing screening vs no-screening) and proportions of CKD screening uptake, using random effect model, overall, by age subgroups (<60 vs ≥60 years old) and by follow-up duration subgroups (<1 year, 1-2 years vs ≥2 years).
- We also extracted and presented CKD screening designs (screening tools, intervals, locations, diagnostic methods, treatment).

Inclusion Criteria	Exclusion Criteria
• Interventional studies: RCTs, quasi-experimental, or pre-post studies • Compared CKD screening vs no screening • Adults aged ≥18 years without a history of CKD • Adults with or without CKD risk factors (e.g., diabetes, hypertension, family history of CKD, frequent NSAID use)	• Adults with known CKD • Adults with symptoms suggesting kidney failure • Adults on renal replacement therapy (dialysis or kidney transplant)

Screening increased CKD detection by 50% among asymptomatic individuals with no prior history of CKD at modest screening uptake (25%)

RESULTS

Outcome	Overall Effect	Subgroups
CKD Detection (RR)	**1.50** (95% CI: 1.46–1.54)	**Age** <60: 1.50 (95% CI : 1.44-1.56), ≥60:1.47 (95% CI : 1.45-1.49) **Follow-up (year)** <1: 1.49 (95% CI: 0.74-3.03),1–2: 1.50 (95% CI: 1.45-1.54) , ≥2: 1.50 (95% CI: 1.46-1.55)
Screening Uptake (%)	**0.25** (95% CI: 0.19–0.32)	**Age** <60: 0.23 (95% CI: 0.15-0.33), ≥60: 0.3 (95% CI: 0.24-0.37); **Follow-up (year)** ,<1 : 0.27 (95% CI: 0.14-0.46) ,1–2 : 0.28 (95% CI: 0.21-0.37) ,≥2 : 0.18 (95% CI: 0.00-0.98)

DISCUSSION

LIMITATIONS

- We are unable to perform subgroup analyses by screening tool and by baseline risk levels to assess whether CKD detection or uptake differ by screening tools due to the limited number of RCTs
- We are also unable to explain the lower CKD screening uptake with longer follow-up versus shorter follow-up due to the quantitative approach used.
- All included RCTs were conducted in high-income countries – results may not generalize to low- and middle-income countries.

STRENGTHS AND POLICY IMPLICATIONS

- This is the first meta-analysis of CKD screening.
- The findings could motivate commissioning of future RCTs on CKD screening.
- Future RCTs can consider :
  - Testing for hematuria – associated with ESRD[6]
  - To examine whether repeated CKD screening at regular intervals leads to better outcomes (lower ESRD and lower mortality)
  - Consider using an SGLT2 inhibitor as treatment
- Future RCTs should strive for complete and consistent reporting of screening designs.

TABLES AND FIGURES

Appendix 1: Prisma flowchart for study selection method

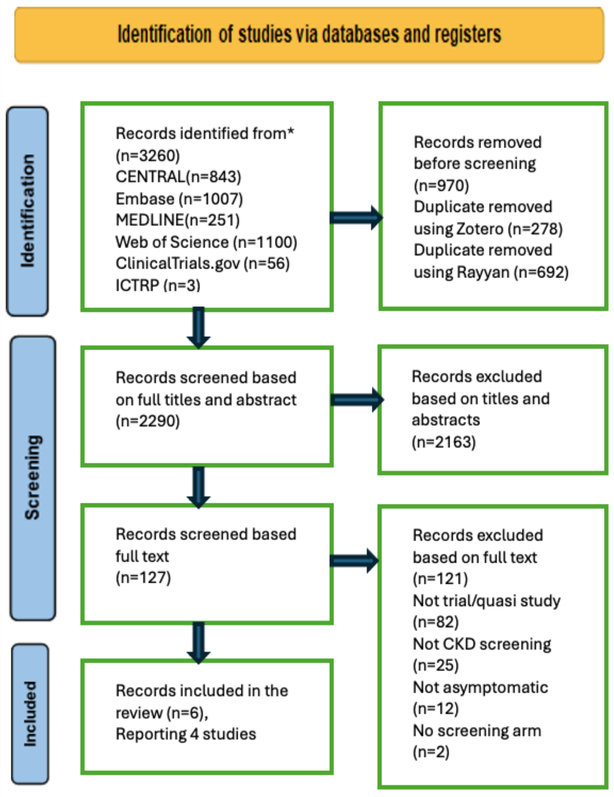


Table 1: Screening design and diagnostic

Study	Screening Design	Diagnostic Method / Criteria	Treatment
Peralta et al. (2020) San Francisco, US	**Tool / biomarker:** Serum creatinine and Cystatin-C using blood test and ACR using urine sample. **Threshold for positive screen:** Combined eGFRcreat and cystatin C equation [eGFRcreat-cys] <60 ml/min per 1.73m² or ACR≥30 mg/g **Screening interval:** One-off **Location:** Primary care practices at the San Francisco Veterans Affairs (VA) Medical Centre	The results of the screening test were used to diagnose CKD.	Renin-angiotensin system (RAS) inhibitors
Kennedy et al. (2019) Hampshire, England	**Tool / biomarker:** Serum creatinine using blood test **Threshold for positive screen:** eGFR<60mL/min/1.73m² **Screening interval:** Not reported **Location:** Primary care clinics	Repeat of the blood test within 2 weeks, using eGFR <60 mL/min/1.73 m² as the threshold to diagnose CKD.	Not reported
Leddy et al. (2019), Pennsylvania, United States	**Tool / biomarker:** Proteinuria, using a home test kit with urine dipstick supported by a smartphone app **Threshold for positive screen:** Based on the colour changes against colour board provided with the test kit, the smartphone app would interpret whether the test was normal or abnormal. **Screening interval:** One-off **Location:** Home testing	ACR ≥ 30 mg/g or protein/creatinine ratio ≥ 150 mg/g)	ACEi or ARB and statin initiation
Tesfaye et al (2023), New South Wales, Victoria and Queensland, Australia	**Tool / biomarker:** Serum creatinine and eGFR with point-of-care testing, for those with moderate to high risk (>3% risk of developing moderate to severe CKD over 5 years, based on QKidney risk calculator). **Threshold for positive screen:** Not specified. But all test results will be forwarded to the patients' primary care doctors. **Screening interval:** Not reported **Location:** Community pharmacies	CKD will be diagnosed by the primary care doctors. How diagnoses would be made was not specified.	Not reported

Figure 1: Forest plot of CKD detection

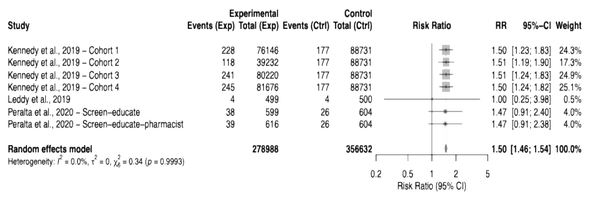
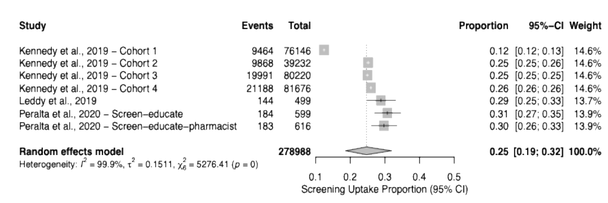


Figure 2: Forest plot of CKD screening uptake



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