

Abstract

Cognitive impairment (CI), which can range from mild cognitive impairment (MCI) to dementia, is common in chronic kidney disease (CKD) and kidney failure and is associated with adverse outcomes. Screening for CI has been studied in the general population, and optimal cut-offs for various instruments exist, but this has not been rigorously explored in the setting of kidney disease where cognition may differ due to comorbidities, uremic toxins and dialysis. In this systematic review, we sought to summarize the performance of screening tools for MCI and dementia across the spectrum of kidney disease.

A search strategy for PubMed, EMBASE, CINAHL, Psych Hub and the Cochrane Library, was developed with the assistance of a medical librarian. Studies that recruited adult patients with CKD or kidney failure (including dialysis and kidney transplantation) who were screened for MCI or dementia using an instrument that was compared to a diagnostic criteria for MCI or dementia, were included. Two reviewers independently identified studies meeting the inclusion criteria and a third reviewer resolved conflicts. Studies that compared cognitive screening instruments to a gold standard and had outcomes such as sensitivity, specificity, PPV, NPV, AUROC were included.

Of 2511 eligible studies, we included 64 in full text review, and 10 unique studies for data abstraction. These studies evaluated the performance of the Mini-Mental Status Exam (MMSE) (6 studies), the Montreal Cognitive Assessment (MoCA) (7 studies), the Modified Mini-Mental State Exam (3MS) (1 study), Mini-Addenbrooke's Cognitive Evaluation (m-ACE) (1 study), and the Kidney Disease Quality of Life (KDQOL) scale (1 study). Optimal cut-offs and performance of screening instruments varied among studies. Meta-analysis is ongoing.

Optimal cut-offs for CI screening in patients with kidney disease are different from those in the general population. Further research is needed to improve screening instruments for CI in the adult CKD and kidney failure populations.

Keywords: mild cognitive impairment, screening instruments, chronic kidney disease

Methodology

Registered protocol in NIHR's PROSPERO, an international prospective register of systematic reviews (Registration ID: CRD42022369285)

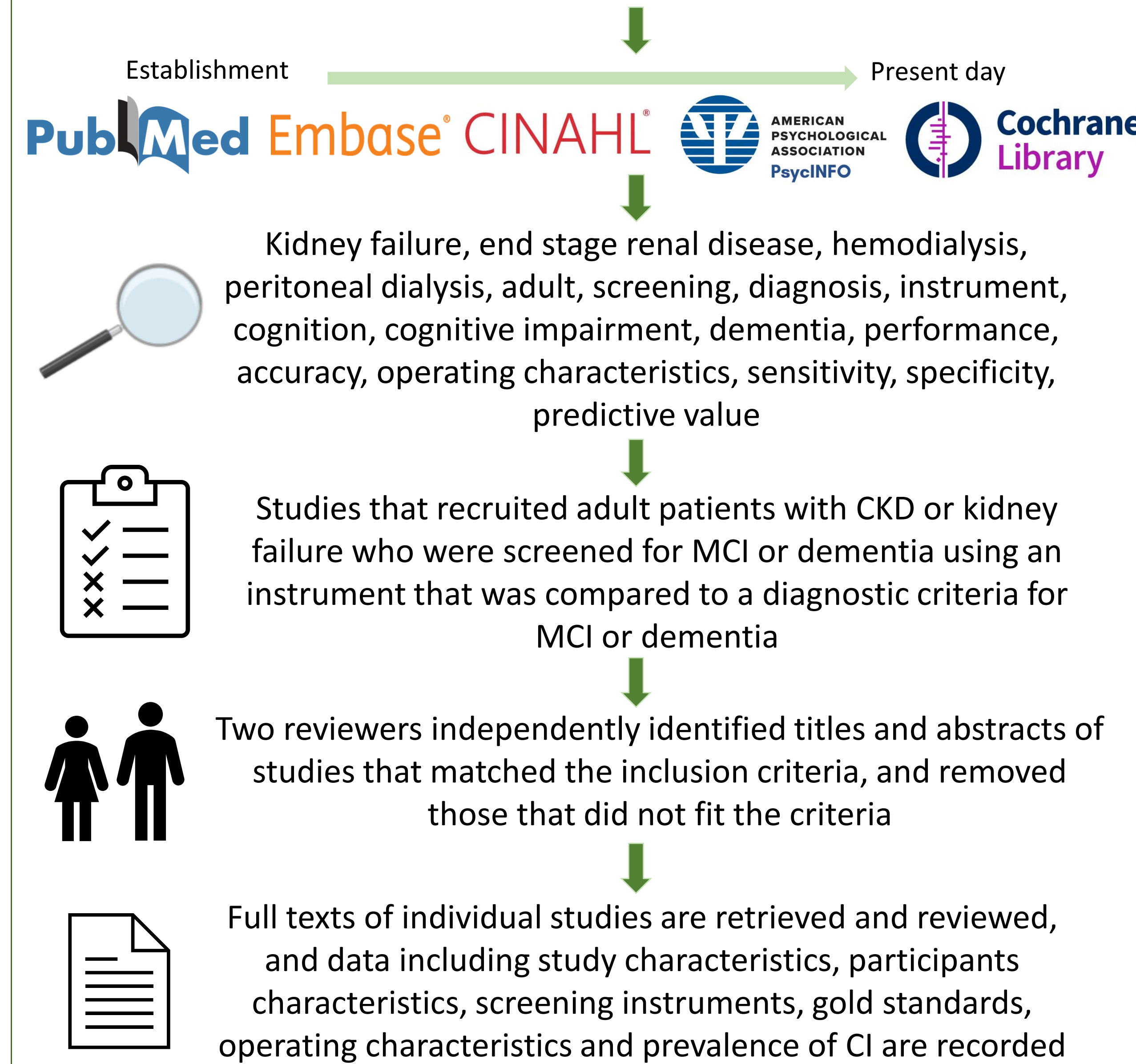
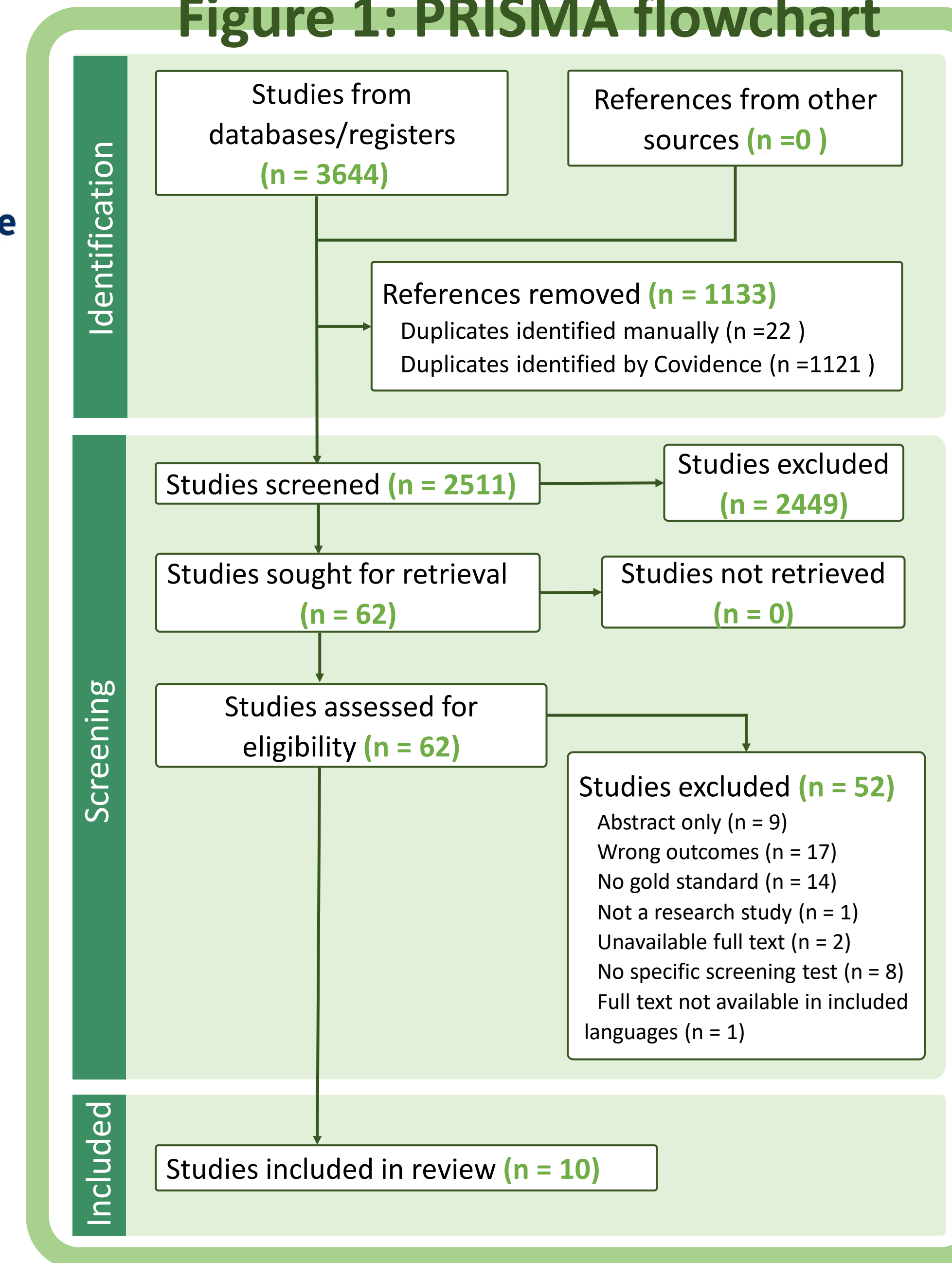


Figure 1: PRISMA flowchart



EDI & SGBA+ considerations

- Equity Diversity and Inclusion (EDI):**
- Diverse research team with unique experiences and backgrounds
 - Greater range of languages for studies that can be included
 - Study population is individuals with kidney failure and many of these individuals often experience reduced quality of life
 - Overall paucity of research being conducted in individuals with kidney failure
- Sex- and gender- based analysis (SGBA+):**
- Given that the included studies only report patients' biological sex, and fail to mention gender, gender-based analysis is impossible.
 - While sex/gender is not expected to significantly affect cognition, it may affect the screening, diagnosis and treatment of MCI/dementia, so we may examine sex as a subgroup if screening instrument operating characteristics differ by sex in included studies

Discussion & Next Steps

- In this systematic review of 10 studies, we found that:
 - The prevalence of CI or dementia in the study populations with CKD/kidney failure is variable (24-81%)
 - A majority (90%) of included studies were limited to evaluating the performance of either the MMSE or MoCA screening tests
 - These screening tools performed sub-optimally and yielded varying results:
 - For the MoCA, the range of optimal cutoff values ranges from 21 to 24, while the typical cutoff for detecting cognitive impairment using the MoCA in the general population is 26
 - For the MMSE, the range of optimal cutoff values ranges from 26-28, while the typical cutoff for detecting cognitive impairment using the MMSE in the general population is 23 or 24
- **Strengths:**
 - Comprehensive search strategy and detailed methodology
- **Limitations:**
 - Only studies published in English, French, Spanish and German were included
 - Heterogeneity in populations, instruments, language
 - Uncertainty associated with the exact etiology of study participants' CI in dialysis (potentially multifactorial)
 - Variability in the gold standard used in each study
- **Next steps:**
 - Assess risk of bias
 - Finish meta-analysis of operating characteristics across screening instruments

Background

- The prevalence of cognitive impairment (CI) in adults with chronic kidney disease and kidney failure is high.
- Mild cognitive impairment (MCI) is a condition that represents an intermediate between normal cognition and dementia, in which the degree of cognitive impairment exceeds that expected by aging alone, but still allows individuals to function independently.
- Dementia is a more severe version of cognitive impairment that renders social or occupational independence impossible.
- CI is associated with outcomes that can adversely affect physical, mental and emotion wellbeing.
- The severity of CI is measured using screening instruments such as the Mini-Mental State Exam (MMSE) and the Montreal Cognitive Assessment (MoCA). Each screening tool is unique and differentially tests subdomains of cognition.
- Operating characteristics for tests vary depending on the population being tested. As such, the cut-offs for screening tools which have been studied and validated in the general population, may not perform similarly in the setting of kidney disease where cognitive function may differ due to comorbidities, uremic toxins, and dialysis.
- We performed a systematic review and meta-analysis to summarize the performance of screening tools for MCI and dementia across the spectrum of kidney disease.

Results

Table 1: Characteristics of included studies and screening tests assessed

Author(Year)	Language	Population	Age [mean(SD)]	Screening Test	Score [mean(SD)]	Domains Assessed by Gold Standard	Prevalence of CI	Optimal reported cutoffs	Sensitivity	Specificity	Area Under the Curve (AUC)
Angermann (2017)	German	Hemodialysis	66(15)	MoCA	24 (4)	memory, orientation, judgement, problem-solving	NR	23.5	99%	74%	NR
Drew (2019)	English	Hemodialysis	64(14)	MoCA	20(4)	Memory, attention and psychomotor speed, executive function	62%	21	86%	55%	0.81
Hobson (2016)	NR	NR	77(8)	M-ACE & MMSE	23(5) & 25 (4)	memory, attention, language, visuospatial skills, and executive function	24%	21; NR	70%; NR	100%; NR	0.96; 0.95
Lee (2018)	Korean	Hemodialysis	65(8)	K-MMSE & K-MoCA	26(3) & 20 (5)	Attention, visuospatial function, language, memory, executive function, working memory	30%	NR; NR	NR; NR	NR; NR	0.72; 0.77
Li (2016)	NR	Peritoneal dialysis	51(14)	3MS	88 (NR)	Memory, language, attention, visuospatial ability, executive function	24%	82	NR	NR	NR
Paraizo (2016)	NR	CKD	57(8)	MoCA	22 (4)	Visuospatial ability, executive function, language, memory, attention, orientation	74%	NR	NR	NR	NR
Puy (2018)	NR	NR	63(11)	MMSE & MoCA	NR (NR) & NR (NR)	Language, visuospatial ability, memory, executive function,	NR	NR; NR	62%; 62%	85%; 100%	NR; NR
Sorenson (2018)	English	Hemodialysis	62(17)	KDQOLCF & MMSE	76 (19) & NR	Executive function, attention, visuospatial ability, memory	81%	60; NR	0.75-0.85%; 0.27%	NR; 77%	NR; 0.507
Tian (2020)	Chinese	Hemodialysis	64(8)	MoCA-BJ & MMSE	21 (NR) & 25 (NR)	Attention, executive function, memory, language, visuospatial ability	NR	24; 26	88%; 70%	75%; 77%	0.891; 0.823
Tiffin-Richards (2014)	German	Hemodialysis	58(14)	MoCA & MMSE	24 (4) & 29 (2)	Memory, language, attention, visuospatial ability, executive function	46%	24; 28	77%; 55%	79%; 75%	0.755; 0.701

CKD, chronic kidney disease; CI, cognitive impairment; NR, not recorded; MoCA, Montreal Cognitive Assessment; M-ACE, Mini-Addenbrooke's Cognitive Evaluation; MMSE, Mini-Mental Status Exam; K-, Korean; 3MS, modified mini-mental status examination; KDQOLCF, kidney disease quality of Life- Cognitive Function; BJ, Beijing