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DEVELOPMENT AND VALIDATION OF MODELS PREDICTING CHRONIC KIDNEY DISEASES AMONG PEOPLE LIVING WITH HIV: PROTOCOL FOR SYSTEMATIC REVIEW

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DEVELOPMENT AND VALIDATION OF MODELS PREDICTING CHRONIC KIDNEY DISEASES AMONG PEOPLE LIVING WITH HIV: PROTOCOL FOR SYSTEMATIC REVIEW

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ABSTRACT

Introduction

Chronic kidney diseases (CKD) are estimated to affect about 9.1% of the global population with a substantially increased risk of the condition (6.8 – 17.2%) among people living with HIV (PLWH). This increased risk is attributed to HIV infection itself, antiretroviral therapy (ART), co-existing viral infections, non-infectious co-morbidities, and traditional risk factors for CKD. Predictive models have been employed in the estimation of prevalent and incident CKD risk in both PLWH and the general population. A predictive model showing an individual's risk of prevalent and/or progression to kidney failure is useful for initiating timely interventions that prevent further worsening of kidney function. This study will systematically review published prediction models developed and/or validated for prevalent and incident CKD in PLWH, describe their characteristics, compare performance, and assess methodological quality and applicability.

Methods and Analysis

Studies with predictive models of interest will be identified by searching MEDLINE, Web of Science, Cumulative Index to Nursing and Allied Health Literature, Cochrane library, and Scopus from inception to May 2022. Title and abstract screening, full-text review, and data extraction will be completed independently by two reviewers. Using appropriate tools designed for predictive modeling investigations, the included papers will be rigorously assessed for bias and applicability. Extracted data will be presented in tables so that published prediction models can be compared qualitatively. Quantitative data on the predictive performance of these models will be synthesized with meta-analyses if appropriate.

Ethics and Dissemination

The findings of the review will be disseminated in peer reviewed journals and seminar presentations to stakeholders. Ethical approval is not required as this is a protocol.

Systematic Review registration

PROSPERO Registration number: CRD42021279694

Keywords: Chronic Kidney diseases, predictive models, prevalence, incidence, HIV, PLWH, systematic review, protocol

Strengths and Limitations

This systematic review protocol follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) 2015 guidelines

This review addresses knowledge gap regarding chronic kidney disease (CKD) prediction models specific for people living with HIV (PLWH)

The review will also incorporate models predicting progression to end-stage renal disease

This review is not limited to randomised controlled trials

In the absence of sufficient number of studies/models, meta-analysis may not be performed

Introduction

Chronic kidney disease (CKD) has become a global threat as it constitutes a sizeable proportion of morbidity and premature deaths [1]. CKD is estimated to affect 697.5million people globally representing a global prevalence of 9.1% [1]. The traditional risk factors for CKD include increasing age, hypertension, diabetes mellitus, and obesity. Impaired renal function is a predictor of hospital admission and poor quality of life as well as increased healthcare expenses [2, 3].

There is a substantially increased risk of developing CKD (6.8 – 17.2%) among people living with HIV (PLWH) [4, 5]. This is corroborated by postulations of HIV infection and antiretroviral therapy (ART) regimens in the acquisition of CKD [6, 7]. CKD could arise among PLWH from the classic HIV-associated nephropathy or immune complex disease, CKD related to non-infectious co-morbidities (hypertension and diabetes), co-existing viral infections (Hepatitis B and C), and CKD from antiretroviral toxicity [8, 9]. CKD is known to contribute to the increased morbidity and mortality among PLWH as the number of PLWH with end-stage renal disease (ESRD) increases globally.

Rationale

Predictive models have been developed to assist with CKD risk evaluation in both the HIV and general population. These predictive models have been employed to identify persons at greater risk of CKD (diagnosis or prognosis) and found to be helpful in clinical decision-making as well as public health interventions to mitigate against CKD [10, 11]. These models utilise biological markers (urinary protein and albumin, serum creatinine and cystine C, uric acid) along with other traditional risk factors for CKD (age, sex, blood pressure readings, and diabetes mellitus) in their formulation. Early detection and management of hypertension, diabetes mellitus, and CKD in this population can help improve renal and cardiovascular outcomes thereby regressing or slowing the progression towards end-stage renal disease (ESRD).

This protocol is for a systematic review with or without meta-analysis of the spectrum of prevalent and/or incident CKD prediction models developed and/or validated in PLWH, to identify existing gaps and guide research endeavours in the future.

Objective

This study aims to conduct a systematic review to identify and characterize predictive models developed and/or validated on prevalent and incident CKD in adult PLWH, evaluate the performances of these models in PLWH and identify existing knowledge gaps as reported in published literature between since inception and May 2022.

Methods and Analysis

The protocol will be conducted in alignment with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) 2015 guidelines [12]. In addition, the CHARMS checklist will be employed to frame the review questions while the PICOTS criteria will be used to determine inclusion and exclusion criteria [13, 14].

Review Questions

The review questions are as follows: 1) are there risk models specifically developed to predict prevalent and/or incident CKD among PLWH; and what are their characteristics? and 2) are there models for predicting prevalent or incident CKD which have been validated in PLWH, and how do they perform in this population? The CHARMS checklist was utilised in the formulation of the review questions [13].

The above questions will form the basis of our review in identifying both prognostic and diagnostic models for CKD, with all types of prediction modelling studies included (development with or without external validation in independent data and external model validation with possible model updates). The scope of the review will be to inform clinical decision-making as it relates to prevalent and incident CKD among PLWH. The review will include diagnostic and prognostic models for CKD as well as models predicting progression to ESRD with reference to HIV diagnosis. PLWH who are ≥ 18 years of age will be our target population.

Patient and public involvement

This review does not require patient or public involvement as it will be based on published works.

Inclusion and exclusion criteria

The PICOTS (patient population, intervention, comparator, outcome, timing setting) framework will be employed in defining the inclusion and exclusion criteria for this review [14]. The population of interest is adult (≥ 18 years) PLWH with emphasis on predictive models for prevalent and incident CKD among the population. The primary outcomes are predictive models for 1) prevalent CKD, 2) incident CKD and 3) progression to ESRD in PLWH. Our secondary outcomes were the evaluation of the performance of the above three groups of models as well as the candidate variables employed in their derivation. Studies included for the review are cross-sectional, cohort, clinical controlled and randomized controlled trials with intent for the models to be used for clinical decision making and public health advocacy measures.

The exclusion criteria will include the following. Studies primarily among paediatric, adolescents, and pregnant women, case-control studies, editorials, letters to editors, models generated from simulation and animal studies as well as those evaluating quality of life among patients with CKD.

Search Strategy

From inception to May 2022, a systematic search of the following electronic databases of peer-reviewed journal articles and online search records will be conducted: MEDLINE, Web of Science, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane library, and Scopus. Keywords relating to population (HIV patients, People living with HIV, People living with HIV/AIDS, HIV infected, ART experienced, ART nave); disease (impaired renal function, impaired kidney function, chronic kidney disease, chronic renal disease, chronic renal insufficiency, chronic kidney failure, end-stage kidney disease, end-stage renal disease); modeling (prevalence, prevalent, incidence, incident, predict, risk, risk scores, prediction models, prediction tools, risk assessment, risk engineering); disease

(impaired renal function, impaired kidney function, chronic (models predicting CKD prevalence and incidence among PLWH, factors associated with the validity of models for PLWH). To accommodate each database, the search phrases will be concatenated. Reference lists of relevant papers will be scanned for eligible studies. Grey literature (such as reports, conference, and workshop proceedings) will be searched using the Google Scholar search engine, as well as important relevant websites such as African Journals Online (AJOL) (hand searches). EndNote reference manager will be used to export references and delete any duplications identified.

Selection of studies

The title and abstract of each paper will be evaluated by two independent reviewers before be ing included in the review. Final selection of papers to be included in the review will be decided after reading the full texts of eligible articles. Disagreements will be resolved through discussion and consensus, or consultation with a third reviewer.

A model/risk assessment tool that predicts prevalent and/or incident CKD, as well as models for progression to end-stage renal disease, must be derived in an adult human population. The area under the receiver operating characteristic curve (AUC) or C-statistic, reclassification percentage, net reclassification improvement (NRI), or integrated discrimination improvement index (IDI) are some analyses being proposed for assessing the qualities of the models.

Assessment of studies

Diagnostic models are those designed for prevalent purposes while prognostic models are designed for incident purposes.

PROBAST (Prediction model Risk Of Bias ASsessment Tool) will be employed to evaluate the quality of all models. PROBAST evaluates both the risk of bias and the application of multivariable prediction (diagnostic and prognostic) models created or validated in primary research. The PROBAST tool will also be involved in the systematic reviews of predictive models for prevalent and incident CKD as well as progression to ESRD in PLWH [15, 16].

Furthermore, the Transparent Reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD statement) will be used to evaluate studies developed or validated for multivariable prediction (either diagnostic or prognostic) model. To achieve this objective, the TRIPOD Statement uses a 22-item checklist [17, 18] in the evaluation of models under consideration.

Disagreements in the use of the above tools for the review will be resolved following consultation with the third reviewer.

Data extraction

The following details will be used to extract data from chosen studies; study specifics (first author, journal name, year of publication, country of study); study population (sample size, age range, sex distribution, number of PLWH, ART-naive or experienced); population characteristics (pre-existing co-morbid conditions: hypertension, diabetes mellitus, stroke, myocardial infarction, dyslipidaemia, congestive heart failure).

In addition, model characteristics (number of participants in the derivation and validation cohorts, number of participants with outcome of interest, number of candidate variables stated as predictors, number and list of variables included in model, type of statistical analysis used in generating model); study designs employed in deriving the models (cross-sectional, cohort, controlled clinical trials, randomized controlled trials); models' outcome data (prevalence and incidence of CKD, number of multivariable prediction scores/models, definition of CKD, CKD equations utilized); and performance (discriminatory [AUC or C-statistic], calibration [difference between observed and predicted rates of hypertension, p-value of corresponding test statistic], re-classification [NRI and IDI values with their accompanying 95% confidence intervals and p-values]) will also be documented. The source of funding and study limitations will be captured. The extracted data will be presented in a tabular (data) form.

Data analysis

The data will be summarized in general (globally), as well as by the World Health Organisation (WHO) regional designation, gender, and study population (PLWH, ART-naive or experienced). A narrative review will be undertaken if a meta-analysis is not possible. The meta-analysis would focus on the performance measures of the identified models with reference to the Area under the receiver operating characteristic (ROC) curve (AUC-ROC), Kolmogorov- Smirnov test, and other appropriate statistical tests. The random effects will be determined using inverse variance weighting and 95% confidence intervals (CI) of pooled estimates while heterogeneity will be determined using the inconsistency index (I^2) [19, 20]. Publication bias will be assessed using funnel plots and when found to be significant, further analysis (Egger's and Begg's tests) will be conducted [21].

Conclusion

This systematic review will provide evidence on the models that predict prevalent and incident CKD among PLWH. The review will also inform on the interventions developed in the prevention and management of CKD among PLWH.

Dissemination

The findings of this review will be published and included as a chapter in a PhD thesis at the University of Cape Town. Furthermore, the findings of this evaluation will be shared with relevant agencies through seminars, conferences, and policy development meetings.

Funding statement

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Author contributions

This systematic review was conceived and designed by OO, NO, and APK. This protocol was initially drafted by OO, NP, AM, NO, BS and APK. Subsequent drafts to the protocol were commented and revisions made by all authors. All authors have approved submission.

Competing interests

The authors declare no competing interests

Acknowledgment

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Data availability statement

Data generated during the review will be made available upon request and at the discretion of study supervisors.

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APPENDIX

Search Strategy

Chronic Kidney disease

"Kidney disease*" OR "kidney failure" OR "Renal disease" OR "Renal insufficiency" OR "Chronic kidney" OR "Chronic renal" OR "CKD" OR "CKF" OR "CRD" OR "end-stage renal" OR "end-stage kidney" OR "end-stage renal" OR "end-stage kidney" OR "uremia" OR "uraemia" OR "dialysis" OR "hemofiltration" OR "haemofiltration" OR "hemodiafiltration" OR "haemodiafiltration" OR "hemodialysis" OR "haemodialysis" OR "renal dialysis"

Nature of association

"incidence" OR "prevalence" OR "occurrence" OR "diagnosis" OR "assessment" OR "identification" OR "screening" OR "progression" OR "end-stage renal"

Modelling and Risk scores

Ingui filter

(Validat$ OR Predict$.ti. OR Rule$) OR (Predict$ AND (Outcome$ OR Risk$ OR Model$)) OR ((History OR Variable$ OR Criteria OR Scor$ OR Characteristic$ OR Finding$ OR Factor$) AND (Predict$ OR Model$ OR Decision$ OR Identif$ OR Prognos$)) OR (Decision$ AND (Model$ OR Clinical$ OR Logistic Models/)) OR (Prognostic AND (History OR Variable$ OR Criteria OR Scor$ OR Characteristic$ OR Finding$ OR Factor$ OR Model$))

Haynes Broad filter

(Predict*[tiab] OR Predictive value of tests[mh] OR Scor*[tiab] OR Observ*[tiab] OR Observer variation[mh])

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification	1a	Identify the report as a protocol of a systematic review
Update	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors:		
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support:		
Sources	5a	Indicate sources of financial or other support for the review
Sponsor	5b	Provide name for the review funder and/or sponsor
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
INTRODUCTION		
Rationale	6	Describe the rationale for the review in the context of what is already known
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
METHODS		
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated
Study records:		
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review

Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

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Primary Subject Heading:	Renal medicine
Secondary Subject Heading:	Epidemiology, Infectious diseases, Public health, HIV/AIDS
Keywords:	HIV & AIDS < INFECTIOUS DISEASES, Chronic renal failure < NEPHROLOGY, EPIDEMIOLOGY, INFECTIOUS DISEASES

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Keywords: Chronic Kidney disease, predictive models, prevalence, incidence, HIV, PLWH, systematic review, protocol

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This review addresses knowledge gap regarding chronic kidney disease (CKD) prediction models specific for people living with HIV (PLWH)

The review will also incorporate models predicting progression to kidney failure requiring kidney replacement therapy

This review is not limited to randomised controlled trials

In the absence of sufficient number of studies/models, meta-analysis may not be performed

Introduction

Chronic kidney disease (CKD) has become a global threat as it constitutes a sizeable proportion of morbidity and premature deaths [1]. CKD is estimated to affect 697.5million people globally representing a global prevalence of 9.1% [1]. The traditional risk factors for CKD include increasing age, hypertension, diabetes mellitus, and obesity. CKD is a predictor of poor quality of life as well as increased healthcare expenses [2, 3].

There is a substantially increased risk of developing CKD (6.8 – 17.2%) among people living with HIV (PLWH) [4, 5]. This is corroborated by postulations of HIV infection and antiretroviral therapy (ART) regimens in the acquisition of CKD [6, 7]. CKD could arise among PLWH from the classic HIV-associated nephropathy or immune complex disease, CKD related to non-infectious co-morbidities (hypertension and diabetes), co-existing viral infections (Hepatitis B and C), and CKD from antiretroviral toxicity [8, 9].

CKD is known to contribute to the increased morbidity and mortality among PLWH as the number of PLWH with kidney failure requiring kidney replacement therapy increases globally [2, 3]. CKD as an important non-infectious cause of morbidity and mortality among PLWH could reverse the gains achieved via ART roll-out [10, 11]. Thus, risk assessments using predictive models remains a veritable tool to mitigating CKD in the populace (and HIV cohort).

Rationale

Predictive models have been developed to assist with CKD risk evaluation in both the HIV and general population. These predictive models have been employed to identify persons at greater risk of CKD (diagnosis or prognosis) and found to be helpful in clinical decision-making as well as public health interventions to mitigate against CKD [12, 13]. These models utilise biological markers (urinary protein and albumin, serum creatinine and cystine C, uric acid) along with other traditional risk factors for CKD (age, sex, blood pressure readings, and diabetes mellitus) in their formulation. Early detection and management of hypertension, diabetes mellitus, and CKD in this population can help improve renal and cardiovascular outcomes thereby regressing or slowing the progression towards kidney failure requiring kidney replacement therapy.

Few studies have reported predictive models for prevalent and incident CKD among PLWH as well as systematic reviews of CKD predictive models in the general population [14–17]. However, none of these studies have provided systematic reviews on CKD predictive models with HIV population in focus.

This protocol is for a systematic review with or without meta-analysis of the spectrum of prevalent and/or incident CKD prediction models developed and/or validated in PLWH, to identify existing gaps and guide research endeavours in the future.

Objective

This study aims to conduct a systematic review to identify and characterize predictive models developed and/or validated on prevalent and incident CKD in adult PLWH, evaluate the performances of these models in PLWH and identify existing knowledge gaps as reported in published literature between since inception and May 2022.

Methods and Analysis

The protocol will be conducted in alignment with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) 2015 guidelines [18]. In addition, the CHARMS checklist will be employed to frame the review questions while the PICOTS criteria will be used to determine inclusion and exclusion criteria [19, 20].

Review Questions

The review questions are as follows: 1) are there risk models specifically developed to predict prevalent and/or incident CKD among PLWH; and what are their characteristics? and 2) are there models for predicting prevalent or incident CKD which have been validated in PLWH, and how do they perform in this population? The CHARMS checklist was utilised in the formulation of the review questions [19].

The above questions will form the basis of our review in identifying both prognostic and diagnostic models for CKD, with all types of prediction modelling studies included (development with or without external validation in independent data and external model validation with possible model updates). The scope of the review will be to inform clinical decision-making as it relates to prevalent and incident CKD among PLWH. The review will include diagnostic and prognostic models for CKD as well as models predicting progression to ESRD with reference to HIV diagnosis. PLWH who are ≥ 18 years of age will be our target population.

Patient and public involvement

This review does not require patient or public involvement as it will be based on published works.

Inclusion and exclusion criteria

The PICOTS (patient population, intervention, comparator, outcome, timing setting) framework will be employed in defining the inclusion and exclusion criteria for this review [20]. The population of interest is adult (≥ 18 years) PLWH with emphasis on predictive models for prevalent and incident CKD among the population. The primary outcomes are predictive models for 1) prevalent CKD, 2) incident CKD and 3) progression to kidney failure requiring kidney replacement therapy in PLWH. Our secondary outcomes were the evaluation of the performance of the above three groups of models as well as the candidate variables employed in their derivation. Studies included for the review are cross-sectional, cohort, clinical controlled and randomized controlled trials with intent for the models to be used for clinical decision making and public health advocacy measures.

The exclusion criteria will include the following. Studies primarily among paediatric, adolescents, and pregnant women, case-control studies, editorials, letters to editors, models generated from simulation and animal studies as well as those evaluating quality of life among patients with CKD.

Search Strategy

From inception to May 2022, a systematic search of the following electronic databases of peer-reviewed journal articles and online search records will be conducted: MEDLINE, Web of Science, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane library, and Scopus. Keywords relating to population (HIV patients, People living with HIV, People living with HIV/AIDS, HIV infected, ART experienced, ART naive); disease (impaired renal function, impaired kidney function, chronic kidney disease, chronic renal disease, chronic renal insufficiency, chronic kidney failure, end-stage kidney disease, end-stage renal disease); modeling (prevalence, prevalent, incidence, incident, predict, risk, risk scores, prediction models, prediction tools, risk assessment, risk engineering); and models predicting CKD prevalence and incidence among PLWH as well as factors associated with the validity of these models. To accommodate each database, the search phrases will be concatenated. Reference lists of relevant papers will be scanned for eligible studies. A search strategy using MEDLINE is attached (See Appendix section). Grey literature (such as reports, conference, and workshop proceedings) will be searched using the Google Scholar search engine, as well as important relevant websites such as African Journals Online (AJOL) (hand searches). EndNote reference manager will be used to export references and delete any duplications identified.

Selection of studies

The title and abstract of each paper will be evaluated by two independent reviewers before be ing included in the review. Final selection of papers to be included in the review will be decided after reading the full texts of eligible articles. Disagreements will be resolved through discussion and consensus, or consultation with a third reviewer.

A model/risk assessment tool that predicts prevalent and/or incident CKD, as well as models for progression to end-stage renal disease, must be derived in an adult human population. The area under the receiver operating characteristic curve (AUC) or C-statistic, reclassification percentage, net reclassification improvement (NRI), or integrated discrimination improvement index (IDI) are some analyses being proposed for assessing the qualities of the models.

Assessment of studies

Diagnostic models are those designed for prevalent purposes while prognostic models are designed for incident purposes.

PROBAST (Prediction model Risk Of Bias ASsessment Tool) will be employed to evaluate the quality of all models. PROBAST evaluates both the risk of bias and the application of multivariable prediction (diagnostic and prognostic) models created or validated in primary research. The PROBAST tool will also be involved in the systematic reviews of predictive models for prevalent and incident CKD as well as progression to ESRD in PLWH [21, 22].

Furthermore, the Transparent Reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD statement) will be used to evaluate studies developed or validated for multivariable prediction (either diagnostic or prognostic) model. To achieve this objective, the TRIPOD Statement uses a 22-item checklist [23, 24] in the evaluation of models under consideration.

Disagreements in the use of the above tools for the review will be resolved following consultation with the third reviewer.

Data extraction

The following details will be used to extract data from chosen studies; study specifics (first author, journal name, year of publication, country of study); study population (sample size, age range, sex distribution, number of PLWH, ART-naive or experienced); population characteristics (pre-existing co-morbid conditions: hypertension, diabetes mellitus, stroke, myocardial infarction, dyslipidaemia, congestive heart failure).

In addition, model characteristics (number of participants in the derivation and validation cohorts, number of participants with outcome of interest, number of candidate variables stated as predictors, number and list of variables included in model, type of statistical analysis used in generating model); study designs employed in deriving the models (cross-sectional, cohort, controlled clinical trials, randomized controlled trials); models' outcome data (prevalence and incidence of CKD, number of multivariable prediction scores/models, definition of CKD, CKD equations utilized); and performance (discriminatory [AUC or C-statistic], calibration [difference between observed and predicted rates of hypertension, p-value of corresponding test statistic], re-classification [NRI and IDI values with their accompanying 95% confidence intervals and p-values]) will also be documented. The source of funding and study limitations will be captured. The extracted data will be presented in a tabular (data) form.

Data analysis

The data will be summarized in general (globally), as well as by the World Health Organisation (WHO) regional designation, gender, and study population (PLWH, ART-naive or experienced). Meta-analysis will be conducted for CKD predictive models in the presence of adequate number of models otherwise a narrative review will be undertaken. The meta-analysis would focus on the performance measures of the identified models with reference to the Area under the receiver operating characteristic (ROC) curve (AUC-ROC), Kolmogorov-Smirnov test, and other appropriate statistical tests. The random effects will be determined using inverse variance weighting and 95% confidence intervals (CI) of pooled estimates while heterogeneity will be determined using the inconsistency index (I^2) [25, 26]. Publication bias will be assessed using funnel plots and when found to be significant, further analysis (Egger's and Begg's tests) will be conducted [27].

Patient and Public involvement statement

This review will involve published articles form the above listed databases and search engines. The selected models predicting CKD would not primarily involve patients.

Ethics and Dissemination

Ethical approval is not required as this is a protocol for a systematic review. The findings of this review will be published in peer-reviewed journals and included as a chapter in a PhD thesis at the University of Cape Town. Furthermore, the findings of this evaluation will be shared with relevant agencies through seminars, conferences, and policy development meetings.

Funding statement

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Author contributions

This systematic review was conceived and designed by OO, NO, and APK. This protocol was initially drafted by OO, NP, AM, NO, BS and APK. Subsequent drafts to the protocol were commented and revisions made by all authors. All authors have approved submission.

Competing interests

The authors declare no competing interests

Acknowledgment

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Data availability statement

Data generated during the review will be made available upon request and at the discretion of study supervisors.

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APPENDIX

Search Strategy

Chronic Kidney disease

"Kidney disease*" OR "kidney failure" OR "Renal disease" OR "Renal insufficiency" OR "Chronic kidney" OR "Chronic renal" OR "CKD" OR "CKF" OR "CRD" OR "end-stage renal" OR "end-stage kidney" OR "end-stage renal" OR "end-stage kidney" OR "uremia" OR "uraemia" OR "dialysis" OR "hemofiltration" OR "haemofiltration" OR "hemodiafiltration" OR "haemodiafiltration" OR "hemodialysis" OR "haemodialysis" OR "renal dialysis"

Nature of association

"incidence" OR "prevalence" OR "occurrence" OR "diagnosis" OR "assessment" OR "identification" OR "screening" OR "progression" OR "end-stage renal"

Modelling and Risk scores

Ingui filter

(Validat$ OR Predict$.ti. OR Rule$) OR (Predict$ AND (Outcome$ OR Risk$ OR Model$)) OR ((History OR Variable$ OR Criteria OR Scor$ OR Characteristic$ OR Finding$ OR Factor$) AND (Predict$ OR Model$ OR Decision$ OR Identif$ OR Prognos$)) OR (Decision$ AND (Model$ OR Clinical$ OR Logistic Models/)) OR (Prognostic AND (History OR Variable$ OR Criteria OR Scor$ OR Characteristic$ OR Finding$ OR Factor$ OR Model$))

Haynes Broad filter

(Predict*[tiab] OR Predictive value of tests[mh] OR Scor*[tiab] OR Observ*[tiab] OR Observer variation[mh])

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification	1a	Identify the report as a protocol of a systematic review
Update	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors:		
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support:		
Sources	5a	Indicate sources of financial or other support for the review
Sponsor	5b	Provide name for the review funder and/or sponsor
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
INTRODUCTION		
Rationale	6	Describe the rationale for the review in the context of what is already known
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
METHODS		
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated
Study records:		
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review

Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

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DEVELOPMENT AND VALIDATION OF RISK MODELS TO PREDICT CHRONIC KIDNEY DISEASE AMONG PEOPLE LIVING WITH HIV: PROTOCOL FOR A SYSTEMATIC REVIEW

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Primary Subject Heading:	Renal medicine
Secondary Subject Heading:	Epidemiology, Infectious diseases, Public health, HIV/AIDS
Keywords:	HIV & AIDS < INFECTIOUS DISEASES, Chronic renal failure < NEPHROLOGY, EPIDEMIOLOGY, INFECTIOUS DISEASES

DEVELOPMENT AND VALIDATION OF RISK MODELS TO PREDICT CHRONIC KIDNEY DISEASE AMONG PEOPLE LIVING WITH HIV: PROTOCOL FOR A SYSTEMATIC REVIEW

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ABSTRACT

Introduction

Chronic kidney disease (CKD) is estimated to affect about 9.1% of the global population with a substantially increased risk of the condition (6.8 – 17.2%) among people living with HIV (PLWH). This increased risk is attributed to HIV infection itself, antiretroviral therapy (ART), co-existing viral infections, non-infectious co-morbidities, and traditional risk factors for CKD. Predictive models have been employed in the estimation of prevalent and incident CKD risk in both PLWH and the general population. A predictive model showing an individual's risk of prevalent and/or progression to kidney failure is useful for initiating timely interventions that prevent further worsening of kidney function. This study will systematically review published prediction models developed and/or validated for prevalent and incident CKD in PLWH, describe their characteristics, compare performance, and assess methodological quality and applicability.

Methods and Analysis

Studies with predictive models of interest will be identified by searching MEDLINE, Web of Science, Cumulative Index to Nursing and Allied Health Literature, Cochrane library, and Scopus from inception to May 2022. Title and abstract screening, full-text review, and data extraction will be completed independently by two reviewers. Using appropriate tools designed for predictive modeling investigations, the included papers will be rigorously assessed for bias and applicability. Extracted data will be presented in tables so that published prediction models can be compared qualitatively. Quantitative data on the predictive performance of these models will be synthesized with meta-analyses if appropriate.

Ethics and Dissemination

The findings of the review will be disseminated in peer-reviewed journals and seminar presentations. Ethical approval is not required as this is a protocol for a systematic review.

Systematic Review registration

PROSPERO Registration number: CRD42021279694

Keywords: Chronic Kidney disease, predictive models, prevalence, incidence, HIV, PLWH, systematic review, protocol

Strengths and Limitations

This systematic review protocol follows the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) 2015 guidelines

This review addresses the knowledge gap regarding chronic kidney disease (CKD) prediction models specific for people living with HIV (PLWH)

The review will also incorporate models predicting progression to kidney failure requiring kidney replacement therapy

This review is not limited to randomised controlled trials

In the absence of a sufficient number of studies/models, meta-analysis may not be performed

Introduction

Chronic kidney disease (CKD) has become a global threat as it constitutes a sizeable proportion of morbidity and premature deaths [1]. CKD is estimated to affect 697.5million people globally representing a global prevalence of 9.1% [1]. The traditional risk factors for CKD include increasing age, hypertension, diabetes mellitus, and obesity. CKD is a predictor of poor quality of life as well as increased healthcare expenses [2, 3].

There is a substantially increased risk of developing CKD (6.8 – 17.2%) among people living with HIV (PLWH) [4, 5]. This is corroborated by postulations of HIV infection and antiretroviral therapy (ART) regimens in the acquisition of CKD [6, 7]. CKD could arise among PLWH from the classic HIV-associated nephropathy or immune complex disease, non-infectious co-morbidities (hypertension and diabetes), co-existing viral infections (Hepatitis B and C), and antiretroviral toxicity [8, 9].

CKD is known to contribute to the increased morbidity and mortality among PLWH as the number of PLWH with kidney failure requiring kidney replacement therapy increases globally [2, 3]. CKD is an important non-infectious cause of morbidity and mortality among PLWH and could reverse the gains achieved via ART roll-out [10, 11]. Thus, risk assessments using predictive models remain a veritable tool for mitigating CKD in the populace (and HIV cohort).

Rationale

Predictive models have been developed to assist with CKD risk evaluation in both the HIV and general population. These predictive models have been employed to identify persons at greater risk of CKD (diagnosis or prognosis) and found to be helpful in clinical decision-making as well as public health interventions to mitigate against CKD [12, 13]. These models utilise biological markers (urinary protein and albumin, serum creatinine and cystine C, uric acid) along with other traditional risk factors for CKD (age, sex, blood pressure readings, and diabetes mellitus) in their formulation. Early detection and management of hypertension, diabetes mellitus, and CKD in this population can help improve renal and cardiovascular outcomes thereby regressing or slowing the progression towards kidney failure requiring kidney replacement therapy.

A few studies have reported predictive models for prevalent and incident CKD among PLWH as well as systematic reviews of CKD predictive models in the general population [14–17]. However, none of these studies have provided systematic reviews on CKD predictive models with the HIV population as the focus.

This protocol is for a systematic review with or without meta-analysis of the spectrum of prevalent and/or incident CKD prediction models developed and/or validated in PLWH, to identify existing gaps and guide research endeavours in the future.

Objective

This study aims to conduct a systematic review to identify and characterize predictive models developed and/or validated on prevalent and incident CKD in adult PLWH, evaluate the performances of these models in PLWH, and identify existing knowledge gaps as reported in published literature.

Methods and Analysis

The protocol will be conducted in alignment with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) 2015 guidelines (See Appendix 1) [18]. In

addition, the CHARMS checklist will be employed to frame the review questions while the PICOTS criteria will be used to determine inclusion and exclusion criteria [19, 20].

Review Questions

The review questions are as follows: 1) are there risk models specifically developed to predict prevalent and/or incident CKD among PLWH; and what are their characteristics? and 2) are there models for predicting prevalent or incident CKD which have been validated in PLWH, and how do they perform in this population? The CHARMS checklist was utilised in the formulation of the review questions [19].

The above questions will form the basis of our review in identifying both prognostic and diagnostic models for CKD, with all types of prediction modelling studies included (development with or without external validation in independent data and external model validation with possible model updates). The scope of the review will be to inform clinical decision-making as it relates to prevalent and incident CKD among PLWH. The review will include diagnostic and prognostic models for CKD as well as models predicting progression to kidney failure requiring kidney replacement therapy with reference to HIV diagnosis. PLWH who are ≥ 18 years of age will be our target population.

Patient and public involvement

This review does not require patient or public involvement as it will be based on published works.

Inclusion and exclusion criteria

The PICOTS (patient population, intervention, comparator, outcome, timing, and setting) framework will be employed in defining the inclusion and exclusion criteria for this review [20]. The population of interest is adult (≥ 18 years) PLWH with emphasis on predictive models for prevalent and incident CKD among the population. The primary outcomes are predictive models for 1) prevalent CKD, 2) incident CKD and 3) progression to kidney failure requiring kidney replacement therapy in PLWH. Our secondary outcomes were the evaluation of the performance of the above three groups of models as well as the candidate variables employed in their derivation. Studies to be included in the review are cross-sectional, cohort, clinical controlled, and randomized controlled trials with the intent for the models to be used for clinical decision-making and public health advocacy measures.

The exclusion criteria will include the following. Studies primarily among paediatric, adolescents, and pregnant women, case-control studies, editorials, letters to editors, models generated from simulation and animal studies as well as those evaluating quality of life among patients with CKD.

Search Strategy

From inception to May 2022, a systematic search of the following electronic databases of peer-reviewed journal articles and online search records will be conducted: MEDLINE, Web of Science, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane library, and Scopus. Keywords relating to population (HIV patients, People living with HIV, People living with HIV/AIDS, HIV infected, ART experienced, ART-naive); disease (impaired renal function, impaired kidney function, chronic kidney disease, chronic renal disease, chronic renal insufficiency, chronic kidney failure, end-stage kidney disease, end-stage renal disease); modeling (prevalence, prevalent, incidence, incident, predict, risk, risk scores, prediction models, prediction tools, risk assessment, risk engineering); and models predicting CKD prevalence and incidence among PLWH as well as factors associated with the validity of these models. To accommodate each database, the search phrases will be concatenated. Reference lists of relevant papers will be scanned for eligible studies.

A search strategy using MEDLINE is attached (See Appendix 2). Grey literature (such as reports, conferences, and workshop proceedings) will be searched using the Google Scholar search engine, as well as important relevant websites such as African Journals Online (AJOL) (hand searches). EndNote reference manager will be used to export references and delete any duplications identified.

Selection of studies

The title and abstract of each paper will be evaluated by two independent reviewers before being in cluded in the review. The final selection of papers to be included in the review will be decided after reading the full texts of eligible articles. Disagreements will be resolved through discussion and consensus, or consultation with a third reviewer.

A model/risk assessment tool that predicts prevalent and/or incident CKD, as well as models for progression to kidney failure requiring kidney replacement therapy, must be derived in an adult human population.
The area under the receiver operating characteristic curve (AUC) or C-statistic, reclassification percentage, net reclassification improvement (NRI), or integrated discrimination improvement index (IDI) are some analyses being proposed for assessing the qualities of the models.

Assessment of studies

Diagnostic models are those designed for prevalent purposes while prognostic models are designed for incident purposes.

PROBAST (Prediction model Risk Of Bias ASsessment Tool) will be employed to evaluate the quality of all models. PROBAST evaluates both the risk of bias and the application of multivariable prediction (diagnostic and prognostic) models created or validated in primary research. The PROBAST tool will also be involved in the systematic reviews of predictive models for prevalent and incident CKD as well as progression to kidney failure requiring kidney replacement therapy in PLWH [21, 22].

Disagreements in the use of the above tool for the review will be resolved following consultation with the third reviewer.

Data extraction

The following details will be used to extract data from chosen studies; study specifics (first author, journal name, year of publication, country of study); study population (sample size, age range, sex distribution, number of PLWH, ART-naive, or experienced); population characteristics (pre-existing co-morbid conditions: hypertension, diabetes mellitus, stroke, myocardial infarction, dyslipidaemia, congestive heart failure).

In addition, model characteristics (number of participants in the derivation and validation cohorts, number of participants with the outcome of interest, number of candidate variables stated as predictors, number and list of variables included in the model, type of statistical analysis used in generating model); study designs employed in deriving the models (cross-sectional, cohort, controlled clinical trials, randomized controlled trials); models' outcome data (prevalence and incidence of CKD, number of multivariable prediction scores/models, definition of CKD, CKD equations utilized); and performance (discriminatory [AUC or C-statistic], calibration [difference between observed and predicted rates of hypertension, p-value of corresponding test statistic], re-classification [NRI and IDI values with their accompanying 95% confidence intervals and p-values]) will also be documented. The source of funding and study limitations will be captured. The extracted data will be presented in a tabular (data) form.

Data analysis

The data will be summarized in general (globally), as well as by the World Health Organisation (WHO) regional designation, gender, and study population (PLWH, ART-naive, or experienced). Meta-analysis will be conducted for CKD predictive models in the presence of an adequate number of models otherwise a narrative review will be undertaken. The meta-analysis would focus on the performance measures of the identified models with reference to the Area under the receiver operating characteristic (ROC) curve (AUC-ROC), Kolmogorov- Smirnov test, and other appropriate statistical tests. The random effects will be determined using inverse variance weighting and 95% confidence intervals (CI) of pooled estimates while heterogeneity will be determined using the inconsistency index (I^2) [23, 24]. Publication bias will be assessed using funnel plots and when found to be significant, further analysis (Egger's and Begg's tests) will be conducted [25].

Patient and Public involvement statement

This review will involve published articles from the above listed databases and search engines. The selected models predicting CKD would not primarily involve patients.

Ethics and Dissemination

Ethical approval is not required as this is a protocol for a systematic review. The findings of this review will be published in peer-reviewed journals and included as a chapter in a PhD thesis at the University of Cape Town. Furthermore, the findings of this evaluation will be shared with relevant agencies through seminars, conferences, and policy development meetings.

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Author contributions

This systematic review was conceived and designed by OO, NO, and APK. This protocol was initially drafted by OO, NP, AM, NO, BS and APK. Revisions and comments made to the protocol were approved by all authors. All authors have approved the submission.

Competing interests

The authors declare no competing interests

Acknowledgment

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Data availability statement

Data generated during the review will be made available upon request and at the discretion of study supervisors.

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APPENDIX 1

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Page
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	N/A
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	7
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	N/A
Support:			
Sources	5a	Indicate sources of financial or other support for the review	7
Sponsor	5b	Provide name for the review funder and/or sponsor	7
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	7
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	3
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	4
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	4
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	5
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	5

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	5
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	5
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	6
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	4, 7
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	4, 6
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	5
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	6
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	6
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	6
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	6
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	6
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	N/A

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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APPENDIX 2

Search Strategy

Chronic Kidney disease

"Kidney disease*" OR "kidney failure" OR "Renal disease" OR "Renal insufficiency" OR "Chronic kidney" OR "Chronic renal" OR "CKD" OR "CKF" OR "CRD" OR "end-stage renal" OR "end-stage kidney" OR "end-stage renal" OR "end-stage kidney" OR "uremia" OR "uraemia" OR "dialysis" OR "hemofiltration" OR "haemofiltration" OR "hemodiafiltration" OR "haemodiafiltration" OR "hemodialysis" OR "haemodialysis" OR "renal dialysis"

Nature of association

"incidence" OR "prevalence" OR "occurrence" OR "diagnosis" OR "assessment" OR "identification" OR "screening" OR "progression" OR "end-stage renal"

Modelling and Risk scores

Ingui filter

(Validat$ OR Predict$.ti. OR Rule$) OR (Predict$ AND (Outcome$ OR Risk$ OR Model$)) OR ((History OR Variable$ OR Criteria OR Scor$ OR Characteristic$ OR Finding$ OR Factor$) AND (Predict$ OR Model$ OR Decision$ OR Identif$ OR Prognos$)) OR (Decision$ AND (Model$ OR Clinical$ OR Logistic Models/)) OR (Prognostic AND (History OR Variable$ OR Criteria OR Scor$ OR Characteristic$ OR Finding$ OR Factor$ OR Model$))

Haynes Broad filter

(Predict*[tiab] OR Predictive value of tests[mh] OR Scor*[tiab] OR Observ*[tiab] OR Observer variation[mh])