National Institute for Health and Care Excellence

Final

Chronic kidney disease

[B] Evidence review for the accuracy of albumin: creatinine ratio versus protein creatinine ratio measurements to quantify proteinuria in children and young people with CKD

NICE guideline NG203

Evidence reviews underpinning recommendations 1.1.12 to 1.1.14 and research recommendations in the NICE guideline

August 2021

Final

These evidence reviews were developed by the Guideline Updates Team

Disclaimer

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Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

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Contents

Accuracy of albumin:creatinine ratio versus protein:creatinine ratio measurements to quantify proteinuria in children and young people with chronic kidney disease (CKD)

1.1 Review question

What is the accuracy of albumin:creatinine ratio versus protein:creatinine ratio measurements to quantify proteinuria in children and young people with CKD?

1.1.1 Introduction

The NICE guideline on chronic kidney disease in adults: assessment and management (NICE guideline CG182) was reviewed in 2017 as part of NICE's surveillance programme. As a result of the review, the decision was made to update the guideline. During the scope of the update, it was decided to extend the guideline to cover the assessment and management of chronic kidney disease in children and young people. As part of the scoping exercise, stakeholders highlighted that the current evidence for albumin:creatinine ratio (ACR) vs protein:creatinine ratio (PCR) agrees with current guidance but noted that PCR is used as a clinical management tool not a screening/identification tool.

The aim of this review is to assess the accuracy of albumin:creatinine ratio versus protein:creatinine ratio measurements to quantify proteinuria in children and young people with CKD. See Appendix A for full details of the review protocol.

1.1.2 Summary of the protocol

Table 1: Protocol summary for accuracy of albumin:creatinine ratio versus protein:creatinine ratio

Population	**Inclusion:** Children and young people (up to 18 years) with suspected or diagnosed chronic kidney disease GFR categories G1 to G5. **Exclusion:** • people receiving renal replacement therapy (RRT) • people with acute kidney injury combined with rapidly progressive glomerulonephritis • pregnant young women • people receiving palliative care
Index text	• Albumin:creatinine ratio • Protein:creatinine ratio
Reference standard	24-hour urine collection
Target condition	Proteinuria
Outcome	**Primary outcome:** • Likelihood ratios (LR) **Secondary outcomes:**

	• Sensitivity • Specificity • PPV • NPV These values will be converted to LR in line with NICE preferred methods (since LRs are not prevalence dependant)

1.1.3 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in Appendix A and the methods section in Appendix B.

Declarations of interest were recorded according to NICE's conflicts of interest policy.

The following methods were specific for this review:

1. The committee was unaware of any established clinical decision thresholds, values of 2.0 for positive likelihood ratio (above which a test would be recommended) and 0.5 for negative likelihood ratio (below which a test would be considered of no clinical use) were used to set 2 clinical decision thresholds for each measure. These values were based on a published paper which suggested a schema to interpret the likelihood ratio findings from diagnostic test accuracy reviews (see Appendix B).

1.1.4 Diagnostic evidence

1.1.4.1 Included studies

A systematic search was carried out to identify diagnostic cross-sectional studies and systematic reviews of diagnostic cross-sectional studies, which found 1,100 references (see Appendix C for the literature search strategy). Based on title and abstract screening, 1,095 references were excluded, and 5 references were ordered for full text screening. None of these 5 references met the inclusion criteria listed in the review protocol (Appendix A). The diagnostic evidence study selection is presented as a PRISMA diagram in Appendix D.

A second set of searches was conducted at the end of the guideline development process for all updated review questions using the original search strategies, to capture papers published whilst the guideline was being developed. This search returned 74 references for this review question, these were screened on title and abstract and all references were excluded at this level. Therefore, no references were ordered for full text screening.

1.1.4.2 Excluded studies

See Appendix K for a list of excluded studies with reasons for exclusion.

1.1.5 Summary of studies included in the diagnostic evidence

No studies were included in this review question.

1.1.6 Summary of the diagnostic evidence

No studies were included in this review question.

1.1.7 Economic evidence

A systematic search was conducted to identify economic evaluations for this review question. The search returned 108 records which were sifted against the review protocol. All

publications were excluded based on title and abstract. The study selection diagram is presented in Appendix H. For more information on the search strategy please see Appendix C.

1.1.8 Summary of included economic evidence

No published cost-effectiveness studies were included in this review question.

1.1.9 Economic model

Economic modelling was not prioritised for this review question.

1.1.10 The committee's discussion and interpretation of the evidence

1.1.10.1. The outcomes that matter most

The committee discussed the impact that true positive, false positive, true negative and false negative ACR and PCR results have on children and young people with CKD. Children and young people with true positive results would have their treatment changed to reduce albumin or protein levels, those with false positive results may undergo unnecessary treatment. Children and young people with true negative results would be correctly reassured that their albumin or protein levels are under control, and those with false negative results would go undertreated with the risk of disease progression.

The committee agreed that the key outcome to correctly quantify proteinuria in children and young people with CKD was sensitivity (and negative likelihood ratios) rather than specificity (and positive likelihood ratios). If the correct quantification of proteinuria is missed, the consequences of disease progression could be serious, and this could lead to irreversible damage to kidney.

The committee noted that there was no evidence for the accuracy of ACR versus PCR measurements to quantify proteinuria in children and young people with CKD. In light of the lack of evidence, the committee discussed the recommendations that had previously been made for adults and, based on their clinical knowledge and experience, agreed that the recommendations for adults for measuring proteinuria were highly relevant for children and young people. Therefore, the committee agreed to extend the adult recommendations to include children and young people.

1.1.10.2 The quality of the evidence

No evidence was identified for this review question. As a result, the committee agreed that a research recommendation should be added to address this gap in the evidence. Details on the research recommendation are described in the next section.

1.1.10.3 Benefits and harms

The committee discussed the recommendations for adults for measuring proteinuria and agreed that, overall, these can be recommended for children and young people as well. It has been recommended, for adults, to use ACR rather than PCR because ACR has greater sensitivity for low levels of proteinuria. Recommendations for adults are also about how the initial detection of proteinuria should be done, how to confirm clinically important proteinuria and in which groups is recommended to measure proteinuria with urine ACR. The committee highlighted that people's circumstances should be considered when interpreting ACR levels because ACR can be affected by different factors (for example, urinary tract infections). It was also highlighted that ACR may vary by time of day. This is why confirmation should be done using a subsequent early morning sample when ACR is between 3 mg/mmol and 70 mg/mmol in the initial detection of proteinuria.

The committee discussed the eGFR threshold for adults without diabetes which is recommended for the quantification of urinary albumin or urinary protein loss. The committee agreed that this threshold does not seem appropriate for children and young people because any reduction in GFR in this population would prompt the quantification of proteinuria. Therefore, a new bullet point was added to set the threshold for creatinine above the upper limit of the age-appropriate reference range for children and young people.

The committee discussed the importance of measuring proteinuria in children and young people with CKD and that high levels of proteinuria are likely to be used to change the treatment in this population but that this has not been investigated in the context of this guideline. Therefore, the committee agreed to make a research recommendation to identify the effect of measuring proteinuria with albumin:creatinine ratio compared to protein:creatinine ratio on the timing of treatment changes in children and young people with CKD and the consequences of the delay in treatment changes on different levels of proteinuria.

1.1.10.4 Cost effectiveness and resource use

No economic evidence was identified for this review question, and economic modelling was not prioritised. The committee noted that after the publication of the 2014 NICE CKD guideline the recommendations in this area, despite, being made only for adults and not for children and young people, were also used to inform practice for the latter groups. They also noted that implementation of those recommendations was often higher for children and young people than for the adult population. Therefore, because the new recommendations made are very similar to those made for adults, the committee were confident they already represented current practice in most areas, and consequently there would not be a substantial resource impact from implementing them.

1.1.10.5 Other factors the committee took into account

The committee highlighted that, based on their clinical knowledge and experience, PCR is the preferred measure of proteinuria in children and young people with nephrotic syndrome. PCR is already recommended for adults as an alternative of ACR when ACR is 70 mg/mmol or more which is a sign of nephrotic syndrome.

The committee highlighted that there is new evidence on adults about equations to estimate ACR from PCR (Weaver 2020). The study concluded that these equations may be useful when an estimate of ACR is desired but only PCR is available. The committee agreed to pass this study to the NICE surveillance team for consideration in future updates of the guideline.

1.1.11 Recommendations supported by this evidence review

This evidence review supports recommendations 1.1.12 to 1.1.14 and the research recommendation on the effect of measuring proteinuria with albumin:creatinine ratio compared with protein:creatinine ratio on the timing of treatment changes in children and young people with CKD (see Appendix L for further details about the research recommendation).

1.1.12 References – included studies

1.1.12.1 Diagnostic

No studies were included in this review question.

1.1.12.2 Economic

No studies were included in this review question.

1.1.12.3 Other

Weaver, R. G., James, M. T., Ravani, P., Weaver, C. G., Lamb, E. J., Tonelli, M., ... & Hemmelgarn, B. R. (2020). Estimating Urine Albumin-to-Creatinine Ratio from Protein-to-Creatinine Ratio: Development of Equations using Same-Day Measurements. Journal of the American Society of Nephrology, 31(3), 591-601.

Appendices

Appendix A – Review protocols

Review protocol for the accuracy of albumin:creatinine ratio versus protein:creatinine ratio measurements to quantify proteinuria in children and young people with CKD

ID	Field	Content
0.	PROSPERO registration number	CRD42020172602
1.	Review title	What is the accuracy of albumin:creatinine ratio versus protein:creatinine ratio measurements to quantify proteinuria in children and young people with CKD?
2.	Review question	What is the accuracy of albumin:creatinine ratio versus protein:creatinine ratio measurements to quantify proteinuria in children and young people with CKD?
3.	Objective	To determine the accuracy of albumin:creatinine ratio versus protein:creatinine ratio measurements to quantify proteinuria in children and young people with CKD?
4.	Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Database of Abstracts of Reviews of Effect (DARE) • Embase (Ovid) • MEDLINE (Ovid) • MEDLINE In-Process (Ovid) • MEDLINE Epub Ahead of Print

		Searches will be restricted by: • English language • Human studies Searches will not be restricted by date. The searches will be re-run 6 weeks before final submission of the review and further studies retrieved for inclusion. The full search strategies for MEDLINE database will be published in the final review.
5.	Condition or domain being studied	Chronic Kidney Disease
6.	Population	**Inclusion**: Children and young people (up to 18 years) with suspected or diagnosed chronic kidney disease GFR categories G1 to G5. **Exclusion**: • people receiving renal replacement therapy (RRT) • people with acute kidney injury combined with rapidly progressive glomerulonephritis

		• pregnant young women • people receiving palliative care.
7.	Test	• Albumin:creatinine ratio • Protein:creatinine ratio
8.	Reference standard	24-hour urine collection
9.	Types of study to be included	• Cross-sectional diagnostic accuracy studies • Systematic reviews of cross-sectional studies
10.	Other exclusion criteria	• Non-English language • Abstracts and conference proceedings • Theses • Non-human studies • Studies from which a 2x2 table cannot be constructed
11.	Context	NICE guidelineCG182 Chronic kidney disease in adults: assessment and management will be updated by this question. The guideline will be extended to cover the assessment and management of chronic kidney disease in children and young people.
12.	Primary outcomes (critical outcomes)	• Likelihood ratios

13.	Secondary outcomes (important outcomes)	• Sensitivity • Specificity • PPV • NPV These values will be converted to LR in line with NICE preferred methods (since LRs are not prevalence dependant)
14.	Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4). Study investigators may be contacted for missing data where time and resources allow. Data will be extracted from the included studies for assessment of study quality and evidence synthesis. Extracted information will include: study setting; study population and participant demographics and baseline characteristics; details of the intervention and control conditions; study methodology; recruitment and study completion rates; outcomes and times of measurement and information for assessment of the risk of bias.
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the QADAS-2 checklist as described in Developing NICE guidelines: the manual.

16.	Strategy for data synthesis	Meta-analysis of diagnostic test accuracy data will be conducted with reference to the Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy (Deeks et al. 2010). Where five or more studies are available for all included strata, a bivariate model will be fitted using the mada package in R v3.4.0, which accounts for the correlations between positive and negative likelihood ratios, and between sensitivities and specificities. Where sufficient data are not available (2-4 studies), separate independent pooling was performed for positive likelihood ratios, negative likelihood ratios, sensitivity and specificity, using Microsoft Excel. Random-effects models (der Simonian and Laird) were fitted for all syntheses, as recommended in the Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy (Deeks et al. 2010).
17.	Analysis of sub-groups	Where data allow, we will conduct subgroup analyses for: • Specific group of family origin • People at high risk of developing progressive CKD (for example, people with diabetes, hypertension or cardiovascular disease, or people recovering from acute kidney injury). • People with a family history of renal disease • Age.
18.	Type and method of review	☐ Intervention ☒ Diagnostic ☐ Prognostic ☐ Qualitative

		☐ Epidemiologic ☐ Service Delivery ☐ Other (please specify)		
19.	Language	English		
20.	Country	England		
21.	Anticipated or actual start date	February 2020		
22.	Anticipated completion date	March 2021		
23.	Stage of review at time of this submission	**Review stage**	**Started**	**Completed**
		Preliminary searches	☐	☐
		Piloting of the study selection process	☐	☐

		Formal screening of search results against eligibility criteria	☐	☐
		Data extraction	☐	☐
		Risk of bias (quality) assessment	☐	☐
		Data analysis	☐	☐
24.	Named contact	**5a. Named contact** Guideline Updates Team **5b Named contact e-mail** GUTprospero@nice.org.uk **5e Organisational affiliation of the review** National Institute for Health and Care Excellence (NICE)		
25.	Review team members	From the Guideline Updates Team: • Mr Chris Carmona • Dr Yolanda Martinez		

		• Ms Omnia Abdulrazeg • Dr Joshua Pink • Mr Rui Martins • Ms Lynda Ayiku
26.	Funding sources/sponsor	This systematic review is being completed by the Guideline Updates Team, which is part of NICE.
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: www.nice.org.uk
29.	Other registration details	
30.	Reference/URL for published protocol	
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as:

		• notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
32.	Keywords	
33.	Details of existing review of same topic by same authors	
34.	Current review status	☐ Ongoing ☐ Completed but not published ☐ Completed and published ☐ Completed, published and being updated ☐ Discontinued
35..	Additional information	

36.	Details of final publication	www.nice.org.uk

Appendix B – Methods

Diagnostic test accuracy evidence

In this guideline, diagnostic test accuracy (DTA) data are classified as any data in which a feature – be it a symptom, a risk factor, a test result or the output of some algorithm that combines many such features – is observed in some people who have the condition of interest at the time of the test and some people who do not. Such data either explicitly provide, or can be manipulated to generate, a 2x2 classification of true positives and false negatives (in people who, according to the reference standard, truly have the condition) and false positives and true negatives (in people who, according to the reference standard, do not).

The 'raw' 2x2 data can be summarised in a variety of ways. Those that were used for decision making in this guideline are as follows:

- **Positive likelihood ratios** describe how many times more likely positive features are in people with the condition compared to people without the condition. Values greater than 1 indicate that a positive result makes the condition more likely.
  - LR^+ = (TP/[TP+FN])/(FP/[FP+TN])
- **Negative likelihood ratios** describe how many times less likely negative features are in people with the condition compared to people without the condition. Values less than 1 indicate that a negative result makes the condition less likely.
  - LR^- = (FN/[TP+FN])/(TN/[FP+TN])
- **Sensitivity** is the probability that the feature will be positive in a person with the condition.
  - sensitivity = TP/(TP+FN)
- **Specificity** is the probability that the feature will be negative in a person without the condition.
  - specificity = TN/(FP+TN)
- **Positive predictive values** describe the probability that a person with a positive screening test has the disease.
  - PPV = TP/ (TP+FP)
- **Negative predictive values** describe probability that a person with a negative screening test doesn't have the disease.
  - NPV = TN/(TN+FN)

The following schema, adapted from the suggestions of Jaeschke et al. (1994), was used to interpret the likelihood ratio findings from diagnostic test accuracy reviews.

Table 2: Interpretation of likelihood ratios

Value of likelihood ratio	Interpretation
LR ≤ 0.1	**Very large** decrease in probability of disease
0.1 < LR ≤ 0.2	**Large** decrease in probability of disease
0.2 < LR ≤ 0.5	**Moderate** decrease in probability of disease
0.5 < LR ≤ 1.0	**Slight** decrease in probability of disease
1.0 < LR < 2.0	**Slight** increase in probability of disease
2.0 ≤ LR < 5.0	**Moderate** increase in probability of disease
5.0 ≤ LR < 10.0	**Large** increase in probability of disease
LR ≥ 10.0	**Very large** increase in probability of disease

The schema above has the effect of setting a minimal important difference for positive likelihoods ratio at 2, and a corresponding minimal important difference for negative likelihood ratios at 0.5. Likelihood ratios (whether positive or negative) falling between these thresholds were judged to indicate no meaningful change in the probability of disease.

Quality assessment

Individual studies were quality assessed using the QUADAS-2 tool, which contains four domains: patient selection, index test, reference standard, and flow and timing. Each individual study was classified into one of the following three groups:

- Low risk of bias – The true effect size for the study is likely to be close to the estimated effect size.
- Moderate risk of bias – There is a possibility the true effect size for the study is substantially different to the estimated effect size.
- High risk of bias – It is likely the true effect size for the study is substantially different to the estimated effect size.

Each individual study was also classified into one of three groups for directness, based on if there were concerns about the population, index features and/or reference standard in the study and how directly these variables could address the specified review question. Studies were rated as follows:

- Direct – No important deviations from the protocol in population, index feature and/or reference standard.
- Partially indirect – Important deviations from the protocol in one of the population, index feature and/or reference standard.
- Indirect – Important deviations from the protocol in at least two of the population, index feature and/or reference standard.

Methods for combining diagnostic test accuracy evidence

Meta-analysis of diagnostic test accuracy data was conducted with reference to the Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy (Deeks et al. 2010).

Where applicable, diagnostic syntheses were stratified by:

- Presenting symptomatology (features shared by all participants in the study, but not all people who could be considered for a diagnosis in clinical practice).
- The reference standard used for true diagnosis.

Where five or more studies were available for all included strata, a bivariate model was fitted using the `mada` package in R v3.4.0, which accounts for the correlations between positive and negative likelihood ratios, and between sensitivities and specificities. Where sufficient data were not available (2-4 studies), separate independent pooling was performed for positive likelihood ratios, negative likelihood ratios, sensitivity and specificity, using Microsoft Excel. This approach is conservative as it is likely to somewhat underestimate test accuracy, due to failing to account for the correlation and trade-off between sensitivity and specificity (see Deeks 2010).

Random-effects models (der Simonian and Laird) were fitted for all syntheses, as recommended in the Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy (Deeks et al. 2010).

In any meta-analyses where some (but not all) of the data came from studies at high risk of bias, a sensitivity analysis was conducted, excluding those studies from the analysis. Results

from both the full and restricted meta-analyses are reported. Similarly, in any meta-analyses where some (but not all) of the data came from indirect studies, a sensitivity analysis was conducted, excluding those studies from the analysis.

Modified GRADE for diagnostic test accuracy evidence

GRADE has not been developed for use with diagnostic studies; therefore a modified approach was applied using the GRADE framework.

The choice of primary outcome for decision making was determined by the committee and GRADE assessments were undertaken using the appropriate method from those listed below.

In all cases, following completion of the GRADE table, the downstream effects of these tests on patient- important outcomes were considered. This could be done explicitly during committee deliberations and reported as part of the discussion section of the review detailing the likely consequences of true positive, true negative, false positive and false negative test results. Alternatively, in reviews where a decision model is being carried (for example, as part of an economic analysis), these consequences may be incorporated here instead.

Using likelihood ratios as the primary outcomes

GRADE assessments were only undertaken for positive and negative likelihood ratios, as the MIDs used to assess imprecision were based on these outcomes but results for sensitivity and specificity are also presented alongside those data.

Evidence from diagnostic accuracy studies was initially rated as high-quality, and then downgraded according to the standard GRADE criteria (risk of bias, inconsistency, imprecision and indirectness) as detailed in Table 3 below.

The committee were consulted to set 2 clinical decision thresholds for each measure: the likelihood ratio above (or below for negative likelihood ratios) which a test would be recommended, and a second below (or above for negative likelihood ratios) which a test would be considered of no clinical use. These were used to judge imprecision (see below). If the committee were unsure which values to pick, then the literature based values of 2 for LR+ and 0.5 for LR- were used based on Table 3, with the line of no effect as the second clinical decision line in both cases.

Table 3: Rationale for downgrading quality of evidence for diagnostic questions using likelihood ratio measures.

GRADE criteria	Reasons for downgrading quality
Risk of bias	Not serious: If less than 33.3% of the weight in a meta-analysis came from studies at moderate or high risk of bias, the overall outcome was not downgraded. Serious: If greater than 33.3% of the weight in a meta-analysis came from studies at moderate or high risk of bias, the outcome was downgraded one level. Very serious: If greater than 33.3% of the weight in a meta-analysis came from studies at high risk of bias, the outcome was downgraded two levels. Outcomes meeting the criteria for downgrading above were not downgraded if there was evidence the effect size was not meaningfully different between studies at high and low risk of bias.
Indirectness	Not serious: If less than 33.3% of the weight in a meta-analysis came from partially indirect or indirect studies, the overall outcome was not downgraded. Serious: If greater than 33.3% of the weight in a meta-analysis came from partially indirect or indirect studies, the outcome was downgraded one level.

GRADE criteria	Reasons for downgrading quality
	Very serious: If greater than 33.3% of the weight in a meta-analysis came from indirect studies, the outcome was downgraded two levels. Outcomes meeting the criteria for downgrading above were not downgraded if there was evidence the effect size was not meaningfully different between direct and indirect studies.
Inconsistency	Concerns about inconsistency of effects across studies, occurring when there is unexplained variability in the treatment effect demonstrated across studies (heterogeneity), after appropriate pre-specified subgroup analyses have been conducted. This was assessed using the I^2 statistic. N/A: Inconsistency was marked as not applicable if data on the outcome was only available from one study. Not serious: If the I^2 was less than 33.3%, the outcome was not downgraded. Serious: If the I^2 was between 33.3% and 66.7%, the outcome was downgraded one level. Very serious: If the I^2 was greater than 66.7%, the outcome was downgraded two levels. Outcomes meeting the criteria for downgrading above were not downgraded if there was evidence the effect size was not meaningfully different between studies with the smallest and largest effect sizes.
Imprecision	If the 95% confidence interval for a positive likelihood ratio spanned a single LR+ clinical decision threshold (e.g. 2), the outcome was downgraded one level, as the data were deemed to be consistent with a meaningful increase in risk and no meaningful predictive value. Similarly, negative likelihood ratios that spanned a single LR- decision threshold (e.g. 0.5) led to downgrading for serious imprecision. Any likelihood ratios that spanned both the LR specific clinical decision threshold and the line of no effect were downgraded twice, as suffering from very serious imprecision. Outcomes meeting the criteria for downgrading above were not downgraded if the confidence interval was sufficiently narrow that the upper and lower bounds would correspond to clinically equivalent scenarios.

The quality of evidence for each outcome was upgraded if either of the following conditions were met:

- Data showed an effect size sufficiently large that it could not be explained by confounding alone.
- All plausible residual confounding is likely to increase our confidence in the effect estimate.

Health economics

Literature reviews seeking to identify published cost–utility analyses of relevance to the issues under consideration were conducted for all questions. In each case, the search undertaken for the clinical review was modified, retaining population and intervention descriptors, but removing any study-design filter and adding a filter designed to identify relevant health economic analyses. In assessing studies for inclusion, population, intervention and comparator, criteria were always identical to those used in the parallel clinical search; only cost–utility analyses were included. Economic evidence profiles, including critical appraisal according to the Guidelines manual, were completed for included studies.

Economic studies identified through a systematic search of the literature are appraised using a methodology checklist designed for economic evaluations (NICE guidelines manual; 2014). This checklist is not intended to judge the quality of a study per se, but to determine whether

an existing economic evaluation is useful to inform the decision-making of the committee for a specific topic within the guideline.

There are 2 parts of the appraisal process. The first step is to assess applicability (that is, the relevance of the study to the specific guideline topic and the NICE reference case); evaluations are categorised according to the criteria in Table 4.

Table 4 Applicability criteria

Level	Explanation
Directly applicable	The study meets all applicability criteria, or fails to meet one or more applicability criteria but this is unlikely to change the conclusions about cost effectiveness
Partially applicable	The study fails to meet one or more applicability criteria, and this could change the conclusions about cost effectiveness
Not applicable	The study fails to meet one or more applicability criteria, and this is likely to change the conclusions about cost effectiveness. These studies are excluded from further consideration

In the second step, only those studies deemed directly or partially applicable are further assessed for limitations (that is, methodological quality); see categorisation criteria in Table 5.

Table 5 Methodological criteria

Level	Explanation
Minor limitations	Meets all quality criteria, or fails to meet one or more quality criteria but this is unlikely to change the conclusions about cost effectiveness
Potentially serious limitations	Fails to meet one or more quality criteria and this could change the conclusions about cost effectiveness
Very serious limitations	Fails to meet one or more quality criteria and this is highly likely to change the conclusions about cost effectiveness. Such studies should usually be excluded from further consideration

Where relevant, a summary of the main findings from the systematic search, review and appraisal of economic evidence is presented in an economic evidence profile alongside the clinical evidence.

Appendix C – Literature search strategies

Background to the search

A NICE information specialist conducted the literature searches for the evidence review. The searches were originally run between the 10th and 12th of March 2020 and updated between the 4th and 16th of September 2020. This search report is compliant with the requirements of PRISMA-S.

The principal search strategy was developed in MEDLINE (Ovid interface) and adapted, as appropriate, for use in the other sources listed in the protocol, taking into account their size, search functionality and subject coverage.

The MEDLINE strategy below was quality assured (QA) by trained NICE information specialist. All translated search strategies were peer reviewed to ensure their accuracy. Both procedures were adapted from the 2016 PRESS Checklist.

The search results were managed in EPPI-Reviewer v5. Duplicates were removed in EPPI-R5 using a two-step process. First, automated deduplication is performed using a high-value algorithm. Second, manual deduplication is used to assess 'low-probability' matches. All decisions made for the review can be accessed via the deduplication history.

English language limits were applied in adherence to standard NICE practice and the review protocol.

Limits to exclude conferences in Embase were applied in adherence to standard NICE practice and the review protocol.

The limit to remove animal studies in the searches was the standard NICE practice, which has been adapted from: Dickersin, K., Scherer, R., & Lefebvre, C. (1994). Systematic Reviews: Identifying relevant studies for systematic reviews. *BMJ*, 309(6964), 1286.

Clinical searches

Databases	Date searched	Version/files	No. retrieved
Cochrane Central Register of Controlled Trials (CENTRAL)	10th March 2020	Issue 3 of 12, March 2020	77
Cochrane Database of Systematic Reviews (CDSR)	10th March 2020	Issue 3 of 12, March 2020	8
Database of Abstracts of Reviews of Effect (DARE)	10th March 2020	Up to 2015	30
Embase (Ovid)	11th March 2020	Embase <1974 to 2020 Week 10>	798

MEDLINE (Ovid)	10th March 2020	Ovid MEDLINE(R) <1946 to March 09, 2020>	696
MEDLINE In-Process (Ovid)	10th March 2020	Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to March 09, 2020>	76
MEDLINE Epub Ahead of Print[a]	10th March 2020	Ovid MEDLINE(R) Epub Ahead of Print <March 09, 2020>	13

Search strategies

Database: Ovid MEDLINE(R) <1946 to March 09, 2020>

Search Strategy:

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1 exp Renal Insufficiency, Chronic/ (112617)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (72595)

3 ((kidney* or renal*) adj1 insufficien*).tw. (21252)

4 ckd*.tw. (22947)

5 ((kidney* or renal*) adj1 fail*).tw. (86345)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (35216)

7 (esrd* or eskd*).tw. (14205)

8 "Chronic Kidney Disease-Mineral and Bone Disorder"/ (3451)

9 or/1-8 (212803)

10 exp Infant/ or Infant Health/ or Infant Welfare/ (1124073)

11 (prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*).ti,ab,in,jn. (838111)

12 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (1888198)

13 Minors/ (2560)

14 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (2310277)

15 exp pediatrics/ (57089)

16 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (811920)

17 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (1995288)

[a] Please search for both development and re-run searches

18 Puberty/ (13169)

19 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*).ti,ab,in,jn. (413410)

20 Schools/ (37046)

21 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (7131)

22 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (459454)

23 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (3867)

24 or/10-23 (5104091)

25 9 and 24 (46252)

26 exp Proteinuria/ (38709)

27 proteinur*.tw. (35335)

28 (albuminur* or microalbuminur*).tw. (15845)

29 or/26-28 (63796)

30 25 and 29 (4376)

31 (acr or uacr or pcr).tw. (448672)

32 Proteins/ (202949)

33 protein*.tw. (2696484)

34 Albumins/ (19336)

35 albumin*.tw. (140129)

36 or/32-35 (2834424)

37 Creatinine/ (55744)

38 creatin*.tw. (193124)

39 37 or 38 (214222)

40 ratio*.tw. (1207641)

41 (36 or 39) and 40 (171229)

42 31 or 41 (611679)

43 30 and 42 (755)

44 limit 43 to english language (719)

45 animals/ not humans/ (4642773)

46 44 not 45 (696)

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to March 09, 2020>

Search Strategy:

---

1 exp Renal Insufficiency, Chronic/ (0)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (9505)

3 ((kidney* or renal*) adj1 insufficien*).tw. (1108)

4 ckd*.tw. (4552)

5 ((kidney* or renal*) adj1 fail*).tw. (6358)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (4867)

7 (esrd* or eskd*).tw. (2009)

8 "Chronic Kidney Disease-Mineral and Bone Disorder"/ (0)

9 or/1-8 (18562)

10 exp Infant/ or Infant Health/ or Infant Welfare/ (0)

11 (prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*).ti,ab,in,jn. (77521)

12 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (0)

13 Minors/ (0)

14 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (307592)

15 exp pediatrics/ (0)

16 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (114791)

17 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (0)

18 Puberty/ (0)

19 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*).ti,ab,in,jn. (58092)

20 Schools/ (0)

21 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (0)

22 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (65895)

23 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (560)

24 or/10-23 (445763)

25 9 and 24 (3406)

26 exp Proteinuria/ (0)

27 proteinur*.tw. (3225)

28 (albuminur* or microalbuminur*).tw. (1839)

29 or/26-28 (4827)

30 25 and 29 (370)

31 (acr or uacr or pcr).tw. (50092)

32 Proteins/ (0)

33 protein*.tw. (240270)

34 Albumins/ (0)

35 albumin*.tw. (12539)

36 or/32-35 (247556)

37 Creatinine/ (0)

38 creatin*.tw. (26453)

39 37 or 38 (26453)

40 ratio*.tw. (211746)

41 (36 or 39) and 40 (18929)

42 31 or 41 (68054)

43 30 and 42 (77)

44 limit 43 to english language (76)

45 animals/ not humans/ (0)

46 44 not 45 (76)

Database: Ovid MEDLINE(R) Epub Ahead of Print <March 09, 2020>

Search Strategy:

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1 exp Renal Insufficiency, Chronic/ (0)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (1357)

3 ((kidney* or renal*) adj1 insufficien*).tw. (147)

4 ckd*.tw. (700)

5 ((kidney* or renal*) adj1 fail*).tw. (733)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (698)

7 (esrd* or eskd*).tw. (307)

8 "Chronic Kidney Disease-Mineral and Bone Disorder"/ (0)

9 or/1-8 (2522)

10 exp Infant/ or Infant Health/ or Infant Welfare/ (0)

11 (prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*).ti,ab,in,jn. (14175)

12 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (0)

13 Minors/ (0)

14 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (48794)

15 exp pediatrics/ (0)

16 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (20053)

17 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (0)

18 Puberty/ (0)

19 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*).ti,ab,in,jn. (12121)

20 Schools/ (0)

21 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (0)

22 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (11391)

23 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (107)

24 or/10-23 (71650)

25 9 and 24 (532)

26 exp Proteinuria/ (0)

27 proteinur*.tw. (320)

28 (albuminur* or microalbuminur*).tw. (199)

29 or/26-28 (498)

30 25 and 29 (47)

31 (acr or uacr or pcr).tw. (6033)

32 Proteins/ (0)

33 protein*.tw. (30904)

34 Albumins/ (0)

35 albumin*.tw. (1618)

36 or/32-35 (31884)

37 Creatinine/ (0)

38 creatin*.tw. (3247)

39 37 or 38 (3247)

40 ratio*.tw. (25981)

41 (36 or 39) and 40 (2669)

42 31 or 41 (8575)

43 30 and 42 (13)

44 limit 43 to english language (13)

45 animals/ not humans/ (0)

46 44 not 45 (13)

Database: Embase <1974 to 2020 Week 10>

Search Strategy:

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1 exp kidney failure/ (350205)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (122286)

3 ((kidney* or renal*) adj1 insufficien*).tw. (29978)

4 ckd*.tw. (49110)

5 ((kidney* or renal*) adj1 fail*).tw. (131849)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (57873)

7 (esrd* or eskd*).tw. (27064)

8 or/1-7 (442165)

9 exp juvenile/ or Child Behavior/ or Child Welfare/ or Child Health/ or infant welfare/ or "minor (person)"/ or elementary student/ (3373773)

10 (prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*).ti,ab,in,ad,jw. (1188085)

11 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,ad,jw. (3572569)

12 exp pediatrics/ (104071)

13 (pediatric* or paediatric* or peadiatric*).ti,ab,in,ad,jw. (1608762)

14 exp adolescence/ or exp adolescent behavior/ or adolescent health/ or high school student/ or middle school student/ (102478)

15 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*).ti,ab,in,ad,jw. (646327)

16 school/ or high school/ or kindergarten/ or middle school/ or primary school/ or nursery school/ or day care/ (101861)

17 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jw. (685244)

18 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (7239)

19 or/9-18 (6320751)

20 8 and 19 (86651)

21 exp proteinuria/ (97326)

22 proteinur*.tw. (56691)

23 (albuminur* or microalbuminur).tw. (14865)

24 or/21-23 (111664)

25 20 and 24 (8933)

26 (acr or uacr or pcr).tw. (736279)

27 protein/ (459008)

28 protein*.tw. (3524695)

29 albumin/ (121191)

30 albumin*.tw. (203246)

31 or/27-30 (3737026)

32 creatinine/ (175952)

33 creatin*.tw. (321711)

34 32 or 33 (391283)

35 ratio*.tw. (1919598)

36 (31 or 34) and 35 (274857)

37 26 or 36 (992990)

38 25 and 37 (1341)

39 limit 38 to english language (1301)

40 nonhuman/ not human/ (4584764)

41 39 not 40 (1255)

42 limit 41 to (conference abstract or conference paper or "conference review") (457)

43 41 not 42 (798)

Cochrane Library

ID	Search	Hits
#1	MeSH descriptor: [Renal Insufficiency, Chronic] explode all trees	6453
#2	(((chronic* or progressi*) near/1 (renal* or kidney*))):ti,ab,kw	9980
#3	(((kidney* or renal*) near/1 insufficien*)):ti,ab,kw	5215
#4	(ckd*):ti,ab,kw	4721
#5	(((kidney* or renal*) near/1 fail*)):ti,ab,kw	15794
#6	(((endstage* or end-stage* or "end stage*") near/1 (renal* or kidney*))):ti,ab,kw	4333
#7	((esrd* or eskd*)):ti,ab,kw	1972
#8	MeSH descriptor: [Chronic Kidney Disease-Mineral and Bone Disorder] this term only	85
#9	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8	25177
#10	MeSH descriptor: [Infant] explode all trees	15691
#11	MeSH descriptor: [Infant Health] this term only	45
#12	MeSH descriptor: [Infant Welfare] this term only	82
#13	((prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies* or toddler*)):ti,ab,kw	85629
#14	((prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies* or toddler*)):so	4898
#15	MeSH descriptor: [Child] explode all trees	1238
#16	MeSH descriptor: [Child Behavior] explode all trees	2007
#17	MeSH descriptor: [Child Health] this term only	87
#18	MeSH descriptor: [Child Welfare] this term only	320
#19	MeSH descriptor: [Minors] this term only	8
#20	((child* or minor or minors or boy* or girl* or kid or kids or young*)):ti,ab,kw	254786
#21	((child* or minor or minors or boy* or girl* or kid or kids or young*)):so	9986
#22	MeSH descriptor: [Pediatrics] explode all trees	646

#23 ((pediatric* or paediatric* or peadiatric*)):ti,ab,kw 32100

#24 ((pediatric* or paediatric* or peadiatric*)):so 30862

#25 MeSH descriptor: [Adolescent] this term only 100696

#26 MeSH descriptor: [Adolescent Behavior] this term only 1330

#27 MeSH descriptor: [Adolescent Health] this term only 23

#28 MeSH descriptor: [Puberty] this term only 293

#29 ((adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*)):ti,ab,kw 135669

#30 ((adolescen* or pubescen* or prepubescen* or pre-pubecen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or juvenil* or youth* or under*age*)):so 3793

#31 MeSH descriptor: [Schools] this term only 1838

#32 MeSH descriptor: [Child Day Care Centers] this term only 221

#33 MeSH descriptor: [Nurseries, Infant] this term only 9

#34 MeSH descriptor: [Schools, Nursery] this term only 37

#35 ((pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*)):ti,ab,kw 93802

#36 ((pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*)):so 1165

#37 (("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*")):ti,ab,kw 14800

#38 {or #10-#37} 404448

#39 #9 and #38 3842

#40 MeSH descriptor: [Proteinuria] explode all trees 2231

#41 (albuminur* or microalbuminur*):ti,ab,kw 3683

#42 (proteinur*):ti,ab,kw 5021

#43 #40 or #41 or #42 8151

#44 #39 and #43 443

#45 (acr or uacr or pcr):ti,ab,kw 14444

#46 MeSH descriptor: [Proteins] explode all trees 116296

#47 (protein*):ti,ab,kw 89019

#48 MeSH descriptor: [Albumins] explode all trees 7640

#49 (albumin*):ti,ab,kw 15504

#50 #46 or #47 or #48 or #49 177752

#51 MeSH descriptor: [Creatinine] this term only 3859

#52 (creatin*):ti,ab,kw 33797

#53 #51 or #52 33797

#54 (ratio*):ti,ab,kw135436

#55 (#50 or #53) and #54 29255

#56 #45 or #55 42446

#57 #44 and #56 150

#58 "conference":pt or (clinicaltrials or trialsearch):so 481429

#59 #57 not #58 85

CRD

1 (MeSH DESCRIPTOR Renal Insufficiency, Chronic EXPLODE ALL TREES) 538 Delete

2 (((chronic* or progressi*) near1 (renal* or kidney*))) 489 Delete

3 (((kidney* or renal*) near1 insufficien*)) 320 Delete

4 ((ckd*)) 93 Delete

5 (((kidney* or renal*) near1 fail*)) 836 Delete

6 (((endstage* or end-stage* or "end stage*") near1 (renal* or kidney*))) 354 Delete

7 ((esrd* or eskd*)) 150 Delete

8 (MeSH DESCRIPTOR Chronic Kidney Disease-Mineral and Bone Disorder) 0 Delete

9 (#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8) 1407 Delete

10 MeSH DESCRIPTOR Proteinuria EXPLODE ALL TREES 145 Delete

11 (albuminur* or microalbuminur*) 140 Delete

12 (proteinur*) 203 Delete

13 (#10 or #11 or #12) 301 Delete

14 (#9 and #13) 140 Delete

15 (acr or uacr or pcr) 420 Delete

16 MeSH DESCRIPTOR Proteins EXPLODE ALL TREES7853 Delete

17	(protein*)	2636	Delete
18	MeSH DESCRIPTOR Albumins EXPLODE ALL TREES	252	Delete
19	(albumin*)	353	Delete
20	(#16 or #17 or #18 or #19)	8747	Delete
21	MeSH DESCRIPTOR Creatinine	114	Delete
22	(creatin*)	745	Delete
23	(#21 or #22)	745	Delete
24	(ratio*)	15294	Delete
25	((#20 or #23) and #24)	2250	Delete
26	(#15 or #25)	2615	Delete
27	(#14 and #26)	58	Delete
28	(#14 and #26) IN DARE	30	Delete
29	(#14 and #26) IN NHSEED	27	Delete
30	(#14 and #26) IN HTA	1	Delete

Cost-effectiveness searches

Databases	Date searched	Version/files	No. retrieved
MEDLINE (Ovid)	10th March 2020	Ovid MEDLINE(R) <1946 to March 09, 2020>	42
MEDLINE in Process (Ovid)	10th March 2020	Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to March 09, 2020>	6
MEDLINE epub (Ovid)	10th March 2020	Ovid MEDLINE(R) Epub Ahead of Print <March 09, 2020>	2
Embase (Ovid)	12th March 2020	Embase <1974 to 2020 Week 10>	60
EconLit (Ovid)	10th March 2020	Econlit <1886 to February 20, 2020>	0

NHS Economic Evaluation Database (NHS EED) (legacy database)	10th March 2020	Up to 2015	27
CRD HTA	10th March 2020	Up to 2018	1

The following search filters were applied to the search strategies in MEDLINE and Embase to identify cost-effectiveness studies:

- Glanville J et al. (2009) Development and Testing of Search Filters to Identify Economic Evaluations in MEDLINE and EMBASE. Alberta: Canadian Agency for Drugs and Technologies in Health (CADTH)

  Several modifications have been made to these filters over the years that are standard NICE practice.

Search strategies

Database: Ovid MEDLINE(R) <1946 to March 09, 2020>

Search Strategy:

---

1 exp Renal Insufficiency, Chronic/ (112617)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (72595)

3 ((kidney* or renal*) adj1 insufficien*).tw. (21252)

4 ckd*.tw. (22947)

5 ((kidney* or renal*) adj1 fail*).tw. (86345)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (35216)

7 (esrd* or eskd*).tw. (14205)

8 "Chronic Kidney Disease-Mineral and Bone Disorder"/ (3451)

9 or/1-8 (212803)

10 exp Infant/ or Infant Health/ or Infant Welfare/ (1124073)

11 (prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*).ti,ab,in,jn. (838111)

12 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (1888198)

13 Minors/ (2560)

14 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (2310277)

15 exp pediatrics/ (57089)

16 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (811920)

17 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (1995288)

18 Puberty/ (13169)

19 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*).ti,ab,in,jn. (413410)

20 Schools/ (37046)

21 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (7131)

22 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (459454)

23 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (3867)

24 or/10-23 (5104091)

25 9 and 24 (46252)

26 exp Proteinuria/ (38709)

27 proteinur*.tw. (35335)

28 (albuminur* or microalbuminur*).tw. (15845)

29 or/26-28 (63796)

30 25 and 29 (4376)

31 (acr or uacr or pcr).tw. (448672)

32 Proteins/ (202949)

33 protein*.tw. (2696484)

34 Albumins/ (19336)

35 albumin*.tw. (140129)

36 or/32-35 (2834424)

37 Creatinine/ (55744)

38 creatin*.tw. (193124)

39 37 or 38 (214222)

40 ratio*.tw. (1207641)

41 (36 or 39) and 40 (171229)

42 31 or 41 (611679)

43	30 and 42 (755)
44	limit 43 to english language (719)
45	animals/ not humans/ (4642773)
46	44 not 45 (696)
47	Economics/ (27142)
48	exp "Costs and Cost Analysis"/ (233116)
49	Economics, Dental/ (1911)
50	exp Economics, Hospital/ (24271)
51	exp Economics, Medical/ (14167)
52	Economics, Nursing/ (3997)
53	Economics, Pharmaceutical/ (2917)
54	Budgets/ (11236)
55	exp Models, Economic/ (14736)
56	Markov Chains/ (14009)
57	Monte Carlo Method/ (27859)
58	Decision Trees/ (10931)
59	econom$.tw. (232004)
60	cba.tw. (9697)
61	cea.tw. (20227)
62	cua.tw. (978)
63	markov$.tw. (17524)
64	(monte adj carlo).tw. (29374)
65	(decision adj3 (tree$ or analys$)).tw. (12967)
66	(cost or costs or costing$ or costly or costed).tw. (449008)
67	(price$ or pricing$).tw. (32702)
68	budget$.tw. (23225)
69	expenditure$.tw. (48234)
70	(value adj3 (money or monetary)).tw. (2046)
71	(pharmacoeconomic$ or (pharmaco adj economic$)).tw. (3446)
72	or/47-71 (905692)
73	"Quality of Life"/ (188956)

74 quality of life.tw. (222791)

75 "Value of Life"/ (5685)

76 Quality-Adjusted Life Years/ (11843)

77 quality adjusted life.tw. (10423)

78 (qaly$ or qald$ or qale$ or qtime$).tw. (8560)

79 disability adjusted life.tw. (2574)

80 daly$.tw. (2349)

81 Health Status Indicators/ (23226)

82 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw. (22011)

83 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (1298)

84 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (4738)

85 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. (28)

86 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (377)

87 (euroqol or euro qol or eq5d or eq 5d).tw. (8561)

88 (qol or hql or hqol or hrqol).tw. (42547)

89 (hye or hyes).tw. (60)

90 health$ year$ equivalent$.tw. (38)

91 utilit$.tw. (166731)

92 (hui or hui1 or hui2 or hui3).tw. (1263)

93 disutili$.tw. (372)

94 rosser.tw. (92)

95 quality of wellbeing.tw. (13)

96 quality of well-being.tw. (377)

97 qwb.tw. (188)

98 willingness to pay.tw. (4287)

99 standard gamble$.tw. (774)

100 time trade off.tw. (1015)

101 time tradeoff.tw. (230)

102 tto.tw. (880)

103 or/73-102 (479552)

104 72 or 103 (1318749)

105 46 and 104 (42)

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to March 09, 2020>

Search Strategy:

---

1 exp Renal Insufficiency, Chronic/ (0)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (9505)

3 ((kidney* or renal*) adj1 insufficien*).tw. (1108)

4 ckd*.tw. (4552)

5 ((kidney* or renal*) adj1 fail*).tw. (6358)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (4867)

7 (esrd* or eskd*).tw. (2009)

8 "Chronic Kidney Disease-Mineral and Bone Disorder"/ (0)

9 or/1-8 (18562)

10 exp Infant/ or Infant Health/ or Infant Welfare/ (0)

11 (prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*).ti,ab,in,jn. (77521)

12 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (0)

13 Minors/ (0)

14 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (307592)

15 exp pediatrics/ (0)

16 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (114791)

17 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (0)

18 Puberty/ (0)

19 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*).ti,ab,in,jn. (58092)

20 Schools/ (0)

21 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (0)

22 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (65895)

23 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (560)

24 or/10-23 (445763)

25 9 and 24 (3406)

26 exp Proteinuria/ (0)

27 proteinur*.tw. (3225)

28 (albuminur* or microalbuminur*).tw. (1839)

29 or/26-28 (4827)

30 25 and 29 (370)

31 (acr or uacr or pcr).tw. (50092)

32 Proteins/ (0)

33 protein*.tw. (240270)

34 Albumins/ (0)

35 albumin*.tw. (12539)

36 or/32-35 (247556)

37 Creatinine/ (0)

38 creatin*.tw. (26453)

39 37 or 38 (26453)

40 ratio*.tw. (211746)

41 (36 or 39) and 40 (18929)

42 31 or 41 (68054)

43 30 and 42 (77)

44 limit 43 to english language (76)

45 animals/ not humans/ (0)

46 44 not 45 (76)

47 Economics/ (0)

48 exp "Costs and Cost Analysis"/ (0)

49 Economics, Dental/ (0)

50 exp Economics, Hospital/ (0)

51 exp Economics, Medical/ (0)

52 Economics, Nursing/ (0)

53 Economics, Pharmaceutical/ (0)

54 Budgets/ (0)

55 exp Models, Economic/ (0)

56 Markov Chains/ (0)

57 Monte Carlo Method/ (0)

58 Decision Trees/ (0)

59 econom$.tw. (44169)

60 cba.tw. (431)

61 cea.tw. (1884)

62 cua.tw. (195)

63 markov$.tw. (5649)

64 (monte adj carlo).tw. (16737)

65 (decision adj3 (tree$ or analys$)).tw. (2337)

66 (cost or costs or costing$ or costly or costed).tw. (94430)

67 (price$ or pricing$).tw. (5640)

68 budget$.tw. (4902)

69 expenditure$.tw. (6293)

70 (value adj3 (money or monetary)).tw. (339)

71 (pharmacoeconomic$ or (pharmaco adj economic$)).tw. (478)

72 or/47-71 (163336)

73 "Quality of Life"/ (0)

74 quality of life.tw. (37873)

75 "Value of Life"/ (0)

76 Quality-Adjusted Life Years/ (0)

77 quality adjusted life.tw. (1674)

78 (qaly$ or qald$ or qale$ or qtime$).tw. (1412)

79 disability adjusted life.tw. (523)

80 daly$.tw. (480)

81 Health Status Indicators/ (0)

82 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw. (2616)

83 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (752)

84 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (734)

85 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. (5)

86 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (18)

87 (euroqol or euro qol or eq5d or eq 5d).tw. (1599)

88 (qol or hql or hqol or hrqol).tw. (7230)

89 (hye or hyes).tw. (8)

90 health$ year$ equivalent$.tw. (2)

91 utilit$.tw. (30976)

92 (hui or hui1 or hui2 or hui3).tw. (187)

93 disutili$.tw. (71)

94 rosser.tw. (5)

95 quality of wellbeing.tw. (7)

96 quality of well-being.tw. (27)

97 qwb.tw. (13)

98 willingness to pay.tw. (920)

99 standard gamble$.tw. (59)

100 time trade off.tw. (116)

101 time tradeoff.tw. (16)

102 tto.tw. (125)

103 or/73-102 (71108)

104 72 or 103 (225081)

105 46 and 104 (6)

Database: Ovid MEDLINE(R) Epub Ahead of Print <March 09, 2020>

Search Strategy:

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1 exp Renal Insufficiency, Chronic/ (0)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (1357)

3 ((kidney* or renal*) adj1 insufficien*).tw. (147)

4 ckd*.tw. (700)

5 ((kidney* or renal*) adj1 fail*).tw. (733)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (698)

7 (esrd* or eskd*).tw. (307)

8 "Chronic Kidney Disease-Mineral and Bone Disorder"/ (0)

9 or/1-8 (2522)

10 exp Infant/ or Infant Health/ or Infant Welfare/ (0)

11 (prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*).ti,ab,in,jn. (14175)

12 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (0)

13 Minors/ (0)

14 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (48794)

15 exp pediatrics/ (0)

16 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (20053)

17 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (0)

18 Puberty/ (0)

19 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*).ti,ab,in,jn. (12121)

20 Schools/ (0)

21 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (0)

22 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (11391)

23 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (107)

24 or/10-23 (71650)

25 9 and 24 (532)

26 exp Proteinuria/ (0)

27 proteinur*.tw. (320)

28 (albuminur* or microalbuminur*).tw. (199)

29 or/26-28 (498)

30	25 and 29 (47)
31	(acr or uacr or pcr).tw. (6033)
32	Proteins/ (0)
33	protein*.tw. (30904)
34	Albumins/ (0)
35	albumin*.tw. (1618)
36	or/32-35 (31884)
37	Creatinine/ (0)
38	creatin*.tw. (3247)
39	37 or 38 (3247)
40	ratio*.tw. (25981)
41	(36 or 39) and 40 (2669)
42	31 or 41 (8575)
43	30 and 42 (13)
44	limit 43 to english language (13)
45	animals/ not humans/ (0)
46	44 not 45 (13)
47	Economics/ (0)
48	exp "Costs and Cost Analysis"/ (0)
49	Economics, Dental/ (0)
50	exp Economics, Hospital/ (0)
51	exp Economics, Medical/ (0)
52	Economics, Nursing/ (0)
53	Economics, Pharmaceutical/ (0)
54	Budgets/ (0)
55	exp Models, Economic/ (0)
56	Markov Chains/ (0)
57	Monte Carlo Method/ (0)
58	Decision Trees/ (0)
59	econom$.tw. (5917)
60	cba.tw. (62)

61 cea.tw. (326)

62 cua.tw. (18)

63 markov$.tw. (697)

64 (monte adj carlo).tw. (1182)

65 (decision adj3 (tree$ or analys$)).tw. (413)

66 (cost or costs or costing$ or costly or costed).tw. (12396)

67 (price$ or pricing$).tw. (891)

68 budget$.tw. (528)

69 expenditure$.tw. (1110)

70 (value adj3 (money or monetary)).tw. (71)

71 (pharmacoeconomic$ or (pharmaco adj economic$)).tw. (52)

72 or/47-71 (20217)

73 "Quality of Life"/ (0)

74 quality of life.tw. (6873)

75 "Value of Life"/ (0)

76 Quality-Adjusted Life Years/ (0)

77 quality adjusted life.tw. (392)

78 (qaly$ or qald$ or qale$ or qtime$).tw. (339)

79 disability adjusted life.tw. (113)

80 daly$.tw. (98)

81 Health Status Indicators/ (0)

82 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw. (448)

83 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (41)

84 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (163)

85 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. (0)

86 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (4)

87 (euroqol or euro qol or eq5d or eq 5d).tw. (367)

88 (qol or hql or hqol or hrqol).tw. (1354)

89 (hye or hyes).tw. (1)

90 health$ year$ equivalent$.tw. (0)

91 utilit$.tw. (4611)

92 (hui or hui1 or hui2 or hui3).tw. (20)

93 disutili$.tw. (13)

94 rosser.tw. (0)

95 quality of wellbeing.tw. (1)

96 quality of well-being.tw. (7)

97 qwb.tw. (3)

98 willingness to pay.tw. (164)

99 standard gamble$.tw. (7)

100 time trade off.tw. (17)

101 time tradeoff.tw. (3)

102 tto.tw. (22)

103 or/73-102 (11771)

104 72 or 103 (30227)

105 46 and 104 (2)

Database: Embase <1974 to 2020 Week 10>

Search Strategy:

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1 exp kidney failure/ (350205)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (122286)

3 ((kidney* or renal*) adj1 insufficien*).tw. (29978)

4 ckd*.tw. (49110)

5 ((kidney* or renal*) adj1 fail*).tw. (131849)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (57873)

7 (esrd* or eskd*).tw. (27064)

8 or/1-7 (442165)

9 exp juvenile/ or Child Behavior/ or Child Welfare/ or Child Health/ or infant welfare/ or "minor (person)"/ or elementary student/ (3373773)

10 (prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*).ti,ab,in,ad,jw. (1188085)

11 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,ad,jw. (3572569)

12 exp pediatrics/ (104071)

13 (pediatric* or paediatric* or peadiatric*).ti,ab,in,ad,jw. (1608762)

14 exp adolescence/ or exp adolescent behavior/ or adolescent health/ or high school student/ or middle school student/ (102478)

15 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*).ti,ab,in,ad,jw. (646327)

16 school/ or high school/ or kindergarten/ or middle school/ or primary school/ or nursery school/ or day care/ (101861)

17 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jw. (685244)

18 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (7239)

19 or/9-18 (6320751)

20 8 and 19 (86651)

21 exp proteinuria/ (97326)

22 proteinur*.tw. (56691)

23 (albuminur* or microalbuminur*).tw. (25778)

24 or/21-23 (112716)

25 20 and 24 (8979)

26 (acr or uacr or pcr).tw. (736279)

27 protein/ (459008)

28 protein*.tw. (3524695)

29 albumin/ (121191)

30 albumin*.tw. (203246)

31 or/27-30 (3737026)

32 creatinine/ (175952)

33 creatin*.tw. (321711)

34 32 or 33 (391283)

35 ratio*.tw. (1919598)

36 (31 or 34) and 35 (274857)

37	26 or 36 (992990)
38	25 and 37 (1348)
39	limit 38 to english language (1307)
40	nonhuman/ not human/ (4584764)
41	39 not 40 (1261)
42	limit 41 to (conference abstract or conference paper or "conference review") (460)
43	41 not 42 (801)
44	exp Health Economics/ (831063)
45	exp "Health Care Cost"/ (286436)
46	exp Pharmacoeconomics/ (199867)
47	Monte Carlo Method/ (39355)
48	Decision Tree/ (12348)
49	econom$.tw. (357094)
50	cba.tw. (12616)
51	cea.tw. (34081)
52	cua.tw. (1464)
53	markov$.tw. (29590)
54	(monte adj carlo).tw. (47282)
55	(decision adj3 (tree$ or analys$)).tw. (22507)
56	(cost or costs or costing$ or costly or costed).tw. (750030)
57	(price$ or pricing$).tw. (55896)
58	budget$.tw. (37719)
59	expenditure$.tw. (72987)
60	(value adj3 (money or monetary)).tw. (3372)
61	(pharmacoeconomic$ or (pharmaco adj economic$)).tw. (8530)
62	or/44-61 (1716744)
63	"Quality of Life"/ (455746)
64	Quality Adjusted Life Year/ (25853)
65	Quality of Life Index/ (2738)
66	Short Form 36/ (27940)
67	Health Status/ (124994)

68 quality of life.tw. (424683)

69 quality adjusted life.tw. (19106)

70 (qaly$ or qald$ or qale$ or qtime$).tw. (19562)

71 disability adjusted life.tw. (3901)

72 daly$.tw. (3834)

73 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw. (40512)

74 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (2356)

75 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (9153)

76 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. (58)

77 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (442)

78 (euroqol or euro qol or eq5d or eq 5d).tw. (19667)

79 (qol or hql or hqol or hrqol).tw. (93552)

80 (hye or hyes).tw. (134)

81 health$ year$ equivalent$.tw. (41)

82 utilit$.tw. (281162)

83 (hui or hui1 or hui2 or hui3).tw. (2210)

84 disutili$.tw. (898)

85 rosser.tw. (119)

86 quality of wellbeing.tw. (42)

87 quality of well-being.tw. (471)

88 qwb.tw. (244)

89 willingness to pay.tw. (8455)

90 standard gamble$.tw. (1092)

91 time trade off.tw. (1673)

92 time tradeoff.tw. (288)

93 tto.tw. (1630)

94 or/63-93 (960389)

95 62 or 94 (2524621)

96 43 and 95 (60)

Database: Econlit <1886 to February 20, 2020>

Search Strategy:

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1 [exp Renal Insufficiency, Chronic/] (0)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (22)

3 ((kidney* or renal*) adj1 insufficien*).tw. (3)

4 ckd*.tw. (5)

5 ((kidney* or renal*) adj1 fail*).tw. (33)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (54)

7 (esrd* or eskd*).tw. (31)

8 ["Chronic Kidney Disease-Mineral and Bone Disorder"/] (0)

9 or/1-8 (101)

10 [exp Infant/ or Infant Health/ or Infant Welfare/] (0)

11 (prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*).ti,ab,in,jn. (5656)

12 [exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/] (0)

13 [Minors/] (0)

14 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (47164)

15 [exp pediatrics/] (0)

16 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (176)

17 [Adolescent/ or Adolescent Behavior/ or Adolescent Health/] (0)

18 [Puberty/] (0)

19 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*).ti,ab,in,jn. (9143)

20 [Schools/] (0)

21 [Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/] (0)

22 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (49443)

23 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (57)

24 or/10-23 (94653)

25 9 and 24 (5)

26 [exp Proteinuria/] (0)

27 proteinur*.tw. (1)

28 (albuminur* or microalbuminur*).tw. (6)

29 or/26-28 (6)

30 25 and 29 (0)

31 (acr or uacr or pcr).tw. (77)

32 [Proteins/] (0)

33 protein*.tw. (614)

34 [Albumins/] (0)

35 albumin*.tw. (4)

36 or/32-35 (617)

37 [Creatinine/] (0)

38 creatin*.tw. (11124)

39 37 or 38 (11124)

40 ratio*.tw. (64433)

41 (36 or 39) and 40 (609)

42 31 or 41 (686)

43 30 and 42 (0)

44 limit 43 to english language [Limit not valid; records were retained] (0)

45 [animals/ not humans/] (0)

46 44 not 45 (0)

CRD

1 (MeSH DESCRIPTOR Renal Insufficiency, Chronic EXPLODE ALL TREES) 538 Delete

2 (((chronic* or progressi*) near1 (renal* or kidney*))) 489 Delete

3 (((kidney* or renal*) near1 insufficien*)) 320 Delete

4 ((ckd*)) 93 Delete

5 (((kidney* or renal*) near1 fail*)) 836 Delete

6 (((endstage* or end-stage* or "end stage*") near1 (renal* or kidney*))) 354 Delete

7 ((esrd* or eskd*)) 150 Delete

8 (MeSH DESCRIPTOR Chronic Kidney Disease-Mineral and Bone Disorder) 0 Delete

9 (#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8) 1407 Delete

10 MeSH DESCRIPTOR Proteinuria EXPLODE ALL TREES 145 Delete

11 (albuminur* or microalbuminur*) 140 Delete

12 (proteinur*) 203 Delete

13 (#10 or #11 or #12) 301 Delete

14 (#9 and #13) 140 Delete

15 (acr or uacr or pcr) 420 Delete

16 MeSH DESCRIPTOR Proteins EXPLODE ALL TREES7853 Delete

17 (protein*) 2636 Delete

18 MeSH DESCRIPTOR Albumins EXPLODE ALL TREES 252 Delete

19 (albumin*) 353 Delete

20 (#16 or #17 or #18 or #19) 8747 Delete

21 MeSH DESCRIPTOR Creatinine 114 Delete

22 (creatin*) 745 Delete

23 (#21 or #22) 745 Delete

24 (ratio*) 15294 Delete

25 ((#20 or #23) and #24) 2250 Delete

26 (#15 or #25) 2615 Delete

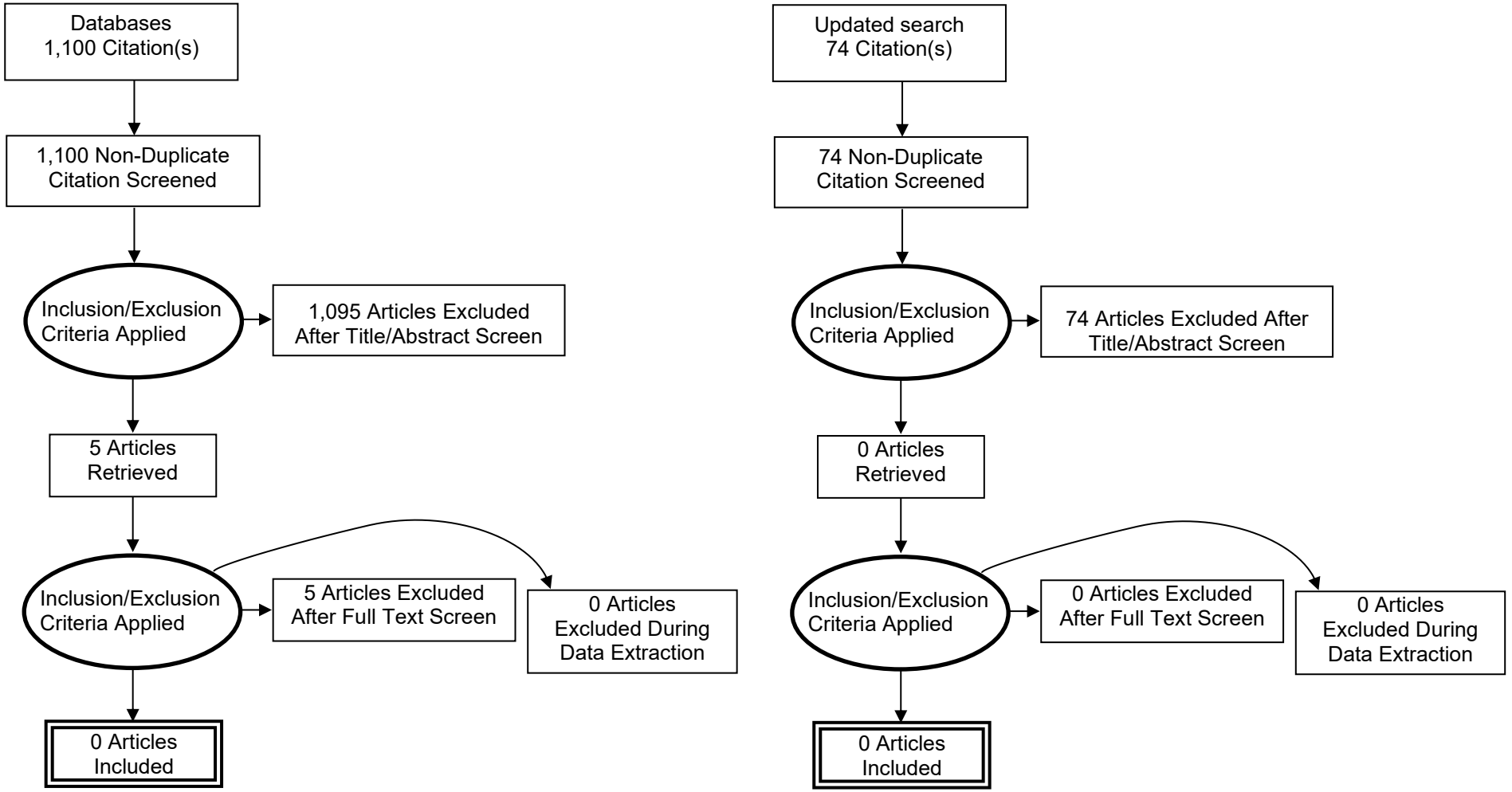
27 (#14 and #26) 58 Delete

28 (#14 and #26) IN DARE 30 Delete

29 (#14 and #26) IN NHSEED 27 Delete

30 (#14 and #26) IN HTA 1 Delete

Appendix D – Diagnostic evidence study selection



Appendix E – Diagnostic evidence

No studies were included in this review question.

Appendix F – Forest plots

No studies were included in this review question.

Appendix G – GRADE tables

No studies were included in this review question.

Appendix H – Economic evidence study selection

Appendix I – Economic evidence tables

No economic studies were included.

Appendix J – Health economic model

This review question was not prioritised for economic modelling.

Appendix K – Excluded studies

Diagnostic studies

Reference	Reason for exclusion
Bashir, S., Hafeez, M.R., Iqbal, J. et al. (2019) Analysis of SPOT urine protein to creatinine ratio as an indicator of 24 hours urinary protein excretion in nephrotic syndrome. Pakistan Journal of Medical and Health Sciences 13(3): 842-844	- Study does not contain a relevant study population [Mean age 25.6 years without subgroup analysis by age]
Garg, S., Gupta, A.K., Rohtgi, A. et al. (2004) Evaluation of random urine sample protein-cretinine ratio as an index of quantitative proteinuria. JK Science 6(3): 134-137	- Study does not contain a relevant study population [Age ranged from 14 to 70 years without subgroup analysis by age]
Kouri, T, Nokelainen, P, Pelkonen, V et al. (2009) Evaluation of the ARKRAY AUTION Eleven reflectometer in detecting microalbuminuria with AUTION Screen test strips and proteinuria with AUTION Sticks 10PA strips. Scandinavian journal of clinical and laboratory investigation 69(1): 52-64	- Study does not contain a relevant study population [Median age of 62 years, range 3 to 95 years without subgroup analysis by age]
Methven, Shona, MacGregor, Mark S, Traynor, Jamie P et al. (2010) Assessing proteinuria in chronic kidney disease: protein-creatinine ratio versus albumin-creatinine ratio. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 25(9): 2991-6	- Study does not contain a relevant study population [Adults]
Zhao, Y.-F., Zhu, L., Liu, L.-J. et al. (2016) Measures of urinary protein and albumin in the prediction of progression of IgA nephropathy. Clinical Journal of the American Society of Nephrology 11(6): 947-955	- Study does not contain a relevant study population [Mean age 35.6 years (range: 14 to 83 years) without subgroup analysis by age]

Appendix L – Research recommendations – full details

L.1.1 Research recommendation

What is the effect of measuring proteinuria with albumin:creatinine ratio compared to protein:creatinine ratio on the timing of treatment changes in children and young people with CKD?

L.1.2 Why this is important

The committee discussed the importance of measuring proteinuria in children and young people with CKD and that high levels of proteinuria are likely to be used to change the treatment in this population but that this has not been investigated in the context of this guideline. Therefore, the committee agreed to make a research recommendation to identify the effect of measuring proteinuria with albumin:creatinine ratio compared to protein:creatinine ratio on the timing of treatment changes in children and young people with CKD and the consequences of the delay in treatment changes on different levels of proteinuria.

L.1.3 Rationale for research recommendation

Importance to 'patients' or the population	It has not been investigated which is the best measure of proteinuria to use for treatment changes in the management of CKD in children and young people. If the correct quantification of proteinuria is missed, the consequences of disease progression could be serious, and this could lead to irreversible kidney damage.
Relevance to NICE guidance	ACR and PCR have been considered in this guideline as measurements of proteinuria and there is a lack of data on their effect on treatment changes. Further evidence might fill in the gap in this area during future updates of the guideline.
Relevance to the NHS	New evidence might affect the management of CKD in children and young people which in turn, might have a resource impact increasing the cost of CKD management by the NHS.
National priorities	High
Current evidence base	No evidence was reviewed for this topic.
Equality considerations	None known

L.1.4 Modified PICO table

Population	**Inclusion:** Children and young people (up to 18 years) with suspected or diagnosed chronic kidney disease GFR categories G1 to G5. **Exclusion:** • people receiving renal replacement therapy (RRT)

	• people with acute kidney injury combined with rapidly progressive glomerulonephritis • pregnant young women people receiving palliative care
Prognostic factor	**Proteinuria:** • Albumin:creatinine ratio • Protein:creatinine ratio
Co-variates	Confounders identified by the studies themselves will be used
Outcome	**Primary outcome:** • Immediate treatment changes • Delayed treatment changes **Secondary outcomes:** • Consequences of delayed treatment changes
Study design	• Prospective cohort studies (retrospective cohort studies will be used if no prospective studies ae found). • Systematic reviews of prospective cohort studies
Timeframe	Long term
Additional information	None