# National Institute for Health and Care Excellence

Final

# Chronic kidney disease

## [C] Evidence reviews for accuracy of reagent strips for detecting protein and blood in urine in children and young people with CKD

*NICE guideline NG203*

*Evidence reviews underpinning recommendations 1.1.11, 1.1.15 to 1.1.16 and research recommendations in the NICE guideline*

*August 2021*

*Final*

*These evidence reviews were developed by the Guideline Updates Team*

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# Accuracy of reagent strips for detecting protein and blood in urine in children and young people with chronic kidney disease (CKD)

## 1.1 Review question

In children and young people, what is the accuracy of reagent strips for detecting protein and blood in urine?

### 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 there is likely to be a difference between children and young people compared to adults at detecting protein and blood in urine using reagent strips.

The aim of this review is to assess the accuracy of reagent strips for detecting protein and blood in urine in children and young people. See Appendix A for full details of the review protocol.

### 1.1.2 Summary of the protocol

**Table 1: PICTO table for accuracy of reagent strips**

| | |
|---|---|
| **Population** | **Inclusion:**<br>Children and young people up to the age of 18 years<br><br>**Exclusion:**<br>• Children and young people receiving renal replacement therapy (RRT)<br>• Children and young people with acute kidney injury combined with rapidly progressive glomerulonephritis<br>• Children and young people receiving palliative care |
| **Index test** | Reagent strips for detecting protein, blood or albumin in urine |
| **Reference standard** | **For all tests**<br>• Mass spectrometry<br><br>**For albumin**<br>• immunonephelometric methods<br><br>**For protein**<br>• turbidimetric or colorimetric assays<br><br>**For haematuria**<br>• Phase-contrast microscopy of fresh urinary sediment |
| **Target condition** | Proteinuria, haematuria, albuminuria |

| | |
|---|---|
| **Outcome** | **Primary outcomes**<br>• Likelihood ratios<br>• Adverse outcomes (for example, test compromised by presence of ascorbic acid in urine)<br><br>**Secondary outcomes**<br>• Specificity<br>• Sensitivity<br>• Positive Predictive Value<br>• Negative Predictive Value<br><br>Outcomes will all be converted to likelihood ratios. |

### 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 on Appendix B.

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

#### Protocol deviation

The committee agreed to use additional reference standards in this review which have been used in published research for adults. The decision to use the additional reference standards was made based on the numbers of studies that used them. While the committee agreed that the standards were not as accurate as the standards in the review protocol, they were accurate enough to merit inclusion because they would aid decision making, and because, on balance, the committee felt that rigid adherence to the reference standards would exclude a lot of relevant literature. Additionally, these measures are all in use in the UK. These reference standards were relevant to test the accuracy of reagent strips to detect proteinuria and albuminuria in children and young people as long as all participants within a study received the same reference standard:

- Spot urinary protein:creatinine ratio
- 24-hour urine protein excretion
- Spot urinary albumin:creatinine ratio
- Albumin concentration analysed by turbidimetric measurement
- Serum creatinine clearance with a modified Schwartz formula.

As a result, outcomes based on these reference standards were not downgraded for indirectness in their GRADE assessment.

### 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 7,863 references (see Appendix C for the literature search strategy). Based on title and abstract screening, 7,831 references were excluded, and 32 references were ordered for full text screening. In total 6 cross-sectional studies were included based on their relevance to the review protocol (Appendix A). The diagnostic evidence study selection is presented as a PRISMA diagram in Appendix D. Included studies reported on proteinuria and albuminuria. There were no studies reporting on haematuria in children and young people.

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 340 references for this review question, these were screened on title and abstract. None of these references were ordered for full text screening because none of them were relevant according to the review protocol (Appendix A).

See section 1.1.13 References – included studies for a list of references for included studies.

#### 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

**Table 2: Summary of studies included in the diagnostic evidence**

| Author and year | Study details | Index test | Reference standard |
|---|---|---|---|
| Agarwal 2004 | **Study location**<br>India<br>**Inclusion criteria**<br>• Age ≤12 years<br>• Underlying nephrotic syndrome<br>**Sample size**<br>50 urine samples from 26 participants | • Urinary dipstick albustix for proteinuria | • Spot urinary protein/creatinine ratio<br>• 24-hour urine protein excretion |
| Biswas 2009 | **Study location**<br>India<br>**Inclusion criteria**<br>• Age ≤12 years<br>• Underlying nephrotic syndrome<br>**Sample size**<br>52 urine samples from 26 participants | • Urinary dipstick for proteinuria | • Spot urinary protein/creatinine ratio<br>• 24-hour urine protein excretion |
| Haysom 2009 | **Study location**<br>Australia<br>**Inclusion criteria**<br>• Healthy Aboriginal and non-Aboriginal children<br>• Boys and girls<br>• Similar proportion from urban, coastal, rural, and remote areas<br>**Sample size**<br>2266 healthy children including 55.1% Aboriginal children from elementary schools | • Multistix-10 SG reagent dipstick for proteinuria | • Spot urine albumin:creatinine dipstick |
| Meinhardt 2003 | **Study location**<br>Switzerland | • Clinitek-Microalbumin | • Albumin concentration was analysed by |

| Author and year | Study details | Index test | Reference standard |
|---|---|---|---|
| | **Inclusion criteria**<br>• Children and adolescents with type 1 diabetes<br>**Sample size**<br>209 specimens of 124 children and adolescents | | turbidimetric measurement |
| Ochigbo 2017 | **Study location**<br>Nigeria<br>**Inclusion criteria**<br>• Severely asphyxiated full-term neonates admitted into the newborn units of the university teaching hospital<br>**Sample size**<br>50 neonates | • Micral-test strips for microalbuminuria | • Serum creatinine clearance with a modified Schwartz formula |
| Sultana 2018 | **Study location**<br>Bangladesh<br>**Inclusion criteria**<br>• Nephrotic syndrome<br>• Bed side proteinuria (3+/4+) by urinary heat coagulation test<br>**Sample size**<br>100 children | • Bed side proteinuria dipstick test | • Spot urinary protein creatinine ratio |

See Appendix E for full evidence tables.

### 1.1.6 Summary of the diagnostic evidence

**Table 3: Summary GRADE table – Proteinuria**

| Index test | Reference standard | Sample size | Likelihood ratio (95% CI) | Quality | Probability of proteinuria (based on LR)[a] |
|---|---|---|---|---|---|
| At baseline Multistix-10 SG | At baseline Albumin:creatinine ratio | Whole sample 2,135 | LR+ 20.92 (15.83, 27.66) | Moderate | Very large increase |
| | | | LR- 0.38 (0.31, 0.47) | Moderate | Moderate decrease |
| At baseline Multistix-10 SG | At baseline Albumin:creatinine ratio | Non-Aboriginal 971 | LR+ 19.52 (13.25, 28.77) | Moderate | Very large increase |
| | | | LR- 0.34 (0.24, 0.48) | Moderate | Moderate decrease |
| At baseline Multistix-10 SG | At baseline Albumin:creatinine ratio | Aboriginal 1,164 | LR+ 22.76 (15.23, 34.01) | Moderate | Very large increase |
| | | | LR- 0.41 (0.32, 0.53) | Low | Moderate decrease |
| At 2 years Multistix-10 SG | At 2 years | Whole sample | LR+ 11.13 (8.06, 15.37) | Moderate | Very large increase |

| Index test | Reference standard | Sample size | Likelihood ratio (95% CI) | Quality | Probability of proteinuria (based on LR)[a] |
|---|---|---|---|---|---|
| | Albumin:creatinine ratio | 1,341 | LR- 0.26 (0.12, 0.57) | Low | Moderate decrease |
| At 2 years Multistix-10 SG | At 2 years Albumin:creatinine ratio | Non-Aboriginal 628 | LR+ 11.19 (7.11, 17.61) | Moderate | Very large increase |
| | | | LR- 0.23 (0.07, 0.81) | Low | Moderate decrease |
| At 2 years Multistix-10 SG | At 2 years Albumin:creatinine ratio | Aboriginal 713 | LR+ 11.09 (7.02, 17.53) | Moderate | Very large increase |
| | | | LR- 0.29 (0.11, 0.76) | Low | Moderate decrease |
| Urinary dipstick albustix | 24-hour urine protein excretion | 50 samples from 26 children | LR+ 42.75 (2.64, 690.58) | Moderate | Very large increase |
| | | | LR- 0.41 (0.22, 0.74) | Low | Moderate decrease |
| Urinary dipstick albustix | Spot urinary protein/creatinine ratio | 50 samples from 26 children | LR+ 9.96 (2.36, 41.99) | Moderate | Large increase |
| | | | LR- 0.48 (0.27, 0.88) | Low | Moderate decrease |
| Urinary protein dipstick | 24-hour urine protein excretion | 52 samples from 26 children | LR+ 22.50 (3.13, 161.25) | Moderate | Very large increase |
| | | | LR- 0.38 (0.20, 0.72) | Low | Moderate decrease |
| Urinary protein dipstick | Spot urinary protein/creatinine ratio | 52 samples from 26 children | LR+ 8.00 (2.48, 25.75) | Moderate | Large increase |
| | | | LR- 0.41 (0.20, 0.83) | Low | Moderate decrease |
| Bed side dipstick test | Spot urinary protein creatinine ratio | 100 | LR+ 3.25 (1.26, 8.40) | Low | Moderate increase |
| | | | LR- 0.03 (0.00, 0.13) | Moderate | Very large decrease |

*(a) See table 5 in Appendix B for the interpretation of likelihood ratios.*

**Table 4: Summary GRADE table – Albuminuria**

| Index test | Reference standard | Sample size | Likelihood ratio (95% CI) | Quality | Probability of proteinuria (based on LR)[a] |
|---|---|---|---|---|---|
| Clinitek-Microalbumin | Turbidimetric measurement | 156 | LR+ 3.35 (2.35, 4.77) | Moderate | Moderate increase |
| | | | LR- 0.15 (0.02, 0.96) | Low | Large decrease |
| Micral-test strips | Serum creatinine clearance | 50 | LR+ 3.92 (0.48, 31.63) | Very low | No meaningful change |
| | | | LR- 0.57 (0.08, 4.07) | Very low | No meaningful change |

*(a) See table 5 in Appendix B for the interpretation of likelihood ratios.*

See Appendix G for full GRADE tables.

### 1.1.7 Economic evidence

A systematic search was conducted to identify economic evaluations for this review question. The search returned 2,419 records which were sifted against the review protocol. Of these publications 2,418 were excluded based on title and abstract. One publication was retrieved but was excluded based on full text inspection. The reason for exclusion can be found in Appendix K. 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 proteinuria results have on children and young people. Children and young people with true positive results would have a repeat test or would undergo protein quantification to confirm proteinuria if they were already diagnosed with CKD. For children and young people where proteinuria was an incidental finding of a dipstick test, additional investigations would help to confirm CKD. Those with false positive results would go unnecessary additional tests or further investigations which may result in increased unnecessary anxiety and health care expense. Children and young people with true negative results would be correctly reassured about their kidney function. Children and young people with false negative results would not undergo further investigations to check their kidney function (those with reagent strips done for other reasons) or to confirm proteinuria (those with CKD) which would affect the treatment they receive to manage their proteinuria.

The committee agreed that negative likelihood ratios were the key outcomes to identify the most accurate reagent strips for detecting proteinuria and albuminuria in children and young people which would rule out significant proteinuria and albuminuria. There was no evidence about the accuracy of reagent strips to detect haematuria in children and young people.

#### 1.1.10.2 The quality of the evidence

Overall, most of the quality of the diagnostic evidence was moderate, with the main reason for downgrading being due to risk of bias of included studies (lack of information on whether index test results were interpreted without knowledge of reference standard results and vice versa).

The committee was unaware of any established clinical decision thresholds, so the literature based 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.

The committee did not feel able to make a recommendation for the use of reagent strips to detect albuminuria because there was less evidence for this type of test and a research recommendation was made.

The committee discussed that only one study reported the analytical technique to measure albumin concentration (turbidimetric measurement) and that the rest of studies reported other reference standards which were not listed in the protocol. The decision to use the additional reference standards is described in section 1.1.3 Methods and process as a deviation protocol. The committee agreed that all reference standards reported by the included studies were relevant to test the accuracy of reagent strips to detect proteinuria and albuminuria in children and young people.

#### 1.1.10.3 Benefits and harms

**Proteinuria**

The evidence showed that reagent strips were less useful to rule-out proteinuria because there was a moderate decreased probability of having proteinuria (shown by a negative reagent strip test) in those with proteinuria (confirmed by a spot albumin:creatinine test) compared to those without confirmed proteinuria (negative likelihood ratios [ranging from 0.23 to 0.41], which were closer to the MID [0.5]). This evidence included the largest study with 2,135 participants. The committee highlighted that ruling out proteinuria was the key outcome because children and young people with true negative results would be correctly reassured about their kidney function and they would not undergo unnecessary additional tests or further investigations which may result in increased unnecessary anxiety and health care expense. Therefore, the committee agreed that reagent strips should not be used to identify proteinuria in children and young people. The evidence was not reviewed for adults and so the committee agreed to retain the 2014 recommendation not to use reagent strips to identify proteinuria in adults unless the strips are capable of specifically measuring albumin at low concentrations and expressing the result as an ACR. The committee also highlighted that these tests are commonly used in clinical practice and agreed to make a further recommendation to offer testing for CKD using eGFRcreatinine and ACR in adults, children and young people with unexplained proteinuria from incidental findings.

The evidence showed that reagent strips were likely to be a significant rule-in test for proteinuria in children and young people at risk of chronic kidney disease (positive likelihood ratios were higher than the MID [2.0] ranging from 3.2 to 22.7). The committee highlighted that ruling out proteinuria with confidence was the key outcome when using reagent strips and that ruling in tests was not very useful. This evidence was used to confirm the decision of recommending not using reagent strips to identify proteinuria in children and young people.

Finally, there was a study including children and young people with nephrotic syndrome. The committee highlighted that nephrotic syndrome was not chronic kidney disease. Therefore, no recommendations were made for this population.

**Albuminuria**

The committee did not agree to recommend the use of reagent strips to detect albuminuria because there was less evidence for this test with only 2 small studies providing evidence on this test (156 and 50 participants respectively). One study included children and young people with type 1 diabetes and the results showed a moderate increased probability of having albuminuria (shown by a positive reagent strip test) in those with albuminuria (confirmed by a turbidimetric measurement) compared to those without confirmed albuminuria (positive likelihood ratio 3.35). The study also showed a large decreased probability of having albuminuria (shown by a negative reagent strip test) in those with albuminuria (confirmed by a turbidimetric measurement) compared to those without confirmed albuminuria (negative likelihood ratio 0.15). This evidence showed that reagent strips might be useful to rule-out albuminuria in children and young people with type 1 diabetes, but this evidence was from a small study (156 participants). The committee agreed to make a research recommendation to gather more evidence on reagent strips to detect

albuminuria in children and young people before making a specific recommendation on this type of reagent strips. The other study included severely asphyxiated full-term neonates, but the reagent strips could not differentiate between neonates with or without albuminuria.

**Haematuria**

There was no evidence about the accuracy of reagent strips to detect haematuria in children and young people, however the committee noted that testing haematuria with reagent strips is similar in both adults and in children and young people. There was already a recommendation on testing haematuria in adults in the 2014 guideline and the committee agreed to add 'children and young people' to the recommendation because this also applies to this population. Children and young people were not considered for the 2014 guideline. The committee recommended further evaluation for children and young people who test positive for haematuria but was unable to be more specific because that evaluation is based in clinical judgment about the likely causes of the haematuria. The committee agreed that there was no need to make a research recommendation on reagent strips to detect haematuria in children and young people because the evidence from adults can be extrapolated to children and young people.

#### 1.1.10.4 Cost effectiveness and resource use

The committee have discussed the suitability of urine reagent strip testing to diagnose and monitor proteinuria in adults, children and young people. It was noted that urinalysis strips were relatively inexpensive and widely available, nonetheless there was wide price variation across products available through the NHS catalogue, ranging from £0.06 to £1.50. Whilst the committee were confident to recommend urinalysis strips for haematuria, the committee felt that even with the low cost the lack of high-quality evidence meant that they did not want to recommend urinalysis strips for proteinuria. The committee felt that the investigation for incidental findings would not result in a large increase in costs, and would likely be outweighed by the benefits or either earlier identification of CKD, or appropriate earlier treatment of proteinuria.

### 1.1.11 Recommendations supported by this evidence review

This evidence review supports recommendations .1.11, 1.1.15 to 1.1.16 and the research recommendation on the accuracy of reagent strips for detecting albumin in urine (see Appendix L for further details about the research recommendation).

### 1.1.12 References – included studies

#### 1.1.12.1 Diagnostic evidence

Agarwal, I., Kirubakaran, C., Markandeyulu et al. (2004) Quantitation of proteinuria by spot urine sampling. Indian Journal of Clinical Biochemistry 19(2): 45-47

Biswas, A, Kumar, R, Chaterjee, A et al. (2009) Quantitation of proteinuria in nephrotic syndrome by spot urine protein creatinine ratio estimation in children. Mymensingh medical journal : MMJ 18(1): 67-71

Haysom, Leigh, Williams, Rita, Hodson, Elisabeth et al. (2009) Diagnostic accuracy of urine dipsticks for detecting albuminuria in indigenous and non-indigenous children in a community setting. Pediatric nephrology (Berlin, Germany) 24(2): 323-31

Meinhardt, U., Ammann, R.A., Fluck, C. et al. (2003) Microalbuminuria in diabetes mellitus - Efficacy of a new screening method in comparison with timed overnight urine collection. Journal of Diabetes and its Complications 17(5): 254-257

Ochigbo, S.O., Udo, J.J., Nlemadi, A.C. et al. (2017) Comparison of the efficacy of serum creatinine and microalbuminuria in early diagnosis of renal injury in asphyxiated infants in calabar, Southern Nigeria. Iranian Journal of Neonatology 8(2): 1-4

Sultana, M N, Majumder, B, Rahman, M J et al. (2018) Dipstick Method versus Spot Urinary Protein Creatinine Ratio for Evaluation of Massive Proteinuria in Childhood Nephrotic Syndrome. Mymensingh medical journal : MMJ 27(2): 369-374

#### 1.1.12.2 Economic evidence

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

# Appendices

## Appendix A – Review protocols

**Review protocol for the accuracy of reagent strips for detecting protein and blood in urine in children and young people**

| ID | Field | Content |
|---|---|---|
| 0. | PROSPERO registration number | CRD42020162554 |
| 1. | Review title | The accuracy of reagent strips for detecting protein and blood in urine in children and young people |
| 2. | Review question | In children and young people, what is the accuracy of reagent strips for detecting protein and blood in urine? |
| 3. | Objective | To evaluate the accuracy of reagent strips at detecting protein- and haematuria in children and young people. |
| 4. | Searches | The following databases will be searched: [Amend if required]<br>• Cochrane Central Register of Controlled Trials (CENTRAL)<br>• Cochrane Database of Systematic Reviews (CDSR)<br>• Embase |

| | | |
|---|---|---|
| | | • MEDLINE<br><br>Searches will be restricted by:<br>• 1995 onwards<br>• English language<br>• Human studies<br>• Children and young people<br><br>The searches will be re-run 6 weeks before final submission of the review and further studies retrieved for inclusion.<br><br>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 the age of 18 years |

| | | |
|---|---|---|
| | | Exclusion:<br>• Children and young people receiving renal replacement therapy (RRT)<br>• Children and young people with acute kidney injury combined with rapidly progressive glomerulonephritis<br>• Children and young people receiving palliative care |
| 7. | Test | Reagent strips for detecting protein, blood or albumin in urine. |
| 8. | Reference standard | For all tests<br>• Mass spectrometry<br><br>For albumin<br>• immunonephelometric methods.<br><br>For protein<br>• turbidimetric or colorimetric assays |

| | | |
|---|---|---|
| | | For haematuria<br>• Phase-contrast microscopy of fresh urinary sediment |
| 9. | Types of study to be included | • Diagnostic cross-sectional studies<br>• Systematic reviews of diagnostic cross-sectional studies |
| 10. | Other exclusion criteria | • non-English language<br>• Abstracts and conference proceedings<br>• Theses<br>• Non-human studies<br>• Studies where a 2x2 table cannot be extracted or derived.<br>• Case control studies |
| 11. | Context | The review will consider the use of reagent strips in any healthcare setting. |

| | | |
|---|---|---|
| 12. | Primary outcomes (critical outcomes) | • Likelihood ratios<br>• Adverse outcomes (for example, test compromised by presence of ascorbic acid in urine) |
| 13. | Secondary outcomes (important outcomes) | • Specificity<br>• Sensitivity<br>• Positive Predictive Value<br>• Negative Predictive Value<br><br>Outcomes will all be converted to likelihood ratios. |

| | | |
|---|---|---|
| 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.<br><br>The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. 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 test and reference standard used; study methodology; recruitment and study completion rates; outcomes and times of measurement and information for assessment of the risk of bias.<br><br>Study investigators may be contacted for missing data where time and resources allow. |
| 15. | Risk of bias (quality) assessment | Risk of bias will be assessed using the QUADAS 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).<br><br>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) will be 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, specific consideration will be given to:<br>• People from black, Asian and other minority ethnic groups<br>• Age under 3. |
| 18. | Type and method of review | ☐ Intervention<br>☒ Diagnostic<br>☐ Prognostic<br>☐ Qualitative<br>☐ Epidemiologic<br>☐ Service Delivery<br>☐ Other (please specify) |
| 19. | Language | English |
| 20. | Country | England |

| | | | | |
|---|---|---|---|---|
| 21. | Anticipated or actual start date | March 2020 | | |
| 22. | Anticipated completion date | December 2020 | | |
| 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**<br>Guideline Updates Team<br><br>**5b Named contact e-mail**<br>GUTprospero@nice.org.uk<br><br>**5e Organisational affiliation of the review**<br>National Institute for Health and Care Excellence (NICE) | | |
| 25. | Review team members | From the Guideline Updates Team:<br>• Mr Chris Carmona<br>• Dr Yolanda Martinez<br>• Mr Rui Maartins<br>• Dr Joshua Pink<br>• 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 |
| 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:<br>• notifying registered stakeholders of publication<br>• publicising the guideline through NICE's newsletter and alerts<br>• 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 | Reagent sticks – urine, proteinuria, albuminuria, haematuria |

| | | | |
|---|---|---|---|
| 33. | Details of existing review of same topic by same authors | None | |
| 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 5: 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 6 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 default values of 2 for LR+ and 0.5 for LR- were used based on Table 5, with the line of no effect as the second clinical decision line in both cases.

**Table 6: 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.<br>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.<br>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.<br>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.<br>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.<br>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.<br>N/A: Inconsistency was marked as not applicable if data on the outcome was only available from one study.<br>Not serious: If the $I^2$ was less than 33.3%, the outcome was not downgraded.<br>Serious: If the $I^2$ was between 33.3% and 66.7%, the outcome was downgraded one level.<br>Very serious: If the $I^2$ was greater than 66.7%, the outcome was downgraded two levels.<br>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.<br>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 7.

**Table 7 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 8.

**Table 8 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.

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# Appendix C Literature search strategies

Accuracy of reagent strips for detecting protein and blood in urine in children and young people with CKD

**Background to the search**

A NICE information specialist conducted the literature searches for the evidence review. The searches were originally run between the 10th to the 19th of February 2020 and updated on the 4th 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 search 1 (CKD population)**

| Databases | Date searched | Version/files | No. retrieved |
|---|---|---|---|
| Cochrane Central Register of Controlled Trials (CENTRAL) | 10th Feb 2020 | Issue 2 of 12, February 2020 | 65 |
| Cochrane Database of Systematic Reviews (CDSR) | 10th Feb 2020 | Issue 2 of 12, February 2020 | 0 |
| Database of Abstracts of Reviews of Effect (DARE) | 10th Feb 2020 | Up to 2015 | 16 |

| | | | |
|---|---|---|---|
| Embase (Ovid) | 10th Feb 2020 | Embase <1974 to 2020 Week 06> | 2328 |
| MEDLINE (Ovid) | 11th Feb 2020 | Ovid MEDLINE(R) <1946 to February 10, 2020> | 635 |
| MEDLINE In-Process (Ovid) | 11th Feb 2020 | Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to February 10, 2020> | 57 |
| MEDLINE Epub Ahead of Print[a] | 11th Feb 2020 | Ovid MEDLINE(R) Epub Ahead of Print <February 10, 2020> | 53 |

**Search strategies:**

Database: Ovid MEDLINE(R) <1946 to February 10, 2020>

Search Strategy:

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1 exp Renal Insufficiency, Chronic/ (112261)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (72306)

3 ((kidney* or renal*) adj1 insufficien*).tw. (21236)

4 ckd*.tw. (22777)

5 ((kidney* or renal*) adj1 fail*).tw. (86254)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (35088)

7 (esrd* or eskd*).tw. (14151)

8 "Chronic Kidney Disease-Mineral and Bone Disorder"/ (3444)

9 or/1-8 (212222)

10 exp Infant/ or Infant Health/ or Infant Welfare/ (1122688)

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. (836467)

12 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (1884908)

13 Minors/ (2556)

14 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (2303530)

15 exp pediatrics/ (56987)

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

16 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (809129)

17 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (1991213)

18 Puberty/ (13168)

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. (412077)

20 Schools/ (36886)

21 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (8704)

22 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (457980)

23 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (3847)

24 or/10-23 (5093050)

25 9 and 24 (46123)

26 "Indicators and Reagents"/ (51841)

27 exp Reagent Kits, Diagnostic/ (19909)

28 reagent*.tw. (83341)

29 (dipstick* or dip-stick*).tw. (3104)

30 (urin* adj3 (test* or strip* or stick*)).tw. (12045)

31 Urinalysis/ (7904)

32 urinalys*.tw. (7179)

33 (diagnos* adj3 (test* or kit*)).tw. (72009)

34 or/26-33 (237233)

35 25 and 34 (758)

36 animals/ not humans/ (4639408)

37 35 not 36 (732)

38 limit 37 to english language (635)

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to February 10, 2020>

Search Strategy:

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1 exp Renal Insufficiency, Chronic/ (0)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (9321)

3 ((kidney* or renal*) adj1 insufficien*).tw. (1092)

4 ckd*.tw. (4447)

5 ((kidney* or renal*) adj1 fail*).tw. (6242)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (4760)

7 (esrd* or eskd*).tw. (1961)

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

9 or/1-8 (18204)

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. (76074)

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. (302432)

15 exp pediatrics/ (0)

16 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (113228)

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. (56890)

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. (65034)

23 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (559)

24 or/10-23 (438341)

25 9 and 24 (3337)

26 "Indicators and Reagents"/ (0)

27 exp Reagent Kits, Diagnostic/ (0)

28 reagent*.tw. (17922)

29 (dipstick* or dip-stick*).tw. (352)

30 (urin* adj3 (test* or strip* or stick*)).tw. (1161)

31 Urinalysis/ (0)

32 urinalys*.tw. (756)

33 (diagnos* adj3 (test* or kit*)).tw. (8660)

34 or/26-33 (28421)

35 25 and 34 (59)

36 animals/ not humans/ (0)

37 35 not 36 (59)

38 limit 37 to english language (57)

Database: Ovid MEDLINE(R) Epub Ahead of Print <February 10, 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. (143)

4 ckd*.tw. (701)

5 ((kidney* or renal*) adj1 fail*).tw. (751)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (689)

7 (esrd* or eskd*).tw. (300)

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

9 or/1-8 (2534)

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. (14161)

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. (48217)

15 exp pediatrics/ (0)

16 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (19895)

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. (12161)

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. (11329)

23 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (102)

24 or/10-23 (71221)

25 9 and 24 (530)

26 "Indicators and Reagents"/ (0)

27 exp Reagent Kits, Diagnostic/ (0)

28 reagent*.tw. (946)

29 (dipstick* or dip-stick*).tw. (51)

30 (urin* adj3 (test* or strip* or stick*)).tw. (199)

31 Urinalysis/ (0)

32 urinalys*.tw. (164)

33 (diagnos* adj3 (test* or kit*)).tw. (2005)

34 or/26-33 (3271)

35 25 and 34 (53)

36 animals/ not humans/ (0)

37 35 not 36 (53)

38 limit 37 to english language (53)

Database: Embase <1974 to 2020 Week 06>

Search Strategy:

---

1 exp kidney failure/ (347908)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (121466)

3 ((kidney* or renal*) adj1 insufficien*).tw. (29887)

4 ckd*.tw. (48701)

5 ((kidney* or renal*) adj1 fail*).tw. (131366)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (57510)

7 (esrd* or eskd*).tw. (26893)

8 or/1-7 (439487)

9 exp juvenile/ or Child Behavior/ or Child Welfare/ or Child Health/ or infant welfare/ or "minor (person)"/ or elementary student/ (3357184)

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. (1181895)

11 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,ad,jw. (3551117)

12 exp pediatrics/ (103541)

13 (pediatric* or paediatric* or peadiatric*).ti,ab,in,ad,jw. (1598303)

14 exp adolescence/ or exp adolescent behavior/ or adolescent health/ or high school student/ or middle school student/ (101886)

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. (641806)

16 school/ or high school/ or kindergarten/ or middle school/ or primary school/ or nursery school/ or day care/ (101356)

17 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jw. (681325)

18 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (7187)

19 or/9-18 (6285274)

20 8 and 19 (86101)

21 urine reagent strip test/ (98)

22 exp test strip/ (4855)

23 urine protein test strip/ (4)

24 reagent*.tw. (132609)

25 (dipstick* or dip-stick*).tw. (5114)

26 (urin* adj3 (test* or strip* or stick*)).tw. (19447)

27 exp urinalysis/ (103604)

28 urinalys*.tw. (13377)

29 (diagnos* adj3 (test* or kit*)).tw. (115370)

30 or/21-29 (366377)

31 20 and 30 (3532)

32 limit 31 to english language (3354)

33 nonhuman/ not human/ (4549751)

34 32 not 33 (3235)

35 limit 34 to (conference abstract or conference paper or "conference review") (907)

36 34 not 35 (2328)

Cochrane Library

| ID | Search | Hits |
|---|---|---|
| #1 | MeSH descriptor: [Renal Insufficiency, Chronic] explode all trees | 6552 |
| #2 | (((chronic* or progressi*) near/1 (renal* or kidney*))):ti,ab,kw | 10433 |
| #3 | (((kidney* or renal*) near/1 insufficien*)):ti,ab,kw | 5332 |
| #4 | (ckd*):ti,ab,kw | 4902 |
| #5 | (((kidney* or renal*) near/1 fail*)):ti,ab,kw | 16700 |
| #6 | (((endstage* or end-stage* or "end stage*") near/1 (renal* or kidney*))):ti,ab,kw | 4594 |
| #7 | ((esrd* or eskd*)):ti,ab,kw | 2098 |
| #8 | MeSH descriptor: [Chronic Kidney Disease-Mineral and Bone Disorder] this term only | 84 |
| #9 | #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 | 26375 |
| #10 | MeSH descriptor: [Infant] explode all trees | 15806 |
| #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 | 87818 |
| #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 | 5066 |
| #15 | MeSH descriptor: [Child] explode all trees | 1215 |
| #16 | MeSH descriptor: [Child Behavior] explode all trees | 2028 |
| #17 | MeSH descriptor: [Child Health] this term only | 88 |
| #18 | MeSH descriptor: [Child Welfare] this term only | 330 |

#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 263836

#21 ((child* or minor or minors or boy* or girl* or kid or kids or young*)):so 10428

#22 MeSH descriptor: [Pediatrics] explode all trees 651

#23 ((pediatric* or paediatric* or peadiatric*)):ti,ab,kw 33804

#24 ((pediatric* or paediatric* or peadiatric*)):so 32074

#25 MeSH descriptor: [Adolescent] this term only 102290

#26 MeSH descriptor: [Adolescent Behavior] this term only 1348

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

#28 MeSH descriptor: [Puberty] this term only 299

#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 140132

#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 3857

#31 MeSH descriptor: [Schools] this term only 1856

#32 MeSH descriptor: [Child Day Care Centers] this term only 223

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

#34 MeSH descriptor: [Schools, Nursery] this term only 38

#35 ((pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*)):ti,ab,kw 96467

#36 ((pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*)):so 1169

#37 (("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*")):ti,ab,kw 14263

#38 {or #10-#37} 415520

#39 #9 and #38 4122

#40 MeSH descriptor: [Indicators and Reagents] this term only 149

#41 MeSH descriptor: [Reagent Kits, Diagnostic] explode all trees 279

#42 (reagent*):ti,ab,kw 1149

#43 (dipstick* or dip-stick*):ti,ab,kw 430

#44 (urin* near/3 (test* or strip* or stick*)):ti,ab,kw 4577

#45 MeSH descriptor: [Urinalysis] this term only 242

#46 urinalys*:ti,ab,kw 4741

#47 (diagnos* near/3 (test* or kit*)):ti,ab,kw 12366

#48 #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 21632

#49 #39 and #48 151

#50 "conference":pt or (clinicaltrials or trialsearch):so 484712

#51 #49 not #50 65 – all CENTRAL

CRD databases

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 Indicators and Reagents 12 Delete

11 MeSH DESCRIPTOR Reagent Kits, Diagnostic EXPLODE ALL TREES 94 Delete

12 (reagent*) 191 Delete

13 (dipstick* or dip-stick*) 60 Delete

14 (urin* near3 (test* or strip* or stick*)) 149 Delete

15 MeSH DESCRIPTOR Urinalysis 71 Delete

16 (urinalys*) 123 Delete

17 (diagnos* near3 (test* or kit*)) 1882 Delete

18 (#10 or #11 or #12 or #13 or #14 or #15 or #16 or #17) 2208 Delete

19 (#9 and #18) 62 Delete

20 (#9 and #18) IN DARE 16 Delete

21 (#9 and #18) IN NHSEED 42 Delete

| | | | |
|---|---|---|---|
| 22 | (#9 and #18) IN HTA | 4 | Delete |

**Cost-effectiveness search 1 (CKD population)**

| Databases | Date searched | Version/files | No. retrieved |
|---|---|---|---|
| MEDLINE (Ovid) | 11th Feb 2020 | Ovid MEDLINE(R) <1946 to February 10, 2020> | 62 |
| MEDLINE in Process (Ovid) | 11th Feb 2020 | Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to February 10, 2020> | 1 |
| MEDLINE epub (Ovid) | 11th Feb 2020 | Ovid MEDLINE(R) Epub Ahead of Print <February 10, 2020> | 2 |
| Embase (Ovid) | 10th Feb 2020 | Embase <1974 to 2020 Week 06> | 165 |
| EconLit (Ovid) | 11th Feb 2020 | Econlit <1886 to January 30, 2020> | 1 |
| NHS Economic Evaluation Database (NHS EED) (legacy database) | 10th Feb 2020 | Up to 2015 | 42 |
| CRD HTA | 10th Feb 2020 | Up to 2018 | 4 |

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 February 10, 2020>

Search Strategy:

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1 exp Renal Insufficiency, Chronic/ (112261)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (72306)

3 ((kidney* or renal*) adj1 insufficien*).tw. (21236)

4 ckd*.tw. (22777)

5 ((kidney* or renal*) adj1 fail*).tw. (86254)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (35088)

7 (esrd* or eskd*).tw. (14151)

8 "Chronic Kidney Disease-Mineral and Bone Disorder"/ (3444)

9 or/1-8 (212222)

10 exp Infant/ or Infant Health/ or Infant Welfare/ (1122688)

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. (836467)

12 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (1884908)

13 Minors/ (2556)

14 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (2303530)

15 exp pediatrics/ (56987)

16 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (809129)

17 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (1991213)

18 Puberty/ (13168)

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. (412077)

20 Schools/ (36886)

21 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (8704)

22 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (457980)

23 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (3847)

24 or/10-23 (5093050)

25 9 and 24 (46123)

26 "Indicators and Reagents"/ (51841)

| | |
|---|---|
| 27 | exp Reagent Kits, Diagnostic/ (19909) |
| 28 | reagent*.tw. (83341) |
| 29 | (dipstick* or dip-stick*).tw. (3104) |
| 30 | (urin* adj3 (test* or strip* or stick*)).tw. (12045) |
| 31 | Urinalysis/ (7904) |
| 32 | urinalys*.tw. (7179) |
| 33 | (diagnos* adj3 (test* or kit*)).tw. (72009) |
| 34 | or/26-33 (237233) |
| 35 | 25 and 34 (758) |
| 36 | animals/ not humans/ (4639408) |
| 37 | 35 not 36 (732) |
| 38 | limit 37 to english language (635) |
| 39 | Economics/ (27129) |
| 40 | exp "Costs and Cost Analysis"/ (232500) |
| 41 | Economics, Dental/ (1910) |
| 42 | exp Economics, Hospital/ (24215) |
| 43 | exp Economics, Medical/ (14162) |
| 44 | Economics, Nursing/ (3996) |
| 45 | Economics, Pharmaceutical/ (2913) |
| 46 | Budgets/ (11222) |
| 47 | exp Models, Economic/ (14702) |
| 48 | Markov Chains/ (13979) |
| 49 | Monte Carlo Method/ (27779) |
| 50 | Decision Trees/ (10895) |
| 51 | econom$.tw. (230853) |
| 52 | cba.tw. (9703) |
| 53 | cea.tw. (20194) |
| 54 | cua.tw. (974) |
| 55 | markov$.tw. (17471) |
| 56 | (monte adj carlo).tw. (29278) |
| 57 | (decision adj3 (tree$ or analys$)).tw. (12880) |

58 (cost or costs or costing$ or costly or costed).tw. (447144)

59 (price$ or pricing$).tw. (32579)

60 budget$.tw. (23156)

61 expenditure$.tw. (48094)

62 (value adj3 (money or monetary)).tw. (2034)

63 (pharmacoeconomic$ or (pharmaco adj economic$)).tw. (3439)

64 or/39-63 (902357)

65 "Quality of Life"/ (188046)

66 quality of life.tw. (221708)

67 "Value of Life"/ (5683)

68 Quality-Adjusted Life Years/ (11815)

69 quality adjusted life.tw. (10390)

70 (qaly$ or qald$ or qale$ or qtime$).tw. (8527)

71 disability adjusted life.tw. (2568)

72 daly$.tw. (2345)

73 Health Status Indicators/ (23201)

74 (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. (21921)

75 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (1293)

76 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (4716)

77 (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)

78 (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)

79 (euroqol or euro qol or eq5d or eq 5d).tw. (8484)

80 (qol or hql or hqol or hrqol).tw. (42323)

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

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

83 utilit$.tw. (166122)

84 (hui or hui1 or hui2 or hui3).tw. (1259)

85 disutili$.tw. (371)

86 rosser.tw. (92)

87 quality of wellbeing.tw. (13)

88 quality of well-being.tw. (378)

89 qwb.tw. (189)

90 willingness to pay.tw. (4247)

91 standard gamble$.tw. (774)

92 time trade off.tw. (1012)

93 time tradeoff.tw. (228)

94 tto.tw. (876)

95 or/65-94 (477612)

96 64 or 95 (1313744)

97 38 and 96 (62)

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to February 10, 2020>

Search Strategy:

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1 exp Renal Insufficiency, Chronic/ (0)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (9321)

3 ((kidney* or renal*) adj1 insufficien*).tw. (1092)

4 ckd*.tw. (4447)

5 ((kidney* or renal*) adj1 fail*).tw. (6242)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (4760)

7 (esrd* or eskd*).tw. (1961)

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

9 or/1-8 (18204)

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. (76074)

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. (302432)

15 exp pediatrics/ (0)

16 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (113228)

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. (56890)

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. (65034)

23 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (559)

24 or/10-23 (438341)

25 9 and 24 (3337)

26 "Indicators and Reagents"/ (0)

27 exp Reagent Kits, Diagnostic/ (0)

28 reagent*.tw. (17922)

29 (dipstick* or dip-stick*).tw. (352)

30 (urin* adj3 (test* or strip* or stick*)).tw. (1161)

31 Urinalysis/ (0)

32 urinalys*.tw. (756)

33 (diagnos* adj3 (test* or kit*)).tw. (8660)

34 or/26-33 (28421)

35 25 and 34 (59)

36 animals/ not humans/ (0)

37 35 not 36 (59)

38 limit 37 to english language (57)

39 Economics/ (0)

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

41 Economics, Dental/ (0)

42 exp Economics, Hospital/ (0)

43 exp Economics, Medical/ (0)

| | |
|---|---|
| 44 | Economics, Nursing/ (0) |
| 45 | Economics, Pharmaceutical/ (0) |
| 46 | Budgets/ (0) |
| 47 | exp Models, Economic/ (0) |
| 48 | Markov Chains/ (0) |
| 49 | Monte Carlo Method/ (0) |
| 50 | Decision Trees/ (0) |
| 51 | econom$.tw. (43282) |
| 52 | cba.tw. (410) |
| 53 | cea.tw. (1829) |
| 54 | cua.tw. (196) |
| 55 | markov$.tw. (5481) |
| 56 | (monte adj carlo).tw. (16541) |
| 57 | (decision adj3 (tree$ or analys$)).tw. (2300) |
| 58 | (cost or costs or costing$ or costly or costed).tw. (92728) |
| 59 | (price$ or pricing$).tw. (5655) |
| 60 | budget$.tw. (4850) |
| 61 | expenditure$.tw. (6210) |
| 62 | (value adj3 (money or monetary)).tw. (345) |
| 63 | (pharmacoeconomic$ or (pharmaco adj economic$)).tw. (517) |
| 64 | or/39-63 (160625) |
| 65 | "Quality of Life"/ (0) |
| 66 | quality of life.tw. (37108) |
| 67 | "Value of Life"/ (0) |
| 68 | Quality-Adjusted Life Years/ (0) |
| 69 | quality adjusted life.tw. (1615) |
| 70 | (qaly$ or qald$ or qale$ or qtime$).tw. (1383) |
| 71 | disability adjusted life.tw. (488) |
| 72 | daly$.tw. (450) |
| 73 | Health Status Indicators/ (0) |

74 (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. (2574)

75 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (746)

76 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (707)

77 (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)

78 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (19)

79 (euroqol or euro qol or eq5d or eq 5d).tw. (1597)

80 (qol or hql or hqol or hrqol).tw. (7123)

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

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

83 utilit$.tw. (30051)

84 (hui or hui1 or hui2 or hui3).tw. (175)

85 disutili$.tw. (71)

86 rosser.tw. (5)

87 quality of wellbeing.tw. (7)

88 quality of well-being.tw. (26)

89 qwb.tw. (11)

90 willingness to pay.tw. (922)

91 standard gamble$.tw. (60)

92 time trade off.tw. (118)

93 time tradeoff.tw. (17)

94 tto.tw. (121)

95 or/65-94 (69425)

96 64 or 95 (220886)

97 38 and 96 (1)

Database: Ovid MEDLINE(R) Epub Ahead of Print <February 10, 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. (143)

4 ckd*.tw. (701)

5 ((kidney* or renal*) adj1 fail*).tw. (751)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (689)

7 (esrd* or eskd*).tw. (300)

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

9 or/1-8 (2534)

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. (14161)

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. (48217)

15 exp pediatrics/ (0)

16 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (19895)

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. (12161)

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. (11329)

23 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (102)

24 or/10-23 (71221)

25 9 and 24 (530)

26 "Indicators and Reagents"/ (0)

27 exp Reagent Kits, Diagnostic/ (0)

28 reagent*.tw. (946)

29 (dipstick* or dip-stick*).tw. (51)

30 (urin* adj3 (test* or strip* or stick*)).tw. (199)

31 Urinalysis/ (0)

32 urinalys*.tw. (164)

33 (diagnos* adj3 (test* or kit*)).tw. (2005)

34 or/26-33 (3271)

35 25 and 34 (53)

36 animals/ not humans/ (0)

37 35 not 36 (53)

38 limit 37 to english language (53)

39 Economics/ (0)

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

41 Economics, Dental/ (0)

42 exp Economics, Hospital/ (0)

43 exp Economics, Medical/ (0)

44 Economics, Nursing/ (0)

45 Economics, Pharmaceutical/ (0)

46 Budgets/ (0)

47 exp Models, Economic/ (0)

48 Markov Chains/ (0)

49 Monte Carlo Method/ (0)

50 Decision Trees/ (0)

51 econom$.tw. (5949)

52 cba.tw. (62)

53 cea.tw. (329)

54 cua.tw. (17)

55 markov$.tw. (725)

56 (monte adj carlo).tw. (1197)

57 (decision adj3 (tree$ or analys$)).tw. (412)

58 (cost or costs or costing$ or costly or costed).tw. (12223)

59 (price$ or pricing$).tw. (869)

60 budget$.tw. (523)

61 expenditure$.tw. (1123)

62 (value adj3 (money or monetary)).tw. (69)

63 (pharmacoeconomic$ or (pharmaco adj economic$)).tw. (47)

64 or/39-63 (20118)

65 "Quality of Life"/ (0)

66 quality of life.tw. (6813)

67 "Value of Life"/ (0)

68 Quality-Adjusted Life Years/ (0)

69 quality adjusted life.tw. (402)

70 (qaly$ or qald$ or qale$ or qtime$).tw. (346)

71 disability adjusted life.tw. (107)

72 daly$.tw. (91)

73 Health Status Indicators/ (0)

74 (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. (455)

75 (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)

76 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (161)

77 (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)

78 (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)

79 (euroqol or euro qol or eq5d or eq 5d).tw. (345)

80 (qol or hql or hqol or hrqol).tw. (1318)

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

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

83 utilit$.tw. (4619)

84 (hui or hui1 or hui2 or hui3).tw. (24)

85 disutili$.tw. (12)

86 rosser.tw. (0)

87 quality of wellbeing.tw. (1)

88 quality of well-being.tw. (6)

89 qwb.tw. (4)

90 willingness to pay.tw. (159)

91 standard gamble$.tw. (8)

92 time trade off.tw. (18)

93 time tradeoff.tw. (3)

94 tto.tw. (19)

95 or/65-94 (11712)

96 64 or 95 (30063)

97 38 and 96 (2)

Database: Embase <1974 to 2020 Week 06>

Search Strategy:

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1 exp kidney failure/ (347908)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (121466)

3 ((kidney* or renal*) adj1 insufficien*).tw. (29887)

4 ckd*.tw. (48701)

5 ((kidney* or renal*) adj1 fail*).tw. (131366)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (57510)

7 (esrd* or eskd*).tw. (26893)

8 or/1-7 (439487)

9 exp juvenile/ or Child Behavior/ or Child Welfare/ or Child Health/ or infant welfare/ or "minor (person)"/ or elementary student/ (3357184)

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. (1181895)

11 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,ad,jw. (3551117)

12 exp pediatrics/ (103541)

13 (pediatric* or paediatric* or peadiatric*).ti,ab,in,ad,jw. (1598303)

14 exp adolescence/ or exp adolescent behavior/ or adolescent health/ or high school student/ or middle school student/ (101886)

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. (641806)

16 school/ or high school/ or kindergarten/ or middle school/ or primary school/ or nursery school/ or day care/ (101356)

17 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jw. (681325)

18 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (7187)

19 or/9-18 (6285274)

20 8 and 19 (86101)

21 urine reagent strip test/ (98)

22 exp test strip/ (4855)

23 urine protein test strip/ (4)

24 reagent*.tw. (132609)

25 (dipstick* or dip-stick*).tw. (5114)

26 (urin* adj3 (test* or strip* or stick*)).tw. (19447)

27 exp urinalysis/ (103604)

28 urinalys*.tw. (13377)

29 (diagnos* adj3 (test* or kit*)).tw. (115370)

30 or/21-29 (366377)

31 20 and 30 (3532)

32 limit 31 to english language (3354)

33 nonhuman/ not human/ (4549751)

34 32 not 33 (3235)

35 limit 34 to (conference abstract or conference paper or "conference review") (907)

36 34 not 35 (2328)

37 exp Health Economics/ (826913)

38 exp "Health Care Cost"/ (284997)

39 exp Pharmacoeconomics/ (199083)

40 Monte Carlo Method/ (39039)

41 Decision Tree/ (12231)

42 econom$.tw. (354598)

43 cba.tw. (12582)

44 cea.tw. (33858)

45 cua.tw. (1449)

46 markov$.tw. (29370)

47 (monte adj carlo).tw. (46934)

48 (decision adj3 (tree$ or analys$)).tw. (22306)

49 (cost or costs or costing$ or costly or costed).tw. (744687)

50 (price$ or pricing$).tw. (55554)

51 budget$.tw. (37480)

52 expenditure$.tw. (72454)

53 (value adj3 (money or monetary)).tw. (3355)

54 (pharmacoeconomic$ or (pharmaco adj economic$)).tw. (8504)

55 or/37-54 (1705739)

56 "Quality of Life"/ (452320)

57 Quality Adjusted Life Year/ (25666)

58 Quality of Life Index/ (2720)

59 Short Form 36/ (27687)

60 Health Status/ (124338)

61 quality of life.tw. (421357)

62 quality adjusted life.tw. (18959)

63 (qaly$ or qald$ or qale$ or qtime$).tw. (19431)

64 disability adjusted life.tw. (3848)

65 daly$.tw. (3786)

66 (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. (40294)

67 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (2341)

68 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (9080)

69 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. (57)

70 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (441)

71 (euroqol or euro qol or eq5d or eq 5d).tw. (19492)

72 (qol or hql or hqol or hrqol).tw. (92843)

73 (hye or hyes).tw. (131)

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

75 utilit$.tw. (279093)

76 (hui or hui1 or hui2 or hui3).tw. (2197)

77 disutili$.tw. (896)

78 rosser.tw. (119)

79 quality of wellbeing.tw. (42)

80 quality of well-being.tw. (469)

81 qwb.tw. (244)

82 willingness to pay.tw. (8386)

83 standard gamble$.tw. (1088)

84 time trade off.tw. (1672)

85 time tradeoff.tw. (288)

86 tto.tw. (1618)

87 or/56-86 (953278)

88 55 or 87 (2507522)

89 36 and 88 (165)

Database: Econlit <1886 to January 30, 2020>

Search Strategy:

---

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 ["Indicators and Reagents"/] (0)

11 [exp Reagent Kits, Diagnostic/] (0)

12 reagent*.tw. (5)

13 (dipstick* or dip-stick*).tw. (0)

14 (urin* adj3 (test* or strip* or stick*)).tw. (13)

15 [Urinalysis/] (0)

16 urinalys*.tw. (5)

17 (diagnos* adj3 (test* or kit*)).tw. (576)

18 or/10-17 (597)

19 9 and 18 (1)

Database: Econlit <1886 to January 30, 2020>

Search Strategy:

---

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 infan*.mp,so. (2786)

11 (baby or babies).mp,so. (1254)

12 minor.mp,so. (3045)

13 minors*.mp,so. (107)

14 boy.mp,so. (161)

15 boys.mp,so. (1551)

16 boyfriend*.mp,so. (9)

17 boyhood.mp,so. (5)

18 girl*.mp,so. (2286)

19 kid.mp,so. (57)

20 kids.mp,so. (311)

21 child*.mp,so. (37654)

22 adolescen*.mp,so. (2132)

23 juvenil*.mp,so. (388)

24 youth*.mp,so. (26679)

25 teen*.mp,so. (1448)

26 under*age*.mp,so. (119)

27 pubescen*.mp,so. (6)

28 [exp pediatrics/] (0)

29 pediatric*.mp,so. (123)

30 paediatric*.mp,so. (35)

31 peadiatric*.mp,so. (0)

32 school*.mp,so. (53109)

33 young*.mp,so. (16636)

34 (("one" or "two" or "three" or "four" or "five" or "six" or "seven" or "eight" or "nine" or "ten" or "eleven" or "twelve" or "thirteen" or "fourteen" or "fifteen" or "sixteen" or "seventeen" or "eighteen") adj2 (year* or age*)).ti,ab. (24835)

35 (("1" or "2" or "3" or "4" or "5" or "6" or "7" or "8" or "9" or "10" or "11" or "12" or "13" or "14" or "15" or "16" or "17" or "18") adj2 (year* or age*)).ti,ab. (15525)

36 ("under 18" or "under eighteen*").ti,ab. (28)

37 or/10-36 (131702)

38 9 and 37 (11)

CRD databases

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 Indicators and Reagents | 12 | Delete |
| 11 | MeSH DESCRIPTOR Reagent Kits, Diagnostic EXPLODE ALL TREES | 94 | Delete |
| 12 | (reagent*) | 191 | Delete |
| 13 | (dipstick* or dip-stick*) | 60 | Delete |
| 14 | (urin* near3 (test* or strip* or stick*)) | 149 | Delete |
| 15 | MeSH DESCRIPTOR Urinalysis | 71 | Delete |
| 16 | (urinalys*) | 123 | Delete |
| 17 | (diagnos* near3 (test* or kit*)) | 1882 | Delete |
| 18 | (#10 or #11 or #12 or #13 or #14 or #15 or #16 or #17) | 2208 | Delete |
| 19 | (#9 and #18) | 62 | Delete |
| 20 | (#9 and #18) IN DARE | 16 | Delete |
| 21 | (#9 and #18) IN NHSEED | 42 | Delete |
| 22 | (#9 and #18) IN HTA | 4 | Delete |

**Clinical search 2 (all populations)**

| Databases | Date searched | Version/files | No. retrieved |
|---|---|---|---|
| Cochrane Central Register of Controlled Trials (CENTRAL) | 19th Feb 2020 | Issue 2 of 12, February 2020 | 218 |
| Cochrane Database of Systematic Reviews (CDSR) | 19th Feb 2020 | Issue 2 of 12, February 2020 | 11 |
| Database of Abstracts of Reviews of Effect (DARE) | 19th Feb 2020 | Up to 2015 | 89 |
| Embase (Ovid) | 19th Feb 2020 | Embase <1974 to 2020 Week 07> | 4536 |

| | | | |
|---|---|---|---|
| MEDLINE (Ovid) | 19th Feb 2020 | Ovid MEDLINE(R) <1946 to February 18, 2020> | 2347 |
| MEDLINE In-Process (Ovid) | 19th Feb 2020 | Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to February 18, 2020> | 105 |
| MEDLINE Epub Ahead of Print[b] | 19th Feb 2020 | Ovid MEDLINE(R) Epub Ahead of Print <February 18, 2020> | 26 |

**Search strategies**

Database: Ovid MEDLINE(R) <1946 to February 18, 2020>

Search Strategy:

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1 exp Infant/ or Infant Health/ or Infant Welfare/ (1122000)

2 (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. (836017)

3 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (1884280)

4 Minors/ (2555)

5 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (2302514)

6 exp pediatrics/ (56966)

7 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (808391)

8 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (1990829)

9 Puberty/ (13151)

10 (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. (411930)

11 Schools/ (36904)

12 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (7121)

13 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (458160)

14 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (3848)

15 or/1-14 (5090977)

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

16 (dipstick* or dip-stick*).tw. (3100)

17 (urin* adj3 (test* or strip* or stick*)).tw. (12033)

18 Urinalysis/ (7897)

19 urinalys*.tw. (7174)

20 or/16-19 (26215)

21 "Indicators and Reagents"/ (51785)

22 exp Reagent Kits, Diagnostic/ (19904)

23 reagent*.tw. (83302)

24 (diagnos* adj3 (test* or kit*)).tw. (71975)

25 or/21-24 (213725)

26 Urine/ (37030)

27 exp Proteinuria/ (38647)

28 Hematuria/ (11800)

29 (urin* or proteinur* or albuminur* or hemoglobinur* or haemoglobinur* or hematur* or haematur*).tw. (466530)

30 or/26-29 (493890)

31 25 and 30 (9448)

32 20 or 31 (33235)

33 15 and 32 (9440)

34 (sensitiv: or predictive value:).mp. or accurac:.tw. (1842609)

35 33 and 34 (2592)

36 animals/ not humans/ (4636390)

37 35 not 36 (2535)

38 limit 37 to english language (2347)

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to February 18, 2020>

Search Strategy:

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

2 (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. (77789)

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

4 Minors/ (0)

5 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (308115)

6 exp pediatrics/ (0)

7 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (115768)

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

9 Puberty/ (0)

10 (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. (58257)

11 Schools/ (0)

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

13 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (66085)

14 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (580)

15 or/1-14 (446380)

16 (dipstick* or dip-stick*).tw. (359)

17 (urin* adj3 (test* or strip* or stick*)).tw. (1184)

18 Urinalysis/ (0)

19 urinalys*.tw. (774)

20 or/16-19 (2111)

21 "Indicators and Reagents"/ (0)

22 exp Reagent Kits, Diagnostic/ (0)

23 reagent*.tw. (18062)

24 (diagnos* adj3 (test* or kit*)).tw. (8805)

25 or/21-24 (26794)

26 Urine/ (0)

27 exp Proteinuria/ (0)

28 Hematuria/ (0)

29 (urin* or proteinur* or albuminur* or hemoglobinur* or haemoglobinur* or hematur* or haematur*).tw. (40148)

30 or/26-29 (40148)

31 25 and 30 (531)

32 20 or 31 (2513)

33 15 and 32 (631)

34 (sensitiv: or predictive value:).mp. or accurac:.tw. (224335)

35 33 and 34 (105)

36 animals/ not humans/ (0)

37 35 not 36 (105)

38 limit 37 to english language (105)

Database: Ovid MEDLINE(R) Epub Ahead of Print <February 18, 2020>

Search Strategy:

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

2 (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. (14110)

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

4 Minors/ (0)

5 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (48388)

6 exp pediatrics/ (0)

7 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (19702)

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

9 Puberty/ (0)

10 (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. (12109)

11 Schools/ (0)

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

13 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (11371)

14 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (95)

15 or/1-14 (71103)

16 (dipstick* or dip-stick*).tw. (50)

17 (urin* adj3 (test* or strip* or stick*)).tw. (198)

18 Urinalysis/ (0)

19 urinalys*.tw. (164)

20 or/16-19 (367)

21 "Indicators and Reagents"/ (0)

22 exp Reagent Kits, Diagnostic/ (0)

23 reagent*.tw. (966)

24 (diagnos* adj3 (test* or kit*)).tw. (2011)

25 or/21-24 (2967)

26 Urine/ (0)

27 exp Proteinuria/ (0)

28 Hematuria/ (0)

29 (urin* or proteinur* or albuminur* or hemoglobinur* or haemoglobinur* or hematur* or haematur*).tw. (5297)

30 or/26-29 (5297)

31 25 and 30 (200)

32 20 or 31 (522)

33 15 and 32 (231)

34 (sensitiv: or predictive value:).mp. or accurac:.tw. (25464)

35 33 and 34 (26)

36 animals/ not humans/ (0)

37 35 not 36 (26)

38 limit 37 to english language (26)

Database: Embase <1974 to 2020 Week 07>

Search Strategy:

---

1 exp juvenile/ or Child Behavior/ or Child Welfare/ or Child Health/ or infant welfare/ or "minor (person)"/ or elementary student/ (3361088)

2 (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. (1183285)

3 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,ad,jw. (3556039)

4 exp pediatrics/ (103667)

5 (pediatric* or paediatric* or peadiatric*).ti,ab,in,ad,jw. (1600432)

6 exp adolescence/ or exp adolescent behavior/ or adolescent health/ or high school student/ or middle school student/ (102013)

7 (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. (642779)

8 school/ or high school/ or kindergarten/ or middle school/ or primary school/ or nursery school/ or day care/ (101477)

9 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jw. (682301)

10 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (7203)

11 or/1-10 (6293316)

12 (dipstick* or dip-stick*).tw. (5118)

13 (urin* adj3 (test* or strip* or stick*)).tw. (19479)

14 exp urinalysis/ (103746)

15 urinalys*.tw. (13406)

16 or/12-15 (121127)

17 urine reagent strip test/ (99)

18 exp test strip/ (4863)

19 urine protein test strip/ (4)

20 reagent*.tw. (132741)

21 (diagnos* adj3 (test* or kit*)).tw. (115608)

22 or/17-21 (251173)

23 urine/ (110885)

24 protein urine level/ (17914)

25 exp proteinuria/ (96970)

26 hematuria/ (44246)

27 hemoglobinuria/ (2081)

28 (urin* or proteinur* or albuminur* or hemoglobinur* or haemoglobinur* or hematur* or haematur*).tw. (669315)

29 or/23-28 (738940)

30 22 and 29 (10960)

31 16 or 30 (127399)

32 11 and 31 (35990)

33 nonhuman/ not human/ (4553644)

34 32 not 33 (34757)

35 limit 34 to english language (32477)

36 limit 35 to (books or chapter or conference abstract or conference paper or "conference review" or letter or note or tombstone) (8359)

37 35 not 36 (24118)

38 (sensitiv: or predictive value:).mp. or accurac:.tw. (2501408)

39 37 and 38 (4536)

Cochrane Library

| ID | Search | Hits |
|---|---|---|
| #1 | MeSH descriptor: [Infant] explode all trees | 15806 |
| #2 | MeSH descriptor: [Infant Health] this term only | 45 |
| #3 | MeSH descriptor: [Infant Welfare] this term only | 82 |
| #4 | ((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 | 87823 |
| #5 | ((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 | 5066 |
| #6 | MeSH descriptor: [Child] explode all trees | 1215 |
| #7 | MeSH descriptor: [Child Behavior] explode all trees | 2028 |
| #8 | MeSH descriptor: [Child Health] this term only | 88 |
| #9 | MeSH descriptor: [Child Welfare] this term only | 330 |
| #10 | MeSH descriptor: [Minors] this term only | 8 |
| #11 | ((child* or minor or minors or boy* or girl* or kid or kids or young*)):ti,ab,kw | 263838 |
| #12 | ((child* or minor or minors or boy* or girl* or kid or kids or young*)):so | 10428 |
| #13 | MeSH descriptor: [Pediatrics] explode all trees | 651 |
| #14 | ((pediatric* or paediatric* or peadiatric*)):ti,ab,kw | 33803 |
| #15 | ((pediatric* or paediatric* or peadiatric*)):so | 32074 |
| #16 | MeSH descriptor: [Adolescent] this term only | 102290 |
| #17 | MeSH descriptor: [Adolescent Behavior] this term only | 1348 |
| #18 | MeSH descriptor: [Adolescent Health] this term only | 23 |
| #19 | MeSH descriptor: [Puberty] this term only | 299 |

#20 ((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 140133

#21 ((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 3857

#22 MeSH descriptor: [Schools] this term only 1856

#23 MeSH descriptor: [Child Day Care Centers] this term only 223

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

#25 MeSH descriptor: [Schools, Nursery] this term only 38

#26 ((pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*)):ti,ab,kw 96467

#27 ((pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*)):so 1169

#28 (("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*")):ti,ab,kw 14263

#29 {or #1-#28} 415525

#30 (dipstick* or dip-stick*):ti,ab,kw 430

#31 (urin* near/3 (test* or strip* or stick*)):ti,ab,kw 4577

#32 MeSH descriptor: [Urinalysis] this term only 242

#33 urinalys*:ti,ab,kw 4742

#34 #30 or #31 or #32 or #33 8714

#35 MeSH descriptor: [Indicators and Reagents] this term only 149

#36 MeSH descriptor: [Reagent Kits, Diagnostic] explode all trees 279

#37 reagent*:ti,ab,kw 1149

#38 (diagnos* near/3 (test* or kit*)):ti,ab,kw 12365

#39 {or #35-#38} 13246

#40 MeSH descriptor: [Urine] this term only 639

#41 MeSH descriptor: [Proteinuria] explode all trees 2247

#42 MeSH descriptor: [Hematuria] this term only 181

#43 (urin* or proteinur* or albuminur* or hemoglobinur* or haemoglobinur* or hematur* or haematur*):ti,ab,kw 74428

#44 {or #40-#43} 74428

#45 #39 and #44 780

#46 #34 or #45 9187

#47 #29 and #46 3414

#48 "conference":pt or (clinicaltrials or trialsearch):so 484712

#49 #47 not #48 1373

#50 (sensitiv* or "predictive value*" or accurac*):ti,ab,kw 100505

#51 MeSH descriptor: [Sensitivity and Specificity] explode all trees 16323

#52 #50 or #51 100989

#53 #49 and #52 229 (11 CDSR, 218 CENTRAL)

CRD databases

1 (dipstick* or dip-stick*) 60 Delete

2 (urin* near3 (test* or strip* or stick*)) 149 Delete

3 (MeSH DESCRIPTOR Urinalysis) 71 Delete

4 (urinalys*) 123 Delete

5 (#1 or #2 or #3 or #4) 263 Delete

6 (MeSH DESCRIPTOR Indicators and Reagents) 12 Delete

7 (MeSH DESCRIPTOR Reagent Kits, Diagnostic EXPLODE ALL TREES) 94 Delete

8 (reagent*) 191 Delete

9 ((diagnos* near3 (test* or kit*)) ) 1882 Delete

10 (#6 or #7 or #8 or #9) 2017 Delete

11 MeSH DESCRIPTOR Urine 39 Delete

12 MeSH DESCRIPTOR Proteinuria EXPLODE ALL TREES 145 Delete

13 MeSH DESCRIPTOR Hematuria 26 Delete

14 (urin* or proteinur* or albuminur* or hemoglobinur* or haemoglobinur* or hematur* or haematur*) 2424 Delete

15 (#11 or #12 or #13 or #14) 2424 Delete

16 (#10 and #15) 143 Delete

17 (#5 or #16) 337 Delete

18 (sensitiv* or "predictive value*" or accurac*) 17726 Delete

19 MeSH DESCRIPTOR Sensitivity and Specificity EXPLODE ALL TREES 4223 Delete

| | | | |
|---|---|---|---|
| 20 | (#18 or #19) | 17802 | Delete |
| 21 | (#17 and #20) | 252 | Delete |
| 22 | (#17 and #20) IN DARE | 89 | Delete |

**Cost-effectiveness search 2 (all populations)**

| Databases | Date searched | Version/files | No. retrieved |
|---|---|---|---|
| MEDLINE (Ovid) | 19th Feb 2020 | Ovid MEDLINE(R) <1946 to February 18, 2020> | 777 |
| MEDLINE in Process (Ovid) | 19th Feb 2019 | Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to February 18, 2020> | 61 |
| MEDLINE epub (Ovid) | 19th Feb 2020 | Ovid MEDLINE(R) Epub Ahead of Print <February 18, 2020> | 17 |
| Embase (Ovid) | 19th Feb 2020 | Embase <1974 to 2020 Week 07> | 1817 |
| EconLit (Ovid) | 19th Feb 2020 | Econlit <1886 to February 13, 2020> | 4 |
| NHS Economic Evaluation Database (NHS EED) (legacy database) | 19th Feb 2020 | Up to 2015 | 154 |
| CRD HTA | 19th Feb 2020 | Up to 2018 | 58 |

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 February 18, 2020>

Search Strategy:

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1 exp Infant/ or Infant Health/ or Infant Welfare/ (1122000)

2 (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. (836017)

3 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (1884280)

4 Minors/ (2555)

5 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (2302514)

6 exp pediatrics/ (56966)

7 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (808391)

8 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (1990829)

9 Puberty/ (13151)

10 (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. (411930)

11 Schools/ (36904)

12 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (7121)

13 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (458160)

14 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (3848)

15 or/1-14 (5090977)

16 (dipstick* or dip-stick*).tw. (3100)

17 (urin* adj3 (test* or strip* or stick*)).tw. (12033)

18 Urinalysis/ (7897)

19 urinalys*.tw. (7174)

20 or/16-19 (26215)

21 "Indicators and Reagents"/ (51785)

22 exp Reagent Kits, Diagnostic/ (19904)

23 reagent*.tw. (83302)

24 (diagnos* adj3 (test* or kit*)).tw. (71975)

25 or/21-24 (213725)

26 Urine/ (37030)

27 exp Proteinuria/ (38647)

28 Hematuria/ (11800)

29 (urin* or proteinur* or albuminur* or hemoglobinur* or haemoglobinur* or hematur* or haematur*).tw. (466530)

30 or/26-29 (493890)

31 25 and 30 (9448)

32 20 or 31 (33235)

33 15 and 32 (9440)

34 Economics/ (27130)

35 exp "Costs and Cost Analysis"/ (232484)

36 Economics, Dental/ (1910)

37 exp Economics, Hospital/ (24227)

38 exp Economics, Medical/ (14163)

39 Economics, Nursing/ (3997)

40 Economics, Pharmaceutical/ (2913)

41 Budgets/ (11227)

42 exp Models, Economic/ (14702)

43 Markov Chains/ (13967)

44 Monte Carlo Method/ (27786)

45 Decision Trees/ (10897)

46 econom$.tw. (230947)

47 cba.tw. (9692)

48 cea.tw. (20186)

49 cua.tw. (973)

50 markov$.tw. (17455)

51 (monte adj carlo).tw. (29279)

52 (decision adj3 (tree$ or analys$)).tw. (12883)

53 (cost or costs or costing$ or costly or costed).tw. (447148)

54 (price$ or pricing$).tw. (32579)

55 budget$.tw. (23158)

56 expenditure$.tw. (48065)

57 (value adj3 (money or monetary)).tw. (2036)

58 (pharmacoeconomic$ or (pharmaco adj economic$)).tw. (3440)

59 or/34-58 (902423)

60 "Quality of Life"/ (188069)

61 quality of life.tw. (221707)

62 "Value of Life"/ (5682)

63 Quality-Adjusted Life Years/ (11787)

64 quality adjusted life.tw. (10366)

65 (qaly$ or qald$ or qale$ or qtime$).tw. (8514)

66 disability adjusted life.tw. (2559)

67 daly$.tw. (2338)

68 Health Status Indicators/ (23201)

69 (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. (21936)

70 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (1293)

71 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (4716)

72 (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)

73 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (376)

74 (euroqol or euro qol or eq5d or eq 5d).tw. (8491)

75 (qol or hql or hqol or hrqol).tw. (42317)

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

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

78 utilit$.tw. (166051)

79 (hui or hui1 or hui2 or hui3).tw. (1259)

80 disutili$.tw. (371)

81 rosser.tw. (92)

82 quality of wellbeing.tw. (13)

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

84 qwb.tw. (188)

85 willingness to pay.tw. (4250)

86 standard gamble$.tw. (773)

87 time trade off.tw. (1012)

88 time tradeoff.tw. (228)

89 tto.tw. (875)

90 or/60-89 (477513)

91 59 or 90 (1313739)

92 33 and 91 (867)

93 limit 92 to english language (792)

94 animals/ not humans/ (4636390)

95 93 not 94 (777)

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to February 18, 2020>

Search Strategy:

---

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

2 (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. (77789)

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

4 Minors/ (0)

5 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (308115)

6 exp pediatrics/ (0)

7 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (115768)

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

9 Puberty/ (0)

10 (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. (58257)

11 Schools/ (0)

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

13 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (66085)

14 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (580)

15 or/1-14 (446380)

16 (dipstick* or dip-stick*).tw. (359)

17 (urin* adj3 (test* or strip* or stick*)).tw. (1184)

18 Urinalysis/ (0)

19 urinalys*.tw. (774)

20 or/16-19 (2111)

21 "Indicators and Reagents"/ (0)

22 exp Reagent Kits, Diagnostic/ (0)

23 reagent*.tw. (18062)

24 (diagnos* adj3 (test* or kit*)).tw. (8805)

25 or/21-24 (26794)

26 Urine/ (0)

27 exp Proteinuria/ (0)

28 Hematuria/ (0)

29 (urin* or proteinur* or albuminur* or hemoglobinur* or haemoglobinur* or hematur* or haematur*).tw. (40148)

30 or/26-29 (40148)

31 25 and 30 (531)

32 20 or 31 (2513)

33 15 and 32 (631)

34 Economics/ (0)

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

36 Economics, Dental/ (0)

37 exp Economics, Hospital/ (0)

38 exp Economics, Medical/ (0)

39 Economics, Nursing/ (0)

40 Economics, Pharmaceutical/ (0)

41 Budgets/ (0)

42 exp Models, Economic/ (0)

43 Markov Chains/ (0)

44 Monte Carlo Method/ (0)

45 Decision Trees/ (0)

46 econom$.tw. (43819)

47 cba.tw. (422)

48 cea.tw. (1886)

49 cua.tw. (200)

50 markov$.tw. (5535)

51 (monte adj carlo).tw. (16651)

52 (decision adj3 (tree$ or analys$)).tw. (2361)

53 (cost or costs or costing$ or costly or costed).tw. (93652)

54 (price$ or pricing$).tw. (5628)

55 budget$.tw. (4818)

56 expenditure$.tw. (6297)

57 (value adj3 (money or monetary)).tw. (347)

58 (pharmacoeconomic$ or (pharmaco adj economic$)).tw. (486)

59 or/34-58 (162065)

60 "Quality of Life"/ (0)

61 quality of life.tw. (38049)

62 "Value of Life"/ (0)

63 Quality-Adjusted Life Years/ (0)

64 quality adjusted life.tw. (1654)

65 (qaly$ or qald$ or qale$ or qtime$).tw. (1404)

66 disability adjusted life.tw. (506)

67 daly$.tw. (463)

68 Health Status Indicators/ (0)

69 (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. (2653)

70 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (748)

71 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (740)

72 (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)

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

74 (euroqol or euro qol or eq5d or eq 5d).tw. (1619)

75 (qol or hql or hqol or hrqol).tw. (7342)

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

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

78 utilit$.tw. (30583)

79 (hui or hui1 or hui2 or hui3).tw. (181)

80 disutili$.tw. (69)

81 rosser.tw. (5)

82 quality of wellbeing.tw. (7)

83 quality of well-being.tw. (28)

84 qwb.tw. (14)

85 willingness to pay.tw. (937)

86 standard gamble$.tw. (61)

87 time trade off.tw. (116)

88 time tradeoff.tw. (17)

89 tto.tw. (123)

90 or/60-89 (70909)

91 59 or 90 (223649)

92 33 and 91 (63)

93 limit 92 to english language (61)

94 animals/ not humans/ (0)

95 93 not 94 (61)

Database: Ovid MEDLINE(R) Epub Ahead of Print <February 18, 2020>

Search Strategy:

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

2 (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. (14110)

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

4 Minors/ (0)

5 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (48388)

6 exp pediatrics/ (0)

7 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (19702)

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

9 Puberty/ (0)

10 (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. (12109)

11 Schools/ (0)

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

13 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (11371)

14 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (95)

15 or/1-14 (71103)

16 (dipstick* or dip-stick*).tw. (50)

17 (urin* adj3 (test* or strip* or stick*)).tw. (198)

18 Urinalysis/ (0)

19 urinalys*.tw. (164)

20 or/16-19 (367)

21 "Indicators and Reagents"/ (0)

22 exp Reagent Kits, Diagnostic/ (0)

23 reagent*.tw. (966)

24 (diagnos* adj3 (test* or kit*)).tw. (2011)

25 or/21-24 (2967)

26 Urine/ (0)

27 exp Proteinuria/ (0)

28 Hematuria/ (0)

29 (urin* or proteinur* or albuminur* or hemoglobinur* or haemoglobinur* or hematur* or haematur*).tw. (5297)

30 or/26-29 (5297)

31 25 and 30 (200)

32 20 or 31 (522)

33 15 and 32 (231)

34 Economics/ (0)

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

36 Economics, Dental/ (0)

37 exp Economics, Hospital/ (0)

38 exp Economics, Medical/ (0)

39 Economics, Nursing/ (0)

40 Economics, Pharmaceutical/ (0)

41 Budgets/ (0)

42 exp Models, Economic/ (0)

43 Markov Chains/ (0)

44 Monte Carlo Method/ (0)

45 Decision Trees/ (0)

46 econom$.tw. (5961)

47 cba.tw. (62)

48 cea.tw. (327)

49 cua.tw. (16)

50 markov$.tw. (720)

51 (monte adj carlo).tw. (1166)

52 (decision adj3 (tree$ or analys$)).tw. (401)

53 (cost or costs or costing$ or costly or costed).tw. (12264)

54 (price$ or pricing$).tw. (882)

55 budget$.tw. (535)

56 expenditure$.tw. (1118)

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

58 (pharmacoeconomic$ or (pharmaco adj economic$)).tw. (48)

59 or/34-58 (20109)

60 "Quality of Life"/ (0)

61 quality of life.tw. (6826)

62 "Value of Life"/ (0)

63 Quality-Adjusted Life Years/ (0)

64 quality adjusted life.tw. (402)

65 (qaly$ or qald$ or qale$ or qtime$).tw. (342)

66 disability adjusted life.tw. (111)

67 daly$.tw. (94)

68 Health Status Indicators/ (0)

69 (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. (457)

70 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (43)

71 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (169)

72 (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)

73 (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)

74 (euroqol or euro qol or eq5d or eq 5d).tw. (348)

75 (qol or hql or hqol or hrqol).tw. (1342)

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

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

78 utilit$.tw. (4582)

79 (hui or hui1 or hui2 or hui3).tw. (21)

80 disutili$.tw. (12)

81 rosser.tw. (0)

82 quality of wellbeing.tw. (1)

83 quality of well-being.tw. (6)

84 qwb.tw. (3)

85 willingness to pay.tw. (163)

86 standard gamble$.tw. (8)

87 time trade off.tw. (18)

88 time tradeoff.tw. (3)

89 tto.tw. (19)

90 or/60-89 (11693)

91 59 or 90 (30040)

92 33 and 91 (17)

93 limit 92 to english language (17)

94 animals/ not humans/ (0)

95 93 not 94 (17)

Database: Embase <1974 to 2020 Week 07>

Search Strategy:

---

1 exp juvenile/ or Child Behavior/ or Child Welfare/ or Child Health/ or infant welfare/ or "minor (person)"/ or elementary student/ (3361088)

2 (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. (1183285)

3 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,ad,jw. (3556039)

4 exp pediatrics/ (103667)

5 (pediatric* or paediatric* or peadiatric*).ti,ab,in,ad,jw. (1600432)

6 exp adolescence/ or exp adolescent behavior/ or adolescent health/ or high school student/ or middle school student/ (102013)

7 (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. (642779)

8 school/ or high school/ or kindergarten/ or middle school/ or primary school/ or nursery school/ or day care/ (101477)

9 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jw. (682301)

10 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (7203)

11 or/1-10 (6293316)

12 (dipstick* or dip-stick*).tw. (5118)

13 (urin* adj3 (test* or strip* or stick*)).tw. (19479)

14 exp urinalysis/ (103746)

15 urinalys*.tw. (13406)

16 or/12-15 (121127)

17 urine reagent strip test/ (99)

18 exp test strip/ (4863)

19 urine protein test strip/ (4)

20 reagent*.tw. (132741)

21 (diagnos* adj3 (test* or kit*)).tw. (115608)

22 or/17-21 (251173)

23 urine/ (110885)

24 protein urine level/ (17914)

25 exp proteinuria/ (96970)

26 hematuria/ (44246)

27 hemoglobinuria/ (2081)

28 (urin* or proteinur* or albuminur* or hemoglobinur* or haemoglobinur* or hematur* or haematur*).tw. (669315)

29 or/23-28 (738940)

30 22 and 29 (10960)

31 16 or 30 (127399)

32 11 and 31 (35990)

33 nonhuman/ not human/ (4553644)

34 32 not 33 (34757)

35 limit 34 to english language (32477)

36 limit 35 to (books or chapter or conference abstract or conference paper or "conference review" or letter or note or tombstone) (8359)

37 35 not 36 (24118)

38 exp Health Economics/ (827822)

39 exp "Health Care Cost"/ (285299)

40 exp Pharmacoeconomics/ (199247)

41 Monte Carlo Method/ (39106)

42 Decision Tree/ (12263)

43 econom$.tw. (355227)

44 cba.tw. (12594)

45 cea.tw. (33941)

46 cua.tw. (1450)

47 markov$.tw. (29412)

48 (monte adj carlo).tw. (47001)

49 (decision adj3 (tree$ or analys$)).tw. (22352)

50 (cost or costs or costing$ or costly or costed).tw. (746071)

51 (price$ or pricing$).tw. (55636)

52 budget$.tw. (37532)

53 expenditure$.tw. (72562)

54 (value adj3 (money or monetary)).tw. (3358)

55 (pharmacoeconomic$ or (pharmaco adj economic$)).tw. (8507)

56 or/38-55 (1708393)

57 "Quality of Life"/ (453173)

58 Quality Adjusted Life Year/ (25711)

59 Quality of Life Index/ (2722)

60 Short Form 36/ (27734)

61 Health Status/ (124456)

62 quality of life.tw. (422214)

63 quality adjusted life.tw. (18994)

64 (qaly$ or qald$ or qale$ or qtime$).tw. (19460)

65 disability adjusted life.tw. (3859)

66 daly$.tw. (3795)

67 (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. (40345)

68 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (2343)

69 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (9099)

70 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. (57)

71 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (441)

72 (euroqol or euro qol or eq5d or eq 5d).tw. (19529)

73 (qol or hql or hqol or hrqol).tw. (93024)

74 (hye or hyes).tw. (131)

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

76 utilit$.tw. (279630)

77 (hui or hui1 or hui2 or hui3).tw. (2199)

78 disutili$.tw. (896)

79 rosser.tw. (119)

80 quality of wellbeing.tw. (42)

81 quality of well-being.tw. (469)

82 qwb.tw. (244)

83 willingness to pay.tw. (8401)

84 standard gamble$.tw. (1091)

85 time trade off.tw. (1672)

86 time tradeoff.tw. (288)

87 tto.tw. (1619)

88 or/57-87 (955047)

89 56 or 88 (2511703)

90 37 and 89 (1817)

Database: Econlit <1886 to February 13, 2020>

Search Strategy:

---

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

2 (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. (5652)

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

4 [Minors/] (0)

5 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (47119)

6 [exp pediatrics/] (0)

7 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (175)

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

9 [Puberty/] (0)

10 (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. (9134)

11 [Schools/] (0)

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

13 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (49346)

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

15 or/1-14 (94513)

16 (dipstick* or dip-stick*).tw. (0)

17 (urin* adj3 (test* or strip* or stick*)).tw. (13)

18 [Urinalysis/] (0)

19 urinalys*.tw. (5)

20 or/16-19 (17)

21 ["Indicators and Reagents"/] (0)

22 [exp Reagent Kits, Diagnostic/] (0)

23 reagent*.tw. (5)

24 (diagnos* adj3 (test* or kit*)).tw. (578)

25 or/21-24 (583)

26 [Urine/] (0)

27 [exp Proteinuria/] (0)

28 [Hematuria/] (0)

29 (urin* or proteinur* or albuminur* or hemoglobinur* or haemoglobinur* or hematur* or haematur*).tw. (79)

30 or/26-29 (79)

31 25 and 30 (1)

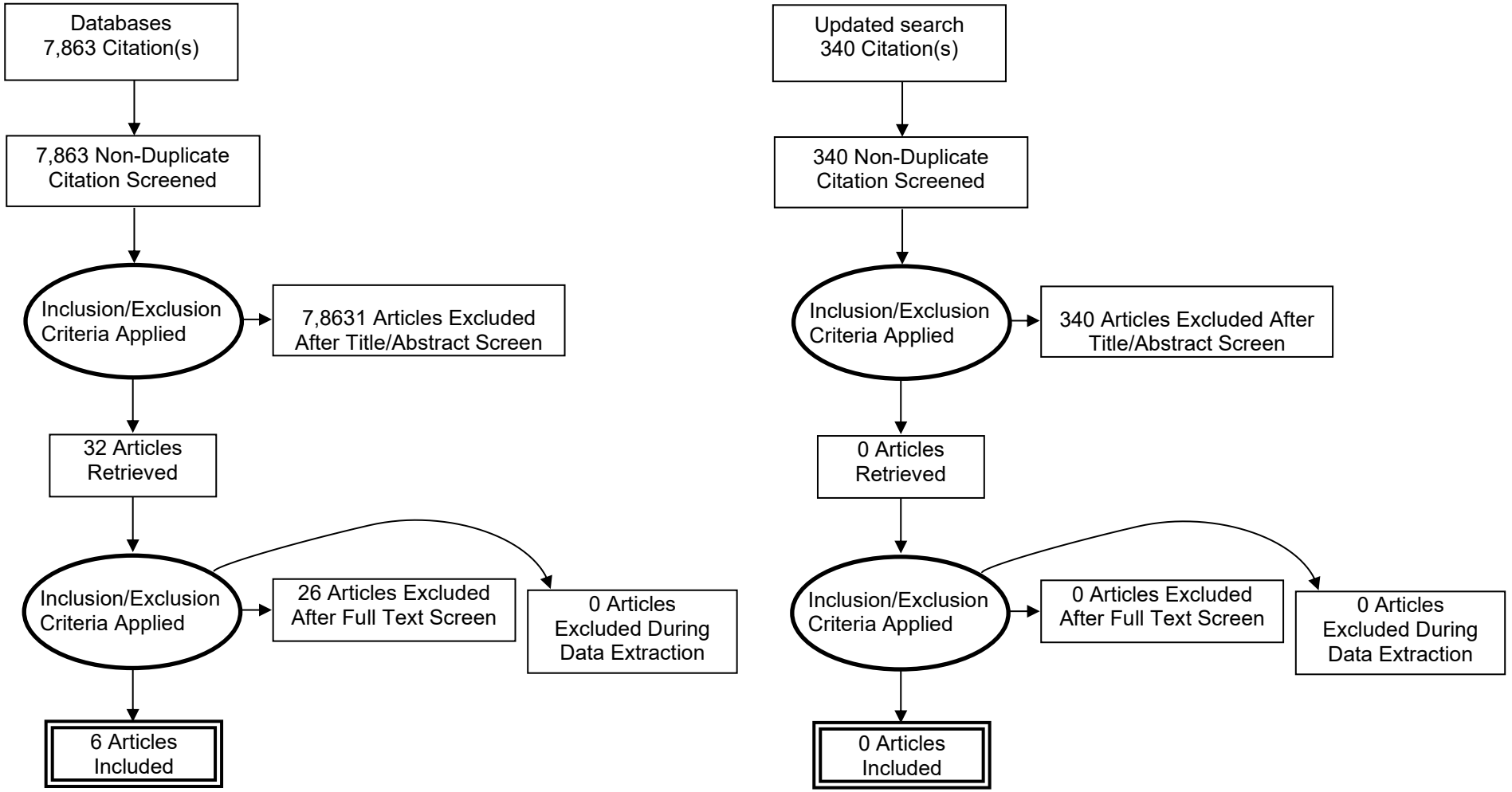
32 20 or 31 (17)

33 15 and 32 (4)

CRD databases

| | | | |
|---|---|---|---|
| 1 | ((dipstick* or dip-stick*)) | 60 | Delete |
| 2 | ((urin* near3 (test* or strip* or stick*))) | 149 | Delete |
| 3 | (MeSH DESCRIPTOR Urinalysis) | 71 | Delete |
| 4 | (urinalys*) | 123 | Delete |
| 5 | (#1 or #2 or #3 or #4) | 263 | Delete |
| 6 | (MeSH DESCRIPTOR Indicators and Reagents) | 12 | Delete |
| 7 | (MeSH DESCRIPTOR Reagent Kits, Diagnostic EXPLODE ALL TREES) | 94 | Delete |
| 8 | (reagent*) | 191 | Delete |
| 9 | ((diagnos* near3 (test* or kit*)) ) | 1882 | Delete |
| 10 | (#6 or #7 or #8 or #9) | 2017 | Delete |
| 11 | (MeSH DESCRIPTOR Urine) | 39 | Delete |
| 12 | (MeSH DESCRIPTOR Proteinuria EXPLODE ALL TREES) | 145 | Delete |
| 13 | (MeSH DESCRIPTOR Hematuria) | 26 | Delete |
| 14 | (urin* or proteinur* or albuminur* or hemoglobinur* or haemoglobinur* or hematur* or haematur*) | 2424 | Delete |
| 15 | (#11 or #12 or #13 or #14) | 2424 | Delete |
| 16 | (#10 and #15) | 143 | Delete |
| 17 | (#5 or #16) | 337 | Delete |
| 18 | (#5 or #16) IN NHSEED | 154 | Delete |
| 19 | (#5 or #16) IN HTA | 58 | Delete |

# Appendix D – Diagnostic evidence study selection



# Appendix E – Diagnostic evidence tables and risk of bias

## Agarwal, 2004

| | |
|---|---|
| **Bibliographic Reference** | Agarwal, I.; Kirubakaran, C.; Markandeyulu; Selvakumar; Quantitation of proteinuria by spot urine sampling; Indian Journal of Clinical Biochemistry; 2004; vol. 19 (no. 2); 45-47 |

**Study Characteristics**

| | |
|---|---|
| **Study type** | Cross-sectional study |
| **Study details** | Study location<br>India<br><br>Study setting<br>Hospital<br><br>Study dates<br>Not reported<br><br>Loss to follow-up<br>None<br><br>Sources of funding<br>Not reported |
| **Inclusion criteria** | Age<br>12 years and younger<br><br>Renal disease<br>Underlying nephrotic syndrome |
| **Sample characteristics** | Sample size<br>50 urine samples from 26 participants |

| | |
|---|---|
| **Index test(s)** | Strips - proteinuria<br>Urinary dipstick albustix was graded as negative, trace 1+ (closest to 30 mg/dl), 2+ (closest to 100 mg/dl), 3+ (closest to 300 mg/dl), and 4+ (>2000 mg/dl) |
| **Reference standard (s)** | Other<br>Spot urinary protein/creatinine ratio with reference ranges <0.2, 0.2 to 3.5, and >3.5. 24-hour urine protein excretion was graded into 3 groups: <4 mg/m²/hr, 4 to 40 mg/m²/hr, and >40 mg/m²/hr |

| **Risk of bias domain** | **Risk of bias judgment** |
|---|---|
| Patient selection: risk of bias | Unclear<br>*(There was no information about how participants were enrolled. Exclusion criteria were not reported)* |
| Patient selection: applicability | Low |
| Index tests: risk of bias | Unclear<br>*(There was no information on whether index test results were interpreted without knowledge of reference standard results)* |
| Index tests: applicability | Low |
| Reference standard: risk of bias | Unclear<br>*(There was no information on whether reference standard results were interpreted without knowledge of index test results)* |
| Reference standard: applicability | Low |
| Flow and timing: risk of bias | Low |
| Overall risk of bias | Moderate |
| Directness | Directly applicable |

## Biswas, 2009

| | |
|---|---|
| **Bibliographic Reference** | Biswas, A; Kumar, R; Chaterjee, A; Ghosh, J K; Basu, K; Quantitation of proteinuria in nephrotic syndrome by spot urine protein creatinine ratio estimation in children.; Mymensingh medical journal : MMJ; 2009; vol. 18 (no. 1); 67-71 |

**Study Characteristics**

| | |
|---|---|
| **Study type** | Cross-sectional study |
| **Study details** | Study location<br>India<br><br>Study setting<br>Hospital<br><br>Study dates<br>Not reported<br><br>Loss to follow-up<br>None<br><br>Sources of funding<br>Not reported |
| **Inclusion criteria** | Age<br>≤12 years old<br><br>Renal disease<br>Underlying nephrotic syndrome |
| **Sample characteristics** | Sample size<br>52 urine samples from 26 participants<br><br>Female<br>30% |
| **Index test(s)** | Strips - proteinuria |

| | |
|---|---|
| | Protein dipstick graded as negative, trace 1+ (closest to 30 mg/dl), 2+ (closest to 100 mg/dl), 3+ (closest to 300 mg/dl), and 4+ (>2000 mg/dl) |
| **Reference standard (s)** | Other<br>Protein/creatinine ratio graded as <0.2, 0.2 to 3.0, >3.0. 24-hour urine protein excretion graded as <4 mg/m²/hr, 4 to 40 mg/m²/hr, and >40 mg/m²/hr |

| **Risk of bias domain** | **Risk of bias judgment** |
|---|---|
| Patient selection: risk of bias | Low |
| Patient selection: applicability | Low |
| Index tests: risk of bias | Unclear<br>*(There was no information on whether index test results were interpreted without knowledge of reference standard results)* |
| Index tests: applicability | Low |
| Reference standard: risk of bias | Unclear<br>*(There was no information on whether reference standard results were interpreted without knowledge of index test results)* |
| Reference standard: applicability | Low |
| Flow and timing: risk of bias | Low |
| Overall risk of bias | Moderate |
| Directness | Directly applicable |

## Haysom, 2009

| | |
|---|---|
| **Bibliographic Reference** | Haysom, Leigh; Williams, Rita; Hodson, Elisabeth; Lopez-Vargas, Pamela; Roy, L Paul; Lyle, David; Craig, Jonathan C; Diagnostic accuracy of urine dipsticks for detecting albuminuria in indigenous and non-indigenous children in a community setting.; Pediatric nephrology (Berlin, Germany); 2009; vol. 24 (no. 2); 323-31 |

**Study Characteristics**

| | |
|---|---|
| **Study type** | Cross sectional |
| **Study details** | Study location<br>Australia<br><br>Study setting<br>Elementary schools<br><br>Study dates<br>2002 - 2004<br><br>Loss to follow-up<br>At baseline 78 out of 2213 did not have ACR measured; at 2 years 17 out of 1358 did not have ACR at follow-up<br><br>Sources of funding<br>National Health and Medical Research Centre for Clinical Excellence in Renal Medicine, the Financial Markets Foundation for Children, and the National Health and Medical Research Council |
| **Inclusion criteria** | Other<br>Healthy Aboriginal and non-Aboriginal children, boys and girls, and in similar proportion from urban, coastal, rural, and remote areas |
| **Exclusion criteria** | Other<br>Non-government schools (private and denominational) have very few Aboriginal enrollments and were not considered for recruitment |
| **Sample characteristics** | Sample size<br>2266 healthy children including 55.1% Aboriginal children<br><br>Female<br>49.0%<br><br>Mean age (SD) |

| | |
|---|---|
| | 8.9 years (2.0 years)<br><br>Other<br>There were more Aboriginal children compared with non-Aboriginal children in the youngest age tertile (37.4% and 28.5%, p<0.0001); and with haematuria at baseline (7.1% and 3.6%, p<0.002) |
| **Index test(s)** | Strips - proteinuria<br>Multistix-10 SG reagent dipstick. The colour was read spectrophotometrically by the Bayer Clinitek 50 urinalysis machine with 4 protein categories: negative/trace (protein <0.30 g/L), 1+ (protein 0.30 g/L), 2+ (protein 1 g/L), 3+ (protein 3 g/L), and 4+ (≥20 g/L) |
| **Reference standard (s)** | Other<br>Spot urine albumin:creatinine dipstick. Colour changes were read spectrophotometrically by the Bayer Clinitek 50 urinalysis machine as a ratio of albumin:creatinine concentration within 3 categories: normal/no pathological albuminuria (ACR <3.4 mg/mmol), microalbuminuria (ACR 3.4-33.9 mg/mmol), and macroalbuminuria (ACR >33.9 mg/mmol) |

| **Risk of bias domain** | **Risk of bias judgment** |
|---|---|
| Patient selection: risk of bias | Low |
| Patient selection: applicability | Low |
| Index tests: risk of bias | Low<br>*(The study nurse was not blinded to the results of either test; however, interpretation of each was quantitative)* |
| Index tests: applicability | Low |
| Reference standard: risk of bias | Low<br>*(The study nurse was not blinded to the results of either test; however, interpretation of each was quantitative)* |
| Reference standard: applicability | Low |
| Flow and timing: risk of bias | Low |

| Risk of bias domain | Risk of bias judgment |
|---|---|
| Overall risk of bias | High |
| Directness | Directly applicable |

## Meinhardt, 2003

| | |
|---|---|
| **Bibliographic Reference** | Meinhardt, U.; Ammann, R.A.; Fluck, C.; Diem, P.; Mullis, P.E.; Microalbuminuria in diabetes mellitus - Efficacy of a new screening method in comparison with timed overnight urine collection; Journal of Diabetes and its Complications; 2003; vol. 17 (no. 5); 254-257 |

**Study Characteristics**

| | |
|---|---|
| **Study type** | Cross-sectional study |
| **Study details** | Study location<br>Switzerland<br><br>Study setting<br>Paediatric diabetes outpatient clinic<br><br>Study dates<br>2000<br><br>Loss to follow-up<br>In 44 out of 209 occasions, urinary albumin could not be assessed in both spot and timed overnight urine<br><br>Sources of funding<br>Not reported |
| **Inclusion criteria** | Other<br>Children and adolescents with type 1 diabetes |
| **Exclusion criteria** | Other |

| | |
|---|---|
| | Fever (>38 C), haematuria (Bayer Multiple Reagent Strip), urinary tract infection (leucocyturia with consecutive positive culture result), and alkaline urine (pH>8), which would explain false positive result in Clinitek-Microalbumin |
| **Sample characteristics** | Sample size<br>209 specimens of 124 children and adolescents<br><br>Female<br>45.1%<br><br>Median (range)<br>11.5 years (interquartile range 8.8, 14.7 years)<br><br>Other<br>Median duration of type 1 diabetes 3.8 years (interquartile range 1.3, 6.7 years); median HbA1c 8.0% (interquartile range 7.2, 8.9%) |
| **Index test(s)** | Strips - albuminuria<br>In the spot urine portion Clinitek-Microalbumin was used to screen for microalbuminuria following the manufacturer's instructions (cut-off 30 mg/l)<br><br>Comments<br>The collected urine was stored for a maximum of 72 h at 4 C |
| **Reference standard (s)** | Turbidimetric or colorimetric assays<br>In the overnight urine portions, the albumin concentration was analysed by turbidimetric measurement of the endpoint of the antigen–antibody reaction (cut-off 30 mg/l) |

| **Risk of bias domain** | **Risk of bias judgment** |
|---|---|
| Patient selection: risk of bias | Low |
| Patient selection: applicability | Low |
| Index tests: risk of bias | Unclear<br>*(There was no information on whether index test results were interpreted without knowledge of reference standard results)* |

| Risk of bias domain | Risk of bias judgment |
|---|---|
| Index tests: applicability | Low |
| Reference standard: risk of bias | Unclear<br>*(There was no information on whether reference standard results were interpreted without knowledge of index test results)* |
| Reference standard: applicability | Low |
| Flow and timing: risk of bias | Low |
| Overall risk of bias | Moderate |
| Directness | Directly applicable |

## Ochigbo, 2017

**Bibliographic Reference** Ochigbo, S.O.; Udo, J.J.; Nlemadi, A.C.; Omololuolaniyo, K.; Comparison of the efficacy of serum creatinine and microalbuminuria in early diagnosis of renal injury in asphyxiated infants in calabar, Southern Nigeria; Iranian Journal of Neonatology; 2017; vol. 8 (no. 2); 1-4

**Study Characteristics**

| | |
|---|---|
| **Study type** | Cross-sectional study |
| **Study details** | Study location<br>Nigeria<br><br>Study setting<br>University teaching hospital<br><br>Study dates<br>2014 |

| | |
|---|---|
| | Loss to follow-up<br>None<br><br>Sources of funding<br>Not reported |
| **Inclusion criteria** | Other<br>Severely asphyxiated full-term neonates admitted into the new-born units of the university teaching hospital. Apgar score of three or less at five minutes of life was considered as severe birth asphyxia |
| **Exclusion criteria** | Other<br>Preterm neonates, febrile infants (Temperature>37.50° C), infants with a past history of congenital or otherwise renal disease, and history of antibiotic use |
| **Sample characteristics** | Sample size<br>50<br><br>Female<br>Male-female ratio of 1.8:1<br><br>Mean age (SD)<br>30.3 (36.2) hours |
| **Index test(s)** | Strips - albuminuria<br>Micral-test strips for microalbuminuria. The results were considered positive when at least two urine samples produce a reaction color corresponding to 20 mg/dl (threshold for microalbuminuria) or more of albumin |
| **Reference standard (s)** | Other<br>Serum creatinine clearance was calculated using a modified Schwartz formula |

| **Risk of bias domain** | **Risk of bias judgment** |
|---|---|
| Patient selection: risk of bias | Low |

| Risk of bias domain | Risk of bias judgment |
|---|---|
| Patient selection: applicability | Low |
| Index tests: risk of bias | Unclear<br>*(There was no information on whether index test results were interpreted without knowledge of reference standard results)* |
| Index tests: applicability | Low |
| Reference standard: risk of bias | Unclear<br>*(There was no information on whether reference standard results were interpreted without knowledge of index test results)* |
| Reference standard: applicability | Low |
| Flow and timing: risk of bias | Unclear<br>*(There was no information about the interval between index test and reference standard)* |
| Overall risk of bias | Moderate |
| Directness | Directly applicable |

## Sultana, 2018

**Bibliographic Reference** Sultana, M N; Majumder, B; Rahman, M J; Moniruzzaman, A M; Suja, A M; Ali, M E; Sarker, Z H; Nabi, S N; Mostakim, M A; Dipstick Method versus Spot Urinary Protein Creatinine Ratio for Evaluation of Massive Proteinuria in Childhood Nephrotic Syndrome.; Mymensingh medical journal : MMJ; 2018; vol. 27 (no. 2); 369-374

**Study Characteristics**

| | |
|---|---|
| **Study type** | Cross-sectional study |
| **Study details** | Study location |

| | |
|---|---|
| | Bangladesh<br><br>Study setting<br>Hospital, department of paediatric nephrology<br><br>Study dates<br>January 2014 to December 2015<br><br>Loss to follow-up<br>None<br><br>Sources of funding<br>Not reported |
| **Inclusion criteria** | Renal disease<br>Nephrotic syndrome<br><br>Other<br>Bed side proteinuria (3+/4+) by urinary heat coagulation test |
| **Exclusion criteria** | Other<br>Gross haematuria, pyuria, polyuria, and polydypsia |
| **Index test(s)** | Strips - proteinuria<br>5 ml urine was collected in test tube and bed side dipstick testing was done for one minute |
| **Reference standard (s)** | Other<br>Urine samples were sent to the laboratory of biochemistry department for estimation of spot urinary protein creatinine ratio |

| **Risk of bias domain** | **Risk of bias judgment** |
|---|---|
| Patient selection: risk of bias | Low |
| Patient selection: applicability | Low |

| Risk of bias domain | Risk of bias judgment |
|---|---|
| Index tests: risk of bias | Unclear<br>*(Proteinuria was reported as positive and negative. Thresholds were not given. There was no information on whether index test results were interpreted without knowledge of reference standard results)* |
| Index tests: applicability | Unclear<br>*(Proteinuria was reported as positive and negative. Thresholds were not given.)* |
| Reference standard: risk of bias | Unclear<br>*(There was no information on whether reference standard results were interpreted without knowledge of index test results)* |
| Reference standard: applicability | Low |
| Flow and timing: risk of bias | Low |
| Overall risk of bias | Moderate |
| Directness | Directly applicable |

# Appendix F – Forest plots

None of the studies included could be combined to produce a pooled effect estimate.

# Appendix G – GRADE tables

## Diagnostic accuracy evidence

### Proteinuria

| No. of studies | Study design | Sample size | Sensitivity (95%CI) | Specificity (95%CI) | Effect size (95%CI) | Risk of bias | Indirectness | Inconsistency | Imprecision | Quality |
|---|---|---|---|---|---|---|---|---|---|---|
| At baseline, whole sample<br>Index test: Multistix-10 SG, positive test = 1+ (protein 0.30 g/L) or more<br>Reference standard: Spot urine albumin:creatinine ratio (ACR) dipstick, positive test ACR ≥3.4-33.9 mg/mmol | | | | | | | | | | |
| 1[a] | Prospective | 2,135 | 0.62 (0.54, 0.69) | 0.97 (0.96, 0.97) | LR+ 20.92 (15.83, 27.66) | Serious[b] | Not serious | N/A | Not serious | Moderate |
| | | | | | LR- 0.38 (0.31, 0.47) | Serious[b] | Not serious | N/A | Not serious | Moderate |
| At baseline, non-Aboriginal<br>Index test: Multistix-10 SG, positive test = 1+ (protein 0.30 g/L) or more<br>Reference standard: Spot urine albumin:creatinine ratio (ACR) dipstick, positive test ACR ≥3.4-33.9 mg/mmol | | | | | | | | | | |
| 1[a] | Prospective | 971 | 0.66 (0.54, 0.77) | 0.96 (0.95, 0.97) | LR+ 19.52 (13.25, 28.77) | Serious[b] | Not serious | N/A | Not serious | Moderate |
| | | | | | LR- 0.34 (0.24, 0.48) | Serious[b] | Not serious | N/A | Not serious | Moderate |
| At baseline, Aboriginal<br>Index test: Multistix-10 SG, positive test = 1+ (protein 0.30 g/L) or more<br>Reference standard: Spot urine albumin:creatinine ratio (ACR) dipstick, positive test ACR ≥3.4-33.9 mg/mmol | | | | | | | | | | |
| 1[a] | Prospective | 1,164 | 0.59 (0.49, 0.69) | 0.97 (0.96, 0.98) | LR+ 22.76 (15.23, 34.01) | Serious[b] | Not serious | N/A | Not serious | Moderate |
| | | | | | LR- 0.41 (0.32, 0.53) | Serious[b] | Not serious | N/A | Serious[c] | Low |
| At 2 years, whole sample<br>Index test: Multistix-10 SG, positive test = 1+ (protein 0.30 g/L) or more | | | | | | | | | | |

| No. of studies | Study design | Sample size | Sensitivity (95%CI) | Specificity (95%CI) | Effect size (95%CI) | Risk of bias | Indirectness | Inconsistency | Imprecision | Quality |
|---|---|---|---|---|---|---|---|---|---|---|
| Reference standard: Spot urine albumin:creatinine dipstick, positive test ACR ≥3.4-33.9 mg/mmol | | | | | | | | | | |
| 1[a] | Prospective | 1,341 | 0.75 (0.52, 0.89) | 0.93 (0.91, 0.94) | LR+ 11.13 (8.06, 15.37) | Serious[b] | Not serious | N/A | Not serious | Moderate |
| | | | | | LR- 0.26 (0.12, 0.57) | Serious[b] | Not serious | N/A | Serious[c] | Low |
| At 2 years – non-Aboriginal<br>Index test: Multistix-10 SG, positive test = 1+ (protein 0.30 g/L) or more<br>Reference standard: Spot urine albumin:creatinine dipstick, positive test ACR ≥3.4-33.9 mg/mmol | | | | | | | | | | |
| 1[a] | Prospective | 628 | 0.77 (0.42, 0.94) | 0.93 (0.90, 0.94) | LR+ 11.19 (7.11, 17.61) | Serious[b] | Not serious | N/A | Not serious | Moderate |
| | | | | | LR- 0.23 (0.07, 0.81) | Serious[b] | Not serious | N/A | Serious[c] | Low |
| At 2 years, Aboriginal<br>Index test: Multistix-10 SG, positive test = 1+ (protein 0.30 g/L) or more<br>Reference standard: Spot urine albumin:creatinine dipstick, positive test ACR ≥3.4-33.9 mg/mmol | | | | | | | | | | |
| 1[a] | Prospective | 713 | 0.72 (0.41, 0.91) | 0.93 (0.91, 0.95) | LR+ 11.09 (7.02, 17.53) | Serious[b] | Not serious | N/A | Not serious | Moderate |
| | | | | | LR- 0.29 (0.11, 0.76) | Serious[b] | Not serious | N/A | Serious[c] | Low |
| Index test: urinary dipstick albustix, positive test 2+ (closest to 100 mg/dl) or more<br>Reference standard: 24-hour urine protein excretion, positive test ≥4 mg/24 h | | | | | | | | | | |
| 1[d] | Cross-sectional | 50 samples from 26 children | 0.59 (0.35, 0.79) | 0.98 (0.81, 0.99) | LR+ 42.75 (2.64, 690.58) | Serious[b] | Not serious | N/A | Not serious | Moderate |
| | | | | | LR- 0.41 (0.22, 0.74) | Serious[b] | Not serious | N/A | Serious[c] | Low |
| Index test: urinary dipstick albustix, positive test 2+ (closest to 100 mg/dl) or more<br>Reference standard: spot urinary protein/creatinine ratio, positive test ≥0.2 mg/mg | | | | | | | | | | |
| 1[d] | Cross-sectional | 50 samples | 0.53 (0.28, 0.77) | 0.94 (0.80, 0.98) | LR+ 9.96 (2.36, 41.99) | Serious[b] | Not serious | N/A | Not serious | Moderate |

| No. of studies | Study design | Sample size | Sensitivity (95%CI) | Specificity (95%CI) | Effect size (95%CI) | Risk of bias | Indirectness | Inconsistency | Imprecision | Quality |
|---|---|---|---|---|---|---|---|---|---|---|
| | | from 26 children | | | LR- 0.48 (0.27, 0.88) | Serious[b] | Not serious | N/A | Serious[c] | Low |
| Index test: urinary protein dipstick, positive test 2+ (closest to 100 mg/dl) or more<br>Reference standard: 24-hour urine protein excretion, positive test ≥4 mg/24 h | | | | | | | | | | |
| 1[e] | Cross-sectional | 52 samples from 26 children | 0.62 (0.37, 0.82) | 0.97 (0.82, 0.99) | LR+ 22.50 (3.13, 161.25) | Serious[b] | Not serious | N/A | Not serious | Moderate |
| | | | | | LR- 0.38 (0.20, 0.72) | Serious[b] | Not serious | N/A | Serious[c] | Low |
| Index test: urinary protein dipstick, positive test 2+ (closest to 100 mg/dl) or more<br>Reference standard: spot urinary protein/creatinine ratio, positive test ≥0.2 mg/mg | | | | | | | | | | |
| 1[e] | Cross-sectional | 52 samples from 26 children | 0.61 (0.34, 0.83) | 0.92 (0.78, 0.97) | LR+ 8.00 (2.48, 25.75) | Serious[b] | Not serious | N/A | Not serious | Moderate |
| | | | | | LR- 0.41 (0.20, 0.83) | Serious[b] | Not serious | N/A | Serious[c] | Low |
| Index test: bed side dipstick test, threshold was not given for a positive test<br>Reference standard: spot urinary protein creatinine ratio, threshold was not given for a positive test | | | | | | | | | | |
| 1[f] | Cross-sectional | 100 | 0.97 (0.91, 0.99) | 0.70 (0.37, 0.90) | LR+ 3.25 (1.26, 8.40) | Serious[b] | Not serious | N/A | Serious[g] | Low |
| | | | | | LR- 0.03 (0.00, 0.13) | Serious[b] | Not serious | N/A | Not serious | Moderate |

a. Haysom 2009
b. Study at moderate risk of bias
c. 95% confidence interval for negative likelihood ratio spanning a clinical decision threshold (0.5).
d. Agarwal 2004
e. Biswas 2009
f. Sultana 2018
g. 95% confidence interval for positive likelihood ratio spanning a clinical decision threshold (2.0).

**Albuminuria**

| No. of studies | Study design | Sample size | Sensitivity (95%CI) | Specificity (95%CI) | Effect size (95%CI) | Risk of bias | Indirectness | Inconsistency | Imprecision | Quality |
|---|---|---|---|---|---|---|---|---|---|---|
| Index test: Clinitek-Microalbumin on spot urine; microalbuminuria (cut-off 30 mg/l)<br>Reference test: turbidimetric measurement of the endpoint of the antigen–antibody reaction in the overnight urine, microalbuminuria (cut-off 30 mg/l) | | | | | | | | | | |
| 1[a] | Cross-sectional | 156 | 0.88 (0.50, 0.98) | 0.73 (0.65, 0.80) | LR+ 3.35 (2.35, 4.77) | Serious[b] | Not serious | N/A | Not serious | Moderate |
| | | | | | LR- 0.15 (0.02, 0.96) | Serious[b] | Not serious | N/A | Serious[c] | Low |
| Index test: Micral-test strips; microalbuminuria = 20 mg/dl or more<br>Reference standard: Serum creatinine clearance calculated with a modified Schwartz formula[d] | | | | | | | | | | |
| 1[e] | Cross-sectional | 50 | 0.50 (0.01, 0.98) | 0.87 (0.75, 0.94) | LR+ 3.92 (0.48, 31.63) | Serious[b] | Not serious | N/A | Very serious[f] | Very low |
| | | | | | LR- 0.57 (0.08, 4.07) | Serious[b] | Not serious | N/A | Very serious[f] | Very low |

a. Meinhardt 2003
b. Study at moderate risk of bias
c. 95% confidence interval for negative likelihood ratio spanning a clinical decision threshold (0.5).
d. Specific levels were not given for ‘elevated’ and ‘normal’ serum creatinine
e. Ochigbo 2017
f. 95% confidence interval for likelihood ratio spanning the LR specific clinical decision threshold and the line of no effect (0.5, 2.0).

# 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 |
|---|---|
| Abitbol, C, Zilleruelo, G, Freundlich, M et al. (1990) Quantitation of proteinuria with urinary protein/creatinine ratios and random testing with dipsticks in nephrotic children. The Journal of pediatrics 116(2): 243-7 | - Not possible to calculate a contingency table from the data specified in the protocol |
| Adamson, C.L., Kumar, S., Sutcliffe, H. et al. (1993) Screening strategies in the detection of microalbuminuria in insulin-dependent diabetic patients. Practical Diabetes 10(4): 142-144 | - Study does not contain relevant population [Participants were 16 to 77 years. There was no subgroup analysis by age] |
| Anigilaje, E.A. and Adedoyin, O.T. (2013) Correlation between dipstick urinalysis and urine sediment microscopy in detecting haematuria among children with sickle cell anaemia in steady state in Ilorin, Nigeria. Pan African Medical Journal 15: 135 | - Not possible to calculate a contingency table from the data specified in the protocol |
| Arm, J P, Peile, E B, Rainford, D J et al. (1986) Significance of dipstick haematuria. 1. Correlation with microscopy of the urine. British journal of urology 58(2): 211-7 | - Study does not contain relevant population [Adults] |
| Bangstad, H J, Try, K, Dahl-Jorgensen, K et al. (1991) New semiquantitative dipstick test for microalbuminuria. Diabetes care 14(11): 1094-7 | - Study does not contain relevant population [Participants were 9 to 73 years old. There was no subgroup analysis by age] |
| Chan, Rebecca Wing-Yan, Chow, Kai-Ming, Tam, Lai-Shan et al. (2005) Can the urine dipstick test reduce the need for microscopy for assessment of systemic lupus erythematosus disease activity?. The Journal of rheumatology 32(5): 828-31 | - Study does not contain relevant population [Participants were 17 to 80 years old. There was no subgroup analysis by age] |
| Chitalia, V.C., Kothari, J., Wells, E.J. et al. (2001) Cost-benefit analysis and prediction of 24-hour proteinuria from the spot urine protein-creatinine ratio. Clinical Nephrology 55(6): 436-447 | - Study does not contain relevant population [Participants were 16 to 58 years old. There was no subgroup analysis by age] |
| Gai, M., Motta, D., Giunti, S. et al. (2006) Comparison between 24-h proteinuria, urinary protein/creatinine ratio and dipstick test in patients with nephropathy: Patterns of proteinuria in dipstick-negative patients. Scandinavian Journal of Clinical and Laboratory Investigation 66(4): 299-308 | - Study does not contain relevant population [Mean age 51.7 years (SD 16.7), range 14 to 89 years without subgroup analysis by age] |
| Gleeson, M J, Connolly, J, Grainger, R et al. (1993) Comparison of reagent strip (dipstick) and microscopic haematuria in urological out-patients. British journal of urology 72(5pt1): 594-6 | - Study does not contain relevant population [Participants were 10 to 94 years old. There was no subgroup analysis by age] |
| Gupta, Gopila, Hemal, Alok, Saha, Abhijeet et al. (2017) Proteinuria in HIV-infected Indian children. Tropical doctor 47(3): 230-233 | - Not possible to calculate a contingency table from the data specified in the protocol [Data was not reported for false and true positives] |
| Hamoudi, A C; Bubis, S C; Thompson, C (1986) Can the cost savings of eliminating urine | - Not possible to calculate a contingency table from the data specified in the protocol |

| Reference | Reason for exclusion |
|---|---|
| microscopy in biochemically negative urines be extended to the pediatric population?. American journal of clinical pathology 86(5): 658-60 | [Biochemical and microscopy results were combined for the different findings including protein, blood, glucose, ketones among others] |
| Jafari Nodoshan, A.A.-H., Shajari, A., Golzar, A. et al. (2015) Urinary screening in primary school children in yazd, iran. Shiraz E Medical Journal 16(1): 1-4 | - Not possible to calculate a contingency table from the data specified in the protocol<br>[Reference test (microscopy) was done in children with abnormal findings] |
| Le Floch, J P, Charles, M A, Philippon, C et al. (1994) Cost-effectiveness of screening for microalbuminuria using immunochemical dipstick tests or laboratory assays in diabetic patients. Diabetic medicine : a journal of the British Diabetic Association 11(4): 349-56 | - Study does not contain relevant population<br>[Participants were 14 to 92 years old. There was no subgroup analysis by age] |
| Ooi, S B; Kour, N W; Mahadev, A (1998) Haematuria in the diagnosis of urinary calculi. Annals of the Academy of Medicine, Singapore 27(2): 210-4 | - Study does not contain relevant population<br>[Participants were 17 to 70 years old. There was no subgroup analysis by age] |
| Pfab, T, Franz, U, Herfeld, F et al. (2006) Rapid immunochromatographic strip test for the detection of albuminuria and brief literature review on albuminuria screening. European journal of medical research 11(1): 3-6 | - Study does not contain relevant population<br>[Participants were 16 to 100 years old. There was no subgroup analysis by age] |
| Salinas, Maria, Lopez-Garrigos, Maite, Flores, Emilio et al. (2018) Urinary albumin strip assay as a screening test to replace quantitative technology in certain conditions. Clinical chemistry and laboratory medicine 57(2): 204-209 | - Study does not contain relevant population<br>[Mainly adults without subgroup in young people (mean age 63 years [SD 17], range 16, 102)] |
| Sekhar, Deepa L, Wang, Li, Hollenbeak, Christopher S et al. (2010) A cost-effectiveness analysis of screening urine dipsticks in well-child care. Pediatrics 125(4): 660-3 | - Study design does not match that specified in the protocol<br>[Decision analysis modelling] |
| Shah, A.A., Iftikhar, N., Ahmed, S. et al. (2015) Usefulness of spot urine protein creatinine ratio in the diagnosis of childhood nephrotic syndrome. Pakistan Paediatric Journal 39(4): 193-197 | - Not possible to calculate a contingency table from the data specified in the protocol |
| Siedner, Mark J, Gelber, Allan C, Rovin, Brad H et al. (2008) Diagnostic accuracy study of urine dipstick in relation to 24-hour measurement as a screening tool for proteinuria in lupus nephritis. The Journal of rheumatology 35(1): 84-90 | - Study does not contain relevant population<br>[Adults] |
| Tai, J. and Tze, W.J. (1990) Evaluation of Micro-Bumintest reagent tablets for screening of microalbuminuria. Diabetes Research and Clinical Practice 9(2): 137-142 | - Study does not contain relevant population<br>[Age of participants was not reported] |
| Tanner, M, Holzer, B, Marti, H P et al. (1983) Frequency of haematuria and proteinuria among Schistosoma haematobium infected children of two communities from Liberia and Tanzania. Acta tropica 40(3): 231-7 | - Reference standard in study does not match that specified in protocol<br>[Study did not use any reference standard] |
| Todenhofer, Tilman, Hennenlotter, Jorg, Witstruk, Marc et al. (2012) Influence of renal excretory function on the performance of urine | - Study does not contain relevant population<br>[Adults] |

| Reference | Reason for exclusion |
|---|---|
| based markers to detect bladder cancer. The Journal of urology 187(1): 68-73 | |
| Trihono, Partini Pudjiastuti; Wulandari, Nanda; Supriyatno, Bambang (2019) Asymptomatic proteinuria in Indonesian adolescent students. Saudi journal of kidney diseases and transplantation : an official publication of the Saudi Center for Organ Transplantation, Saudi Arabia 30(3): 694-700 | - Not possible to calculate a contingency table from the data specified in the protocol<br>[Only participants with positive proteinuria at the second dipstick test were then tested for urinary protein/creatinine ratio] |
| Watson, D., Yang, J.Y.C., Sarwal, R.D. et al. (2019) A novel multi-biomarker assay for non-invasive quantitative monitoring of kidney injury. Journal of Clinical Medicine 8(4): 499 | - Study does not contain relevant population<br>[Age ranged from 2 to 98 years without a subgroup analysis for children and young people] |
| White, A V; Hoy, W E; McCredie, D A (2001) Childhood post-streptococcal glomerulonephritis as a risk factor for chronic renal disease in later life. The Medical journal of Australia 174(10): 492-6 | - Not possible to calculate a contingency table from the data specified in the protocol<br>[The 'abnormal urine' group was not reported separately for proteinuria and haematuria] |
| Zhai, Yi-Hui, Xu, Hong, Zhu, Guang-Hua et al. (2007) Efficacy of urine screening at school: experience in Shanghai, China. Pediatric nephrology (Berlin, Germany) 22(12): 2073-9 | - Not possible to calculate a contingency table from the data specified in the protocol<br>[Participants were divided into groups and each group was tested by reagent dipsticks or by reference standard but not by both methods] |

## Economic studies

| Reference | Reason for exclusion |
|---|---|
| Sekhar, Deepa L, Wang, Li, Hollenbeak, Christopher S et al. (2010) A cost-effectiveness analysis of screening urine dipsticks in well-child care. Pediatrics 125(4): 660-3 | - Cost effectiveness analysis, results reported as cost per CKD diagnosis |

# Appendix L – Research recommendations – full details

## L.1.1 Research recommendation

In children and young people, what is the accuracy of reagent strips for detecting albumin in urine?

## L.1.2 Why this is important

There was limited evidence on the accuracy of reagent strips for albuminuria, so the committee did not make recommendations. There were only 2 studies reporting on reagent strips to detect albuminuria, and only 1 of them showed that reagent strips could be useful at detecting albuminuria in children and young people with type 1 diabetes.

## L.1.3 Rationale for research recommendation

| | |
|---|---|
| Importance to 'patients' or the population | Little is known about the accuracy of reagent strips to detect albuminuria in children and young people. Further evidence would help clinicians to make decisions when testing for albuminuria in children and young people. There might be a benefit of detecting albuminuria in children and young people with type 1 diabetes if further evidence confirms that reagent strips are good at capturing most of the positive cases. This might prevent further kidney damage if cases are not missed. |
| Relevance to NICE guidance | Reagent strips to detect albuminuria have been considered in this guideline and there was a lack of evidence on these tests. Further evidence might fill in the gap in this area during future updates of the guideline. |
| Relevance to the NHS | Evidence would affect the type of test use to measure albumin in urine by the NHS. If additional dipstick tests are recommended in future, this could have an impact on clinical practice and cost for the NHS. |
| National priorities | High |
| Current evidence base | No evidence |
| Equality considerations | None known |

## L.1.4 Modified PICO table

| | |
|---|---|
| Population | **Inclusion:**<br>Children and young people up to the age of 18 years<br><br>**Exclusion:** |

| | |
|---|---|
| | • Children and young people receiving renal replacement therapy (RRT)<br>• Children and young people with acute kidney injury combined with rapidly progressive glomerulonephritis<br>• Children and young people receiving palliative care |
| Index test | Reagent strips for detecting albumin in urine |
| Reference standard | Either spot urine or 24-hour urine collection confirmed by<br>• Immunonephelometric methods<br>• |
| Outcome | **Primary outcomes**<br>• Likelihood ratios<br>• Adverse outcomes (for example, test compromised by presence of ascorbic acid in urine)<br><br>**Secondary outcomes**<br>• Specificity<br>• Sensitivity<br>• Positive Predictive Value<br>• Negative Predictive Value<br><br>Outcomes will all be converted to likelihood ratios. |
| Study design | Cross-sectional study design |
| Timeframe | Short term |
| Additional information | None |