National Institute for Health and Care Excellence

Draft

Chronic kidney disease

[D] Evidence reviews for children and young people who should be tested for CKD

NICE guideline <number>

Evidence review underpinning recommendations 1.1.20, 1.1.22 to 1.1.25 and research recommendations in the NICE guideline

January 2021

Draft for Consultation

These evidence reviews were developed by the Guideline Updates Team

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Children and young people who should be tested for chronic kidney disease (CKD)

1.1 Review question

Which children and young people should be tested for CKD?

1.1.1 Introduction

The NICE guideline on chronic kidney disease in adults: assessment and management (NICE guideline CG182) was reviewed in 2017 as part of NICE's surveillance programme. As a result of the review, the decision was made to update the guideline. During the scoping phase 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 obesity was an independent risk factor for developing chronic kidney disease in children and young people.

The aim of this review is to determine which children and young people should be tested for CKD. See Appendix A for full details of the review protocol.

1.1.2 Summary of the protocol

Table 1: PICO table for children and young people who should be tested for CKD

Population	**Inclusion:** Children and young people (up to the age of 18). **Exclusion:** • people receiving renal replacement therapy (RRT) • people with acute kidney injury combined with rapidly progressive glomerulonephritis • pregnant young women • people receiving palliative care
Prognostic factor	• Congenital renal abnormalities • Acute kidney injury • Blood in urine • Multisystem disease • Low birth weight • Family history of CKD • Obesity
Co-variates	Confounders identified by the studies themselves will be used
Outcomes	Adjusted (unadjusted will only be used if adjusted values are not available) hazard ratios, risk ratios and odds ratios at all reported time points for: • Diagnosis of CKD • CKD progression: change in eGFR • CKD progression: occurrence of end stage kidney disease (ESRD or ESKD as reported by the study) • All-cause mortality

1.1.3 Methods and process

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

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

Protocol deviation

There were studies reporting composite outcomes which were not listed in the protocol of this review. These composite outcomes included CKD diagnosis and hypertension in their definition. The committee discussed these outcomes and agreed that hypertension was a significant condition related to CKD. Therefore, composite outcomes were included as important outcomes, but these were downgraded for indirectness as they were not part of the original protocol.

1.1.4 Prognostic evidence

1.1.4.1 Included studies

A systematic search was carried out to identify cohort studies and systematic reviews of cohort studies, which found 5,365 references (see Appendix C for the literature search strategy). Based on title and abstract screening, 5,330 references were excluded, and 35 references were ordered for full text screening. In total 2 prospective cohort studies and 4 retrospective studies were included based on their relevance to the review protocol (Appendix A). The prognostic evidence study selection is presented as a PRISMA diagram in 0.

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 305 references for this review question, these were screened on title and abstract. Nine references were ordered for full text screening. One reference was included based on its relevance to the review protocol (Appendix A).

Most of the included studies reported acute kidney injury as a risk factor for the diagnosis of CKD. A couple of included studies reported solitary functioning kidney as a risk factor for the diagnosis of CKD. None of the included studies reported on the rest of risk factor listed in the protocol.

See section 1.1.10 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 the primary reason for exclusion.

1.1.5 Summary of studies included in the prognostic evidence

Table 2: Summary of studies included in the prognostic evidence

Author (year)	Study characteristics	Prognostic factor	Outcomes
Benisty (2020) Prospective cohort study	**Study location** Canada **Study setting** Hospital **Duration of follow-up** 6 years and 6 months	• Acute kidney injury	• Diagnosis of CKD (eGFR category G2 [eGFR <90 ml/min/1.73m²] or albuminuria [urine

Author (year)	Study characteristics	Prognostic factor	Outcomes
	Sample size 277 **Inclusion criteria** **Age** <18 years old at paediatric intensive care unit admission **Hospital admission** Paediatric intensive care unit admission		albumin/creatinine >30 mg/g]) • eGFR category G2 or pre-hypertension (≥90 percentile) • eGFR category G2 or hypertension (≥95 percentile)
Harer (2017) Prospective cohort study	**Study location** US **Study setting** Neonatal intensive care unit **Duration of follow-up** 5 years **Sample size** 34 **Inclusion criteria** **Weight** ≤1,500 g **Hospital admission** Neonatal intensive care unit admission before 2 days of life	• Acute kidney injury	• Diagnosis of CKD (eGFR category G2) • Renal dysfunction
Hessey (2019) Retrospective cohort study	**Study location** Canada **Study setting** Paediatric intensive care units **Duration of follow-up** 5 years **Sample size** 2,235 **Inclusion criteria** **Age** ≤18 years old **Hospital admission** First hospitalisation to a paediatric intensive care unit during study period	• Acute kidney injury	• Diagnosis of CKD (≥1 CKD diagnostic codes and/or ≥1 prescription for CKD-specific medication 5 years post-hospital discharge)
Hollander (2016) Retrospective cohort study	**Study location** US **Study setting** Hospital **Duration of follow-up** 6 and 12 months **Sample size** 88 **Inclusion criteria**	• Acute kidney injury	• Diagnosis of CKD (eGFR <60 mL/min/1.73 m2 for longer than 3 months)

Author (year)	Study characteristics	Prognostic factor	Outcomes
	Age <20 years **Condition** Orthotopic heart transplantation		
Poggiali (2019) Retrospective cohort study	**Study location** Brazil **Study setting** Pediatric Nephrourology Unit **Duration of follow-up** Median 8.5 years **Sample size** 162 **Inclusion criteria** **Condition** Congenital solitary functioning kidney	• Solitary functioning kidney (multicystic dysplastic kidney and renal agenesis/hypodysplasia) • Contralateral congenital anomalies of the kidney and urinary tract • Low birth weight in children with solitary functioning kidney	• Diagnosis of CKD (GFR <60 ml/min per 1.73 m² in two consecutive exams with an interval of at least 3 months) • Composite outcome (eGFR <60 ml/min per 1.73 m², hypertension, and proteinuria)
Westland (2013) Retrospective cohort study	**Study location** The Netherlands **Study setting** Paediatric renal centres **Duration of follow-up** Not reported **Sample size** 407 **Inclusion criteria** **Condition** Children with solitary functioning kidney and renal follow-up	• Solitary functioning kidney	• Diagnosis of CKD (eGFR <60 mL/min/1.73 m²) • Renal injury (hypertension, proteinuria, an impaired eGFR, or the use of renoprotective medication)
Williams (2018) Retrospective cohort study	**Study location** Canada **Study setting** Hospital **Duration of follow-up** Median 3.4 years (IQR 1.4, 5.7) **Sample size** 303 **Inclusion criteria** **Age** <18 years **Condition** All first-time recipients who received a non-kidney solid organ transplant	• Acute kidney injury	• Diagnosis of CKD (an average eGFR <60 mL/min per 1.73 m² over any 6-month period starting at day 90 post-transplant) • All-cause mortality

1 See Appendix E for full evidence tables.

1.1.6 Summary of the prognostic evidence

Table 3: Summary GRADE table

Benisty 2020 (prospective cohort study in children and young people admitted to paediatric intensive care unit)

AKI	No AKI	Effect size (95% CI)	Quality	Interpretation of effect[a]
Predictor: any AKI category (reference: no or unknown AKI); Outcome: eGFR category G2 (eGFR <90 ml/min/1.73m2 or ACR >30 mg/g) or BP ≥90th percentile				
69	208	OR 2.2 (1.1 to 4.4)[b]	VERY LOW	Effect
Predictor: any AKI category (reference: no or unknown AKI); Outcome: eGFR category G2 (eGFR <90 ml/min/1.73m2 or ACR >30 mg/g) or BP ≥95th percentile				
69	208	OR 1.7 (0.9 to 3.4)[c]	VERY LOW	Could not differentiate
Predictor: any AKI category (reference: no or unknown AKI); Outcome: eGFR <90 ml/min/1.73m2				
9/66 (13.6%)	13/197 (6.6%)	RR 2.07 (0.93 to 4.61)[d]	LOW	Could not differentiate
Predictor: any AKI category (reference: no or unknown AKI); Outcome: ACR >30 mg/g				
7/68 (10.3%)	25/204 (12.3%)	RR 0.84 (0.38 to 1.85)[d]	VERY LOW	Could not differentiate
Predictor: stage 2 AKI or worse (reference: no or unknown or stage 1 AKI); Outcome: eGFR category G2 (eGFR <90 ml/min/1.73m2 or ACR >30 mg/g) or BP ≥90th percentile				
27	250	OR 6.6 (1.5 to 28.3)[e]	LOW	Effect
Predictor: stage 2 AKI or worse (reference: no or unknown or stage 1 AKI); Outcome: eGFR category G2 (eGFR <90 ml/min/1.73m2 or ACR >30 mg/g) or BP ≥95th percentile				
27	250	OR 1.9 (0.7 to 4.7)[e]	VERY LOW	Could not differentiate
Predictor: stage 2 AKI or worse (reference: no or unknown or stage 1 AKI); Outcome: <90 ml/min/1.73m2				
4/26 (15.4%)	18/237 (7.6%)	RR 2.03 (0.74 to 5.53)[d]	VERY LOW	Could not differentiate
Predictor: stage 2 AKI or worse (reference: no or unknown or stage 1 AKI); Outcome: ACR >30 mg/g				
4/26 (15.4%)	28/246 (11.4%)	RR 1.35 (0.51 to 3.55)[d]	VERY LOW	Could not differentiate

(a): Could not differentiate: 95% CI are not completely between MIDs and crossing line of no effect; Effect: statistically significant and point estimate >MID

(b) Adjusted for: age at follow-up, vasopressor use, nephrotoxic medication use, sepsis during admission, >1 past medical history item at admission, and abnormal baseline eGFR

(c) Adjusted for: age at follow-up, sepsis during admission, >1 past medical history item at admission, and abnormal baseline eGFR

(d) Unadjusted, calculated by reviewer

(e) Adjusted for: age at follow-up, vasopressor use, nephrotoxic medication use, sepsis, >1 past medical history item at admission, abnormal baseline eGFR, and nephrotoxic medication use interaction term with AKI

Harer 2017 (prospective cohort study in children who were admitted to neonatal intensive care unit admission before 2 days of life weighing ≤1,500 g)

AKI	No AKI	Effect size (95% CI)	Quality	Interpretation of effect[a]
Predictor: AKI (reference: no AKI); Outcome: renal dysfunction (eGFR <90 mL/min/1.73 m2 or UPC >0.2 or BP >95th percentile)				

AKI	No AKI	Effect size (95% CI)	Quality	Interpretation of effect[a]
13/20 (65%)	2/14 (14.3%)	RR 4.5 (1.2 to 17.1)[b]	VERY LOW	Effect
Predictor: AKI (reference: no AKI); Outcome: eGFR <90 mL/min/1.73 m2				
7/20 (35%)	2/14 (14.3%)	RR 1.5 (0.8 to 2.5)[b]	VERY LOW	Could not differentiate
Predictor: AKI (reference: no AKI); Outcome: UPC >0.2				
4/20 (20%)	0/14 (0%)	RR 1.9 (0.9 to 2.6)[b]	LOW	Could not differentiate

(a): Could not differentiate: 95% CI are not completely between MIDs and crossing line of no effect; Effect: statistically significant and point estimate >MID

(b) Unclear if relative risk was adjusted

Hessey 2019 (retrospective cohort study in children and young people with a first hospitalisation to a paediatric intensive care unit during study period)

AKI	No AKI	Effect size (95% CI)	Quality	Interpretation of effect[a]
Predictor: AKI (reference: no AKI); Outcome: CKD				
20	23	HR 2.3 (1.3 to 4.3)[b]	HIGH	Effect
Predictor: stage 2/3 AKI (reference: no AKI/stage 1 AKI); Outcome: CKD				
9	34	HR 2.1 (1.0 to 4.4)[b]	MODERATE	Could not differentiate
Predictor: stage 1 AKI (reference: no AKI); Outcome: CKD				
11	23	HR 2.2 (1.1 to 4.5)[b]	MODERATE	Effect
Predictor: stage 2/3 AKI (reference: no AKI); Outcome: CKD				
9	23	HR 2.5 (1.1 to 5.7)[b]	MODERATE	Effect

(a): Could not differentiate: 95% CI are not completely between MIDs and crossing line of no effect; Effect: statistically significant and point estimate >MID

(b) Adjusted for Paediatric Medical Complexity Algorithm and nephrotoxic antibiotic use in the paediatric intensive care unit

Hollander 2016 (retrospective cohort study in children and young people with orthotopic heart transplantation)

AKI	No AKI	Effect size (95% CI)	Quality	Interpretation of effect[a]
Predictor: AKI (reference: no AKI); Outcome: CKD at 6 months				
3/60 (5%)	0/22 (0%)	RR 2.6 (0.14 to 49.14)[b]	VERY LOW	Could not differentiate
Predictor: AKI (reference: no AKI); Outcome: CKD at 12 months				
3/54 (5.6%)	1/22 (4.5%)	RR 1.22 (0.13 to 11.12)[b]	VERY LOW	Could not differentiate

(a): Could not differentiate: 95% CI are not completely between MIDs and crossing line of no effect; Effect: statistically significant and point estimate >MID

(b) Unadjusted, calculated by reviewer

Williams 2017 (retrospective cohort study in children and young people first-time recipients who received a non-kidney solid organ transplant, including heart, lung, liver, and multiorgan transplant [any combination of bowel, liver, stomach, and pancreas])

AKI	No AKI	Effect size (95% CI)	Quality	Interpretation of effect[a]
Predictor: perioperative AKI (reference: no AKI); Outcome: CKD				

AKI	No AKI	Effect size (95% CI)	Quality	Interpretation of effect[a]
203	100	HR 1.84 (0.66 to 5.1)[b]	MODERATE	Could not differentiate
Predictor (up to 3 months after transplant): 1 AKI event (reference: 0 AKI events); Outcome: CKD				
64	221	HR 2.77 (1.13 to 6.8)[c]	MODERATE	Effect
Predictor (up to 3 months after transplant): 2 or more AKI events (reference: 0 AKI events); Outcome: CKD				
18	221	HR 3.53 (0.94 to 13.2)[c]	MODERATE	Could not differentiate
Predictor (up to 6 months after transplant): 1 AKI event (reference: 0 AKI events); Outcome: CKD				
69	206	HR 2.14 (0.79 to 5.8)[c]	LOW	Could not differentiate
Predictor (up to 6 months after transplant): 2 or more AKI events (reference: 0 AKI events); Outcome: CKD				
28	206	HR 2.77 (0.76 to 10.1)[c]	LOW	Could not differentiate
Predictor (up to 12 months after transplant): 1 AKI event (reference: 0 AKI events); Outcome: CKD				
68	195	HR 2.24 (0.54 to 9.25)[c]	LOW	Could not differentiate
Predictor (up to 3 months after transplant): 1 or more AKI events (reference: 0 AKI events); Outcome: mortality				
82	221	HR 1.84 (0.86 to 3.92)[d]	MODERATE	Could not differentiate
Predictor (up to 6 months after transplant): 1 or more AKI events (reference: 0 AKI events); Outcome: mortality				
97	206	HR 2.03 (0.89 to 4.64)[d]	MODERATE	Could not differentiate
Predictor (up to 12 months after transplant): 1 or more AKI events (reference: 0 AKI events); Outcome: mortality				
108	195	HR 1.90 (0.7 to 5.14)[d]	MODERATE	Could not differentiate

(a): Could not differentiate: 95% CI are not completely between MIDs and crossing line of no effect; Effect: statistically significant and point estimate >MID
(b) Adjusted for age, sex, and eGFR at time of transplant
(c) Association of post-transplant AKI episodes with development of CKD accounting for competing risks (death, retransplant). Model was adjusted for age, sex, and glomerular filtration rate at time of transplant
(d) Association of AKI with risk of mortality accounting for competing risk of retransplant. Model was adjusted for age, sex, glomerular filtration rate at time of transplant, and underlying diagnosis

Poggiali 2019 (retrospective cohort study in children with solitary functioning kidney)

Predictor	Reference	Effect size (95% CI)	Quality	Interpretation of effect[a]
Predictor: multicystic dysplastic kidney (reference: hypodysplasia/agenesis); Outcome: CKD				
6/132 (4.5%)	3/30 (10%)	HR 2.52 (0.62 to 10.0)	VERY LOW	Could not differentiate
Predictor: presence of contralateral CAKUT (reference: absence of contralateral CAKUT); Outcome: CKD				

Predictor	Reference	Effect size (95% CI)	Quality	Interpretation of effect[a]
43	119	HR 62.2 (3.7 to 115.7)	LOW	Effect
Predictor: low birth weight (reference: normal birth weight); Outcome: CKD				
32	130	HR 3.31 (0.89 to 12.3)	VERY LOW	Could not differentiate
Predictor: multicystic dysplastic kidney (reference: hypodysplasia/agenesis); Outcome: renal injury events (eGFR <60 ml/min/1.73 m2, hypertension, and proteinuria)				
30/132 (22.7%)	11/30 (36.7%)	HR 2.06 (0.73 to 5.8)	VERY LOW	Could not differentiate
Predictor: presence of contralateral CAKUT (reference: absence of contralateral CAKUT); Outcome: renal injury events (eGFR <60 ml/min/1.73 m2, hypertension, and proteinuria)				
43	119	HR 13.3 (4.3 to 41.2)	LOW	Effect
Predictor: low birth weight (reference: normal birth weight); Outcome: renal injury events (eGFR <60 ml/min/1.73 m2, hypertension, and proteinuria)				
32	130	HR 2.69 (1.03 to 6.98)	VERY LOW	Effect
Predictor: multicystic dysplastic kidney (reference: hypodysplasia/agenesis); Outcome: hypertension				
7/132 (5.3%)	4/30 (13.3%)	HR 3.0 (0.87 to 10.3)	VERY LOW	Could not differentiate
Predictor: presence of contralateral CAKUT (reference: absence of contralateral CAKUT); Outcome: hypertension				
43	119	HR 6.2 (1.78 to 21.5)	LOW	Effect
Predictor: low birth weight (reference: normal birth weight); Outcome: hypertension				
32	130	HR 2.44 (0.71 to 8.42)	VERY LOW	Could not differentiate
Predictor: multicystic dysplastic kidney (reference: hypodysplasia/agenesis); Outcome: proteinuria				
9/132 (6.8%)	3/30 (10%)	HR 2.71 (0.69 to 10.5)	VERY LOW	Could not differentiate
Predictor: presence of contralateral CAKUT (reference: absence of contralateral CAKUT); Outcome: proteinuria				
43	119	HR 1.92 (0.96 to 3.81)	LOW	Could not differentiate
Predictor: low birth weight (reference: normal birth weight); Outcome: proteinuria				
32	130	HR 2.85 (0.79 to 10.2)	VERY LOW	Could not differentiate

(a) Could not differentiate: 95% CI are not completely between MIDs and crossing line of no effect; Effect: statistically significant and point estimate >MID

Westland 2013 (retrospective cohort study in children with solitary functioning kidney and renal follow-up)

Predictor	Reference	Effect size (95% CI)	Quality	Interpretation of effect[a]
Predictor: ipsilateral CAKUT; Outcome: renal injury (hypertension, proteinuria, an impaired eGFR, or the use of renoprotective medication)				

Predictor	Reference	Effect size (95% CI)	Quality	Interpretation of effect[a]
Ipsilateral CAKUT 137	Not reported	OR 1.66 (1.02 to 2.69)[b]	LOW	Effect
Predictor: birth weight <2,500 g; Outcome: renal injury (hypertension, proteinuria, an impaired eGFR, or the use of renoprotective medication)				
Birth weight <2,500 g 56	Birth weight ≥3500, <4000 g 87	OR 2.08 (0.96 to 4.51)[c]	LOW	Could not differentiate
Predictor: acquired SFK; Outcome: renal injury (hypertension, proteinuria, an impaired eGFR, or the use of renoprotective medication)				
Acquired SFK 184	Not reported	OR 1.93 (1.26 to 2.95)[d]	MODERATE	Effect
Predictor: acquired SFK (reference: congenital SFK); Outcome: eGFR <60 mL/min/1.73m2				
Acquired SFK 16/184 (8.7%)	Congenital SFK 9/223 (4%)	RR 2.15 (0.97 to 4.76)[e]	MODERATE	Could not differentiate
Predictor: acquired SFK (reference: congenital SFK); Outcome: proteinuria				
Acquired SFK 50/184 (27.2%)	Congenital SFK 29/223 (13%)	RR 2.08 (1.38 to 3.16)[e]	HIGH	Effect

(a) Could not differentiate: 95% CI are not completely between MIDs and crossing line of no effect; Effect: statistically significant and point estimate >MID
(b) Multivariate analysis included age, acquired SFK, prenatal diagnosis of SFK, birth weight <2,500 g, urinary tract infections, and renal length SDS
(c) Multivariate analysis included age, acquired SFK, ipsilateral CAKUT, prenatal diagnosis of SFK, urinary tract infections, and renal length SDS
(d) Unadjusted
(e) Unadjusted, calculated by reviewer

See Appendix G for full GRADE tables.

1.1.7 Economic evidence

A systematic review was conducted to identify economic evaluations for this review question. The search returned 864 records which were sifted against the review protocol. All records were excluded based on title and abstract. The study selection diagram is presented in **Error! Reference source not found.**. For more information on the search strategy please see **Error! Reference source not found.**.

No published cost-effectiveness studies were included in this review and this question was not prioritised for original economic modelling.

1.1.8 The committee's discussion and interpretation of the evidence

1.1.8.1. The outcomes that matter most

The committee agreed that the key outcomes for identifying which children and young people should be tested for CKD were the diagnosis of CKD, CKD progression and all-cause mortality. All included studies reported the key outcome of diagnosis of CKD. Committee members highlighted that hypertension was a significant condition related to CKD. Therefore, it agreed that composite outcomes including CKD diagnosis and hypertension are also key outcomes for the identification of children and young people who should be tested for CKD. No evidence was found on CKD progression and only one study reported on all-cause mortality. This shortage of evidence on all-cause mortality made it harder to use it for decision making.

1.1.8.2 The quality of the evidence

Overall, the quality of the evidence was from moderate to very low, with the main reasons for downgrading being imprecision of the evidence to identify which prognostic factors could predict the development of CKD. This was shown by imprecision being serious (95% confidence interval crossing one end of the defined minimal clinically important difference [MID] interval [0.8, 1.25]) or very serious (95% confidence interval crossing both ends of the defined MID interval). Risk of bias was also a reason for downgrading the evidence (for example, not collecting data from dropouts, unadjusted risk ratios, confounders only used for composite outcomes).

The committee highlighted that there was a lack of evidence about some of the prognostic factors listed in the protocol (blood in urine, multisystem disease, low birth weight, family history of CKD, and obesity). As a result of this lack of evidence, the committee did not think a strong recommendation for these factors was justified, in spite of their clinical experience that these might be significant prognostic markers for CKD, and instead made a 'consider' recommendation. The committee developed a research recommendation to address this gap in the evidence in the hope that further research could improve the strength of this 'consider' recommendation in future updates of the guideline. The committee was aware that obesity as a risk factor had been raised during the scoping phase of the guideline, but no evidence was identified so the committee felt unable to make a recommendation. Obesity was part of the list of factors added to the research recommendation.

There were studies reporting composite outcomes which were not listed in the protocol of this review. These composite outcomes included CKD diagnosis and hypertension in their definition. The committee discussed these outcomes and agreed that hypertension was a significant condition related to CKD and therefore it was sensible to include composite outcomes. This was recorded as a protocol deviation. Composite outcomes were downgraded for indirectness as they were not part of the original protocol.

1.1.8.3 Discussions about risk factors

The committee agreed that there are important factors that increased the likelihood of a diagnosis of CKD. The included studies showed an association between acute kidney injury and the diagnosis of CKD as well as an association between solitary functioning kidney and the composite outcome of renal injury. These associations were shown by clinically important effect estimates (for example, an odds ratio of 1.93 with 95% confidence interval [CI] 1.26 to 2.95 for solitary functioning kidney and a hazard ratio of 2.3 with 95% CI 1.3 to 4.3 for acute kidney injury).

The committee also highlighted that in clinical practice, children and young people with acute kidney injury and solitary functioning kidney should be followed-up and tested to ensure early identification of CKD. Therefore, the committee agreed to make a recommendation with acute kidney injury and solitary functioning kidney as risk factors which would trigger the offering of testing for CKD.

The committee noted that there was a study including participants receiving a non-kidney solid organ transplant and that these participants are usually at higher risk of CKD because of the use of nephrotoxic medications which could also confound the association between acute kidney injury and CKD in this population. Therefore, no specific recommendations were made for this population.

The committee highlighted that there were no studies reporting on the rest of the factors listed in the protocol but pointed out that they had been added to the protocol because they were considered important in clinical practice. The committee also pointed out that a lack of evidence does not mean that they are not important clinical risk factors. The committee discussed the various risk factors at length and reached a consensus on which were likely to be the most important. Due to the lack of evidence, the committee made a 'consider'

recommendation based on their discussions and added the following risk factors for testing CKD in children and young people:

- low birth weight (≤ 2,500 g)
- diabetes
- hypertension
- cardiovascular disease
- structural renal tract disease
- recurrent renal calculi
- multisystem diseases with potential kidney involvement
- family history of end-stage kidney disease
- hereditary kidney disease
- opportunistic detection of haematuria

The committee highlighted that most of these risk factors were already listed as risk factors in the recommendation for adults and that in their experience, any risk factors in adults are likely to be risk factors in children and young people.

There were 3 recommendations in the 2014 guideline which were specific for adults. The committee agreed that these recommendations were also relevant for children and young people. One recommendation was about monitoring GFR annually in adults taking drugs known to be nephrotoxic, such as calcineurin inhibitors (for example, cyclosporin or tacrolimus), lithium and non-steroidal anti-inflammatory drugs (NSAIDs). Children and young people might be taking some of these drugs which could damage their renal function. Another recommendation was about monitoring the development or progression of CKD for at least 3 years after acute kidney injury which is relevant for adults as well as for children and young people. Finally, it was recommended not to use some factors for testing CKD such as age, gender, ethnicity, obesity (in the absence of metabolic syndrome, diabetes, or hypertension).

1.1.8.4 Cost effectiveness and resource use

No economic evidence was identified for this review question, and economic modelling was not prioritised. The committee highlighted that for CYP requiring testing for CKD, it is usually done in primary care unless the test requires specialist equipment (e.g. a smaller blood pressure cuff), in which case the testing will be done in secondary care. The committee acknowledged that the new recommendations may increase the number of CYP being tested and thus increase costs. This is due to some CYP who had AKI currently being lost to follow up due to there being no mechanism in primary care to flag previous AKI, or during the change from paediatric care to adult care. However, the costs of the tests themselves (a blood test and/or a urine test) are unlikely to significantly increase costs, and once any additional CYP with CKD have been identified, they should then follow a cost-effective pathway for future treatment and monitoring, and therefore these costs will represent an appropriate use of NHS resources.

1.1.9 Recommendations supported by this evidence review

This evidence review supports recommendations 1.1.20, 1.1.22 to 1.1.25 and the research recommendation on the association between risk factors and CKD outcomes in children and young people (see Appendix L for further details about the research recommendation).

1.1.10 References – included studies

1.1.10.1 Prognostic

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Westland, Rik, Kurvers, Roel A J, van Wijk, Joanna A E et al. (2013) Risk factors for renal injury in children with a solitary functioning kidney. Pediatrics 131(2): e478-85

Williams, C, Borges, K, Banh, T et al. (2018) Patterns of kidney injury in pediatric nonkidney solid organ transplant recipients. American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons 18(6): 1481-1488

Appendices

Appendix A – Review protocol

Review protocol for children and young people who should be tested for CKD

ID	Field	Content
0.	PROSPERO registration number	CRD42020172609
1.	Review title	Which children and young people should be tested for CKD?
2.	Review questions	Which children and young people should be tested for CKD?
3.	Objective	To determine which children and young people should be tested for CKD
4.	Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase Searches will be restricted by: • English language • Human studies

		Searches will not be restricted by date. The searches will be re-run 6 weeks before final submission of the review and further studies retrieved for inclusion. The full search strategies for MEDLINE database will be published in the final review.
5.	Condition or domain being studied	Chronic Kidney Disease
6.	Population	Inclusion: Children and young people (up to the age of 18). Exclusion: • people receiving renal replacement therapy (RRT) • people with acute kidney injury combined with rapidly progressive glomerulonephritis • pregnant young women • people receiving palliative care

. WO7.	Prognostic factor	• Congenital renal abnormalities • Acute kidney injury • Blood in urine • Multisystem disease • Low birth weight • Family history of CKD • Obesity
8.	Co- variates	Confounders identified by the studies themselves will be used
9.	Types of study to be included	• Prospective cohort studies (retrospective cohort studies will be used if no prospective studies ae found). • Systematic reviews of prospective cohort studies
10.	Other exclusion criteria	• Abstracts and conference proceedings • Theses • Non-human studies
11.	Context	NICE guideline CG182 chronic kidney disease in adults: assessment and management will be updated by this question. This guideline will be combined with guidelines CG157 chronic kidney disease (stage 4 or 5): management of hyperphosphataemia and NG 8 chronic kidney disease: managing anaemia. The guideline will be extended to cover the assessment and management of chronic kidney disease in children and young people.

12.	Primary outcomes (critical outcomes)	Adjusted (unadjusted will only be used if adjusted values are not available) hazard ratios, risk ratios and odds ratios at all reported time points for: • Diagnosis of CKD • CKD progression: change in eGFR • CKD progression: occurrence of end stage kidney disease (ESRD or ESKD as reported by the study) • All-cause mortality
13.	Secondary outcomes (important outcomes)	None.
14.	Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. 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. 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 QUIPS checklist as described in Developing NICE guidelines: the manual.
16.	Strategy for data synthesis	Where appropriate, risk ratios, odds ratios and hazard ratios will pooled using the inverse-variance method. Outcomes will only be pooled if the same set of predictor variables are used across multiple studies, have adjusted for the same confounders and are on the same scale.
17.	Analysis of sub-groups	If the data can be disambiguated, specific consideration will be given to disease stage at diagnosis
18.	Type and method of review	☐ Intervention ☐ Diagnostic ☒ Prognostic ☐ Qualitative ☐ Epidemiologic ☐ Service Delivery ☐ Other (please specify)
19.	Language	English

20.	Country	England		
21.	Anticipated or actual start date	Feb 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** Guideline Updates Team **5b Named contact e-mail** GUTprospero@nice.org.uk **5e Organisational affiliation of the review** National Institute for Health and Care Excellence (NICE)		
25.	Review team members	From the Guideline Updates Team: • Mr Chris Carmona • Dr Yolanda Martinez • Ms Omnia Abdulrazeg • Dr Joshua Pink • Mr Rui Martins • Ms Lynda Ayiku		
26.	Funding sources/sponsor	This systematic review is being completed by the Guideline Updates Team which is part of NICE.		
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or		

		changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website
29.	Other registration details	
30.	Reference/URL for published protocol	
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
32.	Keywords	Chronic Kidney Disease, eGFR measures, Cystatin C-based equations, MDRD, CKD-EI, Schwartz.

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

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Appendix B – Methods

Association studies

In this guideline, association studies are defined those reporting data showing an association of a predictor (either a single variable or a group of variables) and an outcome variable, where the data are not reported in terms of outcome classification (i.e. diagnostic/prognostic test accuracy). Data were reported as hazard ratios (if measured over time) or odds ratios or risk ratios (if measured at a specific time-point). Data reported in terms of model fit or predictive accuracy were not assessed using this method.

Quality assessment

Individual studies were quality assessed using the QUIPS checklist. Each individual study was classified into one of the following three groups based on an assessment of the overall risk of bias:

- 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, predictors and/or outcomes 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, predictors and/or outcomes.
- Partially indirect – Important deviations from the protocol in one of the population, predictors and/or outcomes.
- Indirect – Important deviations from the protocol in at least two of the population, predictors and/or outcomes.

Methods for combining association studies

Adjusted odds ratios, hazard ratios and risk ratios from multivariate models were only considered for pooling if the same set of predictor variables were used across multiple studies and if the same thresholds to measure predictors were used across studies. This was not the case for any data in this evidence review and so data was presented separately for individual studies.

Minimal clinically important differences (MIDs)

The Core Outcome Measures in Effectiveness Trials (COMET) database was searched to identify published minimal clinically important difference thresholds relevant to this guideline. Identified MIDs were assessed to ensure they had been developed and validated in a methodologically rigorous way, and were applicable to the populations, interventions and outcomes specified in this guideline. In addition, the Guideline Committee were asked to prospectively specify any outcomes where they felt a consensus MID could be defined from their experience. In particular, any questions looking to evaluate non-inferiority (that one

treatment is not meaningfully worse than another) required an MID to be defined to act as a non-inferiority margin. No MIDs were found or defined using this process.

For relative risks and odds ratios where no other MID was available, a default MID interval for dichotomous outcomes of 0.8 to 1.25 was used.

Modified GRADE for association studies

GRADE has not been developed for use with predictive studies; therefore, a modified approach was applied using the GRADE framework. Data from cohort studies was initially rated as high quality, with the quality of the evidence for each outcome then downgraded or not from this initial point.

Table 4: Rationale for downgrading quality of evidence for association studies

GRADE criteria	Reasons for downgrading quality
Risk of bias	Not serious: If the outcome was from a study judged at low risk of bias the l outcome was not downgraded. Serious: If the outcome was from a study judged at moderate risk of bias the outcome was downgraded one level. Very serious: If the outcome was from a study that was judged at high risk of bias, the outcome was downgraded two levels.
Indirectness	Not serious: If the outcome was from a study judged directly applicable, the overall outcome was not downgraded. Serious: If the outcome was from a study judged partially applicable, the outcome was downgraded one level. Very serious: If the outcome was from a study judged indirectly applicable, the outcome was downgraded two levels.
Inconsistency	Results were not synthesised and were presented for individual studies. Inconsistency could therefore not be assessed as was rated as 'not applicable'.
Imprecision	If an MID other than the line of no effect was defined for the outcome, the outcome was downgraded once if the 95% confidence interval for the effect size crossed one line of the MID, and twice if it crosses both lines of the MID. If the line of no effect was defined as an MID for the outcome (in this case for mortality), it was downgraded once if the 95% confidence interval for the effect size crossed the line of no effect (i.e. the outcome was not statistically significant).

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

- Data showing an effect size sufficiently large that it cannot be explained by confounding alone.
- Data where 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 5.

Table 5 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 6.

Table 6 Methodological criteria

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

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

Appendix C – Literature search strategies

Background to the search

A NICE information specialist conducted the literature searches for the evidence review. The searches were originally run on the 19th and 20th of March 2020 and updated on the 7th 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, letters and notes in Embase were applied in adherence to standard NICE practice.

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

Clinical searches

Databases	Date searched	Version/files	No. retrieved	RefMan data
Cochrane Central Register of Controlled Trials (CENTRAL)	19th March 2020	Issue 3 of 12, March 2020	534	391
Cochrane Database of Systematic Reviews (CDSR)	19th March 2020	Issue 3 of 12, March 2020	12	3
Database of Abstracts of Reviews of Effect (DARE)	19th March 2020	Up to 2015	116	116

Embase (Ovid)	19th March 2020	Embase <1974 to 2020 Week 11>	3,623	1728
MEDLINE (Ovid)	19th March 2020	Ovid MEDLINE(R) <1946 to March 17, 2020>	3,022	3001
MEDLINE In-Process (Ovid)	19th March 2020	Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to March 17, 2020>	332	93
MEDLINE Epub Ahead of Print[a]	19th March 2020	Ovid MEDLINE(R) Epub Ahead of Print <March 17, 2020>	57	33

The following search filters were applied in MEDLINE and Embase to identify systematic reviews and prognosis studies:

- Systematic reviews filters:
  - Lee, E. et al. (2012) An optimal search filter for retrieving systematic reviews and meta-analyses. *BMC Medical Research Methodology,* 12(1), 51.

    In MEDLINE, the standard NICE modifications were used: pubmed.tw added; systematic review.pt added from MeSH update 2019.

    In Embase, the standard NICE modifications were used: pubmed.tw added to line medline.tw.
- Prognosis filter:
  - Wilczynski NL, Haynes RB; The Hedges Team. Developing optimal search strategies for detecting clinically sound prognostic studies in MEDLINE. *BMC Medicine*. 2004;2:23 (5 pages). Optimal version used in both MEDLINE and Embase

Search strategies
Database: Ovid MEDLINE(R) <1946 to March 17, 2020> Search Strategy: ---------- 1 exp Renal Insufficiency, Chronic/ (112796) 2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (72744) 3 ((kidney* or renal*) adj1 insufficien*).tw. (21269) 4 ckd*.tw. (23018)

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

5 ((kidney* or renal*) adj1 fail*).tw. (86402)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (35281)

7 (esrd* or eskd*).tw. (14241)

8 "Chronic Kidney Disease-Mineral and Bone Disorder"/ (3454)

9 or/1-8 (213095)

10 exp Infant/ or Infant Health/ or Infant Welfare/ (1125197)

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. (839293)

12 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (1890406)

13 Minors/ (2560)

14 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (2314950)

15 exp pediatrics/ (57169)

16 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (814169)

17 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (1997796)

18 Puberty/ (13179)

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. (414356)

20 Schools/ (37149)

21 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (7135)

22 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (460285)

23 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (3885)

24 or/10-23 (5111691)

25 9 and 24 (46312)

26 prognosis.sh. (497558)

27 diagnosed.tw. (469092)

28 cohort.mp. (538784)

29 predictor:.tw. (316975)

30 death.tw. (600184)

31 exp models, statistical/ (401274)

32 or/26-31 (2349192)

33 exp causality/ (821609)

34 disease progression/ (158832)

35 (risk or risks or caus* or progress*).tw. (4460183)

36 or/33-35 (4735220)

37 32 and 36 (1050582)

38 Glomerular Filtration Rate/ (43388)

39 (glomerul* or GFR* or eGFR* or e-GFR*).tw. (157895)

40 38 or 39 (171256)

41 25 and 37 and 40 (2608)

42 (acr or uacr).tw. (9120)

43 (albumin* and creatin* and ratio*).tw. (5780)

44 42 or 43 (13190)

45 40 and 44 (2508)

46 25 and 45 (269)

47 (MEDLINE or pubmed).tw. (156564)

48 systematic review.tw. (114632)

49 systematic review.pt. (123163)

50 meta-analysis.pt. (112191)

51 intervention$.ti. (120189)

52 or/47-51 (365890)

53 25 and 36 and 52 (570)

54 41 or 46 or 53 (3267)

55 limit 54 to english language (3057)

56 animals/ not humans/ (4646694)

57 55 not 56 (3022)

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to March 17, 2020>

Search Strategy:

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1 exp Renal Insufficiency, Chronic/ (0)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (9603)

3 ((kidney* or renal*) adj1 insufficien*).tw. (1114)

4 ckd*.tw. (4620)

5 ((kidney* or renal*) adj1 fail*).tw. (6399)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (4925)

7 (esrd* or eskd*).tw. (2034)

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

9 or/1-8 (18756)

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. (78382)

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. (310724)

15 exp pediatrics/ (0)

16 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (116250)

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. (58627)

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. (66489)

23 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (569)

24 or/10-23 (450282)

25 9 and 24 (3461)

26 prognosis.sh. (0)

27 diagnosed.tw. (75382)

28 cohort.mp. (70359)

29 predictor:.tw. (44709)

30 death.tw. (69075)

31 exp models, statistical/ (0)

32 or/26-31 (233922)

33 exp causality/ (0)

34 disease progression/ (0)

35 (risk or risks or caus* or progress*).tw. (627974)

36 or/33-35 (627974)

37 32 and 36 (110566)

38 Glomerular Filtration Rate/ (0)

39 (glomerul* or GFR* or eGFR* or e-GFR*).tw. (16735)

40 38 or 39 (16735)

41 25 and 37 and 40 (220)

42 (acr or uacr).tw. (1368)

43 (albumin* and creatin* and ratio*).tw. (928)

44 42 or 43 (1976)

45 40 and 44 (473)

46 25 and 45 (39)

47 (MEDLINE or pubmed).tw. (34279)

48 systematic review.tw. (28123)

49 systematic review.pt. (732)

50 meta-analysis.pt. (40)

51 intervention$.ti. (20667)

52 or/47-51 (65732)

53 25 and 36 and 52 (95)

54 41 or 46 or 53 (335)

55 limit 54 to english language (332)

56 animals/ not humans/ (0)

57 55 not 56 (332)

Database: Ovid MEDLINE(R) Epub Ahead of Print <March 17, 2020>

Search Strategy:

---

1 exp Renal Insufficiency, Chronic/ (0)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (1377)

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

4 ckd*.tw. (704)

5 ((kidney* or renal*) adj1 fail*).tw. (747)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (708)

7 (esrd* or eskd*).tw. (319)

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

9 or/1-8 (2563)

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. (14128)

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. (48638)

15 exp pediatrics/ (0)

16 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (19975)

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. (12133)

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. (11379)

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

24 or/10-23 (71449)

25 9 and 24 (557)

26 prognosis.sh. (0)

27 diagnosed.tw. (10343)

28 cohort.mp. (16278)

29 predictor:.tw. (9194)

30 death.tw. (11038)

31 exp models, statistical/ (0)

32 or/26-31 (41105)

33 exp causality/ (0)

34 disease progression/ (0)

35 (risk or risks or caus* or progress*).tw. (89850)

36 or/33-35 (89850)

37 32 and 36 (20103)

38 Glomerular Filtration Rate/ (0)

39 (glomerul* or GFR* or eGFR* or e-GFR*).tw. (2275)

40 38 or 39 (2275)

41 25 and 37 and 40 (39)

42 (acr or uacr).tw. (267)

43 (albumin* and creatin* and ratio*).tw. (107)

44 42 or 43 (327)

45 40 and 44 (58)

46 25 and 45 (7)

47 (MEDLINE or pubmed).tw. (6838)

48 systematic review.tw. (6596)

49 systematic review.pt. (32)

50 meta-analysis.pt. (27)

51 intervention$.ti. (3917)

52 or/47-51 (13349)

53 25 and 36 and 52 (14)

54 41 or 46 or 53 (57)

55 limit 54 to english language (57)

56 animals/ not humans/ (0)

57 55 not 56 (57)

Database: Embase <1974 to 2020 Week 11>

Search Strategy:

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1 exp kidney failure/ (350445)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (122358)

3 ((kidney* or renal*) adj1 insufficien*).tw. (29985)

4 ckd*.tw. (49147)

5 ((kidney* or renal*) adj1 fail*).tw. (131904)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (57901)

7 (esrd* or eskd*).tw. (27079)

8 or/1-7 (442435)

9 exp juvenile/ or Child Behavior/ or Child Welfare/ or Child Health/ or infant welfare/ or "minor (person)"/ or elementary student/ (3375677)

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. (1188742)

11 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,ad,jw. (3574808)

12 exp pediatrics/ (104140)

13 (pediatric* or paediatric* or peadiatric*).ti,ab,in,ad,jw. (1609815)

14 exp adolescence/ or exp adolescent behavior/ or adolescent health/ or high school student/ or middle school student/ (102538)

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. (646800)

16 school/ or high school/ or kindergarten/ or middle school/ or primary school/ or nursery school/ or day care/ (101920)

17 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jw. (685725)

18 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (7249)

19 or/9-18 (6324586)

20 8 and 19 (86715)

21 prognosis.sh. (569416)

22 diagnosed.tw. (907520)

23 cohort.mp. (1008130)

24 predictor:.tw. (563382)

25 death.tw. (964676)

26 exp models, statistical/ (159256)

27 or/21-26 (3562695)

28 causality/ (2564)

29 disease exacerbation/ (110573)

30 (risk or risks or caus* or progress*).tw. (6991167)

31 or/28-30 (7047990)

32 27 and 31 (1649054)

33 exp glomerulus filtration rate/ (97608)

34 (glomerul* or GFR* or eGFR* or e-GFR*).tw. (263348)

35 33 or 34 (291941)

36 20 and 32 and 35 (4315)

37 (acr or uacr).tw. (27872)

38 (albumin* and creatin* and ratio*).tw. (11333)

39 37 or 38 (35500)

40 35 and 39 (6009)

41 20 and 40 (506)

42 (MEDLINE or pubmed).tw. (247752)

43 exp systematic review/ or systematic review.tw. (284410)

44 meta-analysis/ (182180)

45 intervention$.ti. (193611)

46 or/42-45 (631730)

47 20 and 31 and 46 (1548)

48 36 or 41 or 47 (6072)

49 limit 48 to (conference abstract or conference paper or "conference review" or letter or note) (2143)

50 48 not 49 (3929)

51 limit 50 to english language (3682)

52 nonhuman/ not human/ (4587491)

53 51 not 52 (3623)

Cochrane Library

#1 MeSH descriptor: [Renal Insufficiency, Chronic] explode all trees 6453

#2 (((chronic* or progressi*) near/1 (renal* or kidney*))):ti,ab,kw 9980

#3 (((kidney* or renal*) near/1 insufficien*)):ti,ab,kw 5215

#4 (ckd*):ti,ab,kw 4721

#5 (((kidney* or renal*) near/1 fail*)):ti,ab,kw 15794

#6 (((endstage* or end-stage* or "end stage*") near/1 (renal* or kidney*))):ti,ab,kw 4333

#7 ((esrd* or eskd*)):ti,ab,kw 1972

#8 MeSH descriptor: [Chronic Kidney Disease-Mineral and Bone Disorder] this term only 85

#9 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 25177

#10 MeSH descriptor: [Infant] explode all trees 15691

#11 MeSH descriptor: [Infant Health] this term only 45

#12 MeSH descriptor: [Infant Welfare] this term only 82

#13 ((prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies* or toddler*)):ti,ab,kw 85631

#14 ((prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies* or toddler*)):so 4898

#15 MeSH descriptor: [Child] explode all trees 1238

#16 MeSH descriptor: [Child Behavior] explode all trees 2007

#17 MeSH descriptor: [Child Health] this term only 87

#18 MeSH descriptor: [Child Welfare] this term only 320

#19 MeSH descriptor: [Minors] this term only 8

#20 ((child* or minor or minors or boy* or girl* or kid or kids or young*)):ti,ab,kw 254791

#21 ((child* or minor or minors or boy* or girl* or kid or kids or young*)):so 9986

#22 MeSH descriptor: [Pediatrics] explode all trees 646

#23 ((pediatric* or paediatric* or peadiatric*)):ti,ab,kw 32099

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

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

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

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

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

#29 ((adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*)):ti,ab,kw 135672

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

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

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

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

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

#35 ((pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*)):ti,ab,kw 93803

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

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

#38 {or #10-#37} 404453

#39 #9 and #38 3842

#40 MeSH descriptor: [Glomerular Filtration Rate] this term only 2596

#41 (glomerul* or GFR* or eGFR* or e-GFR*):ti,ab,kw 17719

#42 #40 or #41 17719

#43 #39 and #42 969

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

#45 #43 not #44 546

CRD databases

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

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

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

28 (((ckd*))) 93 Delete

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

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

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

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

33	#25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32	1407	Delete
34	(((glomerul* or GFR* or eGFR* or e-GFR*)))	416	Delete
35	((MeSH DESCRIPTOR Glomerular Filtration Rate EXPLODE ALL TREES))	92	Delete
36	#34 OR #35	416	Delete
37	#33 AND #36	151	Delete

1

2

3 **Cost-effectiveness searches**

4

Databases	Date searched	Version/files	No. retrieved
MEDLINE (Ovid)	19th March 2020	Ovid MEDLINE(R) <1946 to March 17, 2020>	415
MEDLINE in Process (Ovid)	19th March 2020	Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to March 17, 2020>	41
MEDLINE epub (Ovid)	19th March 2020	: Ovid MEDLINE(R) Epub Ahead of Print <March 17, 2020>	4
Embase (Ovid)	19th March 2020	Embase <1974 to 2020 Week 11>	653
EconLit (Ovid)	19th March 2020	Econlit <1886 to March 12, 2020>	0
NHS Economic Evaluation Database (NHS EED) (legacy database)	20th March 2020	Up to 2015	28
CRD HTA	20th March 2020	Up to 2018	7

5

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

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

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

Search strategies

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

Search Strategy:

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1 exp Renal Insufficiency, Chronic/ (112810)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (72758)

3 ((kidney* or renal*) adj1 insufficien*).tw. (21269)

4 ckd*.tw. (23029)

5 ((kidney* or renal*) adj1 fail*).tw. (86405)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (35282)

7 (esrd* or eskd*).tw. (14242)

8 "Chronic Kidney Disease-Mineral and Bone Disorder"/ (3454)

9 or/1-8 (213113)

10 exp Infant/ or Infant Health/ or Infant Welfare/ (1125305)

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. (839402)

12 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (1890646)

13 Minors/ (2560)

14 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (2315397)

15 exp pediatrics/ (57183)

16 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (814385)

17 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (1998055)

18 Puberty/ (13180)

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. (414461)

20 Schools/ (37159)

21 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (7135)

22 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (460368)

23 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (3887)

24 or/10-23 (5112420)

25 9 and 24 (46316)

26 Glomerular Filtration Rate/ (43395)

27 (glomerul* or GFR* or eGFR* or e-GFR*).tw. (157913)

28 26 or 27 (171274)

29 Economics/ (27147)

30 exp "Costs and Cost Analysis"/ (233462)

31 Economics, Dental/ (1911)

32 exp Economics, Hospital/ (24303)

33 exp Economics, Medical/ (14167)

34 Economics, Nursing/ (3997)

35 Economics, Pharmaceutical/ (2918)

36 Budgets/ (11242)

37 exp Models, Economic/ (14771)

38 Markov Chains/ (14037)

39 Monte Carlo Method/ (27895)

40 Decision Trees/ (10959)

41 econom$.tw. (232672)

42 cba.tw. (9706)

43 cea.tw. (20262)

44 cua.tw. (978)

45 markov$.tw. (17565)

46 (monte adj carlo).tw. (29426)

47 (decision adj3 (tree$ or analys$)).tw. (13015)

48 (cost or costs or costing$ or costly or costed).tw. (450052)

49 (price$ or pricing$).tw. (32786)

50 budget$.tw. (23267)

51 expenditure$.tw. (48353)

52 (value adj3 (money or monetary)).tw. (2051)

53 (pharmacoeconomic$ or (pharmaco adj economic$)).tw. (3448)

54 or/29-53 (907619)

55 "Quality of Life"/ (189522)

56 quality of life.tw. (223478)

57 "Value of Life"/ (5685)

58 Quality-Adjusted Life Years/ (11884)

59 quality adjusted life.tw. (10455)

60 (qaly$ or qald$ or qale$ or qtime$).tw. (8590)

61 disability adjusted life.tw. (2586)

62 daly$.tw. (2360)

63 Health Status Indicators/ (23233)

64 (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. (22064)

65 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (1301)

66 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (4757)

67 (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)

68 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (378)

69 (euroqol or euro qol or eq5d or eq 5d).tw. (8606)

70 (qol or hql or hqol or hrqol).tw. (42722)

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

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

73 utilit$.tw. (167187)

74 (hui or hui1 or hui2 or hui3).tw. (1269)

75 disutili$.tw. (375)

76 rosser.tw. (92)

77 quality of wellbeing.tw. (13)

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

79 qwb.tw. (188)

80 willingness to pay.tw. (4302)

81 standard gamble$.tw. (774)

82 time trade off.tw. (1015)

83 time tradeoff.tw. (230)

84 tto.tw. (880)

85 or/55-84 (480838)

86 54 or 85 (1321784)

87 25 and 28 and 86 (415)

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

Search Strategy:

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1 exp Renal Insufficiency, Chronic/ (0)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (9528)

3 ((kidney* or renal*) adj1 insufficien*).tw. (1109)

4 ckd*.tw. (4579)

5 ((kidney* or renal*) adj1 fail*).tw. (6376)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (4906)

7 (esrd* or eskd*).tw. (2021)

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

9 or/1-8 (18651)

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. (77994)

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. (309089)

15 exp pediatrics/ (0)

16 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (115481)

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. (58294)

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. (66229)

23 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (563)

24 or/10-23 (448037)

25 9 and 24 (3439)

26 Glomerular Filtration Rate/ (0)

27 (glomerul* or GFR* or eGFR* or e-GFR*).tw. (16636)

28 26 or 27 (16636)

29 Economics/ (0)

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

31 Economics, Dental/ (0)

32 exp Economics, Hospital/ (0)

33 exp Economics, Medical/ (0)

34 Economics, Nursing/ (0)

35 Economics, Pharmaceutical/ (0)

36 Budgets/ (0)

37 exp Models, Economic/ (0)

38 Markov Chains/ (0)

39 Monte Carlo Method/ (0)

40 Decision Trees/ (0)

41 econom$.tw. (44358)

42 cba.tw. (429)

43 cea.tw. (1916)

44 cua.tw. (200)

45 markov$.tw. (5672)

46 (monte adj carlo).tw. (16783)

47 (decision adj3 (tree$ or analys$)).tw. (2376)

48 (cost or costs or costing$ or costly or costed).tw. (95088)

49 (price$ or pricing$).tw. (5681)

50 budget$.tw. (4918)

51 expenditure$.tw. (6334)

52 (value adj3 (money or monetary)).tw. (342)

53 (pharmacoeconomic$ or (pharmaco adj economic$)).tw. (482)

54 or/29-53 (164315)

55 "Quality of Life"/ (0)

56 quality of life.tw. (38142)

57 "Value of Life"/ (0)

58 Quality-Adjusted Life Years/ (0)

59 quality adjusted life.tw. (1683)

60 (qaly$ or qald$ or qale$ or qtime$).tw. (1417)

61 disability adjusted life.tw. (538)

62 daly$.tw. (492)

63 Health Status Indicators/ (0)

64 (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. (2609)

65 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (751)

66 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (729)

67 (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)

68 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (17)

69 (euroqol or euro qol or eq5d or eq 5d).tw. (1594)

70 (qol or hql or hqol or hrqol).tw. (7251)

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

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

73 utilit$.tw. (31052)

74 (hui or hui1 or hui2 or hui3).tw. (191)

75 disutili$.tw. (70)

76 rosser.tw. (5)

77 quality of wellbeing.tw. (8)

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

79 qwb.tw. (14)

80 willingness to pay.tw. (938)

81 standard gamble$.tw. (59)

82 time trade off.tw. (120)

83 time tradeoff.tw. (16)

84 tto.tw. (125)

85 or/55-84 (71465)

86 54 or 85 (226347)

87 25 and 28 and 86 (41)

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

Search Strategy:

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1 exp Renal Insufficiency, Chronic/ (0)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (1383)

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

4 ckd*.tw. (707)

5 ((kidney* or renal*) adj1 fail*).tw. (746)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (713)

7 (esrd* or eskd*).tw. (320)

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

9 or/1-8 (2569)

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. (14111)

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. (48642)

15 exp pediatrics/ (0)

16 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (19952)

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. (12145)

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. (11383)

23 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (108)

24 or/10-23 (71454)

25 9 and 24 (560)

26 Glomerular Filtration Rate/ (0)

27 (glomerul* or GFR* or eGFR* or e-GFR*).tw. (2274)

28 26 or 27 (2274)

29 Economics/ (0)

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

31 Economics, Dental/ (0)

32 exp Economics, Hospital/ (0)

33 exp Economics, Medical/ (0)

34 Economics, Nursing/ (0)

35 Economics, Pharmaceutical/ (0)

36 Budgets/ (0)

37 exp Models, Economic/ (0)

38 Markov Chains/ (0)

39 Monte Carlo Method/ (0)

40 Decision Trees/ (0)

41 econom$.tw. (5868)

42 cba.tw. (65)

43 cea.tw. (322)

44 cua.tw. (16)

45 markov$.tw. (696)

46 (monte adj carlo).tw. (1168)

47 (decision adj3 (tree$ or analys$)).tw. (416)

48 (cost or costs or costing$ or costly or costed).tw. (12309)

49 (price$ or pricing$).tw. (874)

50 budget$.tw. (532)

51 expenditure$.tw. (1101)

52 (value adj3 (money or monetary)).tw. (72)

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

54 or/29-53 (20062)

55 "Quality of Life"/ (0)

56 quality of life.tw. (6863)

57 "Value of Life"/ (0)

58 Quality-Adjusted Life Years/ (0)

59 quality adjusted life.tw. (400)

60 (qaly$ or qald$ or qale$ or qtime$).tw. (350)

61 disability adjusted life.tw. (106)

62 daly$.tw. (94)

63 Health Status Indicators/ (0)

64 (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. (444)

65 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (40)

66 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (160)

67 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. (1)

68 (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)

69 (euroqol or euro qol or eq5d or eq 5d).tw. (370)

70 (qol or hql or hqol or hrqol).tw. (1366)

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

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

73 utilit$.tw. (4589)

74 (hui or hui1 or hui2 or hui3).tw. (16)

75 disutili$.tw. (12)

76 rosser.tw. (0)

77 quality of wellbeing.tw. (1)

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

79 qwb.tw. (2)

80 willingness to pay.tw. (170)

81 standard gamble$.tw. (7)

82 time trade off.tw. (15)

83 time tradeoff.tw. (2)

84 tto.tw. (22)

85 or/55-84 (11739)

86 54 or 85 (30050)

87 25 and 28 and 86 (4)

Database: Embase <1974 to 2020 Week 11>

Search Strategy:

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1 exp kidney failure/ (350445)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (122358)

3 ((kidney* or renal*) adj1 insufficien*).tw. (29985)

4 ckd*.tw. (49147)

5 ((kidney* or renal*) adj1 fail*).tw. (131904)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (57901)

7 (esrd* or eskd*).tw. (27079)

8 or/1-7 (442435)

9 exp juvenile/ or Child Behavior/ or Child Welfare/ or Child Health/ or infant welfare/ or "minor (person)"/ or elementary student/ (3375677)

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. (1188742)

11 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,ad,jw. (3574808)

12 exp pediatrics/ (104140)

13 (pediatric* or paediatric* or peadiatric*).ti,ab,in,ad,jw. (1609815)

14 exp adolescence/ or exp adolescent behavior/ or adolescent health/ or high school student/ or middle school student/ (102538)

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. (646800)

16 school/ or high school/ or kindergarten/ or middle school/ or primary school/ or nursery school/ or day care/ (101920)

17 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jw. (685725)

18 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (7249)

19 or/9-18 (6324586)

20 8 and 19 (86715)

21 exp glomerulus filtration rate/ (97608)

22 (glomerul* or GFR* or eGFR* or e-GFR*).tw. (263348)

23 21 or 22 (291941)

24 20 and 23 (16336)

25 exp Health Economics/ (831492)

26 exp "Health Care Cost"/ (286589)

27 exp Pharmacoeconomics/ (199933)

28 Monte Carlo Method/ (39392)

29 Decision Tree/ (12362)

30 econom$.tw. (357474)

31 cba.tw. (12620)

32 cea.tw. (34095)

33 cua.tw. (1464)

34 markov$.tw. (29607)

35 (monte adj carlo).tw. (47321)

36 (decision adj3 (tree$ or analys$)).tw. (22522)

37 (cost or costs or costing$ or costly or costed).tw. (750621)

38 (price$ or pricing$).tw. (55938)

39 budget$.tw. (37749)

40 expenditure$.tw. (73045)

41 (value adj3 (money or monetary)).tw. (3375)

42 (pharmacoeconomic$ or (pharmaco adj economic$)).tw. (8531)

43 or/25-42 (1718044)

44 "Quality of Life"/ (456160)

45 Quality Adjusted Life Year/ (25865)

46 Quality of Life Index/ (2740)

47 Short Form 36/ (27969)

48 Health Status/ (125087)

49 quality of life.tw. (425064)

50 quality adjusted life.tw. (19111)

51 (qaly$ or qald$ or qale$ or qtime$).tw. (19568)

52 disability adjusted life.tw. (3906)

53 daly$.tw. (3840)

54 (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. (40531)

55 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (2359)

56 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (9160)

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

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

59 (euroqol or euro qol or eq5d or eq 5d).tw. (19684)

60 (qol or hql or hqol or hrqol).tw. (93641)

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

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

63 utilit$.tw. (281370)

64 (hui or hui1 or hui2 or hui3).tw. (2211)

65 disutili$.tw. (901)

66 rosser.tw. (119)

67 quality of wellbeing.tw. (42)

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

69 qwb.tw. (244)

70 willingness to pay.tw. (8464)

71 standard gamble$.tw. (1092)

72 time trade off.tw. (1674)

73 time tradeoff.tw. (288)

74 tto.tw. (1632)

75 or/44-74 (961184)

76 43 or 75 (2526627)

77 24 and 76 (1077)

78 limit 77 to english language (1031)

79 nonhuman/ not human/ (4587491)

80 78 not 79 (1017)

81 limit 80 to (conference abstract or conference paper or "conference review" or letter or note) (364)

82 80 not 81 (653)

Database: Econlit <1886 to March 12, 2020>

Search Strategy:

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

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

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

4 ckd*.tw. (5)

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

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

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

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

9 or/1-8 (101)

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

11 (prematur* or pre-matur* or preterm* or pre-term* or infan* or newborn* or new-born* or perinat* or peri-nat* or neonat* or neo-nat* or baby* or babies or toddler*).ti,ab,in,jn. (5672)

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. (47291)

15 [exp pediatrics/] (0)

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

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

18 [Puberty/] (0)

19 (adolescen* or pubescen* or prepubescen* or pre-pubescen* or pubert* or prepubert* or pre-pubert* or teen* or preteen* or pre-teen* or juvenil* or youth* or under*age*).ti,ab,in,jn. (9181)

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. (49579)

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

24 or/10-23 (94925)

25 9 and 24 (5)

26 [Glomerular Filtration Rate/] (0)

27 (glomerul* or GFR* or eGFR* or e-GFR*).tw. (12)

28 26 or 27 (12)

29 25 and 28 (0)

CRD databases

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

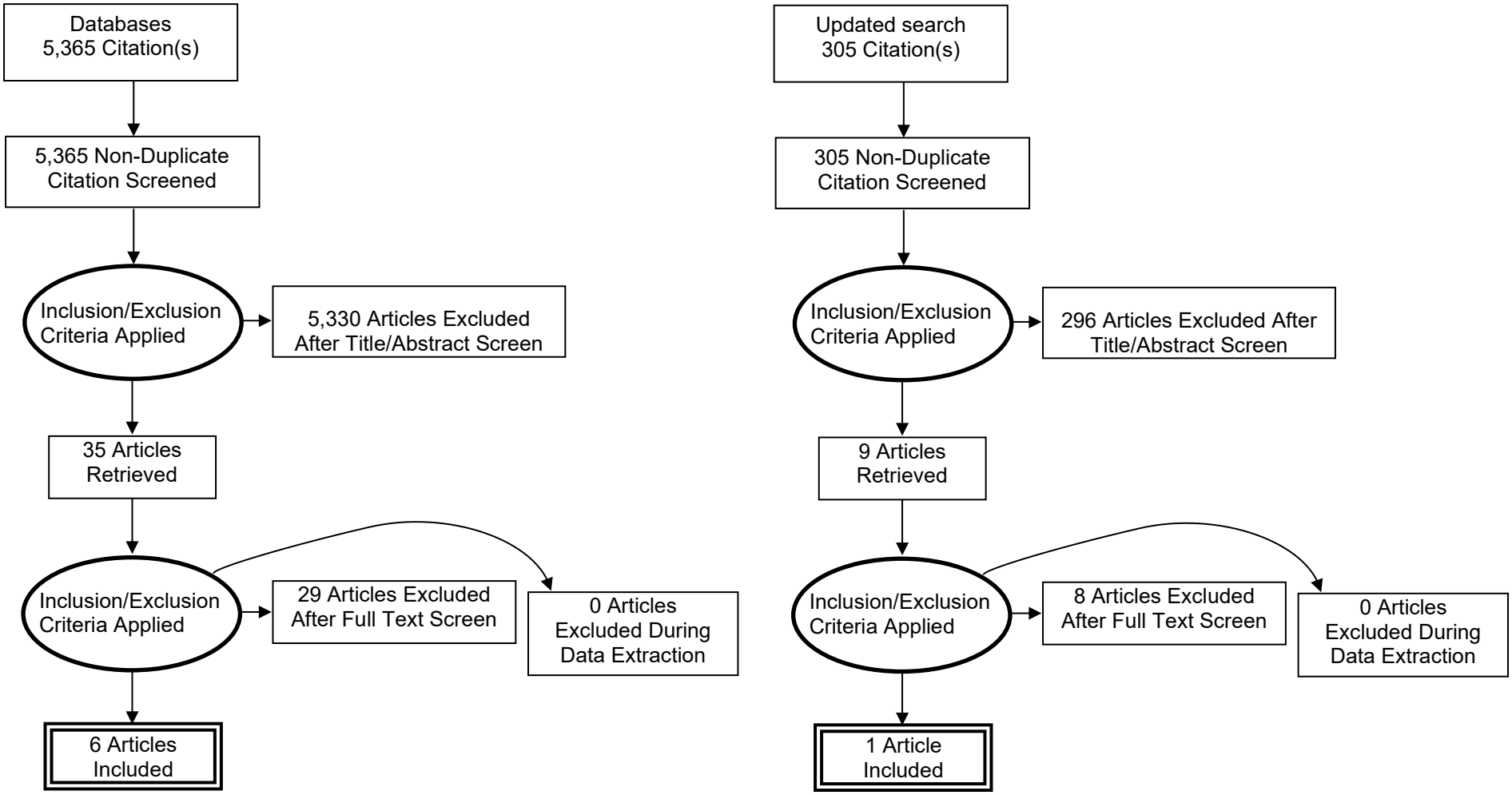
26 (((((chronic* or progressi*) near1 (renal* or kidney*))))) 489 Delete

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

28	(((ckd*)))	93	Delete
29	(((((kidney* or renal*) near1 fail*))))	836	Delete
30	(((((endstage* or end-stage* or "end stage*") near1 (renal* or kidney*)))))	354	Delete
31	((((esrd* or eskd*))))	150	Delete
32	((MeSH DESCRIPTOR Chronic Kidney Disease-Mineral and Bone Disorder))	0	Delete
33	#25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32	1407	Delete
34	(((glomerul* or GFR* or eGFR* or e-GFR*)))	416	Delete
35	((MeSH DESCRIPTOR Glomerular Filtration Rate EXPLODE ALL TREES))	92	Delete
36	#34 OR #35	416	Delete
37	#33 AND #36	151	Delete

1

Appendix D –Prognostic evidence study selection



Appendix E – Prognostic evidence tables

Benisty, 2020

Bibliographic Reference	Benisty, K.; Morgan, C.; Hessey, E.; Huynh, L.; Joffe, A.R.; Garros, D.; Dancea, A.; Sauve, R.; Palijan, A.; Pizzi, M.; Bhattacharya, S.; Doucet, J.A.; Cockovski, V.; Gottesman, R.G.; Goldstein, S.L.; Zappitelli, M.; Kidney and blood pressure abnormalities 6 years after acute kidney injury in critically ill children: a prospective cohort study; Pediatric Research; 2020

Study Characteristics

Study design	Prospective cohort study
Study details	Study location Canada Study setting Hospital Study dates 2005 - 2011 Duration of follow-up 6 years and 6 months Loss to follow-up 102 out of 379 (27%) Sources of funding Canadian Institutes of Health Research and McGill University Health Centre
Inclusion criteria	Age <18 years old at paediatric intensive care unit admission Hospital admission Paediatric intensive care unit admission

Exclusion criteria	Pre-existing renal disease Pre-existing kidney transplant or dialysis; baseline (pre-illness) eGFR <30% normal for age or known chronic kidney conditions (e.g., tubulopathy, glomerular diseases) Other conditions Children admitted to the PICU for cardiac surgery Other criteria Unwillingness to return to the study centre for assessments or lived too far (>3.5-h drive) from the study centre for home visits
Sample characteristics	Sample size 277 (No/unknown AKI: 208; with AKI: 69) Female No/unknown AKI: 38%; with AKI: 45% Mean age (SD) at admission No/unknown AKI: median 1.4 years (IQR 8.1); with AKI: median 3.8 years (IQR 9.0) Mean age (SD) at follow-up No/unknown AKI: median 7.3 years (IQR 8.1); with AKI: median 9.6 years (IQR 9.2) eGFR at baseline No/unknown AKI: median 91 ml/min/1.73m² (IQR 67); with AKI: median 120 ml/min/1.73m² (IQR 29) Abnormal baseline eGFR % eGFR <90 ml/min/1.73 m²: no/unknown AKI (9%); with AKI (2%)
Prognostic factors	Acute kidney injury Defined based on the serum creatinine criteria (SCr) of the Kidney Disease: Improving Global Outcomes (KDIGO) definition (≥1.5 times baseline within 7 days or ≥26.5 µmol/l SCr rise from baseline within 48 h). When baseline SCr was unknown, it was estimated using the Chronic Kidney Disease in Children (CKiD) SCr-based bedside GFR (eGFR) equation; assuming baseline eGFR = 120 ml/min/1.73m2 in children >2 years old and assuming age-specific normative GFR values in children <2 years old. When height was missing, a validated age-based eGFR equation was used to estimate baseline SCr. Severe AKI was also evaluated (≥stage 2; SCr ≥2 times baseline). For primary analyses, patients with no SCr available were classified as non-AKI, as previously performed in adult studies (with a rationale that they were likely less ill and at lower risk for AKI).
Outcomes	Diagnosis of CKD eGFR category G2: presence of eGFR <90 ml/min/1.73m² or albuminuria (urine albumin/creatinine >3 mg/mmol). Additional comments This study reported 2 composite outcomes: 1) eGFR category G2 or pre-hypertension (≥90 percentile); 2) eGFR category G2 or hypertension (≥95 percentile)

Risk of bias

Section	Answer
Study participation	Low risk of bias
Study Attrition	Low risk of bias
Prognostic factor measurement	Low risk of bias
Outcome Measurement	Low risk of bias
Study Confounding	Moderate risk of bias *(Confounders were only used for the composite outcome; missing confounder data was not reported)*
Statistical Analysis and Reporting	Low risk of bias
Overall risk of bias	Moderate
Overall directness	Directly applicable

Harer, 2017

Bibliographic Reference	Harer, M.W.; Pope, C.F.; Conaway, M.R.; Charlton, J.R.; Follow-up of Acute kidney injury in Neonates during Childhood Years (FANCY): a prospective cohort study; Pediatric Nephrology; 2017; vol. 32 (no. 6); 1067-1076

Study Characteristics

Study design	Prospective cohort study
Study details	Study location US Study setting

	Neonatal intensive care unit Study dates 2014 - 2016 Duration of follow-up 5 years Loss to follow-up With AKI: 5 out of 25 (20%); without AKI: 3 out of 17 (18%) Sources of funding University of Virginia Children's Hospital Fellow Grant and the 100 Women Who Care
Inclusion criteria	Weight ≤1,500 g Hospital admission Neonatal intensive care unit admission before 2 days of life
Exclusion criteria	Other conditions Patients with congenital anomalies of the kidney or urinary tract
Sample characteristics	Sample size 34 (with AKI: 20; without AKI: 14) Female With AKI: 50%; without AKI: 71% Mean age (SD) at admission Gestational age: With AKI (median 25 weeks [IQR 24, 26]); without AKI (median 29 weeks [IQR 27, 29]) Mean age (SD) at follow-up With AKI: median 5 years (IQR 4, 5); without AKI: median 5 years (IQR 4, 6) eGFR at follow-up eGFR (Schwartz): with AKI (median 111 [IQR 100, 120]); without AKI (median 124 [IQR 105, 134])
Prognostic factors	Acute kidney injury AKI was classified using the modified KDIGO definition excluding urine output: stage 1 (serum creatinine 1.5 to 1.9 times baseline, ≥0.3 mg/dL increase in 48 hours); stage 2 (serum creatinine 2.0 to 2.9 times baseline); stage 3 (serum creatinine 3 times baseline, ≥2.5 mg/dL increase).

Outcomes	Diagnosis of CKD eGFR <90 mL/min/1.73 m² and urine protein/creatinine >0.2 were reported separately. Additional comments Renal dysfunction was also reported and defined as the presence of any of the following: eGFR <90 mL/min/1.73 m², urine protein/creatinine >0.2 or blood pressure >95th %tile. eGFR was measured with cystatin C and creatinine. Cystatin C was the reference equation.

Risk of bias

Section	**Answer**
Study participation	Low risk of bias
Study Attrition	Moderate risk of bias *(Information was not collected from participants who dropped out)*
Prognostic factor measurement	Low risk of bias
Outcome Measurement	Low risk of bias
Study Confounding	Moderate risk of bias *(Confounders were only used for renal dysfunction; missing confounder data was not reported)*
Statistical Analysis and Reporting	Low risk of bias
Overall risk of bias	Moderate
Overall directness	Partially applicable *(Blood pressure was part of the definition of renal dysfunction.)*

Hessey, 2019

Bibliographic Reference	Hessey, E.; Perreault, S.; Dorais, M.; Roy, L.; Zappitelli, M.; Acute Kidney Injury in Critically Ill Children and Subsequent Chronic Kidney Disease; Canadian Journal of Kidney Health and Disease; 2019; vol. 6

Study Characteristics

Study design	Retrospective cohort study
Study details	Study location Canada Study setting Paediatric intensive care units Study dates 2003 - 2005 Duration of follow-up 5 years Loss to follow-up 264 out of 2499 (11%) Sources of funding Fonds de recherche du Québec—Santé
Inclusion criteria	Age ≤18 years old Hospital admission First hospitalisation to a paediatric intensive care unit during study period
Exclusion criteria	Pre-existing renal disease Pre-admission end-stage renal disease or if this diagnosis was made during index admission; pre-existing renal or urinary tract abnormalities; diagnostic code for CKD or a prescription of CKD-specific medication 12 months before admission; low baseline eGFR (≥1 month old: eGFR < 35 mL/min/1.73m2 using the CKD in Children formula; <1 month old: eGFR <2 standard deviations from mean normative value, because GFR = 35 mL/min/1.73m2 is within 2 standard divisions of the mean normative value. Other criteria Patients with no health care number; patients who could not be linked to provincial data, or did not survive hospitalisation.

Sample characteristics	Sample size 2,235 (Without AKI: 1771; with AKI: 464) Female Without AKI: 44%; with AKI: 46% Mean age (SD) at admission Without AKI: median 3.7 years (IQR 10.3); with AKI: median 3.6 (IQR 10.6) eGFR at baseline Without AKI: median 120 (IQR 36); with AKI: median 120 (IQR 49)
Prognostic factors	Acute kidney injury Acute kidney injury was defined using serum creatinine (SCr) and urine output criteria, based on the KDIGO definition. AKI was classified as stage 1 (SCr rise ≥ 1.5 to 1.9 times baseline in 7 days or ≥26.5 µmol/L within 48 hours or urine output < 0.5 mL/kg/h for 8 hours), stage 2 (SCr rise ≥ 2.0 to 2.9 times baseline or urine output < 0.5 mL/kg/h for 16 hours), and stage 3 (SCr rise ≥ 3.0 times baseline, SCr ≥ 353.6 µmol/L, dialysis treatment for AKI, or eGFR < 35 mL/min/1.73m2 [if >3 months old] or urine output < 0.3 mL/kg/h for 24 hours, or anuric for 12 hours).
Outcomes	Diagnosis of CKD A patient was defined as having CKD if he or she had ≥1 CKD diagnostic codes and/or ≥1 prescription for CKD-specific medication 5 years post-hospital discharge.

Risk of bias

Section	**Answer**
Study participation	Low risk of bias
Study Attrition	Low risk of bias
Prognostic factor measurement	Low risk of bias
Outcome Measurement	Low risk of bias
Study Confounding	Low risk of bias
Statistical Analysis and Reporting	Low risk of bias

Section	Answer
Overall risk of bias	Low
Overall directness	Directly applicable

Hollander, 2016

Bibliographic Reference	Hollander, Seth A; Montez-Rath, Maria E; Axelrod, David M; Krawczeski, Catherine D; May, Lindsay J; Maeda, Katsuhide; Rosenthal, David N; Sutherland, Scott M; Recovery From Acute Kidney Injury and CKD Following Heart Transplantation in Children, Adolescents, and Young Adults: A Retrospective Cohort Study.; American journal of kidney diseases : the official journal of the National Kidney Foundation; 2016; vol. 68 (no. 2); 212-218

Study Characteristics

Study design	Retrospective cohort study
Study details	Study location US Study setting Hospital Study dates 2007 - 2013 Duration of follow-up 6 and 12 months Loss to follow-up None Sources of funding None
Inclusion criteria	Age

	<20 years Condition Orthotopic heart transplantation
Exclusion criteria	Other conditions Undergoing multiorgan (heart-liver) transplantation, requiring extracorporeal membrane oxygenation or ventricular assist device support at any point post-transplantation, or had previously undergone a solid-organ transplantation
Sample characteristics	Sample size 88 (63 with AKI and 25 without AKI) Female With AKI: 43%; without AKI: 48% Mean age (SD) at admission With AKI: median 6.4 years (IQR 0.26, 18.5); without AKI: median 5.2 years (IQR 1, 16.7) Abnormal baseline eGFR % Pre-treatment eGFR <60 ml/min/1.73m²: With AKI (38%) without AKI (20%)
Prognostic factors	Acute kidney injury AKI was defined according to KDIGO criteria. Moderate to severe AKI was defined as AKI stage 2 or higher.
Outcomes	Diagnosis of CKD Defined as eGFR <60 mL/min/1.73 m2 for longer than 3 months. eGFR was calculated using the Schwartz formula.

Risk of bias

Section	**Answer**
Study participation	Low risk of bias
Study Attrition	Moderate risk of bias *(Reasons for loss to follow-up were not provided)*
Prognostic factor measurement	Low risk of bias

Section	Answer
Outcome Measurement	Low risk of bias
Study Confounding	High risk of bias *(No confounders were measured)*
Statistical Analysis and Reporting	Moderate risk of bias *(Adjustment was not done)*
Overall risk of bias	High
Overall directness	Directly applicable

Poggiali, 2019

Bibliographic Reference Poggiali, Isabel V; Simoes E Silva, Ana Cristina; Vasconcelos, Mariana A; Dias, Cristiane S; Gomes, Izabella R; Carvalho, Rafaela A; Oliveira, Maria Christina L; Pinheiro, Sergio V; Mak, Robert H; Oliveira, Eduardo A; A clinical predictive model of renal injury in children with congenital solitary functioning kidney.; Pediatric nephrology (Berlin, Germany); 2019; vol. 34 (no. 3); 465-474

Study Characteristics

Study design	Retrospective cohort study
Study details	Study location Brazil Study setting Paediatric Nephrourology Unit Study dates 1985 - 2015 Duration of follow-up Median follow-up time was 8.5 years

	Loss to follow-up There were 9 missing values concerning the variable proteinuria Sources of funding NIH grants, CAPES grant, partially supported by CNPq grant (Brazilian National Research Council), FAPEMIG grant (Fundação de Amparo à Pesquisa do Estado de Minas Gerais), and the INCT-MM Grant.
Inclusion criteria	Condition Children with congenital solitary functioning kidney
Exclusion criteria	Other conditions Bilateral severe renal hypodysplasia, multiple malformations Other criteria Those who abandoned postnatal follow-up
Prognostic factors	Solitary functioning kidney Solitary functioning kidney was stratified into two phenotypes: multicystic dysplastic kidney and renal agenesis/hypodysplasia. Contralateral congenital anomalies of the kidney and urinary tract was also reported. Low birth weight Low birth weight (<2500 g) in children with solitary functioning kidney
Outcomes	Diagnosis of CKD CKD was defined as GFR <60 ml/min per 1.73 m² in two consecutive exams with an interval of at least 3 months Additional comments Three additional outcomes were reported: 1) proteinuria (urinary protein creatinine ratio above 0.2 or 24-h protein excretion is >150 mg/day in at least two consecutive evaluations); 2) hypertension (no values were given, there was a reference to the fourth report on high blood pressure in children and adolescents); 3) composite event (eGFR <60 ml/min per 1.73 m², hypertension, and proteinuria)

Study arms

Multicystic dysplastic kidney (N = 132)

Sample characteristics	Female 43.9% Other characteristics Birth weight: <2500 g (18.2%); ≥2500 g (81.8%); contralateral congenital anomalies of the kidney and urinary tract: present (21.2%); abscent (78.8%)

Hypodysplasia/agenesis (N = 30)

Sample characteristics	Female 20.0% Other characteristics Birth weight: <2500 g (26.7%); ≥2500 g (73.3%); contralateral congenital anomalies of the kidney and urinary tract: present (50.0%); abscent (50.0%)

Risk of bias

Section	Question	Answer
Study participation	Summary Study participation	Moderate risk of bias *(Unclear how participants were recruited; recruitment period not given only study period was reported; full inclusion criteria not reported)*
Study Attrition	Study Attrition Summary	Moderate risk of bias *(Median follow-up was 8.5 years, only 64.8% participants were followed up for more than 5 years; no reasons were given for participants lost to follow-up; key characteristics were not reported for participants lost to follow-up)*
Prognostic factor measurement	Prognostic factor Measurement Summary	Low risk of bias
Outcome Measurement	Outcome Measurement Summary	Moderate risk of bias *(Values were not given to define hypertension)*
Study Confounding	Study Confounding Summary	High risk of bias *(Confounders were not listed or defined)*
Statistical Analysis and Reporting	Statistical Analysis and Presentation Summary	Moderate risk of bias *(Model development strategy was not reported)*
Overall risk of bias and directness	Risk of Bias	High

Section	Question	Answer
	Directness	Directly applicable

Westland, 2013

Bibliographic Reference	Westland, Rik; Kurvers, Roel A J; van Wijk, Joanna A E; Schreuder, Michiel F; Risk factors for renal injury in children with a solitary functioning kidney.; Pediatrics; 2013; vol. 131 (no. 2); e478-85

Study Characteristics

Study design	Retrospective cohort study
Study details	Study location The Netherlands Study setting Paediatric renal centres Study dates 1992 - 2011 Duration of follow-up Not reported Loss to follow-up None Sources of funding Grant from Fonds NutsOhra Zorgsubsidies, Amsterdam, Netherlands
Inclusion criteria	Condition Children with solitary functioning kidney (SFK) and renal follow-up; SFK was identified by the unilateral absence of (functional) renal tissue on ultrasound or on renal scintigraphy
Exclusion criteria	Other conditions Children with an acquired SFK as a result of renal malignancy; children with an eGFR <30 mL/min/1.73 m2 from birth; and children who died before reaching the age of 1 year.

Sample characteristics	Sample size 407 (223 congenital SFK and 184 acquired SFK) Female Congenital SFK: 34%; acquired SFK: 36% Mean age (SD) at follow-up Congenital SFK: 7.8 years (5.6); acquired SFK: 10.5 years (6.0) eGFR at follow-up Congenital SFK: mean 104 ml/min/1.73 m² (SD 28); acquired SFK: 98 ml/min/1.73 m² (SD 32)
Prognostic factors	Solitary functioning kidney A congenital SFK can be due to unilateral renal agenesis/aplasia or to a multicystic dysplastic kidney. An SFK is acquired when children undergo nephrectomy secondary to congenital anomalies of the kidney and urinary tract (CAKUT) such as pelviureteric junction obstruction, posterior urethral valves, or vesicoureteral reflux, as well as to acute pyelonephritis or renovascular disease. A subdivision was made in patients with or without ipsilateral CAKUT (ie, on the side of the SFK). CAKUT were identified by renal ultrasound in all patients and, on indication, by voiding cystourethrogram. Low birth weight Birth weight <2500 g
Outcomes	Diagnosis of CKD eGFR <60 mL/min/1.73 m². Proteinuria was defined as protein/ creatinine ratio >0.2 mg/mg (>22.6 mg/mmol) in children >2 years of age and as >0.5 mg/mg (>56.6 mg/mmol) for children <2 years of age. Additional comments Renal injury was also reported and defined as hypertension, proteinuria, an impaired eGFR, or the use of renoprotective medication.

Risk of bias

Section	Answer
Study participation	Low risk of bias
Study Attrition	Low risk of bias
Prognostic factor measurement	Low risk of bias

Section	Answer
Outcome Measurement	Low risk of bias
Study Confounding	Low risk of bias
Statistical Analysis and Reporting	Low risk of bias
Overall risk of bias	Low
Overall directness	Partially applicable *(The definition of renal dysfunction also included hypertension and the use of renoprotective medication.)*

Williams, 2018

Bibliographic Reference Williams, C; Borges, K; Banh, T; Vasilevska-Ristovska, J; Chanchlani, R; Ng, V L; Dipchand, A I; Solomon, M; Hebert, D; Kim, S J; Astor, B C; Parekh, R S; Patterns of kidney injury in pediatric nonkidney solid organ transplant recipients.; American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons; 2018; vol. 18 (no. 6); 1481-1488

Study Characteristics

Study design	Retrospective cohort study
Study details	Study location Canada Study setting Hospital Study dates 2002 - 2011

	Duration of follow-up median 3.4 years (IQR 1.4, 5.7) Loss to follow-up None Sources of funding Ashley's Angels Catwalk; Canadian Institutes of Health Research; Astellas Pharma Canada, Inc; Transplant & Regenerative Medicine Centre Catalyst Grant at the Hospital for Sick Children
Inclusion criteria	Age <18 years Condition All first-time recipients who received a non-kidney solid organ transplant, including heart, lung, liver, and multiorgan transplant (any combination of bowel, liver, stomach, and pancreas)
Exclusion criteria	Pre-existing renal disease Haemodialysis or renal failure prior to transplant Other criteria Children followed for fewer than 90 days post-transplant
Sample characteristics	Sample size 303 (203 with AKI and 100 without AKI) Female 44.5% Mean age (SD) at admission Median 3.9 years (IQR 0.7, 11.9) eGFR at baseline Median 108 ml/min/1.73m² (IQR 79.9, 135)
Prognostic factors	Acute kidney injury AKI was defined as an increase in serum creatinine >26.5 µM (0.3 mg/dL) within 48 hours or an increase in serum creatinine >1.5 times the baseline creatinine value within the previous 7 days based on the KDIGO criteria. The number of repeated AKI events was determined over the first year post-transplant
Outcomes	Diagnosis of CKD CKD was defined as an average eGFR <60 mL/min per 1.73 m² over any 6-month period starting at day 90 post-transplant and events were then validated through chart review.

	All-cause mortality Additional comments The association of post-transplant AKI episodes with development of CKD and mortality was reported at 3 time points: up to 3, 6 and 12 months after transplant

Risk of bias

Section	Answer
Study participation	Low risk of bias
Study Attrition	Low risk of bias
Prognostic factor measurement	Low risk of bias
Outcome Measurement	Low risk of bias
Study Confounding	Low risk of bias
Statistical Analysis and Reporting	Low risk of bias
Overall risk of bias	Low
Overall directness	Directly applicable

Appendix F – Forest plots

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

Appendix G – GRADE tables

Benisty 2020 (children and young people admitted to paediatric intensive care unit)

Quality assessment							No of patients		Effect		Quality
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	AKI	No AKI	Relative (95% CI)	Absolute	
Predictor: any AKI category (reference: no or unknown AKI); Outcome: eGFR category G2 (eGFR <90 ml/min/1.73m2 or ACR >30 mg/g) or BP ≥90th percentile											
1[1]	observational studies[2]	serious[3]	not applicable	serious[4]	serious[5]	none	69	208	OR 2.2 (1.1 to 4.4)[6]	-	VERY LOW
Predictor: any AKI category (reference: no or unknown AKI); Outcome: eGFR category G2 (eGFR <90 ml/min/1.73m2 or ACR >30 mg/g) or BP ≥95th percentile											
1[1]	observational studies[2]	serious[3]	not applicable	serious[4]	serious[5]	none	69	208	OR 1.7 (0.9 to 3.4)[7]	-	VERY LOW
Predictor: any AKI category (reference: no or unknown AKI); Outcome: eGFR <90 ml/min/1.73m2											
1[1]	observational studies[2]	serious[3]	not applicable	no serious indirectness	serious[5]	none	9/66 (13.6%)	13/197 (6.6%)	RR 2.07 (0.93 to 4.61)[8]	7 more per 100 (from 0 fewer to 24 more)	LOW
Predictor: any AKI category (reference: no or unknown AKI); Outcome: ACR >30 mg/g											
1[1]	observational studies[2]	serious[3]	not applicable	no serious indirectness	very serious[9]	none	7/68 (10.3%)	25/204 (12.3%)	RR 0.84 (0.38 to 1.85)[8]	2 fewer per 100 (from 8 fewer to 10 more)-	VERY LOW
Predictor: stage 2 AKI or worse (reference: no or unknown or stage 1 AKI); Outcome: eGFR category G2 (eGFR <90 ml/min/1.73m2 or ACR >30 mg/g) or BP ≥90th percentile											
1[1]	observational studies[2]	serious[3]	not applicable	serious[4]	no serious imprecision	none	27	250	OR 6.6 (1.5 to 28.3)[10]	-	LOW
Predictor: stage 2 AKI or worse (reference: no or unknown or stage 1 AKI); Outcome: eGFR category G2 (eGFR <90 ml/min/1.73m2 or ACR >30 mg/g) or BP ≥95th percentile											
1[1]	observational studies[2]	serious[3]	not applicable	serious[4]	very serious[9]	None	27	250	OR 1.9 (0.7 to 4.7)[7]	-	VERY LOW

Predictor: stage 2 AKI or worse (reference: no or unknown or stage 1 AKI); Outcome: <90 ml/min/1.73m2												
1[1]	observational studies[2]	serious[3]	not applicable	no serious indirectness	very serious[9]	none	4/26 (15.4%)	18/237 (7.6%)	RR 2.03 (0.74 to 5.53)[8]	8 more per 100 (from 2 fewer to 34 more)	VERY LOW
Predictor: stage 2 AKI or worse (reference: no or unknown or stage 1 AKI); Outcome: ACR >30 mg/g												
1[1]	observational studies[2]	serious[3]	not applicable	no serious indirectness	very serious[9]	none	4/26 (15.4%)	28/246 (11.4%)	RR 1.35 (0.51 to 3.55)[8]	4 more per 100 (from 6 fewer to 29 more)	VERY LOW

[1] Benisty 2020
[2] Prospective
[3] Study at moderate risk of bias
[4] Partially applicable (composite outcome)
[5] 95% confidence interval crosses one end of a defined MID interval
[6] Adjusted for: age at follow-up, vasopressor use, nephrotoxic medication use, sepsis during admission, >1 past medical history item at admission, and abnormal baseline eGFR
[7] Adjusted for: age at follow-up, sepsis during admission, >1 past medical history item at admission, and abnormal baseline eGFR
[8] Unadjusted, calculated by reviewer
[9] 95% confidence interval crosses both ends of a defined MID interval
[10] Adjusted for: age at follow-up, vasopressor use, nephrotoxic medication use, sepsis, >1 past medical history item at admission, abnormal baseline eGFR, and nephrotoxic medication use interaction term with AKI
ACR: albumin to creatinine ratio; AKI: acute kidney injury; BP: blood pressure; CI: confidence interval; CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate; OR: odds ratio; RR: risk ratio

Harer 2017 (children who were admitted to neonatal intensive care unit admission before 2 days of life weighting ≤1,500 g)

Quality assessment							No of patients		Effect		Quality
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**AKI**	**No AKI**	**Relative (95% CI)**	**Absolute**	
Predictor: AKI (reference: no AKI); Outcome: renal dysfunction (eGFR <90 mL/min/1.73 m2 or UPC >0.2 or BP >95th percentile)											
1[1]	observational studies[2]	serious[3]	not applicable	serious[4]	serious[5]	none	13/20 (65%)	2/14 (14.3%)	RR 4.5 (1.2 to 17.1)[6]	50 more per 100 (from 3 more to 100 more)	VERY LOW
Predictor: AKI (reference: no AKI); Outcome: eGFR <90 mL/min/1.73 m2											

1[1]	observational studies[2]	serious[3]	not applicable	no serious indirectness	very serious[7]	none	7/20 (35%)	2/14 (14.3%)	RR 1.5 (0.8 to 2.5)[6]	7 more per 100 (from 3 fewer to 21 more)	VERY LOW
Predictor: AKI (reference: no AKI); Outcome: UPC >0.2											
1[1]	observational studies[2]	serious[3]	not applicable	no serious indirectness	serious[5]	none	4/20 (20%)	0/14 (0%)	RR 1.9 (0.9 to 2.6)[6]	-	LOW

[1] Harer 2017
[2] Prospective
[3] Study at moderate risk of bias
[4] Partially applicable (Blood pressure was part of the definition of renal dysfunction)
[5] 95% confidence interval crosses one end of a defined MID interval
[6] Unclear if relative risk was adjusted
[7] 95% confidence interval crosses both ends of a defined MID interval
AKI: acute kidney injury; BP: blood pressure; CI: confidence interval; eGFR: estimated glomerular filtration rate; RR: risk ratio; UPC: urine protein/creatinine ratio

Hessey 2019 (children and young people with a first hospitalisation to a paediatric intensive care unit during study period)

Quality assessment							No of patients		Effect		Quality
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**AKI**	**No AKI**	**Relative (95% CI)**	**Absolute**	
Predictor: AKI (reference: no AKI); Outcome: CKD											
1[1]	observational studies[2]	no serious risk of bias	not applicable	no serious indirectness	no serious imprecision	none	20/464 (4.3%)	23/1771 (1.3%)	HR 2.3 (1.3 to 4.3)[3]	2 more per 100 (from 0 more to 4 more)	HIGH
Predictor: stage 2/3 AKI (reference: no AKI/stage 1 AKI); Outcome: CKD											
1[1]	observational studies[2]	no serious risk of bias	not applicable	no serious indirectness	serious[4]	none	9/158 (5.7%)	34/2077 (1.6%)	HR 2.1 (1 to 4.4)[3]	2 more per 100 (from 0 more to 5 more)	MODERATE
Predictor: stage 1 AKI (reference: no AKI); Outcome: CKD											

1[1]	observational studies[2]	no serious risk of bias	not applicable	no serious indirectness	serious[4]	none	11/306 (3.6%)	23/1771 (1.3%)	HR 2.2 (1.1 to 4.5)[3]	2 more per 100 (from 0 more to 4 more)	MODERATE
Predictor: stage 2/3 AKI (reference: no AKI); Outcome: CKD											
1[1]	observational studies[2]	no serious risk of bias	not applicable	no serious indirectness	serious[4]	none	9/158 (5.7%)	23/1771 (1.3%)	HR 2.5 (1.1 to 5.7)[3]	2 more per 100 (from 0 more to 6 more)	MODERATE

[1] Hessey 2019
[2] Retrospective
[3] Adjusted for Pediatric Medical Complexity Algorithm and nephrotoxic antibiotic use in the pediatric intensive care unit
[4] 95% confidence interval crosses one end of a defined MID interval
AKI: acute kidney injury; CI: confidence interval; CKD: chronic kidney disease; HR: hazard ratio

Hollander 2016 (children and young people with orthotopic heart transplantation)

Quality assessment							No of patients		Effect		Quality
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**AKI**	**No AKI**	**Relative (95% CI)**	**Absolute**	
Predictor: AKI (reference: no AKI); Outcome: CKD at 6 months											
1[1]	observational studies[2]	very serious[3]	not applicable	no serious indirectness	very serious[4]	none	3/60 (5%)	0/22 (0%)	RR 2.6 (0.14 to 49.14)[5]	-	VERY LOW
Predictor: AKI (reference: no AKI); Outcome: CKD at 12 months											
1[1]	observational studies[2]	very serious[3]	not applicable	no serious indirectness	very serious[4]	none	3/54 (5.6%)	1/22 (4.5%)	RR 1.22 (0.13 to 11.12)[5]	1 more per 100 (from 4 fewer to 46 more)	VERY LOW

[1] Hollander 2016
[2] Retrospective
[3] Study at high risk of bias
[4] 95% confidence interval crosses both ends of a defined MID interval

[5] Unadjusted, calculated by reviewer
AKI: acute kidney injury; CI: confidence interval; CKD: chronic kidney disease; RR: risk ratio

Williams 2017 (children and young people first-time recipients who received a non-kidney solid organ transplant, including heart, lung, liver, and multiorgan transplant [any combination of bowel, liver, stomach, and pancreas])

Quality assessment							No of patients		Effect		Quality
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	AKI	No AKI	Relative (95% CI)	Absolute	
Predictor: perioperative AKI (reference: no AKI); Outcome: CKD											
1[1]	observational studies[2]	no serious risk of bias	not applicable	no serious indirectness	serious[3]	none	203	100	HR 1.84 (0.66 to 5.1)[4]	-	MODERATE
Predictor (up to 3 months after transplant): 1 AKI event (reference: 0 AKI events); Outcome: CKD											
1[1]	observational studies[2]	no serious risk of bias	not applicable	no serious indirectness	serious[3]	none	64	221	HR 2.77 (1.13 to 6.8)[5]	-	MODERATE
Predictor (up to 3 months after transplant): 2 or more AKI events (reference: 0 AKI events); Outcome: CKD											
1[1]	observational studies[2]	no serious risk of bias	not applicable	no serious indirectness	serious[3]	none	18	221	HR 3.53 (0.94 to 13.2)[5]	-	MODERATE
Predictor (up to 6 months after transplant): 1 AKI event (reference: 0 AKI events); Outcome: CKD											
1[1]	observational studies[2]	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[6]	none	69	206	HR 2.14 (0.79 to 5.8)[5]	-	LOW
Predictor (up to 6 months after transplant): 2 or more AKI events (reference: 0 AKI events); Outcome: CKD											
1[1]	observational studies[2]	no serious risk of bias	not applicable	no serious indirectness	very serious[6]	none	28	206	HR 2.77 (0.76 to 10.1)[5]	-	LOW
Predictor (up to 12 months after transplant): 1 AKI event (reference: 0 AKI events); Outcome: CKD											
1[1]	observational studies[2]	no serious risk of bias	not applicable	no serious indirectness	very serious[6]	none	68	195	HR 2.24 (0.54 to 9.25)[5]	-	LOW

Predictor (up to 3 months after transplant): 1 or more AKI events (reference: 0 AKI events); Outcome: mortality											
1[1]	observational studies[2]	no serious risk of bias	not applicable	no serious indirectness	serious[7]	none	82	221	HR 1.84 (0.86 to 3.92)[8]	-	MODERATE
Predictor (up to 6 months after transplant): 1 or more AKI events (reference: 0 AKI events); Outcome: mortality											
1[1]	observational studies[2]	no serious risk of bias	not applicable	no serious indirectness	serious[7]	none	97	206	HR 2.03 (0.89 to 4.64)[8]	-	MODERATE
Predictor (up to 12 months after transplant): 1 or more AKI events (reference: 0 AKI events); Outcome: mortality											
1[1]	observational studies[2]	no serious risk of bias	not applicable	no serious indirectness	serious[7]	none	108	195	HR 1.90 (0.7 to 5.14)[8]	-	MODERATE

[1] Williams 2017
[2] Retrospective
[3] 95% confidence interval crosses one end of a defined MID interval
[4] Adjusted for age, sex, and eGFR at time of transplant
[5] Association of post-transplant AKI episodes with development of CKD accounting for competing risks (death, retransplant). Model was adjusted for age, sex, and glomerular filtration rate at time of transplant
[6] 95% confidence interval crosses both ends of a defined MID interval
[7] 95% confidence interval crosses line of no effect
[8] Association of AKI with risk of mortality accounting for competing risk of retransplant. Model was adjusted for age, sex, glomerular filtration rate at time of transplant, and underlying diagnosis
AKI: acute kidney injury; CI: confidence interval; CKD: chronic kidney disease; HR: hazard ratio

Poggiali 2019 (children with solitary functioning kidney)

Quality assessment							No of patients		Effect		Quality
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Predictor**	**Reference**	**Relative (95% CI)**	**Absolute**	
Predictor: multicystic dysplastic kidney (reference: hypodysplasia/agenesis); Outcome: CKD											
1[1]	observational studies	very serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	6/132 (4.5%)	3/30 (10%)	HR 2.52 (0.62 to 10.0)	13 more per 100 (from 4 fewer to 55 more)	VERY LOW
Predictor: presence of contralateral CAKUT (reference: absence of contralateral CAKUT); Outcome: CKD											
1[1]	observational studies	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	43	119	HR 62.2 (3.7 to 115.7)	-[4]	LOW
Predictor: low birth weight (reference: normal birth weight); Outcome: CKD											
1	observational studies[1]	very serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	32	130	HR 3.31 (0.89 to 12.3)	-[4]	VERY LOW
Predictor: multicystic dysplastic kidney (reference: hypodysplasia/agenesis); Outcome: renal injury events (eGFR <60 ml/min/1.73 m2, hypertension, and proteinuria)											

1	observational studies[1]	very serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	30/132 (22.7%)	11/30 (36.7%)	HR 2.06 (0.73 to 5.8)	24 more per 100 (from 8 fewer to 56 more)	VERY LOW
Predictor: presence of contralateral CAKUT (reference: absence of contralateral CAKUT); Outcome: renal injury events (eGFR <60 ml/min/1.73 m2, hypertension, and proteinuria)											
1	observational studies[1]	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	43	119	HR 13.3 (4.3 to 41.2)	-[4]	LOW
Predictor: low birth weight (reference: normal birth weight); Outcome: renal injury events (eGFR <60 ml/min/1.73 m2, hypertension, and proteinuria)											
1	observational studies[1]	very serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	32	130	HR 2.69 (1.03 to 6.98)	-[4]	VERY LOW
Predictor: multicystic dysplastic kidney (reference: hypodysplasia/agenesis); Outcome: hypertension											
1	observational studies[1]	very serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	7/132 (5.3%)	4/30 (13.3%)	HR 3.0 (0.87 to 10.3)	22 more per 100 (from 2 fewer to 64 more)	VERY LOW
Predictor: presence of contralateral CAKUT (reference: absence of contralateral CAKUT); Outcome: hypertension											
1	observational studies[1]	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	43	119	HR 6.2 (1.78 to 21.5)	-[4]	LOW
Predictor: low birth weight (reference: normal birth weight); Outcome: hypertension											
1	observational studies[1]	very serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	32	130	HR 2.44 (0.71 to 8.42)	-[4]	VERY LOW
Predictor: multicystic dysplastic kidney (reference: hypodysplasia/agenesis); Outcome: proteinuria											
1	observational studies[1]	very serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	9/132 (6.8%)	3/30 (10%)	HR 2.71 (0.69 to 10.5)	15 more per 100 (from 3 fewer to 57 more)	VERY LOW
Predictor: presence of contralateral CAKUT (reference: absence of contralateral CAKUT); Outcome: proteinuria											
1	observational studies[1]	very serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	43	119	HR 1.92 (0.96 to 3.81)	-[4]	LOW
Predictor: low birth weight (reference: normal birth weight); Outcome: proteinuria											
1	observational studies[1]	very serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	32	130	HR 2.85 (0.79 to 10.2)	-[4]	VERY LOW

[1] Retrospective
[2] Study at high risk of bias
[3] 95% confidence interval crosses both ends of a defined MID interval
[4] Number of events not reported
[5] 95% confidence interval crosses one end of a defined MID interval

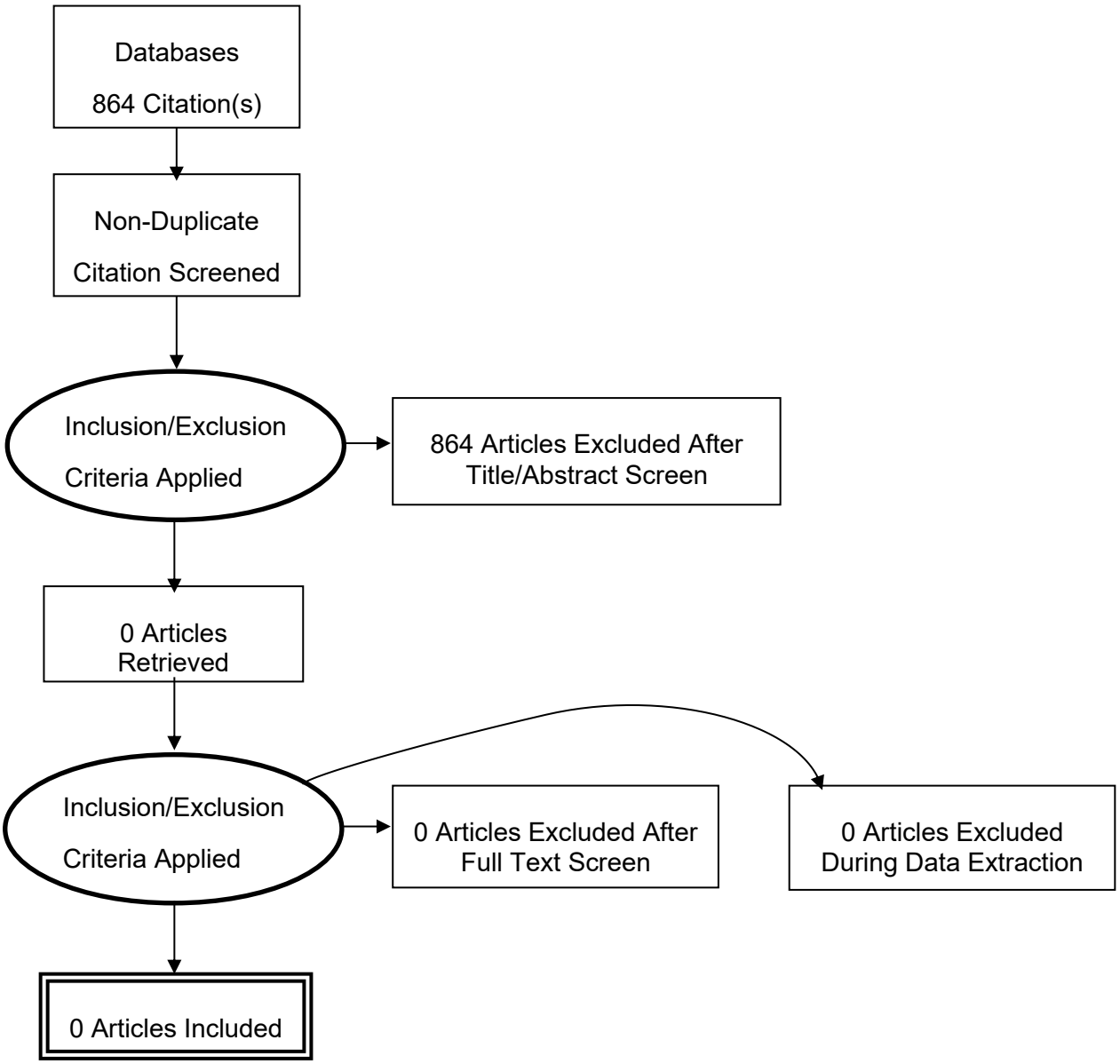
Westland 2013 (children with solitary functioning kidney and renal follow-up)

Quality assessment							No of patients		Effect		Quality
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Predictor**	**Reference**	**Relative (95% CI)**	**Absolute**	
Predictor: ipsilateral CAKUT; Outcome: renal injury (hypertension, proteinuria, an impaired eGFR, or the use of renoprotective medication)											

1[1]	observational studies[2]	no serious risk of bias	not applicable	serious[3]	serious[4]	none	Ipsilateral CAKUT 137	Not reported	OR 1.66 (1.02 to 2.69)[5]	-	LOW
Predictor: birth weight <2,500 g; Outcome: renal injury (hypertension, proteinuria, an impaired eGFR, or the use of renoprotective medication)											
1[1]	observational studies[2]	no serious risk of bias	not applicable	serious[3]	serious[4]	none	Birth weight <2,500 g 56	Birth weight ≥3500, <4000 g 87	OR 2.08 (0.96 to 4.51)[6]	-	LOW
Predictor: acquired SFK; Outcome: renal injury (hypertension, proteinuria, an impaired eGFR, or the use of renoprotective medication)											
1[1]	observational studies[2]	no serious risk of bias	not applicable	serious[3]	no serious imprecision	none	Acquired SFK 184	Not reported	OR 1.93 (1.26 to 2.95)[7]	-	MODERATE
Predictor: acquired SFK (reference: congenital SFK); Outcome: eGFR <60 mL/min/1.73m2											
1[1]	observational studies[2]	no serious risk of bias	not applicable	no serious indirectness	serious[4]	none	Acquired SFK 16/184 (8.7%)	Congenital SFK 9/223 (4%)	RR 2.15 (0.97 to 4.76)[8]	5 more per 100 (from 0 fewer to 15 more)	MODERATE
Predictor: acquired SFK (reference: congenital SFK); Outcome: proteinuria											
1[1]	observational studies[2]	no serious risk of bias	not applicable	no serious indirectness	no serious imprecision	none	Acquired SFK 50/184 (27.2%)	Congenital SFK 29/223 (13%)	RR 2.08 (1.38 to 3.16)[8]	14 more per 100 (from 5 more to 28 more)	HIGH

[1] Westland 2013
[2] Retrospective
[3] Partially applicable (definition of renal dysfunction also included hypertension and use of renoprotective medication)
[4] 95% confidence interval crosses one end of a defined MID interval
[5] Multivariate analysis included age, acquired SFK, prenatal diagnosis of SFK, birth weight <2,500 g, urinary tract infections, and renal length SDS
[6] Multivariate analysis included age, acquired SFK, ipsilateral CAKUT, prenatal diagnosis of SFK, urinary tract infections, and renal length SDS
[7] Unadjusted
[8] Unadjusted, calculated by reviewer
CAKUT: congenital anomalies of the kidney and urinary tract; CI: confidence interval; eGFR: estimated glomerular filtration rate; OR: odds ratio; RR: risk ratio; SFK: solitary functioning kidney

Appendix H – Economic evidence study selection



Appendix I – Economic evidence tables

No published economic studies were included in this review.

Appendix J – Health economic model

This review was not prioritised for economic modelling.

Appendix K – Excluded studies

Prognostic studies

Study	Reason for exclusion
Abitbol, C.L., Chandar, J., Rodriguez, M.M. et al. (2009) Obesity and preterm birth: Additive risks in the progression of kidney disease in children. Pediatric Nephrology 24(7): 1363-1370	- Study does not contain a relevant population All participants had non-diabetic kidney disease
Abitbol, Carolyn L, Bauer, Charles R, Montane, Brenda et al. (2003) Long-term follow-up of extremely low birth weight infants with neonatal renal failure. Pediatric nephrology (Berlin, Germany) 18(9): 887-93	- Study design All participants had extremely low birth weight
Athwani, V., Bhargava, M., Chanchlani, R. et al. (2017) Incidence and Outcome of Acute Cardiorenal Syndrome in Hospitalized Children. Indian Journal of Pediatrics 84(6): 420-424	- Study does not contain a relevant population Children and young people with cardiorenal syndrome
Atmis, B., Karabay-Bayazit, A., Melek, E. et al. (2019) Renal features of bardet biedl syndrome: A single center experience. Turkish Journal of Pediatrics 61(2): 186-192	- Not possible to calculate a contingency table
Bakker, Hanneke, Gaillard, Romy, Franco, Oscar H et al. (2014) Fetal and infant growth patterns and kidney function at school age. Journal of the American Society of Nephrology : JASN 25(11): 2607-15	- Outcome to be predicted do not match that specified in the protocol Microalbuminuria
Bendor, C.D., Bardugo, A., Pinhas-Hamiel, O. et al. (2020) Cardiovascular morbidity, diabetes and cancer risk among children and adolescents with severe obesity. Cardiovascular Diabetology 19(1): 79	- Outcome to be predicted do not match that specified in the protocol No studies were found that assessed the association between severe obesity in childhood and incident chronic kidney disease
Calderon-Margalit, Ronit, Golan, Eliezer, Twig, Gilad et al. (2018) History of Childhood Kidney Disease and Risk of Adult End-Stage Renal Disease. The New England journal of medicine 378(5): 428-438	- Study does not contain a relevant population Adults
Cassidy-Bushrow, Andrea E, Wegienka, Ganesa, Barone, Charles J 2nd et al. (2012) Race-specific relationship of birth weight and renal function among healthy young children. Pediatric nephrology (Berlin, Germany) 27(8): 1317-23	- Outcome to be predicted do not match that specified in the protocol Birth weight Z- score
Chang, Yoosoo, Ryu, Seungho, Choi, Yuni et al. (2016) Metabolically Healthy Obesity and Development of Chronic Kidney Disease: A Cohort Study. Annals of internal medicine 164(5): 305-12	- Study does not contain a relevant population Adults
Chen, Nan, Wang, Weiming, Huang, Yanping et al. (2009) Community-based study on CKD subjects and the associated risk factors. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 24(7): 2117-23	- Study does not contain a relevant population Adults

Study	Reason for exclusion
Correia-Costa, Liane; Azevedo, Ana; Caldas Afonso, Alberto (2019) Childhood Obesity and Impact on the Kidney. Nephron 143(1): 8-11	- Review article but not a systematic review
Das, Sumon Kumar, Mannan, Munim, Faruque, Abu Syed Golam et al. (2016) Effect of birth weight on adulthood renal function: A bias-adjusted meta-analytic approach. Nephrology (Carlton, Vic.) 21(7): 547-65	- Study does not contain a relevant population Adults
Gicchino, M.F., Di Sessa, A., Guarino, S. et al. (2020) Prevalence of and factors associated to chronic kidney disease and hypertension in a cohort of children with juvenile idiopathic arthritis. European Journal of Pediatrics	- Study does not contain a relevant risk factor
Greenberg, Jason H, Zappitelli, Michael, Devarajan, Prasad et al. (2016) Kidney Outcomes 5 Years After Pediatric Cardiac Surgery: The TRIBE-AKI Study. JAMA pediatrics 170(11): 1071-1078	- Study does not contain a relevant population Children and young people with CKD at baseline
Huh, Ji Hye, Yadav, Dhananjay, Kim, Jae Seok et al. (2017) An association of metabolic syndrome and chronic kidney disease from a 10-year prospective cohort study. Metabolism: clinical and experimental 67: 54-61	- Study does not contain a relevant population Adults
Hui, W.F.; Chan, W.K.Y.; Miu, T.Y. (2013) Acute kidney injury in the paediatric intensive care unit: Identification by modified RIFLE criteria. Hong Kong Medical Journal 19(1): 13-19	- Study design Cross-sectional study
Janchevska, Aleksandra, Gucev, Zoran, Tasevska-Rmus, L et al. (2017) Congenital Anomalies of the Kidney and Urinary Tract in Children Born Small for Gestational Age. Prilozi (Makedonska akademija na naukite i umetnostite. Oddelenie za medicinski nauki) 38(1): 53-57	- Study design All participants had congenital anomalies of the kidney and urinary tract (CAKUT)
Kandasamy, Y, Smith, R, Wright, I M R et al. (2014) Reduced nephron endowment in the neonates of Indigenous Australian peoples. Journal of developmental origins of health and disease 5(1): 31-5	- Study design Cross-sectional - Outcome to be predicted do not match that specified in the protocol eGFR reported as median and interquartile range
Lai, S., Sciarra, A., Pierella, F. et al. (2020) Chronic kidney disease and urological disorders: An overview. Current Signal Transduction Therapy 15(2): 224-231	- Review article but not a systematic review
Mammen, Cherry, Al Abbas, Abdullah, Skippen, Peter et al. (2012) Long-term risk of CKD in children surviving episodes of acute kidney injury in the intensive care unit: a prospective cohort study. American journal of kidney diseases : the official journal of the National Kidney Foundation 59(4): 523-30	- Study design All participants had AKI
Moustafa, F.E.-H.; Eid, R.; Hamdy, N. (2020) Pediatric glomerular hematuria: a	- Study design All participants had glomerular haematuria

Study	Reason for exclusion
clinicopathological study. Clinical and Experimental Nephrology 24(7): 613-621	
Nam, Ki Heon, Yun, Hae-Ryong, Joo, Young Su et al. (2018) Changes in obese metabolic phenotypes over time and risk of incident chronic kidney disease. Diabetes, obesity & metabolism 20(12): 2778-2791	- Study does not contain a relevant population Adults
Nishizaki, Naoto, Hirano, Daishi, Nishizaki, Yuji et al. (2014) Increased urinary angiotensinogen is an effective marker of chronic renal impairment in very low birth weight children. Clinical and experimental nephrology 18(4): 642-8	- Study design Case-control study
Okuda, Y., Soohoo, M., Ishikura, K. et al. (2020) Primary causes of kidney disease and mortality in dialysis-dependent children. Pediatric Nephrology	- Study does not contain a relevant population All participants receiving renal replacement therapy (dialysis)
Oz-Sig, O.; Kara, O.; Erdogan, H. (2020) Microalbuminuria and Serum Cystatin C in Prediction of Early-Renal Insufficiency in Children with Obesity. Indian Journal of Pediatrics	- Outcome to be predicted do not match that specified in the protocol
Ramayani, O.R., Djas, Y., Ramayati, R. et al. (2019) Models predicting complication in congenital anomaly kidney and urinary tract. Current Pediatric Research 23(2): 71-76	- Study does not contain a relevant population Unclear if all participants had eGFR category G1
Rocke, K.D., Ferguson, T.S., Younger-Coleman, N.O. et al. (2018) Relationship between early life factors and renal function in Afro-Caribbean young adults: Analysis from the Jamaica 1986 Birth Cohort Study. West Indian Medical Journal 67(2)	- Study does not contain a relevant population Adults
Rutkowski, Boleslaw, Czarniak, Piotr, Krol, Ewa et al. (2013) Overweight, obesity, hypertension and albuminuria in Polish adolescents--results of the Sopkard 15 study. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 28suppl4: iv204-11	- Study design Cross-sectional
Senra, Janaina Campos, Carvalho, Mariana Azevedo, Rodrigues, Agatha Sacramento et al. (2018) An unfavorable intrauterine environment may determine renal functional capacity in adulthood: a meta-analysis. Clinics (Sao Paulo, Brazil) 73: e401	- Study does not contain a relevant population Adults
Shahdadi, H., Sheyback, M., Rafiemanesh, H. et al. (2019) Causes of chronic kidney disease in iranian children: A meta-analysis and systematic review. Annals of Global Health 85(1): 34	- Study design Systematic review of cross-sectional and retrospective studies
Skrunes, Rannveig, Svarstad, Einar, Reisaeter, Anna Varberg et al. (2014) Familial clustering of ESRD in the Norwegian population. Clinical journal of the American Society of Nephrology : CJASN 9(10): 1692-700	- Study does not contain a relevant population Adults

Study	Reason for exclusion
Soto, K., Campos, P., Pinto, I. et al. (2016) The risk of chronic kidney disease and mortality are increased after community-acquired acute kidney injury. Kidney International 90(5): 1090-1099	- Study does not contain a relevant population Some participants had CKD at baseline
Tangirala, Susmitha, Bhaskaranand, Nalini, Kini, Pushpa G et al. (2019) Clinical Profile and Outcome of Children with Congenital Obstructive Uropathy. Indian journal of pediatrics 86(4): 354-359	- Study design All participants had congenital obstructive uropathy
V, H., Nesargi, S.V., Prashantha, Y.N. et al. (2020) Acute kidney injury in sick neonates: a comparative study of diagnostic criteria, assessment of risk factors and outcomes. Journal of Maternal-Fetal and Neonatal Medicine	- Outcome to be predicted do not match that specified in the protocol
Vivante, Asaf, Afek, Arnon, Frenkel-Nir, Yael et al. (2011) Persistent asymptomatic isolated microscopic hematuria in Israeli adolescents and young adults and risk for end-stage renal disease. JAMA 306(7): 729-36	- Study does not contain a relevant population Adults
Westland, Rik, Schreuder, Michiel F, Bokenkamp, Arend et al. (2011) Renal injury in children with a solitary functioning kidney--the KIMONO study. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 26(5): 1533-41	- Secondary publication of an included study that does not provide any additional relevant information
White, Sarah L, Perkovic, Vlado, Cass, Alan et al. (2009) Is low birth weight an antecedent of CKD in later life? A systematic review of observational studies. American journal of kidney diseases : the official journal of the National Kidney Foundation 54(2): 248-61	- Study does not contain a relevant population Adults

Appendix L – Research recommendations – full details

L.1.1 Research recommendation

What is the association between risk factors and CKD outcomes in children and young people?

L.1.2 Why this is important

Prognostic factors are important to identify children and young people at risk of developing CKD but there are few data on which factors are associated to the developing of CKD in this population. To support and strengthen the recommendations developed in this update of the guideline, further research is needed on the factors associated to the development of CKD in children and young people. Long follow-up times should be used to determine which factors remain significant predictors for the developing of CKD overtime.

L.1.3 Rationale for research recommendation

Importance to 'patients' or the population	Limited evidence exists about prognostic factors that are associated to the development of CKD in children and young people. The identification of prognostic factors could help to ensure that children and young people at risk could have an early diagnosis of CKD which in turn could delay CKD progression.
Relevance to NICE guidance	Prognostic factors for the development of CKD in children and young people have been considered in this guideline and there is a lack of data on some of the factors. Further evidence might fill in the gap in this area during future updates of the guideline.
Relevance to the NHS	The identification of prognostic factors for the development of CKD in children and young people could affect the type of children and young people that clinicians identify as being at risk for developing CKD. If new recommendations are made in future, this may increase the number of children and young people being tested and thus increase costs for the NHS.
National priorities	High
Current evidence base	Minimal limited to 2 risk factors: acute kidney injury and solitary functioning kidney.
Equality considerations	None known

L.1.4 Modified PICO table

Population	**Inclusion:** Children and young people (up to the age of 18). **Exclusion:**

	• people receiving renal replacement therapy (RRT) • people with acute kidney injury combined with rapidly progressive glomerulonephritis • pregnant young women • people receiving palliative care • people undergoing non-kidney transplantation
Prognostic factor	• Congenital renal abnormalities • Acute kidney injury • Blood in urine • Multisystem disease • Low birth weight • Family history of CKD • Obesity • Diabetes • Hypertension • Cardiovascular disease • Structural renal tract disease • Recurrent renal calculi
Co-variates	Confounders identified by the studies themselves will be used
Outcome	Adjusted (unadjusted will only be used if adjusted values are not available) hazard ratios, risk ratios and odds ratios at all reported time points for: • Diagnosis of CKD • CKD progression: change in eGFR • CKD progression: occurrence of end stage kidney disease (ESRD or ESKD as reported by the study) • All-cause mortality
Study design	• Prospective cohort studies (retrospective cohort studies will be used if no prospective studies ae found). • Systematic reviews of prospective cohort studies
Timeframe	Long term
Additional information	None