National Institute for Health and Care Excellence

Final

Chronic kidney disease

[E] Evidence review for optimal monitoring frequency

NICE guideline NG203

Evidence reviews underpinning recommendations 1.3.1 and 1.3.2 and research recommendations on optimal monitoring frequency in the NICE guideline

August 2021

Final

These evidence reviews were developed by Guideline Updates Team

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ISBN: 978-1-4731-4233-6

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Optimal monitoring frequency

1.1 Review question

3.2 For adults, children and young people with CKD what is the optimal monitoring frequency based on different rates of decline in eGFR?

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 routine surveillance programme to determine whether new evidence was available that could alter the current recommendations. The surveillance report identified a very large individual patient data meta-analysis (Coresh 2014) that highlights the potential value of smaller declines in eGFR to indicate CKD progression over 1, 2 and 3 years. It was considered to have the capability of identifying patients at high risk of ESRD who are likely to benefit from earlier referral, who will not be highlighted in the current guidance. As a result, the decision was made to update this part of the guideline.

This review question aims to determine the optimal monitoring frequency based on the prognostic importance of a decline in eGFR in adults, children and young people with CKD.

1.1.2 Summary of the protocol

Table 1 Summary of the protocol

Population	**Inclusion:** Adults, children and young people **Exclusion:** • people receiving renal replacement therapy (RRT) • people with acute kidney injury combined with rapidly progressive glomerulonephritis • pregnant women • people receiving palliative care.
Phenomenon of interest	estimated Glomerular Filtration Rate as a predictor of CKD progression. Co-variates include (but are not restricted to): • Ethnicity • Diabetes
Comparator	An absence of risk factors
Outcomes	• CKD progression measured by o Change in eGFR o Incidence of end stage kidney disease • Mortality o All cause o Cardiovascular

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 methods section in Appendix B.

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

Protocol deviations

The protocol included CKD progression based on a minimum of 25% decline in eGFR. However, studies reported declines below 25% (i.e. 20%) or eGFR decline of 1 or 10 mL/min/1.73. As the surveillance review stated that there may be people with CKD who can benefit from early referral, all measurements of eGFR decline were included as the prognostic factor of interest.

1.1.4 Prognostic evidence

1.1.4.1 Included studies

A systematic search was carried out to identify prospective cohort studies and individual participant data (IPD) cohorts, which found 3,074 references (see appendix C for the literature search strategy). Evidence identified in the original guideline (10 references) and evidence found in the search for evidence review N on defining clinically significant decline in eGFR in terms of risk of kidney disease progression (1 reference) were also reviewed. In total, 3,085 references were identified for screening at title and abstract level. During screening 3,013 references excluded. The full texts of 72 articles were reviewed. In total, 8 articles were included based on their relevance to the review protocol (Appendix A). Of these, 3 were IPDs and 5 were prospective cohort studies. There were prospective cohort studies found by the systematic search which were also included in the IPDs. Therefore, any prospective cohort studies in the IPDs were excluded as individual prospective cohort studies (this was noted as the reason for exclusion in Appendix K) to avoid double-counting.

IPDs were Coresh 2014, Lambers Heerspink 2014, and Orlandi 2019 (details for each IPD can be seen below on section 1.1.5 Summary of studies included in prognostic evidence). Lambers Heerspink 2014 included 20 cohorts which overlapped with Coresh 2014. Therefore, results from studies reported in Lambers Heerspink 2014 which did not overlap with Coresh 2014 were presented as additional data at the end of Appendix F.

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 110 references for this review question, these were screened on title and abstract. Three references were ordered for full text screening. None of these references were included based on their relevance to the review protocol (Appendix A).

See appendix D for a PRISMA flow chart showing study selection.

1.1.4.2 Excluded studies

See appendix K for excluded studies with the primary reason for exclusion.

1.1.5 Summary of studies included in prognostic evidence

Table 2 Summary of studies included in prognostic evidence

Study	Study design	Population and sample size (confounders adjusted for)	Prognostic factor	Outcomes [applicability]
Coresh 2014	Individual participant data meta-analysis	22 cohorts with CKD stage 3-5, N = 466,068 (60 year old, non-black, male, no change in eGFR, a first eGFR of 50 ml/min/1.73m2, a systolic blood pressure of 130 mm Hg, a total cholesterol of 5 mmol/L, no history of diabetes or CVD)	20%, 25%, 30%, 40% and 57% eGFR decline	- ESRD (initiation of renal replacement therapy or death due to kidney disease other than acute kidney injury), - all-cause mortality, - cardiovascular mortality [directly applicable]
Harambat 2017	Prospective cohort	Paediatric, N = 704 (age at baseline, sex, Tanner stage, country of residence, cause of CKD, duration of CKD, baseline eGFR, time-dependent systolic and diastolic blood pressure, and time-dependent albumin-to-protein ratio)	Baseline eGFR per ml/min/1.73 m²	ESRD (start of dialysis or pre-emptive transplantation, or eGFR <10 ml/min/1.73 m²) or 50% decline in eGFR [directly applicable]
Ishikura 2014	Prospective cohort	Paediatric, N =447 (Sex, age, CKD stage, congenital anomalies of the kidney and urinary tract, preterm delivery, heavy proteinuria, hypertension, use of antihypertensive drug)	CKD stage 4 and 5.	End stage renal disease (no definition) [directly applicable]
Lambers Heerspink[1] 2014	Individual participant data meta-analysis	37 cohorts (of which only 20 included due to overlap with Coresh 2014), CKD 1-5, N=9,488 (Age, sex, race, baseline eGFR, proteinuria, systolic blood pressure, diabetes and treatment assigned to each study)	30% eGFR decline	ESRD: initiation of treatment with dialysis or transplantation, kidney failure not treated with dialysis or transplantation or doubling of serum creatinine. [directly applicable]

Study	Study design	Population and sample size (confounders adjusted for)	Prognostic factor	Outcomes [applicability]
Lin 2016	Prospective cohort	Paediatric, CKD stage 3-5, N= 5,351 (age, sex, hyperlipidemia, hypoalbuminemia, proteinuria, and systolic BP)	CKD stage 3 – 5	ESRD (no definition) [directly applicable]
Orlandi 2019	Individual participant data meta-analysis	8 cohorts CKD 3-5, N= 23,484 (eGFR 10 unit decrease from baseline. eGFR measured by CKD-EPI equation)	eGFR decline per 10 ml/min/1.73 m²	ESRD: time until dialysis was initiated or when the participant received a kidney transplant. All-cause mortality. [directly applicable]
Subramanian 2019	Prospective cohort	Type 2 diabetes and CKD stage 1-5, N = 91 (Age, diabetes duration (years), urine ACR, HbA1C, hypertension, absent or diminished peripheral pulses)	Baseline eGFR	> 30% decline in eGFR [directly applicable]
Tsai 2017	Prospective cohort	CKD 1-5, N= 4600 (Age, sex, proteinuria (yes vs. no), hypertension (yes vs. no), diabetic nephropathy (yes vs. no), history of CVD, and baseline CKD stage)	eGFR decline per 1 ml/min/1.73 m²	ESRD (not defined) [directly applicable]

CKD: chronic kidney disease; eGFR estimated Glomerular Filtration Rate; ESRD: End-stage renal disease.
(1) See Appendix F1 for details of this study.

See Appendix E for full evidence tables.

1.1.6 Summary of the prognostic evidence

Table 3 Risk of CKD progression (defined as greater than 30% decline in eGFR from baseline eGFR), compared to baseline eGFR, in CKD stage 1-5 with type 2 diabetes

Outcomes	Relative effect (95% CI)	Studies	Quality of the evidence	Interpretation
> 30% eGFR decline in type 2 diabetes, mean 4.8 years	OR 0.98 (0.96 to 1)	1 study	Moderate	Could not differentiate

Table 4 Risk of CKD progression (defined as eGFR percent change1) compared to stable eGFR (0% change), CKD stage 3-5

Outcomes	Relative effect	Study	Quality of the evidence	Interpretation
ESRD, 1 year– 20% decline	HR 2.4 (2.2 to 2.62)	1 study	high	higher risk
ESRD, 1 year– 25% decline	HR 3 (2.6 to 3.46)	1 study	high	higher risk
ESRD, 1 year– 30% decline	HR 4 (3.4 to 4.71)	1 study	high	higher risk
ESRD, 1 year– 40% decline	HR 7.4 (6.1 to 8.98)	1 study	high	higher risk
ESRD, 1 year– 57% decline	HR 21.5 (16.1 to 28.71)	1 study	high	higher risk
ESRD, 2 years – 20% decline	HR 2.9 (2.5 to 3.36)	1 study	high	higher risk
ESRD, 2 years – 25% decline	HR 4 (3.3 to 4.85)	1 study	high	higher risk
ESRD, 2 years – 30% decline	HR 5.4 (4.5 to 6.48)	1 study	high	higher risk
ESRD, 2 years – 40% decline	HR 10.2 (8.2 to 12.69)	1 study	high	higher risk
ESRD, 2 years – 57% decline	HR 32.1 (22.3 to 46.21)	1 study	high	higher risk
ESRD, 3 years – 20% decline	HR 2.5 (2.1 to 2.98)	1 study	high	higher risk
ESRD, 3 years – 25% decline	HR 3.2 (2.4 to 4.27)	1 study	high	higher risk
ESRD, 3 years – 30% decline	HR 5 (3.9 to 6.41)	1 study	high	higher risk
ESRD, 3 years – 40% decline	HR 10.4 (8 to 13.52)	1 study	high	higher risk
ESRD, 3 years – 57% decline	HR 36.8 (27.3 to 49.61)	1 study	high	higher risk

Outcomes	Relative effect	Study	Quality of the evidence	Interpretation
All-cause mortality, 1 year – 20% decline	HR 1.4 (1.31 to 1.5)	1 study	high	higher risk
All-cause mortality, 1 year – 25% decline	HR 1.6 (1.5 to 1.71)	1 study	high	higher risk
All-cause mortality, 1 year – 30% decline	HR 1.9 (1.7 to 2.12)	1 study	high	higher risk
All-cause mortality, 1 year – 40% decline	HR 2.4 (2.2 to 2.62)	1 study	high	higher risk
All-cause mortality, 1 year – 57% decline	HR 3.8 (3.3 to 4.38)	1 study	high	higher risk
All-cause mortality, 2 years – 20% decline	HR 1.4 (1.3 to 1.51)	1 study	high	higher risk
All-cause mortality, 2 years – 25% decline	HR 1.5 (1.4 to 1.61)	1 study	high	higher risk
All-cause mortality, 2 years – 30% decline	HR 1.8 (1.6 to 2.03)	1 study	high	higher risk
All-cause mortality, 2 years – 40% decline	HR 2.3 (2.1 to 2.52)	1 study	high	higher risk
All-cause mortality, 2 years – 57% decline	HR 3.7 (3.2 to 4.28)	1 study	high	higher risk
All-cause mortality, 3 years – 20% decline	HR 1.4 (1.3 to 1.51)	1 study	high	higher risk
All-cause mortality, 3 years – 25% decline	HR 1.5 (1.4 to 1.61)	1 study	high	higher risk
All-cause mortality, 3 years – 30% decline	HR 1.8 (1.6 to 2.03)	1 study	high	higher risk
All-cause mortality, 3 years – 40% decline	HR 2.2 (2 to 2.42)	1 study	high	higher risk
All-cause mortality, 3 years – 57% decline	HR 3.3 (2.7 to 4.03)	1 study	high	higher risk
Cardiovascular mortality, 1 year – 20% decline	HR 1.4 (1.2 to 1.63)	1 study	high	higher risk
Cardiovascular mortality, 1 year – 30% decline	HR 1.7 (1.4 to 2.06)	1 study	high	higher risk
Cardiovascular mortality, 1 year – 40% decline	HR 2.1 (1.6 to 2.76)	1 study	high	higher risk
Cardiovascular mortality, 1 year – 57% decline	HR 2.8 (1.8 to 4.36)	1 study	high	higher risk
Cardiovascular mortality, 2 years – 20% decline	HR 1.3 (1.1 to 1.54)	1 study	high	higher risk
Cardiovascular mortality, 2 years – 30% decline	HR 1.6 (1.3 to 1.97)	1 study	high	higher risk
Cardiovascular mortality, 2 years – 40% decline	HR 1.9 (1.5 to 2.41)	1 study	high	higher risk
Cardiovascular mortality, 2 years – 57% decline	HR 2.6 (1.7 to 3.98)	1 study	high	higher risk
Cardiovascular mortality, 3 years – 20% decline	HR 1.4 (1.2 to 1.63)	1 study	high	higher risk
Cardiovascular mortality, 3 years – 30% decline	HR 1.7 (1.4 to 2.06)	1 study	high	higher risk

Outcomes	Relative effect	Study	Quality of the evidence	Interpretation
Cardiovascular mortality, 3 years – 40% decline	HR 2 (1.7 to 2.35)	1 study	high	higher risk
Cardiovascular mortality, 3 years – 57% decline	HR 2.4 (1.6 to 3.6)	1 study	high	higher risk
1) Percent change in eGFR was calculated as follows: (last eGFR – first eGFR)/(first eGFR) * 100%				

Table 5 Risk of CKD progression (defined as decline greater than 1 mL/min/1.73 in eGFR per year), compared to less than 1 mL/min/1.73, CKD stage 1-5

Outcomes	Relative effect (95% CI)	Studies	Quality of the evidence (GRADE)	Interpretation
End stage renal disease	HR 1.17 (1.16 to 1.18)	1 study	high	Higher risk

Table 6 Risk of CKD progression (defined as decline greater than 10 mL/min/1.73 in eGFR at follow-up or 10 year follow-up), compared to baseline eGFR, CKD stage 3-5

Outcomes	Relative effect (95% CI)	Studies	Quality of the evidence (GRADE)	Interpretation
End stage renal disease	HR 2.54 (2.25 to 2.87)	7 studies	low	Higher risk
Allcause mortality	HR 1.18 (1.14 to 1.22)	1 study	moderate	Higher risk

Table 7 Risk of CKD progression in children

Outcomes	Relative effect(95% CI)	Studies	Quality of the evidence (GRADE)	
ESRD, 12 years minimum follow-up – CKD stage 3b (compared to stage 3a)	HR 2.64 (1.14 to 6.11)	1 study	high	Higher risk
ESRD, 12 years minimum follow-up – CKD stage 4 (compared to stage 3a)	HR 4.82 (3.24 to 7.17)	1 study	high	Higher risk
ESRD or mortality, median 1.5 years follow-up – CKD stage 4 (compared to stage 3)	HR 11.12 (4.22 to 29.3)	1 study	moderate	Higher risk

Outcomes	Relative effect(95% CI)	Studies	Quality of the evidence (GRADE)	
ESRD or mortality, median 1.5 years follow-up – CKD stage 5 (compared to stage 3)	HR 26.95 (7.71 to 94.2)	1 study	moderate	Higher risk
ESRD or 50% decline in eGFR, median 5.18 years follow-up, compared to baseline eGFR (ml/min/1.73), CKD stage 3-5	HR 0.99 (0.98 to 1)	1 study	low	Could not differentiate

Additional evidence from IPDs

The Coresh 2014 IPD was considered to be the key IPD among the 3 IPDs found, and was included in the main analysis.

Additional data was obtained from one individual participant data (IPD) meta-analysis (Lambers Heerspink 2014). The pooled hazard ratio from this IPD could not be included as it contained overlaps with Coresh 2014 IPD meta-analysis. In addition, the individual studies could not be pooled with prospective cohort evidence as method of analysis in Lambers Heerspink 2014 accounts for intervention treatment and control arm as covariates. Therefore, hazard ratios from studies reported in Lambers Heerspink 2014 which do not overlap with Coresh 2014 are presented separately in F.1. The sample sizes of these studies ranged from N=75 to N=1137.

The pooled hazard ratio of ESRD per 30% eGFR decline in studies not reported by Coresh 2014 was HR= 9.77 (95% CI 6.47, 14.75).

An IPD by Orlandi 2019 did not overlap with Coresh 2014 and was included in the main analysis (see Appendix F).

See Appendix G for full GRADE tables.

1.1.7 Economic evidence

A systematic search was conducted to identify economic evaluations for this review question. The search returned 540 records which were sifted against the review protocol. All publications were excluded based on title and abstract. The study selection diagram is presented in Appendix H. For more information on the search strategy please see appendix C.

1.1.8 Summary of included economic evidence

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

1.1.9 Economic model

Economic modelling was not prioritised for this review question.

1.1.10 The committee's discussion and interpretation of the evidence

1.1.10.1. The outcomes that matter most

All prognostic outcomes listed were considered important in this evidence review. The committee noted the key importance of the large individual participant data (IPD) meta-analysis study (Coresh 2014) which provided aggregated data on end stage kidney disease, cardiovascular mortality and mortality. While the committee viewed these outcomes as highly

important for decision making, they also took into account change in eGFR which is a marker of CKD progression.

1.1.10.2 The quality of the evidence

The quality of the evidence ranged from low to high. The main reason for downgrading the quality of the evidence was for inconsistency due to heterogeneity in the pooled estimate of the meta-analyses (these meta-analyses were done with studies from the other 2 IPDs [Lambers Heerspink 2014 and Orlandi 2019] which were not considered as important as Coresh 2014). Studies included ranged from large individual participant data-sets to small prospective cohort studies. Most of the evidence was on adults which was reported by the 3 IPDs and 2 prospective studies (mainly high-quality evidence; N>91 [range 91 to 466,068 participants). The IPD by Coresh 2014 was of high quality. There were 3 prospective studies reporting evidence on children and young people (quality of evidence varied from low to high; N>704 [range 704 to 5351 participants).

The risk of bias for the 3 IPDs was evaluated using the checklist for IPDs rather than for each individual study included in the IPDs.

1.1.10.3 Benefits and harms

The majority of the evidence included for adults showed that with eGFR decline, the risk of kidney disease progression and mortality significantly increases, and this risk significantly increases with increasing eGFR decline (HR> 2.4 for kidney disease progression [HR range 2.4 to 36.8]; HR>1.4 for mortality [HR range 1.4 to 3.3]). The committee agreed this is observed in clinical practice and any person presenting with an increase in eGFR decline would be monitored frequently. The committee reviewed the previous recommendations and agreed on the strength (previous recommendations were already strong) and that they are consistent with the evidence and what occurs in practice. These recommendations were developed to guide the frequency of CKD monitoring taking into account people's preferences and needs. Frequency of monitoring was recommended to be agreed with adults, children and young people with CKD (and their family members or carers, as appropriate). It agreed to clarify monitoring by amending the recommendation to state that repeat assessment is to be agreed with the person with or at risk of CKD.

The committee agreed to extend the recommendation to guide the frequency of monitoring to include rate of change in eGFR or ACR and specific comorbidities, including diabetes, that are known clinical risk factors. There was one small prospective cohort study which could not differentiate risk of greater than 30% eGFR decline in those with type 2 diabetes (evidence was not enough to show otherwise), the committee agreed that in clinical practice, type 2 diabetes would be considered an area of consideration for monitoring. The committee did not think that this was a priority area for research and no research recommendation was developed.

The committee agreed that ACR monitoring should be individualised. For example, ACR might be monitored more frequently in people with high ACR (categories A2 or A3), or if a change in ACR would affect management. The committee made a research recommendation to identify the optimal frequency of ACR monitoring in adults, children and young people with CKD.

The committee discussed whether specific recommendations are needed for children and young people with CKD and decline in eGFR, but agreed that this population would be referred to specialist care and made a recommendation (for further details on recommendations on when to refer children and young people for specialist assessment see evidence review F: The best combination of measures to identify increased risk of progression in adults, children and young people). The evidence showed that there was a significantly higher risk of CKD progression in children and young people with more

advanced CKD (high quality evidence comparing CKD 3a with CKD 3b [HR 2.64] and with CKD 4 [HR 4.82]). The committee also agreed to make a research recommendation to fill in this gap of evidence and to inform future guidance on the timing of review for children and young people, as well as adults, with CKD (see Appendix L).

The committee did not identify any meaningful harms associated with people being monitored for progression of their CKD.

1.1.10.4 Cost effectiveness and resource use

The committee was not presented any formal cost effectiveness evidence. The recommendations are not expected to result in a substantial resource impact as the changes are unlikely to meaningfully increase the number of monitoring appointments. The recommendations mostly remained unchanged from previous guideline in 2014.

1.1.12 Recommendations supported by this evidence review

This evidence review supports recommendations 1.3.1 and 1.3.2 and the research recommendations on optimal monitoring frequency. Other evidence supporting these recommendations can be found in the evidence reviews on defining clinically significant decline in eGFR in terms of risk of kidney disease progression (evidence review N).

1.1.13 References – included studies

Coresh, Josef, Turin, Tanvir Chowdhury, Matsushita, Kunihiro et al. (2014) Decline in estimated glomerular filtration rate and subsequent risk of end-stage renal disease and mortality. JAMA 311(24): 2518-2531

Harambat, Jerome, Kunzmann, Kevin, Azukaitis, Karolis et al. (2017) Metabolic acidosis is common and associates with disease progression in children with chronic kidney disease. Kidney international 92(6): 1507-1514

Ishikura, K., Uemura, O., Hamasaki, Y. et al. (2014) Progression to end-stage kidney disease in Japanese children with chronic kidney disease: Results of a nationwide prospective cohort study. Nephrology Dialysis Transplantation 29(4): 878-884

Lambers Heerspink, Hiddo J, Tighiouart, Hocine, Sang, Yingying et al. (2014) GFR decline and subsequent risk of established kidney outcomes: a meta-analysis of 37 randomized controlled trials. American journal of kidney diseases : the official journal of the National Kidney Foundation 64(6): 860-6

Lin, Ching-Yuang and Huang, Shiuh-Ming (2016) Childhood Albuminuria and Chronic Kidney Disease is Associated with Mortality and End-Stage Renal Disease. Pediatrics and neonatology 57(4): 280-7

Orlandi, P.F., Huang, J., Hoy, W. et al. (2019) A collaborative, individual-level analysis compared longitudinal outcomes across the International Network of Chronic Kidney Disease (iNETCKD) cohorts. Kidney International 96(5): 1217-1233

Subramanian, N., Xu, J., Sayyed Kassem, L. et al. (2019) Absent or diminished pedal pulses and estimated GFR decline in patients with diabetic kidney disease. Renal failure 41(1): 691-697

Tsai, Ching-Wei, Ting, I-Wen, Yeh, Hung-Chieh et al. (2017) Longitudinal change in estimated GFR among CKD patients: A 10-year follow-up study of an integrated kidney disease care program in Taiwan. PloS one 12(4): e0173843

1.1.14.2 Economic

No economic studies were identified for inclusion in this review.

1.1.14.3 Other

QUIPS checklist:

Hayden, J.A., van der Windt, D.A., Cartwright, J.L., Côté, P. and Bombardier, C., 2013. Assessing bias in studies of prognostic factors. *Annals of internal medicine*, *158*(4), pp.280-286.

Appendices

Appendix A – Review protocol

Review protocol for frequency of CKD monitoring

ID	Field	Content
0.	PROSPERO registration number	CRD42020162564
1.	Review title	Optimal monitoring frequency in CKD
2.	Review question	In adults, children and young people with CKD, how frequently should eGFR be monitored (in order to predict future CKD progression)?
3.	Objective	To determine the optimal monitoring frequency based on the prognostic importance of a decline in eGFR in adults, children and young people with CKD.
4.	Searches	The following databases will be searched: Cochrane Database of Systematic Reviews (CDSR) Embase MEDLINE Searches will be restricted by: English language Human studies 2014 or later for adults 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.

ID	Field	Content
5.	Condition or domain being studied	Currently, eGFR is reviewed at least annually in people with CKD to check for decline indicating CKD progression. However, there is new evidence on the potential value of small declines in eGFR to indicate CKD progression over 1, 2 and 3 years. Additionally, there are potentially greater risks of progression in specific sub-groups, for example people with diabetes. This means there may be value in monitoring eGFR more frequently to be able to detect these small declines.
6.	Population	Adults, children and young people with diagnosed chronic kidney disease Exclusion: people receiving renal replacement therapy (RRT) people with acute kidney injury combined with rapidly progressive glomerulonephritis pregnant women people receiving palliative care.
7.	Prognostic factor	estimated Glomerular Filtration Rate as a predictor of CKD progression. Threshold of 25% change in eGFR to be used to mark significant change at various time points.
8.	Comparator	An absence of risk factors'
9.	Types of study to be included	Prospective cohort studies (or retrospective if no prospective available) Cross sectional studies
10.	Other exclusion criteria	Abstracts & conference proceedings Theses Non-English language
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.

ID	Field	Content
12.	Primary outcomes (critical outcomes)	Over the follow up time of the cohort: CKD progression measured by Change in eGFR Incidence of end stage kidney disease Mortality All cause Cardiovascular Co-variates include (but are not restricted to: Ethnicity Diabetes
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 PROBAST checklist as described in Developing NICE guidelines: the manual.
16.	Strategy for data synthesis	Hazard ratios will pooled using the inverse-variance method. Adjusted hazard ratios from multivariate models will only be pooled if the same set of predictor variables are used across multiple studies and are on the same scale and if the same confounders are adjusted for.
17.	Analysis of sub-groups	Where data can be disambiguated, sub-group analysis will be used to stratify by: Rate of progression

ID	Field	Content	
		Age Ethnicity Diabetes Gender hypertension	
18.	Type and method of review	☐	Intervention
		☐	Diagnostic
		☒	Prognostic
		☐	Qualitative
		☐	Epidemiologic
		☐	Service Delivery
		☐	Other (please specify)
19.	Language	English	
20.	Country	England	

Appendix B – Methods

Incorporating published individual patient data meta-analyses

Quality assessment

Individual patient data meta-analyses were quality assessed using guidance published by Tierney and colleagues (Tierney 2015), with each classified into one of the following three groups:

• High quality – It is unlikely that additional relevant and important data would be identified from primary studies compared to that reported in the IPD, and unlikely that any relevant and important studies have been missed by the IPD.

• Moderate quality – It is possible that additional relevant and important data would be identified from primary studies compared to that reported in the IPD, but unlikely that any relevant and important studies have been missed by the IPD.

• Low quality – It is possible that relevant and important studies have been missed by the IPD.

Each IPD was also classified into one of three groups for its applicability as a source of data, based on how closely the review matches the specified review protocol in the guideline. IPDs were rated as follows:

• Fully applicable – The identified IPD fully covers the review protocol in the guideline.

• Partially applicable – The identified IPD fully covers a discrete subsection of the review protocol in the guideline (for example, some of the factors in the protocol only).

• Not applicable – The identified IPD, despite including studies relevant to the review question, does not fully cover any discrete subsection of the review protocol in the guideline.

Using published IPDs as a source of data

If IPDs were identified as being sufficiently applicable and high quality, and were identified sufficiently early in the review process (for example, from the surveillance review or early in the database search), they were used as the primary source of data, rather than extracting information from primary studies. The extent to which this was done depended on the quality and applicability of the IPD, as defined in Table 8. When IPDs were used as a source of primary data, and unpublished or additional data included in the IPD which is not in the primary studies was also included. Data from these IPDs was then quality assessed and presented in GRADE tables as described below, in the same way as if data had been extracted from primary studies. In questions where data was extracted from both IPDs and primary studies, these were cross-referenced to ensure none of the data had been double counted through this process. Where there was overlap between the studies included in IPDs, the most relevant IPD was included in the analysis and data that could be extracted from other IPDs without double counting were presented as additional data.

Table 8: Criteria for using IPDs as a source of data

Quality	Applicability	Use of systematic review
High	Fully applicable	Data from the published IPD were used instead of undertaking a new literature search or data analysis. Searches were only done to cover the period of time since the search date of the IPD.
High	Partially applicable	Data from the published IPD were used instead of undertaking a new literature search and data analysis for the relevant

Quality	Applicability	Use of systematic review
		subsection of the protocol. For this section, searches were only done to cover the period of time since the search date of the IPD. For other sections not covered by the systematic review, searches were undertaken as normal.
Moderate	Fully applicable	Details of included studies were used instead of undertaking a new literature search. Full-text papers of included studies were still retrieved for the purposes of data analysis. Searches were only done to cover the period of time since the search date of the IPD.
Moderate	Partially applicable	Details of included studies were used instead of undertaking a new literature search for the relevant subsection of the protocol. For this section, searches were only done to cover the period of time since the search date of the IPD. For other sections not covered by the IPD, searches were undertaken as normal.

Prognostic studies

Quality assessment

The Quality In Prognosis Studies (QUIPS) was used to assess studies of prognostic factors (Hayden et al 2013). Studies were assessed on the methods of participant recruitment, retention and outcome measurement (as appropriate), with each individual study classified into one of the following three groups:

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

Each individual study was also classified into one of three groups for directness, based on if there were concerns about the population 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, intervention, comparator and/or outcomes.
- Partially indirect – Important deviations from the protocol in one of the population, intervention, comparator and/or outcomes.
- Indirect – Important deviations from the protocol in at least two of the population, intervention, comparator and/or outcomes.

Modified GRADE for prognostic evidence

GRADE has not been developed for use with prognostic test accuracy studies or IPDs; therefore a modified approach was applied using the GRADE framework.

Prospective cohort studies and IPDs were initially rated as high-quality evidence if well conducted, and then downgraded according to the standard GRADE criteria (risk of bias, inconsistency, imprecision and indirectness) as detailed in Table 9 below.

Table 9: Rationale for downgrading quality of evidence for prognostic questions

GRADE criteria	Reasons for downgrading quality
Risk of bias	Not serious: If less than 33.3% of the weight in a meta-analysis came from studies at moderate or high risk of bias, the overall outcome was not downgraded. Serious: If greater than 33.3% of the weight in a meta-analysis came from studies at moderate or high risk of bias, the outcome was downgraded one level. Very serious: If greater than 33.3% of the weight in a meta-analysis came from studies at high risk of bias, the outcome was downgraded two levels. Outcomes meeting the criteria for downgrading above were not downgraded if there was evidence the effect size was not meaningfully different between studies at high and low risk of bias.
Indirectness	Not serious: If less than 33.3% of the weight in a meta-analysis came from partially indirect or indirect studies, the overall outcome was not downgraded. Serious: If greater than 33.3% of the weight in a meta-analysis came from partially indirect or indirect studies, the outcome was downgraded one level. Very serious: If greater than 33.3% of the weight in a meta-analysis came from indirect studies, the outcome was downgraded two levels. Outcomes meeting the criteria for downgrading above were not downgraded if there was evidence the effect size was not meaningfully different between direct and indirect studies.
Inconsistency	Concerns about inconsistency of predictive accuracy across studies, occurring when there is unexplained variability in the predictive accuracy demonstrated across studies (heterogeneity), after appropriate pre-specified subgroup analyses have been conducted. This was assessed using the I^2 statistic. N/A: Inconsistency was marked as not applicable if data on the outcome was only available from one study. Not serious: If the I^2 was less than 33.3%, the outcome was not downgraded. Serious: If the I^2 was between 33.3% and 66.7%, the outcome was downgraded one level. Very serious: If the I^2 was greater than 66.7%, the outcome was downgraded two levels. Outcomes meeting the criteria for downgrading above were not downgraded if there was evidence the effect size was not meaningfully different between studies with the smallest and largest effect sizes.
Imprecision	If the 95% confidence interval for predictive accuracy crossed the line of no effect (HR = 1), the outcome was downgraded one level, as the data were deemed to be imprecise.

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. However, no consensus MIDs were defined and no published MIDs were found.

Interpreting effect

No minimal important differences (MIDs) were identified in this review and therefore the line of no effect (hazard ratio = 1) was used to determine effect. The following interpretations were used:

- There is a higher risk of the outcome if the HR and 95% CI is greater than 1. For example, for the outcome of ESRD, if the prognostic factor is 20% decline in eGFR compared to stable eGFR (0% decline) and the HR with associated 95% CI is greater than 1, than this is interpreted to be a higher risk of ESRD with 20% eGFR decline compared to stable eGFR.
- The evidence could not differentiate between comparators if the 95% CI crosses the line of no effect (HR =1).
- The evidence showed a lower risk of outcome with the prognostic factor compared to comparator if HR < 1 and the 95% CI does not cross the line of no effect.

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 10.

Table 10 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

Level	Explanation
	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 11.

Table 11 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 25th of November 2019 and updated on the 9th 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.

To retrieve evidence on adults that had been published since the search strategies were last run for the former guideline, the search was limited from 2013. No date restrictions were applied to the section of the search strategies on children and young people because this population had not been included in the former guideline.

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

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

Clinical searches

Databases	Date searched	Version/files	No. retrieved
Cochrane Central Register of Controlled Trials (CENTRAL)	25th Nov 2019	Issue 11 of 12, November 2019	310
Cochrane Database of Systematic Reviews (CDSR)	25th Nov 2019	Issue 11 of 12, November 2019	13
Database of Abstracts of Reviews of Effect (DARE)	25th Nov 2019	Up to 2015	116
Embase (Ovid)	25th Nov 2019	Embase <1974 to 2019 Week 47>	1845

MEDLINE (Ovid)	25th Nov 2019	Ovid MEDLINE(R) <1946 to November 22, 2019>	1813
MEDLINE In-Process (Ovid)	25th Nov 2019	Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to November 22, 2019>	124
MEDLINE Epub Ahead of Print	25th Nov 2019	Ovid MEDLINE(R) Epub Ahead of Print <November 22, 2019>	16

Search strategies

Database: Ovid MEDLINE(R) <1946 to November 22, 2019>

Search Strategy:

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1 exp Renal Insufficiency, Chronic/ (110914)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (71116)

3 ((kidney* or renal*) adj1 insufficien*).tw. (21130)

4 ckd*.tw. (22151)

5 ((kidney* or renal*) adj1 fail*).tw. (85720)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (34655)

7 (esrd* or eskd*).tw. (13917)

8 "Chronic Kidney Disease-Mineral and Bone Disorder"/ (3426)

9 or/1-8 (209813)

10 Glomerular Filtration Rate/ (42656)

11 (glomerul* or GFR* or eGFR* or e-GFR*).tw. (155336)

12 10 or 11 (168608)

13 9 and 12 (34940)

14 monitor*.ti. (106000)

15 disease progression/ (155071)

16 (progress* or declin*).ti. (144325)

17 or/14-16 (364489)

18 13 and 17 (4919)

19 prognosis/ (486916)

20 time factors/ (1167642)

21 ((interval* or every or each or per) adj5 (month* or year* or annual* or annum* or week*)).tw. (350135)

22 (treatment adj3 (nonresponse* or failure* or response* or duration or outcome*)).tw,hw. (1097472)

23 (predict* adj2 (value* or treatment* or response* or outcome* or factor*)).tw,hw. (369833)

24 ((review* or recall* or regular* or periodic*) adj3 (interval* or visit* or revisit* or examin* or attend* or test* or retest*)).tw. (58822)

25 (follow* up* or followup*).tw. (883488)

26 (management adj (strateg* or protocol* or plan*)).tw. (33349)

27 natural histor*.tw. (42099)

28 (PPV or NPV).tw. (15156)

29 or/19-28 (3573542)

30 monitor*.ab,hw. (788975)

31 29 and 30 (172713)

32 13 and 31 (727)

33 18 or 32 (5472)

34 limit 33 to english language (5007)

35 animals/ not humans/ (4612069)

36 34 not 35 (4565)

37 limit 36 to ed=20131101-20191125 (2172)

38 exp Infant/ or Infant Health/ or Infant Welfare/ (1114678)

39 (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. (827931)

40 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (1869654)

41 Minors/ (2545)

42 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (2272993)

43 exp pediatrics/ (56538)

44 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (795066)

45 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (1972824)

46 Puberty/ (13111)

47 (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. (406080)

48 Schools/ (36306)

49 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (8682)

50 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (452006)

51 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (3763)

52 or/38-51 (5040018)

53 36 and 52 (1185)

54 37 or 53 (2791)

55 Observational Studies as Topic/ (4459)

56 Observational Study/ (70244)

57 Epidemiologic Studies/ (8151)

58 exp Case-Control Studies/ (1034649)

59 exp Cohort Studies/ (1924233)

60 Cross-Sectional Studies/ (310281)

61 Controlled Before-After Studies/ (444)

62 Historically Controlled Study/ (164)

63 Interrupted Time Series Analysis/ (713)

64 Comparative Study.pt. (1846855)

65 case control$.tw. (107499)

66 case series.tw. (55509)

67 (cohort adj (study or studies)).tw. (155859)

68 cohort analy$.tw. (6225)

69 (follow up adj (study or studies)).tw. (44027)

70 (observational adj (study or studies)).tw. (79587)

71 longitudinal.tw. (193720)

72 prospective.tw. (474287)

73 retrospective.tw. (416121)

74 cross sectional.tw. (265653)

75 or/55-74 (4228210)

76 54 and 75 (1813)

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to November 22, 2019>

Search Strategy:

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1 exp Renal Insufficiency, Chronic/ (0)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (9285)

3 ((kidney* or renal*) adj1 insufficien*).tw. (1097)

4 ckd*.tw. (4383)

5 ((kidney* or renal*) adj1 fail*).tw. (6287)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (4686)

7 (esrd* or eskd*).tw. (1972)

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

9 or/1-8 (18173)

10 Glomerular Filtration Rate/ (0)

11 (glomerul* or GFR* or eGFR* or e-GFR*).tw. (15881)

12 10 or 11 (15881)

13 9 and 12 (3621)

14 monitor*.ti. (14754)

15 disease progression/ (0)

16 (progress* or declin*).ti. (21648)

17 or/14-16 (36230)

18 13 and 17 (263)

19 prognosis/ (0)

20 time factors/ (0)

21 ((interval* or every or each or per) adj5 (month* or year* or annual* or annum* or week*)).tw. (41815)

22 (treatment adj3 (nonresponse* or failure* or response* or duration or outcome*)).tw,hw. (29378)

23 (predict* adj2 (value* or treatment* or response* or outcome* or factor*)).tw,hw. (30832)

24 ((review* or recall* or regular* or periodic*) adj3 (interval* or visit* or revisit* or examin* or attend* or test* or retest*)).tw. (8730)

25 (follow* up* or followup*).tw. (107048)

26 (management adj (strateg* or protocol* or plan*)).tw. (6709)

27 natural histor*.tw. (4581)

28 (PPV or NPV).tw. (3110)

29 or/19-28 (206588)

30 monitor*.ab,hw. (90665)

31 29 and 30 (11266)

32 13 and 31 (65)

33 18 or 32 (313)

34 limit 33 to english language (312)

35 animals/ not humans/ (0)

36 34 not 35 (312)

37 limit 36 to dt=20131101-20191125 (290)

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

39 (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. (75466)

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

41 Minors/ (0)

42 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (299265)

43 exp pediatrics/ (0)

44 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (112197)

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

46 Puberty/ (0)

47 (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. (56034)

48 Schools/ (0)

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

50 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (64787)

51 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (571)

52 or/38-51 (434032)

53 36 and 52 (57)

54 37 or 53 (295)

55 Observational Studies as Topic/ (0)

56 Observational Study/ (89)

57 Epidemiologic Studies/ (0)

58 exp Case-Control Studies/ (1)

59 exp Cohort Studies/ (1)

60 Cross-Sectional Studies/ (0)

61 Controlled Before-After Studies/ (0)

62 Historically Controlled Study/ (0)

63 Interrupted Time Series Analysis/ (0)

64 Comparative Study.pt. (45)

65 case control$.tw. (13463)

66 case series.tw. (11954)

67 (cohort adj (study or studies)).tw. (27266)

68 cohort analy$.tw. (982)

69 (follow up adj (study or studies)).tw. (3332)

70 (observational adj (study or studies)).tw. (15982)

71 longitudinal.tw. (32357)

72 prospective.tw. (59499)

73 retrospective.tw. (67297)

74 cross sectional.tw. (55054)

75 or/55-74 (231768)

76 54 and 75 (124)

Database: Ovid MEDLINE(R) Epub Ahead of Print <November 22, 2019>

Search Strategy:

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1 exp Renal Insufficiency, Chronic/ (0)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (1350)

3 ((kidney* or renal*) adj1 insufficien*).tw. (151)

4 ckd*.tw. (698)

5 ((kidney* or renal*) adj1 fail*).tw. (714)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (658)

7 (esrd* or eskd*).tw. (270)

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

9 or/1-8 (2488)

10 Glomerular Filtration Rate/ (0)

11 (glomerul* or GFR* or eGFR* or e-GFR*).tw. (2245)

12 10 or 11 (2245)

13 9 and 12 (533)

14 monitor*.ti. (1775)

15 disease progression/ (0)

16 (progress* or declin*).ti. (2632)

17 or/14-16 (4381)

18 13 and 17 (33)

19 prognosis/ (0)

20 time factors/ (0)

21 ((interval* or every or each or per) adj5 (month* or year* or annual* or annum* or week*)).tw. (7302)

22 (treatment adj3 (nonresponse* or failure* or response* or duration or outcome*)).tw,hw. (4673)

23 (predict* adj2 (value* or treatment* or response* or outcome* or factor*)).tw,hw. (5515)

24 ((review* or recall* or regular* or periodic*) adj3 (interval* or visit* or revisit* or examin* or attend* or test* or retest*)).tw. (1488)

25 (follow* up* or followup*).tw. (19133)

26 (management adj (strateg* or protocol* or plan*)).tw. (926)

27 natural histor*.tw. (659)

28 (PPV or NPV).tw. (451)

29 or/19-28 (35423)

30 monitor*.ab,hw. (11760)

31 29 and 30 (1995)

32 13 and 31 (10)

33 18 or 32 (43)

34 limit 33 to english language (43)

35 animals/ not humans/ (0)

36 34 not 35 (43)

37 Observational Studies as Topic/ (0)

38 Observational Study/ (1)

39 Epidemiologic Studies/ (0)

40 exp Case-Control Studies/ (0)

41 exp Cohort Studies/ (0)

42 Cross-Sectional Studies/ (0)

43 Controlled Before-After Studies/ (0)

44 Historically Controlled Study/ (0)

45 Interrupted Time Series Analysis/ (0)

46 Comparative Study.pt. (0)

47 case control$.tw. (2373)

48 case series.tw. (1948)

49 (cohort adj (study or studies)).tw. (6613)

50 cohort analy$.tw. (276)

51 (follow up adj (study or studies)).tw. (589)

52 (observational adj (study or studies)).tw. (3215)

53 longitudinal.tw. (6652)

54 prospective.tw. (10717)

55 retrospective.tw. (13743)

56 cross sectional.tw. (8294)

57 or/37-56 (42192)

58 36 and 57 (16)

Database: Embase <1974 to 2019 Week 47>

Search Strategy:

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1 exp kidney failure/ (343634)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (119957)

3 ((kidney* or renal*) adj1 insufficien*).tw. (29764)

4 ckd*.tw. (47834)

5 ((kidney* or renal*) adj1 fail*).tw. (130532)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (56862)

7 (esrd* or eskd*).tw. (26610)

8 or/1-7 (434744)

9 exp glomerulus filtration rate/ (95488)

10 (glomerul* or GFR* or eGFR* or e-GFR*).tw. (259335)

11 9 or 10 (287310)

12 8 and 11 (75738)

13 monitor*.ti. (160901)

14 disease course/ (452148)

15 disease exacerbation/ (106135)

16 (progress* or declin*).ti. (210599)

17 or/13-16 (874287)

18 12 and 17 (10816)

19 therapy delay/ (12152)

20 prognosis/ (561606)

21 ((interval* or every or each or per) adj5 (month* or year* or annual* or annum* or week*)).tw. (613417)

22 (treatment adj3 (nonresponse* or failure* or response* or duration or outcome*)).tw,hw. (1511668)

23 (predict* adj2 (value* or treatment* or response* or outcome* or factor*)).tw,hw. (468327)

24 ((review* or recall* or regular* or periodic*) adj3 (interval* or visit* or revisit* or examin* or attend* or test* or retest*)).tw. (89369)

25 (follow* up* or followup*).tw. (1585604)

26 (management adj (strateg* or protocol* or plan*)).tw. (56224)

27 natural histor*.tw. (64279)

28 (PPV or NPV).tw. (35237)

29 or/19-28 (4109288)

30 monitor*.ab,hw. (1267523)

31 29 and 30 (248139)

32 12 and 31 (2018)

33 18 or 32 (12367)

34 limit 33 to english language (11601)

35 nonhuman/ not human/ (4507607)

36 34 not 35 (10784)

37 limit 36 to (conference abstract or conference paper or "conference review" or letter or note or tombstone) (3353)

38 36 not 37 (7431)

39 limit 38 to dc=20131101-20191125 (3566)

40 exp juvenile/ or Child Behavior/ or Child Welfare/ or Child Health/ or infant welfare/ or "minor (person)"/ or elementary student/ (3325323)

41 (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. (1169531)

42 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,ad,jw. (3512578)

43 exp pediatrics/ (102395)

44 (pediatric* or paediatric* or peadiatric*).ti,ab,in,ad,jw. (1578317)

45 exp adolescence/ or exp adolescent behavior/ or adolescent health/ or high school student/ or middle school student/ (100514)

46 (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. (633967)

47 school/ or high school/ or kindergarten/ or middle school/ or primary school/ or nursery school/ or day care/ (100281)

48 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jw. (672669)

49 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (7057)

50 or/40-49 (6222999)

51 38 and 50 (1755)

52 39 or 51 (4548)

53 Clinical study/ (154378)

54 Case control study/ (149377)

55 Family study/ (25968)

56 Longitudinal study/ (133694)

57 Retrospective study/ (852634)

58 Prospective study/ (566840)

59 Randomized controlled trials/ (170989)

60 58 not 59 (560949)

61 Cohort analysis/ (530540)

62 (Cohort adj (study or studies)).mp. (285045)

63 (Case control adj (study or studies)).tw. (128321)

64 (follow up adj (study or studies)).tw. (61572)

65 (observational adj (study or studies)).tw. (156104)

66 (epidemiologic$ adj (study or studies)).tw. (103391)

67 (cross sectional adj (study or studies)).tw. (202318)

68 or/53-57,60-67 (2544592)

69 52 and 68 (1845)

Cochrane Library

ID	Search	Hits
#1	MeSH descriptor: [Renal Insufficiency, Chronic] explode all trees	6131
#2	(((chronic* or progressi*) near/1 (renal* or kidney*))):ti,ab,kw	9980
#3	(((kidney* or renal*) near/1 insufficien*)):ti,ab,kw	4820
#4	(ckd*):ti,ab,kw	4643
#5	(((kidney* or renal*) near/1 fail*)):ti,ab,kw	15995
#6	(((endstage* or end-stage* or "end stage*") near/1 (renal* or kidney*))):ti,ab,kw	4369
#7	((esrd* or eskd*)):ti,ab,kw	1986
#8	MeSH descriptor: [Chronic Kidney Disease-Mineral and Bone Disorder] this term only	83
#9	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8	25169
#10	MeSH descriptor: [Glomerular Filtration Rate] this term only	2603
#11	(glomerul* or GFR* or eGFR* or e-GFR*):ti,ab,kw	17655
#12	#10 or #11	17655
#13	#9 and #12	5351
#14	(monitor*):ti	9159
#15	MeSH descriptor: [Disease Progression] this term only	6461

#16 (progress* or declin*):ti 11812

#17 #14 or #15 or #16 25779

#18 #13 and #17 515

#19 MeSH descriptor: [Prognosis] this term only 13358

#20 MeSH descriptor: [Time Factors] this term only 63305

#21 (interval* or every or each or per):ti,ab,kw near/5 (month* or year* or annual* or annum* or week*):ti,ab,kw 112177

#22 treatment:ti,ab,kw near/3 (nonresponse* or failure* or response* or duration or outcome*):ti,ab,kw 228558

#23 predict*:ti,ab,kw near/2 (value* or treatment* or response* or outcome* or factor*):ti,ab,kw 31294

#24 ((review* or recall* or regular* or periodic*) near/3 (interval* or visit* or revisit* or examin* or attend* or test* or retest*)):ti,ab,kw 7664

#25 (follow* up* or followup*):ti,ab,kw 273595

#26 (management next (strateg* or protocol* or plan*)):ti,ab,kw 3341

#27 (natural histor*):ti,ab,kw 2983

#28 (PPV or NPV):ti,ab,kw 1889

#29 #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 544941

#30 (monitor*):ab 73784

#31 #29 and #30 33963

#32 #13 and #31 216

#33 #18 or #32 with Cochrane Library publication date Between Nov 2013 and Nov 2019, in Cochrane Reviews, Cochrane Protocols 11

#34 #18 or #32 with Publication Year from 2013 to 2019, in Trials 399

#35 #33 or #34 410

#36 MeSH descriptor: [Infant] explode all trees 15622

#37 MeSH descriptor: [Infant Health] this term only 40

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

#39 ((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 84614

#40 ((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 4967

#41 MeSH descriptor: [Child] explode all trees 1203

#42 MeSH descriptor: [Child Behavior] explode all trees 1962

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

#44 MeSH descriptor: [Child Welfare] this term only 323

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

#46 ((child* or minor or minors or boy* or girl* or kid or kids or young*)):ti,ab,kw 254496

#47 ((child* or minor or minors or boy* or girl* or kid or kids or young*)):so 10193

#48 MeSH descriptor: [Pediatrics] explode all trees 648

#49 ((pediatric* or paediatric* or peadiatric*)):ti,ab,kw 32086

#50 ((pediatric* or paediatric* or peadiatric*)):so 31716

#51 MeSH descriptor: [Adolescent] this term only 101404

#52 MeSH descriptor: [Adolescent Behavior] this term only 1334

#53 MeSH descriptor: [Adolescent Health] this term only 22

#54 MeSH descriptor: [Puberty] this term only 298

#55 ((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 137045

#56 ((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 3706

#57 MeSH descriptor: [Schools] this term only 1815

#58 MeSH descriptor: [Child Day Care Centers] this term only 220

#59 MeSH descriptor: [Nurseries] this term only 9

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

#61 ((pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*)):ti,ab,kw 93294

#62 ((pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*)):so 1144

#63 (("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*")):ti,ab,kw 14230

#64 {or #36-#63} 402239

#65 #18 or #32 700

#66 #64 and #65 138

#67 #35 or #66 483

#68 "conference":pt or (clinicaltrials or trialsearch):so 440437

#69 #67 not #68 323 (CDSR – 13, Central – 310)

CRD databases

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

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

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

4 (ckd*) 93 Delete

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

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

7 (esrd* or eskd*) 150 Delete

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

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

10 MeSH DESCRIPTOR Glomerular Filtration Rate 92 Delete

11 (glomerul* or GFR* or eGFR* or e-GFR*) 416 Delete

12 (#10 or #11) 416 Delete

13 (#9 and #12) 151 Delete

14 (#9 and #12) IN DARE 116 Delete

15 (#9 and #12) IN NHSEED 28 Delete

16 (#9 and #12) IN HTA 7 Delete

Cost-effectiveness searches

Databases	Date searched	Version/files	No. retrieved
MEDLINE (Ovid)	25th Nov 2019	Ovid MEDLINE(R) <1946 to November 22, 2019>	173
MEDLINE in Process (Ovid)	25th Nov 2019	Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to November 22, 2019>	17

MEDLINE epub (Ovid)	25th Nov 2019	Ovid MEDLINE(R) Epub Ahead of Print <November 22, 2019>	27
Embase (Ovid)	25th Nov 2019	Embase <1974 to 2019 Week 47>	385
EconLit (Ovid)	25th Nov 2019	Econlit <1886 to November 14, 2019>	0
NHS Economic Evaluation Database (NHS EED) (legacy database)	25th Nov 2019	Up to 2015	28
CRD HTA	25th Nov 2019	Up to 2018	7

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

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

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

Search strategies
Database: Ovid MEDLINE(R) <1946 to November 22, 2019> Search Strategy: --- 1 exp Renal Insufficiency, Chronic/ (110914) 2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (71116) 3 ((kidney* or renal*) adj1 insufficien*).tw. (21130) 4 ckd*.tw. (22151) 5 ((kidney* or renal*) adj1 fail*).tw. (85720) 6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (34655) 7 (esrd* or eskd*).tw. (13917) 8 "Chronic Kidney Disease-Mineral and Bone Disorder"/ (3426) 9 or/1-8 (209813)

10 Glomerular Filtration Rate/ (42656)

11 (glomerul* or GFR* or eGFR* or e-GFR*).tw. (155336)

12 10 or 11 (168608)

13 9 and 12 (34940)

14 monitor*.ti. (106000)

15 disease progression/ (155071)

16 (progress* or declin*).ti. (144325)

17 or/14-16 (364489)

18 13 and 17 (4919)

19 prognosis/ (486916)

20 time factors/ (1167642)

21 ((interval* or every or each or per) adj5 (month* or year* or annual* or annum* or week*)).tw. (350135)

22 (treatment adj3 (nonresponse* or failure* or response* or duration or outcome*)).tw,hw. (1097472)

23 (predict* adj2 (value* or treatment* or response* or outcome* or factor*)).tw,hw. (369833)

24 ((review* or recall* or regular* or periodic*) adj3 (interval* or visit* or revisit* or examin* or attend* or test* or retest*)).tw. (58822)

25 (follow* up* or followup*).tw. (883488)

26 (management adj (strateg* or protocol* or plan*)).tw. (33349)

27 natural histor*.tw. (42099)

28 (PPV or NPV).tw. (15156)

29 or/19-28 (3573542)

30 monitor*.ab,hw. (788975)

31 29 and 30 (172713)

32 13 and 31 (727)

33 18 or 32 (5472)

34 limit 33 to english language (5007)

35 animals/ not humans/ (4612069)

36 34 not 35 (4565)

37 limit 36 to ed=20131101-20191125 (2172)

38 exp Infant/ or Infant Health/ or Infant Welfare/ (1114678)

39 (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. (827931)

40 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (1869654)

41 Minors/ (2545)

42 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (2272993)

43 exp pediatrics/ (56538)

44 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (795066)

45 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (1972824)

46 Puberty/ (13111)

47 (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. (406080)

48 Schools/ (36306)

49 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (8682)

50 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (452006)

51 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (3763)

52 or/38-51 (5040018)

53 36 and 52 (1185)

54 37 or 53 (2791)

55 Economics/ (27096)

56 exp "Costs and Cost Analysis"/ (230219)

57 Economics, Dental/ (1908)

58 exp Economics, Hospital/ (24042)

59 exp Economics, Medical/ (14141)

60 Economics, Nursing/ (3996)

61 Economics, Pharmaceutical/ (2896)

62 Budgets/ (11194)

63 exp Models, Economic/ (14521)

64 Markov Chains/ (13817)

65 Monte Carlo Method/ (27406)

66 Decision Trees/ (10787)

67 econom$.tw. (227001)

68 cba.tw. (9653)

69 cea.tw. (19987)

70 cua.tw. (963)

71 markov$.tw. (17204)

72 (monte adj carlo).tw. (28842)

73 (decision adj3 (tree$ or analys$)).tw. (12569)

74 (cost or costs or costing$ or costly or costed).tw. (439966)

75 (price$ or pricing$).tw. (32105)

76 budget$.tw. (22890)

77 expenditure$.tw. (47397)

78 (value adj3 (money or monetary)).tw. (1996)

79 (pharmacoeconomic$ or (pharmaco adj economic$)).tw. (3409)

80 or/55-79 (889683)

81 "Quality of Life"/ (184414)

82 quality of life.tw. (217255)

83 "Value of Life"/ (5674)

84 Quality-Adjusted Life Years/ (11586)

85 quality adjusted life.tw. (10173)

86 (qaly$ or qald$ or qale$ or qtime$).tw. (8360)

87 disability adjusted life.tw. (2493)

88 daly$.tw. (2280)

89 Health Status Indicators/ (23098)

90 (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. (21597)

91 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (1282)

92 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (4618)

93 (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)

94 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (373)

95 (euroqol or euro qol or eq5d or eq 5d).tw. (8215)

96 (qol or hql or hqol or hrqol).tw. (41362)

97 (hye or hyes).tw. (59)

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

99 utilit$.tw. (163343)

100 (hui or hui1 or hui2 or hui3).tw. (1241)

101 disutili$.tw. (365)

102 rosser.tw. (91)

103 quality of wellbeing.tw. (13)

104 quality of well-being.tw. (369)

105 qwb.tw. (187)

106 willingness to pay.tw. (4130)

107 standard gamble$.tw. (770)

108 time trade off.tw. (1001)

109 time tradeoff.tw. (225)

110 tto.tw. (869)

111 or/81-110 (469363)

112 80 or 111 (1293968)

113 54 and 112 (173)

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to November 22, 2019>

Search Strategy:

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1 exp Renal Insufficiency, Chronic/ (0)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (9285)

3 ((kidney* or renal*) adj1 insufficien*).tw. (1097)

4 ckd*.tw. (4383)

5 ((kidney* or renal*) adj1 fail*).tw. (6287)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (4686)

7 (esrd* or eskd*).tw. (1972)

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

9 or/1-8 (18173)

10 Glomerular Filtration Rate/ (0)

11 (glomerul* or GFR* or eGFR* or e-GFR*).tw. (15881)

12 10 or 11 (15881)

13 9 and 12 (3621)

14 monitor*.ti. (14754)

15 disease progression/ (0)

16 (progress* or declin*).ti. (21648)

17 or/14-16 (36230)

18 13 and 17 (263)

19 prognosis/ (0)

20 time factors/ (0)

21 ((interval* or every or each or per) adj5 (month* or year* or annual* or annum* or week*)).tw. (41815)

22 (treatment adj3 (nonresponse* or failure* or response* or duration or outcome*)).tw,hw. (29378)

23 (predict* adj2 (value* or treatment* or response* or outcome* or factor*)).tw,hw. (30832)

24 ((review* or recall* or regular* or periodic*) adj3 (interval* or visit* or revisit* or examin* or attend* or test* or retest*)).tw. (8730)

25 (follow* up* or followup*).tw. (107048)

26 (management adj (strateg* or protocol* or plan*)).tw. (6709)

27 natural histor*.tw. (4581)

28 (PPV or NPV).tw. (3110)

29 or/19-28 (206588)

30 monitor*.ab,hw. (90665)

31 29 and 30 (11266)

32 13 and 31 (65)

33 18 or 32 (313)

34 limit 33 to english language (312)

35 animals/ not humans/ (0)

36 34 not 35 (312)

37 limit 36 to dt=20131101-20191125 (290)

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

39 (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. (75466)

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

41 Minors/ (0)

42 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (299265)

43 exp pediatrics/ (0)

44 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (112197)

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

46 Puberty/ (0)

47 (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. (56034)

48 Schools/ (0)

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

50 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (64787)

51 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (571)

52 or/38-51 (434032)

53 36 and 52 (57)

54 37 or 53 (295)

55 Economics/ (0)

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

57 Economics, Dental/ (0)

58 exp Economics, Hospital/ (0)

59 exp Economics, Medical/ (0)

60 Economics, Nursing/ (0)

61 Economics, Pharmaceutical/ (0)

62 Budgets/ (0)

63 exp Models, Economic/ (0)

64 Markov Chains/ (0)

65 Monte Carlo Method/ (0)

66 Decision Trees/ (0)

67 econom$.tw. (42259)

68 cba.tw. (416)

69 cea.tw. (1813)

70 cua.tw. (198)

71 markov$.tw. (5353)

72 (monte adj carlo).tw. (16381)

73 (decision adj3 (tree$ or analys$)).tw. (2236)

74 (cost or costs or costing$ or costly or costed).tw. (90565)

75 (price$ or pricing$).tw. (5496)

76 budget$.tw. (4737)

77 expenditure$.tw. (6167)

78 (value adj3 (money or monetary)).tw. (351)

79 (pharmacoeconomic$ or (pharmaco adj economic$)).tw. (520)

80 or/55-79 (157180)

81 "Quality of Life"/ (0)

82 quality of life.tw. (36630)

83 "Value of Life"/ (0)

84 Quality-Adjusted Life Years/ (0)

85 quality adjusted life.tw. (1554)

86 (qaly$ or qald$ or qale$ or qtime$).tw. (1310)

87 disability adjusted life.tw. (476)

88 daly$.tw. (441)

89 Health Status Indicators/ (0)

90 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw. (2574)

91 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (725)

92 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (717)

93 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. (4)

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

95 (euroqol or euro qol or eq5d or eq 5d).tw. (1595)

96 (qol or hql or hqol or hrqol).tw. (7049)

97 (hye or hyes).tw. (6)

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

99 utilit$.tw. (29472)

100 (hui or hui1 or hui2 or hui3).tw. (172)

101 disutili$.tw. (68)

102 rosser.tw. (5)

103 quality of wellbeing.tw. (6)

104 quality of well-being.tw. (32)

105 qwb.tw. (11)

106 willingness to pay.tw. (877)

107 standard gamble$.tw. (59)

108 time trade off.tw. (121)

109 time tradeoff.tw. (17)

110 tto.tw. (119)

111 or/81-110 (68420)

112 80 or 111 (216678)

113 54 and 112 (17)

Database: Ovid MEDLINE(R) Epub Ahead of Print <November 22, 2019>

Search Strategy:

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1 exp Renal Insufficiency, Chronic/ (0)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (1350)

3 ((kidney* or renal*) adj1 insufficien*).tw. (151)

4 ckd*.tw. (698)

5 ((kidney* or renal*) adj1 fail*).tw. (714)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (658)

7 (esrd* or eskd*).tw. (270)

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

9 or/1-8 (2488)

10	Glomerular Filtration Rate/ (0)
11	(glomerul* or GFR* or eGFR* or e-GFR*).tw. (2245)
12	10 or 11 (2245)
13	9 and 12 (533)
14	Economics/ (0)
15	exp "Costs and Cost Analysis"/ (0)
16	Economics, Dental/ (0)
17	exp Economics, Hospital/ (0)
18	exp Economics, Medical/ (0)
19	Economics, Nursing/ (0)
20	Economics, Pharmaceutical/ (0)
21	Budgets/ (0)
22	exp Models, Economic/ (0)
23	Markov Chains/ (0)
24	Monte Carlo Method/ (0)
25	Decision Trees/ (0)
26	econom$.tw. (5736)
27	cba.tw. (60)
28	cea.tw. (300)
29	cua.tw. (21)
30	markov$.tw. (689)
31	(monte adj carlo).tw. (1140)
32	(decision adj3 (tree$ or analys$)).tw. (386)
33	(cost or costs or costing$ or costly or costed).tw. (12029)
34	(price$ or pricing$).tw. (877)
35	budget$.tw. (516)
36	expenditure$.tw. (1134)
37	(value adj3 (money or monetary)).tw. (61)
38	(pharmacoeconomic$ or (pharmaco adj economic$)).tw. (44)
39	or/14-38 (19661)
40	"Quality of Life"/ (0)

41 quality of life.tw. (6585)

42 "Value of Life"/ (0)

43 Quality-Adjusted Life Years/ (0)

44 quality adjusted life.tw. (387)

45 (qaly$ or qald$ or qale$ or qtime$).tw. (335)

46 disability adjusted life.tw. (91)

47 daly$.tw. (78)

48 Health Status Indicators/ (0)

49 (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. (451)

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

51 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (157)

52 (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)

53 (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)

54 (euroqol or euro qol or eq5d or eq 5d).tw. (342)

55 (qol or hql or hqol or hrqol).tw. (1294)

56 (hye or hyes).tw. (2)

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

58 utilit$.tw. (4641)

59 (hui or hui1 or hui2 or hui3).tw. (18)

60 disutili$.tw. (14)

61 rosser.tw. (0)

62 quality of wellbeing.tw. (1)

63 quality of well-being.tw. (5)

64 qwb.tw. (3)

65 willingness to pay.tw. (155)

66 standard gamble$.tw. (6)

67 time trade off.tw. (17)

68 time tradeoff.tw. (4)

69 tto.tw. (16)

70 or/40-69 (11481)

71 39 or 70 (29428)

72 13 and 71 (27)

73 limit 72 to english language (27)

Database: Embase <1974 to 2019 Week 47>

Search Strategy:

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1 exp kidney failure/ (343634)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (119957)

3 ((kidney* or renal*) adj1 insufficien*).tw. (29764)

4 ckd*.tw. (47834)

5 ((kidney* or renal*) adj1 fail*).tw. (130532)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (56862)

7 (esrd* or eskd*).tw. (26610)

8 or/1-7 (434744)

9 exp glomerulus filtration rate/ (95488)

10 (glomerul* or GFR* or eGFR* or e-GFR*).tw. (259335)

11 9 or 10 (287310)

12 8 and 11 (75738)

13 monitor*.ti. (160901)

14 disease course/ (452148)

15 disease exacerbation/ (106135)

16 (progress* or declin*).ti. (210599)

17 or/13-16 (874287)

18 12 and 17 (10816)

19 therapy delay/ (12152)

20 prognosis/ (561606)

21 ((interval* or every or each or per) adj5 (month* or year* or annual* or annum* or week*)).tw. (613417)

22 (treatment adj3 (nonresponse* or failure* or response* or duration or outcome*)).tw,hw. (1511668)

23 (predict* adj2 (value* or treatment* or response* or outcome* or factor*)).tw,hw. (468327)

24 ((review* or recall* or regular* or periodic*) adj3 (interval* or visit* or revisit* or examin* or attend* or test* or retest*)).tw. (89369)

25 (follow* up* or followup*).tw. (1585604)

26 (management adj (strateg* or protocol* or plan*)).tw. (56224)

27 natural histor*.tw. (64279)

28 (PPV or NPV).tw. (35237)

29 or/19-28 (4109288)

30 monitor*.ab,hw. (1267523)

31 29 and 30 (248139)

32 12 and 31 (2018)

33 18 or 32 (12367)

34 limit 33 to english language (11601)

35 nonhuman/ not human/ (4507607)

36 34 not 35 (10784)

37 limit 36 to (conference abstract or conference paper or "conference review" or letter or note or tombstone) (3353)

38 36 not 37 (7431)

39 limit 38 to dc=20131101-20191125 (3566)

40 exp juvenile/ or Child Behavior/ or Child Welfare/ or Child Health/ or infant welfare/ or "minor (person)"/ or elementary student/ (3325323)

41 (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. (1169531)

42 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,ad,jw. (3512578)

43 exp pediatrics/ (102395)

44 (pediatric* or paediatric* or peadiatric*).ti,ab,in,ad,jw. (1578317)

45 exp adolescence/ or exp adolescent behavior/ or adolescent health/ or high school student/ or middle school student/ (100514)

46 (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. (633967)

47 school/ or high school/ or kindergarten/ or middle school/ or primary school/ or nursery school/ or day care/ (100281)

48 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jw. (672669)

49 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (7057)

50 or/40-49 (6222999)

51 38 and 50 (1755)

52 39 or 51 (4548)

53 exp Health Economics/ (820025)

54 exp "Health Care Cost"/ (283079)

55 exp Pharmacoeconomics/ (197766)

56 Monte Carlo Method/ (37770)

57 Decision Tree/ (11900)

58 econom$.tw. (348116)

59 cba.tw. (12512)

60 cea.tw. (33435)

61 cua.tw. (1428)

62 markov$.tw. (28427)

63 (monte adj carlo).tw. (45214)

64 (decision adj3 (tree$ or analys$)).tw. (21745)

65 (cost or costs or costing$ or costly or costed).tw. (729483)

66 (price$ or pricing$).tw. (54362)

67 budget$.tw. (36782)

68 expenditure$.tw. (71636)

69 (value adj3 (money or monetary)).tw. (3291)

70 (pharmacoeconomic$ or (pharmaco adj economic$)).tw. (8402)

71 or/53-70 (1678772)

72 "Quality of Life"/ (446883)

73 Quality Adjusted Life Year/ (25040)

74 Quality of Life Index/ (2691)

75 Short Form 36/ (27329)

76 Health Status/ (123214)

77 quality of life.tw. (414819)

78 quality adjusted life.tw. (18476)

79 (qaly$ or qald$ or qale$ or qtime$).tw. (18861)

80 disability adjusted life.tw. (3759)

81 daly$.tw. (3707)

82 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw. (39994)

83 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (2275)

84 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (8992)

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

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

87 (euroqol or euro qol or eq5d or eq 5d).tw. (19130)

88 (qol or hql or hqol or hrqol).tw. (91376)

89 (hye or hyes).tw. (129)

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

91 utilit$.tw. (274476)

92 (hui or hui1 or hui2 or hui3).tw. (2159)

93 disutili$.tw. (867)

94 rosser.tw. (118)

95 quality of wellbeing.tw. (40)

96 quality of well-being.tw. (467)

97 qwb.tw. (239)

98 willingness to pay.tw. (8089)

99 standard gamble$.tw. (1081)

100 time trade off.tw. (1653)

101 time tradeoff.tw. (286)

102 tto.tw. (1590)

103 or/72-102 (940105)

104 71 or 103 (2469718)

105 52 and 104 (385)

Database: Econlit <1886 to November 14, 2019>

Search Strategy:

---

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

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (20)

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

4 ckd*.tw. (4)

5 ((kidney* or renal*) adj1 fail*).tw. (32)

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

7 (esrd* or eskd*).tw. (30)

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

9 or/1-8 (98)

10 [Glomerular Filtration Rate/] (0)

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

12 10 or 11 (12)

13 9 and 12 (0)

CRD databases

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

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

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

4 (ckd*) 93 Delete

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

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

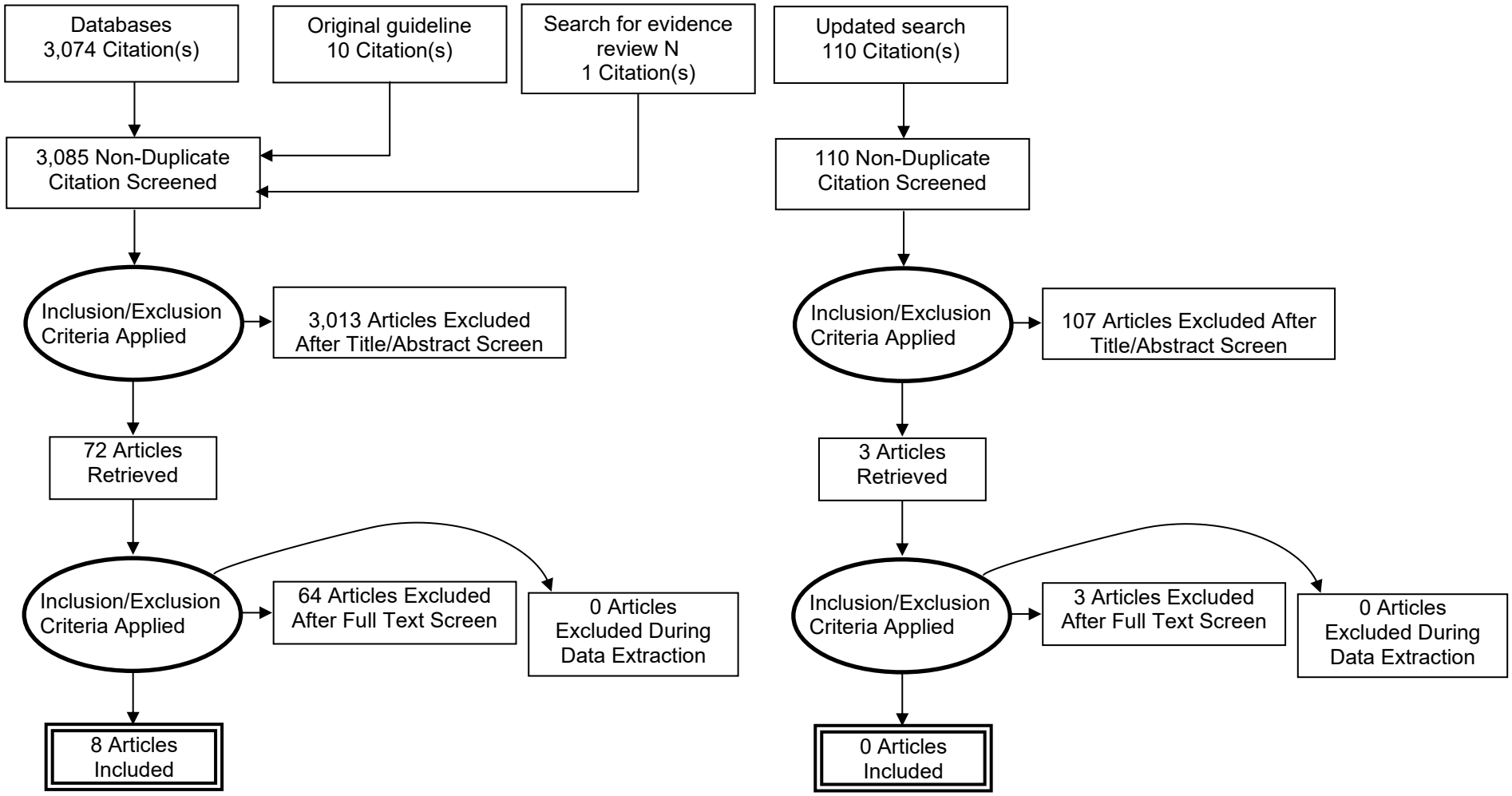
7 (esrd* or eskd*) 150 Delete

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

9	(#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8)	1407	Delete
10	MeSH DESCRIPTOR Glomerular Filtration Rate	92	Delete
11	(glomerul* or GFR* or eGFR* or e-GFR*)	416	Delete
12	(#10 or #11)	416	Delete
13	(#9 and #12)	151	Delete
14	(#9 and #12) IN DARE	116	Delete
15	(#9 and #12) IN NHSEED	28	Delete
16	(#9 and #12) IN HTA	7	Delete

[Add title of review question, then the search strategy.]

Appendix D – Prognostic evidence study selection



Appendix E –Prognostic evidence

Coresh, 2014

Bibliographic Reference	Coresh, Josef; Turin, Tanvir Chowdhury; Matsushita, Kunihiro; Sang, Yingying; Ballew, Shoshana H; Appel, Lawrence J; Arima, Hisatomi; Chadban, Steven J; Cirillo, Massimo; Djurdjev, Ognjenka; Green, Jamie A; Heine, Gunnar H; Inker, Lesley A; Irie, Fujiko; Ishani, Areef; Ix, Joachim H; Kovesdy, Csaba P; Marks, Angharad; Ohkubo, Takayoshi; Shalev, Varda; Shankar, Anoop; Wen, Chi Pang; de Jong, Paul E; Iseki, Kunitoshi; Stengel, Benedicte; Gansevoort, Ron T; Levey, Andrew S; Decline in estimated glomerular filtration rate and subsequent risk of end-stage renal disease and mortality.; JAMA; 2014; vol. 311 (no. 24); 2518-2531

Study Characteristics

Study design	Individual participant data meta-analysis
Study details	Study location Australia, Canada, USA, UK, Netherlands, Korea Study setting Study dates Data analysis between 2012-2014. Sources of funding US National Kidney Foundation and National Institute of Diabetes and Digestive and Kidney Diseases.
Inclusion criteria	CKD cohorts with established cardiovascular and mortality outcomes.
Exclusion criteria	ESRD before baseline period.
Number of participants and recruitment methods	22 cohorts, N=466,068 with eGFR < 60 (N = 1,530,648 total)

Length of follow-up	1 to 3 years
Loss to follow up	Not reported, assumed available data collected.
Outcome(s) of interest	End-stage renal disease (initiation of renal replacement therapy or death due to kidney disease other than acute kidney injury), all-cause mortality and cardiovascular mortality (due to myocardial infarction, heart failure, stroke, or sudden cardiac death).
Prognostic factors or risk factor(s) or sign(s)/symptom(s)	20%, 25%, 30%, 40% and 57% eGFR decline. eGFR calculated using CKD-EPI creatinine equation.
Covariates adjusted for in the multivariable regression modelling	60 year old, non-black, male, no change in eGFR, a first eGFR of 50 ml/min/1.73m2, a systolic blood pressure of 130 mm Hg, a total cholesterol of 5 mmol/L, no history of diabetes or CVD.

Study-level characteristics

	Study (N = 466068)
% Female	
Custom value	20%
Mean age (SD)	
Standardised Mean/SD	74 (10)
Smoking status	
Custom value	6%
Cardiovascular disease *(%)*	

	Study (N = 466068)
Custom value	35%
Black	
Custom value	7%

Section	Question	Answer
Use of a systematic review	Is the IPD meta-analysis part of a systematic review?	*Yes*
Identification of eligible studies	Were All Eligible Trials Identified?	Yes
Ability to obtain IPD data	Were IPD Obtained from Most Trials?	Yes
IPD data integrity	Was the Integrity of the IPD Checked?	Yes
Planned analyses	Were the Analyses Prespecified in Detail?	Yes
Assessment of risk of bias of the included studies	Was the risk of bias of included trials assessed?	Probably no *(Risk of bias assessment not provided, yet all relevant outcomes and time-to-event data were included.)*
Methods of analysis	Were the methods of analysis appropriate overall?	Yes
Reporting standards	Does any report of the results adhere to the Preferred Reporting Items for a Systematic review and Meta-analysis of IPD (The PRISMA-IPD Statement)?	Yes
Overall risk of bias and applicability	Risk of Bias	Low

Section	Question	Answer
	Directness	Directly applicable

Harambat, 2017

Bibliographic Reference Harambat, Jerome; Kunzmann, Kevin; Azukaitis, Karolis; Bayazit, Aysun K; Canpolat, Nur; Doyon, Anke; Duzova, Ali; Niemirska, Anna; Sozeri, Betul; Thurn-Valsassina, Daniela; Anarat, Ali; Bessenay, Lucie; Candan, Cengiz; Peco-Antic, Amira; Yilmaz, Alev; Tschumi, Sibylle; Testa, Sara; Jankauskiene, Augustina; Erdogan, Hakan; Rosales, Alejandra; Alpay, Harika; Lugani, Francesca; Arbeiter, Klaus; Mencarelli, Francesca; Kiyak, Aysel; Donmez, Osman; Drozdz, Dorota; Melk, Anette; Querfeld, Uwe; Schaefer, Franz; 4C Study, Consortium; Metabolic acidosis is common and associates with disease progression in children with chronic kidney disease.; Kidney international; 2017; vol. 92 (no. 6); 1507-1514

Study Characteristics

Study design	Prospective cohort study
Study details	Study location 12 countries (Turkey 48%, Germany 15%, France 9%, Italy 7%, Poland 6%, UK 5%, Austria 2%, Serbia 2%, Switzerland 2%, Lithuania 1%, Portugal 1%, and Czech Republic 1%). Study setting Study dates Not reported Sources of funding Not reported
Inclusion criteria	Age 6-17 years

	eGFR 10 – 60 ml/min/1.73
Exclusion criteria	Transplant active systemic vasculitis renal artery stenosis, coexisting primary cardiovascular anomalies anomalies of the limbs preventing diagnostic procedures
Number of participants and recruitment methods	N=704
Length of follow-up	Median follow-up time was 3.3 (1.5–5.0) years.
Loss to follow up	Not reported
Outcome(s) of interest	ESRD (start of dialysis or pre-emptive transplantation, or eGFR <10 ml/min/1.73 m²) or 50% decline in eGFR.
Prognostic factors or risk factor(s) or sign(s)/symptom(s)	Baseline eGFR per ml/min/1.73 m²
Covariates adjusted for in the multivariable regression modelling	age at baseline, sex, Tanner stage, country of residence, cause of CKD, duration of CKD, baseline eGFR, time-dependent systolic and diastolic blood pressure, and time dependent albumin-to-protein ratio,

Study-level characteristics

	Study (N = 704)
% Female	
Custom value	35%
Mean age (SD)	
MedianIQR	12.3 (9.4 to 14.9)
Comorbidity	
Custom value	53%

Section	Question	Answer
Study participation	Summary Study participation	Low risk of bias
Study Attrition	Study Attrition Summary	Moderate risk of bias
Prognostic factor measurement	Prognostic factor Measurement Summary	Low risk of bias
Outcome Measurement	Outcome Measurement Summary	Low risk of bias
Study Confounding	Study Confounding Summary	Low risk of bias
Statistical Analysis and Reporting	Statistical Analysis and Presentation Summary	Low risk of bias
Overall risk of bias and directness	Risk of Bias	Low
	Directness	Directly applicable

Ishikura, 2014

Bibliographic Reference	Ishikura, K.; Uemura, O.; Hamasaki, Y.; Ito, S.; Wada, N.; Hattori, M.; Ohashi, Y.; Tanaka, R.; Nakanishi, K.; Kaneko, T.; Honda, M.; Progression to end-stage kidney disease in Japanese children with chronic kidney disease: Results of a nationwide prospective cohort study; Nephrology Dialysis Transplantation; 2014; vol. 29 (no. 4); 878-884

Study Characteristics

Study design	Prospective cohort study
Study details	Study location Japan Study setting University and children's hospitals Sources of funding Ministry of Health, Labour and Welfare, Japan.
Inclusion criteria	Confirmed CKD
Exclusion criteria	Transient increases in serum creatinine
Number of participants and recruitment methods	N=447
Length of follow-up	Median 1.49 years (1.16-1.64)
Loss to follow up	None reported.

Outcome(s) of interest	End stage renal disease (no definition provided)
Prognostic factors or risk factor(s) or sign(s)/symptom(s)	CKD stage 4 and 5. eGFR assessed using Schwartz equation.
Covariates adjusted for in the multivariable regression modelling	Sex, age, CKD stage, congenital anomalies of the kidney and urinary tract, preterm delivery, heavy proteinuria, hypertension, use of antihypertensive drug

Study-level characteristics

	Study (N =)
% Female	
Custom value	39%
Mean age (SD)	
Mean/SD	8.6 (4.5)
eGFR	
Mean/SD	39.6 (15.9)

Section	**Question**	**Answer**
Study participation	Summary Study participation	Low risk of bias

Section	Question	Answer
Study Attrition	Study Attrition Summary	Low risk of bias
Prognostic factor measurement	Prognostic factor Measurement Summary	Low risk of bias
Outcome Measurement	Outcome Measurement Summary	Low risk of bias
Study Confounding	Study Confounding Summary	Low risk of bias
Statistical Analysis and Reporting	Statistical Analysis and Presentation Summary	Low risk of bias
Overall risk of bias and directness	Risk of Bias	Low
	Directness	Directly applicable

Lambers Heerspink, 2014

Bibliographic Reference Lambers Heerspink, Hiddo J; Tighiouart, Hocine; Sang, Yingying; Ballew, Shoshana; Mondal, Hasi; Matsushita, Kunihiro; Coresh, Josef; Levey, Andrew S; Inker, Lesley A; GFR decline and subsequent risk of established kidney outcomes: a meta-analysis of 37 randomized controlled trials.; American journal of kidney diseases : the official journal of the National Kidney Foundation; 2014; vol. 64 (no. 6); 860-6

Study Characteristics

Study design	Individual participant data meta-analysis Systematic review conducted on 2007 and individual data requested. Analysis undertaken in 2012.
Study details	Study location

	Not reported Sources of funding AbbVie, Astellas, Janssen, Reata and Vitae.
Inclusion criteria	Confirmed CKD RCTs
Exclusion criteria	No CKD Small (<100) sample size) Insufficient progression of CKD Not RCT
Number of participants and recruitment methods	9488 participants from 37 studies
Length of follow-up	Ranged from mean 17 months to 48 months
Loss to follow up	None reported.
Outcome(s) of interest	ESRD: initiation of treatment with dialysis or transplantation, kidney failure not treated with dialysis or transplantation or doubling of serum creatinine.
Prognostic factors or risk factor(s) or sign(s)/symptom(s)	Percentage change eGFR at 12 months (30%).
Covariates adjusted for in the multivariable regression modelling	Age, sex, race, baseline eGFR, proteinuria, systolic blood pressure, diabetes and treatment assigned to each study.

Additional comments	IPD set overlaps with Coresh 2014. Therefore, hazard ratios from individual studies reported in this IPD were extracted.

Study-level characteristics

	Study (N = 9488)
% Female	
Custom value	37%
Mean age (SD)	
Mean/SD	52 (*empty data*)
eGFR	
Range	16.8 to 99.1

Section	**Question**	**Answer**
Use of a systematic review	Is the IPD meta-analysis part of a systematic review?	Yes, but a pre-specified protocol is not available
Identification of eligible studies	Were All Eligible Trials Identified?	Yes
Ability to obtain IPD data	Were IPD Obtained from Most Trials?	Yes
IPD data integrity	Was the Integrity of the IPD Checked?	Unclear

Section	Question	Answer
Planned analyses	Were the Analyses Prespecified in Detail?	Yes
Assessment of risk of bias of the included studies	Was the risk of bias of included trials assessed?	No
Methods of analysis	Were the methods of analysis appropriate overall?	Probably yes *(Analysis accounted for treatment and control arm as variables.)*
Reporting standards	Does any report of the results adhere to the Preferred Reporting Items for a Systematic review and Meta-analysis of IPD (The PRISMA-IPD Statement)?	Yes
Overall risk of bias and applicability	Risk of Bias	Low
	Directness	Directly applicable

Lin, 2016

Bibliographic Reference	Lin, Ching-Yuang; Huang, Shiuh-Ming; Childhood Albuminuria and Chronic Kidney Disease is Associated with Mortality and End-Stage Renal Disease.; Pediatrics and neonatology; 2016; vol. 57 (no. 4); 280-7

Study Characteristics

Study design	Prospective cohort study

Study details	Study location Taiwan Study setting School and primary care Study dates Samples collected 1992-1996, follow-up 1996 Sources of funding Department of Health, Taiwan
Inclusion criteria	Albuminuria
Exclusion criteria	Refuse to participate Lost to follow-up
Number of participants and recruitment methods	5351
Length of follow-up	10 years.
Loss to follow up	None
Outcome(s) of interest	ESRD (no definition)
Prognostic factors or risk factor(s) or sign(s)/symptom(s)	CKD stage 3 – 5. eGFR measured by Schwartz equation.
Covariates adjusted for in the	age, sex, hyperlipidaemia, hypoalbuminemia, proteinuria, and systolic BP.

multivariable regression modelling	

Study-level characteristics

	Study (N = 5351)
% Female	
M/F Not reported	
Mean age (SD)	
Range	7 to 17
Aetiology primary glomerulonephritis (35%), nephritis secondary to systemic disease (34%), hereditary disease (10%), unknown (10%)	

Section	**Question**	**Answer**
Study participation	Summary Study participation	Low risk of bias
Study Attrition	Study Attrition Summary	Low risk of bias
Prognostic factor measurement	Prognostic factor Measurement Summary	Low risk of bias
Outcome Measurement	Outcome Measurement Summary	Low risk of bias
Study Confounding	Study Confounding Summary	Low risk of bias

Section	Question	Answer
Statistical Analysis and Reporting	Statistical Analysis and Presentation Summary	Low risk of bias
Overall risk of bias and directness	Risk of Bias	Low
	Directness	Directly applicable

Orlandi, 2019

Bibliographic Reference Orlandi, P.F.; Huang, J.; Hoy, W.; Hoy, W.E.; Wang, Z.; Zhang, J.; Cockwell, P.; Healy, H.G.; Fenton, A.; Nessel, L.; Go, A.; Appel, L.; Feldman, H.I.; Oh, K.-H.; Ahn, C.; Chae, D.W.; Han, S.H.; Levin, A.; Djurdjev, O.; Tang, M.; Sola, L.; Rios, P.G.; Gadola, L.; Fukagawa, M.; Hamano, T.; Fujii, N.; Imaizumi, T.; Jha, V.; Yadav, A.K.; Kumar, V.; A collaborative, individual-level analysis compared longitudinal outcomes across the International Network of Chronic Kidney Disease (iNETCKD) cohorts; Kidney International; 2019; vol. 96 (no. 5); 1217-1233

Study Characteristics

Study design	Individual participant data meta-analysis
Study details	Study location Australia, USA, UK, Korea, Uruguay, Japan. Study setting Secondary care Study dates Analysis in 2018 Sources of funding International Society of Nephrology (ISN).

Inclusion criteria	eGFR < 60 Confirmed CKD
Exclusion criteria	Criteria 1 Individual study exclusion criteria varied, included: polycystic kidney disease, systemic vasculitis, HIV, cirrhosis, pregnancy, heart failure and active cancer.
Number of participants and recruitment methods	23484
Length of follow-up	Ranged from 2.7 to 8.1 years in studies. Median 4.1 years
Loss to follow up	Not reported (data censored)
Outcome(s) of interest	ESRD: time until dialysis was initiated or when the participant received a kidney transplant. All-cause mortality.
Prognostic factor(s)	eGFR decline per 10 ml/min/1.73 m²
Covariates adjusted for in the multivariable regression modelling	eGFR 10 unit decrease from baseline. eGFR measured by CKD-EPI equation.

Study-level characteristics

	Study (N = 23484)
% Female	
Custom value	41%

	Study (N = 23484)
Mean age (SD)	
MedianIQR	68 (59 to 75)
Smoking status	
Custom value	9%
eGFR baseline	
MedianIQR	36 (27 to 45)

Section	Question	Answer
Use of a systematic review	Is the IPD meta-analysis part of a systematic review?	Yes, and a pre-specified protocol is available *(iNET-CKD: research protocol was used by studies to conduct research.)*
Identification of eligible studies	Were All Eligible Trials Identified?	Probably no *(No literature search conducted, members of iNET CKD were eligible to participate.)*
Ability to obtain IPD data	Were IPD Obtained from Most Trials?	Yes
IPD data integrity	Was the Integrity of the IPD Checked?	Yes
Planned analyses	Were the Analyses Prespecified in Detail?	Yes

Section	Question	Answer
Assessment of risk of bias of the included studies	Was the risk of bias of included trials assessed?	No
Methods of analysis	Were the methods of analysis appropriate overall?	Yes
Reporting standards	Does any report of the results adhere to the Preferred Reporting Items for a Systematic review and Meta-analysis of IPD (The PRISMA-IPD Statement)?	Partially
Overall risk of bias and applicability	Risk of Bias	Moderate
	Directness	Directly applicable

Subramanian, 2019

Bibliographic Reference Subramanian, N.; Xu, J.; Sayyed Kassem, L.; Simonson, M.; Desai, N.; Absent or diminished pedal pulses and estimated GFR decline in patients with diabetic kidney disease; Renal failure; 2019; vol. 41 (no. 1); 691-697

Study Characteristics

Study design	Prospective cohort study
Study details	Study location Ohio, USA Study setting outpatient clinics in endocrinology and nephrology at University Hospitals Cleveland Medical Centre. Study dates

	Not reported
Inclusion criteria	Age 21-85 years eGFR > 7ml/min/1.73 Diagnosis of diabetes Using revised criteria of American Diabetes Association or use of insulin or oral hyperglycaemic agents
Exclusion criteria	concurrent diagnosis of non-DKD unwillingness or inability to provide informed consent Dialysis Pregnancy, lactation, substance abuse, fever, systemic and urinary-tract infections, or inflammatory disease
Number of participants and recruitment methods	N=91 with type 2 diabetes and CKD
Length of follow-up	Mean 4.8 ± 1.4 years
Loss to follow up	None lost to follow-up
Outcome(s) of interest	> 30% decline in eGFR (CKD-EPI)
Prognostic factors or risk factor(s) or sign(s)/symptom(s)	Baseline eGFR
Covariates adjusted for in the	Age, diabetes duration (years), urine ACR, HbA1C, hypertension, absent or diminished peripheral pulses

multivariable regression modelling	

Study-level characteristics

	Study (N = 91)
% Female	
Custom value	54%
Mean age (SD)	
Mean/SD	58 (11)
Baseline eGFR	
Mean/SD	70.6 (30.5)
HbA1c (%)	
Mean/SD	7.8 (1.8)

Section	**Question**	**Answer**
Study participation	Summary Study participation	Low risk of bias
Study Attrition	Study Attrition Summary	Low risk of bias
Prognostic factor measurement	Prognostic factor Measurement Summary	Low risk of bias

Section	Question	Answer
Outcome Measurement	Outcome Measurement Summary	Low risk of bias
Study Confounding	Study Confounding Summary	Low risk of bias
Statistical Analysis and Reporting	Statistical Analysis and Presentation Summary	Low risk of bias
Overall risk of bias and directness	Risk of Bias	Low
	Directness	Directly applicable

Tsai, 2017

Bibliographic Reference Tsai, Ching-Wei; Ting, I-Wen; Yeh, Hung-Chieh; Kuo, Chin-Chi; Longitudinal change in estimated GFR among CKD patients: A 10-year follow-up study of an integrated kidney disease care program in Taiwan.; PloS one; 2017; vol. 12 (no. 4); e0173843

Study Characteristics

Study design	Prospective cohort study
Study details	Study location Taiwan Study setting China Medical University Hospital Study dates 2003 - 2013

	Sources of funding Taiwan's National Health Insurance
Inclusion criteria	Confirmed CKD Stage 1 - 5 Willing to participate
Exclusion criteria	None reported
Number of participants and recruitment methods	N = 4600 All enrolled patients were followed-up until initiation of long-term renal replacement therapy (haemodialysis, peritoneal dialysis, or transplantation), loss to follow-up, death, or December 31, 2013, whichever occurred first.
Length of follow-up	Mean 2.24 years
Loss to follow up	None reported
Outcome(s) of interest	ESRD (not defined)
Prognostic factors or risk factor(s) or sign(s)/symptom(s)	eGFR decline per 1 ml/min/1.73 m² eGFR calculated by MDRD equation
Covariates adjusted for in the multivariable regression modelling	Age, sex, proteinuria (yes vs. no), hypertension (yes vs. no), diabetic nephropathy (yes vs. no), history of CVD, and baseline CKD stage

Study-level characteristics

	Study (N = 4600)
% Female	
Custom value	43%
Mean age (SD)	
Mean/SD	70.1 (0.2)
Smoking status	
Custom value	9.7%
Baseline eGFR (ml/min/1.73)	
Mean/SD	29.3 (0.31)

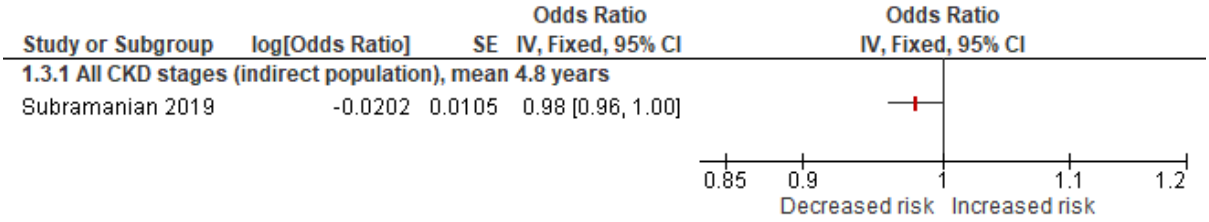
Section	Question	Answer
Study participation	Summary Study participation	Low risk of bias
Study Attrition	Study Attrition Summary	Low risk of bias
Prognostic factor measurement	Prognostic factor Measurement Summary	Low risk of bias
Outcome Measurement	Outcome Measurement Summary	Low risk of bias
Study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

Section	Question	Answer
Overall risk of bias and directness	Risk of Bias	Low
	Directness	Directly applicable

Appendix F – Forest plots

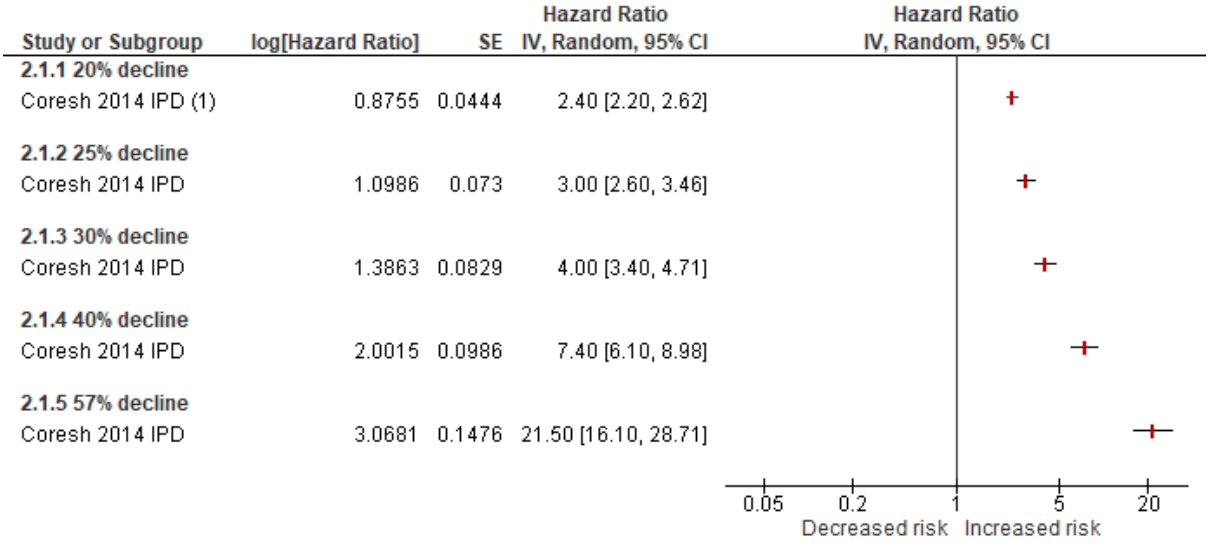
Risk of CKD progression (defined as greater than 30% decline in eGFR from baseline eGFR), compared to baseline eGFR, in CKD stage 1-5 with type 2 diabetes

Figure 1: Greater than 30% decline in type 2 diabetes, CKD 1-5



Risk of CKD progression (defined as eGFR percent change) compared to stable (0% change), CKD stage 3-5

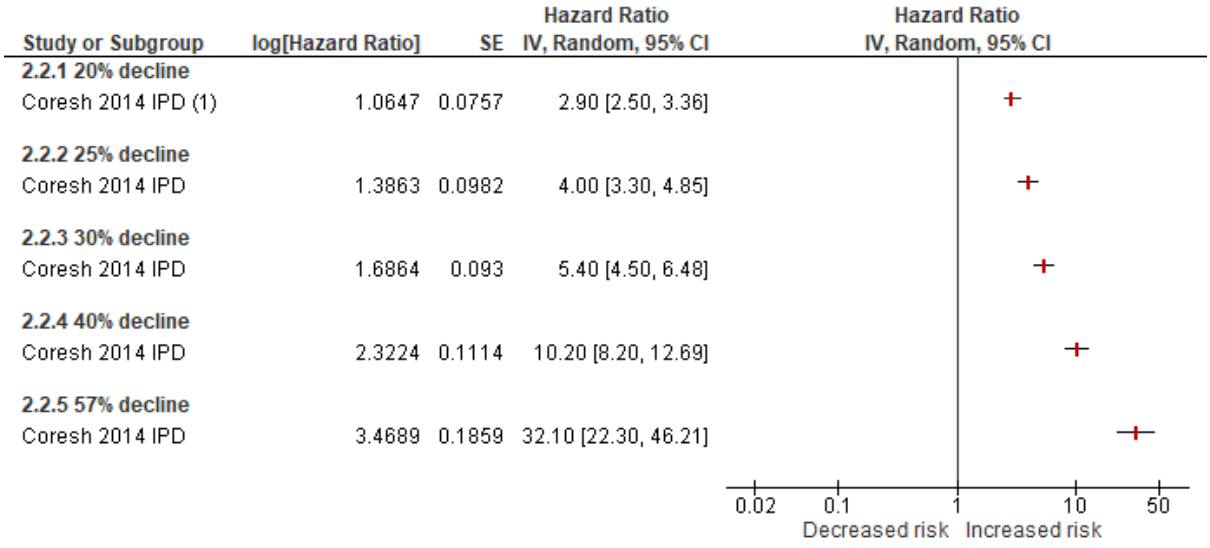
Figure 2: ESRD, 1 year



Footnotes

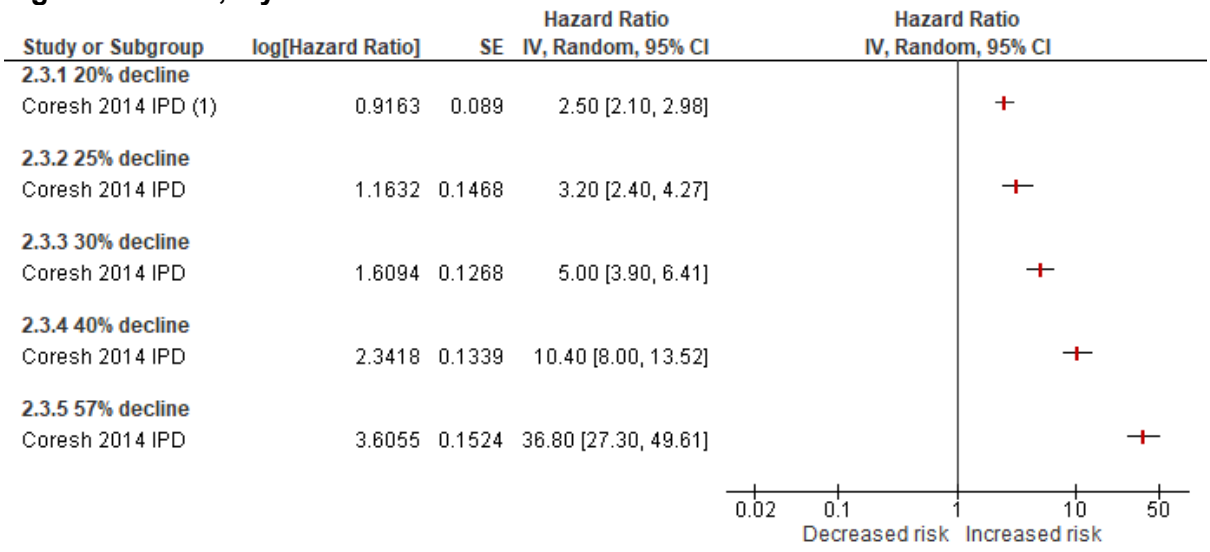
(1) Coresh 2014 adjusted for: age, sez, race/ethnicity, systolic BP, total cholestrol, diabetes, history of CVD and first eGFR.

Figure 3: ESRD, 2 years



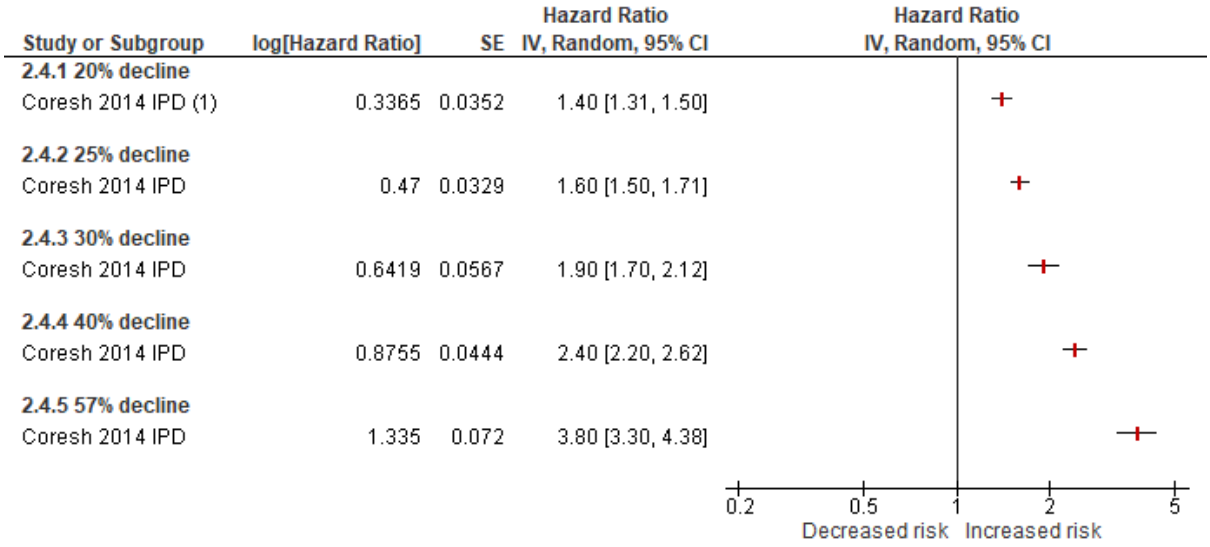
Footnotes
(1) Coresh 2014 adjusted for: age, sez, race/ethnicity, systolic BP, total cholestrol, diabetes, history of CVD and first eGFR.

Figure 4: ESRD, 3 years



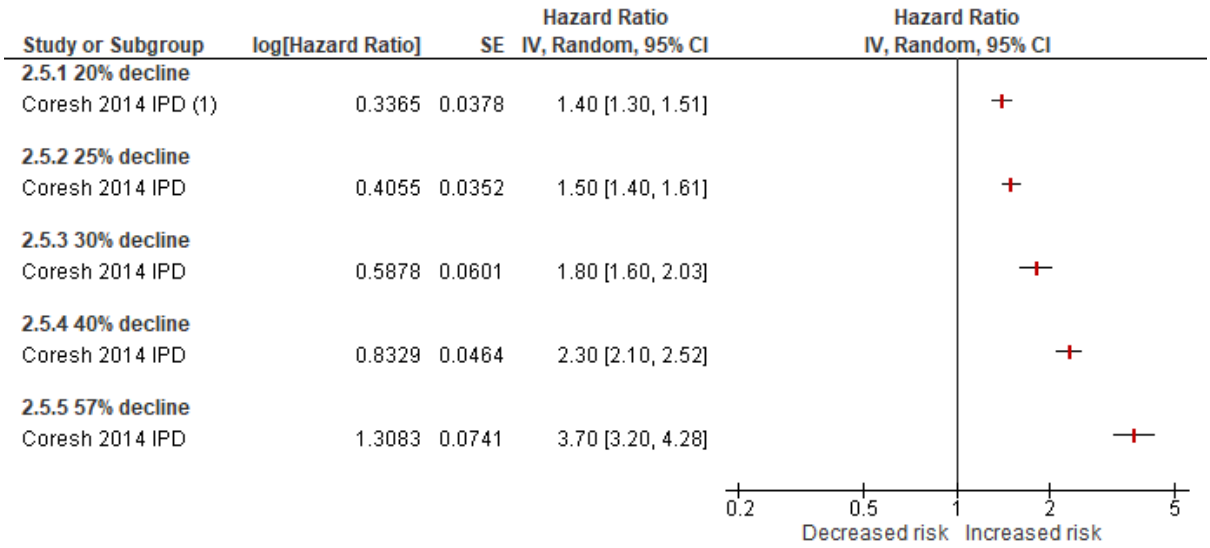
Footnotes
(1) Coresh 2014 adjusted for: age, sez, race/ethnicity, systolic BP, total cholestrol, diabetes, history of CVD and first eGFR.

Figure 5: All-cause mortality, 1 year



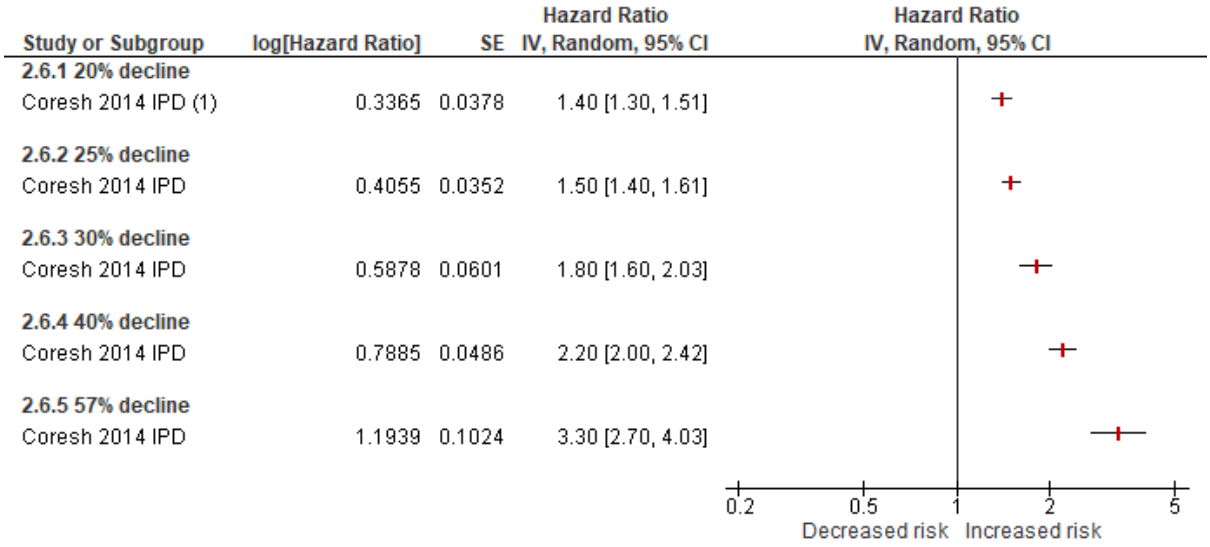
Footnotes
(1) Coresh 2014 adjusted for: age, sez, race/ethnicity, systolic BP, total cholestrol, diabetes, history of CVD and first eGFR.

Figure 6: All-cause mortality, 2 years



Footnotes
(1) Coresh 2014 adjusted for: age, sez, race/ethnicity, systolic BP, total cholestrol, diabetes, history of CVD and first eGFR.

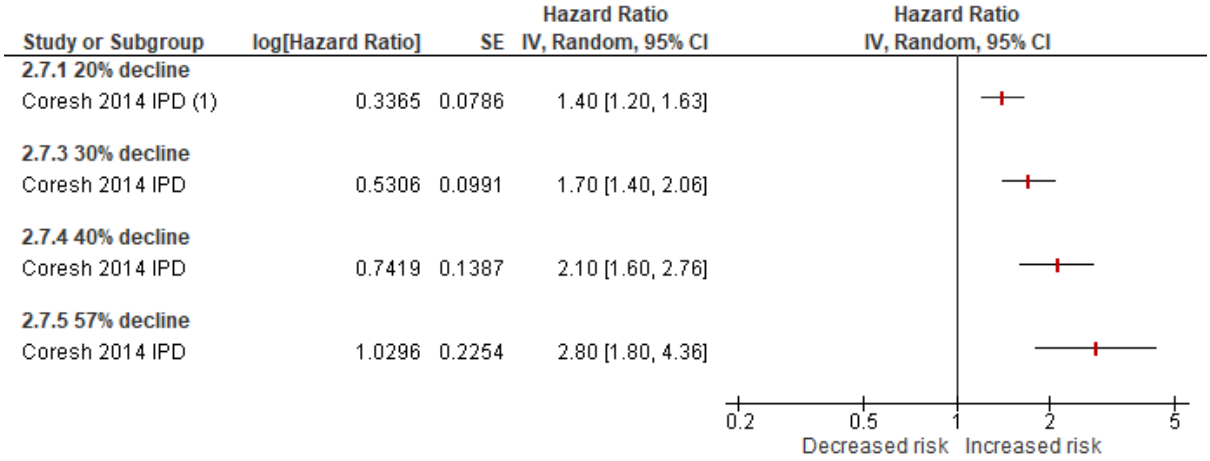
Figure 7: All-cause mortality, 3 years



Footnotes

(1) Coresh 2014 adjusted for: age, sez, race/ethnicity, systolic BP, total cholestrol, diabetes, history of CVD and first eGFR.

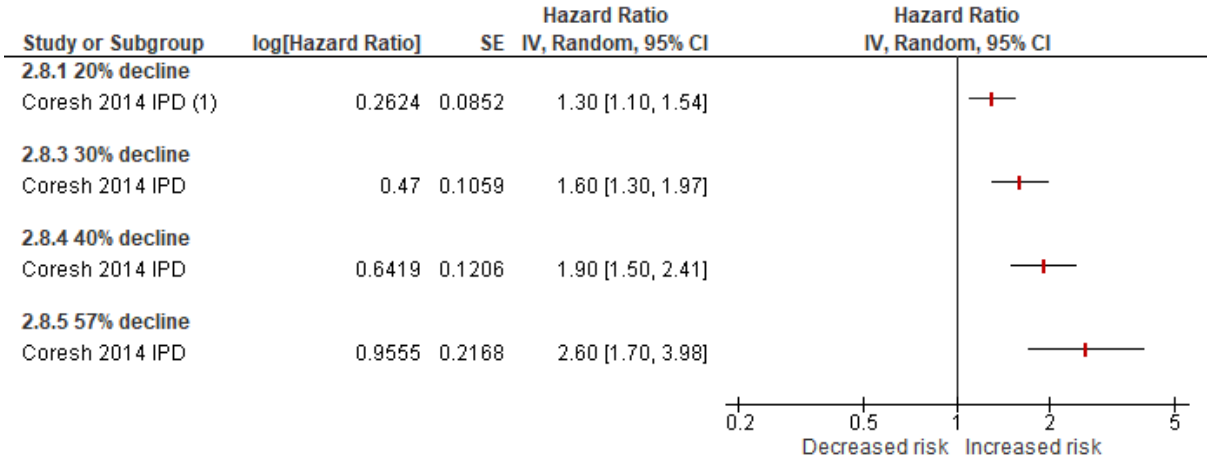
Figure 8: Cardiovascular mortality, 1 year



Footnotes

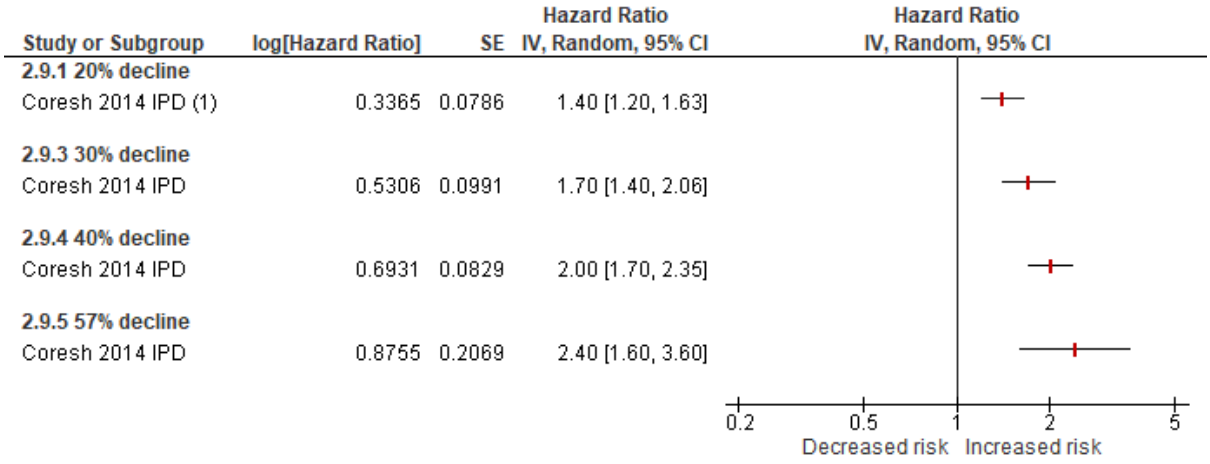
(1) Coresh 2014 adjusted for: age, sez, race/ethnicity, systolic BP, total cholestrol, diabetes, history of CVD and first eGFR.

Figure 9: Cardiovascular mortality, 2 years



Footnotes
(1) Coresh 2014 adjusted for: age, sez, race/ethnicity, systolic BP, total cholestrol, diabetes, history of CVD and first eGFR.

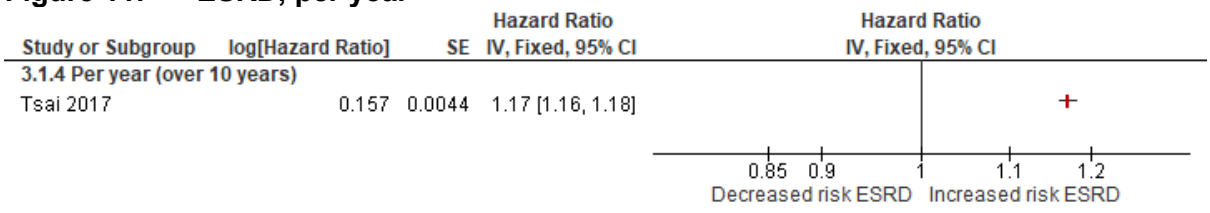
Figure 10: Cardiovascular mortality, 3 years



Footnotes
(1) Coresh 2014 adjusted for: age, sez, race/ethnicity, systolic BP, total cholestrol, diabetes, history of CVD and first eGFR.

Risk of CKD progression (defined as decline greater than 1 mL/min/1.73 in eGFR per year), compared to less than 1 mL/min/1.73, CKD stage 1-5

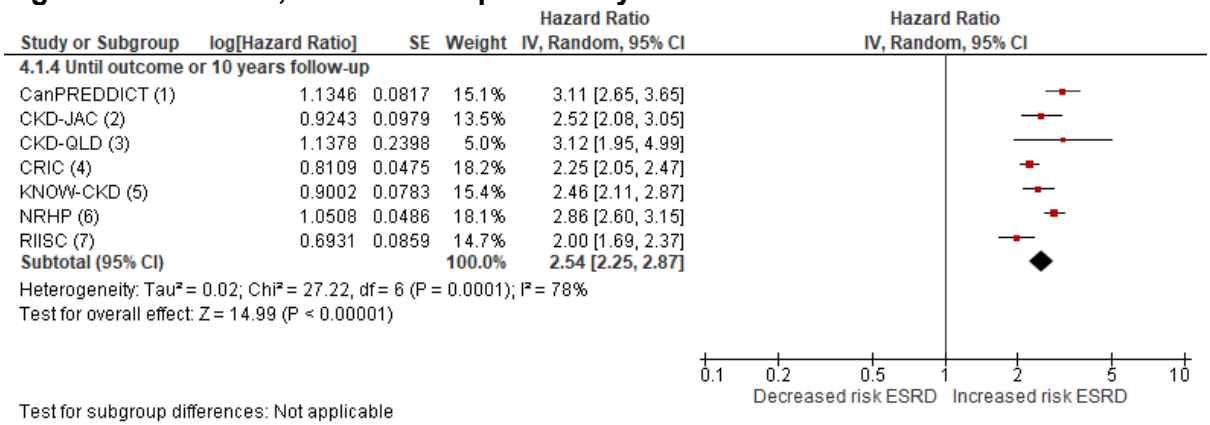
Figure 11: ESRD, per year



Risk of CKD progression (defined as decline greater than 10 mL/min/1.73 in eGFR at follow-up or 10 years follow-up), compared to baseline eGFR, CKD stage 3-5

The pooled hazard ratio for ESRD was not reported by Orlandi 2019 (IPD). Therefore, hazard ratios from studies reported in Orlandi 2019 are presented below (hazard ratios were not reported for one of the cohorts and this is why there are only 7 cohorts reported here instead of the 8 cohorts included in the IPD). The sample sizes of these studies ranged from N=724 to N=11778.

Figure 12: ESRD, until follow-up or at 10 years

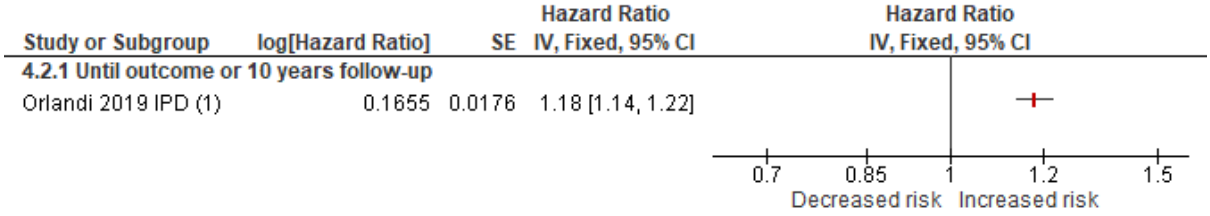


Test for subgroup differences: Not applicable

Footnotes

(1) Canadian Study of Prediction of Death, Dialysis and Interim Cardiovascular Events. Data obtained from Orlandi 2019.
(2) Chronic Kidney Disease Japan Cohort. Data obtained from Orlandi 2019.
(3) Chronic Kidney Disease in Queensland. Data obtained from Orlandi 2019.
(4) Chronic Renal Insufficiency Study (USA). Data obtained from Orlandi 2019.
(5) Korean Cohort Study for Outcome in Patients With Chronic Kidney Disease. Data obtained from Orlandi 2019.
(6) National Renal Healthcare Program (Uraguay). Data obtained from Orlandi 2019.
(7) Renal Impairment in Secondary Care (UK). Data obtained from Orlandi 2019.

Figure 13: All-cause mortality, until follow-up or at 10 years



Footnotes

(1) Individual level data from 7 international cohorts, total sample N=23484 participants. Definition of ESRD differs...

Risk of CKD progression in children

Figure 14: ESRD, 12 years minimum

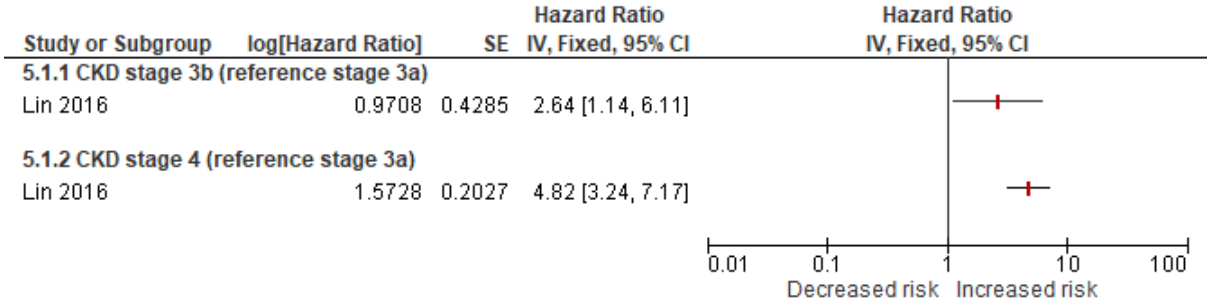


Figure 15: ESRD or mortality, compared to specified reference, median 1.5 years

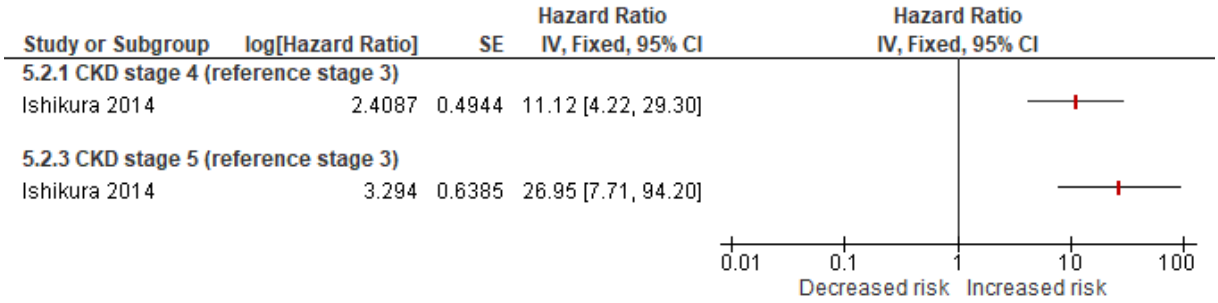
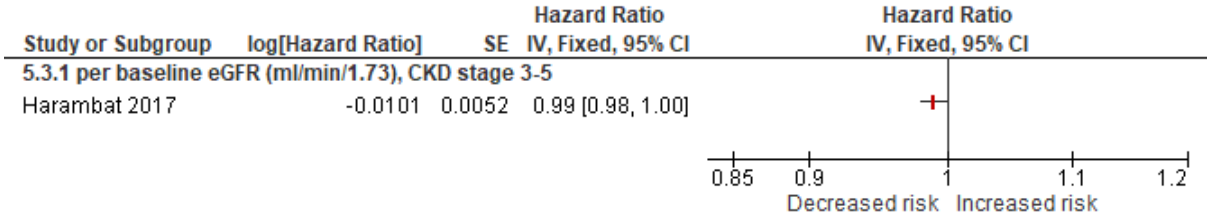


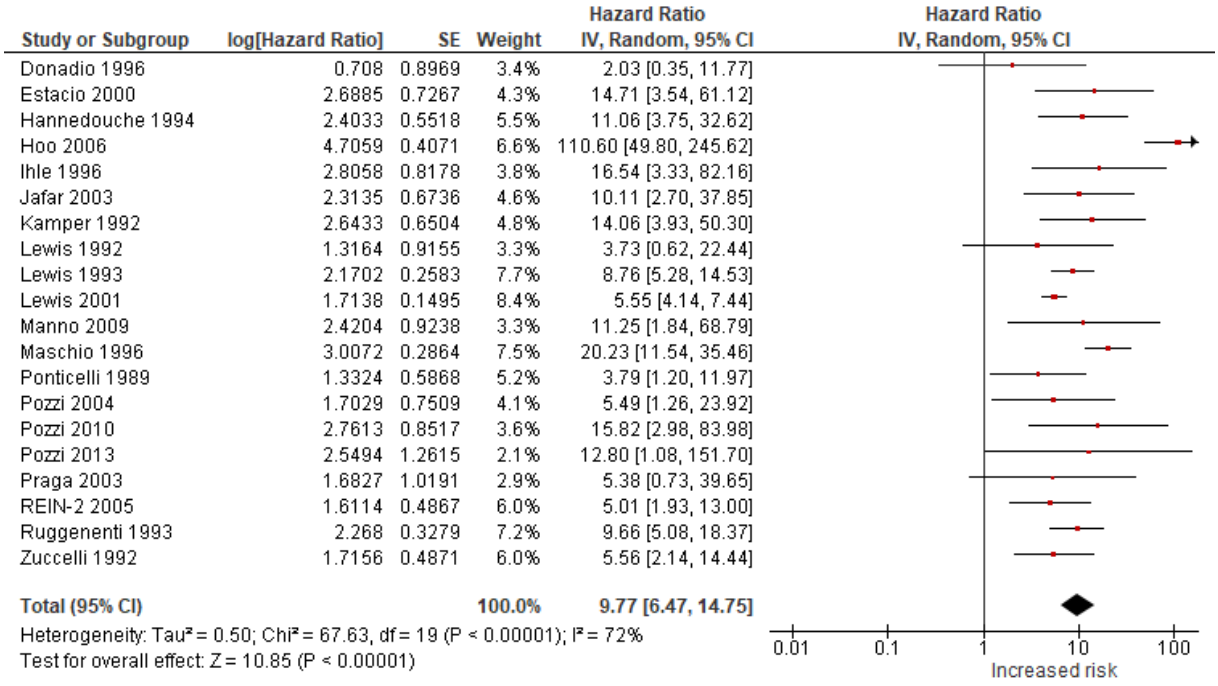
Figure 16: ESRD or 50% decline in eGFR, median 5.18 years follow-up, compared to baseline eGFR, CKD stage 3-5



F.1 Additional data

Additional data was obtained from one individual participant data (IPD) meta-analysis (Lambers Heerspink 2014). The pooled hazard ratio from this IPD could not be included as it contained overlaps with Coresh 2014 IPD meta-analysis. In addition, the individual studies could not be pooled with prospective cohort evidence as method of analysis in Lambers Heerspink 2014 accounts for intervention treatment and control arm as covariates. Therefore, hazard ratios from studies reported in Lambers Heerspink 2014 which do not overlap with Coresh 2014 are presented below. The sample sizes of these studies ranged from N=75 to N=1137.

Figure 17 Risk of ESRD, kidney failure not treated with dialysis or transplantation or doubling of serum creatinine per 30% eGFR decline



Appendix G – GRADE tables

G.1 Risk of CKD progression (defined as greater than 30% decline in eGFR from baseline eGFR), compared to baseline eGFR, in CKD stage 1-5 with type 2 diabetes

Quality assessment							No of patients	Effect	Quality
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**EGFR decline per progression**	**Relative (95% CI)**	
> 30% eGFR decline per baseline eGFR in type 2 diabetes - All CKD stages, mean 4.8 years									
1 (Subramanian 2019)	prospective cohort study	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	NR	OR 0.98 (0.96 to 1)	MODERATE

1 Confidence interval includes 1.

G.2 Risk of CKD progression (defined as eGFR percent change*) compared to stable eGFR (0% change), in CKD stage 3-5

Quality assessment							No of patients	Effect	Quality
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**EGFR decline per % progression,**	**Relative (95% CI)**	
ESRD, 1 year- 20% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 2.4 (2.2 to 2.62)	HIGH

ESRD, 1 year- 25% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 3 (2.6 to 3.46)	HIGH
ESRD, 1 year- 30% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 4 (3.4 to 4.71)	HIGH
ESRD, 1 year- 40% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 7.4 (6.1 to 8.98)	HIGH
ESRD, 1 year- 57% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 21.5 (16.1 to 28.71)	HIGH
ESRD, 2 years - 20% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 2.9 (2.5 to 3.36)	HIGH
ESRD, 2 years - 25% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 4 (3.3 to 4.85)	HIGH
ESRD, 2 years - 30% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 5.4 (4.5 to 6.48)	HIGH
ESRD, 2 years - 40% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 10.2 (8.2 to 12.69)	HIGH
ESRD, 2 years - 57% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 32.1 (22.3 to 46.21)	HIGH
ESRD, 3 years - 20% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 2.5 (2.1 to 2.98)	HIGH
ESRD, 3 years - 25% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 3.2 (2.4 to 4.27)	HIGH
ESRD, 3 years - 30% decline									

1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 5 (3.9 to 6.41)	HIGH
ESRD, 3 years - 40% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 10.4 (8 to 13.52)	HIGH
ESRD, 3 years - 57% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 36.8 (27.3 to 49.61)	HIGH
All-cause mortality, 1 year - 20% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 1.4 (1.31 to 1.5)	HIGH
All-cause mortality, 1 year - 25% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 1.6 (1.5 to 1.71)	HIGH
All-cause mortality, 1 year - 30% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 1.9 (1.7 to 2.12)	HIGH
All-cause mortality, 1 year - 40% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 2.4 (2.2 to 2.62)	HIGH
All-cause mortality, 1 year - 57% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 3.8 (3.3 to 4.38)	HIGH
All-cause mortality, 2 years - 20% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 1.4 (1.3 to 1.51)	HIGH
All-cause mortality, 2 years - 25% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 1.5 (1.4 to 1.61)	HIGH
All-cause mortality, 2 years - 30% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 1.8 (1.6 to 2.03)	HIGH
All-cause mortality, 2 years - 40% decline									

1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 2.3 (2.1 to 2.52)	HIGH
All-cause mortality, 2 years - 57% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 3.7 (3.2 to 4.28)	HIGH
All-cause mortality, 3 years - 20% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 1.4 (1.3 to 1.51)	HIGH
All-cause mortality, 3 years - 25% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 1.5 (1.4 to 1.61)	HIGH
All-cause mortality, 3 years - 30% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 1.8 (1.6 to 2.03)	HIGH
All-cause mortality, 3 years - 40% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 2.2 (2 to 2.42)	HIGH
All-cause mortality, 3 years - 57% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 3.3 (2.7 to 4.03)	HIGH
Cardiovascular mortality, 1 year - 20% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 1.4 (1.2 to 1.63)	HIGH
Cardiovascular mortality, 1 year - 30% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 1.7 (1.4 to 2.06)	HIGH
Cardiovascular mortality, 1 year - 40% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 2.1 (1.6 to 2.76)	HIGH
Cardiovascular mortality, 1 year - 57% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 2.8 (1.8 to 4.36)	HIGH
Cardiovascular mortality, 2 years - 20% decline									

1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 1.3 (1.1 to 1.54)	HIGH
Cardiovascular mortality, 2 years - 30% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 1.6 (1.3 to 1.97)	HIGH
Cardiovascular mortality, 2 years - 40% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 1.9 (1.5 to 2.41)	HIGH
Cardiovascular mortality, 2 years - 57% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 2.6 (1.7 to 3.98)	HIGH
Cardiovascular mortality, 3 years									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	very serious[1]	no serious indirectness	no serious imprecision	none	-	HR 1.77 (1.44 to 2.18)	LOW
Cardiovascular mortality, 3 years - 30% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 1.7 (1.4 to 2.06)	HIGH
Cardiovascular mortality, 3 years - 40% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 2 (1.7 to 2.35)	HIGH
Cardiovascular mortality, 3 years - 57% decline									
1(Coresh 2014)	Individual participant data meta-analysis	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 2.4 (1.6 to 3.6)	HIGH

* Percent change in eGFR was calculated as follows: (last eGFR – first eGFR)/(first eGFR) * 100%.

G.3 Risk of CKD progression (defined as decline greater than 1 mL/min/1.73 in eGFR per year), compared to less than 1 mL/min/1.73, CKD stage 1-5

Quality assessment							No of patients	Effect	Quality
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**EGFR decline per 1 ml/min/1.73**	**Relative (95% CI)**	

							decrease, CKD stages 1-5		
End stage renal disease - Per year (over 10 years)									
1 (Tsai 2017)	prospective cohort study	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 1.17 (1.16 to 1.18)	HIGH

G.4 Risk of CKD progression (defined as decline greater than 10 mL/min/1.73 in eGFR at follow-up or 10 year follow-up), compared to baseline eGFR, CKD stage 3-5

Quality assessment							**No of patients**	**Effect**	**Quality**
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**EGFR decline per 10 ml/min/1.73 decrease, CKD stages 3-5**	**Relative (95% CI)**	
End stage renal disease- Until outcome or 10 years follow-up									
7 studies (data from Orlandi 2019)	prospective cohort study	no serious risk of bias	very serious[1]	no serious indirectness	no serious imprecision	none	-	HR 2.54 (2.25 to 2.87)	LOW
All cause mortality - Until outcome or 10 years follow-up									
1 (Orlandi 2019)	Individual participant data meta-analysis	Serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 1.18 (1.14 to 1.22)	MODERATE

1 I squared statistic > 66.7%.
2 No literature search conducted in IPD.

G.5 Risk of CKD progression in children

Quality assessment	**No of patients**	**Effect**	**Quality**

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	EGFR decline in children	Relative (95% CI)	
ESRD, 12 years minimum follow-up - CKD stage 3b (reference stage 3a)									
1 (Lin 2016)	prospective cohort study	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 2.64 (1.14 to 6.11)	HIGH
ESRD, 12 years minimum follow-up - CKD stage 4 (reference stage 3a)									
1(Lin 2016)	prospective cohort study	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	-	HR 4.82 (3.24 to 7.17)	HIGH
ESRD or mortality, median 1.5 years follow-up - CKD stage 4 (reference stage 3)									
1 (Ishikura 2014)	prospective cohort study	no serious risk of bias	no serious inconsistency	serious[1]	no serious imprecision	none	-	HR 11.12 (4.22 to 29.3)	MODERATE
ESRD or mortality, median 1.5 years follow-up - CKD stage 5 (reference stage 3)									
1(Ishikura 2014)	prospective cohort study	no serious risk of bias	no serious inconsistency	serious[1]	no serious imprecision	none	-	HR 26.95 (7.71 to 94.2)	MODERATE
ESRD or 50% decline in eGFR, median 5.18 years follow-up, compared to baseline eGFR (ml/min/1.73), CKD stage 3-5									
1 (Harambat 2017)	prospective cohort study	no serious risk of bias	no serious inconsistency	serious[1]	serious[2]	none	-	HR 0.99 (0.98 to 1)	LOW

1 Composite outcome.
2 Confidence interval includes HR=1.

Appendix H – Economic evidence study selection

Appendix I – Economic evidence tables

No economic studies were included.

Appendix J – Health economic model

This review question was not prioritised for economic modelling.

Appendix K – Excluded studies

Study	Reason for exclusion
Amin AP, Whaley-Connell AT, Li S et al. (2013) The synergistic relationship between estimated GFR and microalbuminuria in predicting long-term progression to ESRD or death in patients with diabetes: results from the Kidney Early Evaluation Program (KEEP). American journal of kidney diseases : the official journal of the National Kidney Foundation 61(4 Suppl 2): S12	- Retrospective study
Baek, Seung Don, Kim, So Mi, Kang, Jae-Young et al. (2019) A risk scoring model to predict renal progression associated with postcontrast acute kidney injury in chronic kidney disease patients. Medicine 98(5): e14377	- Retrospective study
Barbour SJ, Er L, Djurdjev O et al. (2010) Differences in progression of CKD and mortality amongst Caucasian, Oriental Asian and South Asian CKD patients. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 25(11): 3663-3672	- Retrospective study
Bonneric, S., Karadkhele, G., Couchoud, C. et al. (2020) Sex and glomerular filtration rate trajectories in children. Clinical Journal of the American Society of Nephrology 15(3): 320-329	- No prognostic factor of interest
Boucquemont, J., Metzger, M., Combe, C. et al. (2014) Should we use standard survival models or the illness-death model for interval-censored data to investigate risk factors of chronic kidney disease progression?. PLoS ONE 9(12): e114839	- Compares models for progression, not predictive accuracy of eGFR decline.
Chang, Po-Ya, Chien, Li-Nien, Lin, Yuh-Feng et al. (2016) Risk factors of gender for renal progression in patients with early chronic kidney disease. Medicine 95(30): e4203	- Retrospective study
Chang, Wen-xiu, Arai, Shigeyuki, Tamura, Yoshifuru et al. (2016) Time-dependent risk factors associated with the decline of estimated GFR in CKD patients. Clinical and experimental nephrology 20(1): 58-70	- Retrospective study
de Goeij MC, Liem M, de Jager DJ et al. (2012) Proteinuria as a risk marker for the progression of chronic kidney disease in patients on predialysis care and the role of angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker treatment. Nephron. Clinical practice 121(1-2): c73	- Retrospective study
De Nicola, Luca, Provenzano, Michele, Chiodini, Paolo et al. (2015) Independent Role of Underlying Kidney Disease on Renal Prognosis of Patients with Chronic Kidney Disease under Nephrology Care. PloS one 10(5): e0127071	- No prognostic factor of interest
Eiselt, Jaromir, Rajdl, Daniel, Racek, Jaroslav et al. (2014) Asymmetric dimethylarginine and progression of chronic kidney disease: a one-year follow-up study. Kidney & blood pressure research 39(1): 50-7	- No outcomes of interest included.
Fabiano, Rafaela C G, Araujo, Stanley A, Bambirra, Eduardo A et al. (2017) The Oxford Classification predictors of chronic kidney disease in pediatric	- Retrospective study

Study	Reason for exclusion
patients with IgA nephropathy. Jornal de pediatria 93(4): 389-397	
Fung, Colman Siu Cheung, Wan, Eric Yuk Fai, Chan, Anca Ka Chun et al. (2017) Association of estimated glomerular filtration rate and urine albumin-to-creatinine ratio with incidence of cardiovascular diseases and mortality in chinese patients with type 2 diabetes mellitus - a population-based retrospective cohort study. BMC nephrology 18(1): 47	- No prognostic factor of interest
Furth, Susan L, Cole, Stephen R, Fadrowski, Jeffrey J et al. (2007) The association of anemia and hypoalbuminemia with accelerated decline in GFR among adolescents with chronic kidney disease. Pediatric nephrology (Berlin, Germany) 22(2): 265-71	- No outcomes of interest included.
Furth, Susan L, Cole, Stephen R, Moxey-Mims, Marva et al. (2006) Design and methods of the Chronic Kidney Disease in Children (CKiD) prospective cohort study. Clinical journal of the American Society of Nephrology : CJASN 1(5): 1006-15	- study protocol
Galan, Isabel, Goicoechea, Marian, Quiroga, Borja et al. (2018) Hyperuricemia is associated with progression of chronic kidney disease in patients with reduced functioning kidney mass. Nefrologia : publicacion oficial de la Sociedad Espanola Nefrologia 38(1): 73-78	- No prognostic factor of interest
Go, Alan S, Yang, Jingrong, Tan, Thida C et al. (2018) Contemporary rates and predictors of fast progression of chronic kidney disease in adults with and without diabetes mellitus. BMC nephrology 19(1): 146	- Retrospective study
He, Jiang, Mills, Katherine T, Appel, Lawrence J et al. (2016) Urinary Sodium and Potassium Excretion and CKD Progression. Journal of the American Society of Nephrology : JASN 27(4): 1202-12	- No prognostic factor of interest
Hoefield RA, Kalra PA, Baker P et al. (2010) Factors associated with kidney disease progression and mortality in a referred CKD population. American journal of kidney diseases : the official journal of the National Kidney Foundation 56(6): 1072-1081	- Retrospective study
Hoefield, R A, Kalra, P A, Lane, B et al. (2013) Associations of baseline characteristics with evolution of eGFR in a referred chronic kidney disease cohort. QJM : monthly journal of the Association of Physicians 106(10): 915-24	- Retrospective study
Horne, Kerry L, Packington, Rebecca, Monaghan, John et al. (2017) Three-year outcomes after acute kidney injury: results of a prospective parallel group cohort study. BMJ open 7(3): e015316	- Study design not relevant to protocol
Hoshino, Junichi, Nagai, Kei, Kai, Hirayasu et al. (2018) A nationwide prospective cohort study of patients with advanced chronic kidney disease in Japan: The Reach-J CKD cohort study. Clinical and experimental nephrology 22(2): 309-317	- study protocol
Hsu, Raymond K, Chai, Boyang, Roy, Jason A et al. (2016) Abrupt Decline in Kidney Function Before Initiating Hemodialysis and All-Cause Mortality: The Chronic Renal Insufficiency Cohort (CRIC) Study. American journal of kidney diseases : the official	- Study included in Orlandi 2019 individual level data.

Study	Reason for exclusion
journal of the National Kidney Foundation 68(2): 193-202	
Iimori, S., Naito, S., Noda, Y. et al. (2018) Prognosis of chronic kidney disease with normal-range proteinuria: The CKD-ROUTE study. PLoS ONE 13(1): e0190493	- No prognostic factor of interest Study included in Q3.1.
Inaguma, Daijo, Murata, Minako, Tanaka, Akihito et al. (2017) Relationship between mortality and speed of eGFR decline in the 3 months prior to dialysis initiation. Clinical and experimental nephrology 21(1): 159-168	- Population not relevant. Dialysis patients.
Ix, Joachim H, Biggs, Mary L, Mukamal, Kenneth et al. (2015) Urine Collagen Fragments and CKD Progression-The Cardiovascular Health Study. Journal of the American Society of Nephrology : JASN 26(10): 2494-503	- No prognostic factor of interest
Ju, Hye Young, Kim, Jin Kuk, Hur, Soon Mi et al. (2015) Could mean platelet volume be a promising biomarker of progression of chronic kidney disease?. Platelets 26(2): 143-7	- Study design not relevant
Kaewput, W.; Disorn, P.; Satirapoj, B. (2016) Selective cyclooxygenase-2 inhibitor use and progression of renal function in patients with chronic kidney disease: A single-center retrospective cohort study. International Journal of Nephrology and Renovascular Disease 9: 273-278	- Retrospective study
Kikuchi, Hiroaki, Kanda, Eiichiro, Mandai, Shintaro et al. (2017) Combination of low body mass index and serum albumin level is associated with chronic kidney disease progression: the chronic kidney disease-research of outcomes in treatment and epidemiology (CKD-ROUTE) study. Clinical and experimental nephrology 21(1): 55-62	- No primary outcome of interest.
Kim, Hyoungnae, Park, Jimin, Nam, Ki Heon et al. (2019) The effect of interactions between proteinuria, activity of fibroblast growth factor 23 and serum phosphate on renal progression in patients with chronic kidney disease: a result from the KoreaN cohort study for Outcome in patients With Chronic Kidney Disease study. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association	- Retrospective study
Kim, S., Hwang, S., Jang, H.R. et al. (2019) Creatinine- and cystatin C-based estimated glomerular filtration rate slopes for the prediction of kidney outcome: A comparative retrospective study. BMC Nephrology 20(1): 214	- Retrospective study
Kim, Yoonjin, Shin, Sungjoon, Kim, Kyungsoo et al. (2015) Effect of Urate Lowering Therapy on Renal Disease Progression in Hyperuricemic Patients with Chronic Kidney Disease. The Journal of rheumatology 42(11): 2143-8	- Retrospective study
Koraishy, F.M., Hooks-Anderson, D., Salas, J. et al. (2018) Fast GFR decline and progression to CKD among primary care patients with preserved GFR. International Urology and Nephrology 50(3): 501-508	- Population not relevant.
Kovesdy, Csaba P, Coresh, Josef, Ballew, Shoshana H et al. (2016) Past Decline Versus Current eGFR and	- Studies included in individual data sets. Coresh 2014.

Study	Reason for exclusion
Subsequent ESRD Risk. Journal of the American Society of Nephrology : JASN 27(8): 2447-55	
Koye, Digsu N, Magliano, Dianna J, Reid, Christopher M et al. (2018) Risk of Progression of Nonalbuminuric CKD to End-Stage Kidney Disease in People With Diabetes: The CRIC (Chronic Renal Insufficiency Cohort) Study. American journal of kidney diseases : the official journal of the National Kidney Foundation 72(5): 653-661	- Studies included in individual data sets.
Kuwabara, Masanari, Bjornstad, Petter, Hisatome, Ichiro et al. (2017) Elevated Serum Uric Acid Level Predicts Rapid Decline in Kidney Function. American journal of nephrology 45(4): 330-337	- Retrospective study
Kwan, B., Fuhrer, T., Zhang, J. et al. (2020) Metabolomic Markers of Kidney Function Decline in Patients With Diabetes: Evidence From the Chronic Renal Insufficiency Cohort (CRIC) Study. American Journal of Kidney Diseases	- No prognostic factor of interest
Levin, Adeera, Djurdjev, Ognjenka, Beaulieu, Monica et al. (2008) Variability and risk factors for kidney disease progression and death following attainment of stage 4 CKD in a referred cohort. American journal of kidney diseases : the official journal of the National Kidney Foundation 52(4): 661-71	- Retrospective study
Lorenzo V, Saracho R, Zamora J et al. (2010) Similar renal decline in diabetic and non-diabetic patients with comparable levels of albuminuria. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 25(3): 835-841	- Retrospective study
Lundstrom, Ulrika Hahn, Gasparini, Alessandro, Bellocco, Rino et al. (2017) Low renal replacement therapy incidence among slowly progressing elderly chronic kidney disease patients referred to nephrology care: an observational study. BMC nephrology 18(1): 59	- Retrospective study
Madero, Magdalena, Katz, Ronit, Murphy, Rachel et al. (2017) Comparison between Different Measures of Body Fat with Kidney Function Decline and Incident CKD. Clinical journal of the American Society of Nephrology : CJASN 12(6): 893-903	- Population not relevant. Non-CKD population. Study included in Q3.1.
Marks, Angharad, Fluck, Nicholas, Prescott, Gordon J et al. (2014) Definitions of progression in chronic kidney disease--predictors and relationship to renal replacement therapy in a population cohort with a 6 year follow-up. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 29(2): 333-41	- Retrospective study
McMullan, Ciaran J, Hickson, DeMarc A, Taylor, Herman A et al. (2015) Prospective analysis of the association of ambulatory blood pressure characteristics with incident chronic kidney disease. Journal of hypertension 33(9): 1939-1946	- Population not relevant.
Nacak, Hakan, van Diepen, Merel, Qureshi, Abdul R et al. (2015) Uric acid is not associated with decline in renal function or time to renal replacement therapy	- Retrospective study

Study	Reason for exclusion
initiation in a referred cohort of patients with Stage III, IV and V chronic kidney disease. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 30(12): 2039-45	
Naimark, David M J, Grams, Morgan E, Matsushita, Kunihiro et al. (2016) Past Decline Versus Current eGFR and Subsequent Mortality Risk. Journal of the American Society of Nephrology : JASN 27(8): 2456-66	- Studies included in individual data sets. Secondary study to Kovesdy 2016
Ng, Derek K, Schwartz, George J, Warady, Bradley A et al. (2017) Relationships of Measured Iohexol GFR and Estimated GFR With CKD-Related Biomarkers in Children and Adolescents. American journal of kidney diseases : the official journal of the National Kidney Foundation 70(3): 397-405	- No outcomes of interest included.
Nkuipou-Kenfack, Esther, Duranton, Flore, Gayrard, Nathalie et al. (2014) Assessment of metabolomic and proteomic biomarkers in detection and prognosis of progression of renal function in chronic kidney disease. PloS one 9(5): e96955	- No prognostic factor of interest
Peralta, Carmen A, Vittinghoff, Eric, Bansal, Nisha et al. (2013) Trajectories of kidney function decline in young black and white adults with preserved GFR: results from the Coronary Artery Risk Development in Young Adults (CARDIA) study. American journal of kidney diseases : the official journal of the National Kidney Foundation 62(2): 261-6	- Population not relevant.
Perkins RM, Bucaloiu ID, Kirchner HL et al. (2011) GFR decline and mortality risk among patients with chronic kidney disease. Clinical journal of the American Society of Nephrology : CJASN 6(8): 1879-1886	- Retrospective study
Piccoli, Antonio, Codognotto, Marta, Tabbi, Maria-Grazia et al. (2010) Influence of tonsillectomy on the progression of mesangioproliferative glomerulonephritis. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 25(8): 2583-9	- No outcomes of interest included.
Pontillo, Claudia, Jacobs, Lotte, Staessen, Jan A et al. (2017) A urinary proteome-based classifier for the early detection of decline in glomerular filtration. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 32(9): 1510-1516	- No outcomes of interest included.
Rebholz, Casey M, Grams, Morgan E, Matsushita, Kunihiro et al. (2015) Change in novel filtration markers and risk of ESRD. American journal of kidney diseases : the official journal of the National Kidney Foundation 66(1): 47-54	- Study included in Coresh 2014 individual patient data analysis.
Reichel, H., Zee, J., Tu, C. et al. (2020) Chronic kidney disease progression and mortality risk profiles in Germany: Results from the Chronic Kidney Disease Outcomes and Practice Patterns Study. Nephrology Dialysis Transplantation 35(5): 803-810	- No prognostic factor of interest
Ryom, L, Kirk, O, Lundgren, J D et al. (2013) Advanced chronic kidney disease, end-stage renal disease and	- No prognostic factor of interest

Study	Reason for exclusion
renal death among HIV-positive individuals in Europe. HIV medicine 14(8): 503-8	- Mixed CKD and non-CKD population.
Sawhney, Simon, Marks, Angharad, Fluck, Nick et al. (2017) Post-discharge kidney function is associated with subsequent ten-year renal progression risk among survivors of acute kidney injury. Kidney international 92(2): 440-452	- No prognostic factor of interest - No outcomes of interest included.
Shardlow, Adam, McIntyre, Natasha J, Fluck, Richard J et al. (2017) Associations of fibroblast growth factor 23, vitamin D and parathyroid hormone with 5-year outcomes in a prospective primary care cohort of people with chronic kidney disease stage 3. BMJ open 7(8): e016528	- No prognostic factor of interest Does not include a measure of eGFR decline as prognostic factor.
Shechter, Steven M; Skandari, M Reza; Zalunardo, Nadia (2014) Timing of arteriovenous fistula creation in patients With CKD: a decision analysis. American journal of kidney diseases : the official journal of the National Kidney Foundation 63(1): 95-103	- Study design not relevant
Sood, Manish M, Akbari, Ayub, Manuel, Doug et al. (2017) Time-Varying Association of Individual BP Components with eGFR in Late-Stage CKD. Clinical journal of the American Society of Nephrology : CJASN 12(6): 904-911	- Retrospective study
Sumida, Keiichi, Molnar, Miklos Z, Potukuchi, Praveen K et al. (2016) Association of Slopes of Estimated Glomerular Filtration Rate With Post-End-Stage Renal Disease Mortality in Patients With Advanced Chronic Kidney Disease Transitioning to Dialysis. Mayo Clinic proceedings 91(2): 196-207	- Retrospective study
Tangri, Navdeep, Inker, Lesley A, Hiebert, Brett et al. (2017) A Dynamic Predictive Model for Progression of CKD. American journal of kidney diseases : the official journal of the National Kidney Foundation 69(4): 514-520	- Study design not relevant Prediction model
Totoli, C., Carvalho, A.B., Ammirati, A.L. et al. (2019) Associated factors related to chronic kidney disease progression in elderly patients. PLoS ONE 14(7): e0219956	- Retrospective study
Turin TC, Coresh J, Tonelli M et al. (2012) One-year change in kidney function is associated with an increased mortality risk. American journal of nephrology 36(1): 41-49	- Retrospective study
Turin TC, Coresh J, Tonelli M et al. (2012) Short-term change in kidney function and risk of end-stage renal disease. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 27(10): 3835-3843	- Retrospective study
Vadala, Maria, Castellucci, Massimo, Guarrasi, Giulia et al. (2019) Retinal and choroidal vasculature changes associated with chronic kidney disease. Graefe's archive for clinical and experimental ophthalmology. Albrecht von Graefes Archiv fur klinische und experimentelle Ophthalmologie 257(8): 1687-1698	- Study design not relevant
Van Pottelbergh G, Bartholomeeusen S, Buntinx F et al. (2012) The evolution of renal function and the	- Retrospective study

Study	Reason for exclusion
incidence of end-stage renal disease in patients aged ≥ 50 years. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 27(6): 2297-2303	
Warren, Bethany, Rebholz, Casey M, Sang, Yingying et al. (2018) Diabetes and Trajectories of Estimated Glomerular Filtration Rate: A Prospective Cohort Analysis of the Atherosclerosis Risk in Communities Study. Diabetes care 41(8): 1646-1653	- Study included in Coresh 2014 individual patient data analysis.
Yamanouchi, M., Furuichi, K., Hoshino, J. et al. (2019) Nonproteinuric versus proteinuricphenotypesindiabetic kidney disease: A propensity score-matched analysis of a nationwide, biopsy-based cohort study. Diabetes Care 42(5): 891-902	- No prognostic factor of interest
Zhang, Jun-Jun, Yu, Gui-Zhen, Zheng, Zhao-Hui et al. (2017) Dividing CKD stage 3 into G3a and G3b could better predict the prognosis of IgA nephropathy. PloS one 12(4): e0175828	- Study contains retrospective data.

Appendix L – Research recommendations – full details

L.1.1 Research recommendation

What is the most clinical and cost-effective frequency of review for children and young people with CKD?

L.1.2 Why this is important

No evidence was identified to support any particular strategy for timing of review for children and young people with chronic kidney disease. Because of the lack of evidence, considerable variation in current practice and the likely resource implications of a practice recommendation, the committee made a research recommendation to inform future guidance.

L.1.3 Rationale for research recommendation

Importance to 'patients' or the population	If effective and cost-effective, such an intervention could potentially identify the optimal frequency of reviewing children and young people with CKD and provide benefits in terms of health-related quality of life, time to CKD progression, mortality reduction.
Relevance to NICE guidance	Optimal frequency reviewing children and young people with CKD has been considered in this guideline and there was no evidence. Further evidence might fill in the gap in this area during future updates of the guideline.
Relevance to the NHS	Research in this area will inform NICE recommendations for service delivery and provide information about clinical and cost-effectiveness. Optimal frequency of reviewing children and young people with CKD might potentially reduce unnecessary healthcare resource use and patient treatment burden.
National priorities	High
Current evidence base	There is no evidence on the optimal frequency of review for children and young people with CKD. It is important to have sufficient information on this topic so further evidence based information can be given in regards to the best frequency of reviewing children and young people with CKD.
Equality considerations	None known

L.1.4 Modified PICO table

Population	Children and young people with CKD
Intervention	• 6 monthly review • 2 to 3 monthly review • Monthly review

Comparator	Yearly review (review to include face to face assessment and review of biochemical measures)

Outcome	• Patient, family/carer health-related quality of life
	• All-cause mortality
	• CKD progression measured by
	  ○ Change in eGFR
	  ○ Incidence of end stage kidney disease

Study design	RCT ideally, if not then a prospective cohort study with adequate adjustment for key confounders including age, ethnicity, co-morbidities and some measure of baseline health (e.g. quality of life)
Timeframe	Long term
Additional information	Subgroup data by age groups would inform whether different timings are more appropriate at different developmental stages.

L.1.5 Research recommendation

For adults, children and young people with CKD, what is the optimal monitoring frequency for albumin:creatinine ratio (ACR)?

L.1.6 Why this is important

No evidence was identified to support any particular strategy for timing of monitoring of ACR in adults, children and young people with chronic kidney disease. Because of the lack of evidence, considerable variation in current practice and the likely resource implications of a practice recommendation, the committee made a research recommendation to inform future guidance.

L.1.7 Rationale for research recommendation

Importance to 'patients' or the population	Optimal frequency of ACR monitoring in adults, children and young people with CKD could provide benefits in terms of health-related quality of life, time to CKD progression, mortality reduction.
Relevance to NICE guidance	Optimal frequency of ACR monitoring in adults, children and young people with CKD has been considered in this guideline and there was no evidence. Further evidence might fill in the gap in this area during future updates of the guideline.
Relevance to the NHS	Research in this area will inform NICE recommendations for service delivery and provide information about clinical and cost-effectiveness. Optimal frequency of ACR monitoring in adults, children and young people with CKD might potentially reduce unnecessary healthcare resource use and patient treatment burden.
National priorities	High
Current evidence base	There is no evidence on the optimal frequency of ACR monitoring in adults, children and young

	people with CKD. It is important to have sufficient information on this topic so further evidence-based information can be given in regards to the best frequency of ACR monitoring in adults, children and young people with CKD.
Equality considerations	None known

L.1.8 Modified PICO table

Population	Adults, children and young people with CKD
Intervention	• 6 monthly monitoring of ACR • 2 to 3 monthly monitoring of ACR • Monthly monitoring of ACR
Comparator	Yearly monitoring of ACR
Outcome	• Patient, family/carer health-related quality of life • All-cause mortality
Study design	RCT ideally, if not then a prospective cohort study with adequate adjustment for key confounders including age, ethnicity, co-morbidities and some measure of baseline health (e.g. quality of life)
Timeframe	Long term
Additional information	Subgroups by age.