National Institute for Health and Care Excellence

Draft

Chronic kidney disease:

[N] Evidence review for defining clinically significant decline in eGFR in terms of risk of kidney disease progression

NICE guideline <number>

Evidence review underpinning recommendation 1.3.2 in the NICE guideline

January 2021

Draft for Consultation

These evidence reviews were developed by the Guideline Updates Team

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Defining clinically significant decline in eGFR in terms of risk of kidney disease progression

1.1 Review question

For adults, children and young people with chronic kidney disease (CKD), what constitutes a clinically significant decline in estimated glomerular filtration rate (eGFR) in terms of risk of kidney disease progression?

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 an individual patient data meta-analysis (Coresh 2014; sample size: 1.7 million participants) examining the association of decline in eGFR with two end points: 1) CKD progression (end stage renal disease [initiation of renal replacement therapy]) or 2) all-cause mortality. Results showed that declines in eGFR smaller than a doubling of serum creatinine concentration occurred more commonly and were strongly and consistently associated with the risk of CKD progression and mortality, supporting consideration of lesser declines in eGFR (such as a 30% reduction over 2 years) as an alternative end point for CKD progression to the current 25% in one year. As a result, the decision was made to update this part of the guideline. During scoping, it was agreed to extend the guideline to cover the assessment and management of chronic kidney disease in children and young people in all areas being updated.

The aim of this review is to identify what constitutes a clinically significant decline in eGFR in terms of risk of kidney disease progression. This review identified studies that fulfilled the conditions specified in Table 1. For full details of the review protocol, see Appendix A.

1.1.2 Summary of the protocol

Table 1: PICO table

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	Rate of decline in eGFR
Comparator	In comparative studies, rates of eGFR decline in comparator populations. In other cohorts (for example, epidemiological or prognostic), no comparator is required.

	Where appropriate confounders other than the subgroups of interest should be adjusted for. As a first choice, multivariate/ adjusted analyses from the studies using the confounders identified in the studies themselves will be used.
outcomes	**Primary outcome:** Rate of eGFR decline **Secondary outcomes:** • CKD progression: occurrence of end stage kidney disease (ESRD or ESKD as reported by the study) • Mortality

1.1.3 Methods and process

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

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

Protocol deviation

All included studies were non-comparative. Therefore, none of the risk of bias checklists listed in the protocol could be used. Instead, we used a risk of bias checklist for 'uncontrolled prospective studies' as recommended by the Developing NICE guidelines: the manual (Institute of Health Economics [IHE] checklist for case series). Authors of the checklist suggest removing items that are not applicable for the specific review and we removed items referring to 'intervention and co-intervention' because this review does not contain interventions.

GRADE was not used in this review for the following reasons:

- GRADE is not designed for use in epidemiological reviews.
- Most of the studies could not be meta-analysed because there were significant differences between studies at baseline which resulted in high heterogeneity (I^2 above 90%).
- Imprecision could not be evaluated because there was no effect measure from the evidence of this review as all studies were non-comparative and therefore no values could be used as minimal clinically important differences. The aim of this review was to discuss with the committee the clinically important rate of decline in eGFR in different populations.

The following methods were specific for this review:

1. Secondary outcomes (CKD progression and mortality) are reported as part of the outcomes of the evidence review for the optimal monitoring frequency based on different rates of decline in eGFR (Evidence review E).
2. Some studies reported more than one measure of glomerular filtration rate (GFR). If that was the case, data were extracted in the following order:
   a. Measured GFR (mGFR)
   b. Estimated GFR (eGFR) using CKD-EPI
   c. eGFR using MDRD
   d. eGFR using other equations

3. We extracted the longest follow-up if studies reported more than one follow-up.
4. Most studies reported decline in eGFR with negative values. Studies reporting positive values were changed to negative values for consistency when reporting meta-analysis or forest plots.
5. Comments on included studies:
    a. Bruck 2018 (rate of decline in eGFR was reported for each cohort [these cohorts did not include a comparison group]) reported subgroups by age but sample size was not given for these subgroups. Therefore, data on these subgroups was not added to the forest plots. Bruck 2018 also reported results for the TABLE cohort which was also reported by Minutolo 2020 as part of their pooled results. Therefore, TABLE cohort was not added to the forest plots as a separate cohort.
    b. Grams 2019 (rate of decline in eGFR was reported for each cohort [these cohorts did not include a comparison group]) is a secondary publication of the individual patient data meta-analysis reported by Coresh 2014. Grams was considered to be more relevant for this evidence review because they reported means and standard deviations of the rate of decline in eGFR while Coresh 2014 was considered to be more relevant for the review question 'For adults, children and young people with CKD what is the optimal monitoring frequency based on different rates of decline in eGFR?' (Evidence review E) because the study reported predictive accuracy data.
    c. Hadjadj 2016 reported pooled results (medians) for 3 uncontrolled prospective studies including participants with type 2 diabetes (GENEDIAB, GENESIS and JDRF). Skupien 2019 also reported results (means) for GENEDIAB and GENESIS plus additional participants from the same enrolment centres. Mean results from Skupien 2019 were added to the forest plots and median results from Hadjadj 2016 are reported in a table together with other studies reporting medians.
    d. Inaguma 2017 did not report the sample size for the subgroup with hypertension. Therefore, results could not be added to the forest plots.
    e. Melsom 2019 reported results for Pima Indians but this group was not considered to be a relevant population for the UK. Therefore, data for Pima Indians was not extracted. The data for relevant populations were extracted.
    f. Oyilmaz 2017 did not report the sample size for the subgroup by age. Therefore, results could not be added to the forest plots.
    g. Rowe 1976 reported subgroups by age. The subgroup including participants 17 to 24 years old could not be added to meta-analysis because the subgroup only had one participant.
    h. There were studies reporting subgroups without CKD and with albuminuria (Ozyilmaz 2017; Buyadaa 2020). These were reclassified to CKD if albuminuria was reported as albumin excretion rate ≥30 mg/24 hours; albumin-to-creatine ratio ≥3 mg/mmol or ≥30 mg/g since albuminuria at these levels is diagnostic of CKD.

1.1.4 Epidemiological evidence

1.1.4.1 Included studies

A systematic search was carried out to identify cross-sectional and cohort studies and retrospective individual patient data (IPD) cohorts, which found 9,799 references (see Appendix C for the literature search strategy). Evidence identified in the original guideline (8 references) and references from the NICE surveillance review (1 reference which was found by the systematic search) were also reviewed. There were also relevant references (12 references) found within the systematic search for the review question 'For adults, children

and young people with CKD what is the optimal monitoring frequency based on different rates of decline in eGFR?' In total, 9,819 references were identified for screening at title and abstract level with 9,630 excluded at this level. Full texts were ordered to be screened for 189 references. In total 34 references were included based on their relevance to the review protocol (Appendix A). From these references, 2 were IPDs and 32 were uncontrolled prospective studies. The epidemiological evidence study selection is presented as a PRISMA diagram in Appendix D.

IPDs were Bruck 2018 (European CKD Burden Consortium) and Grams 2019 (CKD Prognosis Consortium). Bruck 2018 reported on 9 uncontrolled prospective studies and Grams 2019 reported on 14 uncontrolled prospective studies. There was no overlap between IPDs or between IPDs and individual uncontrolled prospective studies.

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

See section 1.1.11 References – included studies for a list of references for included studies.

1.1.4.2 Excluded studies

See Appendix K for a list of excluded studies with the primary reason for exclusion.

1.1.5 Summary of studies included in the epidemiological evidence

Table 2: Summary of included studies

Study	Population	mGFR or eGFR	Serum biomarker(s)	Follow-up time
Belangero 2018 SP-CKDkid study	Study design: uncontrolled prospective study Sample size: 209 Children and young people eGFR <60 and >15	eGFR (Schwartz formula)	Creatinine	median 2.5 years
Bruck 2018 European CKD Burden Consortium	Study design: individual patient data Sample size: 18,126 Adults CKD	eGFR (CKD-EPI)	Creatinine	median 5.7 years
Buyadaa 2020 ACCORD & ACCORDION studies	Study design: uncontrolled prospective study Sample size: 10,185 Adults with type 2 diabetes No CKD eGFR ≥ 120 CKD eGFR 90 to 120 CKD eGFR 60 to 90 Albuminuric non-CKD UACR ≥3.4 mg/mmol Albuminuric CKD UACR ≥3.4 mg/mmol	eGFR (MDRD 4-variable)	Creatinine	median 8.8 years

	Non-albuminuric CKD UACR <3.4 mg/mmol			
Chen 2019	Study design: uncontrolled prospective study Sample size: 815 Adults eGFR <59	eGFR (MDRD)	Creatinine	median 5.3 years
Fathallah-Shaykh 2015 CKiD study	Study design: uncontrolled prospective study Sample size: 522 Children and young people with nonglomerular diagnoses and eGFR 30 to 90	mGFR eGFR (CkiD-developed formulae)	mGFR (iohexol) eGFR (creatinine cystatin-C or BUN)	median 4.4 years
Fischer 2016 BAME CRIC & H-CRIC studies	Study design: uncontrolled prospective study Sample size: 3,785 Adults (Non-Hispanic White, Non-Hispanic Black, Hispanic) eGFR 30 to ≥90	eGFR (CRIC equation)	Creatinine cystatin-C or BUN	median 6.8 years
Furth 2007	Study design: uncontrolled prospective study Sample size: 23 Children and young people (White, Non-White [not defined]) eGFR <75	eGFR (Schwartz formula)	Creatinine	3 years
Grams 2019 CKD Prognosis Consortium	Study design: individual patient data Sample size: 3,881,215 Adults eGFR<60 eGFR≥60	eGFR (CKD-EPI)	Creatinine	3 years
Hadjadj 2016	Study design: uncontrolled prospective study Sample size: 1,219 Adults with CKD Type 1 diabetes with retinopathy Type 2 diabetes with proteinuria	eGFR (CKD-EPI)	Creatinine	median 11.9 years
Hwang 2017	Study design: uncontrolled prospective study Sample size: 35 Adults with diabetes and diabetic nephropathy	eGFR (CKD-EPI)	Creatinine	median 2.0 years

Iimori 2018 CKD-ROUTE study	Study design: uncontrolled prospective study Sample size: 927 Adults CKD categories G2 to G5 and normal-range proteinuria CKD category G2 and normal-range proteinuria CKD category G3a and normal-range proteinuria CKD category G3b and normal-range proteinuria CKD categories G4 to G5 and normal-range proteinuria	eGFR (MDRD 3-variable for Japanese)	Creatinine	median 3.0 years
Inaguma 2017 CKD-JAC study	Study design: uncontrolled prospective study Sample size: 2,966 Adults eGFR 45–59 eGFR 30–44 eGFR 15–29 eGFR <15 CKD and Hypertension (SBP ≥140 mmHg and/or DBP ≥90 mmHg) CKD and Hypertension (SBP <140 mmHg and DBP <90 mmHg) CKD and UACR <300 mg/g CKD and UACR 300 to 999 mg/g CKD and UACR ≥1000 mg/g	eGFR (Japanese equation)	Creatinine	median 3.9 years
Kasiske 2015	Study design: uncontrolled prospective study Sample size: 404 Adults Controls Kidney donors	mGFR eGFR (CKD-EPI)	iohexol Creatinine Cystatin-C Creatinine-cystatin-C	3 years
Madero 2017	Study design: uncontrolled prospective study Sample size: 2,489 Adults 70–79 years	eGFR (CKD-EPI)	Cystatin-C	median 8.9 years
Malmgren 2020 OPRA	Study design: uncontrolled prospective study Sample size: 981 Women aged 75 years at baseline eGFR at baseline 63 mL/min/1.73m^2	eGFR (CKD-EPI)	Cystatin-C	10 years
Melsom 2019 RENIS-T6 study	Study design: uncontrolled prospective study Sample size: 1,594 Adults Norwegians without cardiovascular disease, kidney disease, or diabetes	mGFR	iohexol clearance	median 5.6 years

Minutolo 2020 4 studies: TABLE-CKD NEPHRO-SUN RECORD-IT NEPHRO-FEDERICO II	Study design: uncontrolled prospective study Sample size: 2,335 Adults eGFR ≤45	eGFR (CKD-EPI)	Creatinine	median 4.2 years
Moriya 2017 JDCS study	Study design: uncontrolled prospective study Sample size: 1,407 Adults with type 2 diabetes eGFR ≥120 eGFR <120 ≥90 eGFR <90 ≥60 eGFR <60	eGFR (MDRD for Japanese)	Creatinine	8 years
Ozyilmaz 2017 PREVEND study	Study design: uncontrolled prospective study Sample size: 6,471 Adults general population, normoalbuminuria (<30mg/24h), no HTN general population, normoalbuminuria (<30mg/24h), new HTN general population, normoalbuminuria (<30mg/24h), known HTN general population elevated albuminuria (≥30mg/24h), no HTN general population elevated albuminuria (≥30mg/24h), new HTN general population elevated albuminuria (≥30mg/24h), known HTN	eGFR (CKD-EPI)	Creatinine-cystatin-C	median 11.3 years
Pottel 2019 European Kidney Function Consortium Cohorts	Study design: uncontrolled prospective study Sample size: 136 Children and young people with suspected or manifest CKD	mGFR	inulin iohexol Cr-EDTA	average 5.8 years
Pruijm 2018	Study design: uncontrolled prospective study Sample size: 183 Adults eGFR 15 to ≥90 Hypertension without CKD Healthy adults	eGFR (MDRD)	Creatinine	mean 3.0 years
Qin 2015	Study design: uncontrolled prospective study Sample size: 2,518 Adults with normal kidney function	eGFR (CKD-EPI)	Creatinine	median 7.08 years

Reichel 2020 CKDopps (only data from Germany)	Study design: uncontrolled prospective study Sample size: 1,834 Adults eGFR ≥30 ≤60 eGFR ≥15 <30	eGFR (MDRD)	Creatinine	median 2.4 years
Rowe 1976 Baltimore longitudinal study of aging	Study design: uncontrolled prospective study Sample size: 586 Adults general population 17 to 84 years	Not reported	Creatinine	2-year study periods
Skupien 2019 4 studies: Joslin FinnDiane Steno INSERM	Study design: uncontrolled prospective study Sample size: 1,518 Adults Type 1 diabetes with persistent macroalbuminuria in CKD eGFR ≥ 30	eGFR (CKD-EPI)	Creatinine	11 or 12 years
Sukmark 2014	Study design: uncontrolled prospective study Sample size: 203 Adults CKD categories 2 to 4	eGFR (MDRD Abbreviated)	Creatinine	median 3.0 years
Tsai 2014 KMUHIRB-990198	Study design: uncontrolled prospective study Sample size: 621 Adults CKD categories 3 to 5	eGFR (MDRD 4-variable)	Creatinine	mean 3.1 years
Tsai 2019 CMUH105-REC3-068	Study design: uncontrolled prospective study Sample size: 5,092 Adults CKD categories 1 to 5	eGFR (MDRD Abbreviated)	Creatinine	median 2.5 years
Vallianou 2018	Study design: uncontrolled prospective study Sample size: 106 Adults Type 2 diabetes CKD	eGFR (CKD-EPI)	Creatinine	mean 6.3 years
Van Londen 2018	Study design: uncontrolled prospective study Sample size: 349 Adults Kidney donors	mGFR	I-iothalamate I-hippurate	5 years
van Rijn 2018	Study design: uncontrolled prospective study Sample size: 1,955 Adults eGFR ≥15 to ≥90	mGFR eGFR (CKD-EPI MDRD FAS)	mGFR (Cr-EDTA) eGFR (Creatinine)	median 3.4 years

Warren 2018 ARIC study	Study design: uncontrolled prospective study Sample size: 15,517 Adults General population without diabetes undiagnosed diabetes diagnosed diabetes	eGFR (CKD-EPI)	Creatinine	over 26 years
Yoshida 2020	Study design: uncontrolled prospective study Sample size: 2,385 Adults type 1 diabetes, no CKD type 1 diabetes, eGFR <60 and normoalbuminuria (ACR < 30 mg/gCr) type 1 diabetes, ACR ≥ 30 mg/gCr and normal eGFR ≥ 60 type 1 diabetes, eGFR <60 and ACR ≥ 30 mg/gCr type 2 diabetes, no CKD type 2 diabetes, eGFR <60 and normoalbuminuria (ACR < 30 mg/gCr) type 2 diabetes, ACR ≥ 30 mg/gCr and normal eGFR ≥ 60 type 2 diabetes, eGFR <60 and, ACR ≥ 30 mg/gCr	eGFR (MDRD Japanese)	Creatinine	mean 3.0 years
Young 2016 JHS	Study design: uncontrolled prospective study Sample size: 3,653 Adults (African-Americans) General population	eGFR (CKD-EPI)	Creatinine	mean 8.04 years
Yu 2019 ARIC study	Study design: uncontrolled prospective study Sample size: 14,854 Adults (White, African-Americans) general population, normal blood pressure general population, elevated blood pressure general population, stage 1 hypertension general population, stage 2 hypertension without medications general population, stage 2 hypertension with medications	eGFR (CKD-EPI)	Creatinine	30 years

See Appendix E for full evidence tables.

1.1.6 Summary of the epidemiological evidence (negative values mean higher rate of decline)

Table 3 Children and young people with CKD or suspected CKD

Study	Study design	Sample size	Mean decline per year in eGFR ml/min/1.73m^2 (95% CI)	Risk of bias	Indirectness
Fathallah-Shaykh 2015 CKD G2 to G3b	Uncontrolled prospective study	522	-1.10 [-1.45, -0.75]	Low	Directly applicable
Furth 2007 CKD G2 to G5	Uncontrolled prospective study	23	-5.60 [-9.10, -2.10]	Low	Directly applicable
Pottel 2019 Suspected or manifest CKD	Uncontrolled prospective study	136	-2.00 [-2.84, -1.16]	Low	Partially applicable[a]

a) Rate of decline in eGFR was a secondary outcome

Table 4 Children and young people by subgroups

Study	Study design	Sample size	Mean decline per year in eGFR ml/min/1.73m^2 (95% CI)	Risk of bias	Indirectness
Fathallah-Shaykh 2015 CKD G2 to G3b Male	Uncontrolled prospective study	16	-7.50 [-8.33, -6.67]	Low	Directly applicable
Fathallah-Shaykh 2015 CKD G2 to G3b Female	Uncontrolled prospective study	7	-2.90 [-3.86, -1.94]	Low	Directly applicable
Fathallah-Shaykh 2015 CKD G2 to G3b White	Uncontrolled prospective study	19	-5.70 [-6.19, -5.21]	Low	Directly applicable
Fathallah-Shaykh 2015 CKD G2 to G3b Non-White	Uncontrolled prospective study	4	-5.00 [-9.12, -0.88]	Low	Directly applicable
Fathallah-Shaykh 2015 CKD G2 to G3b Hypoalbuminemia	Uncontrolled prospective study	8	-16.30 [-17.69, -14.91]	Low	Directly applicable
Fathallah-Shaykh 2015 CKD G2 to G3b No hypoalbuminemia	Uncontrolled	15	0.80 [0.19, 1.41]	Low	Directly applicable

	prospective study				

a) Rate of decline in eGFR was a secondary outcome

Table 5 Kidney donors

Study	Study design	Sample size	Mean gain per year in eGFR ml/min/1.73m^2 (95% CI)	Risk of bias	Indirectness
Kasiske 2015 Van Londen 2018	Uncontrolled prospective study	530	1.00 [0.84, 1.17]	Low	Directly applicable

Table 6 Adults without CKD; subgroups by age

Study	Study design	Sample size	Mean decline per year in eGFR ml/min/1.73m^2 (95% CI)	Risk of bias	Indirectness
Rowe 1976 25 to 34 years of age	Uncontrolled prospective study	20	-1.09 [-2.46, 0.28]	Low	Directly applicable
Rowe 1976 35 to 44 years of age	Uncontrolled prospective study	64	-0.11 [-0.82, 0.60]	Low	Directly applicable
Rowe 1976 45 to 54 years of age	Uncontrolled prospective study	95	-0.73 [-1.32, -0.14]	Low	Directly applicable
Rowe 1976 55 to 64 years of age	Uncontrolled prospective study	60	-1.64 [-2.44, -0.84]	Low	Directly applicable
Rowe 1976 65 to 74 years of age	Uncontrolled prospective study	36	-1.30 [-2.42, -0.18]	Low	Directly applicable
Rowe 1976 75 to 84 years of age	Uncontrolled prospective study	17	-1.07 [-2.58, 0.44]	Low	Directly applicable

Table 7 Adults without CKD, diabetes, hypertension and albuminuria

Study	Study design	Sample size	Mean decline per year in eGFR ml/min/1.73m^2 (95% CI)	Risk of bias	Indirectness
Kasiske 2015	Uncontrolled prospective study	172	-0.39 [-1.11, 0.33]	Low	Directly applicable
Melsom 2019	Uncontrolled prospective study	1,594	-0.95 [-1.06, -0.84]	Low	Directly applicable
Ozyilmaz 2017	Uncontrolled prospective study	4,397	-0.81 [-0.84, -0.78]	Low	Directly applicable
Pruijm 2018	Uncontrolled prospective study	24	-0.20 [-2.32, 1.92]	Low	Directly applicable
Rowe 1976	Uncontrolled prospective study	293	-0.90 [-1.25, -0.55]	Low	Directly applicable
Warren 2018	Uncontrolled prospective study	13,698	-1.40 [-1.45, -1.35]	Low	Directly applicable

Table 8 Adults without CKD and with diabetes

Study	Study design	Sample size	Mean decline per year in eGFR ml/min/1.73m^2 (95% CI)	Risk of bias	Indirectness
Buyadaa 2020 Type 2 diabetes	Uncontrolled prospective study	775	-2.53 [-2.73, -2.33]	Low	Partially applicable[a]
Moriya 2017 Type 2 diabetes	Uncontrolled prospective study	157	-3.10 [-3.91, -2.29]	Low	Directly applicable
Warren 2018 Undiagnosed diabetes	Uncontrolled prospective study	634	-1.80 [-1.95, -1.65]	Low	Directly applicable

Warren 2018 Diabetes	Uncontrolled prospective study	1185	-2.50 [-2.60, -2.40]	Low	Directly applicable

b) Rate of decline in eGFR was a secondary outcome
UACR: urine albumin:creatinine ratio

Table 9 Adults without CKD and with hypertension

Study	Study design	Sample size	Mean decline per year in eGFR ml/min/1.73m^2 (95% CI)	Risk of bias	Indirectness
Ozyilmaz 2017 New hypertension Albumin <30mg/24h	Uncontrolled prospective study	949	-1.14 [-1.23, -1.05]	Low	Directly applicable
Ozyilmaz 2017 Known hypertension Albumin <30mg/24h	Uncontrolled prospective study	521	-1.16 [-1.28, -1.04]	Low	Directly applicable
Pruijm 2018 Hypertension	Uncontrolled prospective study	47	0.50 [-0.90, 1.90]	Low	Directly applicable

Table 10 Female adults without CKD

Study	Study design	Sample size	Mean decline per year in eGFR ml/min/1.73m^2 (95% CI)	Risk of bias	Indirectness
Ozyilmaz 2017 No hypertension; Albumin <30mg/24h	Uncontrolled prospective study	2,418	-0.86 [-0.90, -0.82]	Low	Directly applicable
Ozyilmaz 2017 New hypertension; Albumin <30mg/24h	Uncontrolled prospective study	370	-1.36 [-1.51, -1.21]	Low	Directly applicable

Ozyilmaz 2017 Known hypertension; Albumin <30mg/24h	Uncontrolled prospective study	271	-1.17 [-1.35, -0.99]	Low	Directly applicable

Table 11 Male adults without CKD

Study	Study design	Sample size	Mean decline per year in eGFR ml/min/1.73m^2 (95% CI)	Risk of bias	Indirectness
Ozyilmaz 2017 No hypertension; Albumin <30mg/24h	Uncontrolled prospective study	1,979	-0.74 [-0.78, -0.70]	Low	Directly applicable
Ozyilmaz 2017 New hypertension; Albumin <30mg/24h	Uncontrolled prospective study	579	-1.00 [-1.10, -0.90]	Low	Directly applicable
Ozyilmaz 2017 Known hypertension; Albumin <30mg/24h	Uncontrolled prospective study	250	-1.14 [-1.32, -0.96]	Low	Directly applicable

Table 12 Adults with CKD

Study (uncontrolled prospective study)	Study design	Sample size	Mean decline per year in eGFR ml/min/1.73m^2 (95% CI)	Risk of bias	Indirectness
Bruck 2018 (Ghent)	Individual patient data analysis	403	-0.77 [-1.08, -0.46]	High	Directly applicable
Bruck 2018 (Nicosia)	Individual patient data analysis	70	-1.48 [-2.47, -0.49]	High	Directly applicable
Bruck 2018 (CIC)	Individual patient data analysis	1,420	-0.34 [-0.66, -0.02]	High	Directly applicable
Bruck 2018 (MAURO)	Individual patient data analysis	719	-1.33 [-1.61, -1.05]	High	Directly applicable
Bruck 2018 (PIRP)	Individual patient data analysis	11,277	-1.65 [-1.75, -1.55]	High	Directly applicable
Bruck 2018 (PECERA)	Individual patient data analysis	939	-2.43 [-2.75, -2.11]	High	Directly applicable

Bruck 2018 (CRISIS)	Individual patient data analysis	2,049	-1.79 [-2.03, -1.55]	High	Directly applicable
Bruck 2018 (LACKABO)	Individual patient data analysis	218	-2.05 [-2.71, -1.39]	High	Directly applicable

Table 13 Female adults with CKD

Study (uncontrolled prospective study)	**Study design**	**Sample size**	**Mean decline per year in eGFR ml/min/1.73m^2 (95% CI)**	**Risk of bias**	**Indirectness**
Bruck 2018 (Ghent)	Individual patient data analysis	157	-0.26 [-0.61, 0.09]	High	Directly applicable
Bruck 2018 (Nicosia)	Individual patient data analysis	20	-1.55 [-3.27, 0.17]	High	Directly applicable
Bruck 2018 (CIC)	Individual patient data analysis	588	0.12 [-0.38, 0.62]	High	Directly applicable
Bruck 2018 (MAURO)	Individual patient data analysis	294	-0.78 [-1.20, -0.36]	High	Directly applicable
Bruck 2018 (PIRP)	Individual patient data analysis	3,992	-1.07 [-1.22, -0.92]	High	Directly applicable
Bruck 2018 (PECERA)	Individual patient data analysis	372	-1.75 [-2.23, -1.27]	High	Directly applicable
Bruck 2018 (CRISIS)	Individual patient data analysis	787	-0.89 [-1.21, -0.57]	High	Directly applicable
Bruck 2018 (LACKABO)	Individual patient data analysis	61	-0.10 [-1.21, 1.01]	High	Directly applicable
Malmgren 2020 eGFR at baseline 63 mL/min/1.73m^2	Uncontrolled prospective study	365	-1.83 [-1.95, -1.71]	Low	Directly applicable
Ozyilmaz 2017 No hypertension; Albumin ≥30mg/24h	Uncontrolled prospective study	92	-1.21 [-1.53, -0.89]	Low	Directly applicable
Ozyilmaz 2017 New hypertension; Albumin ≥30mg/24h	Uncontrolled prospective study	64	-1.50 [-1.82, -1.18]	Low	Directly applicable
Ozyilmaz 2017 Known hypertension; Albumin ≥30mg/24h	Uncontrolled prospective study	39	-1.64 [-2.35, -0.93]	Low	Directly applicable

Table 14 Male adults with CKD

Study (uncontrolled prospective study)	**Study design**	**Sample size**	**Mean decline per year in eGFR**	**Risk of bias**	**Indirectness**

			ml/min/1.73m^2 (95% CI)		
Bruck 2018 (Ghent)	Individual patient data analysis	246	-1.00 [-1.42, -0.58]	High	Directly applicable
Bruck 2018 (Nicosia)	Individual patient data analysis	50	-1.49 [-3.59, 0.61]	High	Directly applicable
Bruck 2018 (CIC)	Individual patient data analysis	832	-0.57 [-1.22, 0.08]	High	Directly applicable
Bruck 2018 (MAURO)	Individual patient data analysis	425	-1.21 [-1.73, -0.69]	High	Directly applicable
Bruck 2018 (PIRP)	Individual patient data analysis	7,285	-1.23 [-1.40, -1.06]	High	Directly applicable
Bruck 2018 (PECERA)	Individual patient data analysis	567	-2.29 [-2.89, -1.69]	High	Directly applicable
Bruck 2018 (CRISIS)	Individual patient data analysis	1,262	-1.03 [-1.39, -0.67]	High	Directly applicable
Bruck 2018 (LACKABO)	Individual patient data analysis	157	-2.47 [-3.82, -1.12]	High	Directly applicable
Ozyilmaz 2017 No hypertension; Albumin ≥30mg/24h	Uncontrolled prospective study	137	-1.16 [-1.50, -0.82]	Low	Directly applicable
Ozyilmaz 2017 New hypertension; Albumin ≥30mg/24h	Uncontrolled prospective study	182	-1.62 [-1.86, -1.38]	Low	Directly applicable
Ozyilmaz 2017 Known hypertension; Albumin ≥30mg/24h	Uncontrolled prospective study	90	-1.93 [-2.40, -1.46]	Low	Directly applicable

Table 15 Adults with CKD and with hypertension

Study	Study design	Sample size	Mean decline per year in eGFR ml/min/1.73m^2 (95% CI)	Risk of bias	Indirectness
Ozyilmaz 2017 New hypertension Albumin ≥30mg/24h	Uncontrolled prospective study	246	-1.59 [-1.78, -1.40]	Low	Directly applicable
Ozyilmaz 2017 Known hypertension Albumin ≥30mg/24h	Uncontrolled prospective study	129	-1.84 [-2.23, -1.45]	Low	Directly applicable

Table 16 Adults with CKD and without diabetes

Study (uncontrolled prospective study)	**Study design**	**Sample size**	**Mean decline per year in eGFR ml/min/1.73m^2 (95% CI)**	**Risk of bias**	**Indirectness**
Bruck 2018 (Ghent)	Individual patient data analysis	259	-0.60 [-0.93, -0.27]	High	Directly applicable
Bruck 2018 (Nicosia)	Individual patient data analysis	28	-1.29 [-2.71, 0.13]	High	Directly applicable
Bruck 2018 (MAURO)	Individual patient data analysis	468	-0.84 [-1.17, -0.51]	High	Directly applicable
Bruck 2018 (PIRP)	Individual patient data analysis	7,150	-1.03 [-1.15, -0.91]	High	Directly applicable
Bruck 2018 (PECERA)	Individual patient data analysis	602	-2.06 [-2.44, -1.68]	High	Directly applicable
Bruck 2018 (CRISIS)	Individual patient data analysis	1,387	-0.97 [-1.24, -0.70]	High	Directly applicable
Bruck 2018 (LACKABO)	Individual patient data analysis	174	-1.54 [-2.27, -0.81]	High	Directly applicable

Table 17 Adults with CKD and diabetes

Study (uncontrolled prospective study)	**Study design**	**Sample size**	**Mean decline per year in eGFR ml/min/1.73m^2 (95% CI)**	**Risk of bias**	**Indirectness**
Bruck 2018 (Ghent)[a]	Individual patient data analysis	144	-1.07 [-1.58, -0.56]	High	Directly applicable
Bruck 2018 (Nicosia)[a]	Individual patient data analysis	42	-1.63 [-3.54, 0.28]	High	Directly applicable
Bruck 2018 (MAURO)[a]	Individual patient data analysis	251	-1.37 [-1.92, -0.82]	High	Directly applicable
Bruck 2018 (PIRP)[a]	Individual patient data analysis	4,127	-1.40 [-1.59, -1.21]	High	Directly applicable
Bruck 2018 (PECERA)[a]	Individual patient data analysis	337	-2.08 [-2.69, -1.47]	High	Directly applicable

Bruck 2018 (CRISIS)[a]	Individual patient data analysis	662	-0.94 [-1.33, -0.55]	High	Directly applicable
Bruck 2018 (LACKABO)[a]	Individual patient data analysis	44	-2.07 [-3.69, -0.45]	High	Directly applicable
Buyadaa 2020 Type 2 diabetes; eGFR ≥60; UACR ≥3.4 mg/mmol	Uncontrolled prospective study	2814	-2.51 [-2.61, -2.41]	Low	Partially applicable[a]
Buyadaa 2020 Type 2 diabetes; eGFR <60; UACR ≥3.4 mg/mmol	Uncontrolled prospective study	330	-1.75 [-1.98, -1.52]	Low	Partially applicable[b]
Buyadaa 2020 Type 2 diabetes; eGFR <60; UACR <3.4 mg/mmol	Uncontrolled prospective study	424	-0.60 [-0.72, -0.48]	Low	Partially applicable[b]
Inaguma 2017 UACR <33.9 mg/mmol[c]	Uncontrolled prospective study	765	-0.54 [-0.87, -0.21]	Low	Partially applicable[b]
Inaguma 2017 UACR 33.9 to 112.89 mg/mmol[c]	Uncontrolled prospective study	857	-2.39 [-2.81, -1.97]	Low	Partially applicable[b]
Inaguma 2017 UACR ≥113 mg/mmol**	Uncontrolled prospective study	1,091	-4.56 [-4.85, -4.27]	Low	Partially applicable[b]
Vallianou 2018 Type 2 diabetes	Uncontrolled prospective study	53	-2.30 [-4.35, -0.25]	High	Partially applicable[b]

a) Diabetes mellitus
b) Rate of decline in eGFR was a secondary outcome
c) Converted from mg/g x 0.113=mg/mmol
UACR: urine albumin:creatinine ratio

Table 18 Adults with CKD categories G1 and G2

Study (uncontrolled prospective study)	**Study design**	**Sample size**	**Mean decline per year in eGFR ml/min/1.73m^2 (95% CI)**	**Risk of bias**	**Indirectness**
Buyadaa 2020 CKD G1, Type 2 diabetes	Uncontrolled prospective study	2,684	-1.31 [-1.39, -1.23]	Low	Partially applicable[a]
Buyadaa 2020 CKD G2, Type 2 diabetes	Uncontrolled prospective study	2,975	-0.91 [-0.98, -0.84]	Low	Partially applicable[a]
Grams 2019 (ADVANCE) eGFR≥60	Individual patient data analysis	7,970	-1.83 [-1.91, -1.75]	High	Directly applicable

Grams 2019 (Geisinger) eGFR≥60	Individual patient data analysis	144,273	-1.87 [-1.88, -1.86]	High	Directly applicable
Grams 2019 (KP Hawaii) eGFR≥60	Individual patient data analysis	9,866	-1.29 [-1.35, -1.23]	High	Directly applicable
Grams 2019 (Maccabi) eGFR≥60	Individual patient data analysis	758,347	-0.75 [-0.75, -0.75]	High	Directly applicable
Grams 2019 (NZDCS) eGFR≥60	Individual patient data analysis	3,479	-3.35 [-3.46, -3.24]	High	Directly applicable
Grams 2019 (RCAV) eGFR≥60	Individual patient data analysis	2,430,178	-1.43 [-1.43, -1.43]	High	Directly applicable
Grams 2019 (SCREAM) eGFR≥60	Individual patient data analysis	480,145	-1.36 [-1.37, -1.35]	High	Directly applicable
Moriya 2017 CKD G1, Type 2 diabetes	Uncontrolled prospective study	355	-1.00 [-1.30, -0.70]	Low	Directly applicable
Moriya 2017 CKD G2, Type 2 diabetes	Uncontrolled prospective study	735	0.30 [0.08, 0.52]	Low	Directly applicable

a) Rate of decline in eGFR was a secondary outcome

Table 19 Adults with CKD categories G3a and G3b

Study	Study design	Sample size	Mean decline per year in eGFR ml/min/1.73m^2 (95% CI)	Risk of bias	Indirectness
Inaguma 2017 CKD G3a Inaguma 2017 CKD G3b Reichel 2020	Uncontrolled prospective study	1,837	-2.08 [-2.36, -1.81]	Low	Partially applicable[a]

CKD G3ab					

a) Rate of decline in eGFR was a secondary outcome

Table 20 Adults with CKD categories G4 and G5

Study	Study design	Sample size	Mean decline per year in eGFR ml/min/1.73m^2 (95% CI)	Risk of bias	Indirectness
Inaguma 2017 CKD G4	Uncontrolled prospective study	1,149	-3.18 [-4.00, -2.36]	Low	Partially applicable[a]
Inaguma 2017 CKD G5	Uncontrolled prospective study	466	-3.75 [-4.33, -3.17]	Low	Partially applicable[a]
Reichel 2020 CKD G4	Uncontrolled prospective study	1,348	-2.00 [-2.26, -1.74]	Low	Partially applicable[a]

a) Rate of decline in eGFR was a secondary outcome

Table 21 Adults with CKD categories G1 to G4

Study	Study design	Sample size	Mean decline per year in eGFR ml/min/1.73m^2 (95% CI)	Risk of bias	Indirectness
Fischer 2016 CKD G1 to G3ab	Uncontrolled prospective study	1,638	-0.48 [-0.54, -0.42]	Low	Partially applicable[a]
Pruijm 2018 CKD G1 to G4	Uncontrolled prospective study	112	-2.00 [-3.11, -0.89]	Low	Directly applicable
Sukmark 2014 CKD G2 to G4	Uncontrolled prospective study	203	-2.25 [-2.75, -1.75]	Moderate	Directly applicable
van Rijn 2018 CKD G1 to G4	Uncontrolled	1,955	-1.50 [-1.56, -1.44]	Low	Directly applicable

	prospective study				

a) Rate of decline in eGFR was a secondary outcome

Table 22 Adults with CKD categories G1 to G3b and type 1 diabetes

Study (uncontrolled prospective study)	**Study design**	**Sample size**	**Mean decline per year in eGFR ml/min/1.73m^2 (95% CI)**	**Risk of bias**	**Indirectness**
Skupien 2019 (FinnDiane)	Uncontrolled prospective study	486	-4.00 [-4.40, -3.60]	Low	Directly applicable
Skupien 2019 (Joslin)	Uncontrolled prospective study	432	-5.20 [-5.65, -4.75]	Low	Directly applicable
Skupien 2019 (Steno)	Uncontrolled prospective study	368	-3.30 [-3.75, -2.85]	Low	Directly applicable
Skupien 2019 (INSERM)	Uncontrolled prospective study	232	-4.10 [-4.65, -3.55]	Low	Directly applicable

Table 23 Adults with CKD categories G3a to G5

Study	**Study design**	**Sample size**	**Mean decline per year in eGFR ml/min/1.73m^2 (95% CI)**	**Risk of bias**	**Indirectness**
Grams 2019 GFR<60, AASK	Individual patient data analysis	664	-1.11 [-1.35, -0.87]	High	Directly applicable
Grams 2019 GFR<60, BC CKD	Individual patient data analysis	8,168	-1.12 [-1.19, -1.05]	High	Directly applicable
Grams 2019 GFR<60, CCF	Individual patient data analysis	14,631	-0.55 [-0.60, -0.50]	High	Directly applicable
Grams 2019 GFR<60, Geisinger	Individual patient data analysis	17,695	-0.41 [-0.46, -0.36]	High	Directly applicable

Grams 2019 GFR<60, KP Hawaii	Individual patient data analysis	3,484	-0.37 [-0.48, -0.26]	High	Directly applicable
Grams 2019 GFR<60, Maccabi	Individual patient data analysis	28,039	-0.38 [-0.42, -0.34]	High	Directly applicable
Grams 2019 GFR<60, MASTERPLAN	Individual patient data analysis	481	-1.27 [-1.49, -1.05]	High	Directly applicable
Grams 2019 GFR<60, MDRD	Individual patient data analysis	301	-2.58 [-2.89, -2.27]	High	Directly applicable
Grams 2019 GFR<60, NZDCS	Individual patient data analysis	909	-1.03 [-1.25, -0.81]	High	Directly applicable
Grams 2019 GFR<60, RENAAL	Individual patient data analysis	728	-4.12 [-4.35, -3.89]	High	Directly applicable
Grams 2019 GFR<60, SCREAM	Individual patient data analysis	33,122	-0.42 [-0.46, -0.38]	High	Directly applicable
Grams 2019 GFR<60, Sunnybrook	Individual patient data analysis	732	-1.63 [-1.89, -1.37]	High	Directly applicable
Moriya 2017 GFR<60, Type 2 diabetes	Uncontrolled prospective study	160	1.30 [0.90, 1.70]	Low	Directly applicable
Reichel 2020 eGFR 15 to 60	Uncontrolled prospective study	1,834	-2.10 [-2.34, -1.86]	Low	Partially applicable[a]

a) Rate of decline in eGFR was a secondary outcome

Table 24 Adults with CKD categories G3b to G5 by sex

Study	Study design	Sample size	Mean decline per year in eGFR ml/min/1.73m^2 (95% CI)	Risk of bias	Indirectness
Minutolo 2020 Male	Pooled analysis of 4 uncontrolled prospective studies	1,311	-2.09 [-2.21, -1.97]	Low	Partially applicable[a]

Minutolo 2020 Female	Pooled analysis of 4 uncontrolled prospective studies	1,024	-1.79 [-1.92, -1.66]	Low	Partially applicable[a]

a) Rate of decline in eGFR was a secondary outcome

Table 25 Adults from Black, Asian and Minority Ethnic (BAME) groups

Study	Study design	Sample size	Mean decline per year in eGFR ml/min/1.73m^2 (95% CI)	Risk of bias	Indirectness
Fischer 2016 CKD G1 to G3ab Non-Hispanic White	Uncontrolled prospective studies	1,638	-0.48 [-0.54, -0.42]	Low	Partially applicable[a]
Fischer 2016 CKD G1 to G3ab Non-Hispanic Black	Uncontrolled prospective studies	1,650	-0.95 [-1.03, -0.87]	Low	Partially applicable[a]
Fischer 2016 CKD G1 to G3ab Hispanic	Uncontrolled prospective studies	497	-1.38 [-1.56, -1.20]	Low	Partially applicable[a]
Young 2016 No CKD African-Americans	Uncontrolled prospective studies	3,653	-1.27 [-1.33, -1.21]	Low	Directly applicable

a) Rate of decline in eGFR was a secondary outcome

Table 26 Uncontrolled prospective studies reporting mean percentage decline

Study	Population	Sample size	Mean % decline per year in eGFR ml/min/1.73m^2 (SD)	Risk of bias	Indirectness
Madero 2017 Health ABC	Adults Aged 70 to 79 years	2,489	3.2% (6.3%)	Low	Directly applicable

Table 27 Uncontrolled prospective studies reporting medians

Study	Population	Sample size	Median decline per year in eGFR ml/min/1.73m^2 (interquartile range)	Risk of bias	Indirectness
Belangero 2018 SP-CKDkid	Children and young people eGFR >15 and <60	209	-1.6 (-6.3, 1.6)	Moderate	Partially applicable[a]
Chen 2019	Adults eGFR<59	815	8.0% (0.4%, 16.8%)	Low	Partially applicable[a]
Hadjadj 2016 SURDIAGENE, DIABHYCAR uncontrolled prospective studies	Adults Type 1 diabetes with retinopathy and CKD	277	-3.4 (-6.4, -1.5)	Low	Partially applicable[a]
Hadjadj 2016 GENEDIAB, GENESIS, JDRF uncontrolled prospective studies	Adults Type 2 diabetes with proteinuria and CKD	942	-3.1 (-5.9, -0.5)	Low	Partially applicable[a]
Hwang 2017	Adults Diabetes and diabetic nephropathy	35	15.6 (4.4, 35.1)	Low	Directly applicable

Study	Population	Sample size	Median decline per year in eGFR ml/min/1.73m^2 (interquartile range)	Risk of bias	Indirectness
Iimori 2018 CKD-ROUTE study	Adults CKD G2 to G5 and normal-range proteinuria	352	-0.69 (-2.53, 1.65)	Low	Partially applicable[a]
Iimori 2018 CKD-ROUTE study	Adults CKD G2 and normal-range proteinuria	36	-2.17 (-3.99, -0.51)	Low	Partially applicable[a]
Iimori 2018 CKD-ROUTE study	Adults CKD G3a and normal-range proteinuria	89	-1.38 (-2.71, 0.0)	Low	Partially applicable[a]
Iimori 2018 CKD-ROUTE study	Adults CKD G3b and normal-range proteinuria	129	-0.31 (-2.19, 1.57)	Low	Partially applicable[a]
Iimori 2018 CKD-ROUTE study	Adults CKD G4 to G5 and normal-range proteinuria	98	0.44 (-1.69, 3.05)	Low	Partially applicable[a]
Qin 2015	Adults Normal kidney function	2,518	1.83 (0.91, 2.74)	Low	Partially applicable[a]
Qin 2015	Male adults Normal kidney function	1,337	1.90 (0.99, 2.84)	Low	Partially applicable[a]
Qin 2015	Female adults Normal kidney function	1,181	1.75 (0.83, 2.68)	Low	Partially applicable[a]
Tsai 2014 KMUHIRB-990198	Adults CKD G3 to G5	621	-1.6 (-3.3, -0.4)	Low	Directly applicable
Tsai 2019 CMUH105-REC3-068	Adults CKD G1 to G5	5,092	-0.87 (-3.62, 3.33)	Low	Directly applicable
Yoshida 2020	Adults Type 1 diabetes without CKD	139	-1.23 (-3.87, 1.03)	Low	Directly applicable
Yoshida 2020	Adults	14	0.44	Low	Directly applicable

Study	Population	Sample size	Median decline per year in eGFR ml/min/1.73m^2 (interquartile range)	Risk of bias	Indirectness
	Type 1 diabetes, eGFR <60 and normo-albuminuria (ACR < 30 mg/gCr)		(-0.47, 2.78)		
Yoshida 2020	Adults Type 1 diabetes, ACR ≥ 30 mg/gCr and normal eGFR ≥ 60	26	-2.18 (-4.34, -0.35)	Low	Directly applicable
Yoshida 2020	Adults Type 1 diabetes, eGFR <60 and ACR ≥ 30 mg/gCr	17	-1.73 (-3.16, -0.22)	Low	Directly applicable
Yoshida 2020	Adults Type 2 diabetes without CKD	1,154	-1.68 (-4.59, 0.24)	Low	Directly applicable
Yoshida 2020	Adults Type 2 diabetes, eGFR <60 and normo-albuminuria (ACR < 30 mg/gCr)	337	-0.22 (-2.22, 2.01)	Low	Directly applicable
Yoshida 2020	Adults Type 2 diabetes, ACR ≥ 30 mg/gCr and normal eGFR ≥ 60	454	-2.68 (-6.15, -0.56)	Low	Directly applicable
Yoshida 2020	Adults Type 2 diabetes, eGFR <60 and ACR ≥ 30 mg/gCr	354	-1.08 (-3.95, 0.79)	Low	Directly applicable
Yu 2019 ARIC study	White adults General population with normal blood pressure	5,341	-1.32 (-1.51, -1.11)	Low	Directly applicable
Yu 2019 ARIC study	African-Americans adults General population with normal blood pressure	859	-1.79 (-2.07, -1.45)	Low	Directly applicable

Study	Population	Sample size	Median decline per year in eGFR ml/min/1.73m^2 (interquartile range)	Risk of bias	Indirectness
Yu 2019 ARIC study	White adults General population with elevated blood pressure	1,281	-1.48 (-1.67, -1.31)	Low	Directly applicable
Yu 2019 ARIC study	African-Americans adults General population with elevated blood pressure	273	-2.10 (-2.34, -1.77)	Low	Directly applicable
Yu 2019 ARIC study	White adults General population with stage 1 hypertension	1,448	-1.47 (-1.66, -1.26)	Low	Directly applicable
Yu 2019 ARIC study	African-Americans adults General population with stage 1 hypertension	610	-2.00 (-2.28, -1.62)	Low	Directly applicable
Yu 2019 ARIC study	White adults General population with stage 2 hypertension without medications	801	-1.71 (-1.93, -1.51)	Low	Directly applicable
Yu 2019 ARIC study	African-Americans adults General population with stage 2 hypertension without medications	573	-2.39 (-2.64, -1.94)	Low	Directly applicable
Yu 2019 ARIC study	White adults General population with stage 2 hypertension with medications	2,132	-1.61 (-1.81, -1.40)	Low	Directly applicable
Yu 2019 ARIC study	African-Americans adults General population with stage 2	1,536	-2.25 (-2.55, -1.79)	Low	Directly applicable

Study	Population	Sample size	Median decline per year in eGFR ml/min/1.73m^2 (interquartile range)	Risk of bias	Indirectness
	hypertension with medications				

a) Rate of decline in eGFR was a secondary outcome

1.1.7 Economic evidence

A systematic review was conducted to identify economic evaluations for this review question. The search returned 1,764 records which were sifted against the review protocol. All records 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.

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

1.1.8 Evidence statements

Table 28 was considered to be the most appropriate way to summarise the evidence and as a result, evidence statements have not been written for this evidence.

Table 28: eGFR decline per year by population subgroups

Population	Risk of bias Indirectness Sample size	eGFR decline per year [ml/min/1.73m^2](based on point estimates)[a, e]
Children and young people		
CKD G2 to G3b	Low Directly applicable N=522	-1.10
CKD G2 to G5	Low Directly applicable N=23	-5.60
Suspected or manifest CKD	Low Partially applicable [b] N=136	-2.00
Children and young people with CKD G2 to G3b	Low Directly applicable	
• Male	N=16	-7.50
• Female	N=7	-2.90
• White	N=19	-5.70
• Non-White	N=4	-5.00
• Hypoalbuminemia	N=8	-16.30
• No hypoalbuminemia	N=15	0.80

Population	Risk of bias Indirectness Sample size	eGFR decline per year [ml/min/1.73m^2](based on point estimates)[a, e]
Kidney donors	Low Directly applicable 530	0.84 to 1.03
Adults without CKD		
Adults without CKD, decline by age	Low Directly applicable	
• 25 -34	20	-1.09
• 35-44	64	-0.11
• 45-54	95	-0.73
• 55-64	60	-1.64
• 65-74	36	-1.30
• 75-84	17	-1.07
• All ages	292	-0.85
Adults without CKD, diabetes, hypertension or albuminuria	Low Directly applicable N>24 (range 24 to 13,698)	-0.20 to -1.40
Adults without CKD and with diabetes	Low Most studies were directly applicable [c] N>157 (range 157 to 1,185	-1.80 to -3.10
Adults without CKD and with hypertension	Low Directly applicable N>47 (range 47 to 949)	0.50 to -1.16
Female adults without CKD	Low Directly applicable N>271 (range 271 to 2,418)	-0.86 to -1.36
Male adults without CKD	Low Directly applicable N>250 (range 250 to 1,979)	-0.74 to -1.14
Adults with CKD		
Adults with CKD	High Directly applicable N>70 (range 70 to 11,277	-0.34 to -2.43
Female adults with CKD	Mainly high Directly applicable N>20 (range 20 to 3,992)	0.12 to -1.83

Population	Risk of bias Indirectness Sample size	eGFR decline per year [ml/min/1.73m^2](based on point estimates)[a, e]
Male adults with CKD	Mainly high Directly applicable N>50 (range 50 to 7,285)	-0.57 to -2.47
Adults with CKD and with hypertension	Low Directly applicable N>129 (range 129 to 246)	-1.59 to -1.84
Adults with CKD and without diabetes	High Directly applicable N>28 (range 28 to 7,150)	-0.60 to -2.06
Adults with CKD and with diabetes	Mainly high Most studies were directly applicable [d] N>42 (range 42 to 4,127)	-0.54 to -4.56
Adults with CKD G1 and G2	Mainly high Most studies were directly applicable [c] N>355 (range 355 to 2,430,178)	0.3. to -3.35
Adults with CKD G3a and G3b	Low Partially applicable [b] N>306 (range 306 to 1,045	-1.92 to -2.30
Adults with CKD G4 and G5	Low Partially applicable [b] N>466 (range 466 to 1,348)	-2.0 to -3.75
Adults with CKD G1 to G4	Mainly low Most studies were directly applicable [c] N>112 (range 112 to 1,955)	-0.48 to -2.25
Adults with CKD G1 to G3b with diabetes	Low Directly applicable N>232 (range 232 to 486)	-3.30 to -5.20
Adults with CKD G3a to G5	Mainly high Most studies were directly applicable [c] N>160 (range 160 to 33,122)	1.30 to -4.12
Male adults with CKD G3b to G5	Low Partially applicable [b]	-2.09

Population	Risk of bias Indirectness Sample size	eGFR decline per year [ml/min/1.73m^2](based on point estimates)[a, e]
	N=1,311	
Female adults with CKD G3b to G5	Low Partially applicable [b] N=1,024	-1.79
Adults from Black, Asian and Minority Ethnic (BAME) groups		
Non-Hispanic Whites with CKD G1 to G3b	Low Partially applicable [b] N=1,638	-0.48
Non-Hispanic Blacks with CKD G1 to G3b	Low Partially applicable [b] N=1,650	-0.95
Hispanics with CKD G1 to G3b	Low Partially applicable [b] N=497	-1.38
African-Americans without CKD	Low Directly applicable N=3,653	-1.27

(a) Negative numbers indicate a decline in eGFR, positive numbers an increase in eGFR.
(b) Rate of decline in eGFR was a secondary outcome.
(c) One study was partially applicable because the rate of decline in eGFR was a secondary outcome.
(d) Three studies were partially applicable because the rate of decline in eGFR was a secondary outcome
(e) Range indicates high and low estimates when more than one study.

1.1.9 The committee's discussion and interpretation of the evidence

1.1.9.1. The outcomes that matter most

The committee agreed that the key outcome for identifying the significant rate of decline in eGFR in different populations was the mean rate of decline per year which was reported by all included studies and for all populations.

1.1.9.2 The quality of the evidence

It was not possible to use GRADE in this review (see section 1.1.3). However, the committee discussed the risk of bias, indirectness and precision of the evidence and agreed that recommendations would be written to reflect that and the clinical importance of the frequency of monitoring in people with CKD. The committee highlighted that the amount of evidence in terms of number of studies and number of participants was large and that most of the studies including adults with CKD had the biggest sample sizes.

The risk of bias was low for most of the uncontrolled prospective studies with the caveat that data was non-comparative. There were 3 uncontrolled prospective studies at moderate risk of bias without a description about how the rate of decline in eGFR was estimated. The individual patient data analyses (IPDs) were at high risk of bias having 2 main reasons for this: 1) there was no explanation about why meta-analysis for the rate of decline in eGFR was not done; and 2) the risk of bias for the included studies in the IPDs was not done.

The rate of decline in eGFR was a secondary outcome in some of the uncontrolled prospective studies. These uncontrolled prospective studies were rated as partially applicable.

Multivariate analyses were not used because all studies were non-comparative. Meta-analysis was done for studies reporting on kidney donors and for studies reporting on adults with CKD categories G3a and G3b (none of these meta-analyses showed evidence of heterogeneity [I^2 0%]). The rest of studies were included in forest plots by population to show trends but pooled results were estimated because there were significant differences between studies at baseline which resulted in high heterogeneity (I^2 above 90%).

1.1.9.3 Discussions about the rate of decline in eGFR in different populations

The committee agreed to keep all bullet points included previously in the recommendation published in 2014 which was largely made based on consensus. The updated evidence showed that the confidence intervals for the rate of decline in eGFR were narrow in the different populations and sample sizes were larger which provided precise evidence to reinforce the previous recommendation.

The committee agreed with the previous discussion in 2014 that underlying individual causes of CKD may have an impact on progression of CKD and that frequency of GFR monitoring could be tailored according to the underlying cause of CKD.

The committee agreed that CKD progression is often non-linear, as discussed in 2014, and that this was important to take into account when determining monitoring frequencies. It is also possible that kidney function and eGFR can often remain stable overtime.

The committee agreed that there were populations with high rates of decline in eGFR per year who would benefit from a tailored frequency of monitoring. The committee noted that the expected rate of decline in eGFR in adults without CKD was about 0.9 ml/min/1.73 m^2 per year and that the following populations showed a higher rate of decline in eGFR per year than the expected rate of decline from the current evidence:

- Children and young people with more advanced CKD (decline in eGFR ranged from -1.10 to -5.60 ml/min/1.73 m^2 per year)
- Adults with more advanced CKD (decline in eGFR ranged from -1.92 to -4.12 ml/min/1.73 m^2 per year)
- Adults with diabetes (decline in eGFR ranged from -1.80 to -5.20 ml/min/1.73 m^2 per year)
- Adults with hypertension (decline in eGFR ranged from -1.16 to -1.84 ml/min/1.73 m^2 per year)

The committee highlighted that the table in the 2014 recommendation of frequency of monitoring already recommended more frequent monitoring in adults with more advanced CKD and it agreed to add diabetes, and hypertension to the list of comorbidities to tailor the frequency of monitoring in these populations based on the higher decline in eGFR shown by the evidence. The committee noted that most adults with CKD have hypertension and that the addition of this condition to the recommendation will not have much of an impact in clinical practice but it was important to highlight that the decline in eGFR can be higher in this population as shown by the evidence. The committee also agreed with the previous discussion in 2014 that monitoring of CKD in adults with heart failure is far more of an issue clinically because the kidney function is often very unstable in these adults and it is important to keep heart failure in the list of conditions to tailor the frequency of GFR monitoring in adults with CKD and hypertension.

As discussed in 2014, the committee agreed that intercurrent illness would also indicate whether additional monitoring was necessary. It was also discussed that the effective arterial blood volume tends to be reduced in adults with CKD, and even minor manipulations in renin-angiotensin blocking drugs or diuretics may result in significant changes in eGFR. Additional monitoring after such changes should therefore be considered.

The evidence showed a higher decline in eGFR in children and young people with more advanced CKD. The committee noted that current practice was to monitor more frequently children and young people who have more advanced CKD (G4 and G5 especially those approaching to puberty). For example, monitoring would be every 4 to 6 weeks for children and young people with CKD G5 who are not on renal replacement therapy. Therefore, clinical expertise would have to guide the frequency of monitoring of children and young people who have more advanced CKD.

The committee agreed that the included evidence covered the different relevant populations for this review question and that there were no gaps in the evidence that needed to be investigated further.

1.1.9.4 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 committee felt that the addition of comorbidities would only slightly increase the number of monitoring appointments and is likely to be in line with current practice. The recommendations now include monitoring for children and young people, and the committee agreed this is unlikely to have a substantial resource impact as it is current practice and there are unlikely to be a large number of people impacted.

1.1.10 Recommendations supported by this evidence review

This evidence review supports recommendations 1.3.2. Other evidence supporting these recommendations can be found in the evidence reviews on optimal monitoring frequency based on different rates of decline in eGFR (evidence review E).

1.1.11 References – included studies

1.1.11.1 Epidemiological evidence

Belangero, Vera M S, Prates, Liliane C, Watanabe, Andreia et al. (2018) Prospective cohort analyzing risk factors for chronic kidney disease progression in children. Jornal de pediatria 94(5): 525-531

Bruck, Katharina, Jager, Kitty J, Zoccali, Carmine et al. (2018) Different rates of progression and mortality in patients with chronic kidney disease at outpatient nephrology clinics across Europe. Kidney international 93(6): 1432-1441

Buyadaa, O., Magliano, D.J., Salim, A. et al. (2020) Risk of rapid kidney function decline, all-cause mortality, and major cardiovascular events in nonalbuminuric chronic kidney disease in type 2 diabetes. Diabetes Care 43(1): 122-129

Chen, Hung-Chih, Lin, Hsuan-Jen, Huang, Chiu-Ching et al. (2019) Maximum Glomerular Filtration Decline Rate is Associated with Mortality and Poor Renal Outcome in Chronic Kidney Disease Patients. Blood purification 48(2): 131-137

Fathallah-Shaykh, Sahar A, Flynn, Joseph T, Pierce, Christopher B et al. (2015) Progression of pediatric CKD of nonglomerular origin in the CKiD cohort. Clinical journal of the American Society of Nephrology : CJASN 10(4): 571-7

Fischer, Michael J, Hsu, Jesse Y, Lora, Claudia M et al. (2016) CKD Progression and Mortality among Hispanics and Non-Hispanics. Journal of the American Society of Nephrology : JASN 27(11): 3488-3497

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

Grams, M.E., Sang, Y., Ballew, S.H. et al. (2019) Evaluating glomerular filtration rate slope as a surrogate end point for ESKD in clinical trials: An individual participant meta-analysis of observational data. Journal of the American Society of Nephrology 30(9): 1746-1755

Hadjadj, Samy, Cariou, Bertrand, Fumeron, Frederic et al. (2016) Death, end-stage renal disease and renal function decline in patients with diabetic nephropathy in French cohorts of type 1 and type 2 diabetes. Diabetologia 59(1): 208-216

Hwang, Subin, Park, Jeeeun, Kim, Jinhae et al. (2017) Tissue expression of tubular injury markers is associated with renal function decline in diabetic nephropathy. Journal of diabetes and its complications 31(12): 1704-1709

Iimori, Soichiro, Naito, Shotaro, Noda, Yumi et al. (2018) Prognosis of chronic kidney disease with normal-range proteinuria: The CKD-ROUTE study. PloS one 13(1): e0190493

Inaguma, Daijo, Imai, Enyu, Takeuchi, Ayano et al. (2017) Risk factors for CKD progression in Japanese patients: findings from the Chronic Kidney Disease Japan Cohort (CKD-JAC) study. Clinical and experimental nephrology 21(3): 446-456

Kasiske, Bertram L, Anderson-Haag, Teresa, Israni, Ajay K et al. (2015) A prospective controlled study of living kidney donors: three-year follow-up. American journal of kidney diseases : the official journal of the National Kidney Foundation 66(1): 114-24

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

Malmgren, L., Mcguigan, F.E., Christensson, A. et al. (2020) Longitudinal Changes in Kidney Function Estimated from Cystatin C and Its Association with Mortality in Elderly Women. Nephron 144(6): 290-298

Melsom, Toralf, Nair, Viji, Schei, Jorgen et al. (2019) Correlation Between Baseline GFR and Subsequent Change in GFR in Norwegian Adults Without Diabetes and in Pima Indians. American journal of kidney diseases : the official journal of the National Kidney Foundation 73(6): 777-785

Minutolo, R., Gabbai, F.B., Chiodini, P. et al. (2020) Sex Differences in the Progression of CKD Among Older Patients: Pooled Analysis of 4 Cohort Studies. American Journal of Kidney Diseases 75(1): 30-38

Moriya, Tatsumi, Tanaka, Shiro, Sone, Hirohito et al. (2017) Patients with type 2 diabetes having higher glomerular filtration rate showed rapid renal function decline followed by impaired glomerular filtration rate: Japan Diabetes Complications Study. Journal of diabetes and its complications 31(2): 473-478

Ozyilmaz, Akin, de Jong, Paul E, Bakker, Stephan J L et al. (2017) Screening for elevated albuminuria and subsequently hypertension identifies subjects in which treatment may be warranted to prevent renal function decline. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 32(suppl2): ii200-ii208

Pottel, Hans, Bjork, Jonas, Bokenkamp, Arend et al. (2019) Estimating glomerular filtration rate at the transition from pediatric to adult care. Kidney international 95(5): 1234-1243

Pruijm, Menno, Milani, Bastien, Pivin, Edward et al. (2018) Reduced cortical oxygenation predicts a progressive decline of renal function in patients with chronic kidney disease. Kidney international 93(4): 932-940

Qin, Xianhui, Wang, Yuejuan, Li, Youbao et al. (2015) Risk factors for renal function decline in adults with normal kidney function: a 7-year cohort study. Journal of epidemiology and community health 69(8): 782-8

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 : official publication of the European Dialysis and Transplant Association - European Renal Association

Rowe, John W., Andres, Reubin, Tobin, Jordan D. et al. (1976) The Effect of Age on Creatinine Clearance in Men: A Cross-sectional and Longitudinal Study2. J Gerontol 31(2): 155-163

Skupien, Jan, Smiles, Adam M, Valo, Erkka et al. (2019) Variations in Risk of End-Stage Renal Disease and Risk of Mortality in an International Study of Patients With Type 1 Diabetes and Advanced Nephropathy. Diabetes care 42(1): 93-101

Sukmark, Theerapon and Sukmark, Supanun (2014) Predictors of faster progression in chronic kidney disease. Journal of the Medical Association of Thailand = Chotmaihet thangphaet 97(8): 812-9

Tsai, C.-W., Huang, H.-C., Chiang, H.-Y. et al. (2019) First-year estimated glomerular filtration rate variability after pre-end-stage renal disease program enrollment and adverse outcomes of chronic kidney disease. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 34(12): 2066-2078

Tsai, Yi-Chun, Chiu, Yi-Wen, Tsai, Jer-Chia et al. (2014) Association of angiopoietin-2 with renal outcome in chronic kidney disease. PloS one 9(10): e108862

Vallianou, N, Stratigou, T, Paikopoulou, A et al. (2018) Monitoring of patients with type 2 diabetes and nephropathy in a specialized diabetic nephropathy clinic seems to be beneficial. Diabetes & metabolic syndrome 12(5): 689-692

van Londen, Marco, Wijninga, Anthony B, de Vries, Jannieta et al. (2018) Estimated glomerular filtration rate for longitudinal follow-up of living kidney donors. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 33(6): 1054-1064

van Rijn, Marieke H C, Metzger, Marie, Flamant, Martin et al. (2018) Performance of creatinine-based equations for estimating glomerular filtration rate changes over time. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association

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

Yoshida, Yui, Kashiwabara, Kosuke, Hirakawa, Yosuke et al. (2020) Conditions, pathogenesis, and progression of diabetic kidney disease and early decliner in Japan. BMJ open diabetes research & care 8(1)

Young, Bessie A, Katz, Ronit, Boulware, L Ebony et al. (2016) Risk Factors for Rapid Kidney Function Decline Among African Americans: The Jackson Heart Study (JHS). American journal of kidney diseases : the official journal of the National Kidney Foundation 68(2): 229-239

Yu, Zhi, Rebholz, Casey M, Wong, Eugenia et al. (2019) Association Between Hypertension and Kidney Function Decline: The Atherosclerosis Risk in Communities (ARIC) Study. American journal of kidney diseases : the official journal of the National Kidney Foundation 74(3): 310-319

1.1.11.3 Other

Matsushita K, Ballew SH, Astor BC, Jong PE, Gansevoort RT, Hemmelgarn BR, et al. (2013) Chronic Kidney Disease Prognosis Consortium: Cohort profile: The chronic kidney disease prognosis consortium. Int J Epidemiol 42: 1660–1668

Tierney, J. F., Vale, C., Riley, R., Smith, C. T., Stewart, L., Clarke, M., & Rovers, M. (2015). Individual participant data (IPD) meta-analyses of randomised controlled trials: guidance on their use. PLoS Med, 12(7), e1001855.

Appendices

Appendix A – Review protocols

Review protocol for 3.1 For adults, children and young people with CKD, what constitutes a clinically significant decline in eGFR in terms of risk of kidney disease progression?

ID	Field	Content
0.	PROSPERO registration number	CRD42020178118
1.	Review title	For adults, children and young people with CKD, what constitutes a clinically significant decline in eGFR in terms of risk of kidney disease progression?
2.	Review question	For adults, children and young people with CKD, what constitutes a clinically significant decline in eGFR in terms of risk of kidney disease progression?
3.	Objective	To determine what constitutes a clinically significant decline in eGFR in terms of risk of kidney disease progression in adults, children and young people with CKD.
4.	Searches	The following databases will be searched: Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE

		Searches will be restricted by: • English language • Human studies Searches will be limited to the date of the previous searches (2014) The searches will be re-run 6 weeks before final submission of the review and further studies retrieved for inclusion. The full search strategies for MEDLINE database will be published in the final review.
5.	Condition or domain being studied	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 smaller declines in eGFR to indicate CKD progression over 1, 2 and 3 years.
6.	Population	Inclusion:

		Adults (over 18 years), children and young people (up to the age of 18) Exclusion: • people receiving renal replacement therapy (RRT) • people with acute kidney injury combined with rapidly progressive glomerulonephritis • pregnant women • people receiving palliative care.
7.	Phenomenon of interest	Rate of decline in estimated glomerular filtration rate (eGFR)
8.	Comparator	In comparative studies, rates of eGFR decline in comparator populations, in other cohorts (for example, epidemiological or prognostic), no comparator is required. Where appropriate confounders other than the subgroups of interest should be adjusted for. As a first choice, multivariate/ adjusted analyses from the studies using the confounders identified in the studies themselves will be used.
9.	Types of study to be included	• Cross sectional studies • Prospective cohort studies • Retrospective Individual Patient Data (IPD) cohorts

10.	Other exclusion criteria	• Population
		  ○ people receiving renal replacement therapy (RRT)
		  ○ people with acute kidney injury combined with rapidly progressive glomerulonephritis
		  ○ pregnant women
		  ○ people receiving palliative care
		• Abstracts and conference proceedings
		• Theses
		• Non-human studies

11.	Context	NICE guideline CG182 chronic kidney disease in adults: assessment and management will be updated by this question. This guideline will be combined with guidelines CG157 chronic kidney disease (stage 4 or 5): management of hyperphosphataemia and NG 8 chronic kidney disease: managing anaemia. The guideline will be extended to cover the assessment and management of chronic kidney disease in children and young people.
12.	Primary outcomes (critical outcomes)	• Rate of eGFR decline (reported as ml/min/1.73 m^2)

		Measure of effect: rate of eGFR decline either as a continuous variable or as a categorical variable (as defined by study)
13.	Secondary outcomes (important outcomes)	• CKD progression: occurrence of end stage kidney disease (ESRD or ESKD as reported by the study) • Mortality
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 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 appropriate checklist – ROBINS-I for cohort studies, JBI checklist for cross sectional studies or JBI checklist for epidemiological studies as described in Developing NICE guidelines: the manual.
16.	Strategy for data synthesis	Where possible (ie where homogeneity can be assumed) rates of eGFR for different populations will be pooled to create pooled estimates of rates of decline. Where appropriate, hazard ratios will be pooled using the inverse-variance method, and risk ratios/odds ratios will be pooled using the Mantel-Haenszel method. Mean differences will be pooled using inverse variance. Adjusted risk ratios/odds ratios from multivariate models will be only pooled if the same set of predictor variables are used across multiple studies and if the same thresholds to measure predictors are used across studies. Fixed- and random-effects models (der Simonian and Laird) will be fitted for all syntheses, with the presented analysis dependent on the degree of heterogeneity in the assembled evidence. Fixed-effects models will be the preferred choice to report, but in situations where the assumption of a shared mean for fixed-effects model are clearly not met, even after appropriate pre-specified subgroup analyses

		are conducted, random-effects results will be presented. Fixed-effects models will be deemed to be inappropriate if one or both of the following conditions is met: • Significant between study heterogeneity in methodology, population, or comparator is identified by the reviewer in advance of data analysis. This decision would need to be made and recorded before any data analysis is undertaken. • The presence of significant statistical heterogeneity, defined as $I^2 \geq 50\%$. Meta-analyses were performed in Cochrane Review Manager v5.3.
17.	Analysis of sub-groups	Data will be stratified by population: • Healthy adults/CYP • Ethnic group • Gender • Age group (children and young people up to 18 years, adults from 19 – 69, Older people from 70 upwards) • Diabetes • Hypertension or CVD • Combinations of the above.
	Type and method of review	☐ Intervention

18.		☐ Diagnostic ☒ Prognostic ☐ Qualitative ☒ Epidemiologic ☐ Service Delivery ☐ Other (please specify)		
19.	Language	English		
20.	Country	England		
21.	Anticipated or actual start date	May 2020		
22.	Anticipated completion date			
23.	Stage of review at time of this submission	**Review stage**	**Started**	**Completed**
		Preliminary searches	☐	☐

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

		• Dr Yolanda Martinez • Mr Rui Maartins • Dr Joshua Pink • Ms Lynda Ayiku
26.	Funding sources/sponsor	This systematic review is being completed by the Guideline Updates Team, which is part of NICE.
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website
29.	Other registration details	None
30.	Reference/URL for published protocol	

31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
32.	Keywords	eGFR variation, Chronic Kidney Disease
33.	Details of existing review of same topic by same authors	none
34.	Current review status	☐ Ongoing ☐ Completed but not published ☐ Completed and published ☐ Completed, published and being updated ☐ Discontinued
35..	Additional information	

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

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Appendix B – Methods

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 29. 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.

Table 29: 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 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.

Non-comparative studies

Studies included in this review were uncontrolled prospective studies. However, the rate of decline in eGFR was an outcome (phenomenon of interest) rather than a prognostic factor. Therefore, the rate of decline in eGFR was analysed using the methods for non-comparative studies (see below).

Quality assessment

The Institute of Health Economics (IHE) checklist for case series was used. There are currently no validated quality checklists available for other non-comparative study types (e.g. survey and audit data). 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.

Methods for combining non-comparative evidence

Where data were possible to meta-analyse, fixed- and random-effects models (der Simonian and Laird) were fitted for all syntheses, with the presented analysis dependent on the degree of heterogeneity in the assembled evidence. Fixed-effects models were the preferred choice to report, but in situations where the assumption of a shared mean for fixed-effects model were clearly not met, random-effects results are presented. Fixed-effects models were deemed to be inappropriate if one or both of the following conditions was met:

- Significant between study heterogeneity in methodology, population, intervention or comparator was identified by the reviewer in advance of data analysis. This decision would need to be made and recorded before any data analysis is undertaken.
- The presence of significant statistical heterogeneity, defined as $I^2 \geq 50\%$.

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

Meta-analyses were performed in Rstudio v1.3.1073.

Modified GRADE for non-comparative evidence

GRADE has not been developed for use with non-comparative studies. Therefore, tables were used to report the effect size, risk of bias and indirectness and summary tables detailing the rates of eGFR decline for different groups were written to substitute GRADE.

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 30.

Table 30 Applicability criteria

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

In the second step, only those studies deemed directly or partially applicable are further assessed for limitations (that is, methodological quality); see categorisation criteria in Table 31.

Table 31 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 7th of April 2020 and updated on the 7th of September 2020. This search report is compliant with the requirements of PRISMA-S.

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

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

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

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

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)	N/A	Not searched on request of Adviser (Chris Carmona)	0
Cochrane Database of Systematic Reviews (CDSR)	7th Apr 2020	Issue 4 of 12, April 2020	34

Database of Abstracts of Reviews of Effect (DARE)	7th Apr 2020	Up to 2015	84
Embase (Ovid)	7th Apr 2020	Embase <1974 to 2020 Week 14>	8047
MEDLINE (Ovid)	7th Apr 2020	Ovid MEDLINE(R) <1946 to April 06, 2020>	5837
MEDLINE In-Process (Ovid)	7th Apr 2020	Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to April 06, 2020>	969
MEDLINE Epub Ahead of Print[a]	7th Apr 2020	Ovid MEDLINE(R) Epub Ahead of Print <April 06, 2020>	180

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

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

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

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

Search strategies
Database: Ovid MEDLINE(R) <1946 to April 06, 2020> Search Strategy: --- 1 exp Renal Insufficiency, Chronic/ (113097) 2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (72983)

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

3 ((kidney* or renal*) adj1 insufficien*).tw. (21279)

4 ckd*.tw. (23155)

5 ((kidney* or renal*) adj1 fail*).tw. (86483)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (35381)

7 (esrd* or eskd*).tw. (14297)

8 "Chronic Kidney Disease-Mineral and Bone Disorder"/ (3457)

9 or/1-8 (213577)

10 Glomerular Filtration Rate/ (43516)

11 (glomerul* or GFR* or eGFR* or e-GFR*).tw. (158294)

12 or/10-11 (171675)

13 (declin* or drop* or reduc* or decreas* or low* or fall* or loss* or less* or chang*).tw. (9268466)

14 exp disease progression/ (175791)

15 (progress* or exacerbat* or significan* or serious* or sever* or warning* or trigger* or threat* or danger* or damag* or harm* or risk* or deteriorat* or wors* or weak* or morbidit* or damag* or mortal* or fatal* or dead* or die or dying* or life*).tw. (9740745)

16 14 or 15 (9775788)

17 12 and 13 and 16 (71643)

18 9 and 17 (21221)

19 prognosis.sh. (499011)

20 diagnosed.tw. (470559)

21 cohort.mp. (541784)

22 predictor:.tw. (318338)

23 death.tw. (601925)

24 exp models, statistical/ (402395)

25 or/19-24 (2357345)

26 18 and 25 (8303)

27 Cross-sectional studies/ (323170)

28 Cross sectional.tw. (276990)

29 27 or 28 (396132)

30 18 and 29 (1782)

31 (MEDLINE or pubmed).tw. (157634)

32 systematic review.tw. (115648)

33 systematic review.pt. (124240)

34 meta-analysis.pt. (112951)

35 intervention$.ti. (120744)

36 or/31-35 (368073)

37 18 and 36 (596)

38 26 or 30 or 37 (9437)

39 limit 38 to ed=20131101-20200407 (4977)

40 exp Infant/ or Infant Health/ or Infant Welfare/ (1126972)

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,jn. (841252)

42 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (1893920)

43 Minors/ (2562)

44 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (2322124)

45 exp pediatrics/ (57315)

46 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (817310)

47 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (2001859)

48 Puberty/ (13192)

49 (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. (415954)

50 Schools/ (37290)

51 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (7149)

52 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (461783)

53 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (3910)

54 or/40-53 (5123706)

55 38 and 54 (2424)

56 39 or 55 (6179)

57 limit 56 to english language (5906)

58 animals/ not humans/ (4653141)

59 57 not 58 (5837)

D Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to April 06, 2020>

Search Strategy:

---

1 exp Renal Insufficiency, Chronic/ (0)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (9584)

3 ((kidney* or renal*) adj1 insufficien*).tw. (1115)

4 ckd*.tw. (4591)

5 ((kidney* or renal*) adj1 fail*).tw. (6395)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (4930)

7 (esrd* or eskd*).tw. (2018)

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

9 or/1-8 (18711)

10 Glomerular Filtration Rate/ (0)

11 (glomerul* or GFR* or eGFR* or e-GFR*).tw. (16608)

12 or/10-11 (16608)

13 (declin* or drop* or reduc* or decreas* or low* or fall* or loss* or less* or chang*).tw. (1399858)

14 exp disease progression/ (0)

15 (progress* or exacerbat* or significan* or serious* or sever* or warning* or trigger* or threat* or danger* or damag* or harm* or risk* or deteriorat* or wors* or weak* or morbidit* or mortal* or fatal* or dead* or die or dying* or life*).tw. (1410001)

16 14 or 15 (1410001)

17 12 and 13 and 16 (7465)

18 9 and 17 (2302)

19 prognosis.sh. (0)

20 diagnosed.tw. (75717)

21 cohort.mp. (70313)

22 predictor:.tw. (44684)

23 death.tw. (69223)

24 exp models, statistical/ (0)

25 or/19-24 (234214)

26 18 and 25 (837)

27 Cross-sectional studies/ (0)

28 Cross sectional.tw. (57219)

29 27 or 28 (57219)

30 18 and 29 (205)

31 (MEDLINE or pubmed).tw. (34428)

32 systematic review.tw. (28184)

33 systematic review.pt. (791)

34 meta-analysis.pt. (43)

35 intervention$.ti. (20717)

36 or/31-35 (65968)

37 18 and 36 (92)

38 26 or 30 or 37 (1026)

39 limit 38 to dt=20131101-20200407 (967)

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

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,jn. (78580)

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

43 Minors/ (0)

44 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (311242)

45 exp pediatrics/ (0)

46 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (116784)

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

48 Puberty/ (0)

49 (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. (58667)

50 Schools/ (0)

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

52 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (66480)

53 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (566)

54 or/40-53 (451042)

55 38 and 54 (225)

56 39 or 55 (978)

57 limit 56 to english language (969)

58 animals/ not humans/ (0)

59 57 not 58 (969)

Database: Ovid MEDLINE(R) Epub Ahead of Print <April 06, 2020>

Search Strategy:

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1 exp Renal Insufficiency, Chronic/ (0)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (1374)

3 ((kidney* or renal*) adj1 insufficien*).tw. (149)

4 ckd*.tw. (716)

5 ((kidney* or renal*) adj1 fail*).tw. (753)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (703)

7 (esrd* or eskd*).tw. (316)

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

9 or/1-8 (2567)

10 Glomerular Filtration Rate/ (0)

11 (glomerul* or GFR* or eGFR* or e-GFR*).tw. (2273)

12 or/10-11 (2273)

13 (declin* or drop* or reduc* or decreas* or low* or fall* or loss* or less* or chang*).tw. (161566)

14 exp disease progression/ (0)

15 (progress* or exacerbat* or significan* or serious* or sever* or warning* or trigger* or threat* or danger* or damag* or harm* or risk* or deteriorat* or wors* or weak* or morbidit* or damag* or mortal* or fatal* or dead* or die or dying* or life*).tw. (183879)

16 14 or 15 (183879)

17 12 and 13 and 16 (1057)

18 9 and 17 (359)

19 prognosis.sh. (0)

20 diagnosed.tw. (10344)

21 cohort.mp. (16285)

22 predictor:.tw. (9172)

23 death.tw. (11195)

24 exp models, statistical/ (0)

25 or/19-24 (41263)

26 18 and 25 (148)

27 Cross-sectional studies/ (0)

28 Cross sectional.tw. (8371)

29 27 or 28 (8371)

30 18 and 29 (27)

31 (MEDLINE or pubmed).tw. (6846)

32 systematic review.tw. (6563)

33 systematic review.pt. (23)

34 meta-analysis.pt. (28)

35 intervention$.ti. (3886)

36 or/31-35 (13291)

37 18 and 36 (22)

38 26 or 30 or 37 (180)

39 limit 38 to english language (180)

Database: Embase <1974 to 2020 Week 14>

Search Strategy:

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1 exp kidney failure/ (353531)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (123820)

3 ((kidney* or renal*) adj1 insufficien*).tw. (30090)

4 ckd*.tw. (50347)

5 ((kidney* or renal*) adj1 fail*).tw. (132535)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (58639)

7 (esrd* or eskd*).tw. (27605)

8 or/1-7 (446229)

9 exp glomerulus filtration rate/ (98896)

10 (glomerul* or GFR* or eGFR* or e-GFR*).tw. (265909)

11 9 or 10 (294700)

12 (declin* or drop* or reduc* or decreas* or low* or fall* or loss* or less* or chang*).tw. (13680001)

13 disease exacerbation/ (111546)

14 (progress* or exacerbat* or significan* or serious* or sever* or warning* or trigger* or threat* or danger* or damag* or harm* or risk* or deteriorat* or wors* or weak* or morbidit* or damag* or mortal* or fatal* or dead* or die or dying* or life*).tw. (14774393)

15 13 or 14 (14796567)

16 11 and 12 and 15 (137424)

17 8 and 16 (46268)

18 prognosis.sh. (571907)

19 diagnosed.tw. (912837)

20 cohort.mp. (1017615)

21 predictor:.tw. (567024)

22 death.tw. (970817)

23 exp models, statistical/ (159577)

24 or/18-23 (3585279)

25 17 and 24 (17991)

26 cross-sectional study/ (341764)

27 Cross sectional.tw. (448173)

28 26 or 27 (532856)

29 17 and 28 (2829)

30 (MEDLINE or pubmed).tw. (249961)

31 exp systematic review/ or systematic review.tw. (287590)

32 meta-analysis/ (183928)

33 intervention$.ti. (194903)

34 or/30-33 (636915)

35 17 and 34 (1747)

36 25 or 29 or 35 (20549)

37 limit 36 to dc=20131101-20200407 (13545)

38 exp juvenile/ or Child Behavior/ or Child Welfare/ or Child Health/ or infant welfare/ or "minor (person)"/ or elementary student/ (3387399)

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,ad,jw. (1193180)

40 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,ad,jw. (3590067)

41 exp pediatrics/ (104560)

42 (pediatric* or paediatric* or peadiatric*).ti,ab,in,ad,jw. (1617395)

43 exp adolescence/ or exp adolescent behavior/ or adolescent health/ or high school student/ or middle school student/ (102996)

44 (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. (649686)

45 school/ or high school/ or kindergarten/ or middle school/ or primary school/ or nursery school/ or day care/ (102315)

46 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jw. (688852)

47 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (7289)

48 or/38-47 (6349586)

49 36 and 48 (4432)

50 37 or 49 (15180)

51 nonhuman/ not human/ (4601462)

52 50 not 51 (14956)

53 limit 52 to (chapter or conference abstract or conference paper or "conference review") (6573)

54 52 not 53 (8383)

55 limit 54 to english language (8047)

Cochrane Library – CDSR only

ID	Search	Hits
#1	MeSH descriptor: [Renal Insufficiency, Chronic] explode all trees	6493
#2	(((chronic* or progressi*) near/1 (renal* or kidney*))):ti,ab,kw	9938
#3	(((kidney* or renal*) near/1 insufficien*)):ti,ab,kw	5244
#4	(ckd*):ti,ab,kw	4694
#5	(((kidney* or renal*) near/1 fail*)):ti,ab,kw	15735
#6	(((endstage* or end-stage* or "end stage*") near/1 (renal* or kidney*))):ti,ab,kw	4309
#7	((esrd* or eskd*)):ti,ab,kw	1967
#8	MeSH descriptor: [Chronic Kidney Disease-Mineral and Bone Disorder] this term only	86
#9	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8	25083
#10	MeSH descriptor: [Glomerular Filtration Rate] this term only	2612
#11	(glomerul* or GFR* or eGFR* or e-GFR*):ti,ab,kw	17658
#12	#10 or #11	17658
#13	(declin* or drop* or reduc* or decreas* or low* or fall* or loss* or less* or chang*):ti,ab,kw	903839
#14	MeSH descriptor: [Disease Progression] explode all trees	7022
#15	(progress* or exacerbat* or significan* or serious* or sever* or warning* or trigger* or threat* or danger* or damag* or harm* or risk* or deteriorat* or wors* or weak* or morbidit* or mortal* or fatal* or dead* or die or dying* or life*):ti,ab,kw	969562
#16	#14 or #15	969811

#17 #12 and #13 and #16 10737

#18 #9 and #17 3932- 34 CDSR

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

11 (((MeSH DESCRIPTOR Glomerular Filtration Rate EXPLODE ALL TREES))) 92 Delete

12 #10 OR #11 416 Delete

13 ((declin* or drop* or reduc* or decreas* or low* or fall* or loss* or less* or chang*)) 36488 Delete

14 MeSH DESCRIPTOR disease progression EXPLODE ALL TREES 704 Delete

15 ((progress* or exacerbat* or significan* or serious* or sever* or warning* or trigger* or threat* or danger* or damag* or harm* or risk* or deteriorat* or wors* or weak* or morbidit* or damag* or mortal* or fatal* or dead* or die or dying* or life*)) 45266 Delete

16 #14 OR #15 45271 Delete

17 #12 AND #13 AND #16 211 Delete

18 #9 AND #17 111 Delete

19 (#9 and #17) IN DARE 84 Delete

20 (#9 and #17) IN NHSEED 21 Delete

21	(#9 and #17) IN HTA	6	Delete

Cost-effectiveness searches

Databases		Date searched	Version/files	No. retrieved
MEDLINE (Ovid)		7th Apr 2020	Ovid MEDLINE(R) <1946 to April 06, 2020>	600
MEDLINE in Process (Ovid)		7th Apr 2020	Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to April 06, 2020>	158
MEDLINE epub (Ovid)		7th Apr 2020	Ovid MEDLINE(R) Epub Ahead of Print <April 06, 2020>	14
Embase (Ovid)		7th Apr 2020	Embase <1974 to 2020 Week 14>	1293
EconLit (Ovid)		7th Apr 2020	Econlit <1886 to April 02, 2020>	0
NHS Economic Evaluation Database (NHS EED) (legacy database)		7th Apr 2020	Up to 2015	21
CRD HTA		7th Apr 2020	Up to 2018	84

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 April 06, 2020>

Search Strategy:

---

1 exp Renal Insufficiency, Chronic/ (113097)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (72983)

3 ((kidney* or renal*) adj1 insufficien*).tw. (21279)

4 ckd*.tw. (23155)

5 ((kidney* or renal*) adj1 fail*).tw. (86483)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (35381)

7 (esrd* or eskd*).tw. (14297)

8 "Chronic Kidney Disease-Mineral and Bone Disorder"/ (3457)

9 or/1-8 (213577)

10 Glomerular Filtration Rate/ (43516)

11 (glomerul* or GFR* or eGFR* or e-GFR*).tw. (158294)

12 or/10-11 (171675)

13 (declin* or drop* or reduc* or decreas* or low* or fall* or loss* or less* or chang*).tw. (9268466)

14 exp disease progression/ (175791)

15 (progress* or exacerbat* or significan* or serious* or sever* or warning* or trigger* or threat* or danger* or damag* or harm* or risk* or deteriorat* or wors* or weak* or morbidit* or damag* or mortal* or fatal* or dead* or die or dying* or life*).tw. (9740745)

16 14 or 15 (9775788)

17 12 and 13 and 16 (71643)

18 9 and 17 (21221)

19 Economics/ (27159)

20 exp "Costs and Cost Analysis"/ (233990)

21 Economics, Dental/ (1911)

22 exp Economics, Hospital/ (24341)

23 exp Economics, Medical/ (14168)

24 Economics, Nursing/ (3997)

25 Economics, Pharmaceutical/ (2920)

26 Budgets/ (11245)

27 exp Models, Economic/ (14805)

28 Markov Chains/ (14078)

29 Monte Carlo Method/ (27977)

30 Decision Trees/ (10985)

31 econom$.tw. (233541)

32 cba.tw. (9714)

33 cea.tw. (20302)

34 cua.tw. (981)

35 markov$.tw. (17621)

36 (monte adj carlo).tw. (29506)

37 (decision adj3 (tree$ or analys$)).tw. (13080)

38 (cost or costs or costing$ or costly or costed).tw. (451647)

39 (price$ or pricing$).tw. (32886)

40 budget$.tw. (23323)

41 expenditure$.tw. (48521)

42 (value adj3 (money or monetary)).tw. (2058)

43 (pharmacoeconomic$ or (pharmaco adj economic$)).tw. (3451)

44 or/19-43 (910408)

45 "Quality of Life"/ (190258)

46 quality of life.tw. (224401)

47 "Value of Life"/ (5693)

48 Quality-Adjusted Life Years/ (11923)

49 quality adjusted life.tw. (10511)

50 (qaly$ or qald$ or qale$ or qtime$).tw. (8628)

51 disability adjusted life.tw. (2603)

52 daly$.tw. (2374)

53 Health Status Indicators/ (23256)

54 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw. (22129)

55 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (1305)

56 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (4787)

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

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

59 (euroqol or euro qol or eq5d or eq 5d).tw. (8667)

60 (qol or hql or hqol or hrqol).tw. (42926)

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

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

63 utilit$.tw. (167831)

64 (hui or hui1 or hui2 or hui3).tw. (1274)

65 disutili$.tw. (381)

66 rosser.tw. (92)

67 quality of wellbeing.tw. (13)

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

69 qwb.tw. (188)

70 willingness to pay.tw. (4338)

71 standard gamble$.tw. (775)

72 time trade off.tw. (1020)

73 time tradeoff.tw. (230)

74 tto.tw. (886)

75 or/45-74 (482608)

76 44 or 75 (1326091)

77 18 and 76 (1109)

78 limit 77 to ed=20131101-20200407 (509)

79 exp Infant/ or Infant Health/ or Infant Welfare/ (1126972)

80 (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. (841252)

81 exp Child/ or exp Child Behavior/ or Child Health/ or Child Welfare/ (1893920)

82 Minors/ (2562)

83 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (2322124)

84 exp pediatrics/ (57315)

85 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (817310)

86 Adolescent/ or Adolescent Behavior/ or Adolescent Health/ (2001859)

87 Puberty/ (13192)

88 (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. (415954)

89 Schools/ (37290)

90 Child Day Care Centers/ or exp Nurseries/ or Schools, Nursery/ (7149)

91 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (461783)

92 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (3910)

93 or/79-92 (5123706)

94 77 and 93 (265)

95 78 or 94 (655)

96 animals/ not humans/ (4653141)

97 95 not 96 (642)

98 limit 97 to english language (600)

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <1946 to April 06, 2020>

Search Strategy:

---

1 exp Renal Insufficiency, Chronic/ (0)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (9584)

3 ((kidney* or renal*) adj1 insufficien*).tw. (1115)

4 ckd*.tw. (4591)

5 ((kidney* or renal*) adj1 fail*).tw. (6395)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (4930)

7 (esrd* or eskd*).tw. (2018)

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

9 or/1-8 (18711)

10 Glomerular Filtration Rate/ (0)

11 (glomerul* or GFR* or eGFR* or e-GFR*).tw. (16608)

12 or/10-11 (16608)

13 (declin* or drop* or reduc* or decreas* or low* or fall* or loss* or less* or chang*).tw. (1399858)

14 exp disease progression/ (0)

15 (progress* or exacerbat* or significan* or serious* or sever* or warning* or trigger* or threat* or danger* or damag* or harm* or risk* or deteriorat* or wors* or weak* or morbidit* or damag* or mortal* or fatal* or dead* or die or dying* or life*).tw. (1410001)

16 14 or 15 (1410001)

17 12 and 13 and 16 (7465)

18 9 and 17 (2302)

19 Economics/ (0)

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

21 Economics, Dental/ (0)

22 exp Economics, Hospital/ (0)

23 exp Economics, Medical/ (0)

24 Economics, Nursing/ (0)

25 Economics, Pharmaceutical/ (0)

26	Budgets/ (0)
27	exp Models, Economic/ (0)
28	Markov Chains/ (0)
29	Monte Carlo Method/ (0)
30	Decision Trees/ (0)
31	econom$.tw. (44634)
32	cba.tw. (430)
33	cea.tw. (1931)
34	cua.tw. (199)
35	markov$.tw. (5692)
36	(monte adj carlo).tw. (16822)
37	(decision adj3 (tree$ or analys$)).tw. (2389)
38	(cost or costs or costing$ or costly or costed).tw. (95668)
39	(price$ or pricing$).tw. (5723)
40	budget$.tw. (4963)
41	expenditure$.tw. (6347)
42	(value adj3 (money or monetary)).tw. (347)
43	(pharmacoeconomic$ or (pharmaco adj economic$)).tw. (483)
44	or/19-43 (165175)
45	"Quality of Life"/ (0)
46	quality of life.tw. (38412)
47	"Value of Life"/ (0)
48	Quality-Adjusted Life Years/ (0)
49	quality adjusted life.tw. (1698)
50	(qaly$ or qald$ or qale$ or qtime$).tw. (1434)
51	disability adjusted life.tw. (559)
52	daly$.tw. (506)
53	Health Status Indicators/ (0)

54 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw. (2630)

55 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (755)

56 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (727)

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

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

59 (euroqol or euro qol or eq5d or eq 5d).tw. (1601)

60 (qol or hql or hqol or hrqol).tw. (7289)

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

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

63 utilit$.tw. (31148)

64 (hui or hui1 or hui2 or hui3).tw. (190)

65 disutili$.tw. (67)

66 rosser.tw. (5)

67 quality of wellbeing.tw. (8)

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

69 qwb.tw. (15)

70 willingness to pay.tw. (932)

71 standard gamble$.tw. (59)

72 time trade off.tw. (116)

73 time tradeoff.tw. (17)

74 tto.tw. (124)

75 or/45-74 (71848)

76 44 or 75 (227526)

77 18 and 76 (174)

78 limit 77 to dt=20131101-20200407 (160)

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

80 (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. (78580)

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

82 Minors/ (0)

83 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,jn. (311242)

84 exp pediatrics/ (0)

85 (pediatric* or paediatric* or peadiatric*).ti,ab,in,jn. (116784)

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

87 Puberty/ (0)

88 (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. (58667)

89 Schools/ (0)

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

91 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jn. (66480)

92 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (566)

93 or/79-92 (451042)

94 77 and 93 (27)

95 78 or 94 (161)

96 animals/ not humans/ (0)

97 95 not 96 (161)

98 limit 97 to english language (158)

Database: Ovid MEDLINE(R) Epub Ahead of Print <April 06, 2020>

Search Strategy:

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1 exp Renal Insufficiency, Chronic/ (0)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (1374)

3 ((kidney* or renal*) adj1 insufficien*).tw. (149)

4 ckd*.tw. (716)

5 ((kidney* or renal*) adj1 fail*).tw. (753)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (703)

7 (esrd* or eskd*).tw. (316)

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

9 or/1-8 (2567)

10 Glomerular Filtration Rate/ (0)

11 (glomerul* or GFR* or eGFR* or e-GFR*).tw. (2273)

12 or/10-11 (2273)

13 (declin* or drop* or reduc* or decreas* or low* or fall* or loss* or less* or chang*).tw. (161566)

14 exp disease progression/ (0)

15 (progress* or exacerbat* or significan* or serious* or sever* or warning* or trigger* or threat* or danger* or damag* or harm* or risk* or deteriorat* or wors* or weak* or morbidit* or damag* or mortal* or fatal* or dead* or die or dying* or life*).tw. (183879)

16 14 or 15 (183879)

17 12 and 13 and 16 (1057)

18 9 and 17 (359)

19 Economics/ (0)

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

21 Economics, Dental/ (0)

22 exp Economics, Hospital/ (0)

23 exp Economics, Medical/ (0)

24 Economics, Nursing/ (0)

25 Economics, Pharmaceutical/ (0)

26 Budgets/ (0)

27 exp Models, Economic/ (0)

28 Markov Chains/ (0)

29 Monte Carlo Method/ (0)

30 Decision Trees/ (0)

31 econom$.tw. (5922)

32 cba.tw. (66)

33 cea.tw. (312)

34 cua.tw. (16)

35 markov$.tw. (699)

36 (monte adj carlo).tw. (1178)

37 (decision adj3 (tree$ or analys$)).tw. (423)

38 (cost or costs or costing$ or costly or costed).tw. (12296)

39 (price$ or pricing$).tw. (866)

40 budget$.tw. (531)

41 expenditure$.tw. (1082)

42 (value adj3 (money or monetary)).tw. (68)

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

44 or/19-43 (20120)

45 "Quality of Life"/ (0)

46 quality of life.tw. (6824)

47 "Value of Life"/ (0)

48 Quality-Adjusted Life Years/ (0)

49 quality adjusted life.tw. (397)

50 (qaly$ or qald$ or qale$ or qtime$).tw. (347)

51 disability adjusted life.tw. (105)

52 daly$.tw. (92)

53 Health Status Indicators/ (0)

54 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw. (442)

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

56 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (159)

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

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

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

60 (qol or hql or hqol or hrqol).tw. (1368)

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

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

63 utilit$.tw. (4567)

64 (hui or hui1 or hui2 or hui3).tw. (17)

65 disutili$.tw. (12)

66 rosser.tw. (0)

67 quality of wellbeing.tw. (1)

68 quality of well-being.tw. (8)

69 qwb.tw. (2)

70 willingness to pay.tw. (166)

71 standard gamble$.tw. (8)

72 time trade off.tw. (18)

73 time tradeoff.tw. (2)

74 tto.tw. (25)

75 or/45-74 (11688)

76 44 or 75 (30064)

77 18 and 76 (14)

Database: Embase <1974 to 2020 Week 14>

Search Strategy:

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1 exp kidney failure/ (353531)

2 ((chronic* or progressi*) adj1 (renal* or kidney*)).tw. (123820)

3 ((kidney* or renal*) adj1 insufficien*).tw. (30090)

4 ckd*.tw. (50347)

5 ((kidney* or renal*) adj1 fail*).tw. (132535)

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (58639)

7 (esrd* or eskd*).tw. (27605)

8 or/1-7 (446229)

9 exp glomerulus filtration rate/ (98896)

10 (glomerul* or GFR* or eGFR* or e-GFR*).tw. (265909)

11 9 or 10 (294700)

12 (declin* or drop* or reduc* or decreas* or low* or fall* or loss* or less* or chang*).tw. (13680001)

13 disease exacerbation/ (111546)

14 (progress* or exacerbat* or significan* or serious* or sever* or warning* or trigger* or threat* or danger* or damag* or harm* or risk* or deteriorat* or wors* or weak* or morbidit* or damag* or mortal* or fatal* or dead* or die or dying* or life*).tw. (14774393)

15 13 or 14 (14796567)

16 11 and 12 and 15 (137424)

17 8 and 16 (46268)

18 exp Health Economics/ (834288)

19 exp "Health Care Cost"/ (287562)

20 exp Pharmacoeconomics/ (200394)

21 Monte Carlo Method/ (39596)

22 Decision Tree/ (12464)

23 econom$.tw. (359487)

24 cba.tw. (12653)

25 cea.tw. (34243)

26 cua.tw. (1474)

27 markov$.tw. (29760)

28 (monte adj carlo).tw. (47537)

29 (decision adj3 (tree$ or analys$)).tw. (22689)

30 (cost or costs or costing$ or costly or costed).tw. (754747)

31 (price$ or pricing$).tw. (56206)

32 budget$.tw. (37925)

33 expenditure$.tw. (73360)

34 (value adj3 (money or monetary)).tw. (3391)

35 (pharmacoeconomic$ or (pharmaco adj economic$)).tw. (8550)

36 or/18-35 (1726118)

37 "Quality of Life"/ (459082)

38 Quality Adjusted Life Year/ (26005)

39 Quality of Life Index/ (2747)

40 Short Form 36/ (28150)

41 Health Status/ (125550)

42 quality of life.tw. (428000)

43 quality adjusted life.tw. (19225)

44 (qaly$ or qald$ or qale$ or qtime$).tw. (19671)

45 disability adjusted life.tw. (3942)

46 daly$.tw. (3874)

47 (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. (40691)

48 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. (2367)

49 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. (9217)

50 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. (59)

51 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. (443)

52 (euroqol or euro qol or eq5d or eq 5d).tw. (19856)

53 (qol or hql or hqol or hrqol).tw. (94388)

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

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

56 utilit$.tw. (283054)

57 (hui or hui1 or hui2 or hui3).tw. (2224)

58 disutili$.tw. (903)

59 rosser.tw. (119)

60 quality of wellbeing.tw. (42)

61 quality of well-being.tw. (474)

62 qwb.tw. (244)

63 willingness to pay.tw. (8528)

64 standard gamble$.tw. (1095)

65 time trade off.tw. (1679)

66 time tradeoff.tw. (288)

67 tto.tw. (1644)

68 or/37-67 (967036)

69 36 or 68 (2539754)

70 17 and 69 (3315)

71 limit 70 to dc=20131101-20200407 (2056)

72 exp juvenile/ or Child Behavior/ or Child Welfare/ or Child Health/ or infant welfare/ or "minor (person)"/ or elementary student/ (3387399)

73 (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. (1193180)

74 (child* or minor or minors or boy* or girl* or kid or kids or young*).ti,ab,in,ad,jw. (3590067)

75 exp pediatrics/ (104560)

76 (pediatric* or paediatric* or peadiatric*).ti,ab,in,ad,jw. (1617395)

77 exp adolescence/ or exp adolescent behavior/ or adolescent health/ or high school student/ or middle school student/ (102996)

78 (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. (649686)

79 school/ or high school/ or kindergarten/ or middle school/ or primary school/ or nursery school/ or day care/ (102315)

80 (pre-school* or preschool* or kindergar* or daycare or day-care or nurser* or school* or pupil* or student*).ti,ab,jw. (688852)

81 ("under 18*" or "under eighteen*" or "under 25*" or "under twenty five*").ti,ab. (7289)

82 or/72-81 (6349586)

83 70 and 82 (706)

84 71 or 83 (2351)

85 nonhuman/ not human/ (4601462)

86 84 not 85 (2299)

87 limit 86 to (chapter or conference abstract or conference paper or "conference review") (948)

88 86 not 87 (1351)

89 limit 88 to english language (1293)

Database: Econlit <1886 to April 02, 2020>

Search Strategy:

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

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

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

4 ckd*.tw. (5)

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

6 ((endstage* or end-stage* or "end stage*") adj1 (renal* or kidney*)).tw. (55)

7 (esrd* or eskd*).tw. (32)

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

9 or/1-8 (102)

10 [Glomerular Filtration Rate/] (0)

11 (glomerul* or GFR* or eGFR* or e-GFR*).tw. (13)

12 or/10-11 (13)

13 (declin* or drop* or reduc* or decreas* or low* or fall* or loss* or less* or chang*).tw. (486384)

14 [exp disease progression/] (0)

15 (progress* or exacerbat* or significan* or serious* or sever* or warning* or trigger* or threat* or danger* or damag* or harm* or risk* or deteriorat* or wors* or weak* or morbidit* or damag* or mortal* or fatal* or dead* or die or dying* or life*).tw. (417375)

16 14 or 15 (417375)

17 12 and 13 and 16 (2)

18 9 and 17 (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 ((((glomerul* or GFR* or eGFR* or e-GFR*)))) 416 Delete

11 (((MeSH DESCRIPTOR Glomerular Filtration Rate EXPLODE ALL TREES))) 92 Delete

12 #10 OR #11 416 Delete

13 ((declin* or drop* or reduc* or decreas* or low* or fall* or loss* or less* or chang*)) 36488 Delete

14 MeSH DESCRIPTOR disease progression EXPLODE ALL TREES 704 Delete

15 ((progress* or exacerbat* or significan* or serious* or sever* or warning* or trigger* or threat* or danger* or damag* or harm* or risk* or deteriorat* or wors* or weak* or morbidit* or damag* or mortal* or fatal* or dead* or die or dying* or life*)) 45266 Delete

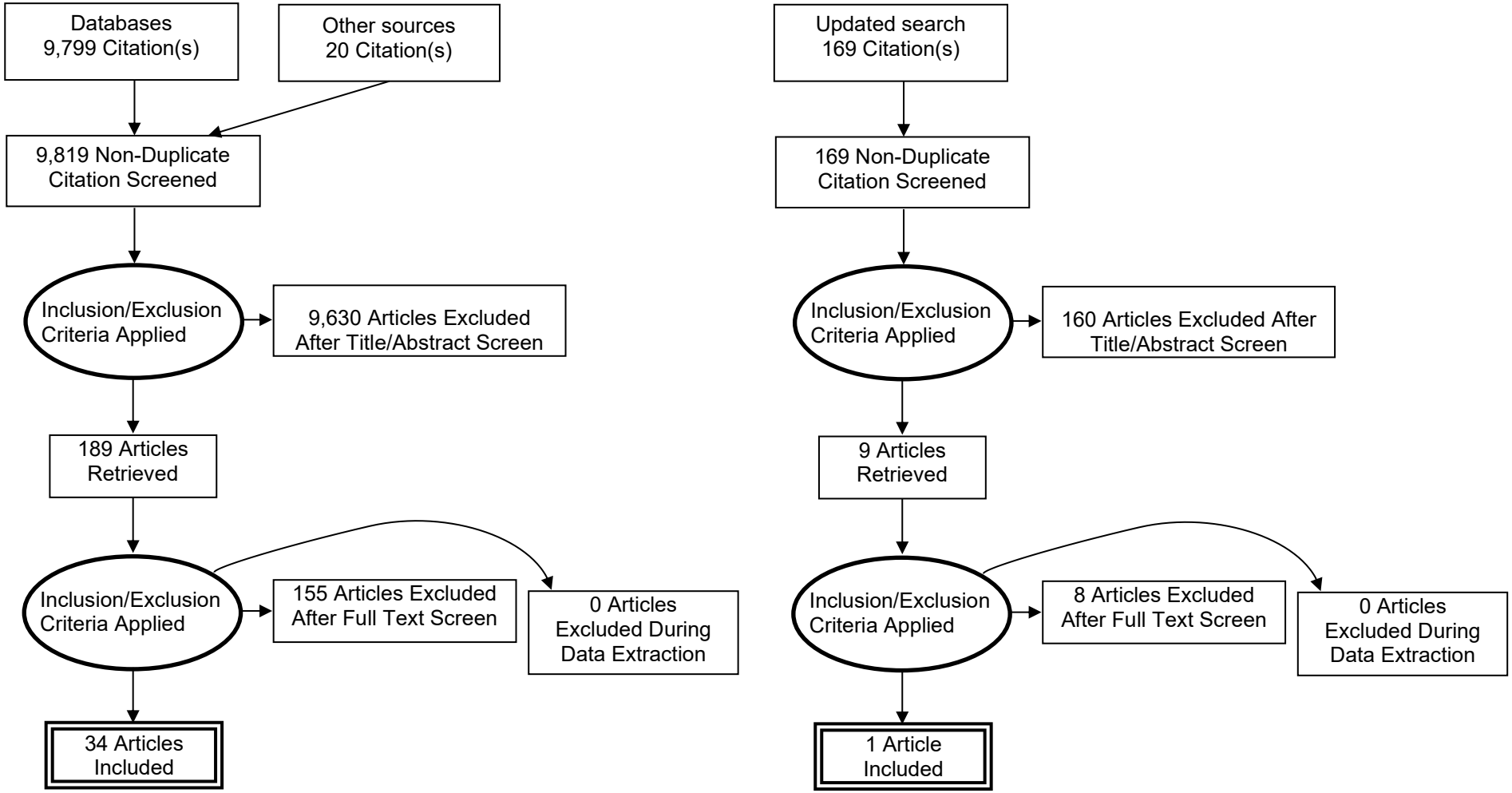
16 #14 OR #15 45271 Delete

17 #12 AND #13 AND #16 211 Delete

18	#9 AND #17	111	Delete
19	(#9 and #17) IN DARE	84	Delete
20	(#9 and #17) IN NHSEED	21	Delete
21	(#9 and #17) IN HTA	6	Delete

1

Appendix D – Epidemiological evidence study selection



Appendix E – Epidemiological evidence tables

Individual patient data

Bruck, 2018

Bibliographic Reference	Bruck, Katharina; Jager, Kitty J; Zoccali, Carmine; Bello, Aminu K; Minutolo, Roberto; Ioannou, Kyriakos; Verbeke, Francis; Volzke, Henry; Arnlov, Johan; Leonardis, Daniela; Ferraro, Pietro Manuel; Brenner, Hermann; Caplin, Ben; Kalra, Philip A; Wanner, Christoph; Castelao, Alberto Martinez; Gorriz, Jose Luis; Hallan, Stein; Rothenbacher, Dietrich; Gibertoni, Dino; De Nicola, Luca; Heinze, Georg; Van Biesen, Wim; Stel, Vianda S; European CKD Burden, Consortium; Different rates of progression and mortality in patients with chronic kidney disease at outpatient nephrology clinics across Europe.; Kidney international; 2018; vol. 93 (no. 6); 1432-1441

Study Characteristics

Study design	Individual participant data meta-analysis Data was reported by cohort without meta-analysis
Study details	Group/Study name European CKD Burden Consortium Dates searched 2000 - 2012 Databases searched PubMed Sources of funding European Renal Association–European Dialysis and Transplant Association (ERA-EDTA) under the Quality European Studies initiative. Other fees were recieved by some of the authors (these fees were from AstraZeneca, Basel, Boëhringer-Ingelheim/Lilly, Merck Sharp, Dohme, a grant from ESTEVE Spain, Vifor-Fresenius Pharma, Fresenius, an educational grant support from Shire, Wiley, Bayer, Resverologix, Novartis.

Study inclusion criteria	CKD CKD patients not undergoing RRT in an outpatient nephrology clinic within Europe and when creatinine follow-up measurements were available
Study exclusion criteria	Sample size Less than 100 participants Other Studies not using eGFR based on serum creatinine equations, intervention trials, and review articles
Phenomenon of interest	Rate of eGFR decline A linear mixed model was used to estimate the rate of change in eGFR over time, taking into account the varying number and spacing of eGFR measurements as well as the variable follow-up duration for each subject. mGFR or eGFR eGFR; CKD-EPI Blood test Creatinine
Included cohorts	All included cohorts 9 cohorts from 5 European countries (n=18,126); CKD patients not on renal replacement therapy, with baseline eGFR <60 ml/min/1.73m² and with at least 2 creatinine measurements.

Study arms

Ghent (Belgium) (N = 403)

Study details	Duration of follow-up Median 5.7 (IQR 4.0, 7.6)
Baseline characteristics	Age Median 69 years (range 61, 77) Female 39.0% Diabetes

	35.7% Hypertension 48.4% Albuminuria Normoalbuminuria (51.3%); microalbuminuria (22.7%); macroalbuminuria (26.0%) eGFR mL/min/1.73m2 Mean 37.7 (SD 11.5)

Nicosia (Cyprus) (N = 70)

Study details	Duration of follow-up Median 3.0 years (IQR 3.0, 3.0)
Baseline characteristics	Age Median 72 years (range 68, 76) Female 28.6% Diabetes 60.0% Hypertension 98.6% Albuminuria Normoalbuminuria (39.1%); microalbuminuria (33.3%); macroalbuminuria (27.5%) eGFR mL/min/1.73m2 Mean 41.2 (SD 11.3)

CIC (Italy) (N = 1420)

Study details	Duration of follow-up Median 0.5 years (IQR 0.0, 1.9)

Baseline characteristics	Age Median 74 years (range 66, 80) Female 41.4% Diabetes 36.6% Hypertension Not applicable Albuminuria Not applicable eGFR mL/min/1.73m2 Mean 33.8 (SD 12.3)

MAURO (Italy) (N = 719)

Study details	Duration of follow-up Median 3.0 (IQR 3.0, 3.0)
Baseline characteristics	Age Median 65 years (range 57, 70) Female 40.9% Diabetes 34.9% Hypertension 94.4% Albuminuria Normoalbuminuria (18.3%); microalbuminuria (28.6%); macroalbuminuria (53.1%) eGFR mL/min/1.73m2 Mean 33.6 (SD 12.0)

PIRP (Italy) (N = 11277)

Study details	Duration of follow-up Median 2.4 years (IQR 1.2, 4.3)
Baseline characteristics	Age Median 74 years (range 67, 80) Female 35.4% Diabetes 36.6% Hypertension 97.8% Albuminuria Normoalbuminuria (41.0%); microalbuminuria (36.6%); macroalbuminuria (22.4%) eGFR mL/min/1.73m2 Mean 30.2 (SD11.9)

TABLE (Italy) (N = 1031)

Study details	Duration of follow-up Median 4.2 years (IQR 2.2, 5.1)
Baseline characteristics	Age Median 69 years (range 58, 76) Female 42.7% Diabetes 26.8% Hypertension 97.1%

	Albuminuria Normoalbuminuria (22.2%); microalbuminuria (24.5%); macroalbuminuria (53.2%) eGFR mL/min/1.73m2 Mean 29.8 (SD 13.8)

PECERA (Spain) (N = 939)

Study details	Duration of follow-up Median 2.5 years (IQR 1.3, 3.0)
Baseline characteristics	Age Median 73 years (range 61, 79) Female 39.6% Diabetes 35.9% Hypertension 91.4% Albuminuria Normoalbuminuria (14.1%); microalbuminuria (28.7%); macroalbuminuria (57.2%) eGFR mL/min/1.73m2 Mean 19.2 (SD 5.4)

CRISIS (UK) (N = 2049)

Study details	Duration of follow-up Median 3.2 years (IQR 1.9, 5.8)
Baseline characteristics	Age Median 67 years (range 56, 75) Female 38.4%

	Diabetes 32.3% Hypertension 95.9% Albuminuria Normoalbuminuria (37.8%); microalbuminuria (29.8%); macroalbuminuria (32.4%) eGFR mL/min/1.73m2 Mean 29.0 (SD 13.3)

LACKABO (UK) (N = 218)

Study details	Duration of follow-up Median 5.2 years (IQR 4.6, 5.4)
Baseline characteristics	Age Median 61 years (range 51, 70) Female 28.0% Diabetes 20.2% Hypertension 83.9% Albuminuria Normoalbuminuria (22.3%); microalbuminuria (28.9%); macroalbuminuria (48.8%) eGFR mL/min/1.73m2 Mean 33.5 (SD 13.5)

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?	Probably yes *(Only missing data was reported)*
Planned analyses	Were the Analyses Prespecified in Detail?	Probably no *(There was no meta-analysis of the rate of decline in eGFR and no discussion about why this was not done; risk of bias of included cohorts was not reported)*
Assessment of risk of bias of the included studies	Was the risk of bias of included trials assessed?	Probably yes *(All relevant outcomes were included and missing data for other outcomes was reported but risk of bias of included studies was not reported)*
Methods of analysis	Were the methods of analysis appropriate overall?	No *(There was no meta-analysis for the rate of decline in eGFR)*
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	High
	Applicability	Directly applicable

Grams, 2019

Bibliographic Reference	Grams, M.E.; Sang, Y.; Ballew, S.H.; Matsushita, K.; Astor, B.C.; Carrero, J.J.; Chang, A.R.; Inker, L.A.; Kenealy, T.; Kovesdy, C.P.; Lee, B.J.; Levin, A.; Naimark, D.; Pena, M.J.; Schold, J.D.; Shalev, V.; Wetzels, J.F.M.; Woodward, M.; Gansevoort, R.T.; Levey, A.S.; Coresh, J.; Evaluating glomerular filtration rate slope as a surrogate end point for ESKD in clinical trials: An individual participant meta-analysis of observational data; Journal of the American Society of Nephrology; 2019; vol. 30 (no. 9); 1746-1755

Study Characteristics

Study design	Individual participant data meta-analysis
Study details	Group/Study name CKD Prognosis Consortium Dates searched Not reported Databases searched Not reported Sources of funding The CKD Prognosis Consortium (CKD-PC) Data Coordinating Center is funded in part by a program grant from the US National Kidney Foundation (which in turn, receives support from industry) and National Institute of Diabetes and Digestive and Kidney Diseases grant. A variety of sources have supported enrollment; data collection, including laboratory measurements; and follow-up in the collaborating cohorts of the CKD-PC. These funding sources include government agencies, such as national institutes of health and medical research councils as well as foundations and industry sponsors. Duration of follow-up 3 years
Study inclusion criteria	Other Cohorts that could participate in all of the 1-, 2-, and 3-year baseline periods and had subsequent longitudinal follow-up for end-stage kidney disease (ESKD) and all-cause mortality; participants ages≥18 years old without ESKD that developed during or before the baseline period.

Study exclusion criteria	None None reported
Phenomenon of interest	Rate of eGFR decline Estimated GFR slope using linear mixed models with an unstructured variance-covariance matrix, random intercept, and random slope for each individual to estimate slope. mGFR or eGFR eGFR; CKD-EPI Blood test Creatinine
Included cohorts	All included cohorts A total of 14 cohorts had the requisite data and agreed to participate. Cohorts included in meta-analysis There was no meta-analysis reported for the rate of decline in eGFR.
Baseline characteristics	Age Mean 57 years (SD 15) Female 25% Ethnicity Black 11% Diabetes 21% eGFR mL/min/1.73m2 Mean 87 (SD 19)

Study arms

AASK eGFR<60 (N = 744)
African American Study of Kidney Disease and Hypertension (AASK)

Baseline characteristics	Age Mean 54 years (SD 11) Female 39% Ethnicity Black 100% Diabetes 0% eGFR mL/min/1.73m2 Mean 42 (SD 11)

BC CKD eGFR<60 (N = 8950)
British Columbia CKD Study (BC CKD)

Baseline characteristics	Age Mean 70 years (SD 13) Female 46% Ethnicity Black 0% Diabetes 44% eGFR mL/min/1.73m2 Mean 32 (SD 11)

CCF eGFR<60 (N = 18873)
Cleveland Clinic CKD Registry Study (CCF)

Baseline characteristics	Age Mean 72 years (SD 11)

	Female 55% Ethnicity Black 12% Diabetes 25% eGFR mL/min/1.73m2 Mean 47 (SD 10)

Geisinger eGFR<60 (N = 19200)
Geisinger Health System (Geisinger)

Baseline characteristics	Age Mean 73 years (SD 12) Female 62% Ethnicity Black 0.8% Diabetes 28% eGFR mL/min/1.73m2 Mean 47 (SD 11)

KP Hawaii eGFR<60 (N = 5468)
Kaiser Permanente Hawaii cohort (KP Hawaii)

Baseline characteristics	Age Mean 71 years (SD 11) Female 53%

	Ethnicity Black 0% Diabetes 52% eGFR mL/min/1.73m2 Mean 47 (SD 10)

Maccabi eGFR<60 (N = 29211)

Maccabi Health System (Maccabi)

Baseline characteristics	Age Mean 74 years (SD 11) Female 50% Ethnicity Black 0% Diabetes 32% eGFR mL/min/1.73m2 Mean 49 (SD 10)

MASTERPLAN eGFR<60 (N = 513)

Multifactorial Approach and Superior Treatment Efficacy in Renal Patients with the Aid of a Nurse Practitioner (MASTERPLAN)

Baseline characteristics	Age Mean 61 years (SD 12) Female 31% Ethnicity Black 0%

	Diabetes 24% eGFR mL/min/1.73m2 Mean 36 (SD 11)

MDRD eGFR<60 (N = 591)
Modification of Diet in Renal Disease Study (MDRD)

Baseline characteristics	Age Mean 52 years (SD 12) Female 38% Ethnicity Black 6.6% Diabetes 3.9% eGFR mL/min/1.73m2 Mean 35 (SD 11)

NZDCS eGFR<60 (N = 1913)
New Zealand Diabetes Cohort Study (NZDCS)

Baseline characteristics	Age Mean 71 years (SD 9) Female 57% Ethnicity Black 0% Diabetes 100%

	eGFR mL/min/1.73m2 Mean 48 (SD 10)

RENAAL eGFR<60 (N = 1139)

Reduction of Endpoints in Non-insulin Dependent Diabetes Mellitus with the Angiotensin II Antagonist Losartan (RENAAL)

Baseline characteristics	Age Mean 60 years (SD 7) Female 37% Ethnicity Black 14% Diabetes 100% eGFR mL/min/1.73m2 Mean 38 (SD 11)

SCREAM eGFR<60 (N = 35049)

Stockholm CREAtinine Measurements Cohort (SCREAM)

Baseline characteristics	Age Mean 69 years (SD 10) Female 61% Ethnicity Black 0% Diabetes 15% eGFR mL/min/1.73m2 Mean 48 (SD 10)

Sunnybrook eGFR<60 (N = 1013)

Sunnybrook Cohort (Sunnybrook)

Baseline characteristics	Age Mean 70 years (SD 13) Female 42% Ethnicity Black 0% Diabetes 52% eGFR mL/min/1.73m2 Mean 35 (SD 12)

All eGFR<60 (N = 122664)

Baseline characteristics	Age Mean 71 years (SD 11) Female 56% Ethnicity Black 3% Diabetes 28% eGFR mL/min/1.73m2 Mean 47 (SD 10)

ADVANCE eGFR≥60 (N = 8457)

The Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation trial (ADVANCE)

Baseline characteristics	Age Mean 66 years (SD 6) Female 40% Ethnicity Black 0.4% Diabetes 100% eGFR mL/min/1.73m2 Mean 83 (SD 13)

Geisinger eGFR≥60 (N = 138682)
Geisinger Health System (Geisinger)

Baseline characteristics	Age Mean 55 years (SD 15) Female 56% Ethnicity Black 1.7% Diabetes 16% eGFR mL/min/1.73m2 Mean 92 (SD 17)

KP Hawaii eGFR≥60 (N = 15140)
Kaiser Permanente Hawaii cohort (KP Hawaii)

Baseline characteristics	Age Mean 58 years (SD 13)

	Female 49% Ethnicity Black 0% Diabetes 67% eGFR mL/min/1.73m2 Mean 86 (SD 16)

Maccabi eGFR≥60 (N = 720012)

Maccabi Health System (Maccabi)

Baseline characteristics	Age Mean 47 years (SD 16) Female 59% Ethnicity Black 0% Diabetes 9% eGFR mL/min/1.73m2 Mean 101 (SD 17)

NZDCS eGFR≥60 (N = 7093)

New Zealand Diabetes Cohort Study (NZDCS)

Baseline characteristics	Age Mean 59 years (SD 13) Female 49%

	Ethnicity Black 0.11% Diabetes 100% eGFR mL/min/1.73m2 Mean 86 (SD 16)

RCAV eGFR≥60 (N = 2408814)

Racial and Cardiovascular Risk Anomalies in CKD Cohort (RCAV)

Baseline characteristics	Age Mean 61 years (SD 13) Female 5.9% Ethnicity Black 16.8% Diabetes 27% eGFR mL/min/1.73m2 Mean 83 (SD 15)

SCREAM eGFR≥60 (N = 460353)

Stockholm CREAtinine Measurements Cohort (SCREAM)

Baseline characteristics	Age Mean 48 years (SD 15) Female 54% Ethnicity Black 0%

	Diabetes 6.2% eGFR mL/min/1.73m2 Mean 97 (SD 17)

All eGFR≥60 (N = 3758551)

Baseline characteristics	Age Mean 56 years (SD 15) Female 24% Ethnicity Black 11% Diabetes 21% eGFR mL/min/1.73m2 Mean 89 (SD 18)

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
Identification of eligible studies	Were All Eligible Trials Identified?	Yes *(Details reported by Matsushita 2013)*
Ability to obtain IPD data	Were IPD Obtained from Most Trials?	Yes *(Details reported by Matsushita 2013)*

Section	Question	Answer
IPD data integrity	Was the Integrity of the IPD Checked?	Probably yes *(Only missing data was reported)*
Planned analyses	Were the Analyses Prespecified in Detail?	Probably yes *(But risk of bias of included studies was not reported)*
Assessment of risk of bias of the included studies	Was the risk of bias of included trials assessed?	Probably yes *(All relevant outcomes were included and missing data for other outcomes was reported but risk of bias of included studies was not reported)*
Methods of analysis	Were the methods of analysis appropriate overall?	No *(Rate of decline in eGFR was not meta-analysed)*
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	High
	Applicability	Directly applicable

Uncontrolled prospective studies

Belangero, 2018

Bibliographic Reference Belangero, Vera M S; Prates, Liliane C; Watanabe, Andreia; Schvartsman, Benita S G; Nussenzveig, Paula; Cruz, Natalia A; Abreu, Ana L S; Paz, Isabel P; Facincani, Inalda; Morgantetti, Fernanda E C; Silva, Andreia O; Andrade, Olberes V B; Camargo, Maria F C; Nogueira, Paulo C Koch; Prospective cohort analyzing risk factors for chronic kidney disease progression in children.; Jornal de pediatria; 2018; vol. 94 (no. 5); 525-531

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Children and young people Study name SP-CKDkid Study location Brazil Study setting Medical centres Study dates 2013 - 2016 Duration of follow-up Median 2.5 years Loss to follow-up 33% at the last follow-up visit (fourth visit) Sources of funding Brazilian Ministry ofHealth through the Program for Institutional Developmentof the Unified Health System
Inclusion criteria	Age Age from 1 to 17 years at the beginning of the study eGFR eGFR <60 mL/min/1.73 m² and >15 mL/min/1.73 m² for at least three months Other Signing of the informed consent form by parents or legal guardians, and of the term of assent by children older than 12 years; and previous follow-up with proper adherence to follow-up for at least three months
Exclusion criteria	Cancer

	Treated in the past 24 months HIV Other Those who planned to move to another city subsequently to the day of invitation to participate in the cohort; any transplant recepient.
Baseline characteristics	Sample size 209 Female 41% Age Median 9.3 years (IQR 5.4, 13.2) eGFR mL/min/1.73m2 Median 33.1 mL/min/1.73m² (IQR 24.9, 40.9)
Phenomenon of interest	Rate of decline in eGFR eGFR was measured at each visit: at the onset of study and at every 6-month visits mGFR or eGFR eGFR from measurements of height and serum creatinine levels using the Schwartz formula Blood test Creatinine

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes

Section	Question	Answer
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	Yes
	Were patients recruited consecutively?	Yes
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Yes
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Partial *(Rate of decline in eGFR was not defined. Study reported that eGFR was measure at baseline and at every 6-month visit during 2 years follow-up.)*
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	Yes
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes

Section	Question	Answer
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Moderate
	Applicability	Partially applicable *(Rate of decline in eGFR was a secondary outcome.)*

Buyadaa, 2020

Bibliographic Reference	Buyadaa, O.; Magliano, D.J.; Salim, A.; Koye, D.N.; Shaw, J.E.; Risk of rapid kidney function decline, all-cause mortality, and major cardiovascular events in nonalbuminuric chronic kidney disease in type 2 diabetes; Diabetes Care; 2020; vol. 43 (no. 1); 122-129

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Adults Study name ACCORD & ACCORDION studies Study location US, Canada

	Study setting 77 centres across the US and Canada Study dates Participants were enrolled between 2003 and 2005 Duration of follow-up 9 years Loss to follow-up 183 out of 10,185 (1.7%) participants without eGFR measurements at follow-up Sources of funding Upported by the NHLBI, by other components of the National Institutes of Health, including the National Institute of Diabetes and Digestive and Kidney Diseases, the National Institute on Aging, and the National Eye Institute, by the Centers for Disease Control and Prevention, and by General Clinical Research Centers; partially supported by the Victorian Government's Operational Infrastructure Support Program.
Inclusion criteria	Age 40 to 79 years Other Type 2 diabetes; the presence of high risk of having cardiovascular event; and HbA1c ≥7.5%
Exclusion criteria	None None reported
Baseline characteristics	Sample size 10,185 Female 38.5% Age Median 62.0 years (IQR 57.7, 67.1) Ethnicity White (62.4%); Black (19.1%); Hispanic (7.1%); Other (11.4%) Diabetes All type 2 diabetes Hypertension

	Not reported Albuminuria/proteinuria Median UACR 1.6 mg/mmol (IQR 0.8, 5.0) eGFR mL/min/1.73m2 Median 89.6 (IQR 75.3, 105.0)
Phenomenon of interest	Rate of decline in eGFR To estimate the rate of eGFR decline, joint longitudinal-survival modeling was used to take into account the possibility of informative censoring due to the shorter follow-up duration of subjects with more rapid decline. The linear mixed model with random intercept and slope was used to model changes in eGFR for each group. mGFR or eGFR eGFR; MDRD (4-variable) equation Blood test Creatinine
Subgroups	Albuminuria eGFR categories

Study arms

No CKD (eGFR ≥120) (N = 791)

Baseline characteristics	Female 41.6% Age Median 59.3 years (IQR 56.5, 63.2) Ethnicity White (53.5%); Black (21.3%); Hispanic (10.5%); Other (14.7%) Diabetes All type 2 diabetes Hypertension

	Not reported Albuminuria/proteinuria Median UACR 1.1 mg/mmol (IQR 0.6, 1.6) eGFR mL/min/1.73m2 Median 130.9 (IQR 123.0, 141.0)

No CKD (eGFR 90 to 120) (N = 2724)

Baseline characteristics	Female 39.0% Age Median 59.7 years (IQR 56.7, 63.5) Ethnicity White (61.3%); Black (21.0%); Hispanic (6.5%); Other (11.2%) Diabetes All type 2 diabetes Hypertension Not reported Albuminuria/proteinuria Median UACR 1.0 mg/mmol (IQR 0.6, 1.6) eGFR mL/min/1.73m2 Median 102.0 (IQR 92.2, 107.1)

No CKD (eGFR 60 to 90) (N = 3026)

Baseline characteristics	Female 39.9% Age Median 102.0 years (IQR 92.2, 107.1) Ethnicity White (66.8%); Black (15.6%); Hispanic (6.6%); Other (11.0%)

	Diabetes All type 2 diabetes Hypertension Not reported Albuminuria/proteinuria Median UACR 0.9 mg/mmol (IQR 0.6, 1.6) eGFR mL/min/1.73m2 Median 78.2 (IQR 71.4, 82.1)

Albuminuric non-CKD (N = 2867)

Baseline characteristics	Female 31.5% Age Median 62.2 years (IQR 57.8, 67.3) Ethnicity White (58.9%); Black (22.2%); Hispanic (7.8%); Other (11.1%) Diabetes All type 2 diabetes Hypertension Not reported Albuminuria/proteinuria Median UACR 10.2 mg/mmol (IQR 5.4, 26.0) eGFR mL/min/1.73m2 Median 90.3 (IQR 7.0, 105.7)

Albuminuric CKD (N = 345)

Baseline characteristics	Female 50.2%

	Age Median 66.0 years (IQR 62.1, 71.2) Ethnicity White (67.3%); Black (14.5%); Hispanic (6.4%); Other (11.8%) Diabetes All type 2 diabetes Hypertension Not reported Albuminuria/proteinuria Median UACR 14.5 mg/mmol (IQR 6.2, 49.0) eGFR mL/min/1.73m2 Median 53.1 (IQR 47.7, 57.3)

Non-albuminuric CKD (N = 432)

Baseline characteristics	Female 58.4% Age Median 66.7 years (IQR 62.4, 72) Ethnicity White (73.3%); Black (9.5%); Hispanic (6.3%); Other (10.9%) Diabetes All type 2 diabetes Hypertension Not reported Albuminuria/proteinuria Median UACR 1.1 mg/mmol (IQR 0.7, 2.0)

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	Yes
	Were patients recruited consecutively?	Unclear
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Partial *(Exclusion criteria were not reported.)*
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	Yes
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes

Section	Question	Answer
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Partially applicable *(Rate of decline in eGFR was a secondary outcome.)*

Chen, 2019

Bibliographic Reference	Chen, Hung-Chih; Lin, Hsuan-Jen; Huang, Chiu-Ching; Chang, Chiz-Tzung; Chou, Che-Yi; Maximum Glomerular Filtration Decline Rate is Associated with Mortality and Poor Renal Outcome in Chronic Kidney Disease Patients.; Blood purification; 2019; vol. 48 (no. 2); 131-137

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Adults Study name None Study location China Study setting

	University hospital Study dates 2004 - 2013 Duration of follow-up Median 5.3 years Loss to follow-up None Sources of funding None
Inclusion criteria	CKD CKD GFR categories G3 to G5 (not on dialysis) Other Participants who had at least 3 readings of eGFR decline available
Exclusion criteria	None None reported
Baseline characteristics	Sample size 815 Female 44.3% Age Median 75 years (IQR 65 to 82) Diabetes 35.5% Hypertension 14.8% Albuminuria/proteinuria Median UPCR 0.86 g/g (IQR 0.36 to 1.88) eGFR mL/min/1.73m2 Median 24.8 (IQR 17.5 to 33.8)

Phenomenon of interest	Rate of decline in eGFR The eGFR decline rate (percentage per year) was calculated as (the present eGFR reading – the previous eGFR reading)/(the time interval between 2 readings in year × previous eGFR). All patients had at least 3 eGFR decline rate readings available and the maximum, the average, the minimum eGFR decline rate were used in the analysis. mGFR or eGFR eGFR; simple MDRD equation Blood test Creatinine
Subgroups	eGFR categories

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	No
	Were patients recruited consecutively?	Unclear
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Yes
	Did patients enter the study at a similar point in the disease?	Yes

Section	Question	Answer
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	No *(There were no losses to follow-up.)*
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Partially applicable *(Rate of decline in eGFR was a secondary outcome.)*

Fathallah-Shaykh, 2015

Bibliographic Reference	Fathallah-Shaykh, Sahar A; Flynn, Joseph T; Pierce, Christopher B; Abraham, Alison G; Blydt-Hansen, Tom D; Massengill, Susan F; Moxey-Mims, Marva M; Warady, Bradley A; Furth, Susan L; Wong, Craig S; Progression of pediatric CKD of nonglomerular origin in the CKiD cohort.; Clinical journal of the American Society of Nephrology : CJASN; 2015; vol. 10 (no. 4); 571-7

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Children and young people Study name CKiD Study location US Study setting Paediatric nephrology centres Study dates 2005 - 2009 Duration of follow-up Median 4.4 years Loss to follow-up None reported Sources of funding The National Institute of Diabetes and Digestive and Kidney Diseases, with additional funding from the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the National Heart, Lung, and Blood Institute.
Inclusion criteria	Age 1 to 16 years eGFR

	Schwartz-eGFR 30 to 90 ml/min per 1.73 m² Other Nonglomerular diagnosis; parental consent and participant assent/consent were obtained according to local requirements.
Exclusion criteria	None None reported
Baseline characteristics	Sample size 522 Female 35.0% Age Median 10 years (IQR 7, 14) Ethnicity African-American 19.0% Diabetes Not reported Hypertension Not reported Albuminuria/proteinuria Median UPCR mg/mg 0.29 (IQR 0.12, 0.82) eGFR mL/min/1.73m2 Median 48 (IQR 36, 64)
Phenomenon of interest	Rate of decline in eGFR Linear mixed models (univariate and multivariate with random intercept and slope) were used to model GFR as a function of time since baseline. mGFR or eGFR GFR was measured by the plasma disappearance of iohexol. At study visits when iohexol GFR was not measured, GFR was estimated as a function of sex, height, serum creatinine, cystatin C, and/or BUN from CKiD-developed formulae (Schwartz 2009).The term "GFR" was used to refer to the combined iohexol measured and eGFR measurements for any participant over follow-up. Blood test GFR (iohexol); eGFR (creatinine, cystatin-C, and/or BUN)

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	Yes
	Were patients recruited consecutively?	Unclear
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Partial *(Exclusion criteria were not reported.)*
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes

Section	Question	Answer
	Were losses to follow-up reported?	No
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Directly applicable

Fischer, 2016

Bibliographic Reference	Fischer, Michael J; Hsu, Jesse Y; Lora, Claudia M; Ricardo, Ana C; Anderson, Amanda H; Bazzano, Lydia; Cuevas, Magdalena M; Hsu, Chi-Yuan; Kusek, John W; Renteria, Amada; Ojo, Akinlolu O; Raj, Dominic S; Rosas, Sylvia E; Pan, Qiang; Yaffe, Kristine; Go, Alan S; Lash, James P; Chronic Renal Insufficiency Cohort (CRIC) Study, Investigators; CKD Progression and Mortality among Hispanics and Non-Hispanics.; Journal of the American Society of Nephrology : JASN; 2016; vol. 27 (no. 11); 3488-3497

Study Characteristics

Study type	Uncontrolled prospective study

Study details	Adults Study name CRIC & H-CRIC Study location US Study setting Recruitment sites included university-based, community based, and private health clinics. Study dates 2003 - 2008 Duration of follow-up Median 6.6 years Loss to follow-up Around 10% Sources of funding Cooperative agreement from the National Institute of Diabetes and Digestive and Kidney Diseases. In addition, this work was supported in part by a list of universities and institutes in the US and a grant from Astra Zeneca.
Inclusion criteria	Age 21 to 74 years CKD Mild to moderate CKD
Exclusion criteria	Cancer Chemotherapy for cancer within 2 years. HIV Other Inability to consent; New York Heart Association class 3 or 4 heart failure; cirrhosis; polycystic kidney disease; prior dialysis therapy or transplant; immunosuppressive therapy within 6 months.
Phenomenon of interest	Rate of decline in eGFR Mean annual change in eGFR was calculated for each participant by averaging 12-month differences in eGFR measured at annual study visits throughout follow up.

	mGFR or eGFR GFR was estimated for participants based on an equation developed in a subgroup of CRIC participants with an iothalamate GFR, which has been demonstrated to have superior accuracy in this cohort compared with other eGFR equations. Blood test Creatinine
Subgroups	Ethnicity

Study arms

Hispanic (N = 497)

Baseline characteristics	Female 42.0% Age Mean 56.3 years (SD 11.7) Diabetes 67.4% Hypertension 89.1% Albuminuria/proteinuria Median urine protein g/24h 0.71 (IQR 0.12, 3.34) eGFR mL/min/1.73m2 Mean 39.0 (SD 15.2)

Non-Hispanic White (N = 1638)

Baseline characteristics	Female 40.0% Age

	Mean 58.9 years (SD 11.0) Diabetes 39.6% Hypertension 78.9% Albuminuria/proteinuria Median urine protein g/24h 0.12 (IQR 0.07, 0.5) eGFR mL/min/1.73m2 Mean 47.7 (SD 17.1)

Non-Hispanic Black (N = 1650)

Baseline characteristics	Female 51.1% Age Mean 58.1 years (SD 10.6) Diabetes 51.4% Hypertension 92.9% Albuminuria/proteinuria Median urine protein g/24h 0.24 (IQR 0.08, 1.07) eGFR mL/min/1.73m2 Mean 43.5 (SD 16.3)

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	Yes
	Were patients recruited consecutively?	Unclear
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Yes
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	Yes
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes

Section	Question	Answer
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Partially applicable *(Rate of decline in eGFR was a secondary outcome.)*

Furth, 2007

Bibliographic Reference Furth, Susan L; Cole, Stephen R; Fadrowski, Jeffrey J; Gerson, Arlene; Pierce, Christopher B; Chandra, Manju; Weiss, Robert; Kaskel, Frederick; Council of Pediatric Nephrology and Urology, New York/New Jersey; Kidney and Urology Foundation of, America; The association of anemia and hypoalbuminemia with accelerated decline in GFR among adolescents with chronic kidney disease.; Pediatric nephrology (Berlin, Germany); 2007; vol. 22 (no. 2); 265-71

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Children and young people Study name Functional Outcomes in Adolescent CKD Study location

	US Study setting Seven clinical sites in the US Study dates 1999 - 2004 Duration of follow-up 3 years Loss to follow-up 16 out of 39 (41.0%) participants with less than one study visit Sources of funding Funded in part by the Kidney and Urology Foundation of America, the National Institute of Diabetes, Digestive and Kidney Disorders, with additional funding from the National Institute of Neurological Disorders and Stroke, National Institute of Child Health and Human Development, and the National Heart, Lung, and Blood Institute, the National Institutes of Health, and the American Kidney Fund's Clinical Scientist in Nephrology Fellowship Program.
Inclusion criteria	Age 11 to 18 years eGFR GFR <75 ml/min/1.73 m² estimated via the Schwartz formula Other Those could read English or Spanish at the 4th grade level. A parent or caregiver gave written informed consent, and adolescents provided written assent.
Exclusion criteria	Renal replacement therapy Prior transplant or on dialysis at study entry
Baseline characteristics	Sample size 23 Female 30.0% Age Mean 14.3 years (SD 2) Ethnicity White 83.0%

	Diabetes Not reported Hypertension Not reported Albuminuria/proteinuria Mean albumin 4.0 (SD 0.5) eGFR mL/min/1.73m2 Mean 51 (SD 27)
Phenomenon of interest	Rate of decline in eGFR Yearly change in GFR was calculated by taking the difference between an adolescent's estimated GFR at successive study visits divided by the difference in calendar time between two successive visits. This is represented by the equation Δij = (yij+1 - yij) / (tij+1 - tij), where yij is the estimated GFR and tij is the visit date for adolescent i at visit j, which yields the "annualised decline in GFR". mGFR or eGFR eGFR; Schwartz formula Blood test Creatinine
Subgroups	Age Gender Ethnicity Albuminuria eGFR categories

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	Yes
	Were patients recruited consecutively?	Unclear
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Yes
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	Yes
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes

Section	Question	Answer
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Directly applicable

Hadjadj, 2016

Bibliographic Reference Hadjadj, Samy; Cariou, Bertrand; Fumeron, Frederic; Gand, Elise; Charpentier, Guillaume; Roussel, Ronan; Kasmi, Ahmed-Amine; Gautier, Jean-Francois; Mohammedi, Kammel; Gourdy, Pierre; Saulnier, Pierre-Jean; Feigerlova, Eva; Marre, Michel; French JDRF Diabetic Nephropathy Collaborative Research Initiative (search for genes determining time to onset of ESRD in T1D patients with proteinuria) and the SURDIAGENE and DIABHYCAR study, groups; Death, end-stage renal disease and renal function decline in patients with diabetic nephropathy in French cohorts of type 1 and type 2 diabetes.; Diabetologia; 2016; vol. 59 (no. 1); 208-216

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Adults Study name GENEDIAB, GENESIS, JDRF, SURDIAGENE, DIABHYCAR cohorts Study location France Study setting Diabetes clinics

	Study dates 1994 - 2012 Sources of funding Grants from the JDRF study (work on type 1 diabetes); the French Ministery of Health and the Association Française des Diabétiques and Groupement pour l'Etude des Maladies Métaboliques et Systémiques (SUGARDIAGENE work); Sanofi-Aventis, the French Ministry of Health, the AFD and the Association Diabète Risque Vasculaire (DIABHYCAR work).
Phenomenon of interest	Rate of decline in eGFR A linear regression was used to compute annual eGFR slope. mGFR or eGFR eGFR; CKD-EPI equation Blood test Creatinine
Subgroups	Diabetes

Study arms

Type 1 diabetes (N = 277)
GENEDIAB, GENESIS, JDRF cohorts

Study details	Duration of follow-up Median 11.9 years Loss to follow-up 138 out of 456 (30.2%) participants.
Inclusion criteria	Other GENEDIAB: severe diabetic retinopathy (proliferative or severe non-proliferative requiring panphotocoagulation), regardless of their nephropathy status. GENESIS: retinopathy and diabetes duration longer than 15 years. JDRF: all patients diagnosed with proteinuria with or without renal failure.
Exclusion criteria	None None reported

Baseline characteristics	Female 41.0% Age Mean 42.1 years (SD 11.5) Hypertension Any hypertensive drug 83.0% Albuminuria/proteinuria Not reported eGFR mL/min/1.73m2 Mean 71.9 (SD 27.3)

Type 2 diabetes (N = 942)
SURDIAGENE, DIABHYCAR cohorts

Study details	Duration of follow-up Median 4.6 years Loss to follow-up SUGARDIAGENE: 1,260 out of 1,468 (85.8%); DIABHYCAR: 2,505 out of 3,137 (79.8%).
Inclusion criteria	Other SURDIAGENE: participants with proteinuria. DIABHYCAR: oral medication, aged ≥50 years, with serum creatinine ≤150 µmol/l and two consecutive urine samples with albumin concentration ≥20 mg/l.
Exclusion criteria	Other SURDIAGENE: non-diabetic renal disease and residing outside the Poitou Charentes region.
Baseline characteristics	Female 29.0% Age Mean 66.3 years (SD 8.7) Hypertension Any hypertensive drug 73.0%

	Albuminuria/proteinuria Mean ACR mg/mmol 112.3 (SD 166.3) eGFR mL/min/1.73m2 Mean 67.6 (SD 22.4)

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	Yes
	Were patients recruited consecutively?	Yes
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Yes
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes

Section	Question	Answer
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	Yes
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Partially applicable *(Rate of decline in eGFR was a secondary outcome.)*

Hwang, 2017

Bibliographic Reference	Hwang, Subin; Park, Jeeeun; Kim, Jinhae; Jang, Hye Ryoun; Kwon, Ghee Young; Huh, Wooseong; Kim, Yoon-Goo; Kim, Dae Joong; Oh, Ha Young; Lee, Jung Eun; Tissue expression of tubular injury markers is associated with renal function decline in diabetic nephropathy.; Journal of diabetes and its complications; 2017; vol. 31 (no. 12); 1704-1709

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Adults Study name None Study location Korea Study setting Tertiary referral centre Study dates 2000 - 2014 Duration of follow-up Median 2.0 years Loss to follow-up 7 out of 122 (5.7%) participants. Sources of funding A grant from the Samsung Biomedical Research Institute Grant
Inclusion criteria	Other Patients with diabetes mellitus who underwent renal biopsy and were confirmed to have diabetic nephropathy.
Exclusion criteria	Other Other coexisting renal disease based on pathologic findings (other types of glomerulonephritis, acute tubular necrosis, or acute interstitial nephritis); those with eGFR <30 mL/min/1.73m² at the time of biopsy; and those who received treatment with immunosuppressants.
Baseline characteristics	Sample size 35 Female 20.0% Age Median 50 years (IQR 43, 59)

	Diabetes Type 1 (6.0%); type 2 (94.0%) Albuminuria/proteinuria Median UPCR (mg/mg Cr) 6.76 (IQR 2.18, 7.61) eGFR mL/min/1.73m2 Median 50 (IQR 43, 66)
Phenomenon of interest	Rate of decline in eGFR A model for time versus eGFR was created using a linear regression analysis, and the absolute values of the slope of the regression line were regarded as GFR decline slopes over time, with a positive value representing a decreasing trajectory of GFR. mGFR or eGFR eGFR; CKD-EPI Blood test Creatinine
Subgroups	Diabetes

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	No
	Were patients recruited consecutively?	Unclear

Section	Question	Answer
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Yes
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	Yes
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Directly applicable

Iimori, 2018

Bibliographic Reference	Iimori, Soichiro; Naito, Shotaro; Noda, Yumi; Sato, Hidehiko; Nomura, Naohiro; Sohara, Eisei; Okado, Tomokazu; Sasaki, Sei; Uchida, Shinichi; Rai, Tatemitsu; Prognosis of chronic kidney disease with normal-range proteinuria: The CKD-ROUTE study.; PloS one; 2018; vol. 13 (no. 1); e0190493

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Adults Study name CKD-ROUTE Study location Japan Study setting University Hospital and its affiliated hospitals Study dates 2010 - 2011 Duration of follow-up Median 3.0 years Loss to follow-up 51 out of 412 (12.3%) participants with normal-range proteinuria; 70 out of 710 (9.8%) participants with abnormal-range proteinuria. Sources of funding The authors received no specific funding for this work.
Inclusion criteria	Age Over 20 years of age eGFR

	CKD categories G2 to G5 (eGFR <15 to 89 ml/min/1.73 m²) Other Newly visiting or referred to the participating nephrology centers for the first time between October 2010 and December 2011;
Exclusion criteria	Renal replacement therapy Transplant; dialysis Cancer Diagnosed or treated within the previous 2 years Other Active gastrointestinal bleeding at enrollment; those who did not provide written informed consent.
Baseline characteristics	Sample size 927 Female 29.8% Age Mean 67 years (SD 14) Diabetes 36.8% Hypertension 89.6% Albuminuria/proteinuria Median UPCR g/gCr 0.64 (IQR 0.64, 2.55) eGFR mL/min/1.73m2 Mean 33.8 (SD 17.8)
Phenomenon of interest	Rate of decline in eGFR Changes in eGFR during the study period were analyzed using repeated measures analysis of variance, followed by Bonferroni post hoc test. mGFR or eGFR eGFR; MDRD 3-variable equation developed by the Japanese Society of Nephrology, to adjust for Japanese physical characteristics: eGFR = 194 × serum creatinine −1.094 × age −0.287 (if female, × 0.739). Blood test

	Creatinine
Subgroups	Albuminuria Proteinuria eGFR categories

Study arms

Normal proteinuria total (N = 352)

Normal-range proteinuria was defined as negative or trace protein by dipstick urinary test at enrollment.

Baseline characteristics	Female 30.7% Age Mean 69 years (SD 13) Diabetes 26.7% Hypertension 81.8% Albuminuria/proteinuria Median UPCR g/gCr 0.08 (IQR 0.03, 0.18) eGFR mL/min/1.73m2 Mean 40.3 (SD 15.6)

Normal proteinuria and G2 (N = 36)

Normal-range proteinuria was defined as negative or trace protein by dipstick urinary test at enrollment. G2 refers to eGFR 60 to 89 mL/min/1.73 m2.

Baseline characteristics	Female 44.4%

	Age Mean 60 years (SD 15) Diabetes 13.9% Hypertension 61.1% Albuminuria/proteinuria Median UPCR g/gCr 0.07 (IQR 0.04, 0.15) eGFR mL/min/1.73m2 Mean 69.9 (SD 7.8)

Normal proteinuria and G3a (N = 89)

Normal-range proteinuria was defined as negative or trace protein by dipstick urinary test at enrollment. G3a refers to eGFR 45 to 59 mL/min/1.73 m2.

Baseline characteristics	Female 20.2% Age Mean 65 years (SD 13) Diabetes 14.6% Hypertension 70.8% Albuminuria/proteinuria Median UPCR g/gCr 0.06 (IQR 0.03, 0.14) eGFR mL/min/1.73m2 Mean 51.5 (SD 4.1)

Normal proteinuria and G3b (N = 129)

Normal-range proteinuria was defined as negative or trace protein by dipstick urinary test at enrollment. G3b refers to eGFR 30 to 44 mL/min/1.73 m2.

Baseline characteristics	Female 28.7% Age Mean 71 years (SD 10) Diabetes 27.1% Hypertension 86.0% Albuminuria/proteinuria Median UPCR g/gCr 0.08 (IQR 0.03, 0.18) eGFR mL/min/1.73m2 Mean 38.2 (SD 4.6)

Normal proteinuria and G4 and 5 (N = 98)

Normal-range proteinuria was defined as negative or trace protein by dipstick urinary test at enrollment. G4 and 5 refers to eGFR <15 to 29 mL/min/1.73 m2.

Baseline characteristics	Female 37.8% Age Mean 75 years (SD 11) Diabetes 41.8% Hypertension 93.9% Albuminuria/proteinuria Median UPCR g/gCr 0.12 (IQR 0.04, 0.27)

	eGFR mL/min/1.73m2 Mean 22.0 (SD 5.1)

Abnormal proteinuria total (N = 575)
Abnormal-range proteinuria was defined as positive proteinuria by the dipstick urinary test.

Baseline characteristics	Female 29.2% Age Mean 66 years (SD 14) Diabetes 43.0% Hypertension 94.4% Albuminuria/proteinuria Median UPCR g/gCr 1.72 (IQR 0.74, 4.20) eGFR mL/min/1.73m2 Mean 29.8 (SD 18.0)

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	Yes

Section	Question	Answer
	Were patients recruited consecutively?	Unclear
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Yes
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	Yes
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Low

Section	Question	Answer
	Applicability	Partially applicable *(Rate of decline in eGFR was a secondary outcome.)*

Inaguma, 2017

Bibliographic Reference Inaguma, Daijo; Imai, Enyu; Takeuchi, Ayano; Ohashi, Yasuo; Watanabe, Tsuyoshi; Nitta, Kosaku; Akizawa, Tadao; Matsuo, Seiichi; Makino, Hirofumi; Hishida, Akira; Chronic Kidney Disease Japan Cohort Study, Group; Risk factors for CKD progression in Japanese patients: findings from the Chronic Kidney Disease Japan Cohort (CKD-JAC) study.; Clinical and experimental nephrology; 2017; vol. 21 (no. 3); 446-456

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Adults Study name CKD-JAC Study location Japan Study setting Nephrology care Study dates 2007 - 2013

	Duration of follow-up Median 3.9 years Loss to follow-up 4 out of 3,087 (0.1%) participants. Sources of funding Kyowa Hakko Kirin Co., Ltd.
Inclusion criteria	Age 20 to 75 years eGFR 10 to 59 mL/min/1.73 m² Other Provision of written informed consent.
Exclusion criteria	Renal replacement therapy Initiation of renal replacement therapy; renal transplantation. Cancer Cancer bearing; cancer treatment in the past 2 years. HIV Other Polycystic kidney disease; cirrhosis; having no information at 6 months after the study onset.
Baseline characteristics	Sample size 2,966 Female 37.9% Age Mean 60. 3 years (SD 11.6) Diabetes 37.7% Albuminuria/proteinuria

	UACR 300 to 99 mg/g Cre (28.2%); UACR ≥1000 mg/g Cre (31.6%) eGFR mL/min/1.73m2 Mean 28.9 (SD 12.2)
Phenomenon of interest	Rate of decline in eGFR The slope of the regression line was calculated based on all eGFRs that had been determined between the onset of the study and the final determination point of eGFR and on the number of days from the onset of the study. mGFR or eGFR eGFR; the following formulae for Japanese individuals were used to calculate eGFR by gender: for males, eGFR (mL/min/1.73 m2) = 194 x [age]-0.287 x [serum creatinine (mg/dL)]-1.094; and for females, eGFR (mL/min/1.73 m2) = 194 x [age]-0.287 x [serum creatinine (mg/dL)]-1.094 x 0.739. Blood test Creatinine
Subgroups	Hypertension Albuminuria eGFR categories

Study arms

eGFR 45 to 59 (N = 306)
Category G3a

Baseline characteristics	Female 36.9% Age Mean 54.7 years (SD 13.4) Diabetes 31.4% Albuminuria/proteinuria UACR 300 to 999 mg/g Cre (21.1%); UACR ≥1000 mg/g Cre (15.4%)

	eGFR mL/min/1.73m2 Mean 50.5 (SD 4.9)

eGFR 30 to 44 (N = 1045)
Category G3b

Baseline characteristics	Female 35.4% Age Mean 59.9 years (SD 12.0) Diabetes 36.3% Albuminuria/proteinuria UACR 300 to 999 mg/g Cre (27.1%); UACR ≥1000 mg/g Cre (21.9%) eGFR mL/min/1.73m2 Mean 37.1 (SD 4.2)

eGFR 15 to 29 (N = 1149)
Category G4

Baseline characteristics	Female 38.6% Age Mean 61.5 years (SD 10.6) Diabetes 38.8% Albuminuria/proteinuria UACR 300 to 999 mg/g Cre (30.4%); UACR ≥1000 mg/g Cre (36.1%) eGFR mL/min/1.73m2 Mean 22.5 (SD 4.3)

eGFR <15 (N = 466)
Category G5

Baseline characteristics	Female 42.7% Age Mean 62.1 years (SD 10.6) Diabetes 42.1% Albuminuria/proteinuria UACR 300 to 999 mg/g Cre (30.0%); UACR ≥1000 mg/g Cre (52.0%) eGFR mL/min/1.73m2 Mean 11.8 years (SD 2.0)

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	Yes
	Were patients recruited consecutively?	Unclear
Study population	Were the characteristics of the patients included in the study described?	Yes

Section	Question	Answer
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Yes
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	Yes
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Partially applicable *(Rate of decline in eGFR was a secondary outcome.)*

Kasiske, 2015

Bibliographic Reference	Kasiske, Bertram L; Anderson-Haag, Teresa; Israni, Ajay K; Kalil, Roberto S; Kimmel, Paul L; Kraus, Edward S; Kumar, Rajiv; Posselt, Andrew A; Pesavento, Todd E; Rabb, Hamid; Steffes, Michael W; Snyder, Jon J; Weir, Matthew R; A prospective controlled study of living kidney donors: three-year follow-up.; American journal of kidney diseases : the official journal of the National Kidney Foundation; 2015; vol. 66 (no. 1); 114-24

Study Characteristics

Study type	Uncontrolled prospective study Some study characteristics were taken from reference 4 (Kasiske BL, Anderson-Haag T, Ibrahim HN, et al. A prospective controlled study of kidney donors: baseline and 6-month follow-up. Am J Kidney Dis. 2013; 62(3):577–586. [PubMed: 23523239]).
Study details	Adults Study name None Study location US Study setting Transplant centres Study dates 2006 - 2012 Duration of follow-up 3 years Loss to follow-up Donors: 21 out of 203 (10.3%); Controls: 28 out of 201 (13.9%) Sources of funding

	The National Institutes of Health.
Inclusion criteria	Age 18 years and older
Exclusion criteria	Cancer Invasive cancer Other Unable or unwilling to give informed consent; allergy to intravenous radiocontrast or seafood; kidney disease (especially proteinuria); active infection; cardiovascular disease; diabetes; psychiatric disorders; and pregnancy.
Phenomenon of interest	Rate of decline in eGFR Slope of the mGFR between 6 and 36 months after donation mGFR or eGFR mGFR; eGFR (CKD-EPI equation, 4-variable formula) Blood test Iohexol; creatinine, cystatin-C
Subgroups	Healthy adults/children and young people Donors and healthy controls Age

Study arms

Controls (N = 201)
Controls were required to meet the same donor eligibility criteria as donors. However, controls did not undergo renal imaging or any invasive testing.

Study details	Loss to follow-up 28 out of 201 (10.3%) participants.
Inclusion criteria	Other Any healthy individual who could theoretically be a donor at the study site, not just siblings of enrolled donors.

Baseline characteristics	Female 67.7% Age Mean 43.1 years (SD 11.9) Ethnicity White 95.0% Diabetes 0% Hypertension 4.5% Albuminuria/proteinuria Median (IQR): UPCR g/g 61 (50,114); UACR mg/g 5.0 (4.0,6.9) eGFR mL/min/1.73m2 Mean (SD): mGFR 96.9 (15.3); eGFR-creatinine 100.1 (16.0); eGFR-cystatinC 102.8 (17.6); eGFR-creatinine-cystatinC 102.0 (16.3)

Donors (N = 203)

Kidney donors were enrolled after acceptance for donation, but before donation had taken place.

Study details	Loss to follow-up 21 out of 203 (13.9%) participants.
Inclusion criteria	Other Any potential living kidney donor.
Baseline characteristics	Female 68.0% Age Mean 43.4 years (SD 11.3) Ethnicity White 94.6% Diabetes

	0% Hypertension 3.0% Albuminuria/proteinuria Median (IQR): UPCR g/g 66 (50,128); UACR mg/g 5.0 (3.8,5.8) eGFR mL/min/1.73m2 Mean (SD): mGFR 96.9 (15.3); eGFR-creatinine 99.2 (14.4); eGFR-cystatinC 103.2 (15.4); eGFR-creatinine-cystatinC 102.0 (13.9)

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	Yes
	Were patients recruited consecutively?	Unclear
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Yes
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes

Section	Question	Answer
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	Yes
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Directly applicable

Madero, 2017

Bibliographic Reference	Madero, Magdalena; Katz, Ronit; Murphy, Rachel; Newman, Anne; Patel, Kushang; Ix, Joachim; Peralta, Carmen; Satterfield, Suzanne; Fried, Linda; Shlipak, Michael; Sarnak, Mark; Comparison between Different Measures of Body Fat with Kidney Function Decline and Incident CKD.; Clinical journal of the American Society of Nephrology : CJASN; 2017; vol. 12 (no. 6); 893-903

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Adults Study name Health ABC Study location US Study setting Field centres Study dates 1997 - 2007 Duration of follow-up Median 8.9 years Loss to follow-up 350 out of 3,075 (11.3%) participants. Sources of funding The Intramural Research Program of the National Institutes of Health and the National Institute on Aging; the National Institute of Nursing Research; and CONACYT.
Inclusion criteria	Age 70 to 79 years Other All Health ABC participants with CT scan measurements at baseline and at least two measurements of cystatin C (the first at the time of abdominal CT).
Baseline characteristics	Sample size 2,489 Female 51.0% Age Mean 74 years (SD 3) Ethnicity

	Black (39.0%) Diabetes 15.0% Hypertension 59.0% Albuminuria/proteinuria Median UACR mg/g 8 (IQR 5,19) eGFR mL/min/1.73m2 Mean eGFR-cystatinC 88 (SD 18)
Phenomenon of interest	Rate of decline in eGFR Change in KF was defined by calculating the rates of change in eGFRcysC using two or three measurements of cystatin C. Linear mixed models with random intercepts and slopes were used to estimate and compare linear trends in mean eGFR. mGFR or eGFR eGFR; estimated using the formula: 133 x minutes (Scys/0.8,1)-0.499 x maximum (Scys/0.8,1)-1.328 x 0.996age (x 0.932 for women). This formula was developed from the pooling of several cohorts with measured GFR. Blood test Cystatin-C
Subgroups	Age

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes

Section	Question	Answer
	Were the cases collected in more than one centre?	Yes
	Were patients recruited consecutively?	Unclear
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Partial *(Exclusion criteria were not reported.)*
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	Yes
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Low

Section	Question	Answer
	Applicability	Directly applicable

Malmgren, 2020

Bibliographic Reference	Malmgren, L.; Mcguigan, F.E.; Christensson, A.; Akesson, K.E.; Longitudinal Changes in Kidney Function Estimated from Cystatin C and Its Association with Mortality in Elderly Women; Nephron; 2020; vol. 144 (no. 6); 290-298

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Adults Study name Osteoporosis Prospective Risk Assessment (OPRA) cohort Study location Sweden Study setting Bone health study Study dates Recruitment was from 1995 to 1998 Duration of follow-up 10 years

	Loss to follow-up 616 out of 981 (62.8%) Sources of funding This work was supported by grants from the Swedish Research Council (2018-02981); Greta and Johan Kock Foundation; A. Påhlsson Foundation; A. Osterlund Foundation; H Järnhardt Foundation; King Gustav V 80-year Fund; Swedish Rheumatism Foundation; Royal Physiographic Society of Lund; Swedish Kidney Foundation, Njurstiftelsen; Skåne University Hospital Research Fund; and Research and Development Council of Region, Skåne, Sweden.
Inclusion criteria	Other Women were randomly selected without exclusion criteria
Baseline characteristics	Sample size 981 Female 100% Age All 75 years old at baseline Diabetes 7% Hypertension 39% eGFR mL/min/1.73m2 CKD-EPIcysC, mL/min/1.73m²: mean 63 (SD 18)
Phenomenon of interest	Rate of decline in eGFR Change in kidney function over time using a mixed model with a random intercept. In this model, kidney function (eGFR estimated by CKD -EPIcysC) was used as a linear variable using all 3 time points (ages 75, 80, and 85 years). mGFR or eGFR eGFR; CKD-EPIcysC equation Blood test cystatin-C

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	Unclear
	Were patients recruited consecutively?	Unclear
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Yes
	Did patients enter the study at a similar point in the disease?	Unclear
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	Yes
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes

Section	Question	Answer
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Directly applicable

Melsom, 2019

Bibliographic Reference Melsom, Toralf; Nair, Viji; Schei, Jorgen; Mariani, Laura; Stefansson, Vidar T N; Harder, Jennifer L; Jenssen, Trond G; Solbu, Marit D; Norvik, Jon Viljar; Looker, Helen; Knowler, William C; Kretzler, Matthias; Nelson, Robert G; Eriksen, Bjorn O; Correlation Between Baseline GFR and Subsequent Change in GFR in Norwegian Adults Without Diabetes and in Pima Indians.; American journal of kidney diseases : the official journal of the National Kidney Foundation; 2019; vol. 73 (no. 6); 777-785

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Adults
Phenomenon of interest	Rate of decline in eGFR GFR measurements were analysed in a linear mixed regression model with a random intercept and slope using an unstructured covariance matrix.
Subgroups	Ethnicity

Study arms

RENIS cohort (N = 1594)
Norwegians

Study details	Study name RENIS-T6 Study location Norway Study setting Community-based Study dates 2007 - 2015 Duration of follow-up Median 5.6 years Loss to follow-up 295 out of 1,564 (18.8%) participants. Sources of funding The Northern Norway Regional Health Authority and a grant from Boehringer Ingelheim.
Inclusion criteria	Age 50 to 62 years Other Those who did not report cardiovascular disease, kidney disease, or diabetes.
Exclusion criteria	Other Technical failure in GFR measurement; diabetes at baseline according to their fasting plasma samples or hemoglobin A1c levels.
Baseline characteristics	Sample size 1,594 Female 51.0%

	Age Mean 58.1 years (SD 3.8) Diabetes 0% Hypertension Antihypertensive medication (18.0%) Albuminuria/proteinuria Median UACR mg/g 2.0 (IQR 0.9, 4.8) eGFR mL/min/1.73m2 Mean 93.8 (SD 14.3)
Phenomenon of interest	mGFR or eGFR mGFR Blood test Iohexol

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	No
	Were patients recruited consecutively?	Yes
Study population	Were the characteristics of the patients included in the study described?	Yes

Section	Question	Answer
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Yes
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	Yes
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Directly applicable

Minutolo, 2020

Bibliographic Reference	Minutolo, R.; Gabbai, F.B.; Chiodini, P.; Provenzano, M.; Borrelli, S.; Garofalo, C.; Bellizzi, V.; Russo, D.; Conte, G.; De Nicola, L.; Sex Differences in the Progression of CKD Among Older Patients: Pooled Analysis of 4 Cohort Studies; American Journal of Kidney Diseases; 2020; vol. 75 (no. 1); 30-38

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Adults Study name 4 cohorts: TABLE-CKD; NEPHRO-SUN; RECORD-IT; NEPHRO-FEDERICO II Study location Italy Study setting Nephrology clinics Study dates 1999 - 2017 Duration of follow-up Median 4.2 years Loss to follow-up 13 out of 3212 (0.4%) participants. Sources of funding This research did not receive any grant, funds, fees, or support.
Inclusion criteria	CKD Consecutive patients with CKD under stable nephrology care for at least 6 months
Exclusion criteria	Renal replacement therapy

	Cancer Active malignancy Other Acute kidney injury in the 6 months before the baseline visit, or advanced liver or heart disease. Additional exclusion criteria were undefined cause of CKD and poor adherence to therapy in TABLE-CKD and immunosuppressive drugs, pregnancy, and urinary protein excretion >5 g/d in NEPHRO-FEDERICO II. For the purposes of the present study, additional exclusion criteria were duplicate patients, missing information for follow-up, and eGFR >45 mL/min/1.73 m². This latter criterion was used to focus on patients with moderate to advanced CKD, which previous studies have shown is the threshold for the onset of the major CKD complications and notable change in the risk for ESKD and death.
Baseline characteristics	Sample size TABLE-CKD (n=955); NEPHRO-SUN (n=351); RECORD-IT (n=702); NEPHRO-FEDERICO II (n=327) Female 43.8% Age Mean 67.1 years (SD 14.0) Diabetes 29.2% Albuminuria/proteinuria Median proteinuria g/d 0.55 (IQR 0.17, 1.40) eGFR mL/min/1.73m2 Mean 26.9 (SD 10.4)
Phenomenon of interest	Rate of decline in eGFR Slope of change in eGFR mGFR or eGFR eGFR; CKD-EPI Blood test Creatinine
Subgroups	Gender

Study arms

Men (N = 1311)	
Baseline characteristics	Sample size TABLE-CKD (n=531); NEPHRO-SUN (n=195); RECORD-IT (n=404); NEPHRO-FEDERICO II (n=181) Age Mean 67.1 years (SD 13.9) Diabetes 28.5% Albuminuria/proteinuria Median proteinuria g/d 0.69 (IQR 0.19, 1.60) eGFR mL/min/1.73m2 Mean 27.6 (SD 10.2)
Women (N = 1024)	
Baseline characteristics	Sample size TABLE-CKD (n=424); NEPHRO-SUN (n=156); RECORD-IT (n=298); NEPHRO-FEDERICO II (n=146) Age Mean 67.1 years (SD 14.2) Diabetes 30.0% Albuminuria/proteinuria Median proteinuria g/d 0.45 (IQR 0.14-1.10) eGFR mL/min/1.73m2 Mean 26.0 (SD 10.6)

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	Yes
	Were patients recruited consecutively?	Yes
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Yes
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	Yes
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes

Section	Question	Answer
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Partially applicable *(Rate of decline in eGFR was a secondary outcome.)*

Moriya, 2017

Bibliographic Reference Moriya, Tatsumi; Tanaka, Shiro; Sone, Hirohito; Ishibashi, Shun; Matsunaga, Satoshi; Ohashi, Yasuo; Akanuma, Yasuo; Haneda, Masakazu; Katayama, Shigehiro; Patients with type 2 diabetes having higher glomerular filtration rate showed rapid renal function decline followed by impaired glomerular filtration rate: Japan Diabetes Complications Study.; Journal of diabetes and its complications; 2017; vol. 31 (no. 2); 473-478

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Adults Study name JDCS Study location

	Japan Study setting Part of a nationwide multi-centred randomised trial in hospitals specialising in diabetes care. Study dates 1996 - 2004 Duration of follow-up 8 years Loss to follow-up 33.5% Sources of funding The Ministry of Health, Labor and Welfare of Japan
Inclusion criteria	Age 40 to 70 years Other Type 2 diabetes and HbA1C levels of >6.5%; serum creatinine measurements for at least 3 years.
Exclusion criteria	Other Non-diabetic nephropathy, nephrotic syndrome, serum creatinine levels >120 μmol/l, patients without baseline diabetic retinopathy assessment.
Baseline characteristics	Sample size 1,407 Female 47.4% Age Mean 59 years (SD 7) Diabetes All with type 2 diabetes Albuminuria/proteinuria Median UACR 16.2 mg/gCr (range 0.1, 299.5) eGFR mL/min/1.73m2 Mean 87.5 (SD 29.1)

Phenomenon of interest	Rate of decline in eGFR The annual eGFR decline rates of each patient were calculated as the regression coefficients of univariate linear regression models. mGFR or eGFR eGFR; MDRD formula modified for Japanese population Blood test Creatinine
Subgroups	eGFR categories

Study arms

G1 eGFR ≥120 (N = 157)

Baseline characteristics	Female 59.9% Age Mean 60 years (SD 7) Diabetes All with type 2 diabetes Hypertension Treated with antihypertensive agent 28.0%

G2 eGFR ≥90 <120 (N = 355)

Baseline characteristics	Female 53.0% Age Mean 57 years (SD 7) Diabetes All with type 2 diabetes

	Hypertension Treated with antihypertensive agent 23.7%
G3 eGFR ≥60 <90 (N = 735)	
Baseline characteristics	Female 40.0% Age Mean 59 years (SD 7) Diabetes All with type 2 diabetes Hypertension Treated with antihypertensive agent 28.1%
G4 eGFR <60 (N = 160)	
Baseline characteristics	Female 56.9% Age Mean 62 years (SD 5) Diabetes All with type 2 diabetes Hypertension Treated with antihypertensive agent 21.4%

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	Yes
	Were patients recruited consecutively?	Unclear
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Yes
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	Yes
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes

Section	Question	Answer
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Directly applicable

Ozyilmaz, 2017

Bibliographic Reference Ozyilmaz, Akin; de Jong, Paul E; Bakker, Stephan J L; Visser, Sipke T; Thio, Chris; Gansevoort, Ron T; PREVEND Study, Group; Screening for elevated albuminuria and subsequently hypertension identifies subjects in which treatment may be warranted to prevent renal function decline.; Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association; 2017; vol. 32 (no. suppl2); ii200-ii208

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Adults Study name PREVEND Study location The Netherlands Study setting General population invited to visit a study outpatient clinic

	Study dates Baseline screening in 1997 - 1998 Duration of follow-up Median 11.3 years Loss to follow-up None Sources of funding grants from the Dutch Kidney Foundation and the University Medical Center Groningen, The Netherlands. Reagents for assessments of cystatin C were provided by Gentian AS (Moss, Norway).
Inclusion criteria	Age 20 to 75 years
Exclusion criteria	Other Self-reported diabetes or known kidney disease at baseline.
Phenomenon of interest	Rate of decline in eGFR To calculate annual change in eGFR per individual a linear regression line was drawn through all available eGFR values. mGFR or eGFR eGFR; CKD-EPI creatinine-cystatinC equation Blood test Creatinine; cystatin-C
Subgroups	Age Gender Hypertension Albuminuria

Study arms

Normoalbuminuria and no hypertension (N = 4397)

Elevated albuminuria was defined as an albumin concentration ≥20 mg/L in the first morning urine sample confirmed by an albumin excretion ≥30 mg/day in two 24-h urines. Hypertension was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg or the use of antihypertensive medication.

Baseline characteristics	Female 55.0% Age Mean 46 years (SD 11) Ethnicity Caucasian 95.9% Albuminuria/proteinuria Median UACR mg/mmol 0.7 (IQR 0.3, 4.7) eGFR mL/min/1.73m2 Mean 99.1 (SD 14.5)

Normoaluminuria and new hypertension (N = 949)

Elevated albuminuria was defined as an albumin concentration ≥20 mg/L in the first morning urine sample confirmed by an albumin excretion ≥30 mg/day in two 24-h urines. Hypertension was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg or the use of antihypertensive medication.

Baseline characteristics	Female 39.0% Age Mean 56 years (SD 12) Ethnicity Caucasian 97.9% Albuminuria/proteinuria Median UACR mg/mmol 0.9 (IQR 0.3, 4.8) eGFR mL/min/1.73m2 Mean 90.7 (SD 16.1)

Normoalbuminuria and known hypertension (N = 521)

Elevated albuminuria was defined as an albumin concentration ≥20 mg/L in the first morning urine sample confirmed by an albumin excretion ≥30 mg/day in two 24-h urines. Hypertension was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg or the use of antihypertensive medication. Hypertension was considered to be known when the subject involved reported use of blood pressure-lowering medication or was known to use such medication from pharmacy records.

Baseline characteristics	Female 52.0% Age Mean 60 years (SD 10) Ethnicity Caucasian 94.8% Albuminuria/proteinuria Median UACR mg/mmol 1.0 (IQR 0.3, 5.6) eGFR mL/min/1.73m2 Mean 84.1 (SD 17.4)

Elevated albuminuria and no hypertension (N = 229)

Elevated albuminuria was defined as an albumin concentration ≥20 mg/L in the first morning urine sample confirmed by an albumin excretion ≥30 mg/day in two 24-h urines. Hypertension was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg or the use of antihypertensive medication.

Baseline characteristics	Female 40.0% Age Mean 50 years (SD 12) Ethnicity Caucasian 94.3% Albuminuria/proteinuria Median UACR mg/mmol 4.0 (IQR 1.3, 79.2)

	eGFR mL/min/1.73m2 Mean 92.9 (SD 17.6)

Elevated albuminuria and new hypertension (N = 246)

Elevated albuminuria was defined as an albumin concentration ≥20 mg/L in the first morning urine sample confirmed by an albumin excretion ≥30 mg/day in two 24-h urines. Hypertension was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg or the use of antihypertensive medication.

Baseline characteristics	Female 26.0% Age Mean 58 years (SD 11) Ethnicity Caucasian 98.0% Albuminuria/proteinuria Median UACR mg/mmol 4.4 (IQR 1.3, 64.6) eGFR mL/min/1.73m2 Mean 85.8 (SD 18.7)

Elevated albuminuria and known hypertension (N = 129)

Elevated albuminuria was defined as an albumin concentration ≥20 mg/L in the first morning urine sample confirmed by an albumin excretion ≥30 mg/day in two 24-h urines. Hypertension was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg or the use of antihypertensive medication. Hypertension was considered to be known when the subject involved reported use of blood pressure-lowering medication or was known to use such medication from pharmacy records.

Baseline characteristics	Female 30.0% Age Mean 62 years (SD 9) Ethnicity Caucasian 95.3%

	Albuminuria/proteinuria Median UACR mg/mmol 5.7 (IQR 1.6, 104.7) eGFR mL/min/1.73m2 Mean 74.5 (SD 21.0)

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	No
	Were patients recruited consecutively?	Unclear
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Yes
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes

Section	Question	Answer
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	No *(There were no losses to follow-up.)*
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Directly applicable

Pottel, 2019

Bibliographic Reference	Pottel, Hans; Bjork, Jonas; Bokenkamp, Arend; Berg, Ulla; Asling-Monemi, Kajsa; Selistre, Luciano; Dubourg, Laurence; Hansson, Magnus; Littmann, Karin; Jones, Ian; Sjostrom, Per; Nyman, Ulf; Delanaye, Pierre; Estimating glomerular filtration rate at the transition from pediatric to adult care.; Kidney international; 2019; vol. 95 (no. 5); 1234-1243

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Children and young people Study name European Kidney Function Consortium Study location There were 6 different cohorts from Europe but only a subset of the cohort from France (Lyon) was used to report the rate of decline in GFR during transition age from paediatric to adult care. Study setting Transition paediatric to adult care Study dates 2004 - 2016 Duration of follow-up Average 5.8 years Loss to follow-up None Sources of funding This research received no specific grant from any funding agency.
Inclusion criteria	Other Non transplanted patients with serial data passing through the transition age of 18 years (i.e., at least 1 measurement of GFR before and at least 1 after the age of 18).
Exclusion criteria	None None reported
Baseline characteristics	Sample size 136 Female 51.5% Age Mean 14.6 years (SD 2.2)

Phenomenon of interest	Rate of decline in eGFR Mean slope of the regression lines calculated per patient. mGFR or eGFR mGFR Blood test Inulin renal clearance

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	No
	Were patients recruited consecutively?	Unclear
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Partial *(Exclusion criteria were not reported.)*
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes

Section	Question	Answer
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	No *(There were no losses to follow-up.)*
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Partially applicable *(Rate of decline in eGFR was a secondary outcome.)*

Pruijm, 2018

Bibliographic Reference	Pruijm, Menno; Milani, Bastien; Pivin, Edward; Podhajska, Agata; Vogt, Bruno; Stuber, Matthias; Burnier, Michel; Reduced cortical oxygenation predicts a progressive decline of renal function in patients with chronic kidney disease.; Kidney international; 2018; vol. 93 (no. 4); 932-940

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Adults Study name None Study location Switzerland Study setting Outpatient clinic (participants with CKD and participants with hypertension); healthy controls were recruited by local advertisement. Study dates Not reported Duration of follow-up Mean 3 years Loss to follow-up Participants with CKD (8 out of 120, 6.6%); participants with hypertension (15 out of 62, 24.1%); controls (20 out of 44, 45.4%). Sources of funding Grants from the Swiss National Science Foundation.
Inclusion criteria	Age ≥ 18 years
Exclusion criteria	Renal replacement therapy CKD patients could not participate if they were on renal replacement therapy, had a single kidney, had autosomal dominant polycystic kidney disease, or acute kidney injury during the previous 6 months, according to the KDIGO definition. Other Contraindication to MRI such as claustrophobia or the presence of a pacemaker or other implanted metallic device, or the presence of life-threatening comorbidities with a short life expectancy.

Phenomenon of interest	Rate of decline in eGFR The rate of change of eGFR slope was based on all available creatinine-based eGFR values from baseline until the last follow-up visit. mGFR or eGFR eGFR; MDRD Blood test Creatinine
Subgroups	Healthy adults/children and young people Hypertension

Study arms

CKD (N = 112)

CKD was defined as an eGFR ≤60 ml/min per 1.73 m2 or the presence of albuminuria, irrespective of its cause.

Baseline characteristics	Female 31.9% Age Mean 56 years (SD 14) Diabetes 25.0% Hypertension 79.8% eGFR mL/min/1.73m2 Mean 55 (SD 29)

Arterial hypertension without CKD (N = 47)

Arterial hypertension was defined as a mean office blood pressure ≥140/90 mm Hg measured on more than 1 occasion or an office blood pressure <140/90 mm Hg while taking 1 or more antihypertensive drugs.

Baseline characteristics	Female 35.0% Age Mean 56 years (SD 11) Diabetes 16.7% Hypertension 100% eGFR mL/min/1.73m2 Mean 90 (SD 15)

Healthy controls (N = 24)

Controls were normotensive, untreated healthy individuals without a history of kidney disease or other concomitant morbidity and without structural renal abnormalities on a screening ultrasound scan.

Baseline characteristics	Female 48.0% Age Mean 47 years (SD 11) Diabetes 0% Hypertension 0% eGFR mL/min/1.73m2 Mean 97 (SD 14)

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	No
	Were patients recruited consecutively?	Unclear
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Yes
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	Yes
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes

Section	Question	Answer
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Directly applicable

Qin, 2015

Bibliographic Reference Qin, Xianhui; Wang, Yuejuan; Li, Youbao; Xie, Di; Tang, Genfu; Wang, Binyan; Wang, Xiaobin; Xu, Xin; Xu, Xiping; Hou, Fanfan; Risk factors for renal function decline in adults with normal kidney function: a 7-year cohort study.; Journal of epidemiology and community health; 2015; vol. 69 (no. 8); 782-8

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Adults Study name None Study location China Study setting Epidemiological study of metabolic syndrome conducted in rural communities. Study dates 2003 - 2011

	Duration of follow-up Median 7.08 years Loss to follow-up 383 out of 2901 (13.2%) participants. Sources of funding The Major State Basic Research Development Program of China, the Public Welfare and Health Sector Research Project and Major Scientific and Technological Planning Project of Guangzhou City, and the National Nature and Science Grant.
Exclusion criteria	Cancer Other Coronary heart disease or stroke, hypertension, diabetes, or with any missing data about age, sex, height, weight, waist circumference, smoking status, drinking status, systolic blood pressure, diastolic blood pressure, fasting plasma glucose, total cholesterol, triglyceride, high-density lipoprotein cholesterol, self-reported health status change, education and physical activity levels, age <40 years, and participants with baseline eGFR <60 mL/min/1.73 m².
Baseline characteristics	Sample size 2518 Female 46.9% Age Mean 50.2 years (SD 5.9) eGFR mL/min/1.73m2 Mean 108.3 (SD 13.4)
Phenomenon of interest	Rate of decline in eGFR The annual eGFR change was calculated as (eGFR at baseline - eGFR at revisit)/follow-up year. mGFR or eGFR eGFR; CKD-EPI Blood test Creatinine
Subgroups	Gender

Study arms

Men (N = 1337)	
Baseline characteristics	Age Mean 51.0 years (SD 5.9) eGFR mL/min/1.73m2 Mean 107.1 (SD 13.1)
Women (N = 1181)	
Baseline characteristics	Age Mean 49.3 years (SD 5.7) eGFR mL/min/1.73m2 Mean 109.5 (SD 13.6)

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	No
	Were patients recruited consecutively?	Unclear
Study population	Were the characteristics of the patients included in the study described?	Yes

Section	Question	Answer
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Yes
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	Yes
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Partially applicable *(Rate of decline in eGFR was a secondary outcome.)*

Reichel, 2020

Bibliographic Reference	Reichel, H.; Zee, J.; Tu, C.; Young, E.; Pisoni, R.L.; Stengel, B.; Duttlinger, J.; Lonnemann, G.; Robinson, B.M.; Pecoits-Filho, R.; Fliser, D.; Chronic kidney disease progression and mortality risk profiles in Germany: results from the Chronic Kidney Disease Outcomes and Practice Patterns Study; Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association; 2020

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Adults Study name CKDopps Study location Germany Study setting Nephrology practices Study dates 2013 - 2018 Duration of follow-up Median 2.4 years Loss to follow-up 163 out of 1,834 (8.8%) participants. Sources of funding The Dialysis Outcomes and Practice Patterns Study (DOPPS) Program is funded by a consortium of private industry, public funders, and professional societies.

Inclusion criteria	eGFR eGFR between 15 and 60 mL/min/1.73m² Other Those who provided written consent; at least 6 months of eGFR data.
Exclusion criteria	Other Those who reached end-stage kidney disease before 6 months.
Baseline characteristics	Sample size 1,834 Female 42.0% Age Median 75 years (IQR 67, 80) Diabetes 42.0% Hypertension 85.0% Albuminuria/proteinuria Normal to mildly increased (19%), moderately increased (17%), very high (13%), nephrotic range (6%), missing (45%) eGFR mL/min/1.73m2 Median 25 (IQR 21, 31)
Phenomenon of interest	Rate of decline in eGFR Individual patient-level linear models were used to estimate changes in eGFR over each patient's follow-up time. mGFR or eGFR eGFR; MDRD Blood test Creatinine
Subgroups	eGFR categories

Study arms

eGFR ≥30 (N = 486)	
Baseline characteristics	Female 36.0% Age Median 73 years (IQR 64, 78) Diabetes 39.0% Hypertension 86.0% Albuminuria/proteinuria Normal to mildly increased (27%), moderately increased (17%), very high (12%), nephrotic range (3%), missing (41%) eGFR mL/min/1.73m2 Median 40 (IQR 35, 48)
eGFR <30 (N = 1348)	
Baseline characteristics	Female 45.0% Age Median 75 years (IQR 68, 81) Diabetes 42.0% Hypertension 85.0% Albuminuria/proteinuria Normal to mildly increased (16%), moderately increased (17%), very high (13%), nephrotic range (7%), missing (47%)

	eGFR mL/min/1.73m2 Median 23 (IQR 19, 26)

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	Yes
	Were patients recruited consecutively?	Yes
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Yes
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes

Section	Question	Answer
	Were losses to follow-up reported?	Yes
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Partially applicable *(Rate of decline in eGFR was a secondary outcome.)*

Rowe, 1976

Bibliographic Reference	Rowe, John W.; Andres, Reubin; Tobin, Jordan D.; Norris, Arthur H.; Shock, Nathan W.; The Effect of Age on Creatinine Clearance in Men: A Cross-sectional and Longitudinal Study2; J Gerontol; 1976; vol. 31 (no. 2); 155-163

Study Characteristics

Study type	Uncontrolled prospective study

Study details	Adults Study name Baltimore Longitudinal Study of Aging Study location US Study setting Community-dwelling volunteers Study dates 1961 - 1971 Duration of follow-up 2 years Loss to follow-up Not reported Sources of funding Not reported
Inclusion criteria	Age 17 to 96 years Other Community-dwelling men
Exclusion criteria	Other Nephrolithiasis; Urinary tract infection; Gout; Prostatectomy; Congestive heart failure; Coronary heart disease; Cerebrovascular disease; Diabetes mellitus; Abnormal urinalysis; Miscellaneous renal disease.
Baseline characteristics	Sample size 586
Phenomenon of interest	Rate of decline in eGFR In longitudinal analysis the annual rate of change of creatinine clearance was computed as the slope of the regression line for each subject with three of more "normal" data points. mGFR or eGFR eGFR; equation not reported

	Blood test Creatinine
Subgroups	Age

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	No
	Were patients recruited consecutively?	Unclear
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Yes
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes

Section	Question	Answer
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	No
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	No
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Directly applicable

Skupien, 2019

Bibliographic Reference Skupien, Jan; Smiles, Adam M; Valo, Erkka; Ahluwalia, Tarunveer S; Gyorgy, Beata; Sandholm, Niina; Croall, Stephanie; Lajer, Maria; McDonnell, Kevin; Forsblom, Carol; Harjutsalo, Valma; Marre, Michel; Galecki, Andrzej T; Tregouet, David-Alexandre; Wu, Chun Yi; Mychaleckyj, Josyf C; Nickerson, Helen; Pragnell, Marlon; Rich, Stephen S; Pezzolesi, Marcus G; Hadjadj, Samy; Rossing, Peter; Groop, Per-Henrik; Krolewski, Andrzej S; Variations in Risk of End-Stage Renal Disease and Risk of Mortality in an International Study of Patients With Type 1 Diabetes and Advanced Nephropathy.; Diabetes care; 2019; vol. 42 (no. 1); 93-101

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Adults Loss to follow-up Not reported Sources of funding The JDRF DNCRI subproject “Search for genes determining time to onset of ESRD in type 1 diabetes patients with proteinuria”, National Institutes of Health grants, Joslin Diabetes Research Center grant, the Folkhalsan Research Foundation, the Wilhelm and Else Stockmann Foundation, the Liv och Halsa Society, Helsinki University Central Hospital Research Funds, and the Academy of Finland.
Inclusion criteria	eGFR eGFR ≥30 mL/min/1.73 m² Other Type 1 diabetes; those who were alive within 1 year of follow-up and had at least a 42-month follow-up if free from ESRD.
Exclusion criteria	None None reported
Phenomenon of interest	Rate of decline in eGFR Both the eGFR time-series data and times to ESRD or censoring were used to obtain estimates of mean rates of renal (eGFR) decline in the cohorts, an approach that is robust with regard to heterogeneity of baseline renal function (eGFR) at enrollment and variable duration of follow-up. mGFR or eGFR eGFR; CKD-EPI Blood test Creatinine
Subgroups	Diabetes

Study arms

Joslin cohort (N = 432)

Study details	Study location US Study setting Diabetes clinic Study dates 1991 - 2013 Duration of follow-up 11 to 12 years
Baseline characteristics	Female 42.8% Age Median 37 years (IQR 32, 43) Hypertension Antihypertensive treatment 74.8% Albuminuria/proteinuria Median UACR mg/g 718 (IQR 420, 1,337) eGFR mL/min/1.73m2 Median 88 (IQR 69, 109)

FinnDiane cohort (N = 486)

Study details	Study location Finland Study setting Nationwide multicenter study Study dates 1997 - 2013 Duration of follow-up 11 to 12 years

Baseline characteristics	Female 39.7% Age Median 39 years (IQR 32, 48) Hypertension Antihypertensive treatment 94.8% Albuminuria/proteinuria Median UACR mg/g 321 (IQR 122, 786) eGFR mL/min/1.73m2 Median 70 (IQR 49, 93)

Steno cohort (N = 368)

Study details	Study location Denmark Study setting Diabetes centre Study dates 1993 - 2009 Duration of follow-up Approximately 16 years
Baseline characteristics	Female 38.9% Age Median 40 years (IQR 33, 48) Hypertension Antihypertensive treatment 81.5% Albuminuria/proteinuria Median UACR mg/g 581 (IQR 273, 1,489)

	eGFR mL/min/1.73m2 Median 75 (IQR 58, 96)
INSERM cohort (N = 232)	
Study details	Study location France Study setting Participants from GENEDIAB, GENESIS and other centres Study dates Recruitment was 1993 - 1998 Duration of follow-up 11 to 12 years
Baseline characteristics	Female 40.1% Age Median 41 years (IQR 32, 50) Hypertension Antihypertensive treatment 82.3% Albuminuria/proteinuria Median urinary albumin mg/L 497 (IQR 181, 1110) eGFR mL/min/1.73m2 Median 74 (IQR 56, 94)

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	Yes
	Were patients recruited consecutively?	Yes
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Partial *(Exclusion criteria were not reported.)*
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	No
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes

Section	Question	Answer
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Directly applicable

Sukmark, 2014

Bibliographic Reference	Sukmark, Theerapon; Sukmark, Supanun; Predictors of faster progression in chronic kidney disease.; Journal of the Medical Association of Thailand = Chotmaihet thangphaet; 2014; vol. 97 (no. 8); 812-9

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Adults Study name None Study location Thailand Study setting Community hospital

	Study dates 2008 - 2011 Duration of follow-up Median 3.0 years Loss to follow-up 33 out of 203 (16.2%) participants. Sources of funding Not reported
Inclusion criteria	CKD CKD categories 2 to 4
Exclusion criteria	Cancer Advanced stage cancer Other Serious systemic disease, refractory congestive heart failure, decompensated cirrhosis.
Baseline characteristics	Sample size 203 Female 45.8% Age Mean 65.7 years (SD 13.2) Diabetes 72.4% Albuminuria/proteinuria Dipsticks proteinuria: negative (23.1%); trace (24.4%); 1+ (21.9%); 2+ (16.2%); 3+ (14.4%) eGFR mL/min/1.73m2 Median 34.9 (range 15.1, 88.4)
Phenomenon of interest	Rate of decline in eGFR Decline overtime

	mGFR or eGFR eGFR; MDRD abbreviated equation Blood test Creatinine

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	No
	Were patients recruited consecutively?	Yes
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Yes
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes

Section	Question	Answer
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Partial *(There was no description about how the rate of decline in eGFR was estimated.)*
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	Yes
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Moderate
	Applicability	Directly applicable

Tsai, 2019

Bibliographic Reference	Tsai, C.-W.; Huang, H.-C.; Chiang, H.-Y.; Chung, C.-W.; Chiu, H.-T.; Liang, C.-C.; Yu, T.; Kuo, C.-C.; First-year estimated glomerular filtration rate variability after pre-end-stage renal disease program enrollment and adverse outcomes of chronic kidney disease; Nephrology,

dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association; 2019; vol. 34 (no. 12); 2066-2078

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Adults Study name CMUH105-REC3-068 Study location Taiwan Study setting Participants were enrolled from a Medical University Hospital Study dates 2003 - 2015 Duration of follow-up Median 2.5 years Loss to follow-up Not reported Sources of funding Ministry of Science and Technology of Taiwan
Inclusion criteria	Age 18 years CKD Based either on the working diagnoses of nephrologists or in accordance with the criteria outlined in the National Kidney Foundation (NKF) KDOQI guidelines Other

	Those who remained dialysis free for at least 12 months and had at least three eGFR measurements in the first year of the pre-ESRD program.
Exclusion criteria	None None reported
Baseline characteristics	Sample size 5,092 Female 43.5% Age Median 67.5 years (IQR 56.8, 76.3) Diabetes 33.7% Hypertension 51.5% Albuminuria/proteinuria Median UPCR 774 mg/g (IQR 212, 2101); median UACR 255 mg/g (IQR 47, 1494) eGFR mL/min/1.73m2 Median 34.3 (IQR 19.7, 50.0)
Phenomenon of interest	Rate of decline in eGFR Slope of the eGFR change in the first year by using a multilevel model including both a random intercept and slope with all eGFR measurements clustered within the patients mGFR or eGFR eGFR; abbreviated MDRD Blood test Creatinine

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	No
	Were patients recruited consecutively?	Yes
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Partial *(Exclusion criteria were not reported.)*
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	No
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes

Section	Question	Answer
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Directly applicable

Tsai, 2014

Bibliographic Reference	Tsai, Yi-Chun; Chiu, Yi-Wen; Tsai, Jer-Chia; Kuo, Hung-Tien; Lee, Su-Chu; Hung, Chi-Chih; Lin, Ming-Yen; Hwang, Shang-Jyh; Kuo, Mei-Chuan; Chen, Hung-Chun; Association of angiopoietin-2 with renal outcome in chronic kidney disease.; PloS one; 2014; vol. 9 (no. 10); e108862

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Adults Study name KMUHIRB-990198 Study location Taiwan Study setting Tertiary hospital

	Study dates 2006 - 2013 Duration of follow-up Mean 3.1 years Loss to follow-up 2.9% Sources of funding No support or funding to report
Inclusion criteria	CKD CKD categories 3 to 5 Other Those who had follow-up for one year at least in an integrated CKD program
Exclusion criteria	None None reported
Baseline characteristics	Sample size 621 Female 44.6% Age Mean 65.3 years (SD 12.7) Diabetes 38.5% Hypertension 85.7% Albuminuria/proteinuria UPCR >1 g/g 275 (49.3%) eGFR mL/min/1.73m2 Mean 21.8 (SD 12.6)

Phenomenon of interest	Rate of decline in eGFR The decline in renal function was assessed by the eGFR slope, defined as the regression coefficient between eGFR and time in units of ml/min per 1.73m² per year. All eGFR values available from enrollment to the end of the observation period were included for calculation. At least three eGFR values were required to estimate the eGFR slope. mGFR or eGFR eGFR; 4-variable MDRD Blood test Creatinine

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	No
	Were patients recruited consecutively?	Yes
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Partial *(Exclusion criteria were not reported.)*
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes

Section	Question	Answer
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	Yes
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Directly applicable

Vallianou, 2018

Bibliographic Reference	Vallianou, N; Stratigou, T; Paikopoulou, A; Apostolou, T; Vlassopoulou, B; Tsagarakis, S; Ioannidis, G; Monitoring of patients with type 2 diabetes and nephropathy in a specialized diabetic nephropathy clinic seems to be beneficial.; Diabetes & metabolic syndrome; 2018; vol. 12 (no. 5); 689-692

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Adults Study name None Study location Greece Study setting Not reported Study dates 2016 Duration of follow-up Mean 6.3 years Loss to follow-up Not reported Sources of funding Not reported
Inclusion criteria	Other None reported
Exclusion criteria	None None reported
Baseline characteristics	Sample size 106 Female 72.6%

	Age Mean 65 years (SD 10) Ethnicity All Caucasians Diabetes All type 2 diabetes Albuminuria/proteinuria Albuminuria: normo <30 (14.1%); micro 30 to 299 (36.6%); macro ≥300 (49.3%) eGFR mL/min/1.73m2 Mean 50 (SD 21)
Phenomenon of interest	Rate of decline in eGFR Annual eGFR deterioration mGFR or eGFR eGFR; CKD-EPI Blood test Creatinine

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	No

Section	Question	Answer
	Were patients recruited consecutively?	Unclear
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	No
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	No
	Were the relevant outcomes measured using appropriate objective/subjective methods?	No *(Rate of decline in eGFR was reported as 'annual eGFR deterioration' without a description of how it was estimated.)*
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	No
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes

Section	Question	Answer
Overall Risk of Bias	Risk of Bias	High
	Applicability	Partially applicable *(Rate of decline in eGFR was a secondary outcome.)*

van Londen, 2018

Bibliographic Reference van Londen, Marco; Wijninga, Anthony B; de Vries, Jannieta; Sanders, Jan-Stephan F; de Jong, Margriet F C; Pol, Robert A; Berger, Stefan P; Navis, Gerjan; de Borst, Martin H; Estimated glomerular filtration rate for longitudinal follow-up of living kidney donors.; Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association; 2018; vol. 33 (no. 6); 1054-1064

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Adults Study name None Study location The Netherlands Study setting University Medical Centre

	Study dates 1994 - 2012 Duration of follow-up 5 years Loss to follow-up 28 out of 377 (7.4%) participants. Sources of funding Veni grant from the Dutch Organization for Scientific Research
Inclusion criteria	Other Kidney donors who were normotensive or had an adequately regulated blood pressure with a maximum of two antihypertensive drugs.
Exclusion criteria	Other People with history of diabetes (or an abnormal glucose tolerance test), kidney disease or cardiovascular events who were excluded from kidney donation.
Baseline characteristics	Sample size 349 Female 54% Age Mean 51 years (SD 10) Ethnicity All Caucasians Albuminuria/proteinuria Mean proteinuria mg/L 0.09 (SD 0.14) eGFR mL/min/1.73m2 Mean mGFR-normalised for body surface area 103 mL/min/1.73m² (SD 16)
Phenomenon of interest	Rate of decline in eGFR Slopes were calculated as the difference in GFR between two time points divided by the time between these time points. mGFR or eGFR mGFR; normalised for body surface area

	Blood test I-iothalamate and I-hippurate infusion

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	No
	Were patients recruited consecutively?	Yes
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Yes
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes

Section	Question	Answer
	Were losses to follow-up reported?	Yes
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Directly applicable

van Rijn, 2018

Bibliographic Reference van Rijn, Marieke H C; Metzger, Marie; Flamant, Martin; Houillier, Pascal; Haymann, Jean-Philippe; van den Brand, Jan A J G; Froissart, Marc; Stengel, Benedicte; NephroTest Study, Group; Performance of creatinine-based equations for estimating glomerular filtration rate changes over time.; Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association; 2018

Study Characteristics

Study type	Uncontrolled prospective study

Study details	Adults Study name NephroTest study Study location France Study setting Nephrology Study dates Not reported Duration of follow-up Median 3.4 years Loss to follow-up None Sources of funding Grants from INSERM, French Ministry of Health, Agence de la Biome´decine, AURA, Roche, the Radboud Institute for Health Sciences, and the Dutch Kidney Foundation.
Inclusion criteria	Age Adults CKD CKD categories 1 to 4 Other People who were not on dialysis nor living with a kidney transplant, who were referred by nephrologists to three physiology departments for extensive annual workups.
Exclusion criteria	Other Baseline measured GFR <15 mL/min/1.73m² and missing serum creatinine data.
Baseline characteristics	Sample size 1,955 Female 33.1% Age

	Mean 58.7 years (SD 15.2) Ethnicity African origin 13.9% Diabetes 27.5% Hypertension 90.9% Albuminuria/proteinuria UACR mg/mmol 3 to 29 (33.8%); ≥30 (30.6%) eGFR mL/min/1.73m2 Mean (SD): mGFR 44.0 (19.0); eGFR with CKD-EPI 46.4 (22.2); eGFR with MDRD 44.5 (20.9)
Phenomenon of interest	Rate of decline in eGFR Absolute and relative slopes for mGFR and eGFR by using a linear mixed model with random intercept and slope. mGFR or eGFR mGFR; eGFR both CKD-EPI and MDRD Blood test Cr-EDTA renal clearance for mGFR; creatinine for eGFR

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	No

Section	Question	Answer
	Were patients recruited consecutively?	Yes
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Yes
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	No *(There were no losses at follow-up.)*
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Low

Section	Question	Answer
	Applicability	Directly applicable

Warren, 2018

Bibliographic Reference	Warren, Bethany; Rebholz, Casey M; Sang, Yingying; Lee, Alexandra K; Coresh, Josef; Selvin, Elizabeth; Grams, Morgan E; Diabetes and Trajectories of Estimated Glomerular Filtration Rate: A Prospective Cohort Analysis of the Atherosclerosis Risk in Communities Study.; Diabetes care; 2018; vol. 41 (no. 8); 1646-1653

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Adults Study name ARIC Study location US Study setting Four U.S. communities (Forsyth County, NC; Jackson, MS; suburban Minneapolis,MN; and Washington County, MD). Study dates 1987 - 2013 Duration of follow-up Over 26 years

	Loss to follow-up None Sources of funding National Heart, Lung, and Blood Institute; National Institutes of Health; National Institute of Diabetes and Digestive and Kidney Diseases.
Inclusion criteria	Other Not reported
Exclusion criteria	Other eGFR ≤15 mL/min/1.73 m² or end-stage renal disease at baseline; those who were not black or white race or who were black from the Minnesota or Maryland sites due to small sample size (n = 103), and those missing eGFR measurements.
Phenomenon of interest	Rate of decline in eGFR To estimate individual eGFR slopes over time, linear mixed-effects models with random intercepts and random slopes were used. These models were fit on diabetes status at baseline as a nominal variable to adjust the baseline level of eGFR and included an interaction term between diabetes status at baseline and time to estimate annual decline in eGFR by diabetes categories. mGFR or eGFR eGFR; CKD-EPI Blood test Creatinine
Subgroups	Diabetes

Study arms

No diabetes (N = 13698)

Baseline characteristics	Female 55.2% Age Mean 54.5 years (SD 5.7) Ethnicity

	Race–center: Forsyth County, NC–white (23.5%); Forsyth County, NC–black (2.9%); Jackson, MS–black (21.1%); Minneapolis, MN–white (26.8%); Washington County, MD–white (25.7%) Hypertension 31.4% eGFR mL/min/1.73m2 Mean 102.6 (SD 14.7)

Undiagnosed diabetes (N = 634)

Undiagnosed diabetes was defined as a fasting glucose ≥126 mg/dL or non-fasting glucose ≥200 mg/dL without medication or physician diagnosis.

Baseline characteristics	Female 48.4% Age Mean 56.0 years (SD 5.7) Ethnicity Race–center: Forsyth County, NC–white (16.7%); Forsyth County, NC–black (4.4%); Jackson, MS–black (31.1%); Minneapolis, MN–white (23.2%); Washington County, MD–white (24.6%) Hypertension 59.8% eGFR mL/min/1.73m2 Mean 103.3 (SD 17.5)

Diagnosed diabetes (N = 1185)

Diagnosed diabetes was defined as a self-report of physician diagnosis or use of glucose-lowering medication.

Baseline characteristics	Female 57.6% Age Mean 56.4 years (SD 5.7) Ethnicity

	Race–center: Forsyth County, NC–white (16.0%); Forsyth County, NC–black (4.8%); Jackson, MS–black (41.7%); Minneapolis, MN–white (12.7%); Washington County, MD–white (24.7%) Hypertension 60.1% eGFR mL/min/1.73m2 Mean 102.3 (SD 20.9)

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	Yes
	Were patients recruited consecutively?	Unclear
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Partial *(Inclusion criteria were not reported.)*
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes

Section	Question	Answer
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	No *(There were no losses to follow-up.)*
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Directly applicable

Yoshida, 2020

Bibliographic Reference Yoshida, Yui; Kashiwabara, Kosuke; Hirakawa, Yosuke; Tanaka, Tetsuhiro; Noso, Shinsuke; Ikegami, Hiroshi; Ohsugi, Mitsuru; Ueki, Kohjiro; Mita, Tomoya; Watada, Hirotaka; Koya, Daisuke; Mise, Koki; Wada, Jun; Shimizu, Miho; Wada, Takashi; Ito, Yumi; Narita, Ichiei; Kashihara, Naoki; Nangaku, Masaomi; Matsuyama, Yutaka; Conditions, pathogenesis, and progression of diabetic kidney disease and early decliner in Japan.; BMJ open diabetes research & care; 2020; vol. 8 (no. 1)

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Adults Study name None Study location Japan Study setting Patients with diabetes attending hospitals Study dates Not reported Duration of follow-up Mean 3.0 years Loss to follow-up Not reported Sources of funding Japan Agency for Medical Research and Development
Inclusion criteria	Other Diabetes diagnosed by Japanese guidelines
Exclusion criteria	Other Those with diabetes other than type 1 or type 2 diabetes; those whose measurement intervals were within 3 months; those who started maintenance dialysis during follow-up.
Baseline characteristics	Sample size 2,385 Female

	37% Age Median 64 years (IQR 55, 71) Diabetes Type 1 and type 2 diabetes eGFR mL/min/1.73m2 Median 70 (IQR 56, 85)
Phenomenon of interest	Rate of decline in eGFR To determine yearly eGFR decline rate, the differences between baseline and final measurements were calculated and divided by the follow-up period. mGFR or eGFR eGFR; MDRD adjusted for Japanese ethnicity Blood test Creatinine
Subgroups	Albuminuria eGFR categories

Study arms

Type 1 diabetes - No DKD (N = 134)

Type 1 diabetes without diabetic kidney disease (DKD)

Baseline characteristics	Female 55% Age Median 50 years (IQR 37, 62) eGFR mL/min/1.73m2 Median 87 (IQR 75, 100)

Type 1 diabetes - Low eGFR (N = 9)

Type 1 diabetes and eGFR <60 mL/min/1.73 m2 and normoalbuminuria (UACR <30 mg/gCr)

Baseline characteristics	Female 56% Age Median 67 years (IQR 63, 72) eGFR mL/min/1.73m2 Median 50 (IQR 43, 54)

Type 1 diabetes - Albuminuria (N = 27)

Type 1 diabetes and UACR ≥30 mg/gCr and normal eGFR (≥60 mL/min/1.73 m2)

Baseline characteristics	Female 48% Age Median 57 years (IQR 48, 62) eGFR mL/min/1.73m2 Median 77 (IQR 70-90)

Type 1 diabetes - Low eGFR and albuminuria (N = 14)

Type 1 diabetes and eGFR <60 mL/min/1.73 m2 and UACR ≥30 mg/gCr

Baseline characteristics	Female 43% Age Median 55 years (IQR 47, 66) eGFR mL/min/1.73m2 Median 40 (IQR 27, 56)

Type 1 diabetes - Overall (N = 184)

All participants with type 1 diabetes

Baseline characteristics	Female 53% Age Median 53 years (IQR 40, 64) eGFR mL/min/1.73m2 Median 82 (IQR 69, 97)

Type 2 diabetes - No DKD (N = 993)

Type 2 diabetes without DKD

Baseline characteristics	Female 36% Age Median 63 years (IQR 54, 70) eGFR mL/min/1.73m2 Median 78 (IQR 70-91)

Type 2 diabetes - Low eGFR (N = 266)

Type 2 diabetes and eGFR <60 mL/min/1.73 m2 and normoalbuminuria (UACR <30 mg/gCr)

Baseline characteristics	Female 38% Age Median 71 years (IQR 65, 76) eGFR mL/min/1.73m2 Median 52 (IQR 46, 56)

Type 2 diabetes - Albuminuria (N = 481)

Type 2 diabetes and UACR ≥30 mg/gCr and normal eGFR (≥60 mL/min/1.73 m2)

Baseline characteristics	Female 35% Age Median 62 years (IQR 54, 69) eGFR mL/min/1.73m2 Median 77 (IQR 68, 90)

Type 2 diabetes - Low eGFR and albuminuria (N = 414)
Type 2 diabetes and eGFR <60 mL/min/1.73 m2 and UACR ≥30 mg/gCr

Baseline characteristics	Female 35% Age Median 66 years (IQR 60, 75) eGFR mL/min/1.73m2 Median 44 (IQR 33, 52)

Type 2 diabetes - Overall (N = 2154)
All participants with type 2 diabetes

Baseline characteristics	Female 36% Age Median 65 years (IQR 57, 72) eGFR mL/min/1.73m2 Median 70 (IQR 56, 83)

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	Yes
	Were patients recruited consecutively?	Yes
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Yes
	Did patients enter the study at a similar point in the disease?	Yes
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	No
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes

Section	Question	Answer
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Directly applicable

Young, 2016

Bibliographic Reference Young, Bessie A; Katz, Ronit; Boulware, L Ebony; Kestenbaum, Bryan; de Boer, Ian H; Wang, Wei; Fulop, Tibor; Bansal, Nisha; Robinson-Cohen, Cassianne; Griswold, Michael; Powe, Neil R; Himmelfarb, Jonathan; Correa, Adolfo; Risk Factors for Rapid Kidney Function Decline Among African Americans: The Jackson Heart Study (JHS).; American journal of kidney diseases : the official journal of the National Kidney Foundation; 2016; vol. 68 (no. 2); 229-239

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Adults Study name JHS Study location US Study setting Participants were recruited from tri-county region (Hinds, Madison, and Rankin) of metropolitan Jackson.

	Study dates 2000 - 2013 Duration of follow-up Mean 8.04 years Loss to follow-up 21 out of 5,301 (0.39%) participants. Sources of funding Dr Young's National Institutes of Health; National Institute of Diabetes and Digestive and Kidney Diseases; National Heart, Lung and Blood Institute; National Institute on Minority Health and Health Disparities; and Veterans Affairs Puget Sound Health Care System.
Inclusion criteria	Other Participants originally recruited as part of the Atherosclerosis Risk in Communities (ARIC) study (ages 35-85 years). Additional younger and older participants were recruited as part of the JHS family study, such that ages of all recruited participants at baseline ranged from 21-94.
Exclusion criteria	Other Participants without serum creatinine measured at examinations 1 or 3, those on dialysis (self report) at examination 1, those who died prior to examination 3, and those who were lost to follow-up were excluded from analyses.
Baseline characteristics	Sample size 3,653 Female 63% Age Mean 54 years (SD 12) Ethnicity All African-Americans Diabetes 19% Hypertension 59% Albuminuria/proteinuria Median UACR mg/g 5.7 [IQR 3.8, 10.5]

	eGFR mL/min/1.73m2 Mean 96 (SD 20)
Phenomenon of interest	Rate of decline in eGFR The relative decline in eGFR was modeled by estimating the subject-specific slope between time and natural log-transformed eGFR. mGFR or eGFR eGFR; CKD-EPI Blood test Creatinine

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	Yes
	Were patients recruited consecutively?	Unclear
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Partial *(Recruitment protocol was published in a previous paper.)*
	Did patients enter the study at a similar point in the disease?	Yes

Section	Question	Answer
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	Yes
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Directly applicable

Yu, 2019

Bibliographic Reference	Yu, Zhi; Rebholz, Casey M; Wong, Eugenia; Chen, Yuan; Matsushita, Kunihiro; Coresh, Josef; Grams, Morgan E; Association Between Hypertension and Kidney Function Decline: The Atherosclerosis Risk in Communities (ARIC) Study.; American journal of kidney diseases : the official journal of the National Kidney Foundation; 2019; vol. 74 (no. 3); 310-319

Study Characteristics

Study type	Uncontrolled prospective study
Study details	Adults Study name ARIC Study location US Study setting Participants were recruited from 4 communities in the US: Forsyth County, NC; Jackson, MS; suburbs of Minneapolis, MN; and Washington County, MD. Study dates 1987 - 2017 Duration of follow-up 30 years Loss to follow-up Whites (72.8%); African-Americans (73.7%) Sources of funding National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health; National Heart, Lung, and Blood Institute; and Department of Health and Human Services.
Inclusion criteria	Age Middle-aged (45 to 64 years old at baseline) Other White and African-American men and women
Exclusion criteria	Other Participants were excluded if they had missing data for hypertension status at baseline, missing measurement of serum creatinine at baseline, eGFR <60 mL/min/1.73 m2 at baseline, prevalent ESKD, self-reported race other than white or African American, or missing covariates.

Phenomenon of interest	Rate of decline in eGFR Random intercepts and random slopes were used to account for individual variations in eGFR at baseline and its change. mGFR or eGFR eGFR; CKD-EPI Blood test Creatinine
Subgroups	Ethnicity Hypertension

Study arms

White Normal BP (N = 5341)

Normal blood pressure (BP) defined as systolic blood pressure (SBP) <120 mm Hg and diastolic blood pressure (DBP) <80 mm Hg

Baseline characteristics	Female 57.1% Age Mean 53.5 years (SD 5.5) Diabetes 3.7% eGFR mL/min/1.73m2 Mean 101.5 (SD 11.2)

White Elevated BP (N = 1281)

Elevated BP defined as SBP ≥120 SBP <130 mm Hg and DBP <80 mm Hg

Baseline characteristics	Female 49.9%

	Age Mean 56.1 years (SD 5.6) Diabetes 6.9% eGFR mL/min/1.73m2 Mean 99.5 (SD 10.9)

White Stage 1 HTN (N = 1448)

Stage 1 hypertension (HTN) defined as 130≥ SBP <140 mm Hg or 80≥ DBP <90 mm Hg

Baseline characteristics	Female 43.5% Age Mean 55.0 years (SD 5.7) Diabetes 6.4% eGFR mL/min/1.73m2 Mean 99.5 (SD 11.3)

White Stage 2 HTN without medications (N = 801)

Stage 2 HTN defined as SBP ≥140 mm Hg or DBP ≥90 mm Hg; without use of antihypertensive medication in the last 2 weeks

Baseline characteristics	Female 47.6% Age Mean 56.7 years (SD 5.6) Diabetes 7.6% eGFR mL/min/1.73m2 Mean 99.0 (SD 11.3)

White Stage 2 HTN with medications (N = 2132)

Stage 2 HTN defined as SBP ≥140 mm Hg or DBP ≥90 mm Hg; with use of antihypertensive medication in the last 2 weeks

Baseline characteristics	Female 51.9% Age Mean 56.8 years (SD 5.4) Diabetes 15.3% eGFR mL/min/1.73m2 Mean 96.5 (SD 12.7)

African-American Normal BP (N = 859)

Normal BP defined as SBP <120 mm Hg and DBP <80 mm Hg

Baseline characteristics	Female 62.5% Age Mean 52.2 years (SD 5.6) Diabetes 10.2% eGFR mL/min/1.73m2 Mean 114.8 years (SD 15.5)

African-American Elevated BP (N = 273)

Elevated BP defined as SBP ≥120 SBP <130 mm Hg and DBP <80 mm Hg

Baseline characteristics	Female 65.6% Age Mean 54.5 years (SD 6.1)

	Diabetes 12.5% eGFR mL/min/1.73m2 Mean 115.7 (SD 14.0)

African-American Stage 1 HTN (N = 610)

Stage 1 HTN defined as 130≥ SBP <140 mm Hg or 80≥ DBP <90 mm Hg

Baseline characteristics	Female 53.8% Age Mean 52.9 years (SD 5.6) Diabetes 10.7% eGFR mL/min/1.73m2 Mean 114.4 years (SD 15.9)

African-American Stage 2 HTN without medications (N = 573)

Stage 2 HTN defined as SBP ≥140 mm Hg or DBP ≥90 mm Hg; without use of antihypertensive medication in the last 2 weeks

Baseline characteristics	Female 48.3% Age Mean 54.6 years (SD 5.7) Diabetes 14.0% eGFR mL/min/1.73m2 Mean 113.2 (SD 15.7)

African-American Stage 2 HTN with medications (N = 1536)

Stage 2 HTN defined as SBP ≥140 mm Hg or DBP ≥90 mm Hg; with use of antihypertensive medication in the last 2 weeks	
Baseline characteristics	Female 67.6% Age Mean 55.0 years (SD 5.7) Diabetes 24.3% eGFR mL/min/1.73m2 Mean 109.6 (SD 18.6)

Quality appraisal and risk of bias

Section	Question	Answer
Study objective	Was the hypothesis/aim/objective of the study clearly stated?	Yes
Study design	Was the study conducted prospectively?	Yes
	Were the cases collected in more than one centre?	Yes
	Were patients recruited consecutively?	Unclear
Study population	Were the characteristics of the patients included in the study described?	Yes
	Were the eligibility criteria (i.e. inclusion and exclusion criteria) for entry into the study clearly stated?	Partial *(Inclusion criteria were not reported.)*
	Did patients enter the study at a similar point in the disease?	Yes

Section	Question	Answer
Outcome measure	Were relevant outcome measures established a priori?	Yes
	Were the relevant outcomes measured using appropriate objective/subjective methods?	Yes
Statistical analysis	Were the statistical tests used to assess the relevant outcomes appropriate?	Yes
Results and conclusions	Was follow-up long enough for important events and outcomes to occur?	Yes
	Were losses to follow-up reported?	Yes
	Did the study provide estimates of random variability in the data analysis of relevant outcomes?	Yes
	Were the conclusions of the study supported by results?	Yes
Competing interests and sources of support	Were both competing interests and sources of support for the study reported?	Yes
Overall Risk of Bias	Risk of Bias	Low
	Applicability	Directly applicable

Appendix F – Forest plots

Figure 1: Rate of decline in eGFR ml/min/1.73m^2 per year in children and young people (negative values mean higher rate of decline)

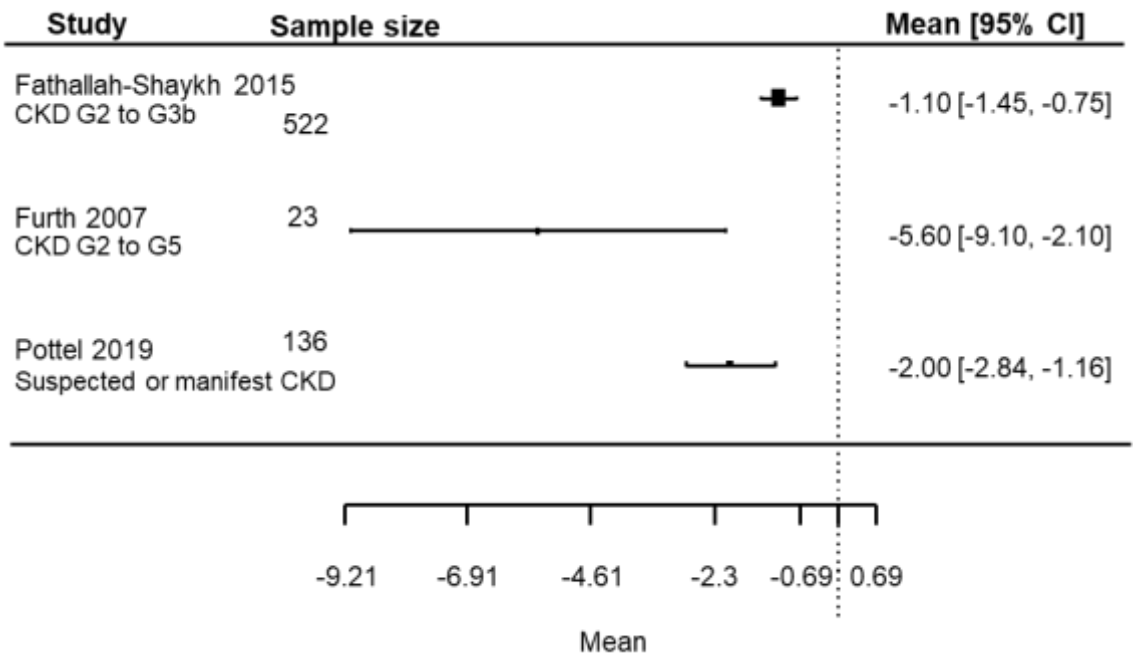

Study
Sample size
Mean [95% CI]
Fathallah-Shaykh 2015
CKD G2 to G3b
522
-1.10 [-1.45, -0.75]
Furth 2007
CKD G2 to G5
23
-5.60 [-9.10, -2.10]
Pottel 2019
Suspected or manifest CKD
136
-2.00 [-2.84, -1.16]
-9.21
-6.91
-4.61
-2.3
-0.69
0.69
Mean

Figure 2: Rate of decline in eGFR ml/min/1.73m^2 per year in subgroups of children and young people (negative values mean higher rate of decline)

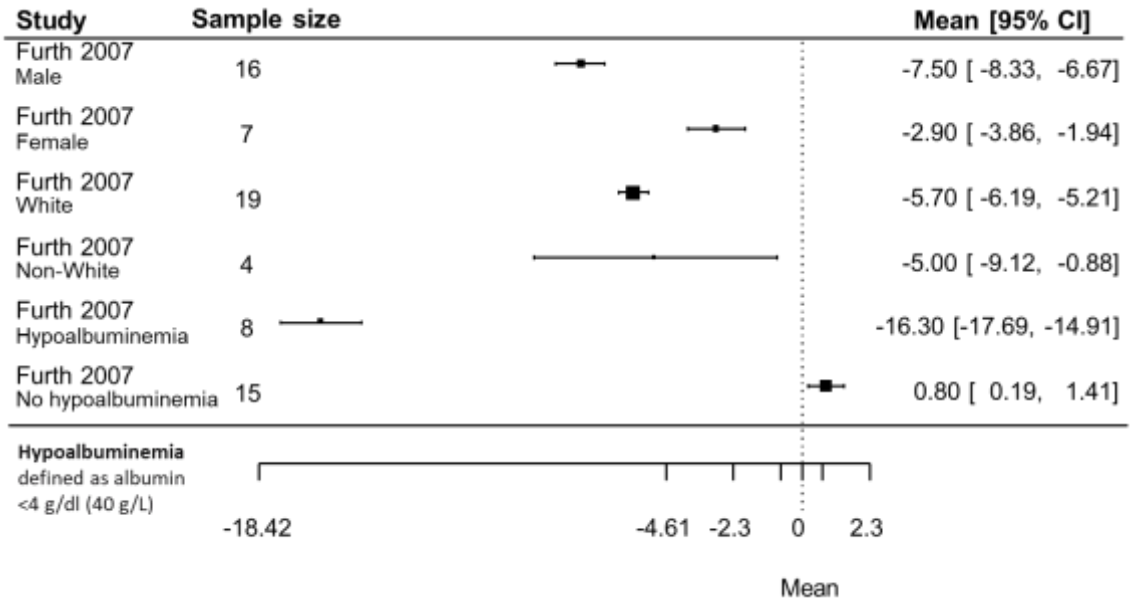


Figure 3: Rate of gain in eGFR ml/min/1.73m^2 per year in kidney donors (positive values mean higher rate of gain)

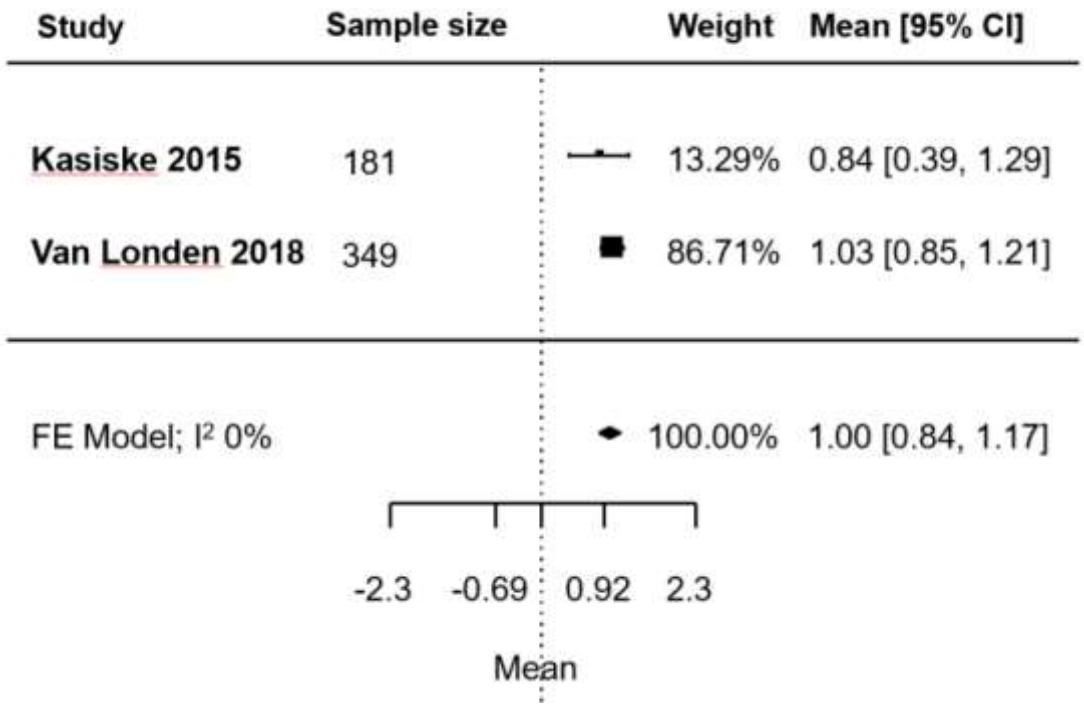


Figure 4: Rate of decline in eGFR ml/min/1.73m^2 per year in adults without CKD; subgroups by age (negative values mean higher rate of decline)

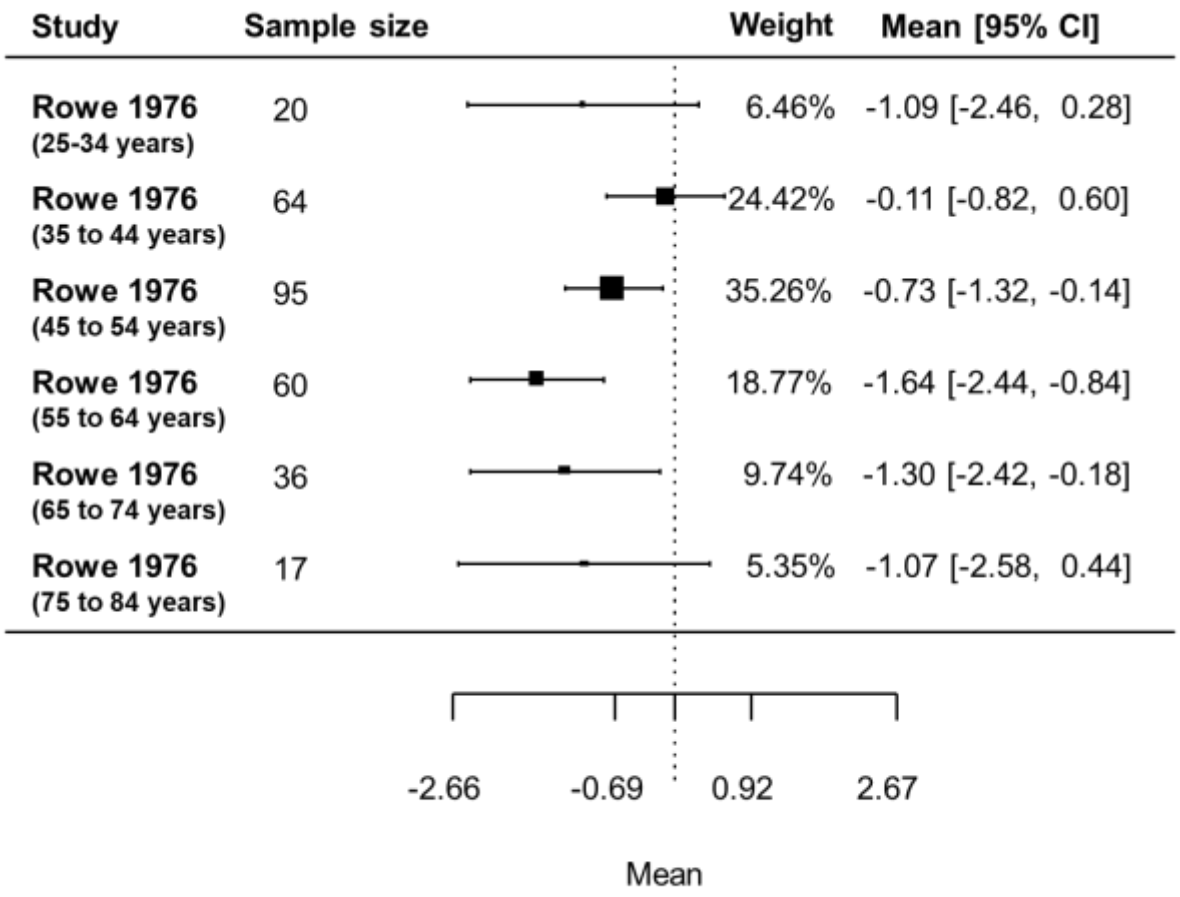


Figure 5: Rate of decline in eGFR ml/min/1.73m^2 per year in adults without CKD, diabetes, hypertension and albuminuria (negative values mean higher rate of decline)

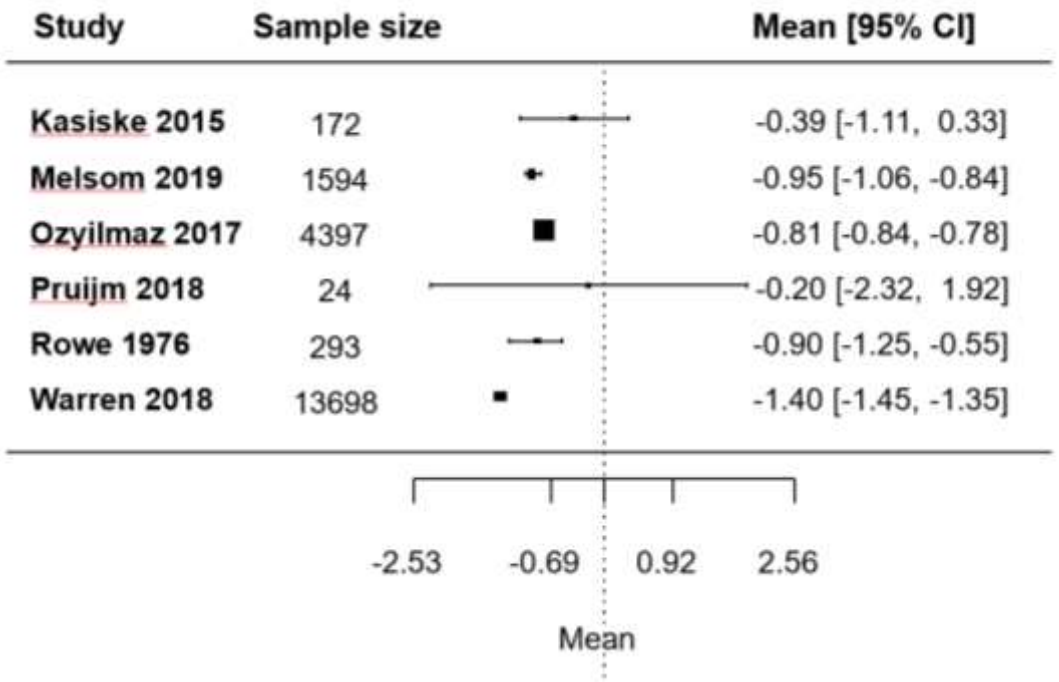


Figure 6: Rate of decline in eGFR ml/min/1.73m^2 per year in adults without CKD and with diabetes (negative values mean higher rate of decline)

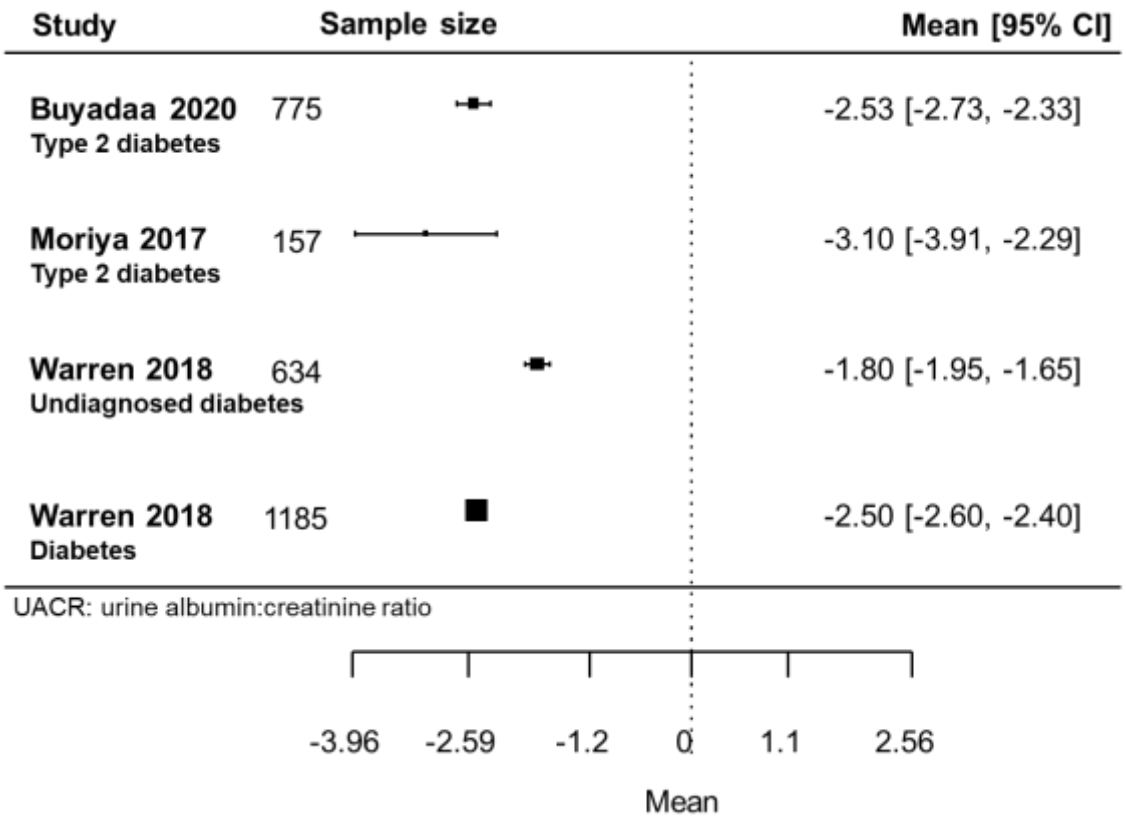


Figure 7: Rate of decline in eGFR ml/min/1.73m^2 per year in adults without CKD and with hypertension (negative values mean higher rate of decline)

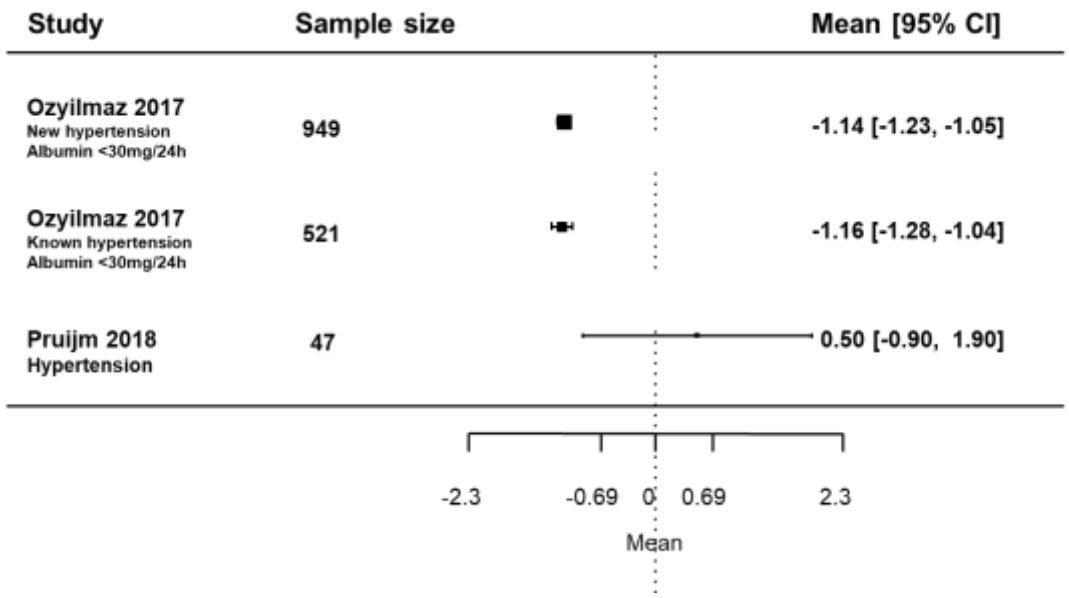


Figure 8: Rate of decline in eGFR ml/min/1.73m^2 per year in female adults without CKD (negative values mean higher rate of decline)

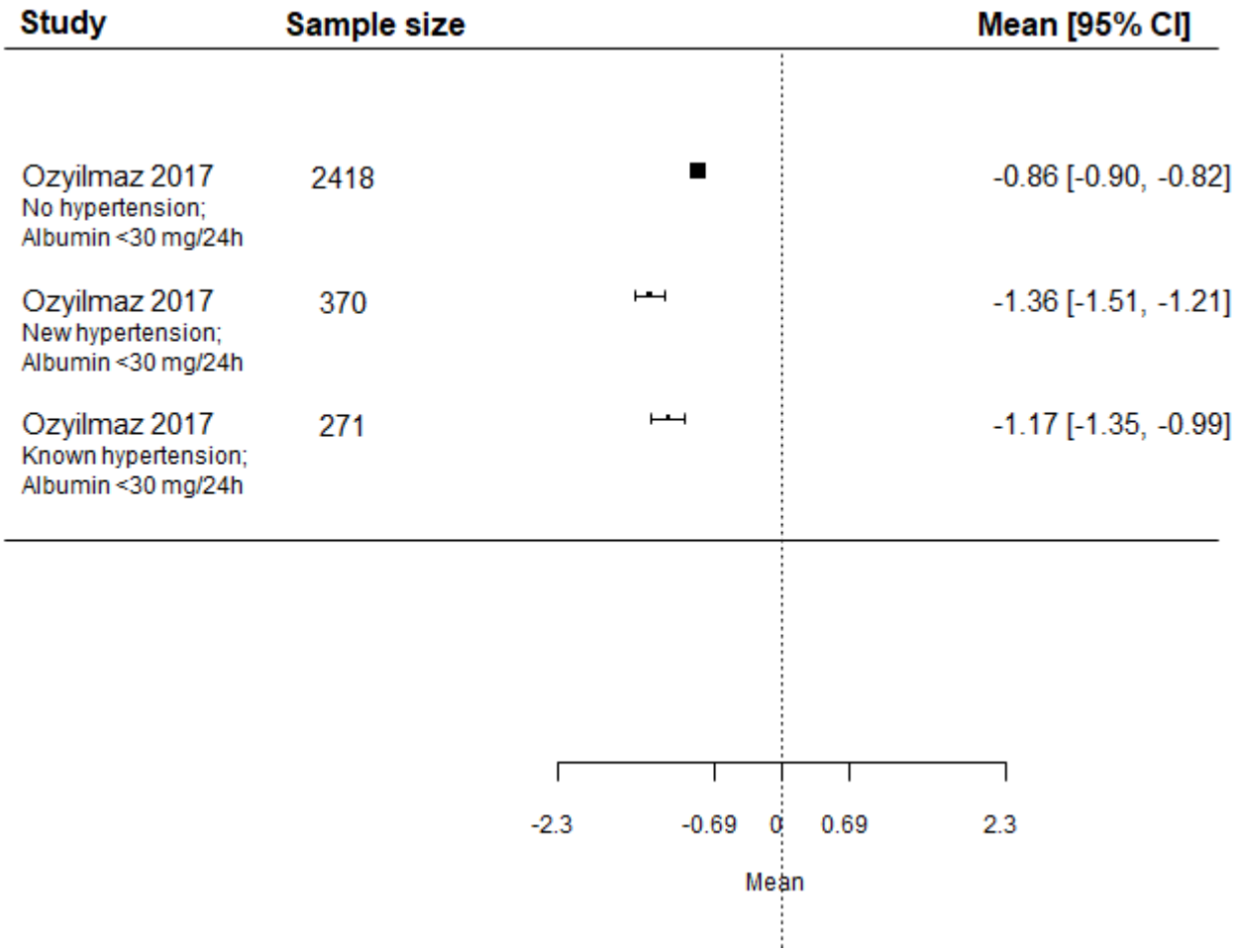


Figure 9: Rate of decline in eGFR ml/min/1.73m^2 per year in male adults without CKD (negative values mean higher rate of decline)

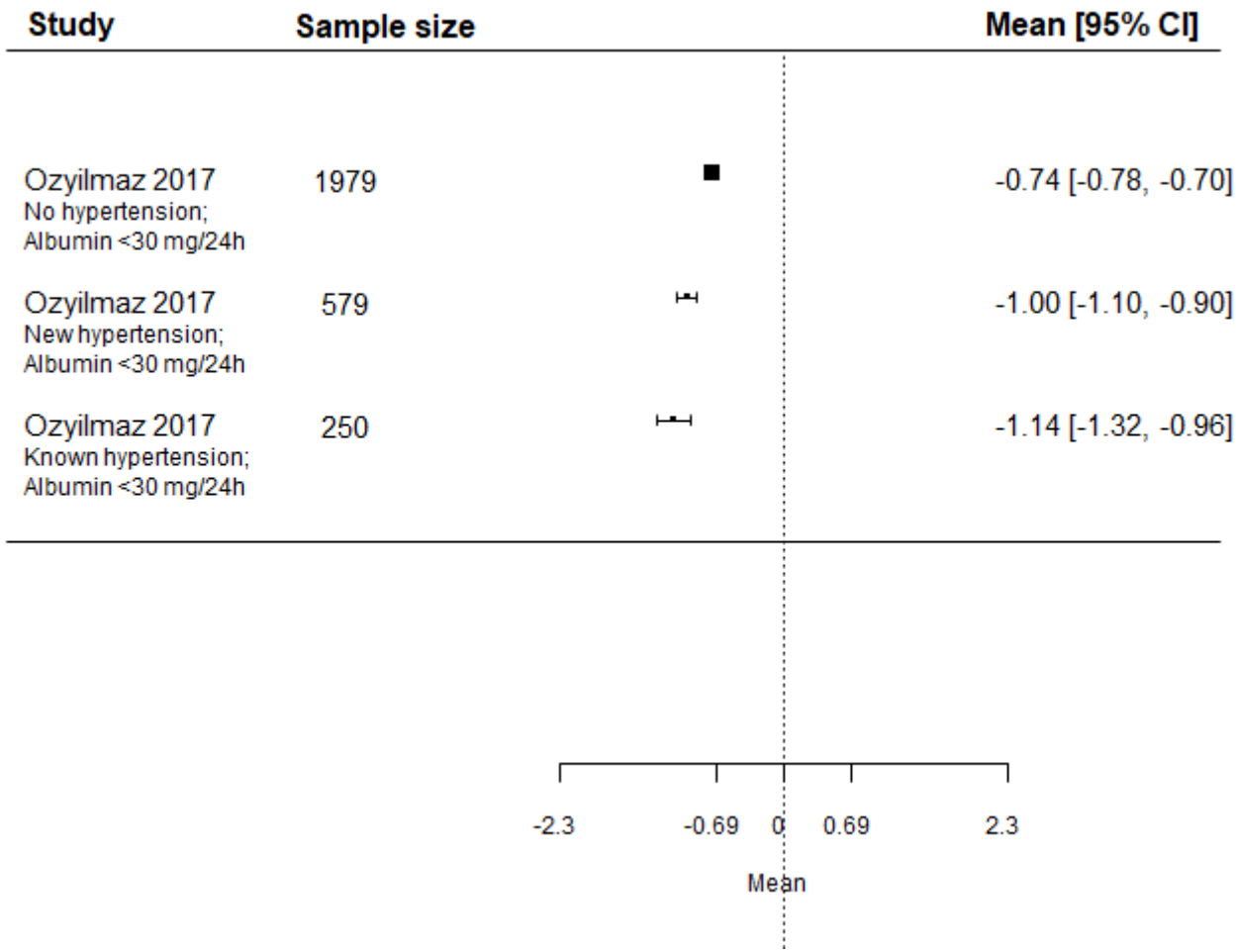


Figure 10: Rate of decline in eGFR ml/min/1.73m^2 per year in adults with CKD (negative values mean higher rate of decline)

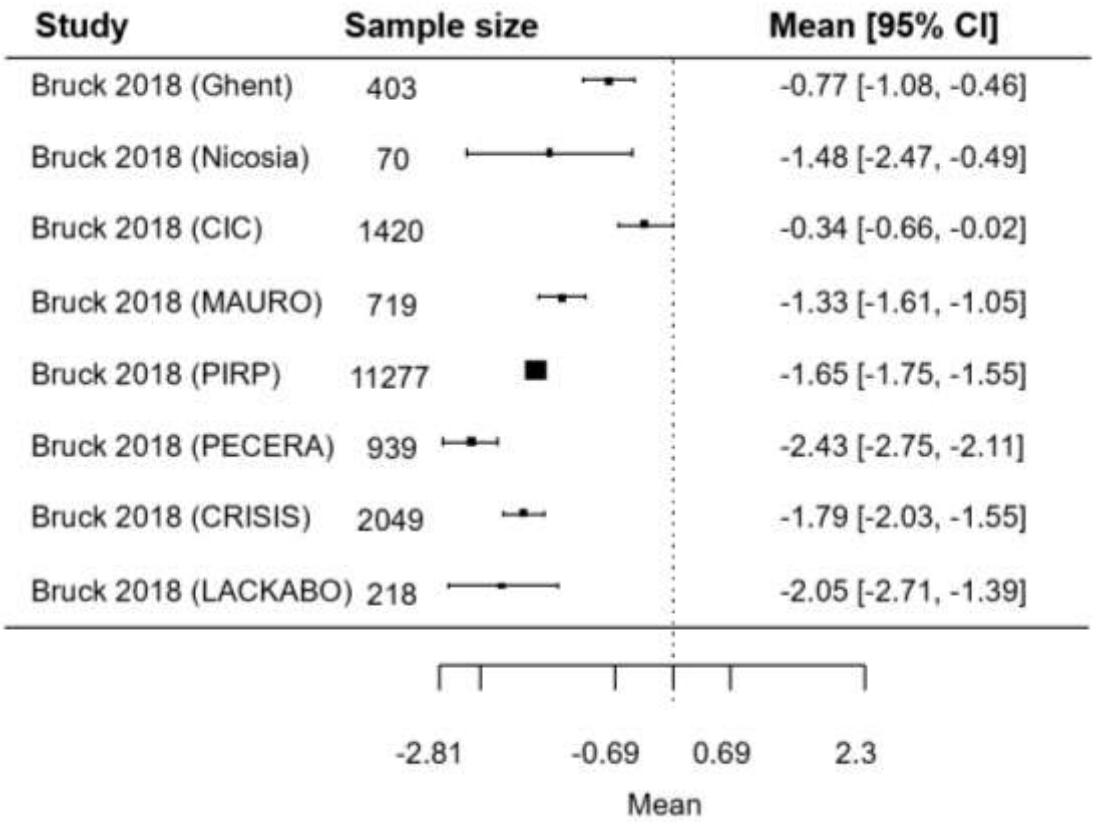


Figure 11: Rate of decline in eGFR ml/min/1.73m^2 per year in female adults with CKD (negative values mean higher rate of decline)

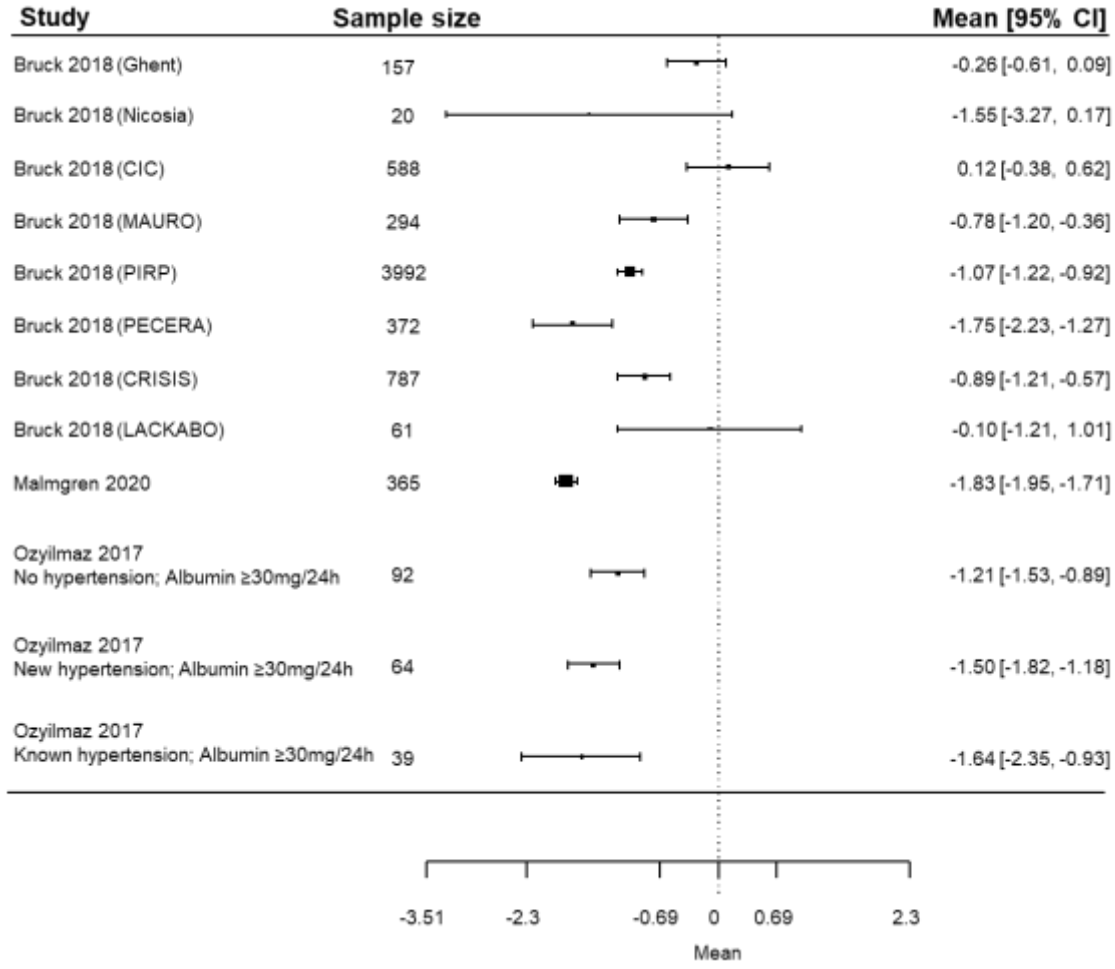


Figure 12: Rate of decline in eGFR ml/min/1.73m^2 per year in male adults with CKD (negative values mean higher rate of decline)

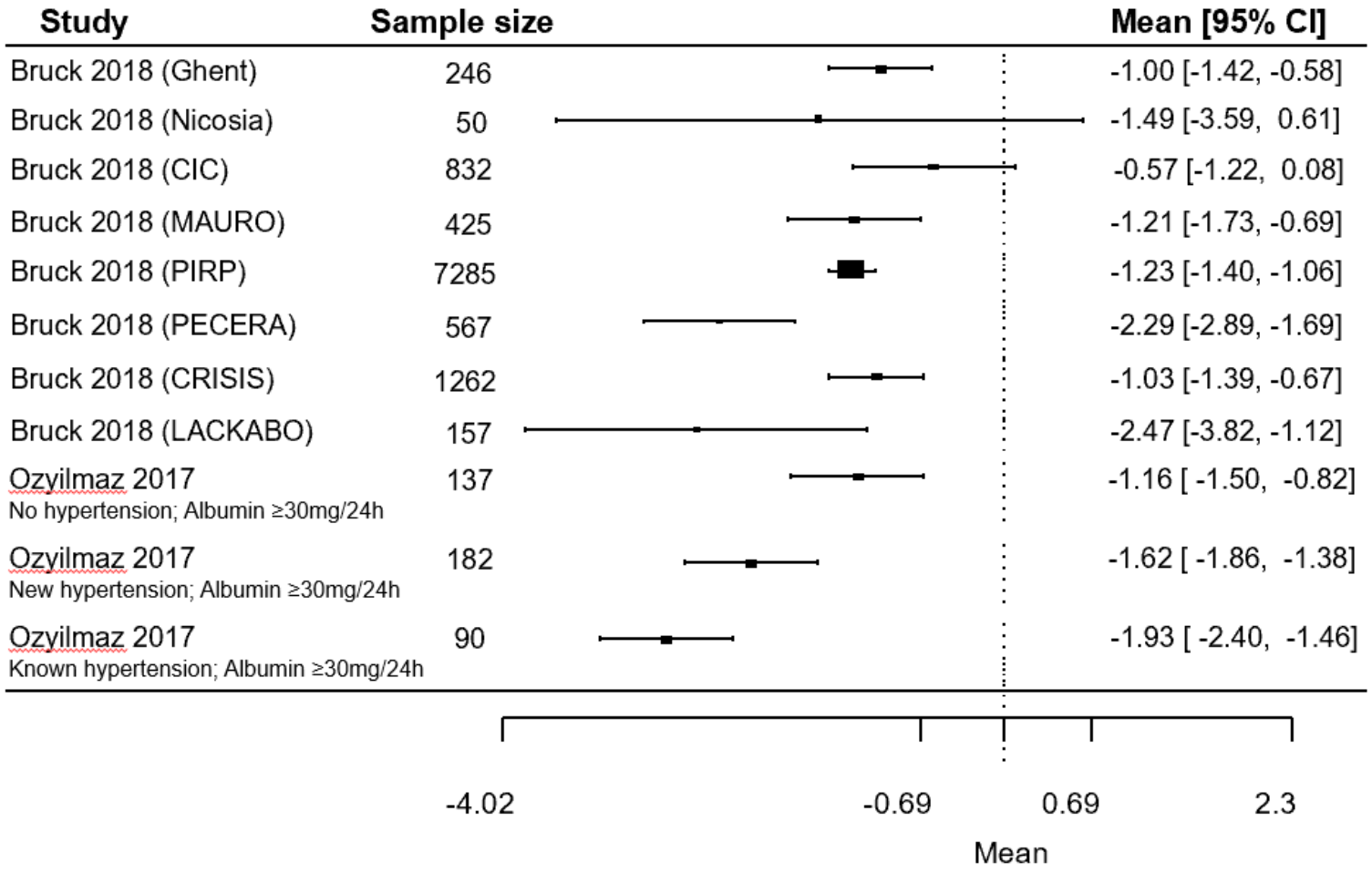


Figure 13: Rate of decline in eGFR ml/min/1.73m^2 per year in adults with CKD and with hypertension (negative values mean higher rate of decline)

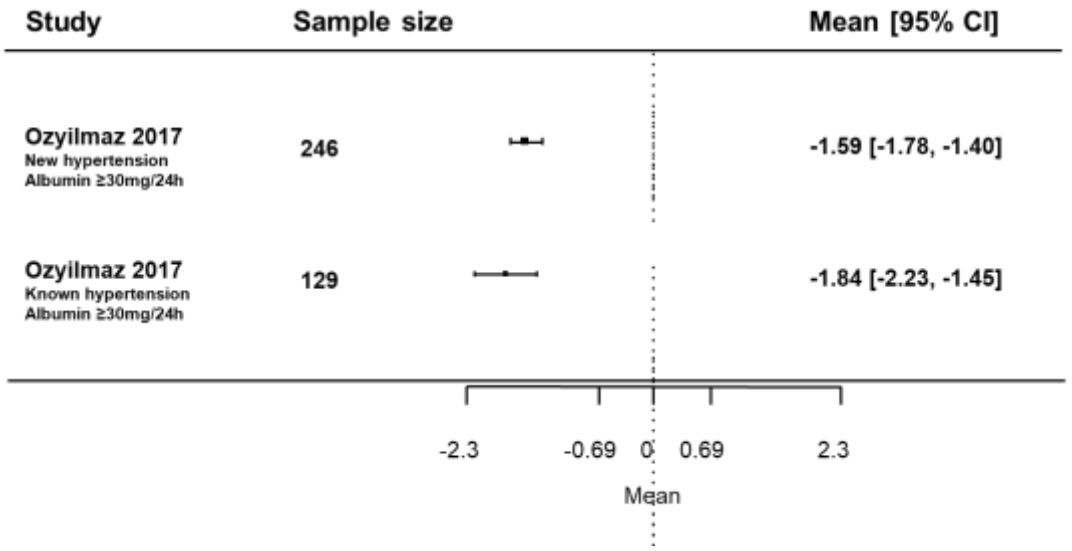


Figure 14: Rate of decline in eGFR ml/min/1.73m^2 per year in adults with CKD and without diabetes (negative values mean higher rate of decline)

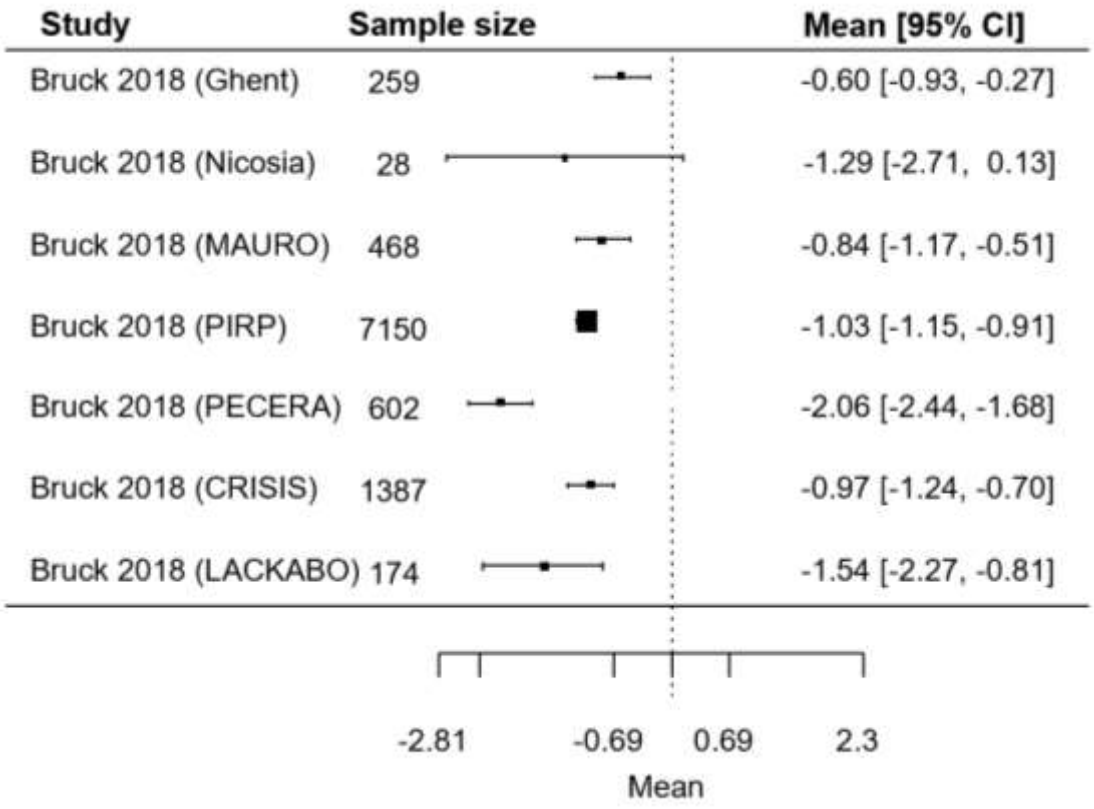


Figure 15: Rate of decline in eGFR ml/min/1.73m^2 per year in adults with CKD and diabetes (negative values mean higher rate of decline)

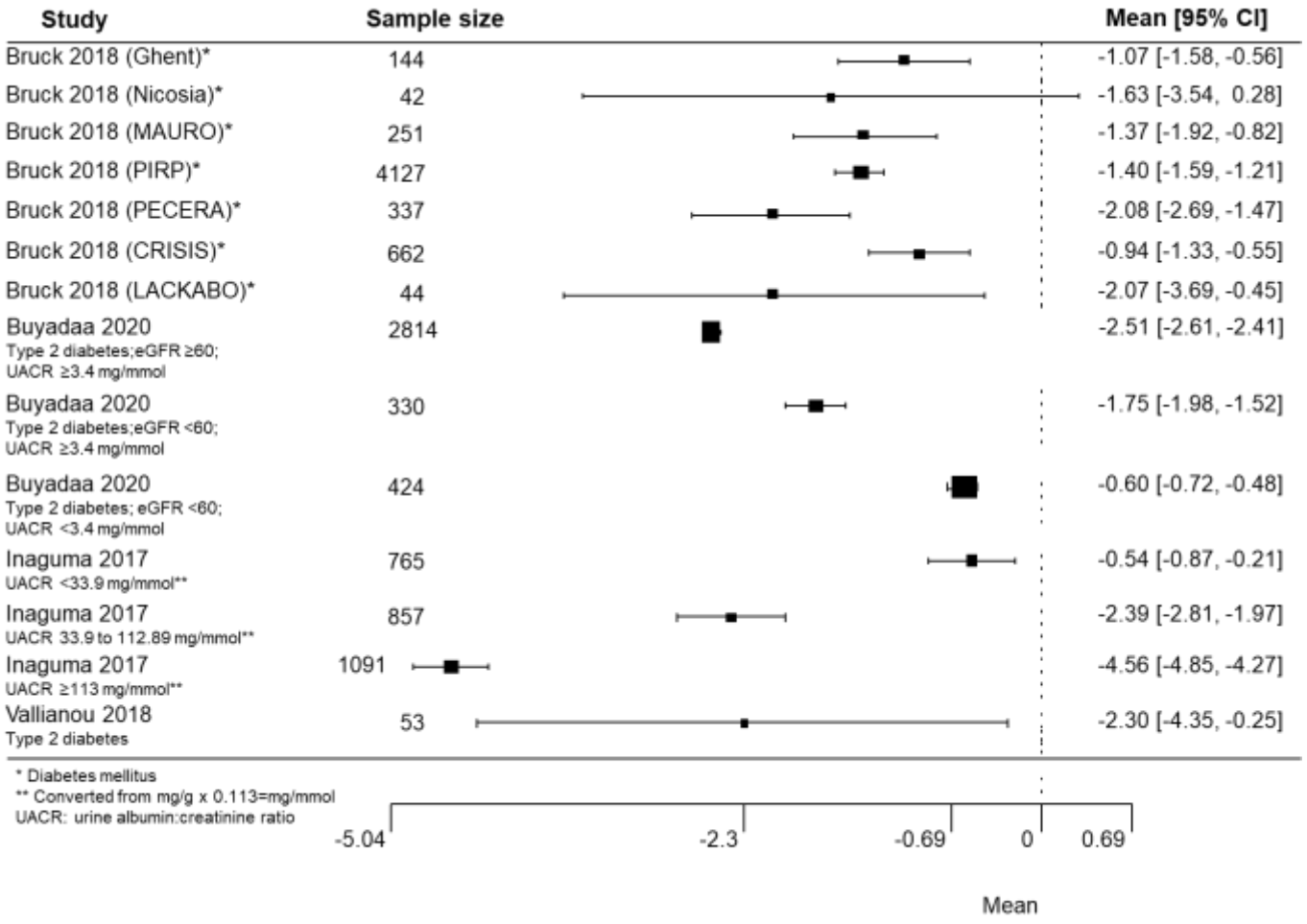


Figure 16: Rate of decline in eGFR ml/min/1.73m^2 per year in adults with CKD categories G1 and G2 (negative values mean higher rate of decline)

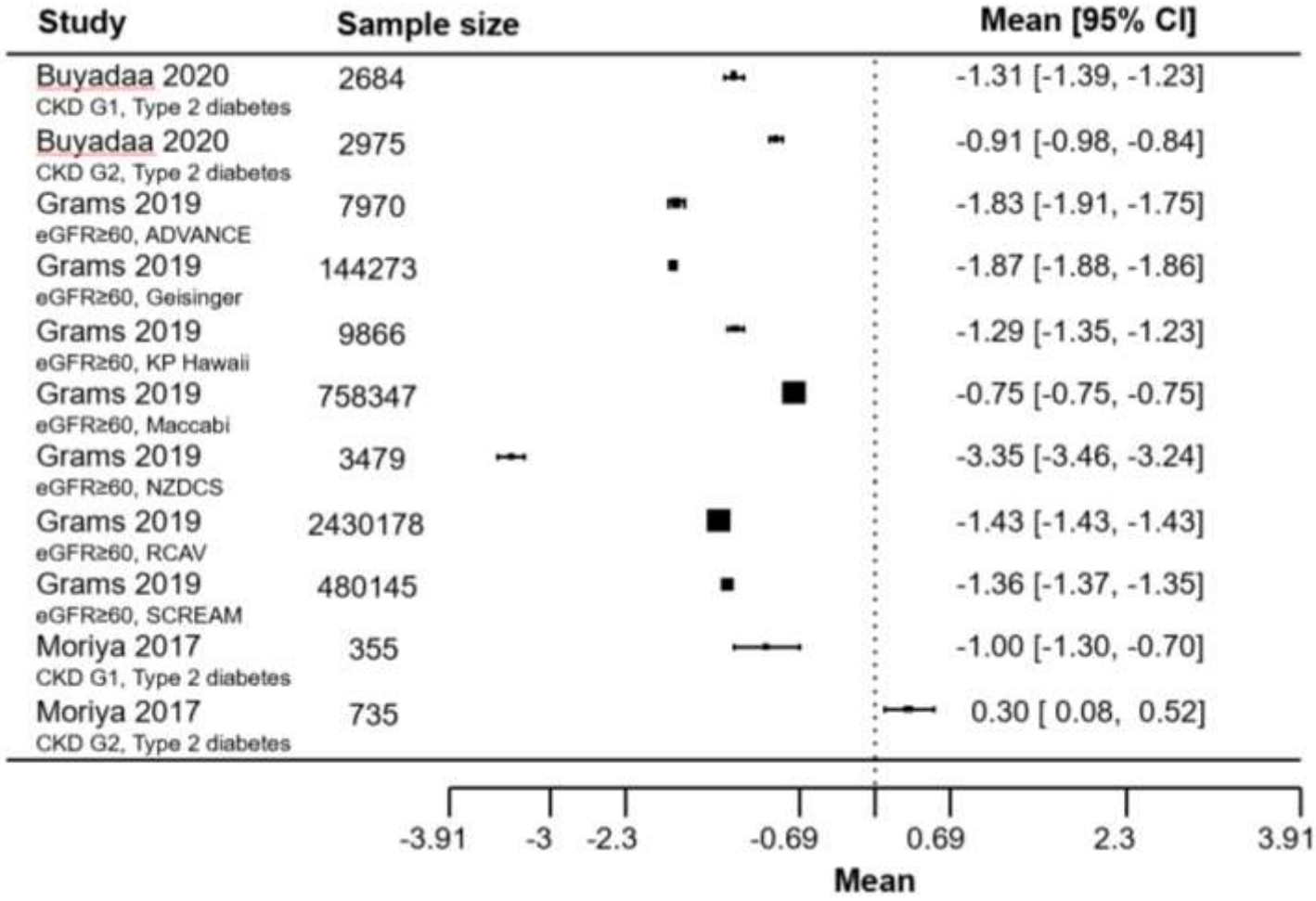


Figure 17: Rate of decline in eGFR ml/min/1.73m^2 per year in adults with CKD categories G3a and G3b (negative values mean higher rate of decline)

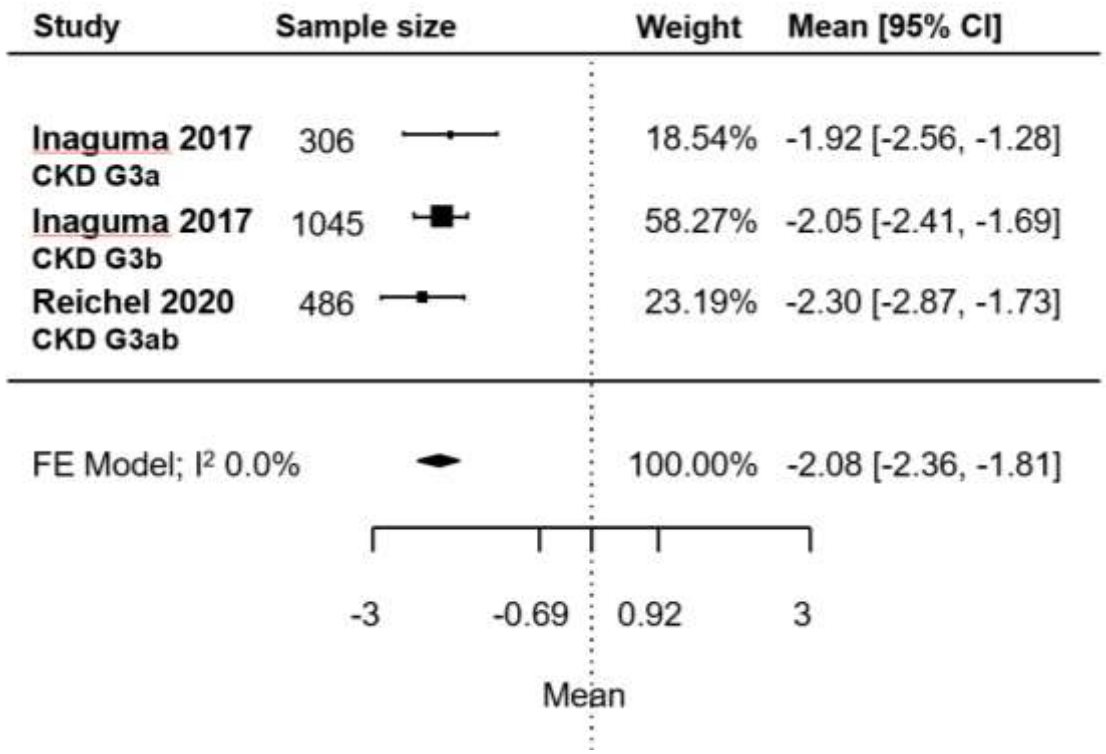


Figure 18: Rate of decline in eGFR ml/min/1.73m^2 per year in adults with CKD categories G4 and G5 (negative values mean higher rate of decline)

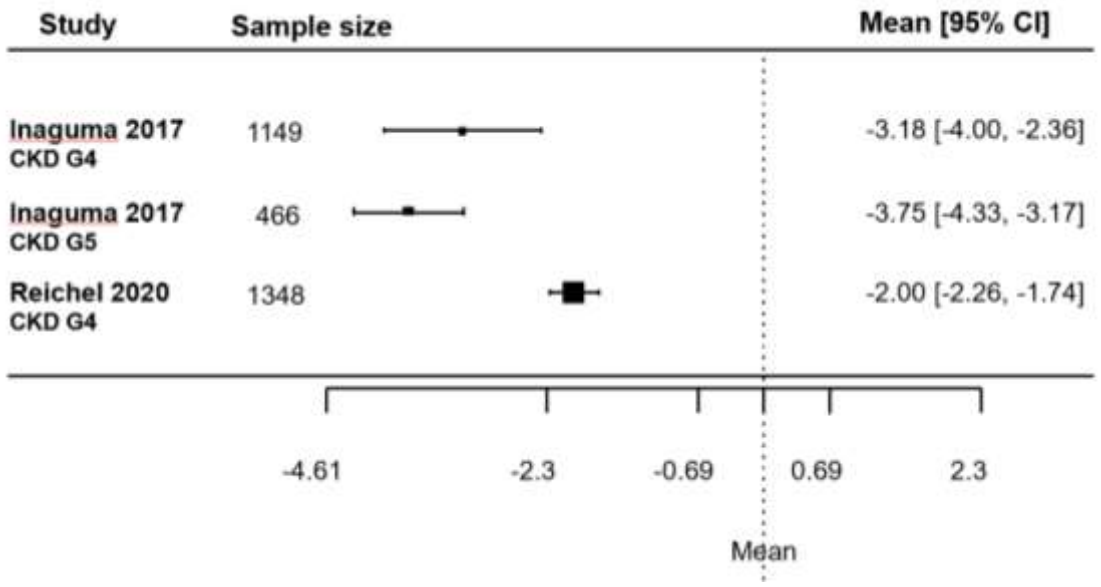


Figure 19: Rate of decline in eGFR ml/min/1.73m^2 per year in adults with CKD categories G1 to G4 (negative values mean higher rate of decline)

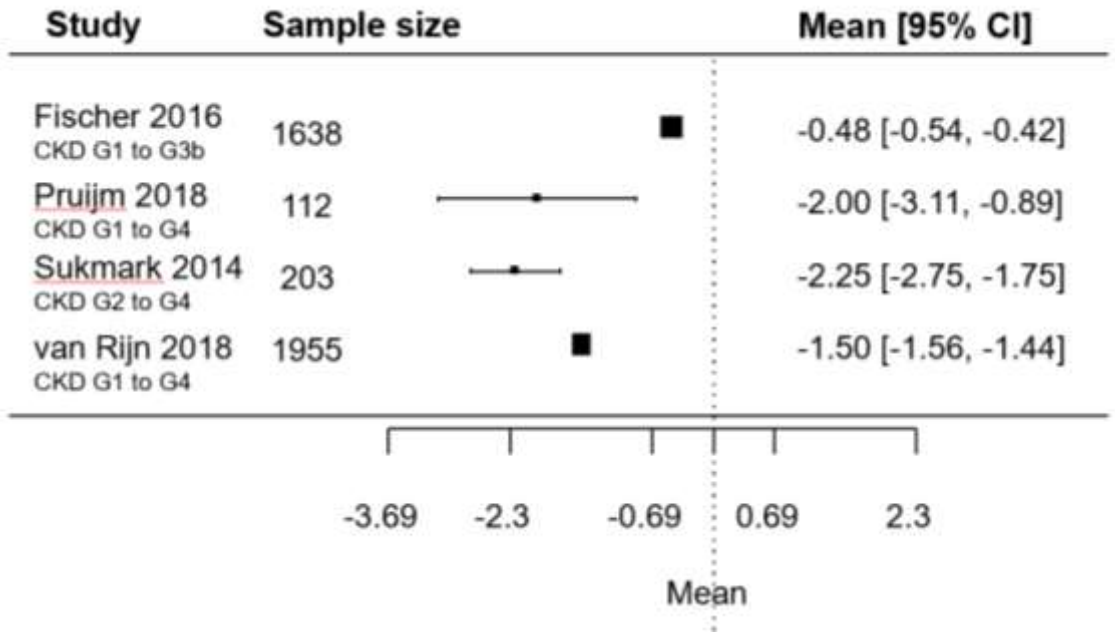


Figure 20: Rate of decline in eGFR ml/min/1.73m^2 per year in adults with CKD categories G1 to G3b and type 1 diabetes (negative values mean higher rate of decline)

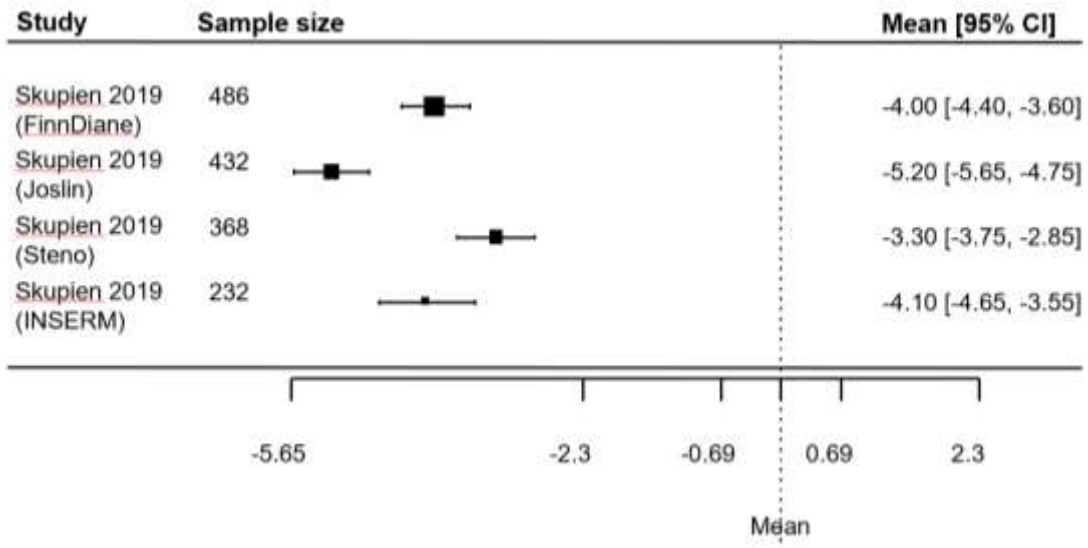


Figure 21: Rate of decline in eGFR ml/min/1.73m^2 per year in adults with CKD categories G3a to G5 (negative values mean higher rate of decline)

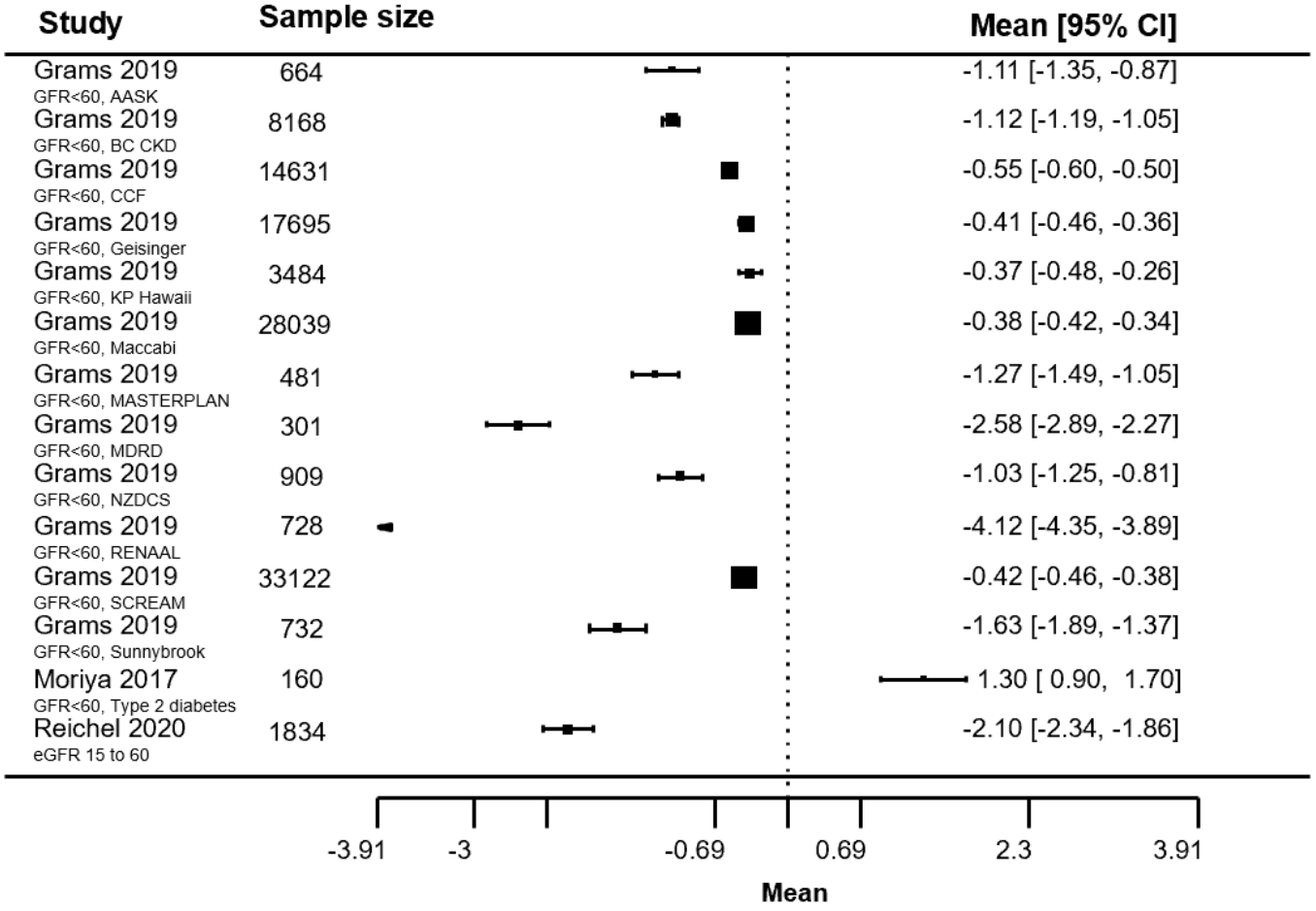


Figure 22: Rate of decline in eGFR ml/min/1.73m^2 per year in adults with CKD categories G3b to G5 by sex (negative values mean higher rate of decline)

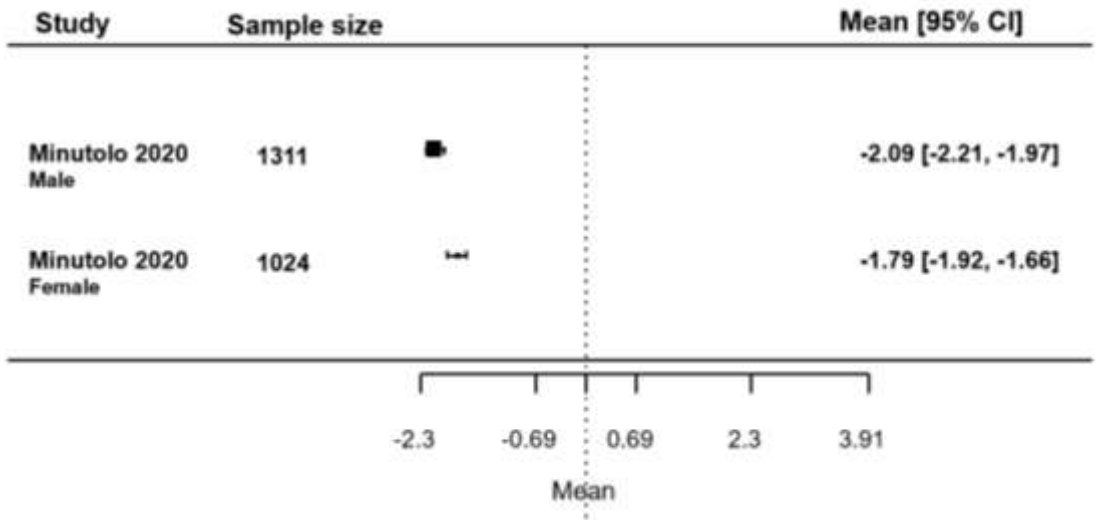
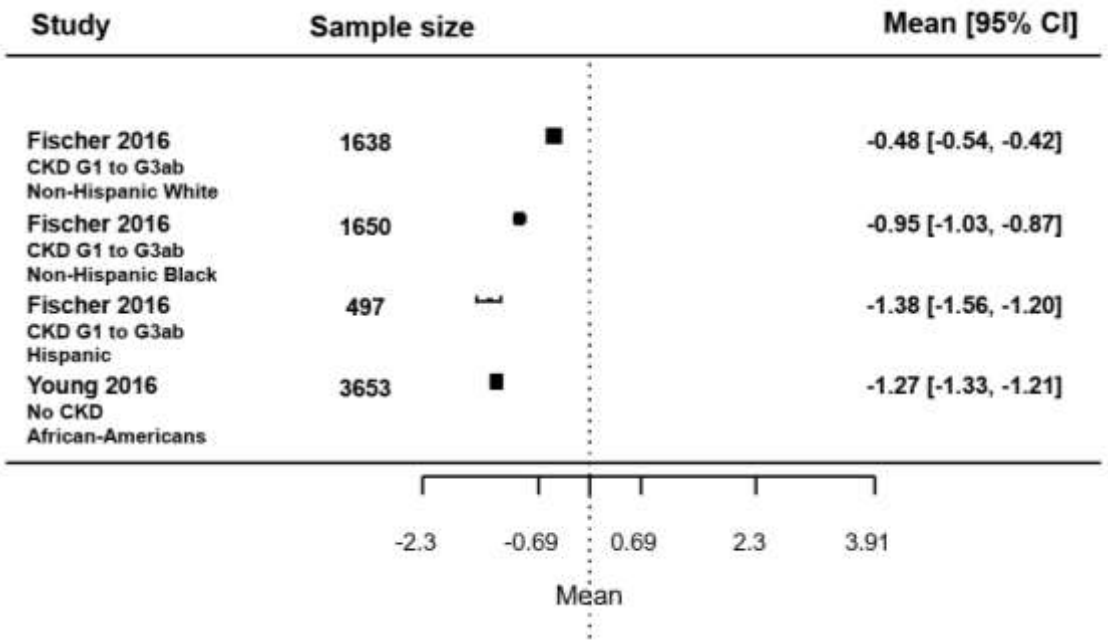


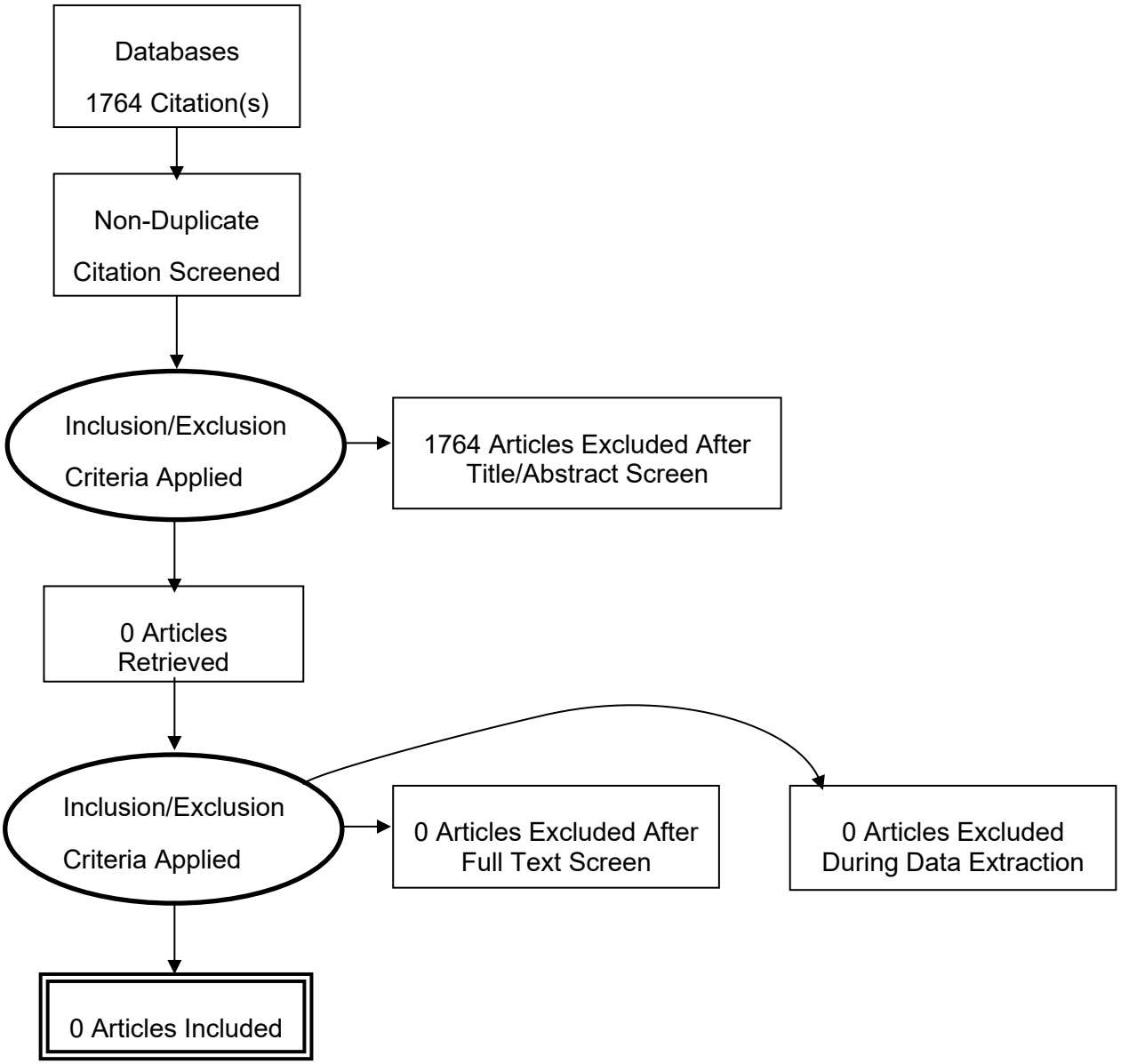
Figure 23: Rate of decline in eGFR ml/min/1.73m^2 per year adults from Black, Asian and Minority Ethnic groups (negative values mean higher rate of decline)



Appendix G – GRADE tables

GRADE tables were not used in this evidence review.

Appendix H – Economic evidence study selection



Appendix I – Economic evidence tables

No published economic studies were included in this review.

Appendix J – Health economic model

This review was not prioritised for economic modelling.

Appendix K – Excluded studies

Epidemiologic evidence

Study	Reason for exclusion
Agampodi, S B, Amarasinghe, G S, Naotunna, P G C R et al. (2018) Early renal damage among children living in the region of highest burden of chronic kidney disease of unknown etiology (CKDu) in Sri Lanka. BMC nephrology 19(1): 115	- Study does not contain outcomes of interest *Decline in eGFR not reported*
Agarwal, Rajiv, Duffin, Kevin L, Laska, Dennis A et al. (2014) A prospective study of multiple protein biomarkers to predict progression in diabetic chronic kidney disease. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 29(12): 2293-302	- Data not reported in an extractable format *eGFR slope only reported for a couple of examples in the supplementary file*
Al-Eisa, A.A., Al-Hajri, A., Al-Shuaib, S. et al. (2017) Early-onset microalbuminuria in children with type 1 diabetes in Kuwait. Current Pediatric Research 21(2): 254-259	- Not a relevant study design *Retrospective study*
Ali, I., Chinnadurai, R., Ibrahim, S.T. et al. (2020) Predictive factors of rapid linear renal progression and mortality in patients with chronic kidney disease. BMC Nephrology 21(1): 345	- Not a relevant study design *Retrospective study*
Ali, O., Mohiuddin, A., Mathur, R. et al. (2013) A cohort study on the rate of progression of diabetic chronic kidney disease in different ethnic groups. BMJ Open 3(2): e001855	- Data not reported in an extractable format *Annual decline in eGFR without a measure of dispersion*
Anand, Shuchi, Kondal, Dimple, Montez-Rath, Maria et al. (2017) Prevalence of chronic kidney disease and risk factors for its progression: A cross-sectional comparison of Indians living in Indian versus U.S. cities. PloS one 12(3): e0173554	- Study does not contain outcomes of interest *Rate of decline in eGFR not reported*
Arora, Pradeep, Jalal, Kabir, Gupta, Anu et al. (2017) Progression of kidney disease in elderly stage 3 and 4 chronic kidney disease patients. International urology and nephrology 49(6): 1033-1040	- Data not reported in an extractable format *Data only reported graphically*

Study	Reason for exclusion
Bansal, Nisha, Xie, Dawei, Tao, Kelvin et al. (2016) Atrial Fibrillation and Risk of ESRD in Adults with CKD. Clinical journal of the American Society of Nephrology : CJASN 11(7): 1189-96	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Barr, Elizabeth Lm, Barzi, Federica, Hughes, Jaquelyne T et al. (2018) Contribution of cardiometabolic risk factors to estimated glomerular filtration rate decline in Indigenous Australians with and without albuminuria - the eGFR Follow-up Study. Nephrology (Carlton, Vic.) 23(7): 682-689	- Study does not contain phenomenon of interest *Decline is not reported overtime (only 1 follow-up)*
Barr, Elizabeth Lm, Reutens, Anne, Magliano, Dianna J et al. (2017) Cystatin C estimated glomerular filtration rate and all-cause and cardiovascular disease mortality risk in the general population: AusDiab study. Nephrology (Carlton, Vic.) 22(3): 243-250	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Barzi, Federica, Jones, Graham R D, Hughes, Jaquelyne T et al. (2018) Trajectories of eGFR decline over a four year period in an Indigenous Australian population at high risk of CKD-the eGFR follow up study. Clinical biochemistry 53: 58-64	- Does not contain a relevant population *Indigenous Australian*
Bernier-Jean, A., Prince, R.L., Lewis, J.R. et al. (2020) Dietary plant and animal protein intake and decline in estimated glomerular filtration rate among elderly women: a 10-year longitudinal cohort study. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association	- Conference abstract
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	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Camelo, Lidyane V, Giatti, Luana, Ladeira, Roberto Marini et al. (2018) Racial disparities in renal function: the role of racial discrimination. The Brazilian Longitudinal Study of Adult Health	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*

Study	Reason for exclusion
(ELSA-Brasil). Journal of epidemiology and community health 72(11): 1027-1032	
Cassidy-Bushrow, Andrea E, Wegienka, Ganesa, Barone, Charles J 2nd et al. (2012) Race-specific relationship of birth weight and renal function among healthy young children. Pediatric nephrology (Berlin, Germany) 27(8): 1317-23	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Catalina, Sanchez Basto, Katherine, Puerto Nino Angie, Nicolas, Fernandez et al. (2019) The natural history of solitary post-nephrectomy kidney in a pediatric population. International braz j urol : official journal of the Brazilian Society of Urology 45(6): 1227-1237	- Not a relevant study design *Retrospective study*
Cea Soriano, Lucia, Johansson, Saga, Stefansson, Bergur et al. (2015) Cardiovascular events and all-cause mortality in a cohort of 57,946 patients with type 2 diabetes: associations with renal function and cardiovascular risk factors. Cardiovascular diabetology 14: 38	- Not a relevant study design *Retrospective study*
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	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Chang, Wen Xiu, Asakawa, Shinichiro, Toyoki, Daigo et al. (2015) Predictors and the Subsequent Risk of End-Stage Renal Disease - Usefulness of 30% Decline in Estimated GFR over 2 Years. PloS one 10(7): e0132927	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Chen, Jenny H C, Hughes, Peter, Woodroffe, Claudia et al. (2019) Pre- and postdonation kidney function in donors of a kidney paired donation with unique criteria for donor glomerular filtration rate - a longitudinal cohort analysis. Transplant international : official journal of the European Society for Organ Transplantation 32(3): 291-299	- Not a relevant study design *Retrospective longitudinal cohort analysis*
Chen, Ping-Min; Wada, Takashi; Chiang, Chih-Kang (2017) Prognostic value of proteinuria and	- Not a relevant study design *Retrospective study*

Study	Reason for exclusion
glomerular filtration rate on Taiwanese patients with diabetes mellitus and advanced chronic kidney disease: a single center experience. Clinical and experimental nephrology 21(2): 307-315	
Chin, Andrew I, Nguyen, Tuan A, Dinesh, Kumar P et al. (2015) Late acceleration of glomerular filtration rate decline is a risk for hemodialysis catheter use in patients with established nephrology chronic kidney disease care. Hemodialysis international. International Symposium on Home Hemodialysis 19(3): 379-85	- Not a relevant study design *Retrospective study*
Chiou, Yuan-Yow, Lin, Ching-Yuang, Chen, Mei-Ju et al. (2016) Etiology and pediatric chronic kidney disease progression: Taiwan Pediatric Renal Collaborative Study. Journal of the Formosan Medical Association = Taiwan yi zhi 115(9): 752-63	- Not a relevant study design *Retrospective study*
Coll-De-Tuero, G., Comas-Cufi, M., Rodriguez-Poncelas, A. et al. (2019) Prognostic value of the estimated glomerular filtration rate decline in hypertensive patients without chronic kidney disease. American Journal of Hypertension 32(9): 890-899	- Not a relevant study design *Retrospective study*
Colombo, M., McGurnaghan, S.J., Bell, S. et al. (2020) Predicting renal disease progression in a large contemporary cohort with type 1 diabetes mellitus. Diabetologia 63(3): 636-647	- Not a relevant study design *Retrospective study*
Coppo, Rosanna, Lofaro, Danilo, Camilla, Roberta R et al. (2017) Risk factors for progression in children and young adults with IgA nephropathy: an analysis of 261 cases from the VALIGA European cohort. Pediatric nephrology (Berlin, Germany) 32(1): 139-150	- Not a relevant study design *Retrospective*
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	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*

Study	Reason for exclusion
Cueto-Manzano, Alfonso M, Cortes-Sanabria, Laura, Martinez-Ramirez, Hector R et al. (2014) Prevalence of chronic kidney disease in an adult population. Archives of medical research 45(6): 507-13	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
D'hoore, Eric, Neirynck, Nathalie, Schepers, Eva et al. (2015) Chronic kidney disease progression is mainly associated with non-recovery of acute kidney injury. Journal of nephrology 28(6): 709-16	- Secondary publication of an included study that does not provide any additional relevant information *Reported by Bruck 2018*
Das, Sumon Kumar, Afsana, Syeda Momena, Elahi, Shahriar Bin et al. (2019) Renal insufficiency among urban populations in Bangladesh: A decade of laboratory-based observations. PloS one 14(4): e0214568	- Study does not contain outcomes of interest *Decline in eGFR not reported*
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	- Secondary publication of an included study that does not provide any additional relevant information *This cohort is included by Minutolo 2020*
Devetzis, Vasilios, Daryadel, Arezoo, Roumeliotis, Stefanos et al. (2015) C-Terminal Fragment of Agrin (CAF): A Novel Marker for Progression of Kidney Disease in Type 2 Diabetics. PloS one 10(12): e0143524	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Dutra, Marina Constante, Uliano, Estevao Jose Muller, Machado, Danubia Felippe Grassi de Paula et al. (2014) Assessment of kidney function in the elderly: a population-based study. Jornal brasileiro de nefrologia : 'orgao oficial de Sociedades Brasileira e Latino-Americana de Nefrologia 36(3): 297-303	- Data not reported in an extractable format *Decline in eGFR by age reported as a scatter chart*
Eastwood, S.V., Chaturvedi, N., Sattar, N. et al. (2019) Impact of Kidney Function on Cardiovascular Risk and Mortality: A Comparison of South Asian and European Cohorts. American Journal of Nephrology 50(6): 425-433	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Ebert, Natalie, Jakob, Olga, Gaedeke, Jens et al. (2017) Prevalence of reduced kidney function	- Study does not contain phenomenon of interest

Study	Reason for exclusion
and albuminuria in older adults: the Berlin Initiative Study. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 32(6): 997-1005	*Rate of decline in eGFR not reported*
Ermini, G, Tosetti, C, Zocchi, D et al. (2019) Type 2 diabetes treatment and progression of chronic kidney disease in Italian family practice. Journal of endocrinological investigation 42(7): 787-796	- Not a relevant study design *Retrospective study*
Evans, Marie, Grams, Morgan E, Sang, Yingying et al. (2018) Risk Factors for Prognosis in Patients With Severely Decreased GFR. Kidney international reports 3(3): 625-637	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Fabiano, Rafaela C G, Araujo, Stanley A, Bambirra, Eduardo A et al. (2017) The Oxford Classification predictors of chronic kidney disease in pediatric patients with IgA nephropathy. Jornal de pediatria 93(4): 389-397	- Not a relevant study design *Retrospective study*
Fassett, Robert G; Geraghty, Dominic P; Coombes, Jeff S (2014) The impact of pre-intervention rate of kidney function change on the assessment of CKD progression. Journal of nephrology 27(5): 515-9	- Not a relevant study design *Retrospective study*
Fenton, Anthony, Montgomery, Emma, Nightingale, Peter et al. (2018) Glomerular filtration rate: new age- and gender- specific reference ranges and thresholds for living kidney donation. BMC nephrology 19(1): 336	- Not a relevant study design *Retrospective study*
Fliser, Danilo, Franek, Edward, Joest, Markus et al. (1997) Renal function in the elderly: Impact of hypertension and cardiac function. Kidney International 51(4): 1196-1204	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Fuhrman, Dana Y, Schneider, Michael F, Dell, Katherine M et al. (2017) Albuminuria, Proteinuria, and Renal Disease Progression in Children with CKD. Clinical journal of the American Society of Nephrology : CJASN 12(6): 912-920	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*

Study	Reason for exclusion
Furth, Susan L, Pierce, Chris, Hui, Wun Fung et al. (2018) Estimating Time to ESRD in Children With CKD. American journal of kidney diseases : the official journal of the National Kidney Foundation 71(6): 783-792	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
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	- Not a relevant study design *Retrospective study*
Gonzalez-Quiroz, Marvin, Smpokou, Evangelia-Theano, Silverwood, Richard J et al. (2018) Decline in Kidney Function among Apparently Healthy Young Adults at Risk of Mesoamerican Nephropathy. Journal of the American Society of Nephrology : JASN 29(8): 2200-2212	- Does not contain a relevant population *[Participants were subgroup based on their baseline decline in eGFR]*
Grams, Morgan E, Li, Liang, Greene, Tom H et al. (2015) Estimating time to ESRD using kidney failure risk equations: results from the African American Study of Kidney Disease and Hypertension (AASK). American journal of kidney diseases : the official journal of the National Kidney Foundation 65(3): 394-402	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Guo, Yidan, Cui, Liufu, Ye, Pengpeng et al. (2018) Change of Kidney Function Is Associated With All-Cause Mortality and Cardiovascular Diseases: Results From the Kailuan Study. Journal of the American Heart Association 7(21): e010596	- Study does not contain phenomenon of interest *Decline is not reported overtime (only 1 follow-up)*
Halbesma, Nynke, Kuiken, Dirk-Sjoerd, Brantsma, Auke H et al. (2006) Macroalbuminuria is a better risk marker than low estimated GFR to identify individuals at risk for accelerated GFR loss in population screening. Journal of the American Society of Nephrology : JASN 17(9): 2582-2590	- Study does not contain phenomenon of interest *Decline is not reported overtime (only 1 follow-up)*
Hemmelgarn, B.R., Zhang, J., Manns, B.J. et al. (2006) Progression of kidney dysfunction in the community-dwelling elderly. Kidney International 69(12): 2155-2161	- Data not reported in an extractable format *Sample sizes for subgroup analysis were not reported*

Study	Reason for exclusion
Hering, Dagmara, Marusic, Petra, Duval, Jacqueline et al. (2017) Effect of renal denervation on kidney function in patients with chronic kidney disease. International journal of cardiology 232: 93-97	- Does not contain a relevant population *All participants went through renal denervation*
Hirano, K., Kobayashi, D., Kohtani, N. et al. (2019) Optimal follow-up intervals for different stages of chronic kidney disease: a prospective observational study. Clinical and Experimental Nephrology 23(5): 613-620	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Hirst, J.A., Ordonez Mena, J.M., Taylor, C.J. et al. (2020) Prevalence of chronic kidney disease in the community using data from OxRen: A UK population-based cohort study. British Journal of General Practice 70(693): e285-e293	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Huang, J., Hoy, W., Levin, A. 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	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Imamura, Yoshihiko, Takahashi, Yasunori, Hayashi, Toshihide et al. (2019) Usefulness of multidisciplinary care to prevent worsening renal function in chronic kidney disease. Clinical and experimental nephrology 23(4): 484-492	- Not a relevant study design *Retrospective study*
Janki, Shiromani, Dols, Leonienke F C, Timman, Reinier et al. (2017) Five-year follow-up after live donor nephrectomy - cross-sectional and longitudinal analysis of a prospective cohort within the era of extended donor eligibility criteria. Transplant international : official journal of the European Society for Organ Transplantation 30(3): 266-276	- Study does not contain phenomenon of interest *Decline is not reported overtime (only 1 follow-up)*
Jiang, G., Luk, A.O.Y., Tam, C.H.T. et al. (2019) Progression of diabetic kidney disease and trajectory of kidney function decline in Chinese patients with Type 2 diabetes. Kidney International 95(1): 178-187	- Data not reported in an extractable format *Definition of the type of decline not reported in the main text (slow, curvilinear, progressive, accelerated decline). Supplementary information not available from the British Library during COVID-19 pandemic*

Study	Reason for exclusion
Kachimanga, Chiyembekezo, Kamwezi, Richard, Wroe, Emily B et al. (2019) Screening for chronic kidney disease in rural Malawi: results from a diabetic clinic. BMC research notes 12(1): 375	- Not a relevant study design *Retrospective study*
Kalyesubula, Robert, Hau, Jeffrey P, Asiki, Gershim et al. (2018) Impaired renal function in a rural Ugandan population cohort. Wellcome open research 3: 149	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Kamdem, Felicite, Lekpa, Fernando Kemta, Doualla, Marie Solange et al. (2017) Prevalence and risk factors of chronic kidney disease in newly diagnosed and untreated hypertensive patients in cameroon: A cross-sectional study. Saudi journal of kidney diseases and transplantation : an official publication of the Saudi Center for Organ Transplantation, Saudi Arabia 28(5): 1144-1149	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Kanda, Eiichiro, Usui, Tomoko, Kashihara, Naoki et al. (2018) Importance of glomerular filtration rate change as surrogate endpoint for the future incidence of end-stage renal disease in general Japanese population: community-based cohort study. Clinical and experimental nephrology 22(2): 318-327	- Not a relevant study design *Retrospective study*
Kanda, Takeshi, Takeda, Ayano, Hirose, Hiroshi et al. (2018) Temporal trends in renal function and birthweight in Japanese adolescent males (1998-2015). Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 33(2): 304-310	- Study does not contain outcomes of interest *Decline in eGFR not reported*
Kang, Eunjeong, Han, Miyeun, Kim, Hyunsuk et al. (2017) Baseline General Characteristics of the Korean Chronic Kidney Disease: Report from the KoreaN Cohort Study for Outcomes in Patients With Chronic Kidney Disease (KNOW-CKD). Journal of Korean medical science 32(2): 221-230	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Kang, Ji-Hyoun, Park, Dong-Jin, Lee, Kyung-Eun et al. (2017) Comparison of clinical,	- Study does not contain phenomenon of interest

Study	Reason for exclusion
serological, and prognostic differences among juvenile-, adult-, and late-onset lupus nephritis in Korean patients. Clinical rheumatology 36(6): 1289-1295	*Rate of decline in eGFR not reported*
Kara, Ekrem, Sahin, Osman Zikrullah, Kizilkaya, Bayram et al. (2017) Fasting in Ramadan is not associated with deterioration of chronic kidney disease: A prospective observational study. Saudi journal of kidney diseases and transplantation : an official publication of the Saudi Center for Organ Transplantation, Saudi Arabia 28(1): 68-75	- Study does not contain phenomenon of interest *Decline is not reported overtime (only 1 follow-up)*
Kataoka-Yahiro, Merle, Davis, James, Gandhi, Krupa et al. (2019) Asian Americans & chronic kidney disease in a nationally representative cohort. BMC nephrology 20(1): 10	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Kerschbaum, J., Bitter, S., Weitlaner, M. et al. (2020) Arterial hypertension as a risk factor for reduced glomerular filtration rate after living kidney donation. Journal of Clinical Medicine 9(2): 338	- Not a relevant study design *Retrospective study*
Khalil, A., Yaqub, M.S., Taber, T. et al. (2020) Correlation and Prediction of Living-Donor Remaining Function by Using Predonation Computed Tomography-Based Volumetric Measurements: Role of Remaining Kidney Volume. Experimental and clinical transplantation : official journal of the Middle East Society for Organ Transplantation 18(1): 39-47	- Not a relevant study design *Retrospective study*
Khalil, Amani A, Abed, Mona A, Ahmad, Muayyad et al. (2018) Under-diagnosed chronic kidney disease in Jordanian adults: prevalence and correlates. Journal of renal care 44(1): 12-18	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Khalsa, D.D.K.; Beydoun, H.A.; Carmody, J.B. (2016) Prevalence of chronic kidney disease risk factors among low birth weight adolescents. Pediatric Nephrology 31(9): 1509-1516	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*

Study	Reason for exclusion
Khan, Yusra Habib, Sarriff, Azmi, Adnan, Azreen Syazril et al. (2017) Progression and outcomes of non-dialysis dependent chronic kidney disease patients: A single center longitudinal follow-up study. Nephrology (Carlton, Vic.) 22(1): 25-34	- Not a relevant study design *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	- Secondary publication of an included study that does not provide any additional relevant information *Related to Iimori 2018*
Kim, Jong Ho, Kim, Sang Soo, Kim, In Joo et al. (2017) Nonalbumin proteinuria is a simple and practical predictor of the progression of early-stage type 2 diabetic nephropathy. Journal of diabetes and its complications 31(2): 395-399	- Data not reported in an extractable format *Average decline in eGFR without a measure of dispersion*
Kim, K.-S., Park, S.W., Cho, Y.-W. et al. (2018) Higher prevalence and progression rate of chronic kidney disease in elderly patients with type 2 diabetes mellitus. Diabetes and Metabolism Journal 42(3): 224-232	- Not a relevant study design *Retrospective study*
Knoop, Thomas, Vikse, Bjorn Egil, Mwakimonga, Angela et al. (2017) Long-term outcome in 145 patients with assumed benign immunoglobulin A nephropathy. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 32(11): 1841-1850	- Data not reported in an extractable format *Annual change in eGFR without a measure of dispersion*
Kon, Soichiro, Konta, Tsuneo, Ichikawa, Kazunobu et al. (2018) Association between renal function and cardiovascular and all-cause mortality in the community-based elderly population: results from the Specific Health Check and Guidance Program in Japan. Clinical and experimental nephrology 22(2): 346-352	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Koraishy, F.M., Hooks-Anderson, D., Salas, J. et al. (2018) Fast GFR decline and progression to	- Not a relevant study design *Retrospective study*

Study	Reason for exclusion
CKD among primary care patients with preserved GFR. International Urology and Nephrology 50(3): 501-508	
Kovesdy, Csaba P, Coresh, Josef, Ballew, Shoshana H et al. (2016) Past Decline Versus Current eGFR and Subsequent ESRD Risk. Journal of the American Society of Nephrology : JASN 27(8): 2447-55	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
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	- Secondary publication of an included study that does not provide any additional relevant information *Fischer 2016 reports results in the whole sample and Koye 2018 only reports on participants with diabetes.*
Kuo, I-Ching, Huang, Jiun-Chi, Wu, Pei-Yu et al. (2017) A Low Geriatric Nutrition Risk Index Is Associated with Progression to Dialysis in Patients with Chronic Kidney Disease. Nutrients 9(11)	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
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	- Secondary publication of an included study that does not provide any additional relevant information *Related to Fischer 2016*
Kwon, Hanna, Lee, Dong-Gi, Kang, Hee Cheol et al. (2016) Incidence of isolated dipstick hematuria and its association with the glomerular filtration rate: a cross-sectional study from the Korean National Health and Nutrition Examination Survey V (2010-2012). International urology and nephrology 48(4): 451-6	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Lalan, Shwetal, Jiang, Shuai, Ng, Derek K et al. (2018) Cardiometabolic Risk Factors, Metabolic Syndrome, and Chronic Kidney Disease Progression in Children. The Journal of pediatrics 202: 163-170	- Study does not contain phenomenon of interest *Decline is not reported overtime (only 1 follow-up)*

Study	Reason for exclusion
Lang, Joshua, Katz, Ronit, Ix, Joachim H et al. (2018) Association of serum albumin levels with kidney function decline and incident chronic kidney disease in elders. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 33(6): 986-992	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Le, WeiBo, Liang, ShaoShan, Chen, Hao et al. (2014) Long-term outcome of IgA nephropathy patients with recurrent macroscopic hematuria. American journal of nephrology 40(1): 43-50	- Not a relevant study design *Retrospective study*
Lee, Kyungho, Shin, Jungho, Park, Jeeeun et al. (2018) First-year GFR slope and long-term renal outcome in IgA nephropathy. European journal of clinical investigation 48(6): e12936	- Not a relevant study design *Retrospective study*
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	- Data not reported in an extractable format *Annual decline in eGFR without a measure of dispersion*
Lindeman, Robert D.; Tobin, Jordan D.; Shock, Nathan W. (1984) Association between blood pressure and the rate of decline in renal function with age. Kidney International 26(6): 861-868	- Study does not contain phenomenon of interest *Rate of decline in renal function was measured using creatinine clearance without estimating glomerular filtration rate*
Liu, J.-J., Liu, S., Gurung, R.L. et al. (2020) Risk of progressive chronic kidney disease in individuals with early-onset type 2 diabetes: a prospective cohort study. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 35(1): 115-121	- Data not reported in an extractable format *Annual decline in eGFR without a measure of dispersion*
Liyanage, Polwatta Liyanage Gayani Chandima, Lekamwasam, Sarath, Weerarathna, Thilak Priyantha et al. (2018) Prevalence of normoalbuminuric renal insufficiency and associated clinical factors in adult onset diabetes. BMC nephrology 19(1): 200	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*

Study	Reason for exclusion
Lunyera, J., Stanifer, J.W., Davenport, C.A. et al. (2020) Life course socioeconomic status, allostatic load, and kidney health in black americans. Clinical Journal of the American Society of Nephrology 15(3): 341-348	- Secondary publication of an included study that does not provide any additional relevant information *Related to Young 2016*
Ma, Irene, Guo, Maggie, Muruve, Daniel et al. (2018) Sociodemographic associations with abnormal estimated glomerular filtration rate (eGFR) in a large Canadian city: a cross-sectional observation study. BMC nephrology 19(1): 198	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Madala, Nomandla D, Thusi, Gertrude P, Assounga, Alain G H et al. (2014) Characteristics of South African patients presenting with kidney disease in rural KwaZulu-Natal: a cross sectional study. BMC nephrology 15: 61	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Mahmood, Usman, Healy, Helen G, Kark, Adrian et al. (2017) Spectrum (characteristics) of patients with chronic kidney disease (CKD) with increasing age in a major metropolitan renal service. BMC nephrology 18(1): 372	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Malmgren, Linnea, McGuigan, Fiona E, Berglundh, Sofia et al. (2015) Declining Estimated Glomerular Filtration Rate and Its Association with Mortality and Comorbidity Over 10 Years in Elderly Women. Nephron 130(4): 245-55	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Mandelli, Sara, Riva, Emma, Tettamanti, Mauro et al. (2015) Mortality Prediction in the Oldest Old with Five Different Equations to Estimate Glomerular Filtration Rate: The Health and Anemia Population-based Study. PloS one 10(8): e0136039	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Maple-Brown, Louise J, Hughes, Jaquelyne T, Ritte, Rebecca et al. (2016) Progression of Kidney Disease in Indigenous Australians: The eGFR Follow-up Study. Clinical journal of the American Society of Nephrology : CJASN 11(6): 993-1004	- Study does not contain phenomenon of interest *Decline is not reported overtime (only 1 follow-up)*

Study	Reason for exclusion
Martin Benlloch, J; Roman Ortiz, E; Mendizabal Oteiza, S (2016) Long-term safety in living kidney donors for paediatric transplantation. Single-centre prospective study. Nefrologia : publicacion oficial de la Sociedad Espanola Nefrologia 36(6): 674-678	- Study does not contain outcomes of interest *Rate of decline in eGFR not reported* - Study not reported in English *Spanish*
Massie, A.B., Holscher, C.M., Henderson, M.L. et al. (2020) Association of Early Postdonation Renal Function with Subsequent Risk of End-Stage Renal Disease in Living Kidney Donors. JAMA Surgery 155(3): e195472	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Matsushita, Kunihiro, Chen, Jingsha, Sang, Yingying et al. (2016) Risk of end-stage renal disease in Japanese patients with chronic kidney disease increases proportionately to decline in estimated glomerular filtration rate. Kidney international 90(5): 1109-1114	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Matsushita, Kunihiro, Coresh, Josef, Sang, Yingying et al. (2015) Estimated glomerular filtration rate and albuminuria for prediction of cardiovascular outcomes: a collaborative meta-analysis of individual participant data. The lancet. Diabetes & endocrinology 3(7): 514-25	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Melsom, Toralf, Solbu, Marit Dahl, Schei, Jorgen et al. (2018) Mild Albuminuria Is a Risk Factor for Faster GFR Decline in the Nondiabetic Population. Kidney international reports 3(4): 817-824	- Secondary publication of an included study that does not provide any additional relevant information *Related to Melsom 2019*
Mirijello, Antonio, Viazzi, Francesca, Fioretto, Paola et al. (2018) Association of kidney disease measures with risk of renal function worsening in patients with type 1 diabetes. BMC nephrology 19(1): 347	- Data not reported in an extractable format *Rate of decline in eGFR reported graphically*
Mok, Yejin, Matsushita, Kunihiro, Sang, Yingying et al. (2016) Association of Kidney Disease Measures with Cause-Specific Mortality: The Korean Heart Study. PloS one 11(4): e0153429	- Not a relevant study design *Retrospective study*

Study	Reason for exclusion
Murai-Takeda, A., Kanda, T., Azegami, T. et al. (2019) Low birth weight is associated with decline in renal function in Japanese male and female adolescents. Clinical and Experimental Nephrology 23(12): 1364-1372	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Mwasongwe, Stanford, Min, Yuan-I, Booth, John N 3rd et al. (2018) Masked hypertension and kidney function decline: the Jackson Heart Study. Journal of hypertension 36(7): 1524-1532	- Study does not contain phenomenon of interest *Decline is not reported overtime (only 1 follow-up)*
Na, J C, Park, J S, Yoon, M-G et al. (2018) Long-term Follow-up of Living Kidney Donors With Chronic Kidney Disease at 1 Year After Nephrectomy. Transplantation proceedings 50(4): 1018-1021	- Not a relevant study design *Retrospective study*
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 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	- Not a relevant study design *Retrospective study*
Nagai, Kei, Sairenchi, Toshimi, Irie, Fujiko et al. (2016) Relationship between Estimated Glomerular Filtration Rate and Cardiovascular Mortality in a Japanese Cohort with Long-Term Follow-Up. PloS one 11(6): e0156792	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
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	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Nakanga, Wisdom P, Prynn, Josephine E, Banda, Louis et al. (2019) Prevalence of impaired renal function among rural and urban populations: findings of a cross-sectional study in Malawi. Wellcome open research 4: 92	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*

Study	Reason for exclusion
Oh, Se Won, Kim, Sejoong, Na, Ki Young et al. (2014) Glomerular filtration rate and proteinuria: association with mortality and renal progression in a prospective cohort of a community-based elderly population. PloS one 9(4): e94120	- Study does not contain phenomenon of interest *Decline is not reported overtime (only 1 follow-up)*
Ohno, Michiya, Deguchi, Fumiko, Izumi, Kumiko et al. (2014) Correlation between renal function and common risk factors for chronic kidney disease in a healthy middle-aged population: a prospective observational 2-year study. PloS one 9(11): e113263	- Study does not contain phenomenon of interest *Decline is not reported overtime (only 1 follow-up)*
Oliveira, I.O., Mintem, G.C., Oliveira, P.D. et al. (2020) Uric acid is independent and inversely associated to glomerular filtration rate in young adult Brazilian individuals. Nutrition, Metabolism and Cardiovascular Diseases 30(8): 1289-1298	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Omuse, Geoffrey, Maina, Daniel, Mwangi, Jane et al. (2017) Comparison of equations for estimating glomerular filtration rate in screening for chronic kidney disease in asymptomatic black Africans: a cross sectional study. BMC nephrology 18(1): 369	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Ortega-Romero, M., Mendez-Hernandez, P., Cruz-Angulo, M.D.C. et al. (2019) Chronic Kidney Disease in Children Aged 6-15 Years and Associated Risk Factors in Apizaco, Tlaxcala, Mexico, a Pilot Study. Nephron 143(4): 264-273	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Oshima, Megumi, Toyama, Tadashi, Haneda, Masakazu et al. (2018) Estimated glomerular filtration rate decline and risk of end-stage renal disease in type 2 diabetes. PloS one 13(8): e0201535	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Pallayova, M., Rayner, H., Taheri, S. et al. (2015) Is there a difference in progression of renal disease between South Asian and white European diabetic adults with moderately reduced kidney function?. Journal of Diabetes and its Complications 29(6): 761-765	- Study does not contain phenomenon of interest *Decline is not reported overtime (only 1 follow-up)*

Study	Reason for exclusion
Pawlak-Bratkowska, M., Stanczyk, M., Baranska, D. et al. (2015) Influence of low birth weight on blood pressure and kidney volume in healthy 2-3 years old children. Pediatria Polska 90(5): 372-377	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Penno, Giuseppe, Solini, Anna, Bonora, Enzo et al. (2018) Defining the contribution of chronic kidney disease to all-cause mortality in patients with type 2 diabetes: the Renal Insufficiency And Cardiovascular Events (RIACE) Italian Multicenter Study. Acta diabetologica 55(6): 603-612	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Piscitelli, Pamela, Viazzi, Francesca, Fioretto, Paola et al. (2017) Predictors of chronic kidney disease in type 1 diabetes: a longitudinal study from the AMD Annals initiative. Scientific reports 7(1): 3313	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Polonia, Jorge, Azevedo, Andre, Monte, Miguel et al. (2017) Annual deterioration of renal function in hypertensive patients with and without diabetes. Vascular health and risk management 13: 231-237	- Not a relevant study design *Retrospective study*
Rein, Philipp, Saely, Christoph H, Vonbank, Alexander et al. (2014) Usefulness of serial decline of kidney function to predict mortality and cardiovascular events in patients undergoing coronary angiography. The American journal of cardiology 113(2): 215-21	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Ricardo, Ana C, Yang, Wei, Sha, Daohang et al. (2019) Sex-Related Disparities in CKD Progression. Journal of the American Society of Nephrology : JASN 30(1): 137-146	- Data not reported in an extractable format *Annual slope in eGFR without a measure of dispersion*
Rios, Alvaro, Lorca, Eduardo, Garmendia, Maria Luisa et al. (2016) Estimated glomerular filtration rate, urine albumin excretion, and survival among patients consulting in public Chilean public primary care clinics. Renal failure 38(3): 397-403	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Rocke, K.D., Ferguson, T.S., Younger-Coleman, N.O. et al. (2018) Relationship between early	- Data not reported in an extractable format

Study	Reason for exclusion
life factors and renal function in Afro-Caribbean young adults: Analysis from the Jamaica 1986 Birth Cohort Study. West Indian Medical Journal 67(2)	*Rate of decline in eGFR not reported*
Rucci, Paola, Mandreoli, Marcora, Gibertoni, Dino et al. (2014) A clinical stratification tool for chronic kidney disease progression rate based on classification tree analysis. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 29(3): 603-10	- Not a relevant study design *Retrospective study*
Rule, Andrew D, Gussak, Hiie M, Pond, Gregory R et al. (2004) Measured and estimated GFR in healthy potential kidney donors. American Journal of Kidney Diseases 43(1): 112-119	- Not a relevant study design *Retrospective study*
Saito, Takako, Uchida, Keiko, Ishida, Hideki et al. (2015) Changes in glomerular filtration rate after donation in living kidney donors: a single-center cohort study. International urology and nephrology 47(2): 397-403	- Not a relevant study design *Retrospective study*
Salvador-Gonzalez, B., Mestre-Ferrer, J., Soler-Vila, M. et al. (2017) Chronic kidney disease in hypertensive subjects >=60 years treated in Primary Care. Nefrologia 37(4): 406-414	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Samuel, Susan M, Palacios-Derflingher, Luz, Tonelli, Marcello et al. (2014) Association between First Nations ethnicity and progression to kidney failure by presence and severity of albuminuria. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne 186(2): e86-94	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Sanchez, Otto A, Ferrara, Laine K, Rein, Sarah et al. (2018) Hypertension after kidney donation: Incidence, predictors, and correlates. American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons 18(10): 2534-2543	- Not a relevant study design *Retrospective study*

Study	Reason for exclusion
Saydah, Sharon H, Xie, Hui, Imperatore, Giuseppina et al. (2018) Trends in Albuminuria and GFR Among Adolescents in the United States, 1988-2014. American journal of kidney diseases : the official journal of the National Kidney Foundation 72(5): 644-652	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Schaefer, Joao Carlos Fantini, Pereira, Mariana Soares, de Jesus, Clovisa Reck et al. (2015) Kidney function estimate among subjects aged 18-59 years in Tubarao, Santa Catarina: a population-based study. Jornal brasileiro de nefrologia : 'orgao oficial de Sociedades Brasileira e Latino-Americana de Nefrologia 37(2): 185-91	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Sebastiao, Y.V., Cooper, J.N., Becknell, B. et al. (2020) Prediction of kidney failure in children with chronic kidney disease and obstructive uropathy. Pediatric Nephrology	- Kidney failure risk equation in children and young people *This study was included in the evidence review identifying kidney failure prediction equations*
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	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Shardlow, Adam, McIntyre, Natasha J, Fluck, Richard J et al. (2016) Chronic Kidney Disease in Primary Care: Outcomes after Five Years in a Prospective Cohort Study. PLoS medicine 13(9): e1002128	- Study does not contain phenomenon of interest *Decline is not reported overtime (only 1 follow-up)*
Shimizu, Miho, Furuichi, Kengo, Toyama, Tadashi et al. (2018) Decline in estimated glomerular filtration rate is associated with risk of end-stage renal disease in type 2 diabetes with macroalbuminuria: an observational study from JDNCS. Clinical and experimental nephrology 22(2): 377-387	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Slack, TK and Wilson, DM (1976) Normal renal function: CIN and CPAH in healthy donors before and after nephrectomy. Mayo Clinic proceedings 51(5): 296-300	- Data not reported in an extractable format *Decline in eGFR without a measure of dispersion*

Study	Reason for exclusion
Soylemezoglu, Oguz, Duzova, Ali, Yalcinkaya, Fatos et al. (2012) Chronic renal disease in children aged 5-18 years: a population-based survey in Turkey, the CREDIT-C study. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 27suppl3: iii146-51	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Sumida, Keiichi, Molnar, Miklos Z, Potukuchi, Praveen K et al. (2017) Changes in Albuminuria and Subsequent Risk of Incident Kidney Disease. Clinical journal of the American Society of Nephrology : CJASN 12(12): 1941-1949	- Not a relevant study design *Retrospective study*
Suzuki, Akira, Obi, Yoshitsugu, Hayashi, Terumasa et al. (2019) Visit-to-visit variability in estimated glomerular filtration rate predicts hospitalization and death due to cardiovascular events. Clinical and experimental nephrology 23(5): 661-668	- Data not reported in an extractable format *Rate of decline in eGFR not reported*
Suzuki, H., Inoue, T., Dogi, M. et al. (2014) Decline of renal function and progression of left ventricular hypertrophy are independently determined in chronic kidney disease stages 3-5. Pulse 2(14): 29-37	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Tanaka, Kenichi, Watanabe, Tsuyoshi, Takeuchi, Ayano et al. (2017) Cardiovascular events and death in Japanese patients with chronic kidney disease. Kidney international 91(1): 227-234	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Thomas, Bernadette, Matsushita, Kunihiro, Abate, Kalkidan Hassen et al. (2017) Global Cardiovascular and Renal Outcomes of Reduced GFR. Journal of the American Society of Nephrology : JASN 28(7): 2167-2179	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Trihono, Partini Pudjiastuti; Rhodia, Lia; Karyanti, Mulya Rahma (2018) Kidney Disease Profiles Among Adolescents In Indonesia. Acta medica Indonesiana 50(4): 283-290	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Tsai, Ching-Wei, Ting, I-Wen, Yeh, Hung-Chieh et al. (2017) Longitudinal change in estimated	- Study does not contain phenomenon of interest

Study	Reason for exclusion
GFR among CKD patients: A 10-year follow-up study of an integrated kidney disease care program in Taiwan. PloS one 12(4): e0173843	*Decline is not reported overtime (only 1 follow-up)*
van Deventer, Hendrick E, Paiker, Janice E, Katz, Ivor J et al. (2011) A comparison of cystatin C- and creatinine-based prediction equations for the estimation of glomerular filtration rate in black South Africans. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 26(5): 1553-8	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Viazzi, F., Ceriello, A., Fioretto, P. et al. (2018) Changes in albuminuria and renal outcome in patients with type 2 diabetes and hypertension: A real-life observational study. Journal of Hypertension 36(8): 1719-1728	- Not a relevant study design *Retrospective study*
Vistisen, D., Andersen, G.S., Hulman, A. et al. (2019) Progressive decline in estimated glomerular filtration rate in patients with diabetes after moderate loss in kidney functiond even without albuminuria. Diabetes Care 42(10): 1886-1894	- Not a relevant study design *Retrospective study*
Vora, Amit N, Stanislawski, Maggie, Grunwald, Gary K et al. (2017) Association Between Chronic Kidney Disease and Rates of Transfusion and Progression to End-Stage Renal Disease in Patients Undergoing Transradial Versus Transfemoral Cardiac Catheterization-An Analysis From the Veterans Affairs Clinical Assessment Reporting and Tracking (CART) Program. Journal of the American Heart Association 6(4)	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Wang, Jeffrey, Lewis, Joshua R, Byrnes, Elizabeth et al. (2020) Serum Midkine, estimated glomerular filtration rate and chronic kidney disease-related events in elderly women: Perth Longitudinal Study of Aging Women. Scientific reports 10(1): 14499	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Wang, Jiali, Zhao, Lijun, Zhang, Junlin et al. (2020) CLINICOPATHOLOGIC FEATURES AND PROGNOSIS OF TYPE 2 DIABETES	- Study does not contain phenomenon of interest

Study	Reason for exclusion
MELLITUS AND DIABETIC NEPHROPATHY IN DIFFERENT AGE GROUPS: MORE ATTENTION TO YOUNGER PATIENTS. Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists 26(1): 51-57	*Rate of decline in eGFR not reported*
Wang, Jinwei, Wang, Fang, Liu, Shiwei et al. (2017) Reduced Kidney Function, Albuminuria, and Risks for All-cause and Cardiovascular Mortality in China: A Population-based Cohort Study. BMC nephrology 18(1): 188	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Wang, Jinwei, Wang, Fang, Saran, Rajiv et al. (2018) Mortality risk of chronic kidney disease: A comparison between the adult populations in urban China and the United States. PloS one 13(3): e0193734	- Data not reported in an extractable format *Decline in eGFR reported graphically*
Wen, Chi Pang, Matsushita, Kunihiro, Coresh, Josef et al. (2014) Relative risks of chronic kidney disease for mortality and end-stage renal disease across races are similar. Kidney international 86(4): 819-27	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Weng, Shuo-Chun, Tarng, Der-Cherng, Chen, Chyong-Mei et al. (2014) Estimated glomerular filtration rate decline is a better risk factor for outcomes of systemic disease-related nephropathy than for outcomes of primary renal diseases. PloS one 9(4): e92881	- Data not reported in an extractable format *Annual decline in eGFR without a measure of dispersion*
Wetzels, J.F.M., Kiemeney, L.A.L.M., Swinkels, D.W. et al. (2007) Age- and gender-specific reference values of estimated GFR in Caucasians: The Nijmegen Biomedical Study. Kidney International 72(5): 632-637	- Data not reported in an extractable format *Annual decline in eGFR without a measure of dispersion*
Wong, Craig S, Pierce, Christopher B, Cole, Stephen R et al. (2009) Association of proteinuria with race, cause of chronic kidney disease, and glomerular filtration rate in the chronic kidney disease in children study. Clinical journal of the American Society of Nephrology : CJASN 4(4): 812-9	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*

Study	Reason for exclusion
Wu, Jianwei, Jia, Jiaokun, Li, Zhaoxia et al. (2018) Association of estimated glomerular filtration rate and proteinuria with all-cause mortality in community-based population in China: A Result from Kailuan Study. Scientific reports 8(1): 2157	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Xie, Yan, Bowe, Benjamin, Xian, Hong et al. (2016) Renal Function Trajectories in Patients with Prior Improved eGFR Slopes and Risk of Death. PloS one 11(2): e0149283	- Not a relevant study design *Retrospective study*
Xie, Yan, Bowe, Benjamin, Xian, Hong et al. (2016) Estimated GFR Trajectories of People Entering CKD Stage 4 and Subsequent Kidney Disease Outcomes and Mortality. American journal of kidney diseases : the official journal of the National Kidney Foundation 68(2): 219-228	- Not a relevant study design *Retrospective study*
Yang, Wei, Xie, Dawei, Anderson, Amanda H et al. (2014) Association of kidney disease outcomes with risk factors for CKD: findings from the Chronic Renal Insufficiency Cohort (CRIC) study. American journal of kidney diseases : the official journal of the National Kidney Foundation 63(2): 236-43	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*
Yu, Mi-Yeon, Kim, Dong Ki, Park, Jung Hwan et al. (2018) Albuminuria during treatment with angiotensin type II receptor blocker is a predictor for GFR decline among non-diabetic hypertensive CKD patients. PloS one 13(8): e0202676	- Study does not contain phenomenon of interest *Rate of decline in eGFR not reported*