

Item S1. Data analysis overview and analytic notes for some of individual studies

Overview:

As previously described,¹ the collaborating cohorts were asked to compile a dataset with approximately 40 variables (key exposures [serum creatinine to estimate GFR and albuminuria], covariates [e.g., age, sex, race/ethnicity, diabetes], and outcomes [laboratory tests and hypertension]). To be consistent across cohorts, the CKD-PC Data Coordinating Center sent definitions for those variables to participating cohorts. We instructed studies not to impute any variables.

For 42 of the 55 cohorts in this specific study, the Data Coordination Center at Johns Hopkins University conducted the analysis; the remainder ran the standard code written in STATA by the Data Coordinating Center and shared the output with the Data Coordinating Center. The standard code was designed to automatically save all estimates and variance-covariance matrices needed for the meta-analysis. Then, the Data Coordinating Center meta-analyzed the estimates across cohorts using STATA.

As detailed in our previous reports,^{2,3} each cohort was instructed to standardize their serum creatinine and report its method when available. The reported creatinine standardization allows grouping studies into studies that reported using a standard IDMS traceable method or conducted some serum creatinine standardization to IDMS traceable methods (ARIC, AusDiab, BIS, CanPREDDICT, CARE FOR HOME, ESTHER, GCKD, Geisinger, Gonryo, Gubbio, Maccabi, MASTERPLAN, MMKD, NHANES, PREVEND, Rancho Bernardo, RCAV, REGARDS, RSIII, SCREAM, SEED, SRR-CKD, Takahata) and studies where the creatinine standardization was not done (AASK, ADVANCE, Aichi, BC CKD, Beijing, CCF, ChinaNS, CHS, CIRCS, CKD-JAC, CRIB, Framingham, IPHS, KHS, MDRD, MESA, MRC, NZDCS, Ohasama, Pima, RENAAL, Sunnybrook, Taiwan MJ, ULSAM, ZODIAC). For those cohorts without standardization, the creatinine levels were reduced by 5%, the calibration factor used to adjust non-standardized MDRD Study samples to IDMS.^{2,4} We did not adjust creatinine levels in those studies with unknown standardization status (JMS, Mt Sinai, NIPPON DATA80, NIPPON DATA90, NIPPON DATA2010, PSP-CKD and SMART).

We calculated eGFR using the CKD-EPI equation: $eGFR_{CKD-EPI} = 141 \times (\text{minimum of standardized serum creatinine [mg/dL]/}\kappa \text{ or } 1)^{\alpha} \times (\text{maximum of standardized serum creatinine [mg/dL]/}\kappa \text{ or } 1)^{-1.209} \times 0.993^{\text{age}} \times (1.018 \text{ if female}) \times (1.159 \text{ if black})$, where κ is 0.7 if female and 0.9 if male and α is -0.329 if female and -0.411 if male.⁵ The selection of knots for eGFR and ACR was based on clinical thresholds.⁶

Notes for individual studies:

1. General population cohorts

ChinaNS: Anti-hypertensive medication use was not available.

2. High-risk cohorts

ADVANCE: This study is an intervention study which includes participants with diabetes only.

Geisinger: Due to the requirement of ACR measurement for analyses and the clinical indications that are associated with measurement in this health system dataset, this cohort was categorized as a high-risk cohort for all outcomes except phosphorus and PTH, and as a CKD cohort for outcomes phosphorus and PTH. Urine protein-to-creatinine ratio was converted to urine albumin-to-creatinine ratio by dividing by 2.655 for men and 1.7566 for women.

Maccabi: Due to the requirement of ACR measurement for analyses and the clinical indications that are associated with measurement in this health system dataset, this cohort was categorized as a high-risk cohort. Urine protein-to-creatinine ratio was converted to urine albumin-to-creatinine ratio by dividing by 2.655 for men and 1.7566 for women.

Mt Sinai BioMe: Due to the requirement of ACR measurement for analyses and the clinical indications that are associated with measurement in this health system dataset, this cohort was categorized as a high-risk cohort for all outcomes except phosphorus and PTH, and as a CKD cohort for outcomes phosphorus and PTH. Urine

protein-to-creatinine ratio was converted to urine albumin-to-creatinine ratio by dividing by 2.655 for men and 1.7566 for women.

PIMA: History of CVD was not available.

SCREAM: This cohort does not have data on BMI, smoking and blood pressure. Due to the requirement of ACR measurement for analyses and the clinical indications that are associated with measurement in this health system dataset, this cohort was categorized as a high-risk cohort for all outcomes except phosphorus and PTH, and as a CKD cohort for outcomes phosphorus and PTH.

ZODIAC: Anti-hypertensive medication use was not available.

3. CKD cohorts

AASK: Urine protein-to-creatinine ratio was converted to urine albumin-to-creatinine ratio by dividing by 2.655 for men and 1.7566 for women.

CanPREDDICT: This cohort does not have data on smoking. Urine protein-to-creatinine ratio was converted to urine albumin-to-creatinine ratio by dividing by 2.655 for men and 1.7566 for women.

CRIB: History of heart failure was not available. Use of thiazide diuretics, loop diuretics or potassium sparing diuretics was combined. Individual use of each type of diuretics was not available.

Gonryo: This cohort does not have data on smoking.

MASTERPLAN: This study measured urine albumin-to-creatinine ratio in patients with albuminuria in the low range, urine protein-to-creatinine ratio in patients with overt proteinuria. Urine protein-to-creatinine ratio was converted to urine albumin-to-creatinine ratio by dividing by 2.655 for men and 1.7566 for women.

MDRD: Anti-hypertensive medication use was not available. Urine protein-to-creatinine ratio was converted to urine albumin-to-creatinine ratio by dividing by 2.655 for men and 1.7566 for women.

PSP-CKD: Urine protein-to-creatinine ratio was converted to urine albumin-to-creatinine ratio by dividing by 2.655 for men and 1.7566 for women.

RCAV: This cohort does not have data on smoking. Subset of eGFR<60 of this cohort was included in the analysis thus categorized as a CKD cohort.

RENAAL: History of CVD was not available.

SRR-CKD: This cohort does not have data on smoking. There may be some overlap with the SCREAM cohort, which would capture participants with advanced CKD in the region of Stockholm. Use of thiazide diuretics, loop diuretics or potassium sparing diuretics was combined. Individual use of each type of diuretics was not available.

Sunnybrook: This cohort includes patients seen in the nephrology clinics at Sunnybrook Hospital in Toronto, Ontario, Canada with CKD stage 3-5 or proteinuric CKD stage 1-2. Urine protein-to-creatinine ratio was converted to urine albumin-to-creatinine ratio by dividing by 2.655 for men and 1.7566 for women.

Diabetes Definition Information:

Study	Diabetes definition requested: <i>Glycated hemoglobin A1c \geq6.5% or fasting glucose \geq7.0 mmol/L (\geq126 mg/dL) or non-fasting glucose \geq11.1 mmol/L (\geq200 mg/dL) or use of glucose lowering drugs (ADA 2010 criteria). Self-report of physician diagnosed diabetes can be included. Any differences from the above noted below:</i>
CKD Cohorts	
AASK	All participants were free of diabetes as this was an exclusion criterion to have a known history of diabetes.
BC CKD	
CanPREDDICT	
CARE FOR HOME	Diabetes was defined as diabetes mellitus reported by the patients or the nephrologist and/or intake of diabetic medication and/or fasting plasma glucose > 126 mg/dl at inclusion.
CCF	Diabetes was defined using ICD-9 codes: 250.x
CKD-JAC	
CRIB	Diabetes was defined by clinical diagnosis. This study did not collect use of anti-diabetic medications.
GCKD	Diabetes was defined as HbA1c \geq 6.5% or use of at least one antidiabetic medication.
Gonryo	
MASTERPLAN	This study did not use non-fasting glucose or glycated hemoglobin to define diabetes.
MDRD	This study did not collect use of anti-diabetic medications.
MMKD	All participants in this study do not have diabetes.
PSP-CKD	
RCAV	Diabetes was defined using ICD-9 codes: 250.x
RENAAL	All participants had type 2 diabetes defined as those patients who were diagnosed after the age of 30, who did not require insulin within six months of diagnosis, and who had no history of diabetic ketoacidosis.
SRR-CKD	This study did not collect use of anti-diabetic medications. Diabetes was defined by a clinical diagnosis in medical records.
Sunnybrook	
General Population Cohorts	
Aichi	
ARIC	
AusDiab	This study incorporated 2-h plasma glucose after oral glucose tolerance test in addition to the definition for this meta-analysis. This study did not collect use of anti-diabetic medications.
Beijing	This study incorporated 2-h plasma glucose after oral glucose tolerance test in addition to the definition for this meta-analysis. This study did not collect use of anti-diabetic medications.
BIS	Diabetes was defined as glycated hemoglobin A1c \geq 6.5% or use of glucose lowering drugs
ChinaNS	Diabetes was defined by fasting glucose \geq 7.0 mmol/L (\geq 126 mg/dL) or use of glucose lowering drugs (ADA 2010 criteria) or self-report of physician diagnosed diabetes.
CHS	
CIRCS	
ESTHER	
Framingham	
Gubbio	
IPHS	
JMS	
KHS	
MESA	

MRC	Diabetes was classified according to self-report of a medical diagnosis, use of antidiabetic medication, or the presence of a high random blood glucose measurement.
NHANES	
NIPPON DATA80	This study did not collect use of anti-diabetic medications.
NIPPON DATA90	This study did not include anti-diabetic medication use to define diabetes.
NIPPON DATA2010	This study did not include anti-diabetic medication use to define diabetes.
Ohasama	This study did not collect use of anti-diabetic medications.
PREVEND	
Rancho Bernardo	This study incorporated 2-h plasma glucose after oral glucose tolerance test in addition to the definition for this meta-analysis.
REGARDS	
RSIII	Type 2 diabetes was defined as a fasting blood glucose concentration of 7.0 mmol/L or higher, a non-fasting blood glucose concentration of 11.1 mmol/L or higher (when fasting samples were unavailable), or the use of blood glucose-lowering drugs.
SEED	
Taiwan MJ	
Takahata	
ULSAM	Diabetes was diagnosed as fasting plasma glucose ≥ 7.0 mmol/l (≥ 126 mg/dl) or 2-h postload glucose level 11.1 mmol/l (≥ 200 mg/dl) or by the use of oral hypoglycaemic agents or insulin at both examinations.
High Risk Cohorts	
ADVANCE	This study is an intervention study which includes participants with type 2 diabetes diagnosed at the age of 30 or older only.
Geisinger	Diabetes was defined using ICD-9 codes: 250.x
Maccabi	Diabetes was defined using ICD-9 codes: 250.x
Mt Sinai BioMe	Diabetes was defined using eMERGE Network's type 2 diabetes algorithm developed at Icahn School of Medicine at Mount Sinai.
NZDCS	This study includes only individuals with type 2 diabetes.
Pima	This study incorporated 2-h plasma glucose after oral glucose tolerance test in addition to the definition for this meta-analysis. Self reported diagnosis was accepted only if documented in the medical record.
SCREAM	Diabetes was defined using ICD-10 codes: E10, E11, E13
SMART	
ZODIAC	This study includes only individuals with type 2 diabetes. This study has not collected data on fasting glucose.

Missing Covariates Table:

Study	Region	N	BMI	Smoking	DM	History of CVD
CKD Cohorts						
AASK	USA	1094	0 (0%)	0 (0%)	0 (0%)	0 (0%)
BC CKD	Canada	11880	5463 (46%)	0 (0%)	0 (0%)	0 (0%)
CanPREDDICT	Canada	2061	2025 (98%)	2061 (100%)	0 (0%)	0 (0%)
CARE FOR HOME	Germany	369	348 (94%)	24 (7%)	229 (62%)	0 (0%)
CCF	USA	19249	2881 (15%)	0 (0%)	0 (0%)	0 (0%)
CKD-JAC	Japan	2679	254 (9%)	342(13%)	0 (0%)	0 (0%)
CRIB	UK	375	N<5	0 (0%)	0 (0%)	0 (0%)
GCKD	Germany	5159	52 (1%)	14 (0%)	0 (0%)	N<5
Geisinger CKD†	USA	24611	2549 (10%)	0 (0%)	0 (0%)	0 (0%)
Gonryo	Japan	3009	1393 (46%)	3009 (100%)	937 (31%)	0 (0%)
MASTERPLAN	Netherlands	670	0 (0%)	14 (2%)	N<5	9 (1%)
MDRD	USA	1736	N<5	5 (0%)	10 (1%)	0 (0%)
MMKD	Multi [§]	202	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Mt Sinai BioMe CKD†	USA	3521	554 (16%)	260 (7%)	0 (0%)	0 (0%)
PSP-CKD	UK	9434	3768 (40%)	0 (0%)	0 (0%)	0 (0%)
RCAV	USA	127812	13342 (10%)	127812 (100%)	0 (0%)	0 (0%)
RENAAL	Multi [¶]	1512	1512 (100%)	N<5	0 (0%)	1512 (100%)
SCREAM CKD†	Sweden	33232	33232 (100%)	33232 (100%)	0 (0%)	0 (0%)
SRR-CKD	Sweden	3051	544 (18%)	3051 (100%)	0 (0%)	0 (0%)
Sunnybrook	Canada	3010	1838 (61%)	0 (0%)	0 (0%)	0 (0%)
General Population Cohorts						
Aichi	Japan	4987	0 (0%)	89 (2%)	0 (0%)	0 (0%)
ARIC*	USA	11889	34 (0%)	436 (4%)	17 (0%)	281 (2%)
AusDiab*	Australia	11198	170 (2%)	178 (2%)	69 (1%)	32 (0%)
Beijing	China	1533	0 (0%)	N<5	61 (4%)	N<5
BIS	Germany	2055	N<5	0 (0%)	0 (0%)	0 (0%)
ChinaNS*	China	46810	228 (0%)	35 (0%)	44 (0%)	4766 (10%)
CHS*	USA	2984	48 (2%)	55 (2%)	0 (0%)	0 (0%)
CIRCS	Japan	11916	N<5	8 (0%)	0 (0%)	0 (0%)
ESTHER*	Germany	9744	10 (0%)	284 (3%)	0 (0%)	10 (0%)
Framingham*	USA	2956	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Gubbio	Italy	1684	0 (0%)	0 (0%)	0 (0%)	0 (0%)
IPHS	Japan	97769	437 (0%)	0 (0%)	0 (0%)	0 (0%)
JMS	Japan	5124	6 (0%)	0 (0%)	0 (0%)	0 (0%)
KHS	Korean	243779	12080 (1%)	0 (0%)	0 (0%)	0 (0%)
MESA*	USA	6796	0 (0%)	34 (1%)	0 (0%)	0 (0%)
MRC	UK	12367	765 (6%)	31 (0%)	0 (0%)	96 (1%)
NHANES	USA	56017	540 (1%)	2741 (5%)	69 (0%)	3343 (6%)
NIPPON DATA80*	Japan	10382	N<5	15 (0%)	N<5	0 (0%)
NIPPON DATA90	Japan	7612	N<5	0 (0%)	0 (0%)	0 (0%)
NIPPON DATA2010	Japan	2749	N<5	8 (0%)	6 (0%)	0 (0%)
Ohasama	Japan	3300	46 (1%)	641 (19%)	89 (3%)	0 (0%)
PREVEND	Netherlands	8060	74 (1%)	0 (0%)	274 (3%)	0 (0%)
Rancho Bernardo	USA	1484	7 (0%)	8 (1%)	0 (0%)	0 (0%)
REGARDS	USA	27727	79 (0%)	101 (0%)	137 (0%)	8 (0%)
RSIII	Netherlands	3519	67 (2%)	10 (0%)	0 (0%)	0 (0%)
SEED*	Singapore	7028	7 (0%)	N<5	51 (1%)	5 (0%)
Taiwan MJ	Taiwan	501704	149 (0%)	0 (0%)	0 (0%)	0 (0%)

Takahata	Japan	3524	0 (0%)	N<5	115 (3%)	0 (0%)
ULSAM	Sweden	1123	N<5	32 (3%)	0 (0%)	0 (0%)
High Risk Cohorts						
ADVANCE	Multi**	11033	22 (0%)	13 (0%)	0 (0%)	0 (0%)
Geisinger	USA	65051	10497 (16%)	0 (0%)	0 (0%)	0 (0%)
Maccabi	Israel	264255	125292 (47%)	0 (0%)	0 (0%)	0 (0%)
Mt Sinai BioMe	USA	8109	1642 (20%)	540 (7%)	7 (0%)	7 (0%)
NZDCS*	New Zealand	31622	604 (2%)	163 (1%)	0 (0%)	0 (0%)
Pima	USA	5074	37 (1%)	2119 (42%)	0 (0%)	5074 (100%)
SCREAM	Sweden	260047	260047 (100%)	260047 (100%)	0 (0%)	0 (0%)
SMART	Netherlands	3691	6 (0%)	34 (1%)	0 (0%)	0 (0%)
ZODIAC	Netherlands	1632	3 (0%)	18 (1%)	0 (0%)	0 (0%)
* Studies with only hypertension						
† CKD population from three administrative high risk cohorts, not included in the total N						
§ Participants are from Austria, Germany, and Italy						
¶ Participants are from Argentina, Austria, Brazil, Canada, Chile, China, Costa Rica, Czech Republic, Denmark, France, Germany, Hungary, Israel, Italy, Japan, Malaysia, Mexico, Netherlands, New Zealand, Peru, Portugal, Russia, Singapore, Slovakia, Spain, United Kingdom, United States of America, Venezuela						
** Participants are from Australia, Canada, China, Czech Republic, Estonia, France, Germany, Hungary, India, Ireland, Italy, Lithuania, Malaysia, Netherlands, New Zealand, Philippines, Poland, Russia, Slovakia, United Kingdom						

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