

Cohort Profile

Cohort Profile: Taiwan Kidney Outcome (TAKO) and Taiwan Kidney Outcome Omics (TAKOO) cohorts

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Keywords: chronic kidney disease; end-stage kidney disease; hemodialysis; cardiovascular disease; osteoporosis; cerebrovascular disease; dementia.

Key Features

- The study focuses on kidney disease patients in Taiwan which has one of the highest global rates of end-stage kidney disease. It comprises two cohorts from the Kaohsiung Medical University healthcare system: the Taiwan Kidney Outcome study (TAKO, 2005–21), a retrospective clinical cohort, and the Taiwan Kidney Outcome Omics study (TAKOO, since 2016), a prospective subcohort of TAKO enriched with multiomics data.
- The TAKO cohort includes 11 495 chronic kidney disease (CKD) patients and 1663 end-stage kidney disease (ESKD) patients, while TAKOO comprises 498 CKD patients and 347 ESKD patients. Participants are followed up every three months for CKD patients and 2–3 times per week for hemodialysis patients.
- Both cohorts have comprehensive clinical data including medical history, comorbidities, medications, and laboratory results. The TAKOO cohort additionally has multiomics data including genomics, proteomics, metabolomics, gut microbiome, and environmental toxins.
- The study has already yielded important findings about protein-bound uremic toxins, cognitive function in hemodialysis patients, and the effects of various medications on gut microbiota composition.
- A key strength is the comprehensive multiomics approach in the TAKOO cohort but limitations include a relatively small sample size and short follow-up period for some analyses.

Received: 17 February 2025; Editorial Decision: 22 July 2025; Accepted: 5 August 2025

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Why were the cohorts set up?

Taiwan has a very high incidence and prevalence of end-stage kidney disease (ESKD) [1]. The Taiwan National Health Insurance (NHI) system—established in 1995 as a government-run, single-payer program covering over 99% of its 23 million residents—ensuring broad access to healthcare, including dialysis, has reported the world's highest hemodialysis (HD) incidence, exceeding 500 per million population annually [2]. Chronic kidney disease (CKD) is a major public health issue [3] with significant healthcare costs [4]. Therefore, the Taiwan Kidney Outcome (TAKO) cohort, a retrospective clinical cohort based on electronic health records (EHR) from 2005 to 2021, was established to collect comprehensive clinical data on disease progression, risk factors, and treatment outcomes across a large population of CKD and end-stage kidney disease (ESKD) patients. The Taiwan Kidney Outcome Omics (TAKOO) subcohort was created within this framework in 2016 to focus on intensive multiomics profiling (e.g. genomics, proteomics, metabolomics). These cohorts serve complementary purposes: TAKO provides a wide lens for population-level insights, while TAKOO's detailed molecular data support hypothesis-driven studies, such as identifying novel biomarkers or mechanisms of CKD progression. Together, they offer a platform to explore kidney disease interplay with comorbidities like diabetes, hypertension, hyperlipidemia, gout, cardiovascular disease, and cerebrovascular disease for breakthroughs in diagnostics, therapeutics, and prognostics.

A multiomics approach enables us an understanding of the underlying mechanisms of kidney disease to better develop personalized treatments based on individual patient characteristics. Taiwan has a unique population with diverse genetic backgrounds and environmental exposures, making it an ideal location for studying the genetics and epigenetics of kidney disease. Finally, a multiomics approach allows the identification of biomarkers for early progression and risk stratification in kidney disease, improving patient outcomes and reducing healthcare costs. The TAKOO cohort, comprising a subgroup of participants with comprehensive multiomics data holds significant value for future research.

Who is in the cohort?

The TAKO cohort comprises 13 158 participants (11 495 with CKD and 1663 with ESKD) recruited from Kaohsiung Medical University Hospital, Kaohsiung Municipal Siaogang Hospital, and Kaohsiung Municipal Ta-Tung Hospital between 2005 and 2021. The TAKOO subcohort consists of 845 participants (498 CKD and 347 ESKD) recruited from 2016 for prospective follow-up. All 845 TAKOO participants are a subset of the 13 158 TAKO participants, selected for prospective follow-up and multiomics profiling from 2016. The TAKO and TAKOO cohorts primarily consist of Han Chinese participants, reflecting the demographic makeup of southern Taiwan.

All eligible patients with CKD were identified through the EHRs of participating hospitals based on the following criteria: age ≥ 18 years and either (i) estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73 m² for at least three months, or (ii) persistent proteinuria for more than three months, consistent with Kidney Disease Improving Global Outcomes (KDIGO) guidelines [5], supplemented in TAKO by the International Classification of Diseases (ICD) codes,

specifically ICD-9 codes (585–589) before 2016 and ICD-10 codes (I12, I13, N00, N01, N02, N03, N04, N05, N07, N11, N14, N17, N18, N19, Q61) after 2016. For the TAKO cohort (2005–21), all patients meeting these criteria were consecutively included. The TAKOO cohort (2016–21) is a prospective subcohort of TAKO, in which participants were additionally consented for longitudinal follow-up and multiomics analysis. Recruitment ended in 2021, and no additional participants have been enrolled thereafter. All CKD participants in the TAKO and TAKOO cohorts are under nephrologists' care and originally joined the pre-ESKD multidisciplinary care program launched by Taiwan NHI system to offer appropriate CKD education, track the patient's health status, and provide necessary information and communication to patients and family members [6, 7].

ESKD participants in the TAKO and TAKOO cohorts are older than 18 years and have undergone maintenance dialysis for at least 90 days. All patients receive regular HD with high-efficiency dialyzers three times per week at 250 to 300 ml/min blood flow rate and 500 ml/min on dialysate flow, with the sessions lasting 3.5–4 hours. Since TAKOO is a prospective cohort, there are specific exclusion criteria: patients who are likely to die within 6 months, have solid organ or bone marrow transplantation, active cancer, or cancer treatment within last 6 months; those with chronic respiratory failure with room air saturation $< 90\%$ or heart failure New York Heart Association Stage IV, those who have human immunodeficiency virus infection or Child B or C stage liver cirrhosis, or individuals who refused to provide informed consent (Table 1).

Longitudinal patient information is extracted from the EHR including sociodemographic data (age, sex, and years of education), the primary cause of kidney disease (hypertension, diabetes, glomerulonephritis, and others), dialysis information (time on dialysis, dialysis access), medical history, comorbidities, medications, and biochemical data.

The baseline characteristics of CKD and ESKD participants in both cohorts are summarized in Tables 2 and 3, respectively. In total, 11 495 CKD patients in the TAKO cohort and 498 patients in the TAKOO cohort (Table 2) were recruited, with 1663 ESKD patients in the TAKO cohort and 347 patients in the TAKOO cohort (Table 3).

The CKD participants in the TAKO cohort had a mean age of 64.8 years and 58.6% were male, with diabetes (41.5%) and hypertension (61.6%) being the most prevalent comorbidities. The most common causes of CKD were diabetes (36.4%) and glomerulonephritis (30.6%). The mean eGFR was 32.6 ml/min/1.73 m² by the creatinine-based CKD epidemiology collaboration (CKD-EPI), with 4801 (47.1%) participants classified as stages 1–3, 2755 (27.0%) as stage 4, and 2633 (25.8%) as stage 5. Frequently used medications included antihypertensives (63.8%), angiotensin-converting enzyme inhibitors (ACEI)/angiotensin II receptor blockers (ARBs) (48.1%), and statins (31.4%). The CKD participants in the TAKOO cohort had a mean age of 65.7 years and 64.9% males. The proportions of diabetes (47.8%) and hypertension (82.5%) were higher, with glomerulonephritis (35.1%) and diabetes (24.7%) being the primary CKD causes. Antihypertensives (85.9%), ACEI/ARBs (61.6%), and statins (55.0%) were commonly prescribed. The mean eGFR was 34.4 ml/min/1.73 m² with 275 (55.2%) participants classified as stages 1–3, 126 (25.3%) as stage 4, and 97 (19.5%) as stage 5.

Table 1. Inclusion and exclusion criteria for the TAKO and TAKOO cohorts

Criteria	TAKO cohort	TAKOO cohort (subcohort of TAKO)
Participants	CKD and ESKD patients from Kaohsiung Medical University Healthcare System	Subset of CKD and ESKD patients from TAKO cohort
Inclusion—CKD	Age >18 years; diagnosed with CKD (eGFR <60 ml/min/1.73 m ² or proteinuria >3 months per KDIGO guidelines) via EHR (ICD-9 pre-2016: e.g. 585.x, 403.x; ICD-10 post-2016: e.g. N18.x, I12.x); under nephrologists' care in pre-ESKD program	Same as TAKO CKD criteria
Inclusion—ESKD	Age >18 years; maintenance dialysis ≥90 days (EHR dialysis records; ICD-9 pre-2016: e.g. V45.1; ICD-10 post-2016: e.g. Z99.2)	Age >18 years; maintenance dialysis ≥90 days (dialysis unit records linked to EHR; ICD-10: e.g. N18.6)
Exclusion—CKD	None specified	None specified
Exclusion—ESKD	None specified	Likely to die within 6 months; solid organ or bone marrow transplantation; active cancer or cancer treatment within last 6 months; chronic respiratory failure (room air saturation <90%); heart failure NYHA Stage IV; HIV infection; Child B or C liver cirrhosis; legal attendance; refusal of informed consent
Recruitment Period	2005–21	2016–21
Data Source	Retrospective EHR-based	Prospective with clinical sample collection and biobank storage

CKD, chronic kidney disease; ESKD, end-stage kidney disease; EHR, electronic health records; eGFR, estimated glomerular filtration rate; KDIGO, Kidney Disease Improving Global Outcomes; NYHA, New York Heart Association; HIV, human immunodeficiency virus. TAKO uses retrospective EHR data; TAKOO applies prospective exclusions at enrollment.

In the TAKO HD cohort of 1663 participants, the mean age was 61.5 years, with 56.0% males. Diabetes (47.9%) and glomerulonephritis (31.2%) were the leading causes of ESKD, with hypertension (68.4%) and diabetes (52.3%) the prevalent comorbidities. Commonly used medications include antihypertensives (59.2%), erythropoiesis-stimulating agents (ESAs) (82.7%), and phosphate binders (70.5%). In the TAKOO HD subcohort of 347 participants, the mean age was 59.7 years and 53.9% were males. Glomerulonephritis (42.4%) and diabetes (30.8%) were the primary causes of ESKD, with hypertension (74.6%) and diabetes (48.1%) the most common comorbidities. Medications frequently prescribed included antihypertensives (65.4%), ESAs (85.0%), and phosphate binders (73.2%). Other detailed baseline characteristics are shown in [Tables 2](#) and [3](#). As of the most recent follow-up, a total of 5139 deaths (39.0%) occurred in the TAKO cohort, including 4443 (38.7%) among CKD patients and 696 (41.9%) among ESKD patients. In the TAKOO subcohort, 141 deaths (16.7%) were observed, including 49 (9.8%) among CKD patients and 92 (26.5%) among ESKD patients.

How often have they been followed up?

All participants were recruited from 2005 to 2021 in the TAKO cohort and from 2016 to 2021 in the TAKOO cohort. For CKD patients, follow-up has occurred every three months, with two to three visits per week for HD patients, and continues to be recorded every three months based on the EHRs. The cognitive function evaluation was performed among TAKOO HD subjects in 2016, 2017, and 2020. Loss to follow-up was defined as patients who left the Kaohsiung Medical University Hospital care system, most often due to address changes. As of the most recent follow-up, 1589 (13.8%) patients with CKD and 45 (9.0%) patients with ESKD on HD were lost to follow-up. Despite this limitation, vital status and cause of death remain fully ascertainable

through linkage with Taiwan National Death Registry. In contrast, the TAKOO cohort achieved complete follow-up through the proactive engagement of dedicated nurses, educators, and care managers, ensuring comprehensive longitudinal data collection.

What has been measured?

The TAKO and TAKOO cohorts are comprehensively assessed to collect a wide array of clinical, biochemical, and omics data (TAKOO cohort only) to evaluate health outcomes and risks. Clinical information included comorbidities, medications, and clinical examination records (cardiovascular, lung, brain, bone, and eye health). Nutritional status was assessed using the Subjective Global Assessment (SGA). EHR data were standardized using consistent ICD coding (ICD-9 before 2016, ICD-10 after 2016), with missing or inconsistent records flagged and reviewed by trained staff to ensure data quality in the TAKO cohort. Regular audits were conducted to verify the accuracy of key variables such as eGFR and dialysis status, addressing potential variations in coding practices over time. Information on comorbidities such as diabetes, hypertension, cardiovascular diseases, and malignancies was retrieved from EHRs. Clinical outcomes were identified using ICD codes and physician diagnoses, with cardiovascular outcomes like myocardial infarction, heart failure, stroke, and both cardiovascular and noncardiovascular death specifically defined. Major adverse cardiovascular events (MACE) were measured as a composite of outcomes, including death, heart failure, stroke, and peripheral artery disease. Laboratory measurements include a range of hematological, metabolic, and inflammatory markers analyzed through automated systems and immunoassays. Key biomarkers included albumin, lipids, electrolytes, C-reactive protein, and kidney function markers such as creatinine and eGFR, calculated using modification of diet in renal disease

Table 2. The baseline characteristics of CKD participants in the Taiwan Kidney Outcome (TAKO) and Taiwan Kidney Outcome Omics (TAKOO) cohort

	CKD patients in TAKO cohort (N = 11 495)	No.	CKD patients in TAKOO cohort (N = 498)	No.
Age	64.8 ± 14.1	11 495	65.7 ± 12.5	498
Age group		11 495		498
<40 years	676 (5.9%)		20 (4.0%)	
40–65 years	4565 (39.7%)		187 (37.6%)	
65–80 years	4749 (41.3%)		233 (46.8%)	
>80 years	1505 (13.1%)		58 (11.6%)	
Male gender (%)	6735 (58.6%)	11 495	323 (64.9%)	498
Smoking history (%)	2021 (19.8%)	10 187	92 (18.5%)	497
Cause of chronic kidney disease		10 344		498
Hypertension	996 (9.6%)		57 (11.4%)	
Diabetes mellitus	3763 (36.4%)		123 (24.7%)	
Glomerulonephritis	3168 (30.6%)		175 (35.1%)	
Others	2417 (23.4%)		143 (28.7%)	
Body mass index (kg/m ²)	25.3 ± 4.4	9143	25.5 ± 4.0	498
Systolic blood pressure (mmHg)	139.8 ± 20.9	9356	136.5 ± 17.4	498
Diastolic blood pressure (mmHg)	78.2 ± 13.3	9350	76.2 ± 10.9	498
Comorbidities				
Diabetes mellitus (%)	4772 (41.5%)	11 495	238 (47.8%)	498
Hypertension (%)	7081 (61.6%)	11 495	411 (82.5%)	498
Hyperlipidemia (%)	4311 (37.5%)	11 495	345 (69.3%)	498
Coronary artery disease (%)	1827 (15.9%)	11 495	111 (22.3%)	498
Heart failure (%)	1413 (12.3%)	11 495	48 (9.6%)	498
Cerebrovascular disease (%)	1584 (13.8%)	11 495	83 (16.7%)	498
Atrial fibrillation (%)	367 (3.2%)	11 495	18 (3.6%)	498
Peripheral artery disease (%)	459 (4.0%)	11 495	31 (6.2%)	498
Medications				
Anti-hypertensive drugs	7337 (63.8%)	11 495	428 (85.9%)	498
ACEI/ARB	5534 (48.1%)	11 495	307 (61.6%)	498
β-blocker	3617 (31.5%)	11 495	200 (40.2%)	498
Diabetic medication	4161 (36.2%)	11 495	194 (39.0%)	498
Insulin	2125 (18.5%)	11 495	56 (11.2%)	498
Statin	3606 (31.4%)	11 495	274 (55.0%)	498
Loop diuretics	3235 (28.1%)	11 495	77 (15.5%)	498
Clinical laboratory data				
Hemoglobin (mg/dl)	11.3 ± 2.3	10 087	12.3 ± 2.1	498
Albumin (mg/dl)	4.0 ± 0.6	9725	4.3 ± 0.4	498
GOT (IU/l)	28.4 ± 20.2	6814	30.9 ± 35.7	334
GPT (IU/l)	24.1 ± 19.8	9599	24.2 ± 23.1	411
Blood urea nitrogen (mg/dl)	40.0 ± 24.9	10 079	34.9 ± 20.3	498
Creatinine (mg/dl)	3.1 ± 2.5	10 190	2.6 ± 1.8	498
Uric acid (mg/dl)	7.5 ± 2.1	9616	6.6 ± 1.7	498
Sodium (mmol/l)	138.2 ± 3.6	9671	138.4 ± 2.8	498
Potassium (mmol/l)	4.2 ± 0.6	9795	4.2 ± 0.5	498
Calcium (mg/dl)	9.1 ± 1.3	9224	9.2 ± 0.5	498
Phosphate (mg/dl)	4.1 ± 1.1	9251	3.9 ± 2.0	498
Parathyroid hormone (pg/ml)	119.7 ± 152.5	5726	111.3 ± 155.7	391
Total cholesterol (mg/dl)	187.7 ± 56.8	9636	170.7 ± 37.2	498
High-density lipoprotein (mg/dl)	43.5 ± 13.9	9126	46.8 ± 15.0	487
Low-density lipoprotein (mg/dl)	105.0 ± 41.8	9323	93.1 ± 30.6	498
Triglycerides (mg/dl)	150.4 ± 118.9	9660	139.4 ± 94.4	498
C-reactive protein (mg/l)	11.7 ± 29.7	7125	7.8 ± 27.2	422
eGFR (calculated by MDRD)	30.3 ± 21.5	10 189	31.8 ± 17.8	498
CKD stage by MDRD		10 189		498
Stage 1-3	4455 (43.7%)		255 (51.2%)	
Stage 4	2948 (28.9%)		143 (28.7%)	
Stage 5	2786 (27.3%)		100 (20.1%)	
eGFR (calculated by CKD-EPI)	32.6 ± 23.2	10 189	34.4 ± 19.8	498
CKD stage by CKD-EPI		10 189		498
Stage 1-3	4801 (47.1%)		275 (55.2%)	
Stage 4	2755 (27.0%)		126 (25.3%)	
Stage 5	2633 (25.8%)		97 (19.5%)	

GOT, Glutamic Oxaloacetic Transaminase; GPT, Glutamic Pyruvic Transaminase; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; eGFR, estimated glomerular filtration rate; MDRD, modification of diet in renal disease; CKD-EPI, chronic kidney disease Epidemiology Collaboration.

(MDRD) and CKD-EPI equations. In-depth clinical examinations included echocardiography, lung function tests, neuroimaging, and bone mineral density (BMD) assessments, along

with cognitive function measurements via standardized tests such as the Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA).

Table 3. The baseline characteristics of ESKD (hemodialysis) participants in the Taiwan Kidney Outcome (TAKO) and Taiwan Kidney Outcome Omics (TAKOO) cohort

	HD patients in TAKO cohort (N = 1663)	N	HD patients in TAKOO cohort (N = 347)	N
Age	61.5 ± 13.8	1663	59.7 ± 11.5	347
Age group		1663		347
<40 years	112 (6.7%)		23 (6.6%)	
40–64 years	871 (52.4%)		202 (58.2%)	
65–79 years	533 (32.1%)		112 (32.3%)	
80–99 years	147 (8.8%)		10 (2.9%)	
Male gender (%)	932 (56.0%)	1663	187 (53.9%)	347
Cause of ESKD		1658		347
Hypertension	172 (10.4%)		29 (8.4%)	
Diabetes mellitus	795 (47.9%)		122 (35.2%)	
Glomerulonephritis	517 (31.2%)		147 (42.4%)	
Others	174 (10.5%)		49 (14.1%)	
Comorbidities				
Diabetes mellitus (%)	889 (53.5%)	1663	148 (42.7%)	347
Hypertension (%)	1360 (81.8%)	1663	268 (77.2%)	347
Hyperlipidemia (%)	752 (45.2%)	1663	131 (37.9%)	346
Coronary artery disease (%)	385 (23.2%)	1663	59 (17.1%)	346
Heart failure (%)	486 (29.2%)	1663	76 (21.9%)	347
Cerebrovascular disease (%)	244 (14.7%)	1663	31 (8.9%)	347
Atrial fibrillation (%)	82 (4.9%)	1663	16 (4.6%)	347
Medications				
Anti-hypertensive drugs	1468 (88.3%)	1663	164 (47.3%)	347
ACEI/ARB	1111 (66.8%)	1663	86 (24.8%)	347
β-blocker	993 (59.7%)	1663	104 (30.0%)	347
Diabetic medication	923 (55.5%)	1663	113 (32.6%)	347
Insulin	706 (42.5%)	1663	58 (16.7%)	347
Statin	679 (40.8%)	1663	95 (27.4%)	347
Clinical laboratory data				
Hemoglobin (mg/dl)	10.3 ± 1.4	1643	10.7 ± 1.2	347
Albumin (mg/dl)	3.8 ± 0.4	1635	3.9 ± 0.3	347
GOT (IU/l)	23.5 ± 116.1	1642	17.2 ± 9.7	347
GPT (IU/l)	19.9 ± 38.4	1642	14.3 ± 9.1	347
Blood urea nitrogen (mg/dl)	65.4 ± 22.5	1640	66.0 ± 14.1	347
Creatinine (mg/dl)	8.8 ± 2.7	1640	10.2 ± 2.1	347
Uric acid (mg/dl)	6.8 ± 1.9	1626	7.5 ± 1.5	345
Sodium (mmol/l)	136.8 ± 3.6	1642	138.4 ± 3.2	347
Potassium (mmol/l)	4.5 ± 0.8	1642	4.6 ± 0.6	347
Calcium (mg/dl)	9.0 ± 1.3	1635	9.3 ± 0.9	347
Phosphate (mg/dl)	5.1 ± 1.5	1634	4.7 ± 1.1	347
Parathyroid hormone (pg/ml)	380.1 ± 343.5	1584	418.4 ± 359.6	345
Alkaline Phosphatase (IU/l)	171.6 ± 192.3	1077	233.5 ± 231.8	345
Total cholesterol (mg/dl)	169.8 ± 46.6	1616	167.9 ± 39.5	347
High-density lipoprotein (mg/dl)	44.2 ± 15.4	1218	41.6 ± 12.7	323
Low-density lipoprotein (mg/dl)	93.4 ± 35.8	1129	95.0 ± 32.3	347
Triglycerides (mg/dl)	136.7 ± 103.2	1616	149.7 ± 95.9	347
C-reactive protein (mg/l)	15.1 ± 34.5	1392	2.4 ± 4.2	346
Ferritin (ng/ml)	442.6 ± 476.9	1610	467.6 ± 330.8	346
Aluminum (ng/ml)	15.1 ± 14.5	1529	20.5 ± 14.6	345
Zinc (μg/dl)	82.1 ± 20.8	1297	96.2 ± 17.4	346
Hemodialysis information				
Body weight before hemodialysis	62.5 ± 13.5	1239	63.0 ± 12.1	347
Body weight after hemodialysis	60.3 ± 13.0	1239	60.6 ± 11.7	347
Dialysis dose, Single pool Kt/V	1.5 ± 0.3	1362	1.6 ± 0.2	345
Urea reduction ratio (URR)	0.7 ± 0.1	1362	0.7 ± 0.1	345

ESKD, end-stage kidney disease; GOT, Glutamic Oxaloacetic Transaminase; GPT, Glutamic Pyruvic Transaminase; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker; HD, hemodialysis.

The TAKOO cohort also has multiomics data including genomics using the Taiwan Biobank single-nucleotide polymorphism (SNP) chip, proteomics through the platforms Olink and Luminex, metabolomics via ultra-high-performance liquid chromatography–tandem mass spectrometry method (UPLC-MS/MS), and trace elements assessed by inductively coupled plasma mass spectrometry (ICP-MS) (Table 4). The SNP chip utilized a custom SNP array [Taiwan Biobank Phase 2.0] developed on the ThermoFisher Axiom platform,

informed by whole-genome sequencing data from 946 participants to optimize variant selection for the Han Chinese population. The array includes ~686 000 markers, covering common variants, rare disease genes, drug metabolism loci, and copy number variation regions. Genomic data were collected for 139 HD and 53 CKD patients using a customized SNP chip optimized for the Han Chinese population (detailed in Supplementary Data). Also, 184 proteins were included in Olink Proteomics CVD II and CVD III panels

Table 4. Biochemical and multiomics variables collected from the TAKOO cohort and methods

Omics layers	Method (Technology and Platform)	Panels
Genetics	Single-Nucleotide Polymorphism (SNP) chip	Whole Genome Genotyping Array from Affymetrix (Santa Clara, CA, USA)
Target Proteomics	Proximity Extension Assay (PEA) technology by Olink proteomics	Olink CVD II and III panels (Supplementary Table 1)
Target Proteomics	Luminex multiplex immunobead assay by MILLIPLEX MAP technology (Luminex)	Bone turnover biomarkers (DKK1, FGF23, Leptin, OC, OPN, OPG, SOST, RANKL) Novel cardiovascular biomarkers (IL-6, IL-1 β , GDF-15, FST, PTX3, PLGF, Galectin-3, Cathepsin D, Endocan-1) Pro-inflammation cytokines (IL-1 β , IL-6, IL-8, TNF- α)
Target Proteomics	Meso-Scale Discovery (MSD) platform as multiplex sandwich immunoassays detection by electrochemiluminescence (ECL) technology	
Target Metabolomics	ultra-high-performance liquid chromatography–tandem mass spectrometry method (UPLC-MS/MS)	Protein-bound uremic toxins (indoxyl sulfate, p-cresyl sulfate, indole-3 acetic acid, and hippuric acid) Short chain fatty acid (lactic acid, acetic acid, propionic acid, isobutyric acid, butyric acid, 2-methylbutyric acid, isovaleric acid, valeric acid, 3-methylvaleric acid, isocaproic acid, and caproic acid) Trimethylamine-N-oxide (TMAO) associated metabolites (choline, carnitine, trimethylamine [TMA], [TMAO], γ -butyrobetaine) Indole metabolites Blood amino acids Phenol metabolites
Target trace metal elements	Inductively coupled plasma mass spectrometry (ICP-MS)	Vanadium (V), Chromium (Cr), Manganese (Mn), Cobalt (Co), Copper (Cu), Gallium (Ga), Arsenic (As), Selenium (Se), Strontium (Sr), and Cadmium (Cd)
Environmental toxins	ultra-high-performance liquid chromatography–tandem mass spectrometry method (UPLC-MS/MS)	Per- and Polyfluorinated Substances (PFAS)
Clinical biochemical data		Hemoglobin, albumin, high sensitivity C-reactive protein, total cholesterol, low-density lipoprotein, triglycerides, ion calcium, phosphate, blood urea nitrogen, phosphorous, alanine transaminase, alkaline phosphatase, magnesium, parathyroid hormone, aluminum, sodium, potassium, and zinc levels
Gut microbiota		16 s rRNA amplicon sequencing, shotgun metagenomics analysis

DKK1, Dickkopf-related protein 1; FGF23, fibroblast growth factor 23; OC, osteocalcin; OPN, osteopontin; OPG, osteoprotegerin; SOST; RANKL, nuclear factor kappa-ligand; IL-6, interleukin-6; IL-1 β , interleukin-1 beta; GDF-15, Growth Differentiation Factor 15; FST, follistatin; PTX3, Pentraxin-3; PLGF, placental growth factor.

([Supplementary Table 1](#)). Additionally, gut microbiome profiles were obtained through 16S rRNA sequencing and shotgun metagenomics, providing insights into microbial composition and functional capacities. Environmental toxins and epigenetic data were also measured, with a particular focus on uremic toxins. Detailed information on study variables and examination procedures is illustrated in [Fig. 1](#), [Supplementary Table 2](#) and available in the [Supplementary Data](#). Looking ahead, the study team plans to explore opportunities to augment the TAKO cohort with additional omics data, potentially through phased expansion or linkage with existing biobanks such as the Taiwan Biobank, to enhance the cohort’s capacity for future multiomics research.

What has been found? Key findings and publications

Three papers have been published regarding the relationship between protein-bound uremic toxins and various health

outcomes in patients with CKD undergoing HD. Our study investigated the relationship between the free form of indoxyl sulfate (IS) and p-cresyl sulfate (PCS) and cardiovascular (CV)-related proteins in 333 stable HD patients [8], reporting that IS and PCS were associated with several CV-related proteins involved in endothelial barrier function, the complement system, cell adhesion, phosphate homeostasis, and inflammation, and that higher levels of fibroblast growth factor 23 (FGF23) were related to increased risk of acute coronary syndrome (ACS) [8]. The other studies investigated the association of uremic toxins such as IS, PCS, indole-3 acetic acid (IAA), and hippuric acid (HA) on cognitive function in HD patients [9]. In our study, we observed a negative association between cognitive function and free IS, free PCS, and IAA in patients undergoing HD [9]. Notably, there was no observed correlation between serum HA levels and the cognitive function status in these patients [9].

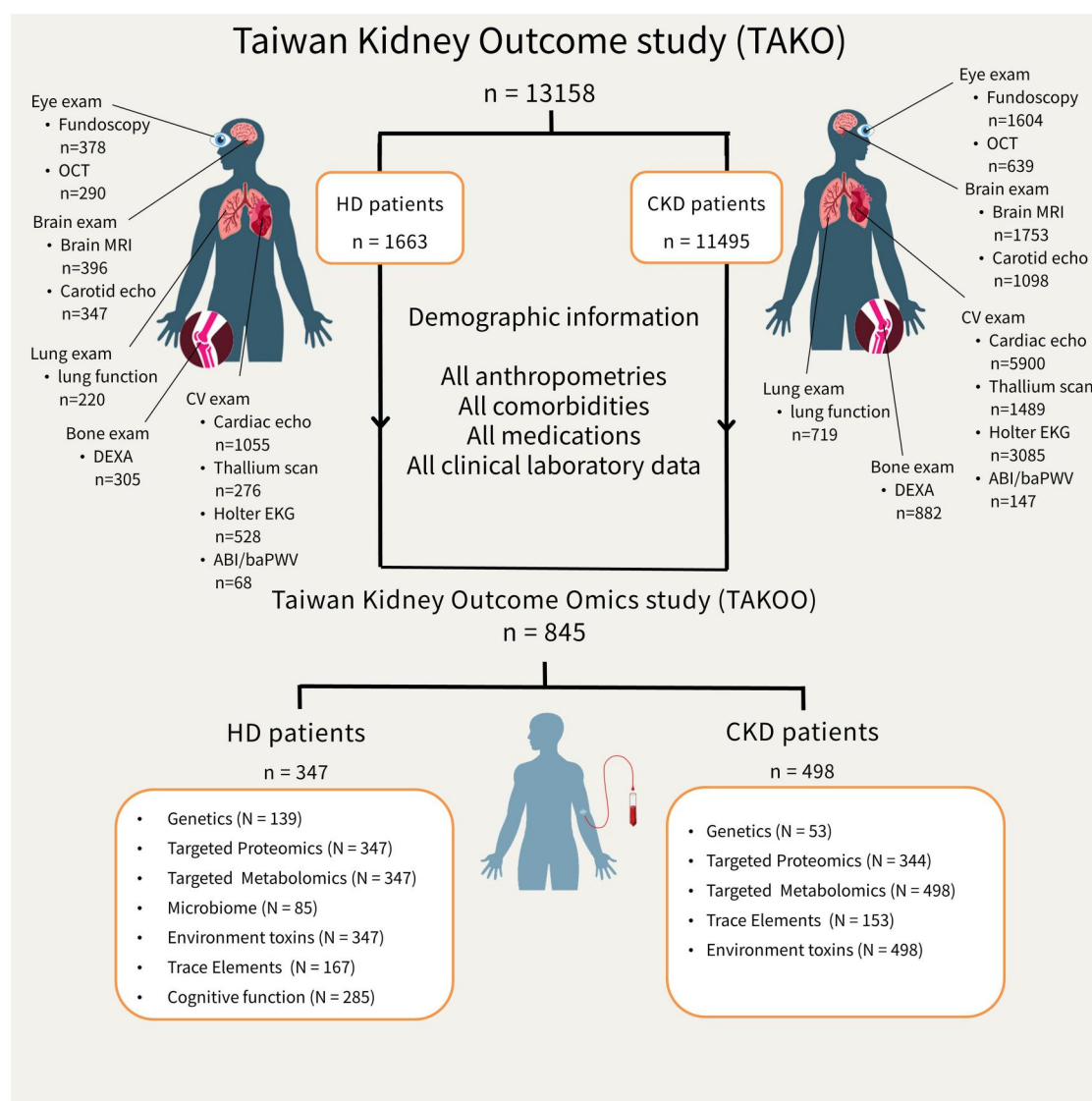


Figure 1. The study variables of chronic kidney disease (CKD) and end-stage kidney disease patients (ESKD) enrolled in the Taiwan Kidney Outcome (TAKO) and Taiwan Kidney Outcome Omics (TAKOO) studies. ABI, ankle-brachial index; baPWV, brachial-ankle pulse wave velocity; CV, cardiovascular; echo, echocardiogram; DEXA, bone density scan; EKG, electrocardiogram; HD, hemodialysis; MRI, magnetic resonance imaging; OCT, optical coherence tomography.

Another study investigated the effects of antacid drugs, proton pump inhibitor (PPI) and histamine-2 blocker (H2-blocker), on the gut microbiota composition in HD patients [10], reporting that PPI significantly changed the gut microbiota composition in HD patients compared to H2-blocker users or controls, and caution was raised against the overuse of PPIs [10]. Differences in the gut microbial composition of HD patients treated with and without β -blockers and between ferric citrate and calcium carbonate phosphate binders have also been reported [11, 12], with ferric citrate therapy resulting in a more diverse microbiome community compared to calcium carbonate therapy in HD patients with phosphate binder treatment [12], and increased abundance of *Flavonifractor* genus with β -blocker treatment [11].

A study explored the association between circulating IAA levels and mitogen-activated protein kinase cascade-associated proteins in patients undergoing HD [13], showing that IAA was positively associated with stem cell factor and may be involved in the regulation of cell proliferation, hematopoietic cells, and the Janus kinase-signal transducer and activator of transcription signaling pathway [13].

Another study evaluated the relationship between ankle-brachial index (ABI) and brachial-ankle pulse wave velocity (baPWV) and cognitive impairment in patients receiving HD, reporting that a low ABI or high baPWV was associated with lower cognitive function in these patients [14].

What are the main strengths and weaknesses?

First, the cohort size is relatively small which could limit the generalizability of the findings to other populations. Additionally, small sample numbers are reported for some outcomes, possibly reducing the statistical power to detect significant associations. However, the research team plans to continue the follow-up to collect more data until 2027, supported by funding from the National Science and Technology Council, which will enhance the statistical power of the study and provide a more comprehensive analysis of the relationship between the measured variables and outcomes. Furthermore, the lack of dietary data may limit the ability to adjust for potential confounding factors. Finally, the relatively short follow-up period (to date) limits our ability to

capture the long-term effects of the exposures on the outcomes, therefore, the data collection will continue to collect more outcome and confounding information. Despite these limitations, the study provides valuable insights into the associations between multiomics and renal disease, highlighting the need for larger and more comprehensive studies with a longer follow-up to confirm and extend these findings.

Can I get hold of the data? Where can I find out more?

Although the study database is not publically available, any potential collaborations are welcomed and considered on a case-by-case basis. Specific requests can be sent to the corresponding author, Dr Ping-Hsun Wu (970392kmuh@gmail.com).

Ethics approval

The TAKO and TAKOO cohort study was approved by the Institutional Review Board of Kaohsiung Medical University (KMUHIRB-G(II)-20160024, KMUHIRB-E(I)-20160095, KMUHIRB-E(II)-20220255, KMUHIRB-E(I)-20220272, KMUHIRB-E(II)-20220269, and KMUHIRB-E(II)-20220286).

Acknowledgements

We acknowledge the contributors who were involved in the data collection, including Pei-Ni Hsiao, Tzu-Hui Chen, Shih-Ming Hsiao, Shu-Li Wang, Shu-An Yang, Hung-Tien Kuo, Jia-Jung Lee, Chi-Chih Hung, Lee-Moay Lim, Pei-Yu Wu, Jiun-Chi Huang, Sheng-Wen Niu, Hugo You-Hsien Lin, Tien-Chi Huang, Yi-Hsueh Liu, Chung-Hwan Chen, and Ming-Chen Tsai.

Author contributions

Conceptualization, Ping-Hsun Wu, Yi-Ting Lin, Yi-Wen Chiu, and Mei-Chuan Kuo; Data curation, Ping-Hsun Wu, Yi-Ting Lin, Ming-Yen Lin, Teng-Hui Huang, and Yun-Shiuan Chuang; Study design and analysis plan, Ping-Hsun Wu, Yi-Ting Lin, Yi-Wen Chiu, and Mei-Chuan Kuo; Statistical analysis, Ping-Hsun Wu, Yi-Ting Lin, and Teng-Hui Huang; Funding acquisition, Ping-Hsun Wu and Yi-Ting Lin; Investigation, Ping-Hsun Wu, Yi-Ting Lin, Po-Yu Liu; Writing—first draft, Ping-Hsun Wu, Yi-Ting Lin; Writing—review & editing, Yi-Chun Tsai, Szu-Chia Chen, I-Ching Kuo, Wei-Chung Tsai, Hsiu-Fen Lin, Tien-Ching Lee, Pei-Kang Liu, Yi-Wen Chiu, Jer-Ming Chang, Shang-Jyh Hwang, and Mei-Chuan Kuo.

Supplementary data

[Supplementary data](#) is available at *IJE* online.

Conflict of interest

None declared.

Funding

The funding sources did not play any role in the design or conduct of the study, collection, management, analysis, interpretation of the data, or preparation, review, or approval of the manuscript. The study was funded by grants from the Ministry of Science and Technology, Taiwan

(MOST 111-2314-B-037-032-MY3 and MOST 111-2314-B-037-083-MY3), Kaohsiung Medical University Hospital, Taiwan (KMUH-DK(C)113003, KMUH-DK(B)110003-4, KMUH112-2M08, KMUH-DK(C)114002, KMUH112-2R76, KMU H111-1M60, KMUH111-1R73, and KMUH110-0M73), and Kaohsiung Medical University, Taiwan (NHRIMU-111-I003-2, NHRIMU-113-I005, NYCUMU-112-I006, KT112P012, KT113P006, NHRIMU-114-I001, and S11209).

Data availability

See “Can I get hold of the data?” above.

Use of artificial intelligence (AI) tools

AI tools were not used in this study or writing the paper.

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