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Outpatient acute kidney disease detection by national and institutional health data

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Abstract

Background The development of diagnostic definitions for acute kidney disease in outpatients (AKD_{OPT}) remains an unattained goal because of consensus gaps and data silos in health-care systems.

Methods Our team developed the Acute Kidney Injury Detection System (AKIDS) to screen for undiagnosed AKD_{OPT} using National Health Insurance MediCloud data and institutional electronic medical records. The criteria for AKD_{OPT} were a >50% change in maximum and minimum serum creatinine levels or a >35% change in corresponding estimated glomerular filtration rate values within the 180 days before an appointed outpatient visit. In this retrospective cohort study, the associations between AKD_{OPT} and composite kidney outcome (CKO; e.g., end-stage kidney disease, a >40% drop in estimated glomerular filtration rate, or a 2-fold or more increase in serum creatinine), all-cause mortality, and de novo non-dialysis chronic kidney disease (CKD-ND) were evaluated using multivariable Cox proportional hazards models.

Results Of 79,838 eligible adult patients screened by the AKIDS, 12,510 (15.7%) have AKD_{OPT}. The adjusted absolute risk increases for 1-year incident CKO, mortality, and de novo CKD-ND for patients with AKD_{OPT} relative to those without are 79.0 (95% confidence interval 78.9–79.1), 25.3 (25.2–25.3), and 54.8 (54.7–54.9) per 1000 patients, respectively. The adjusted hazard ratios for 1-year CKO, mortality, and de novo CKD-ND are 16.2 (14.2–18.5), 2.6 (2.4–2.9), and 3.5 (3.1–3.9), respectively.

Conclusions By integrating the national-local data using the AKIDS, this study comprehensively characterizes a previously unrecognized phenotype, AKD_{OPT}, illustrating the potential of healthcare big data in transforming global approaches to AKD patterns and prevention.

Plain Language Summary

Acute kidney disease occurs when the kidneys do not fully recover after acute kidney injury, leading to waste and fluid buildup in the body. In outpatient settings, acute kidney disease (AKD_{OPT}) diagnosis is often missed because of unclear diagnostic criteria and limited data sharing across hospitals. To address this, we developed the Acute Kidney Injury Detection System (AKIDS) to identify AKD_{OPT} using kidney function data shared across hospitals in Taiwan. AKD_{OPT} was defined by sudden changes in specific markers important for kidney function within six months before an outpatient visit. Of the adult outpatients screened, the AKIDS identified 15.7% with AKD_{OPT}. These patients faced higher risks of kidney failure, death, or developing chronic kidney disease within one year. Our study highlights how seamlessly integrated healthcare data can help identify previously unrecognized kidney injuries and improve kidney disease management.

Acute kidney injury (AKI) poses a substantial burden on health-care systems worldwide, particularly in terms of in-hospital mortality and the long-term risk of chronic kidney disease (CKD)[1]. Diagnosing AKI patients is the first step for any initiative to reduce disease burden, such as International Society of Nephrology's 0by25 initiative aimed at preventing all avoidable deaths from AKI worldwide by 2025. However, the health-care data silos across hospitals have made it challenging to identify AKI or acute kidney disease (AKD) in outpatient settings (AKI_{OPT} or AKD_{OPT})[2,3]. Therefore, prior studies have largely focused on establishing clinical decision support systems based on local electronic medical records for AKI and AKD in inpatient settings[4–6], leaving AKI_{OPT} and AKD_{OPT} a crucial missing piece in AKI detection network and a sizable portion of patients undetected without timely management[7].

Beyond data silos, the absence of an agreed-upon diagnostic criteria, such as the appropriate diagnostic timeframe, further complicates AKI_{OPT} or AKD_{OPT} detection. Community-acquired AKI, typically

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diagnosed in emergency or inpatient settings based on acute reverse patterns of serum creatinine (S-Cre), is the most closely related phenotype to AKI_{OPT}[8]. In 2019, Leither et al. first defined AKI_{OPT} using a 3-year S-Cre variation in single-institution electronic medical records[9]. However, the median interval between baseline and diagnosis-defining S-Cre measurements spanned 225 days, inconsistent with the conventional definition of AKI as abrupt decrease in kidney function within hours to 7 days[10]. A new approach to diagnose AKD_{OPT} using data of a shorter timeframe is urgently needed and take precedence over AKI_{OPT}, since frequent S-Cre measurements (e.g., within a 7-day window), are not standard in outpatient settings.

Health Information Exchange MediCloud platform of the Taiwan National Health Insurance (NHI) program presents such an opportunity. Since 2017, it has enabled medical centers to integrate laboratory, medication, imaging, and surgery information from local electronic medical records with information from other hospitals in near real time[11]. With NHI's MediCloud, we were able to systematically identify AKD_{OPT} patients by using the S-Cre levels and estimated glomerular filtration rate (eGFR) values in the 180 days before an outpatient visit. We have previously proposed the AKD_{OPT} diagnosis criteria as a >50% change in S-Cre and a >35% change in eGFR over a 180-day period, and demonstrated that AKD_{OPT} among patients with advanced CKD was associated with accelerated progression to end-stage kidney disease (ESKD)[12]. In the present study, guided by our operational definition of AKD_{OPT}, we design and integrate the Acute Kidney Injury Detection System (AKIDS) into the backend of the outpatient Health Information System at China Medical University Hospital (CMUH) to characterize the one-year natural course of AKD_{OPT}. AKD_{OPT} is present in 15.7% of the outpatients screened by the AKIDS and is associated with a 16.2-fold significant increase in the risk of composite kidney outcomes (CKOs), a 2.6-fold risk of mortality, and a 3.5-fold risk of de novo CKD within one year.

Methods

Study population for epidemiological characterization of AKD_{OPT}

The abbreviations frequently used in the current study are listed in Supplementary Table 1. The iHi Data Platform of CMUH contains the carefully verified and validated medical records of 3,077,895 patients who had sought care at CMUH between January 1, 2003, and December 31, 2020[13–15]. The AKIDS database contains the screening results for each appointed outpatient visits screened by AKIDS since December 2017. By using the iHi Data Platform and AKIDS database in this retrospective cohort study, we included all appointed outpatient visits screened by AKIDS between December 1, 2017, and June 30, 2019 as the source population and kept patients' first appointed visits. The index date was the first appointed outpatient visit. Patients younger than 18 or older than 90 years old, those with 2 or more nephrology department visits in prior 90 days or had nephrology visit on the index visit date, those with ESKD requiring renal replacement therapy (RRT), those with cancer history, or those with an unknown AKD_{OPT} status were excluded (Fig. 1). Patients who were classified as unknown AKD_{OPT} when there was only one S-Cre measurement available in the 180 days prior to the index appointed outpatient visits and their characteristics were presented in Supplementary Data 1. Sociodemographic variables, baseline comorbidities, and medications history within a 1-year window prior to the index date and biochemical measurements within a 3-month window prior to the index date were obtained from the iHi Data Platform. Supplementary Table 2 presents the methods and definitions used for kidney function measurement. For calculating the monthly cumulative incidence of AKD_{OPT}, we used appointed outpatient visits screened by AKIDS between December 1, 2017, and May 31, 2020 among eligible adults meeting the criteria mentioned above in Fig. 1. Sample size calculation was not performed for this retrospective observational study, as it utilized pre-existing data recorded during the hospital-wide implementation of AKIDS in the backend system. Given the high volume of outpatient visits at CMUH, the sample size is expected to be sufficient for the study's objectives. This study was approved by the Institutional Review Board (IRB) of CMUH (107-REC1-070; 111-REC3-138; 111-REC2-022). A waiver of informed consent was granted by the IRB of CMUH as the study was retrospective in nature, utilizing pre-existing medical record data with minimal risk to participants.

AKIDS for AKD_{OPT} Screening

We developed AKIDS to enable automatic AKD_{OPT} screening and dialysis risk assessment, and provide suggestions for the nephrology referral in outpatient setting (Supplementary Fig. 1). Between December 2017 and May 2020, we incorporated the AKIDS into the backend of the outpatient Health Information System of CMUH to investigate the natural course of AKD_{OPT}. The AKIDS utilized the minimal and maximum S-Cre levels observed during the past 180 days of the index date to define AKD_{OPT}, with the minimal S-Cre level during this period served as the baseline S-Cre. AKD_{OPT} in the 180 days prior to the index date was defined per the following criteria: (1) a >50% absolute change between the maximum S-Cre and minimum S-Cre (baseline S-Cre), or (2) a >35% absolute change between the maximum eGFR (baseline eGFR) and minimum eGFR. AKD_{OPT} was divided into two subtypes based on the last two (i.e., penultimate and ultimate) S-Cre measurements in the 180 days prior to the index date: deteriorating (>0.3 mg/dL increase) and stable (otherwise). We developed a risk matrix that utilizes patient's AKD_{OPT} subgroup (i.e., no, stable, and deteriorating AKD_{OPT}) and ultimate eGFR level (i.e., ≥ 60, 45 to <60, and <45 ml/min/1.73m^2) to stratify the risk of one-year CKO. Patients were identified by AKIDS as having high-risk AKD_{OPT} and were considered to require a nephrology clinic referral when their ultimate eGFR within 180 days prior to the index visit was less than 45 ml/min/1.73 m^2. A 180-day diagnostic window for AKD_{OPT} was used because it was the maximum time period accessible from the NHI MediCloud and this diagnostic window has been supported by our prior study and another study[12,16]. The median interval between the measurement of the minimum and maximum S-Cre was 77 days (interquartile range: 23–105 days), indicating that most cases of AKD_{OPT} occurred within 90 days prior to the index date. Several sensitivity analyses using different definitions of AKD_{OPT} were conducted. From our unpublished prospective study of 98 enrolled patients with AKD_{OPT} who were deemed to require nephrology referral through activated AKIDS, 61% had neutrophil gelatinase-associated lipocalin levels exceeding 131.7 ng/mg creatinine, supporting the biomarker's validation of our operational algorithm's accuracy in diagnosing AKD_{OPT}[17]. Detailed information was provided in the Supplementary Table 3.

Clinical outcomes of interest

The outcomes of interest included a CKO, all-cause mortality, and de novo non-dialysis CKD (CKD-ND) during the 1-year follow-up after the index outpatient visit. CKO was defined as follows: (1) progression to ESKD, as indicated by the initiation of hemodialysis or peritoneal dialysis, or kidney transplantation, as indicated by the records of a catastrophic illness certificate issued by Taiwan's Ministry of Health and Welfare[15]; (2) a >40% decrease of eGFR at any outpatient follow-up, compared with the baseline eGFR; or (3) a twofold or higher increase in S-Cre at any outpatient follow-up, compared with the baseline S-Cre. Dates of death were verified using the National Death Registry maintained by Taiwan's Ministry of Health and Welfare. For patients without CKD at baseline, de novo CKD-ND was indicated if a patient had at least two outpatient eGFR values of <60 mL/min/1.73 m^2 during the 3–12 months after the index date but did not progress to ESKD. Supplementary Table 2 presents the definitions of CKD stage progression, kidney function recovery, and nephrology care.

Statistics and reproducibility

The incidence of AKD_{OPT} for each month between December 2017 and May 2020 was calculated by dividing the number of patients with AKD_{OPT} by the total number of outpatients by month, and the monthly incidence of AKD_{OPT} requiring referral was calculated based on the number of patients with AKD_{OPT} requiring referral divided by the number of AKD_{OPT} patients

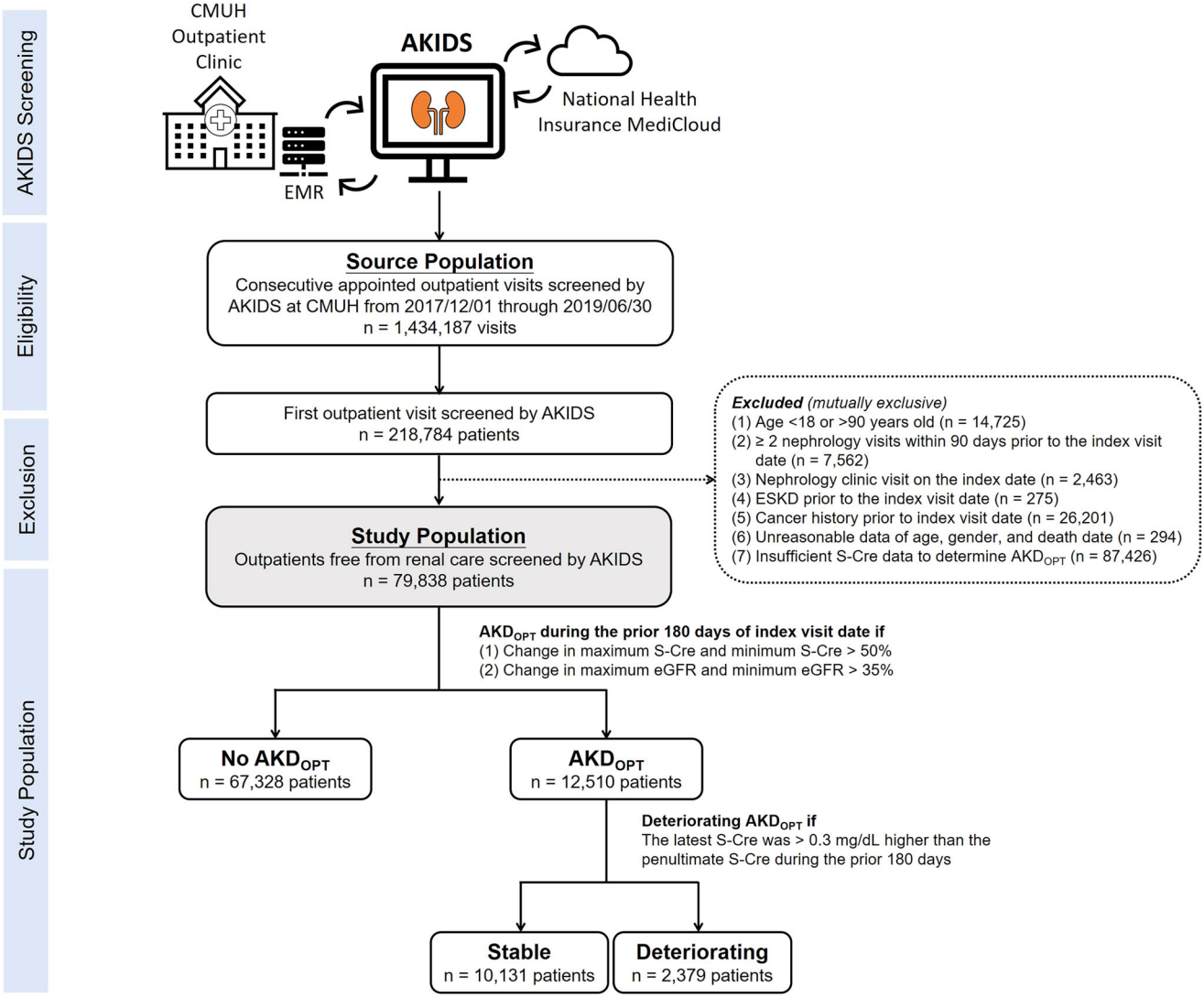

Fig. 1 | Process for selecting the study population of outpatients screened by the Acute Kidney Injury Detection System (AKIDS). AKIDS automatically integrated the local EMR data and data from National Health Insurance MediCloud to screen for AKI status among appointed adult outpatients. This study included all appointed outpatient visits screened by AKIDS between December 1, 2017, and June 30, 2019 as the source population and kept patients' first appointed visits. The index date was the first appointed outpatient visit. Patients younger than 18 or older than 90 years old, those with 2 or more nephrology department visits in prior 90 days or had nephrology visit on the index visit date, those with ESKD, those with cancer history, or those with an unknown AKD$_{OPT}$ status were excluded. The final study population included 79,838 outpatients, of which 12,510 patients had AKD$_{OPT}$. AKD$_{OPT}$ acute kidney disease in outpatient settings, CMUH China Medical University Hospital, EMR electronic medical records, eGFR estimated glomerular filtration rate, ESKD end-stage kidney disease, S-Cre serum creatinine.

by month. The numerical data used in calculating the incidence were provided in Supplementary Data 2. The associations of AKD$_{OPT}$ with the risk of outcomes were evaluated using separate multivariable Cox proportional hazards models[18,19]. We modeled the effect of AKD$_{OPT}$ on cause-specific hazard of outcomes other than death, with consideration for the competing risk of overall death[20]. The PROC PHREG procedure in SAS was used to perform regression analysis of survival data based on the Cox proportional hazards model[21]. All enrolled patients were followed up until June 30, 2020, dialysis initiation, death, or loss to follow-up (LTFU). Cox models accounted for LTFU, whichever occurred earlier, were initially adjusted for sociodemographic variables and comorbidities (Model 1), followed by adjustments for baseline nephrotoxic agent exposure (Model 2) and then baseline S-Cre and hemoglobin levels (Model 3). The censoring time for CKO and de novo CKD-ND was the date of the last patient visit, as recorded in the iHi Data Platform; this is because these two outcomes were actively confirmed through clinical investigation[18,19]. Because we used the National Death Registry to capture all death events without any missing event, the censoring time for mortality was the date of death for patients who died during the 1-year follow-up and the last day of study period for patients who did not die. We compared the adjusted hazard ratios (aHRs) and risk differences between the non-AKD$_{OPT}$ and AKD$_{OPT}$ groups as well as between the non-AKD$_{OPT}$, deteriorating-AKD$_{OPT}$, and stable-AKD$_{OPT}$ groups. The proportional hazards assumption was confirmed with the parallel time-to-event curves. Adjusted absolute risks were estimated using the method proposed by Austin[22]. Missing values for body mass index, smoking status, and hemoglobin levels were imputed through a multiple-imputation method that was executed using the Multivariate Imputation by Chained Equations package in R (number of imputations was 20; number of iterations was 100)[23]. The PROC MIANALYZE procedure in SAS was used to combine results from multiple imputations (if multiple datasets were imputed) and provide a final set of estimates. The MODELEFFECTS statement is used to specify the estimation of model effects, and stderr specifies the standard errors[24,25]. Subgroup analysis of age, sex, comorbidities, nephrotoxic agent exposure, diagnostic S-Cre source, and baseline

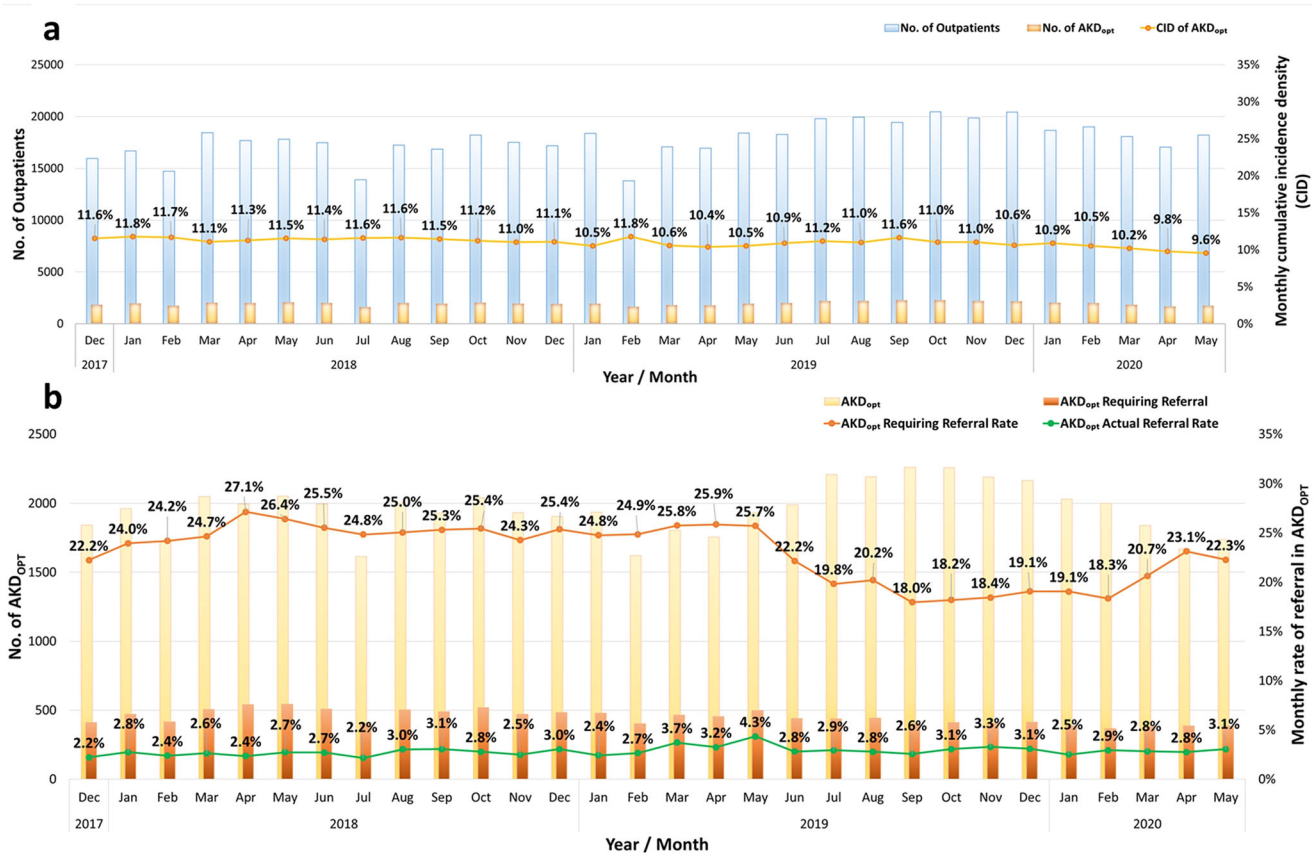

Fig. 2 | Epidemiology profile of AKD_{OPT} from December 2017 to May 2020 among eligible adult outpatients free from nephrology care, ESKD, and cancer. **a** Monthly occurrence (yellow bars) and cumulative incidence (orange line) of AKD_{OPT}. **b** Monthly occurrence (orange bars) and rate of AKD_{OPT} requiring nephrology clinic referral (red line), in addition to rate of actual nephrology clinic referral in 1 month (green line). The numerical data used in calculating the incidence were provided in Supplementary Data 2. AKD_{OPT} acute kidney disease in outpatient settings, CID cumulative incidence density, ESKD end-stage kidney disease.

CKD stage were conducted. We plotted adjusted time-to-event curves for 1-year probabilities of outcomes against follow-up time and compared them between the non-AKD_{OPT}, and AKD_{OPT} groups by using a log-rank test using R program[25]. The adjusted cumulative incidence function data underlying the time-to-event curves were provided in the Supplementary Data 3. A risk matrix was constructed to stratify study population according to AKD_{OPT} status and ultimate eGFR measurements (≥ 60, 45 to <60, and <45 mL/min/1.73 m^2) and the aHR for each outcome were calculated based on Model 3. A two-sided α value of 0.05 was considered to indicate statistical significance. All statistical analyses were performed using SAS (version 9.4; SAS Institute Inc., Cary, NC, USA) and R (version 3.5.1; R Foundation for Statistical Computing, Vienna, Austria).

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Results

Epidemiology and clinical characteristics of AKD_{OPT}

Between December 2017 and May 2020, the monthly cumulative incidence of AKD_{OPT} was stable among eligible population, with the average incidence being 11.0% (95% confidence interval [CI] 10.8–11.2%), and the top 3 clinical divisions that had the highest number of AKD_{OPT} requiring nephrology referral were cardiology, urology, and gastroenterology (Fig. 2; Supplementary Figs. 2, 3). Moreover, 23.0% (95% CI 21.9–24.0%) of the patients with AKD_{OPT} were considered to be high risk and required nephrology referral, but only 2.8% (95% CI 2.6–2.9%) of the patients with AKD_{OPT} actually had a nephrology clinic follow-up in the same month. In the sensitivity analyses of limiting eligible outpatient visits with at both diagnostic S-Cre measurements from CMUH's outpatient setting or with at least one S-Cre measurements from CMUH's outpatient, the average incidence of AKD_{OPT} decreased to 2.9% (95% CI, 2.8–3.0%) and 6.1% (95% CI 5.9–6.3%), respectively. However, the proportion of high-risk AKD_{OPT} remained high (32.3% [30.4–34.2%] and 28.5% [27.1–29.9%]) and the rate of AKD_{OPT} patients having nephrology follow-up remained low (4.3% [3.8–4.8%] and 3.5% [3.3–3.7%]; Supplementary Figs. 4, 5).

Of the 79,838 eligible outpatients (study population), 12,510 (15.7%) were identified by the AKIDS as having AKD_{OPT}, with 81.0% of them having stable AKD_{OPT} and 19.0% having deteriorating AKD_{OPT}. Compared with patients without AKD_{OPT}, those with AKD_{OPT} were older, were more likely to be a former or active tobacco smoker or alcohol drinker, and had a higher burden of comorbidities such as diabetes and hypertension (Table 1). Patients with AKD_{OPT} were more likely to have an advanced CKD stage (eGFR <60 mL/min/1.73 m^2) (18.3% vs 10.5%), had higher blood urea nitrogen and pooled urine albumin-to-creatinine ratio levels but lower serum albumin and hemoglobin levels than did those without AKD_{OPT} (Table 1 and Supplementary Data 4). Because the setting of the S-Cre measurements used to screen for AKD_{OPT} could only be verified if the measurements were from the on-site electronic medical records and because the inclusion of S-Cre from inpatient measurements may interfere the AKD_{OPT} detection, we provided the distribution of S-Cre source. Only 45.2% of the study population had their maximum and minimum S-Cre measurements solely from the outpatient setting, 20.9% from inpatient and 34% from other institutions via the NHI Health Information Exchange (Table 1). The patients with AKD_{OPT} had significantly higher 1-year CKO (12.4% vs. 0.5%), all-cause mortality (8.2% vs. 1.4%), and de novo CKD-ND rates (7.8% vs. 1.6%) than did those without AKD_{OPT}.

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Table 1 | Baseline demographic and clinical characteristics of the AKD_{OPT} study population selected from CMUH for the period between December 2017 and June 2019

Characteristic	Available *n* (%)	Total (*n* = 79838)	Non-AKD_{OPT} [α] (*n* = 67328)	AKD_{OPT} [β] (*n* = 12510)	AKD_{OPT} Subtype		*P*-value [f]	
					Stable [γ] (*n* = 10131)	Deteriorating [δ] (*n* = 2379)	α vs β	γ vs δ
Demographic information								
Age (year)	79838 (100)	59.1 (45.7, 69.5)	58.3 (44.9, 68.5)	63.9 (50.4, 75.2)	63.3 (49.3, 75.0)	65.6 (54.2, 76.4)	5.52×10^{-224}	7.16×10^{-13}
Female	79838 (100)	39692 (49.7)	33255 (49.4)	6437 (51.5)	5308 (52.4)	1129 (47.5)	2.27×10^{-05}	1.45×10^{-05}
Ever smoke	77977 (97.7)	23443 (30.1)	18902 (28.8)	4541 (36.7)	3665 (36.6)	876 (37.2)	2.11×10^{-9}	0.5608
Ever drink	52717 (66)	10210 (19.4)	7459 (17.8)	2751 (25.6)	2248 (25.5)	503 (26.3)	2.02×10^{-75}	0.4852
Body mass index (kg/m^2)	65726 (82.3)	24.8 (22.1, 27.8)	24.9 (22.2, 27.9)	24.3 (21.6, 27.5)	24.2 (21.4, 27.3)	25.1 (22.3, 28.2)	3.22×10^{-34}	1.40×10^{-16}
Comorbidities								
Diabetes mellitus	79838 (100)	20231 (25.3)	15594 (23.2)	4637 (37.1)	3662 (36.2)	975 (41.0)	1.81×10^{-236}	1.10×10^{-05}
Hypertension	79838 (100)	27890 (34.9)	21718 (32.3)	6172 (49.3)	4843 (47.8)	1329 (55.9)	2.15×10^{-296}	1.48×10^{-12}
Nephrotoxic or AKI predisposing agents within 90 days prior								
Any of the following agents	79838 (100)	46810 (58.6)	37703 (56)	9107 (72.8)	7466 (73.7)	1641 (69.0)	6.67×10^{-269}	3.29×10^{-06}
NSAIDs	79838 (100)	21463 (26.9)	17361 (25.8)	4102 (32.8)	3449 (34.0)	653 (27.5)	3.28×10^{-9}	6.97×10^{-10}
Contrast	79838 (100)	14151 (17.7)	10353 (15.4)	3798 (30.4)	3355 (33.1)	443 (18.6)	$0.00 \times 10^{+00}$	1.53×10^{-43}
Antimicrobials	79838 (100)	5665 (7.1)	3549 (5.3)	2116 (16.9)	1891 (18.7)	225 (9.5)	$0.00 \times 10^{+00}$	4.24×10^{-27}
Chemotherapy immunotherapy	79838 (100)	138 (0.2)	109 (0.2)	29 (0.2)	26 (0.3)	3 (0.1)	0.0838	0.2335
ACEIs	79838 (100)	3412 (4.3)	2483 (3.7)	929 (7.4)	793 (7.8)	136 (5.7)	2.36×10^{-80}	4.10×10^{-04}
ARBs	79838 (100)	16970 (21.3)	13445 (20.0)	3525 (28.2)	2739 (27.0)	786 (33.0)	2.37×10^{-94}	4.70×10^{-09}
Diuretics	79838 (100)	13682 (17.1)	8916 (13.2)	4766 (38.1)	3950 (39.0)	816 (34.3)	$0.00 \times 10^{+00}$	2.25×10^{-05}
Kidney function dynamics within 180 days prior								
S-Cre measurement (mg/dL)								
Maximum	79838 (100)	0.9 (0.8, 1.2)	0.9 (0.7, 1.1)	1.3 (1.0, 1.9)	1.3 (0.9, 1.8)	1.5 (1.2, 2.1)	$0.00 \times 10^{+00}$	3.11×10^{-86}
Minimum (baseline)	79838 (100)	0.8 (0.6, 1.0)	0.8 (0.6, 1.0)	0.7 (0.6, 1.0)	0.7 (0.5, 1.0)	0.9 (0.7, 1.2)	2.76×10^{-62}	7.66×10^{-158}
Ultimate	79838 (100)	0.8 (0.7, 1.0)	0.8 (0.7, 1.01)	0.9 (0.7, 1.3)	0.8 (0.6, 1.1)	1.5 (1.2, 2.1)	1.88×10^{-105}	$0.00 \times 10^{+00}$
Penultimate	79838 (100)	0.9 (0.70, 1.1)	0.9 (0.7, 1.0)	0.9 (0.7, 1.3)	0.9 (0.7, 1.3)	1.0 (0.7, 1.3)	1.69×10^{-182}	0.0004
eGFR measurement (mL/min/1.73m^2)								
Maximum (baseline)	79838 (100)	93.6 (76.6, 107)	93.9 (77.7, 106.7)	91.5 (69.2, 109.5)	94.1 (74.3, 112)	77.3 (52.9, 96.5)	3.15×10^{-13}	1.63×10^{-130}
Minimum	79838 (100)	81.6 (60.7, 97.7)	85.2 (67.6, 99.6)	49.9 (32.1, 72.2)	52.5 (33.7, 76.6)	41.2 (27.0, 57.0)	$0.00 \times 10^{+00}$	8.05×10^{-83}
Ultimate	79838 (100)	89.4 (69.9, 103.5)	90.7 (73.0, 103.8)	78.5 (49.8, 100.9)	86.8 (61.8, 105.3)	42.3 (28.3, 57.7)	$0.00 \times 10^{+00}$	$0.00 \times 10^{+00}$
Penultimate	79838 (100)	88.3 (68.4, 102.9)	89.7 (71.9, 103.4)	74.5 (48.3, 98.5)	74.8 (48.3, 99.8)	73.2 (48.0, 94.8)	$0.00 \times 10^{+00}$	0.0044
Baseline eGFR ≥ 60 mL/min/1.73 m^2	79838 (100)	70453 (88.2)	60234 (89.5)	10219 (81.7)	8583 (84.7)	1636 (68.8)	8.74×10^{-136}	3.03×10^{-73}
Diagnostic S-Cre source [b]	79838 (100)						$0.00 \times 10^{+00}$	1.92×10^{-208}
Pattern O		36087 (45.2)	33870 (50.3)	2217 (17.7)	1365 (13.5)	852 (35.8)		
Pattern A		8111 (10.2)	4711 (7.0)	3400 (27.2)	3219 (31.8)	181 (7.6)		
Pattern M		8524 (10.7)	6771 (10.1)	1753 (14.0)	1378 (13.6)	375 (15.8)		
Pattern C		27116 (34.0)	21976 (32.6)	5140 (41.1)	4169 (41.2)	971 (40.8)		
Pooled uACR (mg/g cre)	17705 (22.2)	18.7 (7.2, 72.6)	16.2 (6.6, 6.0)	46.4 (13.5, 247.0)	44.9 (12.9, 218.3)	50.9 (15.3, 359.8)	1.39×10^{-163}	0.0045

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Table 1 (continued) | Baseline demographic and clinical characteristics of the AKD_{OPT} study population selected from CMUH for the period between December 2017 and June 2019

Characteristic	Available *n* (%)	Total (*n* = 79838)	Non-AKD_{OPT} [α] (*n* = 67328)	AKD_{OPT} [β] (*n* = 12510)	AKD_{OPT} Subtype		*P*-value [f]	
					Stable [γ] (*n* = 10131)	Deteriorating [δ] (*n* = 2379)	α vs β	γ vs δ
Proteinuria	79838 (100)	8373 (10.49)	5933 (8.81)	2440 (19.5)	1875 (18.51)	565 (23.75)	2.29×10^{-281}	6.37×10^{-09}
Hemoglobin (g/dL)	56297 (70.5)	13.4 (12, 14.6)	13.6 (12.4, 14.7)	12.1 (10.6, 13.5)	12 (10.6, 13.4)	12.5 (10.7, 14)	$0.00 \times 10^{+00}$	1.78×10^{-12}
One-year outcomes								
CKO[c]	79838 (100)	1858 (2.3)	312 (0.5)	1546 (12.4)	1112 (11.0)	434 (18.2)	$0.00 \times 10^{+00}$	3.27×10^{-22}
ESKD		96 (0.1)	22 (0.03)	74 (0.6)	39 (0.4)	35 (1.5)	1.28×10^{-61}	5.05×10^{-10}
eGFR drop > 40%		1702 (2.13)	291 (0.4)	1411 (11.2)	995 (9.8)	416 (17.5)	$0.00 \times 10^{+00}$	2.04×10^{-26}
Twofold or more increase in S-Cre		783 (1.0)	51 (0.1)	732 (5.9)	556 (5.5)	176 (7.4)	$0.00 \times 10^{+00}$	3.55×10^{-04}
All-cause mortality	79838 (100)	1942 (2.4)	923 (1.4)	1019 (8.2)	860 (8.5)	159 (6.7)	$0.00 \times 10^{+00}$	3.77×10^{-03}
De novo CKD-ND[d]	70453 (88.2)	1769 (2.5)	972 (1.6)	797 (7.8)	588 (6.9)	209 (12.8)	6.37×10^{-299}	2.63×10^{-16}
CKD stage progression[e]	8994 (11.3)	883 (9.8)	410 (6.0)	473 (22.4)	279 (19.3)	194 (29.4)	9.9×10^{-110}	2.0×10^{-07}
Kidney function recovery for AKD_{OPT}[f]	12510 (15.7)							
Absolute recovery		7343 (58.7)	–	1721 (23.4)	1294 (22.4)	427 (27.1)	–	9.62×10^{-05}
General recovery, absolute change		7343 (58.7)	–	5138 (70.0)	4113 (71.3)	1025 (65.1)	–	2.17×10^{-06}
General recovery, relative change		7343 (58.7)	–	3054 (41.6)	2307 (40.0)	747 (47.5)	–	9.88×10^{-08}
No. of nephrology visit ≥2 in 90 days	79838 (100)	733 (0.9)	398 (0.6)	335 (2.7)	219 (2.2)	116 (4.9)	7.80×10	1.58×10^{-13}

ACEIs angiotensin-converting enzyme inhibitors, AKD_{OPT} acute kidney disease in outpatient settings, *ARBs* angiotensin II receptor antagonists, *CKD* chronic kidney disease, *CKO* composite kidney outcome, *eGFR* estimated glomerular filtration rate, *ESKD* end-stage kidney disease, *ND* nondialysis, *NSAID* nonsteroidal anti-inflammatory drug, *S-Cre* serum creatinine, *uACR* urine albumin-to-creatinine ratio, *uPCR* urine protein-to-creatinine ratio.

[a]Continuous variables, expressed as medians and interquartile ranges (IQRs), were compared using the nonparametric Wilcoxon rank-sum test. Categorical variables, expressed as frequencies (percentages), were compared using a chi-square test.

[b]Pattern O: both maximum and minimum S-Cre measurements were obtained from outpatient settings; Pattern A: both S-Cre measurements were obtained from inpatient settings; Pattern M: one S-Cre measurement was obtained from inpatient settings, and the other was obtained from outpatient settings; Pattern C: at least one S-Cre measurement was obtained from the National Health Insurance MediCloud platform.

[c]CKO was defined as an ESKD diagnosis or the presence of kidney transplantation records from the National Health Insurance program's Catastrophic Illness Database, a ≥ 40% decrease in outpatient eGFR relative to the baseline eGFR value, or a twofold or more increase in outpatient S-Cre during the follow-up period.

[d]For patients without CKD at baseline, de novo CKD-ND was defined as having at least two outpatient eGFR values of <60 mL/min/1.73m^2 during 3–12 months after the index date but did not progress to ESKD.

[e]For patients with CKD stage ≥3 at baseline, stage progression was defined according to the lowest outpatient eGFR or dialysis use 3–12 months after the index date.

[f]For patients with AKD_{OPT}, absolute kidney function recovery was defined as a minimum outpatient S-Cre level during follow-up that was less than or equal to the baseline S-Cre level. General recovery with absolute change was defined as a minimum outpatient S-Cre level during follow-up that was no more than the baseline S-Cre level plus 0.2 mg/dL. General recovery with relative change was defined as a minimum outpatient S-Cre level during follow-up that was no more than 1.1 times the baseline S-Cre level. The denominators for AKD_{OPT}, stable AKD_{OPT}, and deteriorating AKD_{OPT} were 7343, 5768, and 1575, respectively.

Table 2 | Hazard ratios, absolute risk, and their corresponding 95% confidence intervals for 1-year CKOs, all-cause mortality, and de novo CKD associated with AKD_{OPT} and its subtypes (data with multiple imputation)

One-year Outcomes	Case / Non-case	Person-Months (P-M)	Incidence (per 1000 P-M)	Hazard Ratio				Absolute Risk (per 1000 pts) [c]
				Crude	Model 1 [a,b]	Model 2 [a,b]	Model 3 [a,b]	Model 3 [a]
CKO								
Non-AKD_{OPT}	312/67016	740218	0.42	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	(Ref)
AKD_{OPT}	1546/10964	121067	12.77	29.7 (26.3–33.5)	21.6 (19.1–24.5)	18.3 (16.1–20.9)	16.2 (14.2–18.5)	79.0 (78.9–79.1)
Stable	1112/9019	98466	11.29	26.3 (23.2–29.8)	19.7 (17.3–22.4)	15.9 (13.9–18.2)	14.3 (12.5–16.4)	70.2 (70.1–70.3)
Deteriorating	434/1945	22601	19.20	44.6 (38.6–51.6)	29.2 (25.2–33.9)	26.6 (22.9–31.0)	22.7 (19.5–26.4)	109.7 (109.5–109.9)
All-cause mortality								
Non-AKD_{OPT}	923/66405	799987	1.15	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	(Ref)
AKD_{OPT}	1019/11491	143019	7.12	6.2 (5.6–6.7)	3.8 (3.5–4.2)	3.1 (2.8–3.4)	2.6 (2.4–2.9)	25.3 (25.2–25.3)
Stable	860/9271	115599	7.44	6.4 (5.9–7.1)	4.1 (3.7–4.5)	3.2 (2.9–3.5)	2.8 (2.5–3.1)	27.3 (27.2–27.3)
Deteriorating	159/2220	27420	5.80	5 (4.2–5.9)	2.9 (2.4–3.4)	2.6 (2.2–3.1)	2.1 (1.8–2.6)	17.9 (17.8–17.9)
De novo *CKD-ND*								
Non-AKD_{OPT}	972/59262	657408	1.48	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	(Ref)
AKD_{OPT}	797/9422	103246	7.72	5.2 (4.7–.7)	3.2 (2.9–3.5)	3.0 (2.7–3.4)	3.5 (3.1–3.9)	54.8 (54.7–54.9)
Stable	588/7995	86667	6.78	4.6 (4.1–5.1)	2.9 (2.6–3.2)	2.7 (2.4–3.0)	3.3 (2.9–3.7)	51.3 (51.2–51.4)
Deteriorating	209/1427	16579	12.61	8.5 (7.3–9.8)	4.6 (4.0–5.4)	4.5 (3.8–5.2)	4.1 (3.5–4.8)	64.2 (64.0–64.4)

[a]*Model* 1: adjusted for age, sex, body mass index, smoking status, diabetes, hypertension, cerebrovascular disease, dementia, renal disease, congestive heart failure; *Model 2*: further adjusted for nephrotoxic agents (e.g., NSAIDs, contrast agents, ACEIs/ARBs, antimicrobials, and diuretics in the previous 90 days); *Model 3*: further adjusted for baseline S-Cre and hemoglobin levels.
[b]*The* censoring time for LTFU was determined through outcome ascertainment.
[c]Absolute risk from the Cox proportional model (Model 3) was calculated using methods proposed by Austin (doi: 10.1016/j.jclinepi.2009.03.012). This risk represents the number of patients per 1000 patients with outcomes attributable to AKD_{OPT} or its subgroups.
ACEIs angiotensin-converting enzyme inhibitors, *AKD_{OPT}* acute kidney disease in outpatient settings, *ARBs* angiotensin II receptor antagonists, *CKD* chronic kidney disease, *CKO* composite kidney outcome, *LTFU* loss to follow-up, *ND*, nondialysis, *NSAIDs* nonsteroidal anti-inflammatory drugs, S-Cre serum creatinine.

Associations of AKD_{OPT} with CKO and all-cause mortality

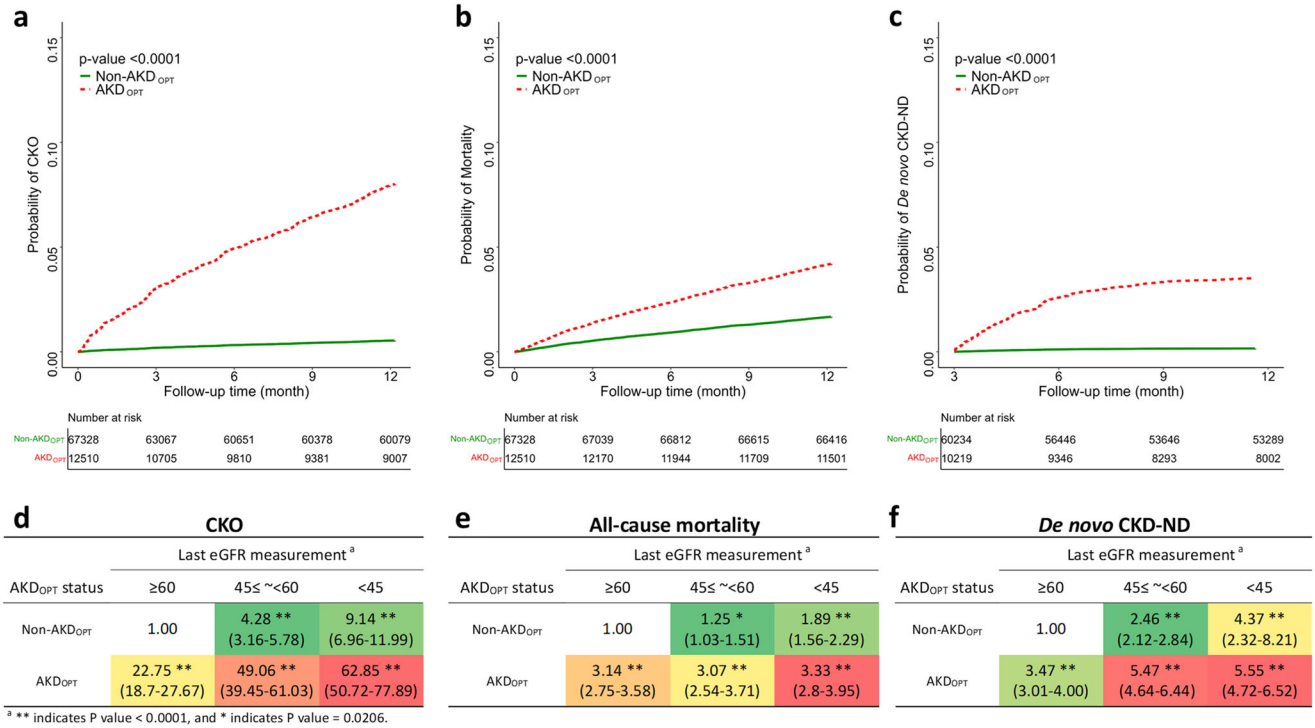
During the 1-year follow-up, 1942 patients died and 1858 had CKO (96 had ESKD; 1702 had a > 40% decrease in eGFR; 783 had a twofold increase in S-Cre levels; not mutually exclusive). The incidence of 1-year CKO was notably higher in patients with AKD_{OPT} than in those without AKD_{OPT} (12.77 vs 0.42 per 1000 person-months); the adjusted absolute risk was 79 (95% CI 78.9–79.1) per 1000 persons. The corresponding difference for deteriorating AKD_{OPT} was even higher, reaching 109.7 (95% CI 109.5–109.9) per 1000 persons (Table 2). The 1-year mortality rate was significantly higher in patients with AKD_{OPT} than in those without AKD_{OPT} (7.12 vs 1.15 per 1000 person-months); the adjusted absolute risk was 25.3 (95% CI 25.2–25.3) per 1000 persons. The absolute risk of mortality was higher in patients with stable AKD_{OPT} than in those with deteriorating AKD_{OPT}. Moreover, the aHRs for 1-year CKO and mortality in the AKD_{OPT} group relative to the non-AKD_{OPT} group were 16.2 (14.2–18.5) and 2.6 (2.4–2.9), respectively (Table 2). The aHRs for 1-year CKO and mortality in the deteriorating-AKD_{OPT} group relative to the non-AKD_{OPT} group were 22.7 (19.5–26.4) and 2.1 (1.8–2.6), respectively; the same aHRs in the stable-AKD_{OPT} group relative to the non-AKD_{OPT} group were 14.3 (12.5–16.4) and 2.8 (2.5–3.1), respectively. Among patients without baseline CKD, the corresponding aHRs for 1-year de novo CKD-ND in the AKD_{OPT}, deteriorating-AKD_{OPT}, and stable-AKD_{OPT} groups relative to the non-AKD_{OPT} group were 3.5 (3.1–3.9), 4.1 (3.5–4.8), and 3.3 (2.9–3.7), respectively. For each outcome, the time-to-event curves were significant different between AKD_{OPT} and non-AKD_{OPT} groups, as well as across AKD_{OPT} subgroups (Fig. 3a–c and Supplementary Fig. 6a–c).

Of patients who were younger than 65 years or those were free from comorbidities such as diabetes, hypertension, or CKD at baseline, having AKD_{OPT} was associated with a significantly higher risk of 1-year CKO, mortality, and de novo CKD-ND (Supplementary Fig. 7). The risk matrix demonstrated that the aHR for each outcome exhibited a gradient increase from low-risk (non-AKD_{OPT} and ultimate eGFR of ≥60) to high-risk patients (AKD_{OPT} and ultimate eGFR of <45) (Fig. 3d–f and Supplementary Fig. 6d–f).

We conducted various sensitivity analyses to ensure the robustness of our results. The aHR and absolute risks from these analyses aligned with our main findings under different conditions: (1) without multiple imputation (Supplementary Table 4), (2) with diagnostic S-Cre measurements exclusively from CMUH's outpatients (Supplementary Table 5) and with at least one diagnostic S-Cre from CMUH's outpatients (Supplementary Table 6), () with at least one outpatient S-Cre during follow-up (Supplementary Table 7), (4) with diagnostic S-Cre taken within the standard 90-day AKD diagnostic window (Supplementary Table 8), and (5) with diagnostic S-Cre taken from CMUH's outpatients within 90-day window (Supplementary Table 9). By applying the most stringent definition for AKD_{OPT}, we found larger effect sizes for the aHRs and adjusted absolute risks (Supplementary Table 9), which implies that our original definition might have underestimated the clinical impact of AKD_{OPT}. For the 87,426 patients initially excluded because of an unknown AKD_{OPT} status, we adopted the CMUH's median outpatient S-Cre levels (adjusted for age, sex, and CKD status) as the baseline S-Cre. The association of AKD_{OPT} with 1-year CKO, mortality, and de novo CKD remained significant, albeit with a reduced effect size (Supplementary Table 10).

Recovery pattern of AKD_{OPT} and nephrology follow-up

Of the patients with AKD_{OPT}, 23.4%, 70.0%, and 41.6% experienced recovery to their baseline S-Cre levels (absolute recovery), recovery to ≤0.2 mg/dL above baseline levels, and recovery to ≤1.1 times the baseline



d CKO

AKD_{OPT} status	Last eGFR measurement [a] ≥60	45≤ ~<60	<45
Non-AKD_{OPT}	1.00	4.28 ** (3.16-5.78)	9.14 ** (6.96-11.99)
AKD_{OPT}	22.75 ** (18.7-27.67)	49.06 ** (39.45-61.03)	62.85 ** (50.72-77.89)

e All-cause mortality

AKD_{OPT} status	Last eGFR measurement [a] ≥60	45≤ ~<60	<45
Non-AKD_{OPT}	1.00	1.25 * (1.03-1.51)	1.89 ** (1.56-2.29)
AKD_{OPT}	3.14 ** (2.75-3.58)	3.07 ** (2.54-3.71)	3.33 ** (2.8-3.95)

f *De novo* CKD-ND

AKD_{OPT} status	Last eGFR measurement [a] ≥60	45≤ ~<60	<45
Non-AKD_{OPT}	1.00	2.46 ** (2.12-2.84)	4.37 ** (2.32-8.21)
AKD_{OPT}	3.47 ** (3.01-4.00)	5.47 ** (4.64-6.44)	5.55 ** (4.72-6.52)

[a] ** indicates P value < 0.0001, and * indicates P value = 0.0206.

Fig. 3 | Risk of outcomes associated with AKD_{OPT}. a–c Adjusted 1-year time-to-event curve for CKOs, all-cause mortality, and de novo CKD, respectively, categorized according to AKD_{OPT} status. Variables used for adjustment in the Cox proportional hazards models are described in Model 3. The sample sizes are 79,838 for (**a**, **b**) and 70,453 for (**c**). **d–f** Corresponding risk matrix accounting for the ultimate eGFR and AKD_{OPT} for CKOs, all-cause mortality, and de novo CKD, respectively. The associations of AKD_{OPT} with the risk of outcomes were evaluated using separate multivariable Cox proportional hazards models. The number represents the aHR (95% CI) of each outcome of interest from Model 3 based on the ultimate eGFR and AKD_{OPT} (lower aHRs in green and higher aHRs in red). aHR adjusted hazard ratio, AKD_{OPT} acute kidney disease in outpatient settings, CI confidence interval, CKD chronic kidney disease, CKOs composite kidney outcomes, eGFR estimated glomerular filtration rate, ND nondialysis.

levels within 1 year, respectively (Table 1). However, compared with the patients with stable AKD_{OPT} (22.4%), those with deteriorating AKD_{OPT} had a higher absolute recovery rate (27.1%). This may be attributed to the fact that patients with deteriorating AKD_{OPT} were more likely to be regularly followed by nephrologists (12.2% vs 7.0%) and were follow-up sooner (23 days vs 48 days), compared to those with stable AKD_{OPT}. Among the patients with CKD at baseline, 22.4%, 19.3%, and 29.4% of the patients with AKD_{OPT} (all), stable AKD_{OPT}, and deteriorating AKD_{OPT} had CKD stage progression, respectively (Table 1). The nephrology follow-up rate within 90 days following the index date was 2.7%, 2.2%, and 4.9% for the patients with AKD_{OPT}, stable AKD_{OPT}, and deteriorating AKD_{OPT}, respectively.

Discussion

During the 30-month period since the AKIDS was implemented in the backend of CMUH's Health Information System, AKIDS identified 11.0% AKD_{OPT} cases on average per month in the outpatient setting; the AKD_{OPT} trend was stable without any notable variation. We observed that AKD_{OPT} could significantly accelerate kidney failure and lead to premature death within 1 year. Our risk matrix could facilitate the task of performing dose–response risk assessments for identifying the AKD_{OPT} phenotype. We observed the 1-year kidney recovery was 23.4%, indicating the AKD_{OPT}'s nature is partly reversible and not just a one-way ticket towards irreversible rapid progression of CKD. The prognostic predictive value of the AKIDS bolsters its potential benefits for enhancing kidney health at the population level.

Few studies have investigated AKI in outpatient settings. The most critical challenge for such investigations pertains to identifying a reference (baseline) S-Cre level and time frame for defining (peak) S-Cre levels for AKI_{OPT} diagnosis. Leither et al. defined AKI in outpatient settings using a moving average of S-Cre measurements during an 18-month baseline period and peak S-Cre levels during the following 18-month exposure period, without incorporating cross-hospital S-Cre data[9]. They reported that the cumulative incidence of AKI_{OPT} was 1.4% throughout the 18-month exposure period. The true incidence of AKI_{OPT} may be therefore underestimated[26]. The same research group implemented a project involving the use of machine learning to predict AKI_{OPT}; the group modified the baseline period to 365 days, allowing the use of even earlier S-Cre levels if no recent measurements were available[26]. In Tolan et al.'s study of an outpatient laboratory alerting mechanism, they defined AKI_{OPT} as S-Cre increase within 180 days, the same diagnostic window as our AKD_{OPT}[16]. Although the phenotype the authors stated was AKI_{OPT}, it actually more resembles the AKD_{OPT} phenotype in our study, according to the latest AKI care guidelines[10]. The present study demonstrated how advances in health-care informatics and cloud-based data sharing can aid in AKD_{OPT} detection and reshape clinical practice for this often undiagnosed condition. Our proposed AKD_{OPT} diagnosis system enables the automatic, systematic, large-scale identification of this previously neglected phenotype. AKD_{OPT} imposes a substantial burden on medical centers, however only less than 3% of patients with AKD_{OPT} were actually identified and followed by nephrology care within 90 days. Failure to address AKD_{OPT} represents a missed opportunity to reverse kidney damage and prevent progression to an incident or persistent change in CKD stage.

The phenotype identified by AKIDS was, as anticipated, significantly associated with compromised kidney survival. This finding echoes our previous study that underscored the role AKD_{OPT} in accelerating CKD progression among pre-ESKD patients[12]. Considering the high prevalence of AKD_{OPT} detected by the AKIDS, the referral of all patients with detected AKD to nephrology clinics could overwhelm the relevant health-care system. To avoid unnecessary referrals, we developed a risk matrix to identify high-risk patients who require nephrology follow-up (Fig. 3). The AKIDS

could identify over 77.1% (74/96) of new onset ESKD cases and 83.2% (1546/1858) of incident CKO cases within a year (Table 1). Additionally, the specificity of AKIDS was 84.4% (67306/79742) and 85.9% (67016/77980) for ESKD and CKO cases, respectively. The effectiveness of AKIDS suggests its potential for inclusion in the current CKD detection network, allowing early intervention to improve kidney survival and potentially leading to substantial global healthcare savings.

The development of de novo CKD-ND and the downgrade of CKD after AKD_{OPT} underscore a dynamic transition within the AKI–CKD continuum. For patients with a baseline eGFR value of ≥60 mL/min/1.73 m^2, AKD_{OPT} may represent the first hit and exhibit a stronger prognostic association with CKO compared with that in patients who already have CKD. This is supported by a significant interaction effect on the association between AKD_{OPT} and CKO risk observed in the subgroup analysis stratified by baseline CKD status (Supplementary Fig. 7). Whether early detection of AKD_{OPT} can change the disease course requires prospective evidence. The primary objectives of the present study were to establish consensus in the definition of and develop an alert system for the commonly missed AKD_{OPT}; we next aim to conduct an effectiveness investigation of AKIDS through a pragmatic clinical trial.

The key strength of this research lies in its use of the NHI's National MediCloud platform, which provided us with an unprecedented means of detecting AKD_{OPT}. High-quality follow-up ascertainment using the National Death Registry and the CMUH data platform completed the data ecosystem for this study. However, this study has several limitations. First, no consensus has been reached on how AKI_{OPT} or AKD_{OPT} is diagnosed. Our proposed system uses a 180-day diagnostic time frame, which is longer than the 90 days recommended in current inpatient AKD diagnostic guidelines from KDIGO[10]. Nevertheless, the longer diagnostic time window has been supported by our prior study on CKD patients[12], Tolan et al.'s study (180-day)[16], and Leither et al's study (18-month) of AKI in outpatient setting[9]. Additionally, the NHI's MediCloud platform provides all available biochemical data for the 180 days prior to the index clinic visit, allowing us to redefine the diagnostic window for AKD_{OPT}. Moreover, when we restricted the diagnostic window to 90 days, the inferences remained the same (Supplementary Tables 8 and 9). Second, we did not differentiate the source of diagnostic S-Cre measurements to maximize data interoperability with NHI's MediCloud, which does not specify their sources. In the sensitivity analyses, limiting the S-Cre measurements from CMUH's outpatient setting resulted in a lower AKD_{OPT} incidence, but the practice gap between the expected and actual nephrology referrals for high-risk AKD_{OPT} patients and the risk of CKO associated with AKD_{OPT} remained high (Supplementary Figs. 4, 5; Supplementary Tables 5, 6, 9). The AKIDS system is designed to detect all AKD within a 180-day window for patients visiting outpatient clinics, without limiting the detection to cases originating in the outpatient setting. From a clinical practice perspective, including S-Cre measurements from both inpatient and outpatient settings offers a more comprehensive view of the patient's kidney function history, supporting continuous care. Third, the methods used for S-Cre measurements may differ across hospitals and hence may potentially introduce measurement errors. However, hospitals are required to perform calibration and quality inspection regularly, which could minimize the misclassification issues in the study[11]. Fourth, AKIDS was unable to determine the AKD status for a significant proportion of outpatients who had only one S-Cre measurement prior to their visit, which may have led to an underestimation of the AKD_{OPT} burden. However, excluding patients with unknown AKD_{OPT} status is unlikely to have impacted our findings, as these patients were younger, had fewer comorbidities, and experienced fewer outcomes of interest (Supplementary Data 1). Additionally, the hazard ratio and the absolute risk of 1-year CKO associated with the AKD_{OPT} status—estimated from median-imputed baseline S-Cre—were relatively smaller than that in the study population (Supplementary Table 10). Finally, we cannot rule out the possibility of residual confounding and selection bias, such as genetic background and environmental factors, leading to an underestimation of the clinical importance of AKD_{OPT} and overadjustment for variables that might be present in relevant the causal pathway, such as primary kidney disease.

This study developed an AKIDS to examine the epidemiological profile of AKD_{OPT} in an outpatient population by fully integrating national and local medical data ecosystems. Our findings indicate that a significant number of AKD patients remain undiagnosed in the outpatient settings. Without timely intervention, these patients face a significantly increased risk of progression to ESKD and mortality. This application of big data not only addresses the gap in existing CKD prevention strategies by targeting the AKI–CKD continuum but also highlights the potential use of health-care-related big data in kidney disease prevention and treatment worldwide. Our next steps involve replicating our findings in different health-care systems with high-quality, interoperable data flows and verifying the effectiveness of the AKIDS for reducing ESKD and mortality rates among patients with AKD_{OPT}.

Data availability

The patient-level data that support the findings of this study are available on request from the corresponding author, CCK. The patient-level data are not publicly available due to them containing information that could compromise research participant privacy, according to the Institutional Review Board and the Information Management Committee of China Medical University Hospital. The summary data for Figs. 2 and 3 is in Supplementary Data 2 and Supplementary Data 3, respectively.

Code availability

Code for prediction model development is provided at https://doi.org/10.5281/zenodo.15094219[25]. Further details of all the code developed during the study are available from chinchik@gmail.com on reasonable request.

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Author contributions

H.-Y.C. and C.-C.K. (corresponding author) had full access to all the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis. H.-Y.C., H.-C.Y., and C.-C.K. established the AKIDS and designed the study; H.-C.Y., D.R.C., I.-W.T., J.-S.W., Y.-L.C., Y.-C.L., M.-C.H., and C.-C.K. participated in the AKIDS implementation and data collection; Z.-H.L. managed and analyzed data; H.-Y.C. and C.-C.K. monitored data analytic quality; H.-Y.C., H.-C.Y., B.C., D.R.C, H.-L.C., and C.-C.K. provided interpretation of data; M.-C.H. and T.-L.K.T. provided administrative and technical advice; H.-Y.C., Z.-H.L., and C.-C.K. drafted the manuscript; H.-C.Y. and C.-C.K. coordinated study and provided funding support; All authors reviewed and approved the final version of the manuscript.

Competing interests

The authors declare no competing interests.

Additional information

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