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Outcomes for Older People with Screening Detected Versus Existing Chronic Kidney Disease: Cohort Study with Data Linkage

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Abstract

Background Chronic Kidney Disease (CKD) is a common health problem, associated with increased risk of cardiovascular disease (CVD), end stage kidney disease (ESKD), and premature death. A third of people aged ≥70 years have CKD, many of whom are undiagnosed, but little is known about the value of screening.

Aim To compare the risk of adverse health outcomes between people with an existing diagnosis of CKD and those identified on screening. To identify factors associated with mortality in CKD.

Design Prospective cohort study of 892 primary care patients aged ≥ 60 years with CKD (existing and screening detected) in Oxfordshire, with data linkage to civil death registry and secondary care.

Methods Hazard Ratios (HR) and 95% Confidence Intervals (CI) were estimated using Cox proportional-hazard models to compare the risk of all-cause mortality, hospitalisation, CVD, ESKD separately, and as a composite between CKD groups, as well as to identify factors associated with mortality.

Results After a median follow-up of 3-5 years, 49 people died, 493 were hospitalised, 57 had an incident CVD event, and 0 had an ESKD event. There was no difference in the composite outcome between those existing CKD and those identified on screening (HR 0.94, CI 0.67-1.33). Older age (HR 1.10, CI 1.06-1.15), male sex (HR 2.31, CI 1.26-4.24), and heart failure (HR 5.18, CI 2.45-10.97) were associated with increased risk of death.

Conclusion Screening older people for CKD may be of value, as their risk of short-term mortality, hospitalisation, and CVD is comparable to people routinely diagnosed. Larger studies with longer

follow-up in more diverse and representative populations of older adults are needed to corroborate these findings.

Keywords

Chronic Kidney Disease | Screening | Prognosis | Primary Care | Cohort Studies

How this fits in

Chronic kidney disease (CKD) is a common health problem in older adults, estimated to affect up to 35% of people over 70 years old. CKD is associated with a significantly increased risk of cardiovascular disease (CVD) and premature death. Many people are living with CKD undiagnosed, but little is known about the potential benefit of screening older people for the condition. Our findings show that the risk of short-term mortality, hospitalisation, and CVD is comparable in people diagnosed through screening to those diagnosed routinely in primary care. This suggests that screening older people for CKD may be of value, to increase detection and enable disease-modifying treatment to be initiated at an earlier stage. Larger studies with longer follow-up in more diverse and representative populations of older adults are needed to corroborate these findings.

Introduction

Chronic kidney disease (CKD) is a common and increasing health problem, with an estimated prevalence of 13.9% in adults in England.[1] This is largely attributed to the ageing population and rising prevalence of type 2 diabetes and hypertension.[2,3] CKD is a heterogenous group of disorders characterised by an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73m^2 and/or other measures of kidney damage, including a urine albumin creatinine ratio (ACR) > 3mg/mmol, present for at least three months.[4] CKD is a powerful and independent risk factor for cardiovascular disease (CVD) and premature death.[5,6] Whilst most people with CKD will not develop end stage kidney disease (ESKD) in their lifetime, the burden of CVD is substantial, even in early stages of CKD. Early detection of CKD is recommended to address cardiovascular risk, slow CKD progression, and reduce those developing ESKD.[7] This can be achieved through blood pressure control, renin-angiotensin system (RAS) inhibitors and sodium-glucose co-transporter 2 (SGLT2) inhibitors, which have been shown to prevent adverse cardiovascular and kidney outcomes in people with CKD.[8,9]

CKD is often asymptomatic, particularly in the early stages and consequently many people are living with the condition undiagnosed.[10,11] Screening for CKD can be useful in identifying unrecognised cases, but full population screening is low yield and may not be cost effective.[12,13] Screening programmes in high-risk groups, including those with diabetes and hypertension are well established.[4,14] It is estimated that up to 35% of people over 70 years of age are living with CKD in part due to age-related decline in kidney function.[3] However, despite this high prevalence, targeted CKD screening of older adults is not routinely implemented in clinical practice, and its potential value has not been well explored.

In 2013, the Oxford Renal Cohort (OxRen) Study was established to screen an older population of people in primary care for CKD.[15] This study showed that nearly half of people with CKD (44%) had not

previously been diagnosed.[10] The present study aimed to link OxRen data with clinical outcomes from NHS Digital to determine the value of screening for CKD in an older primary care population. The aim was to compare the risk of adverse health outcomes between people with an existing diagnosis of CKD and those with screening detected CKD. The primary objective was to compare the risk of all-cause mortality, hospitalisation, CVD and ESKD between these CKD groups. The secondary objective was to identify factors associated with adverse health outcomes in patients with CKD.

Methods

Study Design & Study Population

The OxRen Study was the largest national CKD observational study, recruiting 3207 individuals aged ≥ 60 years from primary care practices in Oxfordshire, England, from November 2013 to July 2017.[15] Individuals entered the OxRen CKD cohort either based on an existing diagnosis of CKD in their primary care record, or through screening. Screening detected CKD was defined by an eGFR <60 mL/min/1.73 m^2 and/or a urine ACR ≥3 mg/mmol which persisted on repeat measurement 3 months later. Screening also identified a group of individuals with transiently impaired kidney function whose eGFR and/or urine ACR returned to normal at the second screening visit. Detailed methodology of the OxRen study is described elsewhere.[10,15]

The present study, known as the New onset Kidney Impairment (NewKI) study recruited participants from the OxRen CKD cohort. Individuals were invited to take part in a baseline assessment and to provide written informed consent for their NHS number and date of birth to be linked to the Office for National Statistics (ONS) civil death registry and Hospital Episode Statistics (HES) Admitted Patient Care (APC) data. These data were provided by NHS Digital and enabled us to follow participants over time to conduct a population-based prospective cohort study.

Outcome Measures

The primary outcome measure was a composite of all-cause mortality, hospitalisation for any cause, CVD, or ESKD. Secondary outcome measures included each individual component of the composite primary outcome measure. Additional outcome measures were factors associated with mortality in people with CKD.

The primary outcome measures were reported according to CKD subgroup, which were defined as 1) people with an existing diagnosis of CKD (existing CKD), 2) people with newly diagnosed CKD after screening (screening detected CKD), and 3) people with transiently reduced kidney function identified on screening (transiently impaired kidney function).

Outcome Ascertainment

Information concerning vital status and cause of death was ascertained until the 2nd of July 2021. Due to a lag in HES data CVD events were ascertained until the 21st of March 2020 and ESKD events were ascertained until the 30 of November 2019. International Classification of Diseases 10th revision (ICD-10) codes were used to define CVD and ESKD events (code lists are shown in Supplementary Appendix 1 and 2, respectively). All CVD and ESKD events recorded prior to study entry were considered as prevalent and excluded from analysis of the incidence.

Factors associated with mortality

We investigated the association between various characteristics and mortality in people with CKD. This included the following sociodemographic and lifestyle variables: age, sex, ethnicity (white vs non-white), body-mass index (BMI), waist-to-hip ratio (WHR), smoking status (never, former, or current),

alcohol intake (in grams per week), and level of education. Level of education was coded as follows: primary only (if the participants answered they had no qualifications), secondary (if the participants answered they had A-levels, GCSEs, or O-levels), and higher education (if the participants answered they had university or postgraduate studies). We also investigated blood pressure and co-morbidities including hypertension, diabetes, ischaemic heart disease, heart failure, atrial fibrillation, peripheral vascular disease, other cardiovascular disease, renal disease, urinary tract infection, thyroid disease, anaemia, osteopenia, and osteoporosis.

Statistical Analysis

Sociodemographic, lifestyle, and co-morbidity variables were tabulated and reported as median and interquartile range (IQR) for continuous variables, or frequency and percentage for categorical variables. These baseline characteristics were reported separately for each CKD subgroup.

Cox proportional-hazards models were used to estimate Hazard Ratios (HR) and 95% Confidence Intervals (CI) for the association of CKD subgroups and other factors associated with all-cause mortality, hospitalisation for any cause, CVD and ESKD. Kaplan-Meier (KM) curves and log-rank tests were used to compare survival between CKD subgroups, age groups, and men and women.

All analyses were conducted with R version 4.2.0 (Vienna, Austria) using the 'survival' and 'survminer' packages.

Power calculation

A previous UK observational study reported that 69% of people routinely diagnosed with new CKD had died by the end of study follow-up at 5.5 years.[16] In the absence of UK data for people with CKD

detected by screening, we used data from a French cohort of patients testing positive for CKD in two measurements 3 months apart. The mortality in this cohort was 38% after 3 years of follow-up.[17] Using the sample size for the existing CKD and screening detected CKD groups in our study, and a 5% level of statistical significance, we estimated our statistical power to be sufficient (>99%) to detect such difference in mortality between groups. We expected this difference to be much lower after adjustment for age and other determinants of mortality. However, even if the ratio between both groups was as low as 1.27, we would still have greater than 80% power. Smaller differences in the risk of death may suggest screening is helpful at identifying people with similar risk of death as those already diagnosed routinely.

Results

In total, 902 participants consented for linkage of their data to NHS Digital. Data for 892 participants were available for the analysis, of whom 257 (28.8%) had an existing diagnosis of CKD, 185 had screening detected CKD (20.7%), and 450 (50.4%) had transiently reduced kidney function.

The characteristics of the study participants by CKD subgroup is shown in Table 1. There was a higher proportion of females in the existing CKD group (53.3%), whilst in the screening detected CKD group there was a higher proportion of males (54.1%). The median eGFR was lower in those with an existing diagnosis of CKD, compared with those identified on screening (55.04 mL/min/1.73m^2 vs. 65.00 mL/min/1.73m^2). Most patients did not have albuminuria, and median urine ACR was similar across CKD groups (Existing CKD; 2.45 mg/mmol, Screening detected CKD; 2.80 mg/mmol). People with an existing CKD diagnosis had a higher burden of hypertension, diabetes, and ischaemic heart disease, compared to those with screening detected CKD.

All-cause mortality

In the overall cohort, after a median 4.59 (IQR 3.69 to 5.34) years of follow-up, 49 (5.43%) study participants died (Table 2). The probability of survival beyond 5 years was 0.94 (95% CI 0.92-0.96). The leading cause of death was cancer, accounting for 45.0% of all deaths (n = 22), followed by cardiovascular disease which contributed to 27.0% of the deaths (n = 13).

There was no difference in all-cause mortality between CKD subgroups before or after adjustment for confounders (Table 2). Figure 1 illustrates the Kaplan-Meier survival probability over time stratified by CKD group.

Supplementary Table 1 shows estimates of the factors associated with all-cause mortality in people with CKD, including those with an existing diagnosis of CKD and screening detected CKD. Men with CKD had more than twice the risk of dying from any cause as women with CKD (HR 2.50, 95% CI 1.36-4.60). The association of sex with all-cause mortality remained statistically significant even after adjusting for age (HR 2.31, 95% CI 1.26-4.24). Age was also associated with all-cause mortality in people with CKD. Per each additional year of age, the risk of death increased by 11% (HR 1.11, 95% CI 1.06-1.15). The association of age with all-cause mortality was not attenuated following adjustment for sex (HR 1.10, 95% CI 1.06-1.15). Supplementary Figures 2 and 3 illustrate the Kaplan-Meier survival probability over time stratified by sex and age.

A person with CKD and a medical history of heart failure had a large increase in the risk of all-cause mortality (HR 8.19, 95% CI 3.94-16.99) compared to those with CKD but without heart failure. After adjustment for age and sex, the association persisted but was attenuated (HR 5.18, 95% CI 2.45-10.97).

Cardiovascular disease and end-stage kidney disease

Prior to enrolment in the study, 57 (6.4%) participants had already had a CVD event and were therefore excluded from the incident analysis. After a median follow-up of 3.06 years (IQR 1.63-3.88), 135 (15.1%) of the study participants had an incident CVD event.

There was no difference in CVD incidence between CKD subgroups before or after adjustment for confounders (Supplementary Table 2). No participants had an ESKD event during the study period. No further analysis was therefore conducted for this outcome.

Hospitalisation

After a median follow-up of 1.62 (IQR: 0.57-3.14) years, 493 (55.3%) of the study participants had a hospitalisation event. There was no difference in hospitalisation incidence between CKD subgroups before or after adjustment for confounders (Supplementary Table 3).

Composite outcome

After a median follow-up of 1.62 (IQR 0.57-3.14) years, 495 (55.3%) of the study participants had a composite outcome event. There was no difference in the incidence of the composite outcome between CKD subgroups before or after adjustment for confounders (fully adjusted HR 0.94, 95% CI 0.67-1.33). The results from the crude, adjusted and fully adjusted models are shown in Table 3.

Discussion

Summary of key findings

In this unique prospective cohort of older adults in English primary care, we found no difference in short-term mortality, hospitalisation due to any cause, or CVD incidence between people with an established diagnosis of CKD and those identified through screening.

Older age (per 1 year fully adjusted HR 1.10, 95% CI 1.06-1.15), male sex (fully adjusted HR 2.31, 95% CI 1.26-4.24), and heart failure (fully adjusted HR 5.18, 95% CI 2.45-10.97) were associated with increased risks of death in people with CKD.

Comparison with existing literature

Previous screening programmes have identified large numbers of people with undiagnosed CKD[18], but population-based screening has not been shown to be cost-effective.[12,13] Targeted screening of high-risk groups, including those with diabetes and hypertension is recommended in many healthcare settings.[4,14] Several systematic reviews have evaluated the effectiveness of targeted CKD screening in the community.[13,19] These reviews identified significant variation in the assessment of CKD, with many screening programmes not following KDIGO guidance on diagnosing CKD, relying on either a single abnormal result or eGFR alone. This has limited the value of these programmes in drawing conclusions on the effectiveness of screening. Moreover, new interventions such as SGLT2 inhibitors have recently been recommended for use in people with CKD, warranting a re-evaluation of the potential benefits and cost-effectiveness of CKD screening.[20]

Older adults are not routinely screened for CKD and its potential value has not previously been extensively explored. A cost-utility analysis of a Canadian CKD screening programme, using assessment of eGFR, found that it was not cost-effective overall or in older adults.[12] They explored the impact of screening on the risk of ESKD and mortality. The analysis was based on the premise that screening would be expected to identify patients with no previous diagnosis who could then receive a RAS inhibitor. In subgroups of people aged <65 and ≥65 years old, the cost per quality adjusted life year (QALY) gained associated with screening was $C200100 Canadian dollars (approximately £116675) and $C93700 (approximately £54635), respectively. Conversely, in subgroups of people with and without diabetes, the cost per QALY gained was $22600 (approximately £13177) and $572000 (approximately £333525), respectively.[12] However, this study used eGFR to diagnose CKD and potentially failed to identify individuals with proteinuria, who are at higher risk of adverse outcomes and more likely to benefit from intervention. The study was also published prior to the availability of SGLT2 inhibitors, and their potential impact was subsequently not considered in the analysis.

Strengths and limitations

To our knowledge, this is the first study to compare short-term health outcomes in older primary care populations who were screened for CKD. A significant strength of this study is that CKD was diagnosed using Kidney Disease Improving Global Outcomes (KDIGO) guidance.[21] Our CKD screening process included an assessment of both eGFR and proteinuria, which was repeated after 3 months. Outcomes were assessed through data linkage with NHS Digital, enabling us to access data on deaths and hospitalisations, which are highly regarded in terms of their quality.

Although the magnitude of the observed difference in mortality between the CKD groups was as anticipated, the observed mortality rate in the cohort was lower than expected. This may have impacted our ability to detect a difference in mortality between those with existing CKD diagnosis and

those with screening detected CKD. Moreover, due to a relatively short follow-up period and a cohort of patients with early stages of CKD, we did not identify any cases of ESKD.

Selection bias is a limitation of our study. The study population was comprised largely of people of White ethnicity, which has implications for the generalisability of our findings to the broader population of older adults both in the UK and other countries. Ethnicity is an established risk factor for mortality in people with CKD.[22] Nearly all the participants in our study were of White ethnicity, and this prevented us from investigating associations of ethnicity with death and other outcomes. This may have also led to a lower overall mortality rate in the cohort.

Individuals were recruited into the present study based on the CKD groups they were originally assigned in the OxRen study; existing CKD, screening detected CKD and screening detected transiently impaired kidney function. Kidney function may have changed over time and those with transiently impaired kidney function may have progressed to chronic kidney disease. This may have resulted in misclassification bias, impacting on our ability to detect differences between the groups.

Confounding is a potential limitation of our analysis exploring factors associated with mortality in people with CKD. We adjusted for age and sex in the models, but it is possible that other variables, including cardiovascular co-morbidities, prescribed medications, eGFR and urine ACR confounded the associations we observed.

Implications for research and clinical practice

Our study suggests that screening older people in primary care for CKD may be of value, as the risk of mortality and other adverse health outcomes are comparable to those with an established diagnosis of CKD. Individuals with transiently impaired kidney function also had comparable outcomes, likely

reflecting a group at higher risk of adverse outcomes than those with normal kidney function. Understanding what happens to the kidney function of those with transiently impaired kidney function over time would be valuable and the lack of follow-up data on the kidney function in this group is a limitation of the present study.

Older patients with CKD have several long-term conditions and this requires holistic care from the general practitioner. There was no difference in cardiovascular events between subgroups and the main cause of death overall was cancer. The frequency of co-morbidities in this age group may be the reason that there is no difference seen in outcomes. The group with heart failure were at particularly high risk and may be a group most likely to benefit from screening for CKD to optimise management.

The screening detected CKD population we identified had relatively preserved eGFR and few had albuminuria. This could limit the potential of this group to benefit from interventions, such as RAS inhibitors and SGLT2 inhibitors, given that their risk of CVD and progressive CKD will be comparatively lower than other groups with high CKD prevalence such as those with diabetes.

Our study population was small and not representative of the broader population of older adults in the UK. The characteristics of a larger and more diverse screening detected older CKD population needs to be established, including the prevalence of proteinuric kidney disease and proportions of those with more advanced kidney disease. This would help to determine cardiovascular risk and likelihood to benefit from interventions such as RAS inhibitors and SGLT2 inhibitors in higher risk patients. Future studies therefore need larger, older, and more diverse study populations with longer follow-up, to determine whether CKD screening is cost-effective and improves clinical outcomes and quality of life for older adults.

Conclusions

Our findings show that the risk of short-term mortality, hospitalisation, and CVD is comparable in older people with CKD diagnosed through screening to those diagnosed routinely in primary care. This suggests that screening older people for CKD may be of value, to increase detection and enable disease-modifying treatment to be initiated at an earlier stage. Larger studies with longer follow-up in more diverse and representative populations of older adults are needed to corroborate these findings and determine whether CKD screening is effective in this group.

Declarations

Ethics approval and consent to participate

Ethical approval for the study was granted by the Yorkshire & The Humber Bradford Leeds Research Ethics Committee (REC reference: 17/YH/0429). Informed written consent was provided by all participants included in the study.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

JMOM, WM, JH declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work. AF has received financial support to facilitate her attendance at the European Renal Association conference in Stockholm from Astra-Zeneca. CJT has received consulting fees from Astra-Zeneca, Roche and Bayer outside the submitted work. NJ has received a grant from the Wellcome Trust to support his Doctoral Research Fellowship which is unrelated to the work in this manuscript. He has received consulting fees from OXON Epidemiology and received payment whilst working as a presenter for NB Medical, a national GP education organisation. He is an unpaid trustee of the charities Cardiac Risk in the Young and Scoliosis Support and Research. FDRH has received consulting fees from BI, AZ, and Pfizer unrelated to this work. CJT, NJ and FDHR have no other relationships or activities that could appear to have influenced the submitted work.

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406 **Authors' contributions**

407

408 The OxRen and NewKI studies were conceived and designed by FDRH who also obtained the funding.
409 JH and JMOM designed this study and JMOM and AF analysed the data. AF, JMOM, and JH initially
410 drafted the manuscript under the supervision of FDRH. CJT was a member of the OxRen and NewKI
411 study teams. CJT and NJ edited the revised manuscript. All authors read the final version of the
412 manuscript and agreed to be listed as co-authors.

413

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415

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419

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422

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425 data entry and cleaning, patient recruitment (led by Research Nurses Heather Rutter, Pippa
426 Whitbread).

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Patient and public involvement

Two patient representatives sit on the Study Steering Committee, which meets on a six-monthly basis to assess the progress of participant recruitment and follow up, review, and contribute to study materials and oversee the ethical and safe conduct of the research.

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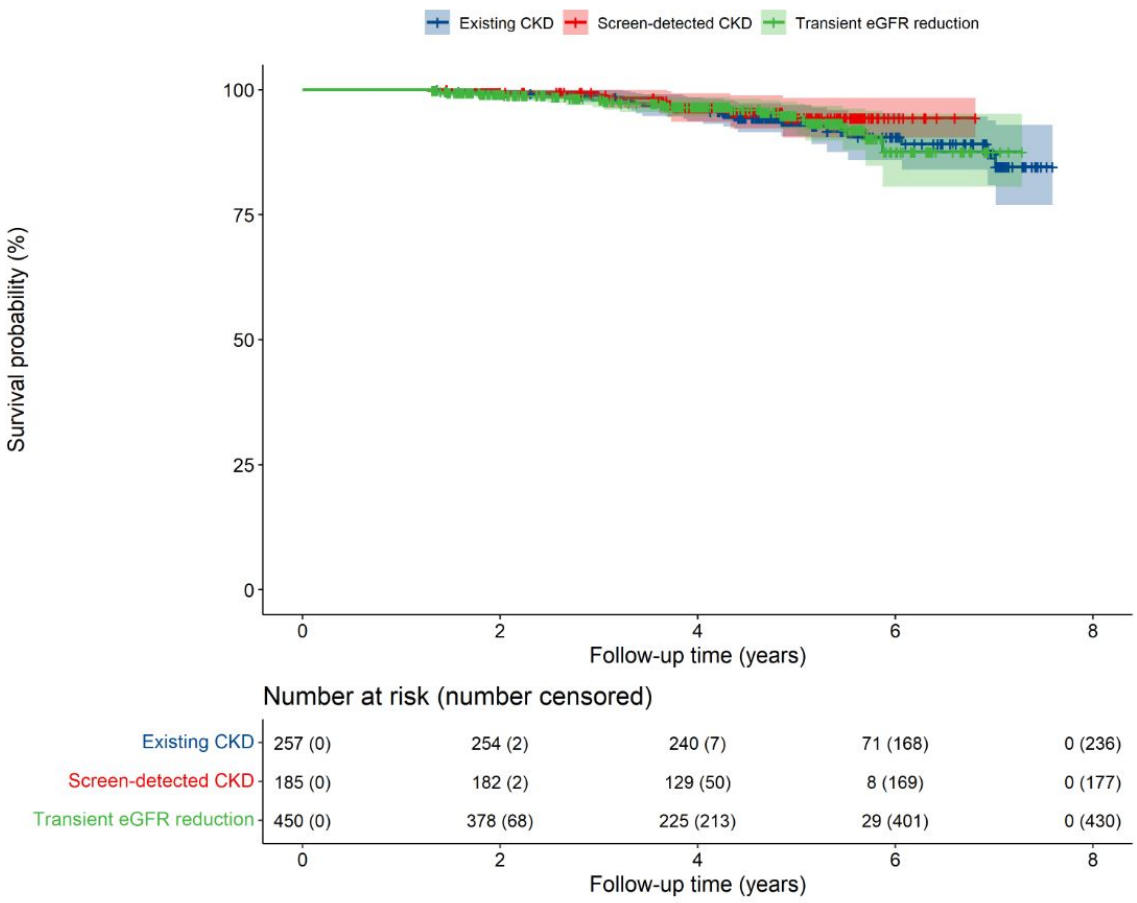

Figure 1: Kaplan-Meier survival probability over time stratified by CKD group.

Table 1: Baseline characteristics of people with CKD stratified by CKD category.

Variable	Existing CKD N = 257		Screening detected CKD N = 185		Transiently impaired kidney function N = 250	
Gender, n (%)						
Men	120	(46.69)	100	(54.05)	205	(45.56)
Women	137	(53.31)	85	(45.95)	245	(54.44)
Age (years), Median (IQR)	75.03	(70.46 - 79.02)	73.74	(69.38 - 77.82)	72.89	(69.09 - 78.31)
Smoking Status, n (%)						
Never	133	(51.75)	97	(52.43)	256	(56.89)
Former	116	(45.14)	77	(41.62)	180	(40.00)
Current	8	(3.11)	11	(5.95)	14	(3.11)
Ethnicity, n (%)						
White	253	(98.44)	181	(97.84)	444	(98.67)
Non-white	4	(1.56)	4	(2.16)	6	(1.33)
Education, n (%)						
Primary only	87	(33.85)	71	(38.38)	153	(34.00)
Secondary	97	(37.74)	68	(36.76)	170	(37.78)
Higher education	73	(28.40)	46	(24.86)	127	(28.22)
Medical history of						
Hypertension, n (%)	166	(64.59)	107	(57.84)	224	(49.78)
Diabetes, n (%)	56	(21.79)	22	(11.89)	54	(12.00)
Ischaemic Heart Disease, n (%)	57	(22.18)	27	(14.59)	69	(15.33)
Heart Failure, n (%)	10	(3.89)	9	(4.86)	15	(3.33)
Atrial Fibrillation, n (%)	41	(15.95)	15	(8.11)	47	(10.44)
Other Cardiovascular Disease, n (%)	22	(8.56)	9	(4.86)	27	(6.00)
Peripheral Vascular Disease, n (%)	9	(3.50)	8	(4.32)	20	(4.44)
Renal Disease, n (%)	216	(84.05)	43	(23.24)	64	(14.22)
UTI, n (%)	108	(42.02)	75	(40.54)	205	(45.56)
Thyroid Disease, n (%)	32	(12.45)	21	(11.35)	54	(12.00)
Anaemia, n (%)	30	(11.67)	16	(8.65)	46	(10.22)
Osteopenia, n (%)	20	(7.78)	13	(7.03)	24	(5.33)
Osteoporosis, n (%)	18	(7.00)	13	(7.03)	34	(7.56)
Alcohol intake (g), median (IQR)	2	(1 - 7)	4	(1 - 10)	3	(0 - 10)
BMI (kg/m²), median (IQR)	26.9	(24.69 - 30.45)	27.22	(24.32 - 30.86)	26.85	(23.75 - 30.64)
WHR, median (IQR)	0.92	(0.84 - 0.97)	0.91	(0.85 - 0.98)	0.9	(0.84 - 0.97)
Systolic blood pressure (mmHg), median (IQR)	131	(120 - 144)	136	(124 - 149)	135	(123 - 146)
Diastolic blood pressure (mmHg), median (IQR)	78	(70 - 85)	80	(72 - 86)	80	(72 - 87)
eGFR (mL/min/1.73m2), median (IQR)	55.04	(45.91 - 63.95)	65	(57 - 77.75)	67	(59 - 80)
Urine ACR (mg/mmol), median (IQR)	2.45	(0.8 - 2.5)	2.8	(1.95 - 7.5)	2.45	(1.1 - 2.5)

Table 2: Hazard Ratios (HR) and 95% Confidence Intervals (CI) for the association of CKD categories with all-cause mortality among participants in the NewKI study

Category	Median follow-up (years)	PYs	N	n	MR	Crude model		Age & Sex adjusted		Multivariable model *	
Existing CKD	4.93	1350	257	21	15.56	1.00	(Reference)	1.00	(Reference)	1.00	(Reference)
Screening detected CKD	4.57	838	185	8	9.548	0.74	(0.32 to 1.69)	0.81	(0.35 to 1.87)	0.41	(0.11 to 1.56)
Transiently impaired kidney function	4.00	1756	450	20	11.39	0.95	(0.510 to 1.78)	1.16	(0.61 to 2.19)	0.96	(0.35 to 2.65)

Abbreviations: PYs: sum of follow-up time at risk in years for all participants in the category; **N:** number of participants in the category; **n:** number of deaths in the category; **MR:** mortality rate (i.e. the quotient of number of deaths by the sum of follow-up time at risk).

* Multivariable model was adjusted for age, sex, smoking status and medical history of diabetes, hypertension, ischaemic heart disease, heart failure, other cardiovascular disease, eGFR and urine ACR.

Table 3: Hazard Ratios (HR) and 95% Confidence Intervals (CI) for the association of CKD categories with the composite outcome among participants in the NewKI study.

Category	Median follow-up (years)	PYs	N	n	IR	Crude model		Age & Sex adjusted		Multivariable model *	
Existing CKD	4.93	1350	257	81	60	1.00	(Reference)	1.00	(Reference)	1.00	(Reference)
Screening detected CKD	4.57	838	185	65	77.58	1.11	(0.88 to 1.4)	1.16	(0.92 to 1.47)	0.94	(0.67 to 1.33)
Transiently impaired kidney function	4.00	1756	450	251	142.9	0.83	(0.68 to 1.02)	0.89	(0.72 to 1.09)	0.77	(0.55 to 1.07)

Abbreviations: PYs: sum of follow-up time at risk in years for all participants in the category; **N:** number of participants in the category; **n:** number of composite outcome cases in the category; **IR:** incidence rate, per 1,000 person-years (i.e. the quotient of number of composite outcome cases by the sum of follow-up time at risk).

* Multivariable model was adjusted for age, sex, smoking status and medical history of diabetes, hypertension, ischaemic heart disease, heart failure, other cardiovascular disease, eGFR and urine ACR.