Supplemental Materials

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Supplemental Methods

Measurements of kidney function and damage

Estimated glomerular filtration rate (eGFR) was calculated with creatinine (eGFRcr) using the 2021 Chronic Kidney Disease Epidemiology (CKD-EPI) Collaboration equation[1] and with cystatin C (eGFRcys) using the 2012 CKD-EPI equation[S2]. Urine albumin-to-creatinine ratio (ACR), urine protein-to-creatinine ratio (PCR), and urine dipstick protein were extracted. To harmonize measures, we converted PCR and urine dipstick to ACR values using an established conversion equation.[S3]

Covariates

Age and sex were determined via linkage to the unique 10-digit personal identification number. Specific medications were extracted from the Dispensed Drug Registry, including renin-angiotensin-aldosterone system (RAAS) inhibitors, diuretics, hypertension medications, and statins. Comorbidities including hypertension, diabetes, history of coronary heart disease, stroke, heart failure, peripheral artery disease, atrial fibrillation, liver disease, cancer, and chronic obstructive pulmonary disease, were ascertained using clinical diagnosis and procedure codes extracted from the Regional Healthcare Utilization Database and high potassium (>5 mmol/L) and anemia (hemoglobin<12 g/dL for female and <13 g/dL for male) were ascertained from the closest laboratory values prior to the plasma creatinine or cystatin C measurement (**Table S6**).

Outcomes

We calculated eGFR decline as the percent change from the baseline eGFR based on plasma creatinine or cystatin C to the latest subsequent follow-up measurement within the next 5 years. Percent change was assessed both continuously and as a binary outcome defined as more than 30% decline.

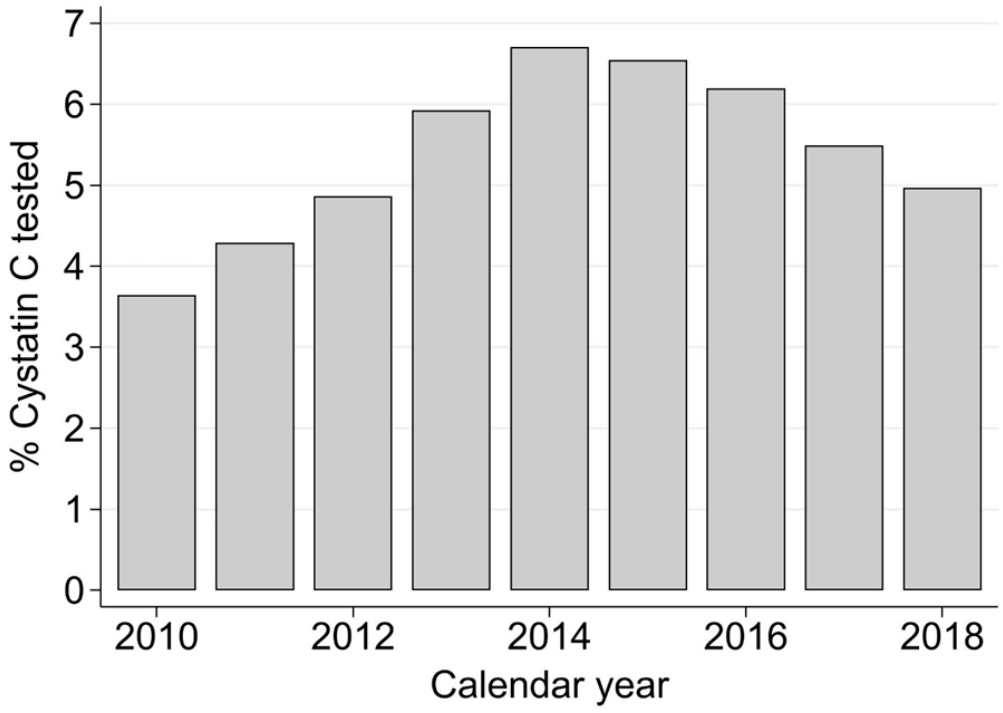
Analyses

First, we described the number of participants with cystatin C testing by year and then, using 2014 as a cross-sectional sample, compared people who received creatinine and cystatin C testing with those who received creatinine testing alone. Proportions for categorical variables and mean values of continuous variables were used to describe the characteristics by cystatin C testing status. Second, we used logistic regression to examine associations of all covariates with cystatin C testing status in a multivariate model. A missing indicator was used to handle missing data for ACR. To test whether there were different characteristics associated with cystatin C testing among people missing additional assessment of kidney function, we performed analyses stratified by albuminuria testing status.

Third, we evaluated the frequency of re-testing of cystatin C within 5 years and evaluated characteristics associated with retesting using multivariate logistic regression. In order to ensure adequate follow-up, we evaluated re-testing among those with a first cystatin C test prior to 2014.

Finally, within those individuals who had cystatin C testing prior to 2014 and re-testing 1 to 5 years later, we compared the percent change in eGFRcr with the percent change in eGFRcys, estimating the sensitivity and specificity of 30% decline in eGFRcr for detecting a 30% decline in eGFRcys.

Figure S1. Proportion with cystatin C testing by calendar year among individuals with measured creatinine.

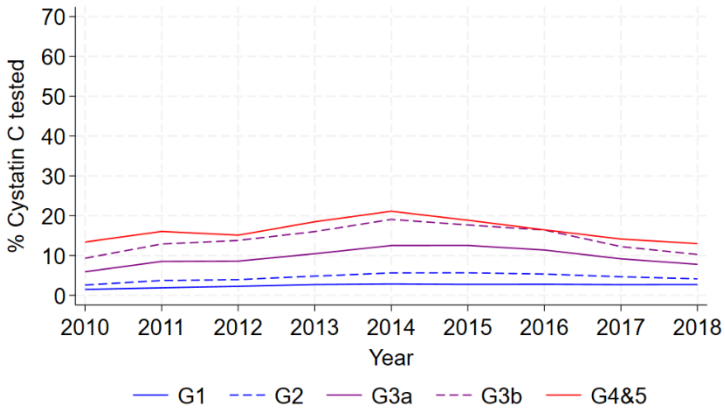


year	N*	Creatinine only	Creatinine and cystatin C	% cystatin C tested
2010	529,996	510,679	19,317	3.64
2011	562,036	537,929	24,107	4.29
2012	518,709	493,470	25,239	4.87
2013	534,151	502,500	31,651	5.93
2014	552,909	515,809	37,100	6.71
2015	560,570	523,862	36,708	6.55
2016	568,561	533,323	35,238	6.20
2017	579,278	547,475	31,803	5.49
2018	536,958	510,267	26,691	4.97
Overall	1,369,183	1,216,514	152,669	11.15

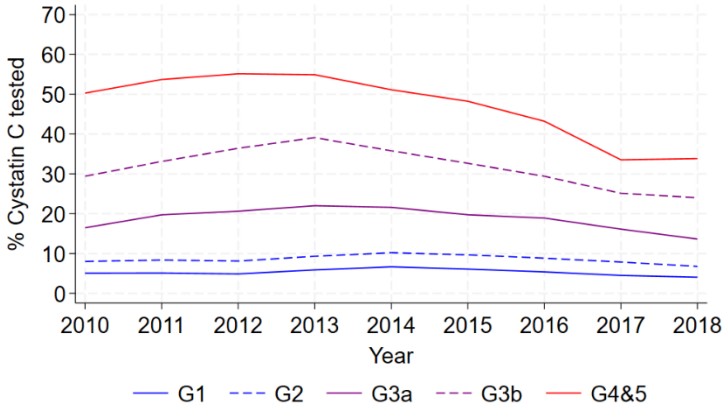
*Total number of individuals with any creatinine measured within the year.

Figure S2. Trends in proportion of the population with cystatin C testing by year, stratified by G- and A-stage.

A. ACR missing



B. Stage A1 (ACR <30 mg/g)



C. Stages A2/A3 (ACR ≥30 mg/g)

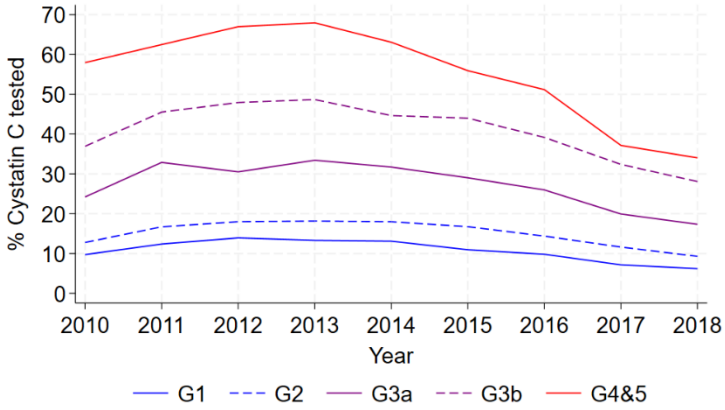
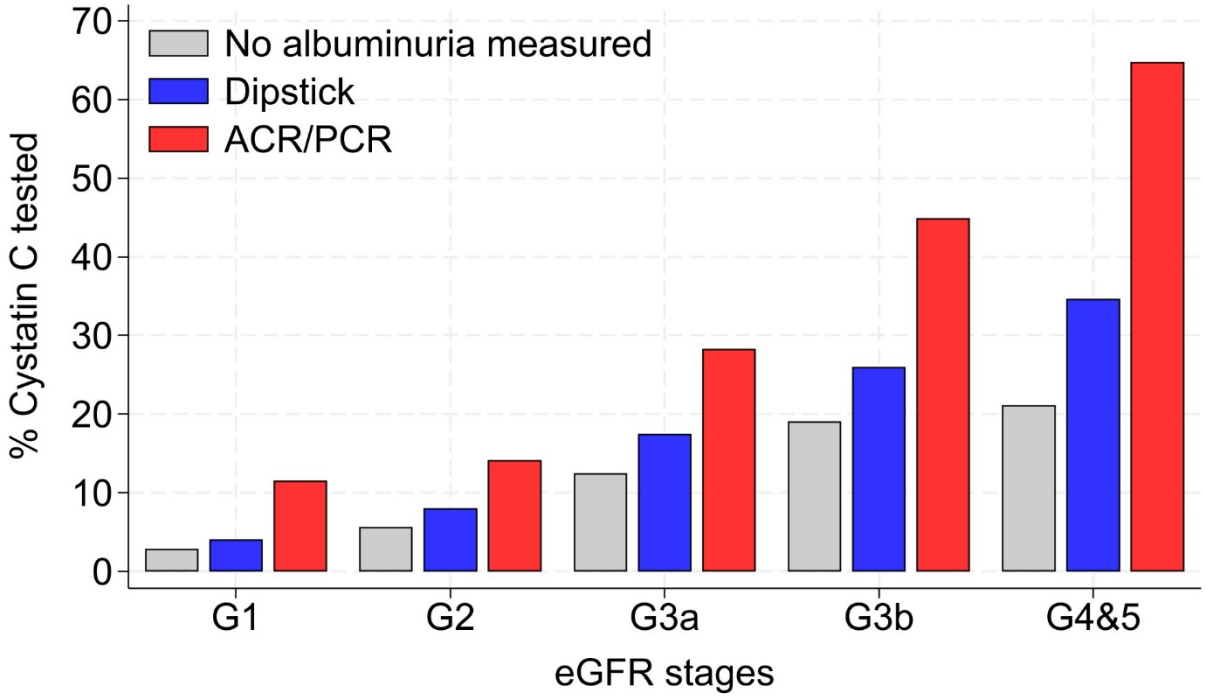


Figure S3. Percent with cystatin C testing in 2014, stratified by eGFRcr stages and albuminuria testing status.



Supplementary References

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S3. Fu EL, Levey AS, Coresh J, et al. Accuracy of GFR Estimating Equations in Patients with Discordances between Creatinine and Cystatin C-Based Estimations. *J Am Soc Nephrol*. Mar 30 2023;doi:10.1681/ASN.0000000000000128

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S6. Carrero JJ, Fu EL, Sang Y, et al. Discordances Between Creatinine- and Cystatin C-Based Estimated GFR and Adverse Clinical Outcomes in Routine Clinical Practice. *Am J Kidney Dis*. Nov 2023;82(5):534-542. doi:10.1053/j.ajkd.2023.04.002