

Cognitive Impairment

A Novel Risk Factor for Rapid Kidney Function Decline and Incident CKD in Middle-Aged Adults

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Key Points

- Early cognitive impairment and dementia raise the risk of developing CKD.
- Early cognitive impairment and dementia are linked to faster kidney function decline.

Abstract

Background Emerging evidence suggests that better cognition is associated with a lower risk of CKD. However, whether early-onset cognitive impairment (CI) at baseline is linked to rapid eGFR decline or incident CKD remains unclear.

Methods We conducted a prospective cohort study of 5761 World Trade Center responders (mean age, 53.8±7.9 years) without CKD at baseline, followed for a mean of 4.2±1.9 years. CI was defined as a Montreal Cognitive Assessment (MoCA) score ≤23, with a subgroup analysis for baseline dementia (MoCA ≤18). Primary outcomes included annual eGFR change and rapid eGFR decline (<−5 ml/min per 1.73 m² per year). The secondary outcome was incident CKD (eGFR <60 ml/min per 1.73 m² or diagnosis code). Multivariable Cox proportional hazards models and linear regressions were used for binary and continuous outcomes, respectively. Sensitivity analyses included looking at the effect of baseline mild CI (MoCA score 19–23), propensity matching for demographics, baseline age younger than 60 years, removal of baseline post-traumatic stress disorder/depression or baseline head trauma/stroke/cardiovascular disease, and after exclusion of those who died during follow-up.

Results At baseline, 1446 (25%) individuals had CI, while 89 (2%) had dementia. The mean baseline eGFR was 91.1 ml/min per 1.73 m², with an overall decline of −1.2 ml/min per 1.73 m² per year. Rapid eGFR decline occurred in 550 (10%) individuals. After adjusting for age, sex, race and ethnicity, comorbidities, World Trade Center exposure, screened post-traumatic stress disorder, and baseline eGFR, CI and dementia were significantly associated with rapid eGFR decline (adjusted hazard ratio [aHR], 1.63 and 2.42, respectively; both $P < 0.001$) and faster annual eGFR decline. Findings were consistent across all sensitivity analyses. In addition, 248 (4%) individuals developed incident CKD. Both baseline CI (aHR, 1.72; $P < 0.001$) and dementia (aHR, 2.77; $P = 0.010$) were significantly associated with incident CKD.

Conclusions Among middle-aged individuals without CKD, early-onset CI was independently associated with rapid eGFR decline and incident CKD. These findings warrant validation in other cohorts.

Kidney360 6: 2130–2144, 2025. doi: <https://doi.org/10.34067/KID.0000000880>

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Received: March 20, 2025 **Accepted:** June 20, 2025

Published Online Ahead of Print: June 25, 2025

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Introduction

A mild decline in eGFR of approximately 0.75 ml/min per 1.73 m² per year is expected with normal kidney aging.¹ However, a greater-than-expected decline is a key indicator of CKD development and progression.² Well-established risk factors for rapid eGFR decline include age, sex, race, socioeconomic status, genetic predisposition, albuminuria, and comorbidities such as diabetes mellitus and hypertension (HTN).^{3,4} Less is known about risk factors for rapid eGFR decline in middle-aged individuals with normal kidney function.³

Patients with advanced CKD and ESKD have a higher incidence of cognitive impairment (CI),^{5–10} which are linked to poorer health care outcomes.¹¹ Furthermore, rapid eGFR decline has been associated with cognitive decline.^{7,10,12,13} Cognitive dysfunction has been observed even in early eGFR decline, possibly due to vascular brain injury or related neuroinflammation.⁹ Most studies have explored CKD as a predictor and CI as an outcome, often relying on cross-sectional designs. Yet although mechanisms that are linked to CKD are also related to early neurodegenerative processes, few studies have considered the reverse hypothesis. One study that reported that, in patients with CKD, the presence of CI was associated with more rapid eGFR decline.⁷ In addition, previous studies examining cognition and kidney disease have focused on older adults (65 years or older) at a time when neurodegeneration has already commenced for most people.^{10,12–15} A recent longitudinal study reported increased risk of CI in middle-aged individuals with CKD.¹⁶ Thus, although robust epidemiologic evidence links CKD to future cognitive decline, the potential role of neuro CIs to predict eGFR decline in middle-aged individuals without CKD remains unclear.

CI has been linked to an increased risk of cardiovascular disease (CVD),^{17,18} while higher cognitive function is associated with a lower risk of HTN.¹⁹ Both CVD and HTN are well-established risk factors for CKD. A recent Mendelian randomization (MR) study suggested a causal association between better cognitive function and a lower risk of CKD.²⁰ Despite the strong epidemiologic link between CKD and CI, whether baseline cognitive function predicts kidney function decline remains unclear. We hypothesized that baseline CI is associated with an increased risk of rapid eGFR decline and incident CKD in middle-aged individuals without preexisting kidney disease. To test this hypothesis, we analyzed data from the World Trade Center (WTC) responder cohort.²¹

Methods

Setting

The WTC responder cohort presents a unique opportunity to study this association in a relatively young population, where CKD is uncommon, yet early-onset CI is prevalent.²² This setting allows us to examine the temporal relationship between CI and kidney function decline with minimized confounding. The WTC responder cohort undergoes protocolized annual assessments of eGFR and cognition, providing a unique opportunity to examine whether CI predicts future GFR decline and/or CKD.

Data Source and Study Population

Data were obtained from the WTC Health and Wellness Study, a prospective health monitoring program that follows first responders present at the WTC after the September 11, 2001, terrorist attacks, as previously described.²¹ Participant screening and enrollment began 1 month after the response effort concluded, following the final extinguishment of fires. Annual assessments include medical history, physical examinations, and mental health evaluations. Serum creatinine (SCr) measurements became available in January 2015 due to electronic medical record constraints, defining the starting point of this study. WTC responders undergo scheduled annual visits, during which data were collected for this study. This study was approved by the Stony Brook University Institutional Review Board (604,113; WTC Health and Wellness Study).

Inclusion and Exclusion Criteria

SCr measurements were obtained during routine annual outpatient visits per protocol, regardless of clinical status. SCr measurements during hospitalizations were excluded to ensure eGFR assessments reflected steady-state kidney function. Individuals were included if they had at least two outpatient SCr measurements between January 1, 2015, and December 31, 2022 (Figure 1 and Supplemental Figure 1). Participants were excluded if they had a history of ESKD (defined as prior renal transplantation or dialysis before study initiation or during follow-up) or CKD at baseline (eGFR <60 ml/min per 1.73 m² or preexisting International Classification of Diseases (ICDs) 9 or 10 CKD codes at the time of the first eGFR measurement). eGFR was calculated using the 2021 race-free CKD-Epidemiology Collaboration equation.²³ Participants were followed for a mean duration of 4.2±1.9 years.

Exposure Measures

Global cognitive status was assessed using the Montreal Cognitive Assessment (MoCA), a 30-point screening tool evaluating short-term memory, visuospatial abilities, executive function, attention, concentration, working memory, language, and orientation.²⁴ The MoCA has shown high accuracy in diagnosing mild CI (MCI) and was selected based on its proven sensitivity and reliability. To reduce test-retest bias, alternative versions were used at each testing occasion. A conservative cutoff of MoCA ≤23 was used to detect CI, while severe CI, defined as dementia, was classified as MoCA ≤18.^{25,26} MoCA scores were recorded at the start of the observation period (T₀), corresponding to the time of the initial eGFR measurement (Supplemental Figure 1). MoCA change per year was calculated as the total difference between last and first MoCA measurement divided by total-years of follow-up. MoCA change per year <0 was classified as “worsening MoCA scores,” while ≥0 was classified as “improving MoCA scores.”

Outcome Measures

The primary outcome measures were.

1. *Mean annual eGFR change*, calculated as the difference between the first (baseline) and last eGFR measurement, divided by the follow-up duration (years).

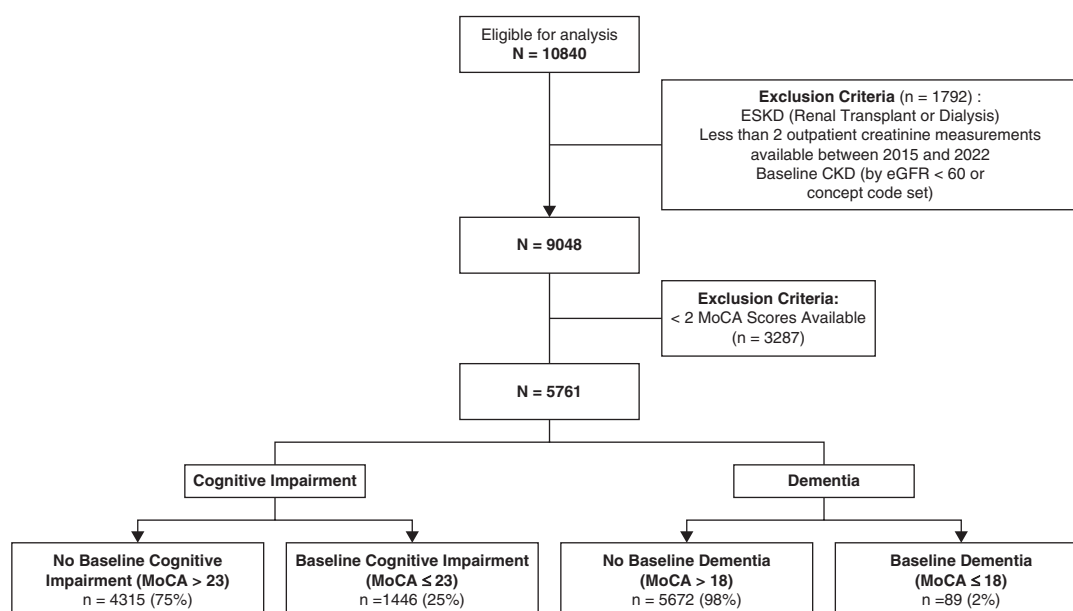


Figure 1. Flow chart of cohort. MoCA, Montreal Cognitive Assessment.

2. *Rapid eGFR decline*, defined as a mean annual eGFR change ≤ -5 ml/min per 1.73 m^2 per year.^{27–29}

The secondary outcome measure was incident CKD defined as an eGFR < 60 ml/min per 1.73 m^2 or the presence of a CKD diagnosis code at the last visit during the observation period.

Combining diagnosis codes with eGFR measurements has been shown to improve CKD classification accuracy³⁰ (see sensitivity analyses for further validation). Incident CKD was considered a secondary kidney outcome due to its lower incidence in this cohort ($n=248$, 4%).

Covariates

Baseline demographics and health history were assessed at the time of the first eGFR measurement (T_0 ; Supplemental Figure 1).

Race and Ethnicity

Participants were classified as: White (White/non-Hispanic or Caucasian) or Non-White Asian [non-Hispanic], Black [Hispanic and non-Hispanic], Hispanic [not Black]/Mexican, or other [non-Hispanic].

WTC Exposure

Exposure assessments were conducted during WTC responders' intake visits using exhaustive self-reported questionnaires and validated in interviews conducted at responders' second visits. Exposure activities and experiences included location/duration of work, responder activities during cleanup, and types of exposures observed during response activities. The severity of exposure during WTC response efforts was categorized into five levels, as previously described²²: *No/Low* Exposure—no exposure or low exposure with protective personal equipment; *Mild* Exposure—moderate duration of low-level exposure; *Moderate* Exposure—prolonged low-level exposure; *High*

Exposure—moderate duration of high-risk activity; *Severe* Exposure—prolonged high-risk activity; and *Unknown*—insufficient exposure data.

Psychiatric Variables

Mental health symptom severity was also assessed at T_0 using validated inventories of behavioral symptoms. Depression was measured using the Patient Health Questionnaire-9 at annual WTC health visits. Individuals with Patient Health Questionnaire-9 scores ≥ 10 were classified as having “screened depression”.³¹ Post-traumatic stress disorder (PTSD) was measured using the 17-item PTSD checklist. Individuals with PTSD checklist scores ≥ 44 were classified as having “screened PTSD.”³²

Other Covariates

Other covariates were defined as follows.

- *Educational Attainment*. “BA/BS+” (≥ 4 -year college degree) or “<BA/BS” (< 4 -year college degree).
- *Diabetes Mellitus*. ICD-9/10 codes, self-reported diagnosis (questionnaires), or fasting glucose > 130 mg/dl.
- *HTN*. ICD-9/10 codes, self-reported diagnosis, or recorded BP of systolic > 160 mm Hg or diastolic > 100 mm Hg.
- *CVD*. Composite of stroke, angina, myocardial infarction, coronary artery disease, heart failure, or abnormal heart rhythm, determined via ICD-9/10 codes and self-reported diagnosis.
- *Obesity*. ICD-9/10 codes or a recorded body mass index (BMI) $> 30 \text{ kg/m}^2$.

Statistical Analysis

Continuous variables were compared using the Student t test or Kruskal-Wallis test as appropriate. Categorical variables were compared using chi-squared tests or Fisher exact test when applicable. Cox Proportional Hazards Models³³ were used to estimate hazard ratios for rapid

eGFR decline and incident CKD outcomes. These models were constructed in a series of successive steps, with CI or dementia as the exposure variables (depending on the analysis) and binary kidney outcomes as the dependent variables.

The analysis began with an unadjusted model, followed by sequential adjustments for:

1. Demographics (age, sex, race and ethnicity).
2. Baseline comorbidities (diabetes, HTN, CVD, BMI).
3. WTC exposure.
4. Screened baseline PTSD status (which was closely correlated with CI and dementia in previous WTC studies³⁴).
5. Baseline eGFR.

The reference group for rapid eGFR decline was the “stable” eGFR group, defined as a mean rate of eGFR change > -1 ml/min per 1.73 m^2 per year. Linear regression models were used to estimate β -coefficients for the association between CI or dementia (depending on the analysis) and eGFR change per year, in a similar series of successive models. Individuals with missing data were removed from regressions, allowing for a complete case analysis. Interactions between study variables were not assessed. Regression analyses were conducted in the same manner for main and sensitivity analyses.

Time-to-event data were used to generate unadjusted cumulative incidence curves for rapid eGFR decline during follow-up. The cumulative incidence function was estimated using the Kaplan-Meier estimate of the survival function,³⁵ as no competing risks were evaluated in this study.

The Holm-Bonferroni correction was applied to regression analyses to account for adjustment for multiplicity testing, resulting in an adjusted P value.³⁶ A two-tailed P value of <0.05 was considered statistically significant. All statistical analyses were performed using SAS version 9.4³⁷ (Cary, NC). Data visualization was performed using the *ggsurvfit*³⁸ and *forestplot*³⁹ packages in R version 4.3.1.⁴⁰

Sensitivity Analyses

To examine the importance of balancing participants, propensity score matching (PSM)⁴¹ was employed using greedy nearest-neighbor matching to balance cohorts based on baseline age, sex, and race and ethnicity. To assess whether advanced baseline age acted as an effect modifier in the observed associations, sensitivity analyses were performed in which individuals 60 years or older were excluded from the overall cohort. An additional sensitivity analysis was conducted excluding all individuals who baseline screened PTSD or depression.

For those with baseline CI, the incident CKD outcome was further analyzed using only the eGFR-based definition and the combined outcomes of incident CKD+eGFR decline.

To determine whether an association was present between baseline MCI and proposed kidney outcomes, additional subgroup analyses were performed for individuals with baseline MoCA scores ≥ 19 , with baseline MCI defined as MoCA between 19 and 23.⁴² Another sensitivity analysis assessed the association of worsening MoCA trajectories with rapid decline and incident CKD.

Additional sensitivity analyses were performed after excluding individuals who died during the observation period and those with removing traditional risk factors for CI development (stroke, head trauma, neurodegenerative disease, and CVD).

Results

Participant Characteristics

In a cohort of 5761 WTC responders, 1446 (25%) had CI and 89 (2%) had dementia at baseline (Figure 1 and Supplemental Table 1). The mean age was 53.8 ± 7.9 years, 92% were male, and 84% were White/non-Hispanic. The mean baseline eGFR was 91.1 ml/min per 1.73 m^2 . Individuals without CI or dementia had slightly more eGFR measurements and a longer follow-up period. Overall, eGFR declined by -1.2 ± 4.0 ml/min per 1.73 m^2 per year during the mean follow-up period of 4.2 ± 1.9 years. Those with CI were older, less likely to be White, had lower education, and higher WTC exposure, as well as a greater prevalence of diabetes, depression, and PTSD. A similar pattern was seen in individuals with dementia.

The Association of Baseline CI and Dementia with Change in eGFR per Year

Individuals with CI (versus no CI) experienced a greater annual eGFR decline (-1.5 ± 4.8 versus -1.1 ± 3.7 ml/min per 1.73 m^2 per year, $P = 0.006$; Table 1). Those with dementia (versus no dementia) had a more pronounced decline (-3.0 ± 5.3 versus -1.2 ± 4.0 ml/min per 1.73 m^2 per year, $P = 0.002$; Supplemental Table 1).

After adjusting for demographics, comorbidities, WTC exposure, PTSD, and baseline eGFR, baseline CI (versus no CI; $\beta = -0.34$ [-0.58 to -0.11], P adjusted = 0.024) and baseline dementia (versus no dementia; $\beta = -1.51$ [-2.36 to -0.66], P adjusted = 0.004) were significantly associated with greater eGFR decline (Figure 2 and Supplemental Figure 2).

Sensitivity Analyses

1. *PSM for Demographics*: individuals with baseline CI (versus no CI) had greater eGFR decline (-1.9 ± 4.7 versus -1.1 ± 3.6 ml/min per 1.73 m^2 per year, $P = 0.009$; Table 2). Among PSM-matched individuals, dementia did not significantly affect eGFR decline (Supplemental Table 2).
2. *Baseline Age Younger than 60 Years*: individuals with CI and dementia had greater annual eGFR decline, compared with those without (Table 3 and Supplemental Table 3). In multivariable analyses, baseline CI (versus no CI) remained significantly associated with greater eGFR decline per year ($\beta = -0.32$; 95% confidence interval, -0.58 to -0.07 ; P adjusted = 0.039; Figure 2). The association of baseline dementia (versus no dementia) was of borderline statistical significance ($\beta = -0.94$; 95% confidence interval, -1.96 to 0.06 ; P adjusted = 0.064; Supplemental Figure 2).
3. *No PTSD or Depression at Baseline*: CI and dementia were associated with greater annual eGFR decline (Table 4 and Supplemental Table 4). In multivariable analyses, both baseline CI (versus no CI; $\beta = -0.30$; 95% confidence

Table 1. Characteristics and outcomes of individuals with and without cognitive impairment (overall cohort)

Variable	Overall 5761	No Baseline CI (MoCA >23) 4315 (75%)	Baseline CI (MoCA ≤23) 1446 (25%)	P Value
Age (yr)	53.8±7.9	53.1±7.7	55.8±8.2	<0.001
Sex				0.49
Male	5282 (92%)	3950 (92%)	1332 (92%)	
Female	479 (8%)	365 (8%)	114 (8%)	
Race and ethnicity				<0.001
Missing	195 (3%)	104 (2%)	91 (6%)	
Non-White ^a	708 (12%)	481 (11%)	227 (16%)	
White (non-Hispanic)	4858 (84%)	3730 (86%)	1128 (78%)	
Education				<0.001
<BA/BS	3549 (62%)	2621 (61%)	928 (64%)	
BA/BS or higher	1633 (28%)	1317 (31%)	316 (22%)	
Missing	579 (10%)	377 (9%)	202 (14%)	
Comorbidities				
CVD ^b	361 (6%)	247 (6%)	114 (8%)	0.003
Diabetes	594 (10%)	423 (10%)	171 (12%)	0.029
HTN	1834 (32%)	1360 (32%)	474 (33%)	0.37
Obesity	3080 (53%)	2315 (54%)	765 (53%)	0.62
BMI (kg/m ²)	31.2±5.4	31.2±5.4	31.1±5.3	0.52
Missing	37 (0.6%)	22 (0.5%)	15 (1%)	
WTC exposure				0.004
No exposure/low exposure	272 (5%)	219 (5%)	53 (4%)	
Mild exposure	2969 (52%)	2275 (53%)	694 (48%)	
Moderate exposure	1836 (32%)	1334 (31%)	502 (35%)	
High exposure	380 (7%)	275 (6%)	105 (7%)	
Severe exposure	108 (2%)	80 (2%)	28 (2%)	
Missing	196 (3%)	132 (3%)	64 (4%)	
Screened depression	647 (11%)	464 (11%)	183 (13%)	0.028
Missing	170 (3%)	109 (3%)	61 (4%)	
Screened PTSD	690 (12%)	474 (11%)	216 (15%)	<0.001
Missing	117 (2%)	82 (2%)	35 (2%)	
Baseline MoCA score	25.2±2.7	26.4±1.7	21.5±1.7	<0.001
eGFR variables				
First eGFR measurement (ml/min per 1.73 m ²)	91.1±12.8	91.5±12.8	90.1±12.9	<0.001
Last eGFR measurement (ml/min per 1.73 m ²)	86.7±14.3	87.1±14.1	85.7±14.9	0.001
No. of eGFR available	4.0 (3.0–6.0)	5.0 (3.0–6.0)	4.0 (3.0–5.0)	<0.001
Duration of follow-up (yr)	4.2±1.9	4.4±1.8	3.7±1.9	<0.001
Kidney outcomes				
eGFR change per year (ml/min per 1.73 m ² per year)	−1.2±4.0	−1.1±3.7	−1.5±4.8	0.006
Rapid eGFR decline (≤−5 ml/min per 1.73 m ² per year)	550 (10%)	358 (8%)	192 (13%)	<0.001
Incident CKD	248 (4%)	167 (4%)	81 (6%)	0.005

Data expressed as mean±SD or frequency (%) as appropriate. BMI, body mass index; CI, cognitive impairment; CVD, cardiovascular disease; HTN, hypertension; MoCA, Montreal Cognitive Assessment; PTSD, post-traumatic stress disorder; PPE, protective personal equipment; WTC, World Trade Center.

^aConsidered “non-White” if individuals reported themselves to be Asian (non-Hispanic), Black (Hispanic and non-Hispanic), Hispanic (not Black)/Mexican, or other (non-Hispanic).

^bCardiovascular disease was defined as a composite variable of stroke, angina, myocardial infarction, coronary artery disease, heart failure, or abnormal heart rhythm.

interval, −0.55 to −0.05; *P* adjusted = 0.040; [Figure 2](#)) and baseline dementia (versus no dementia; β = −1.96; 95% confidence interval −2.93 to −0.98; *P* adjusted = 0.001; [Supplemental Figure 2](#)) were significantly associated with greater eGFR decline per year.

The Association of Baseline CI and Dementia with Rapid eGFR Decline

Of 5761 responders, 550 (10%) experienced rapid eGFR decline. Individuals with CI (versus no CI) were more likely to have rapid eGFR decline (13% versus 8%,

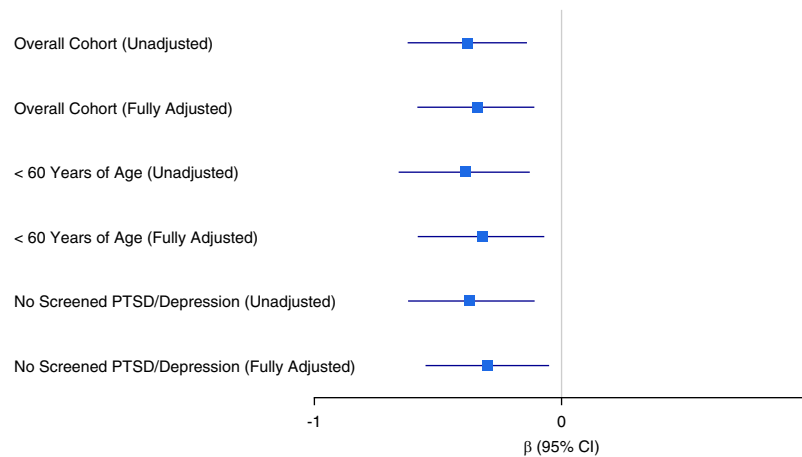


Figure 2. Association of baseline CI with eGFR change per year. Forest plot displaying association between baseline CI and eGFR change per year for overall, younger than 60 years, and no PTSD/depression cohorts. Fully adjusted models adjusted for age, sex, race and ethnicity, comorbidities (diabetes, HTN, CVD, baseline BMI), WTC exposure, screened baseline PTSD (in overall and younger than 60 years cohorts), and baseline eGFR. BMI, body mass index; CI, cognitive impairment; CVD, cardiovascular disease; HTN, hypertension; PTSD, post-traumatic stress disorder; WTC, World Trade Center; 95% CI, 95% confidence interval.

$P < 0.001$; Figure 3 and Table 1). Dementia (versus no dementia) showed a more pronounced effect (25% versus 9%, $P < 0.001$; Figure 4 and Supplemental Table 1).

Multivariable analysis showed that both CI (versus no CI; adjusted hazard ratio [aHR], 1.61 [1.32 to 1.96]; P adjusted < 0.001) and dementia (versus no dementia; aHR, 2.40 [1.46 to 3.94]; P adjusted = 0.004) were significantly associated with rapid eGFR decline (Figure 5 and Supplemental Figure 3).

Sensitivity Analyses

1. *PSM for Demographics*: individuals with baseline CI (versus no CI) had more rapid eGFR decline (12% versus 9%, $P = 0.003$; Table 2). Individuals with dementia (versus no dementia) were also more likely to experience rapid eGFR decline (not statistically significant: 24% versus 18%, $P = 0.26$; Supplemental Table 2).
2. *Baseline Age Younger than 60 years*: individuals with baseline CI and dementia were more likely to experience rapid eGFR decline (Table 3 and Supplemental Table 3) compared with those without. In multivariable analyses, baseline CI (versus no CI; aHR, 1.55 [1.22 to 1.97]; P adjusted = 0.003; Figure 5) and dementia (versus no dementia; aHR, 2.50 [1.28 to 4.88]; P adjusted = 0.035; Supplemental Figure 3) remained significantly associated with an increased hazard of rapid eGFR decline.
3. *No PTSD or Depression at Baseline*: individuals with baseline CI and dementia were more likely to exhibit rapid eGFR decline, compared with those without (Table 4 and Supplemental Table 4). In multivariable analyses, baseline CI (versus no CI; aHR, 1.56 [1.26 to 1.93]; P adjusted < 0.001 ; Figure 5) and dementia (versus no dementia; aHR, 2.68 [1.55 to 4.62]; P adjusted = 0.004; Supplemental Figure 3) remained significantly associated with an increased hazard of rapid eGFR decline.

The Association of Baseline CI/Dementia with Incident CKD

Two hundred and forty-eight (4%) developed incident CKD. CI (versus no CI) was associated with higher CKD risk (6% versus 4%, $P = 0.005$; Table 1), and dementia (versus no dementia) showed a stronger association (10% versus 4%, $P = 0.007$; Supplemental Table 1). Multivariable models showed CI (versus no CI; aHR, 1.73 [1.29 to 2.31]; P adjusted = 0.002) and dementia (versus no dementia; aHR, 2.80 [1.29 to 6.09]; P adjusted = 0.038) were significantly linked to incident CKD (Figure 6 and Supplemental Figure 4). Compared with individuals without baseline CI, those with CI had a greater incidence of CKD stages 3b (0.6% versus 0.4%) and 4 (0.1% versus 0%). No individuals in the cohort developed incident CKD stage 5 or ESKD.

Sensitivity Analyses

The low number of incident CKD cases based on ICD codes (0.8%) led to an alternative eGFR-based definition, confirming CI (versus no CI) as significantly associated with incident CKD (aHR, 1.76 [1.29 to 2.40]; P adjusted = 0.003; Figure 6). All incident CKD cases in individuals with baseline dementia were determined only by eGFR.

Owing to the low number of incident CKD cases, additional sensitivity analyses were not performed.

Other Sensitivity Analyses

The Association of Baseline CI with Incident CKD and Rapid eGFR Decline (Combined Outcome)

Ninety-five (2%) developed the combined outcome of incident CKD and rapid eGFR decline. CI (versus no CI) was associated with higher risk (3% versus 1%, $P = 0.005$). Multivariable models showed that CI (versus no CI; aHR, 2.56 [1.66 to 3.99]; $P < 0.001$) was significantly linked to combined kidney outcome. The numbers of individuals with baseline dementia were too small for this analyses.

Table 2. Characteristics and outcomes of individuals with and without cognitive impairment (propensity score matched for age, sex, and race and ethnicity)

Variable	Overall 2652	No Baseline CI (MoCA >23) 1326 (50%)	Baseline CI (MoCA ≤23) 1326 (50%)	P Value
Age (yr)	55.1±7.5	55.0±7.3	55.2±7.6	0.43
Sex				1.00
Male	2436 (92%)	1218 (92%)	1218 (92%)	
Female	216 (8%)	108 (8%)	108 (8%)	
Race and ethnicity				1.00
Non-White ^a	440 (17%)	220 (17%)	220 (17%)	
White (non-Hispanic)	2212 (83%)	1106 (83%)	1106 (83%)	
Education				<0.001
<BA/BS	1692 (64%)	808 (61%)	884 (67%)	
BA/BS or higher	685 (26%)	393 (30%)	292 (22%)	
Missing	275 (10%)	125 (9%)	150 (11%)	
Comorbidities				
CVD ^b	181 (7%)	80 (6%)	101 (8%)	0.11
Diabetes	326 (12%)	166 (13%)	160 (12%)	0.72
HTN	915 (35%)	481 (36%)	434 (33%)	0.055
Obesity	1506 (57%)	803 (61%)	703 (53%)	<0.001
BMI (kg/m ²)	31.4±5.4	31.8±5.5	31.1±5.3	<0.001
Missing	18 (0.7%)	6 (0.5%)	12 (0.9%)	
WTC exposure				0.113
No exposure/low exposure	130 (5%)	78 (6%)	52 (4%)	
Mild exposure	1320 (50%)	669 (50%)	651 (49%)	
Moderate exposure	879 (33%)	432 (33%)	447 (34%)	
High exposure	176 (7%)	80 (6%)	96 (7%)	
Severe exposure	57 (2%)	31 (2%)	26 (2%)	
Unknown	90 (3%)	36 (3%)	54 (4%)	
Screened depression	333 (13%)	159 (12%)	174 (13%)	0.30
Missing	87 (3%)	33 (2%)	54 (4%)	
Screened PTSD	355 (13%)	151 (11%)	204 (15%)	0.002
Missing	56 (2%)	24 (2%)	32 (2%)	
Baseline MoCA score	24.0±2.9	26.3±1.7	21.6±1.7	<0.001
eGFR variables				
First eGFR measurement (ml/min per 1.73 m ²)	90.2±12.7	90.1±12.5	90.4±12.9	0.56
Last eGFR measurement (ml/min per 1.73 m ²)	85.8±14.3	85.7±14.0	85.8±14.7	0.88
No. of eGFR available	4.0 (3.0–6.0)	5.0 (3.0–6.0)	4.0 (3.0–5.0)	<0.001
Duration of follow-up	4.1±1.9	4.3±1.8	3.9±1.9	<0.001
Kidney outcomes				
eGFR change per year (ml/min per 1.73 m ² per year)	−1.3±4.2	−1.1±3.6	−1.9±4.7	0.009
Rapid eGFR decline (≤−5 ml/min per 1.73 m ² per year)	276 (10%)	114 (9%)	162 (12%)	0.003

Data expressed as mean±SD or frequency (%) as appropriate. BMI, body mass index; CI, cognitive impairment; CVD, cardiovascular disease; HTN, hypertension; MoCA, Montreal Cognitive Assessment; PTSD, post-traumatic stress disorder; PPE, protective personal equipment; WTC, World Trade Center.

^aConsidered “non-White” if individuals reported themselves to be Asian (non-Hispanic), Black (Hispanic and non-Hispanic), Hispanic (not Black)/Mexican, or other (non-Hispanic).

^bCardiovascular disease was defined as a composite variable of stroke, angina, myocardial infarction, coronary artery disease, heart failure, or abnormal heart rhythm.

Association of Baseline MCI with Kidney Outcomes

After excluding individuals with a baseline dementia (MoCA ≤19), 5672 individuals were eligible for analysis, of which 4315 (76%) did not have baseline MCI and 1357 (24%) were classified as baseline MCI (Supplemental Table 5). Consistent with our primary cohort in fully adjusted models, baseline MCI (versus no MCI) remained significantly associated with greater eGFR decline per year

(Supplemental Figure 5), rapid eGFR decline (Supplemental Figure 6), and incident CKD (Supplemental Figure 7).

Exclusion of Mortality during Follow-Up

To prevent residual confounding from unmeasured variables leading to death, in a sensitivity analysis, we removed 62 (1%) individuals in our study who died by the end of follow-up. Consistent with our primary cohort, in

Table 3. Characteristics and outcomes of individuals with and without cognitive impairment in individuals with baseline age younger than 60 years

Variable	Overall 4594	No Baseline CI (MoCA >23) 3542 (77%)	Baseline CI (MoCA ≤23) 1052 (23%)	P Value
Age (yr)	50.8±5.4	50.4±5.5	51.9±5.1	<0.001
Sex				0.94
Male	4173 (91%)	3218 (91%)	955 (91%)	
Female	421 (9%)	324 (9%)	97 (9%)	
Race and ethnicity				<0.001
Missing	130 (3%)	74 (2%)	56 (5%)	
Non-White ^a	617 (13%)	424 (12%)	193 (18%)	
White (non-Hispanic)	3847 (84%)	3044 (86%)	803 (76%)	
Education				<0.001
<BA/BS	2880 (63%)	2179 (62%)	701 (67%)	
BA/BS or higher	1314 (29%)	1091 (31%)	223 (21%)	
Missing	400 (9%)	272 (8%)	128 (12%)	
Comorbidities				
CVD ^b	213 (5%)	157 (4%)	56 (5%)	0.23
Diabetes	401 (9%)	294 (8%)	107 (10%)	0.059
HTN	1299 (28%)	988 (28%)	311 (30%)	0.29
Obesity	2522 (55%)	1923 (54%)	599 (57%)	0.13
BMI (kg/m ²)	31.3±5.4	31.3±5.4	31.5±5.3	0.31
Missing	32 (0.7%)	19 (0.5%)	13 (1%)	
WTC exposure				0.093
No exposure/low exposure	212 (5%)	175 (5%)	37 (4%)	
Mild exposure	2535 (55%)	1983 (56%)	552 (52%)	
Moderate exposure	1356 (30%)	1026 (29%)	330 (32%)	
High exposure	277 (6%)	207 (6%)	70 (7%)	
Severe exposure	71 (2%)	53 (2%)	18 (2%)	
Unknown	143 (3%)	98 (3%)	45 (4%)	
Screened depression	523 (11%)	383 (11%)	140 (13%)	0.015
Missing	121 (3%)	79 (2%)	42 (4%)	
Screened PTSD	561 (12%)	401 (11%)	160 (15%)	<0.001
Missing	88 (2%)	63 (2%)	25 (2%)	
Baseline MoCA score	25.4±2.6	26.5±1.7	21.6±1.6	<0.001
eGFR variables				
First eGFR measurement (ml/min per 1.73 m ²)	92.8±12.6	92.9±12.5	92.3±12.7	0.14
Last eGFR measurement (ml/min per 1.73 m ²)	88.6±13.7	88.7±13.6	88.1±13.9	0.18
No. of eGFR available	5.0 (3.0–6.0)	5.0 (3.0–6.0)	4.0 (3.0–5.0)	<0.001
Duration of follow-up	4.3±1.8	4.5±1.8	3.9±1.9	<0.001
Kidney outcomes				
eGFR change per year (ml/min per 1.73 m ² per year)	−1.1±3.8	−1.0±3.6	−1.4±4.6	0.010
Rapid eGFR decline (≤−5 ml/min per 1.73 m ² year)	395 (9%)	273 (8%)	122 (12%)	<0.001

Data expressed as mean±SD or frequency (%) as appropriate. BMI, body mass index; CI, cognitive impairment; CVD, cardiovascular disease; HTN, hypertension; MoCA, Montreal Cognitive Assessment; PTSD, post-traumatic stress disorder; PPE, protective personal equipment, WTC, World Trade Center.

^aConsidered “non-White” if individuals reported themselves to be Asian (non-Hispanic), Black (Hispanic and non-Hispanic), Hispanic (not Black)/Mexican, or other (non-Hispanic).

^bCardiovascular disease was defined as a composite variable of stroke, angina, myocardial infarction, coronary artery disease, heart failure, or abnormal heart rhythm.

fully adjusted models, both baseline CI (versus no CI) and baseline dementia (versus no dementia) remained significantly associated with greater eGFR decline per year (Supplemental Figure 8). Rapid eGFR decline (Supplemental Figure 9) and incident CKD (Supplemental Figure 10).

Exclusion of Preexisting Head Trauma, Stroke, and CVD

After excluding 405 individuals with stroke, baseline CVD, and head trauma, 5586 individuals were available

for analysis, of which 1391 (25%) were classified as having baseline CI and 85 (2%) were classified as having baseline dementia. Consistent with our primary cohort, in fully adjusted models, both baseline CI (versus no CI) and baseline dementia (versus no dementia) remained significantly associated with greater eGFR decline per year (Supplemental Figure 11). Rapid eGFR decline (Supplemental Figure 12) and incident CKD (Supplemental Figure 13).

Table 4. Characteristics and outcomes of individuals with and without cognitive impairment in individuals without screened baseline post-traumatic stress disorder or depression

Variable	Overall 4869	No Baseline CI (MoCA >23) 3686 (76%)	Baseline CI (MoCA ≤23) 1183 (24%)	P Value
Age (yr)	53.7±8.0	53.1±7.8	55.8±8.3	<0.001
Sex				0.42
Male	4497 (92%)	3398 (92%)	1099 (93%)	
Female	372 (8%)	288 (8%)	84 (7%)	
Race and ethnicity				<0.001
Missing	170 (3%)	92 (3%)	78 (7%)	
Non-White ^a	577 (12%)	396 (11%)	181 (15%)	
White (non-Hispanic)	4122 (85%)	3198 (87%)	924 (78%)	
Education				<0.001
<BA/BS	2937 (60%)	2192 (59%)	745 (63%)	
BA/BS or higher	1432 (29%)	1163 (32%)	269 (23%)	
Missing	500 (10%)	331 (9%)	169 (14%)	
Comorbidities				
CVD ^b	286 (6%)	198 (5%)	85 (7%)	0.020
Diabetes	465 (10%)	344 (9%)	121 (10%)	0.36
HTN	1502 (31%)	1129 (31%)	373 (32%)	0.56
Obesity	2560 (53%)	1949 (53%)	611 (52%)	0.46
BMI (kg/m ²)	31.0±5.3	31.0±5.3	30.9±5.2	0.60
Missing	32 (0.7%)	19 (0.5%)	13 (1%)	
WTC exposure				0.051
No exposure/low exposure	232 (5%)	184 (5%)	48 (4%)	
Mild exposure	2598 (53%)	2007 (54%)	591 (50%)	
Moderate exposure	1514 (31%)	1113 (30%)	401 (34%)	
High exposure	291 (6%)	215 (6%)	76 (6%)	
Severe exposure	73 (2%)	55 (1%)	18 (2%)	
Missing	161 (3%)	112 (3%)	49 (4%)	
Baseline MoCA score	25.3±2.7	26.5±1.7	21.6±1.6	<0.001
eGFR variables				
First eGFR measurement (ml/min per 1.73 m ²)	91.0±12.8	91.4±12.8	89.8±13.0	<0.001
Last eGFR measurement (ml/min per 1.73 m ²)	86.7±14.2	87.1±14.0	85.5±14.7	<0.001
No. of eGFR available	4.0 (3.0–6.0)	5.0 (3.0–6.0)	4.0 (3.0–5.0)	<0.001
Duration of follow-up (yr)	4.2±1.9	4.4±1.8	3.6±1.9	<0.001
Kidney outcomes				
eGFR change per year (ml/min per 1.73 m ² per year)	−1.2±3.9	−1.1±3.7	−1.5±4.5	0.011
Rapid eGFR decline (≤−5 ml/min per 1.73 m ² per year)	462 (9%)	303 (8%)	159 (13%)	<0.001

Data expressed as mean±SD or frequency (%) as appropriate. BMI, body mass index; CI, cognitive impairment; CVD, cardiovascular disease; HTN, hypertension; MoCA, Montreal Cognitive Assessment; PTSD, post-traumatic stress disorder; PPE, protective personal equipment; WTC, World Trade Center.

^aConsidered “non-White” if individuals reported themselves to be Asian (non-Hispanic), Black (Hispanic and non-Hispanic), Hispanic (not Black)/Mexican, or other (non-Hispanic).

^bCardiovascular disease was defined as a composite variable of stroke, angina, myocardial infarction, coronary artery disease, heart failure, or abnormal heart rhythm.

Association of Worsening MoCA Scores with Kidney Outcomes

Of the 5761 individuals analyzed, 3022 (51%) showed worsening of MoCA scores over the follow-up period. Individuals with worsening MoCA scores did not have significantly different rates of either rapid decline (9% versus 10%, $P = 0.087$) or incident CKD (5% versus 4%, $P = 0.198$; Supplemental Table 6). In fully adjusted models, worsening MoCA scores were not significantly associated with either rapid decline (aHR, 1.09 [0.99 to 1.18]; $P = 0.068$) or incident CKD (aHR, 1.12 [0.96 to 1.30]; $P = 0.143$; Supplemental Figure 14). Based on our previous studies,

while MoCA is very sensitive in detection of MCI or dementia, the trajectory of MoCA is not a reliable estimate of progressive cognitive decline.

Discussion

We recently reported that WTC responders are at higher risk for early-onset MCI and dementia.^{10,12–15} Previous studies on cognition and kidney function have primarily focused on older populations,^{10,12–15} while those involving younger individuals have been limited by cross-sectional

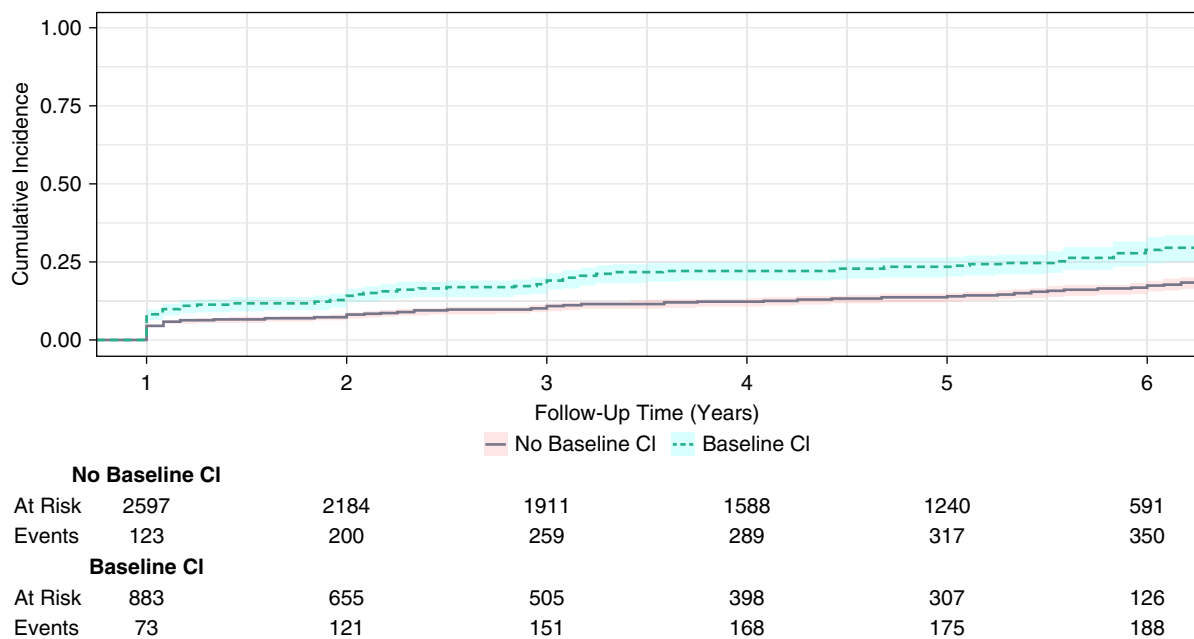


Figure 3. Cumulative incidence plot for rapid eGFR decline outcome in individuals with and without baseline CI. Cumulative (unadjusted) incidence plot for rapid GFR decline for individuals with (dashed) and without (solid) CI during the observation period.

designs.^{6,43} To the best of our knowledge, this is the first study to report that, among middle-aged individuals without CKD, baseline CI is associated with an increased risk of accelerated eGFR decline. This association remained significant after adjusting for multiple risk factors, as well as multiple sensitivity analyses: PSM for demographics; in

individuals younger than 60 years; and in those without baseline PTSD or depression; without baseline head trauma, stroke, and CVD; and after exclusion of those who died during follow-up. In addition, baseline CI was linked to an increased risk of incident CKD and the combined risk of incident CKD and rapid eGFR decline in

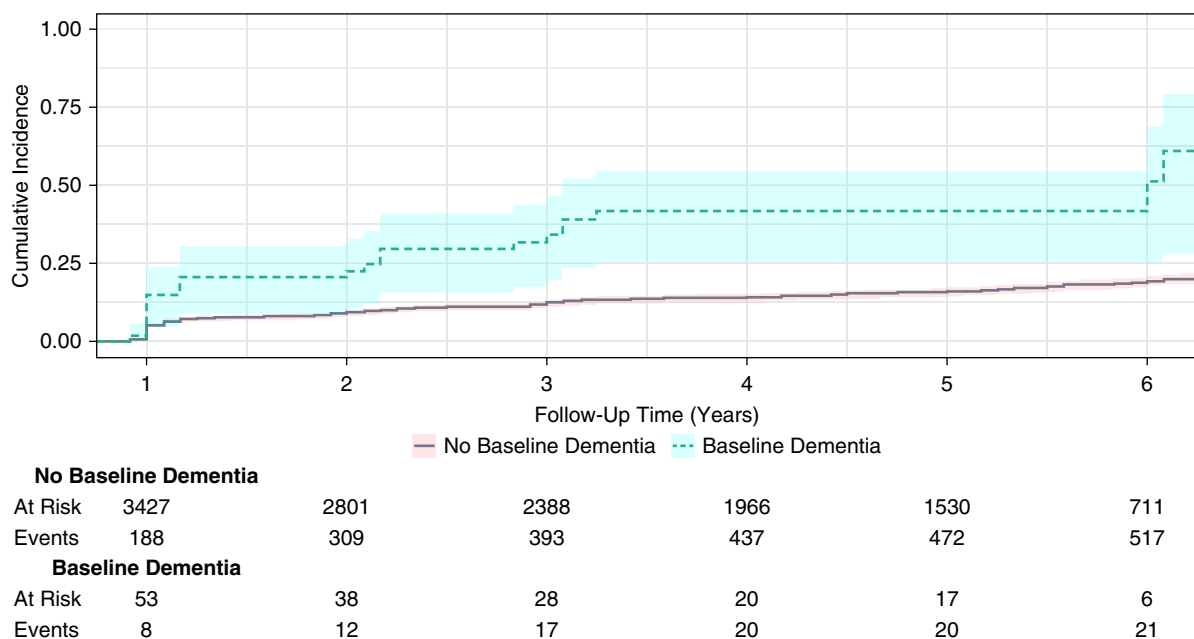


Figure 4. Cumulative incidence plot for rapid eGFR decline outcome in individuals with and without baseline dementia. Cumulative (unadjusted) incidence plot for rapid GFR decline for individuals with (dashed) and without (solid) dementia during the observation period.

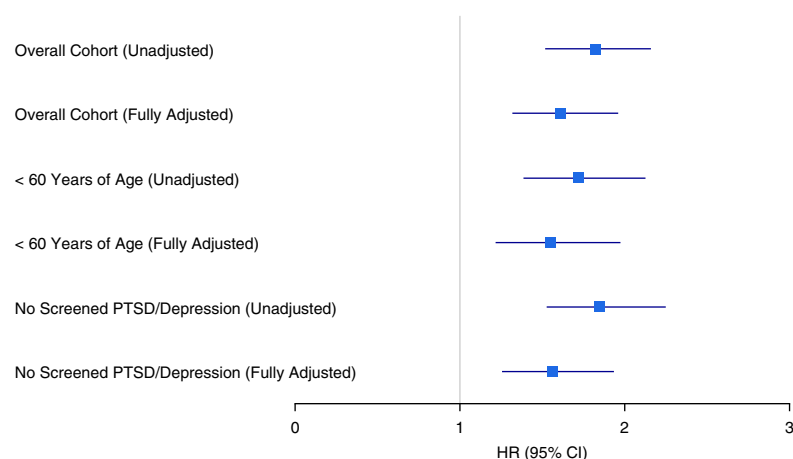


Figure 5. Association of baseline CI with rapid eGFR decline (≤ -5 ml/min per 1.73 m^2 per year). Forest plot displaying association between baseline CI and rapid eGFR decline for overall, younger than 60 years, and no PTSD/depression cohorts. Fully adjusted models adjusted for age, sex, race and ethnicity, comorbidities (diabetes, HTN, CVD, baseline BMI), WTC exposure, screened baseline PTSD (in overall and younger than 60 years of age cohorts), and baseline eGFR.

multivariable models. Even MCI was a risk factor for kidney outcomes. Severe CI (*i.e.*, dementia) at baseline showed similar associations, although due to the very low sample size of individuals with baseline dementia, after propensity matching for demographics, the association with eGFR decline was not statistically significant. The association between baseline dementia and kidney outcomes requires replication in larger cohorts due to the limited subgroup size.

A key strength of this study is the availability of longitudinal, granular data on mental health and protocolized annual GFR measurements from the WTC database, which enabled a robust analysis of the relationship between brain and kidney disease. Furthermore, the early onset of CI in WTC responders offers a unique opportunity to evaluate the effect of brain aging on kidney function in middle-aged individuals without preexisting kidney disease.

Advanced CKD can lead to accelerated cognitive decline, potentially through vascular injury, inflammation, and uremic toxins.^{44,45} Interestingly, similar inflammatory mechanisms are often linked to MCI and dementia, particularly in Alzheimer disease and related dementias. However, the exact mechanism linking CI to an increased risk of rapid kidney function decline in individuals without pre-existing kidney disease remains unclear. Our findings suggest that the association between eGFR decline and CI is stronger in individuals with more severe CI, *i.e.*, dementia. A recent MR study involving 396,600 UK Biobank participants, all without baseline CKD or dementia, demonstrated that better cognitive function is causally associated with a lower risk of CKD.²⁰ Another MR study found that genetically predicted decreased kidney function is associated with biologic aging (telomere attrition).⁴⁶ Emerging evidence suggests a “systemic aging phenotype,” in which physiologic aging occurs concurrently in multiple organs,

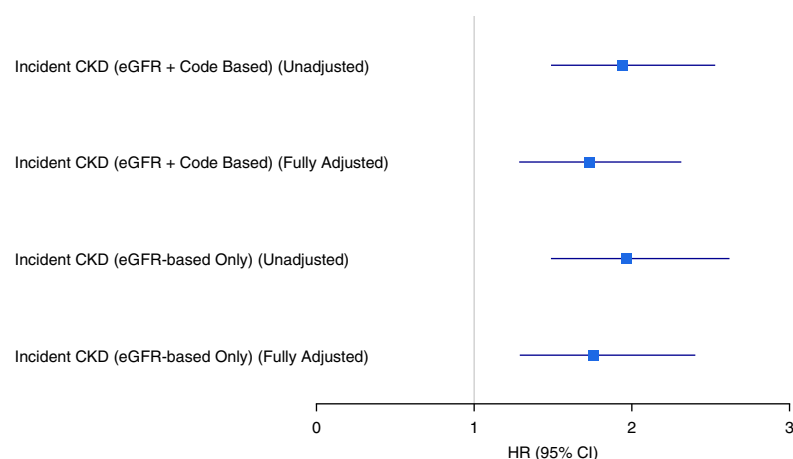


Figure 6. Association of baseline CI with incident CKD. Forest plot displaying association between baseline CI and incident CKD (eGFR+code-based versus eGFR-based only) among the overall cohort. Fully adjusted models adjusted for age, sex, race and ethnicity, comorbidities (diabetes, HTN, CVD, baseline BMI), WTC exposure, screened baseline PTSD, and baseline eGFR.

including the kidney and brain. Alzheimer's disease has been associated with accelerated aging in the kidneys.⁴⁷ Individuals with CI may exhibit a systemic aging phenotype, in which brain and kidney function decline in parallel. We previously reported that early-onset CI in WTC responders is linked to cortical atrophy on brain imaging.⁴⁸ However, this form of dementia may be a tauopathy, distinct from typical Alzheimer's disease,^{49,50} and may involve neuroinflammation.^{51,52} Systemic inflammation, a well-known contributor to CKD pathogenesis,⁵³ could also play a role in kidney injury in these individuals. For example, the nucleotide-binding oligomerization domain-like receptor pyrin domain-containing 3 inflammasome is known to be involved in the pathogenesis of both CKD⁵⁴ and Alzheimer's disease.⁵⁵ Microvascular disease in the brain and kidneys has been correlated.^{9,56} In addition, endothelial dysfunction is associated with the progression of CKD⁵⁷ and neurodegenerative diseases.⁵⁸ CI is linked to a higher incidence of clinical risk factors of CKD, such as diabetes, HTN, obesity, and CVD.^{17–19,59–62} Finally, impaired cognition has been associated with reduced health literacy,⁶³ which may influence health-related behaviors and contribute to kidney damage. Further research is needed to elucidate the pathophysiologic pathways and patient-related factors linking neurodegenerative disorders with kidney aging and CKD.

We previously reported that exposure to toxic chemicals during the September 11, 2001, rescue efforts (WTC exposure) is associated with early-onset dementia in WTC responders.²² Emerging data suggest an association between chronic environmental toxin exposure and GFR decline or CKD.⁶⁴ WTC exposure lasted 9 months, which is long for an exposure event but relatively brief for occupational exposures. These exposures occurred 14 years before the start of our study, when individuals were still free of CKD. Although WTC exposures could have contributed to eGFR decline, the association between rapid GFR decline and incident CKD with CI remained independent of WTC exposure and baseline eGFR. Together, these results may imply that the relationship between CI and CKD is independent of exposure, potentially resulting from a shared inflammatory mechanism, or that exposures causing early-onset dementia may concurrently be damaging the kidneys.

PTSD and depression are both linked to CI^{65,66} and eGFR decline.^{67,68} We previously reported that PTSD is a risk factor for rapid eGFR decline in young WTC responders.⁶⁸ However, most studies on kidney and cognitive dysfunction have not accounted for comorbid PTSD or depression. In this study, we show that the association between eGFR decline and CI in middle-aged adults is independent of baseline screened PTSD and depression.

Our findings have important clinical implications. Rapid GFR decline, a hallmark of CKD progression toward kidney failure, may be slowed or halted with appropriate interventions.⁶⁹ Monitoring kidney function more closely in high-risk individuals, such as those with CI, may enable the early initiation of preventive strategies. Given the association between kidney function decline and CI, clinicians may need to implement routine cognitive assessments in patients with CKD, particularly in populations

with known environmental exposures. In addition, integrating kidney function monitoring into neurologic evaluations could allow for earlier interventions aimed at slowing both kidney dysfunction and neurodegeneration. Whether treatment of CI can slow eGFR decline remains unknown, but it should be the focus of future interventional studies.

This study has several limitations. First, we lacked data on proteinuria, medications used for the treatment of CKD and CI, and drugs that can be toxic to the kidneys and brain. Second, the WTC cohort, which was almost universally used in stable unionized jobs at the time of exposure, is relatively well-educated and mostly male and White. These factors limit the generalizability of our findings. Previous studies on cognitive function and CKD found that this association was not influenced by sex.^{10,11,20,70} The influence of race and ethnicity in the association of CKD and dementia is less well studied and should be a focus of future research. Third, the relatively young age of our cohort and low prevalence of medical comorbidities resulted in few cases of incident CKD and baseline dementia. Advanced kidney outcomes, such as incident ESKD, were not evaluated. Moreover, our GFR calculation was based on SCr, which can be influenced by muscle mass. However, we have adjusted for BMI in all our multivariable models. Fourth, our diagnosis of CI and dementia relied on a sole screening tool (MoCA). However, as previously mentioned, MoCA has demonstrated high accuracy in diagnosing CI and is associated with cortical atrophy on brain imaging. We used alternative versions at each testing occasion to reduce test-retest bias. Fifth, there are potential biases related to self-reported data. Sixth, individuals with baseline CI and dementia had less follow-up than those without. This was likely due to older age and poor cognition. Seventh, the competing of death and cardiovascular events were not assessed. Finally, it is important to acknowledge the possibility of residual confounding due to unmeasured variables. For example, health-related behaviors, which could influence both cognitive function and kidney health, were not accounted for in this study.

In conclusion, we report that prevalent CI is significantly associated with the risk of rapid eGFR decline in WTC responders without baseline kidney disease. CI may also be associated with the risk of incident CKD. These findings suggest that patients with CI may require close monitoring of kidney function, regardless of their age or comorbid psychiatric conditions. Furthermore, our results underscore the need for targeted screening strategies, particularly in high-risk occupational groups, and highlight the importance of refining CKD management guidelines to consider neurocognitive outcomes. Future studies should validate these findings in larger, more diverse cohorts and explore whether targeted interventions can mitigate the progression of both cognitive and kidney dysfunction.

Disclosures

Disclosure forms, as provided by each author, are available with the online version of the article at <http://links.lww.com/KN9/B157>.

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Funding

F.M. Koraishy, National Institutes of Health (R21OH012237-01). S.A.P. Clouston, National Institutes of Health (NIH/NIA R01 AG049953). S.S. Hedayati, National Institute of Diabetes and Digestive and Kidney Diseases (R01DK124379). B.J. Luft, Centers for Disease Control and Prevention (CDC/NIOSH 75D301-22-C-15522).

Declarative Statements

This study includes clinical experimentation and received Institutional Review Board or Ethics Committee approval. The need to obtain informed patient consent was waived. This study includes clinical experimentation and complies with the Declaration of Helsinki.

Data Availability Statements

Partial restrictions to the data and/or materials apply. Deidentified participant data is available upon request to the corresponding author. Who can access the data: Anyone whose proposed use of the data has been received and approved. Types of analyses: Any purpose of interest to the WTC responder population. Mechanisms of data availability: After completion of a signed data access agreement. Any additional restrictions: No specific dates can be released publicly.

Supplemental Material

This article contains the following supplemental material online at <http://links.lww.com/KN9/B158>.

Supplemental Figure 1. Study timeline and distribution of enrollment into cohort.

Supplemental Figure 2. Association of baseline dementia with eGFR change per year.

Supplemental Figure 3. Association of baseline dementia with rapid eGFR decline (≤ -5 ml/min per 1.73 m² per year).

Supplemental Figure 4. Association of baseline dementia with incident CKD.

Supplemental Figure 5. Association of baseline MCI with eGFR change per year.

Supplemental Figure 6. Association of baseline MCI with rapid eGFR decline (≤ -5 ml/min per 1.73 m² per year).

Supplemental Figure 7. Association of baseline MCI with incident CKD.

Supplemental Figure 8. Association of baseline CI/dementia with eGFR change per year (no mortality).

Supplemental Figure 9. Association of baseline CI/dementia with rapid eGFR decline (≤ -5 ml/min per 1.73 m² per year; no mortality).

Supplemental Figure 10. Association of baseline CI/dementia with incident CKD (no mortality).

Supplemental Figure 11. Association of baseline CI/dementia with eGFR change per year (no CI risk factors).

Supplemental Figure 12. Association of baseline CI/dementia with rapid eGFR decline (≤ -5 ml/min per 1.73 m² per year; No CI risk factors).

Supplemental Figure 13. Association of baseline CI/dementia with incident CKD (no CI risk factors).

Supplemental Figure 14. Association of worsening MoCA scores with kidney outcomes.

Supplemental Table 1. Characteristics and outcomes of individuals with and without dementia.

Supplemental Table 2. Characteristics and outcomes of individuals with and without dementia (propensity score matched for age, sex, and race and ethnicity).

Supplemental Table 3. Characteristics and outcomes of individuals with and without Dementia in individuals with baseline age younger than 60 years.

Supplemental Table 4. Characteristics and outcomes of individuals with and without dementia in individuals without baseline PTSD or depression.

Supplemental Table 5. Characteristics and outcomes of individuals with and without MCI.

Supplemental Table 6. Characteristics and outcomes of individuals with worsening MoCA scores.

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