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Association of Electronic Cigarette Use with Chronic Kidney Disease in NHANES 2017-2020: A Cross-Sectional Replication Study

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Abstract

Combustible cigarettes (CCs) are a modifiable risk factor for chronic kidney disease (CKD) however the impact of electronic cigarettes (ECs) is not well defined. A recent cross-sectional analysis of NHANES 2017-2020 data reported 2.5-fold higher CKD odds in current EC users, with risk increasing with use frequency (Li *et al.*, 2025). However, methodological concerns—including failure to segment by CC current, former, and never use; sampling irregularities; and sensitivity analyses on insufficient harm events—called the validity into question and prompted this replication study. Using the complete NHANES 2017-2020 pre-pandemic dataset (N = 8109 adults), we stratified participants by CC use history to minimize confounding from non-independent tobacco exposures. EC use was defined as past 5-day use—the only consistent metric across cycles. CKD was assessed using Li *et al.*'s binary definitions and the KDIGO CKD Heat Map for graded risk of progression. Analyses progressed through unweighted, population-weighted, and propensity-matched case-control stages, adjusting for age, sex, race, diabetes, hypertension, obesity, and CC duration/cessation timing. Results showed no evidence of an association between current EC use and CKD prevalence or risk progression across all segments and definitions (CC current and former users: $ps>0.05$; CC never users: only 1 CKD diagnosis among EC users), contrasting the original findings. Unadjusted lower CKD rates in EC users were driven by younger age and lower comorbidity burden; frequent EC use reflected recent CC cessation. Limitations include cross-sectional design, single-timepoint measurements, and sparse harm events in EC cohorts which limited the statistical power. This study underscores the critical importance of precise exposure characterization and segmentation in tobacco-related observational research to avoid misattribution of CC-related risks to ECs. It highlights systematic flaws in prior NHANES

analyses and advocates for enhanced survey metrics—such as EC duration, past 30-day use, and time since CC cessation—in future waves. These findings reinforce the need for methodological rigor to most precisely evaluate associations between risk and use of nicotine products.

Keywords

Nicotine, E-Cigarette, Chronic Kidney Disease, Cross-Sectional Study, Replication Study

1. Introduction

Chronic kidney disease is the 8th leading cause of mortality in the U.S., with a prevalence of over 35 million adults [1]. Risk factors include age, diabetes, hypertension, and obesity. Another critical yet modifiable risk factor is combustible cigarette (CC) smoking; consequently, evaluating the association of electronic cigarette (EC) use with this disease is relevant. A recent analysis (Li *et al.*, 2025) performed a retrospective cross-sectional analysis of the NHANES 2017-2020 database to investigate this research question [2]. The authors reported that current EC use was associated with 2.5-fold higher odds of CKD and that CKD risk was also positively correlated with the frequency of EC use. As described below, multiple aspects of the analysis appeared not to conform to best practices for optimizing precision and accuracy [3]. Therefore, a replication study was performed to verify the findings.

2. Methods

Data were downloaded from the NHANES "Pre-Pandemic" dataset spanning 2017-2020. The separate 2017-2018 and 2019-2020 files were not used, as they are already incorporated into the 2017-2020 dataset. NHANES data were accessed Oct. 1-20, 2025, and contained only de-identified information.

Definitions:

- EC current use was assessed as use in the past 5 days (SMQ690H, SMQ849). In 2019, the NHANES discontinued asking about EC ever-use and EC past 30-day use (SMQ900, SMQ905), so this was the only metric available for the complete 2017-2020 dataset (see the Discussion for suggestions for future NHANES waves).
- Current established CC use was derived from two variables: (a) smoking 100+ cigarettes/lifetime and (b) currently smoking cigarettes "every day" or "some days" (vs. not at all").
- CC former established use was derived from two variables: (a) smoked 100+ cigarettes/lifetime and (b) now smoking "not at all" (vs. "every day" or "some days").
- CC never established use was defined as having smoked < 100 cigarettes/lifetime.
- The glomerular filtration rate (GFR) was calculated via the 2021 CKD-EPI

Creatinine Equation, which estimates the glomerular filtration rate (eGFR) using age, sex, and serum creatinine as variables.

$$eGFR\ (mL/min/1.73m^2) = 142 \times \min(SCr/\kappa, 1)\alpha \times \max(SCr/\kappa, 1) - 1.200 \times 0.9938^{AGE} \times 1.012\ [\text{if female}]$$

where:

SCr (serum creatinine) in mg/dL (LBXSCR in NHANES)

$K = 0.7$ (females) or 0.9 (males)

$\alpha = -0.241$ (females) or -0.302 (males)

AGE in years

- CKD metrics (see **Figure 1**)
  - ➢ The KDIGO CKD Heat Map provides a more precise assessment of early screening for chronic kidney disease (CKD) in the general population, specifically the risk of progression, morbidity, and mortality [4]. The columns represent the albumin/creatinine ratios, and the rows represent the estimated glomerular filtration rates. The color coding represents the risk of progression to CKD. Five gradations of risk exist: low risk of progression to CKD, moderate risk, high risk, very high risk and highest risk. Note that a definitive assessment of CKD requires the presence of

A. CKD Heat Map (KDIGO, 2012)

	A1 (<30)	*A2 (30-299)*	*A3 (≥300)*
G1 (GFR ≥90)	**Low risk**	**Moderate**	**High**
G2 (60-90)	**Low**	**Moderate**	**High**
G3a (45-60)	**Moderate**	**High**	**Very high**
G3b (30-45)	**High**	**Very high**	**Very high**
G4 (15-30)	**Very high**	**Very high**	**Highest**
G5 (<15)	**Highest**	**Highest**	**Highest risk**

Albuminuria stages

A1: Normal to mildly increased (<30 mg/g creatinine)
A2: Moderately increased (30-299)
A3: Severely increased (≥300)

Glomerular Filtration Rate (GFR) stages

G1: Normal or high (≥90 mL/min/1.73 m²)
G2: Mildly decreased (60-90)
G3a: Mild to moderately decreased (45-60)
G3b: Moderately to severely decreased (30-45)
G4: Severely decreased (15-30)
G5: Kidney failure (<15)

B. CKD Narrower Definition (Li et al., 2025)

	A1 (<30)	*A2 (30-299)*	*A3 (≥300)*
G1 (GFR ≥90)	**Negative**	**Negative**	**Positive**
G2 (60-90)	**Negative**	**Negative**	**Positive**
G3a (45-60)	**Negative**	**Negative**	**Positive**
G3b (30-45)	**Negative**	**Negative**	**Positive**
G4 (15-30)	**Negative**	**Negative**	**Positive**
G5 (<15)	**Negative**	**Negative**	**Positive**

C. CKD Broader Definition (Li et al., 2025)

	A1 (<30)	*A2 (30-299)*	*A3 (≥300)*
G1 (GFR ≥90)	**Negative**	**Positive**	**Positive**
G2 (60-90)	**Negative**	**Positive**	**Positive**
G3a (45-60)	**Positive**	**Positive**	**Positive**
G3b (30-45)	**Positive**	**Positive**	**Positive**
G4 (15-30)	**Positive**	**Positive**	**Positive**
G5 (<15)	**Positive**	**Positive**	**Positive**

(Panel A) KDIGO CKD Heat Map [4]. The columns represent the albumin/creatinine ratio, and the rows represent the estimated glomerular filtration rate. The color coding represents the risk of CKD progression, morbidity, and mortality (green represents low risk, yellow represents moderate risk, and red represents high risk). (Panel B) CKD narrow definition from Li *et al.* [2]. An albumin/creatinine ratio of 300+ represents a positive result. (Panel C) CKD broad definition from Li *et al.* [2]. An albumin/creatinine ratio of 30+ or an eGFR < 60 represents a positive result. CKD (chronic kidney disease); KDIGO (Kidney Disease: Improving Global Outcomes).

Figure 1. CKD assessment scales.

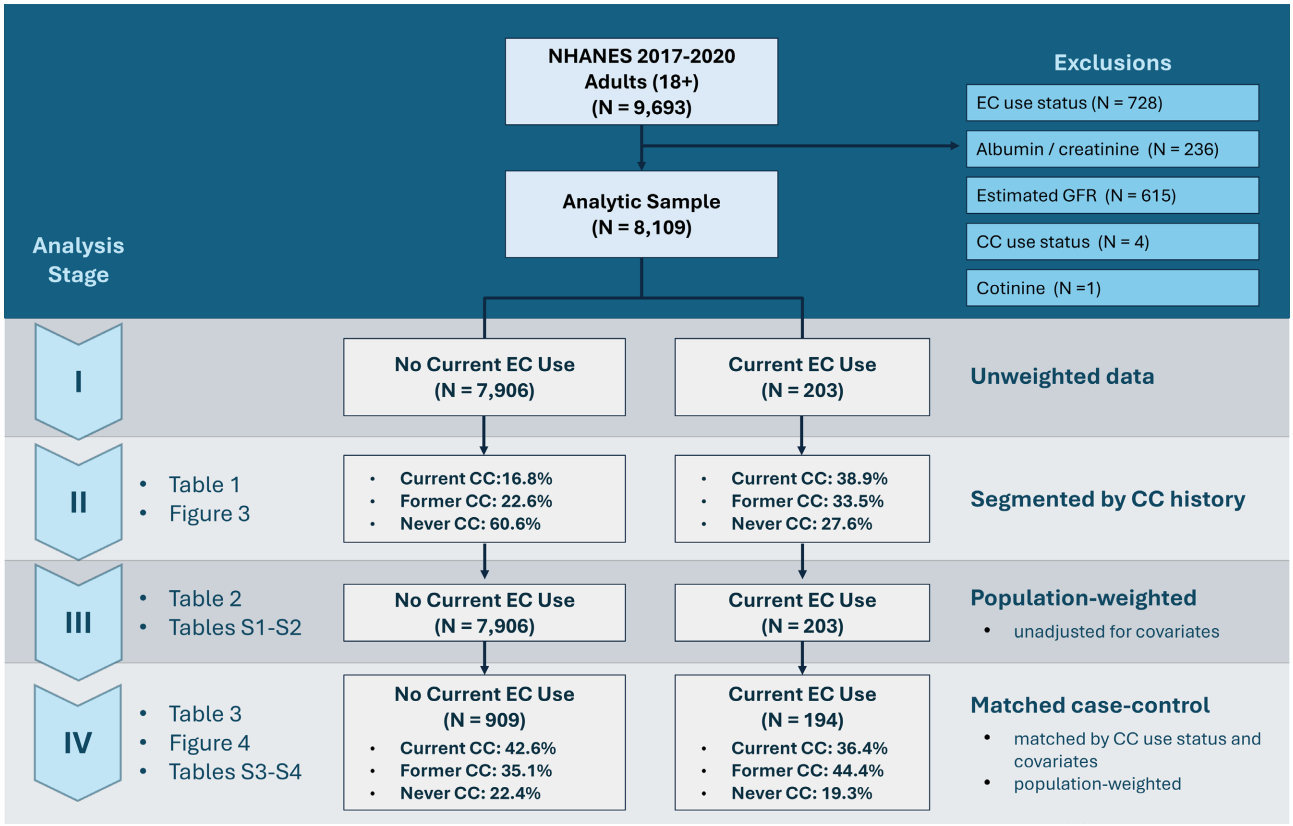


Figure 2. Analysis flow diagram.

symptoms for at least 3 months and a clinical evaluation in addition to the Heat Map metrics.

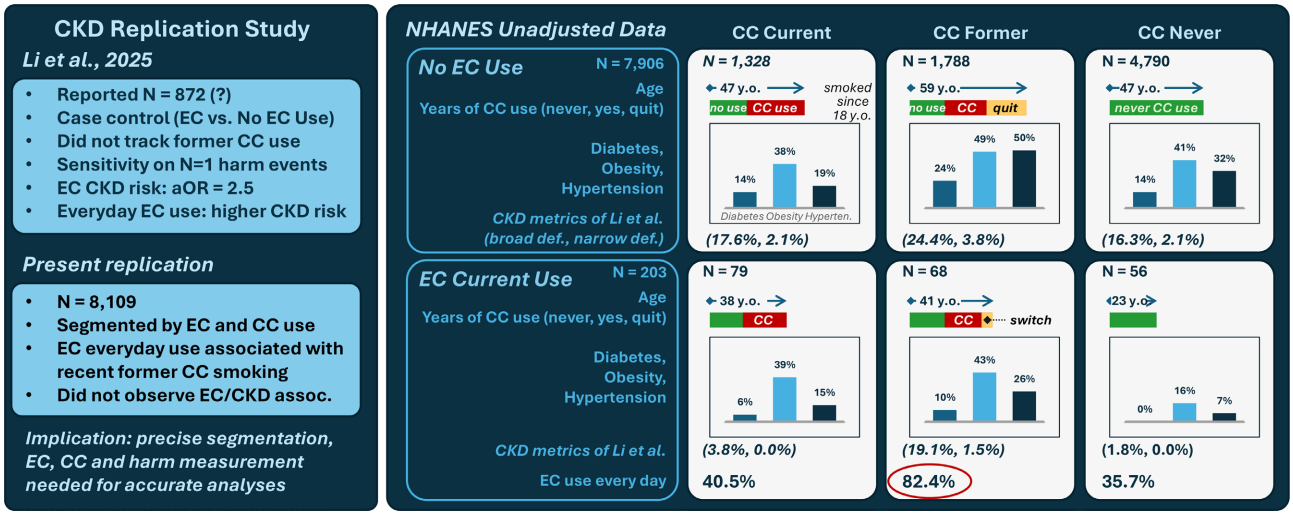
- Li *et al.* utilized two definitions of CKD, which had lower precision (binary scales representing a positive or negative result). In the narrow definition, an albumin/creatinine ratio of 300+ represents a positive result.
- In the broader definition of Li *et al.*, an albumin/creatinine ratio of 30+ or an eGFR < 60 represents a positive result.

3. Results

3.1. Overview

The present replication study involved analyzing the dataset through four stages of adjustments of imbalances between cohorts: I) the unweighted sample, II) the unweighted sample, segmented by CC and EC use, III) the population-weighted sample, and IV) the matched case-control sample.

Figure 3 provides a comparison of the results of the present replication study vs. Li *et al.*, showing differences in sample size generation and precision of segmentation and accounting for former CC use and divergence in the association of EC use with CKD prevalence. Critical differences between segments (in the unadjusted data) are also illustrated in the figure. These differences are discussed further below.



(Left panel) Comparison of results, Li *et al.*, 2025, and the present replication study. (Right panel) Unweighted data segmented by CC use (current, former, never) and EC use. Each white panel represents a segment, including sample size, mean age, mean history of CC use, key, and prevalence of CKD (using the definitions of Li *et al.*). History of CC use is color coded: green represents years of never use, red represents years of CC smoking, and yellow represents years of cessation or switching to EC.

Figure 3. Overview.

3.2. Step I: Unweighted Analytic Sample

An attempt was made to replicate the analysis dataset of the authors. As shown in Figure 2, from a starting sample of N = 9693 adults, the retained analytic sample of N = 8109 consisted of 203 EC-current-users and 7906 non-EC current-users after the exclusions were enumerated owing to missing data. The missing data for the 1584 excluded individuals primarily pertained to EC use status, albumin/creatinine levels, and metrics used to calculate the estimated GFR.

3.3. Step II: Unweighted Sample (Segmented by CC and EC Use)

NHANES unweighted data (*i.e.*, raw data) are provided in Table 1. Consistent with best practices, the sample was segmented by CC and EC use histories. This was necessary to minimize confounding due to the nonindependence of CC and EC use patterns[3].

In the unweighted data, large between-group imbalances existed in the demographic covariates associated with CKD risk. The EC groups had lower rates of diabetes, hypertension and obesity than did the non-EC groups. Segmentation by CC use history revealed additional segment-specific differences. EC users who were previously CC users had stopped smoking much more recently than former CC users who were not EC users (5.3 vs. 20.1 years quit, respectively). Those individuals who had completely switched from CC use to EC use also had much higher rates of daily EC use than did those who were CC dual-users or never-users (82.4% vs. 40.5% and 35.7%, respectively) and were older than CC never-users were (41.3 years old vs. 22.8 years old). Thus, daily EC use was most often observed in cohorts at higher risk for CKD due to non-EC covariates (older age, long-term CC users who had quit in recent years).

Table 1. Unweighted analysis sample (segmented by CC and EC use).

Characteristic		CC Current Use (N = 1407)		CC Former Use (N = 1856)		CC Never Use (N = 4846)	
		EC Non-Use	EC Use	EC Non-Use	EC Use	EC Non-Use	EC Use
Sample size (% of all EC users or nonusers)	N (%)	1328 (16.8%)	79 (38.9%)	1788 (22.6%)	68 (33.5%)	4790 (60.6%)	56 (27.6%)
Age (years)	Mean (SD)	47.4 (15.4)	38.4 (14.2)	58.6 (16.5)	41.3 (16.2)	47.0 (18.5)	22.8 (6.9)
Male (% of column segment)	N (%)	765 (57.6%)	38 (48.1%)	1094 (61.2%)	44 (64.7%)	1955 (40.8%)	39 (69.6%)
Non-Hispanic White	N (%)	493 (37.1%)	47 (59.5%)	828 (46.3%)	41 (60.3%)	1411 (29.5%)	25 (44.6%)
Diabetes diagnosis or medication	N (%)	184 (13.9%)	5 (6.3%)	422 (23.6%)	7 (10.3%)	667 (13.9%)	0 (0.0%)
BMI ≥ 30 kg/m^2	N (%)	501 (38.2%)	30 (38.5%)	859 (48.8%)	29 (42.6%)	1958 (41.4%)	9 (16.1%)
BP, systolic (mm Hg)	N (%)	124.9 (19.3)	116.1 (14.5)	127.7 (19.6)	120.7 (14.7)	122.7 (18.9)	116.3 (12.1)
BP ≥140 mm Hg or antihypertensive medication	N (%)	445 (35.8%)	14 (18.7%)	830 (49.4%)	17 (26.2%)	1421 (32.1%)	4 (7.4%)
Duration of regular CC smoking (years)	Mean (SD)	29.0 (15.8)	21.9 (14.6)	20.9 (14.2)	18.9 (14.6)	N/A	N/A
Current CPD	Mean (SD)	10.8 (8.3)	10.2 (9.6)	N/A	N/A	N/A	N/A
Time quit CC (years)	Mean (SD)	N/A	N/A	20.1 (15.5)	5.3 (7.5)	N/A	N/A
EC use every day (5/5 days)	N (%)	N/A	32 (40.5%)	N/A	56 (82.4%)	N/A	20 (35.7%)
Cotinine Serum (LBXCOT; ng/ml)	Mean (SD)	234.7 (148.8)	218.3 (139.1)	27.6 (105.5)	236.7 (172.7)	10.3 (66.9)	85.6 (96.3)
LBXCOT ≥ 10	N (%)	1262 (95.0%)	75 (94.9%)	221 (12.4%)	61 (89.7%)	291 (6.1%)	37 (66.1%)
Albumin/Creatinine (URDACT, unitless)							
URDACT < 30	N (%)	1137 (85.6%)	76 (96.2%)	1505 (84.2%)	56 (82.4%)	4183 (87.3%)	55 (98.2%)
URDACT 30 - 299	N (%)	163 (12.3%)	3 (3.8%)	215 (12.0%)	11 (16.2%)	508 (10.6%)	1 (1.8%)
URDACT ≥ 300*	**N (%)**	**28 (2.1%)**	**0 (0.0%)**	**68 (3.8%)**	**1 (1.5%)**	**99 (2.1%)**	**0 (0.0%)**
eGFR (mL/min/1.73m^2)							
eGFR < 60	N (%)	72 (5.4%)	0 (0.0%)	253 (14.1%)	2 (2.9%)	290 (6.1%)	0 (0.0%)
eGFR < 60 or URDACT ≥ 30**	**N (%)**	**234 (17.6%)**	**3 (3.8%)**	**436 (24.4%)**	**13 (19.1%)**	**781 (16.3%)**	**1 (1.8%)**
***CKD (narrower definition of Li *et al.*)**	**Unadjusted RR**	***Ref***	**0.00**	***Ref***	**0.39**	***Ref***	**0.00**
****CKD (broader definition of Li *et al.*)**	**Unadjusted RR**	***Ref***	**0.22**	***Ref***	**0.78**	***Ref***	**0.11**

CC: combusted cigarettes; EC: e-cigarettes; CC Current Use: at least 100 lifetime CCs (established use) and use in the past 30 days (current established use); CC Former Use: former established use; CC Never Use: never established use; EC use: use in the past 5 days. BP: systolic blood pressure; BMI: body mass index; CPD: cigarettes per day; CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate (see also Methods and Figure 1).

Li *et al.* utilized two definitions of CKD, both of which are reported in Table 1. A broader definition included individuals with a glomerular filtration rate (GFR) < 60 or an albumin/creatinine ratio ≥ 30. A narrower definition was limited to individuals with an albumin/creatinine ratio ≥ 300. In the raw data, the prevalence of CKD, according to the broader definition, was markedly lower in each EC-using group (vs. the comparator EC nonuse group): current smokers (3.8% vs. 17.6%), former smokers (19.1% vs. 24.4%), and never smokers (1.8% vs. 16.3%). Using this broader definition of CKD, the unadjusted RR for EC users vs. nonusers was 0.22 for CC current users, 0.78 for CC former users, and 0.11 for CC never users. The lower prevalence of CKD in EC users held true for the narrower definition of CKD as well. For EC users, only 1 harm event was reported for CC former-users (RR 0.39 vs. EC nonusers), and no harm events were reported for EC users who were CC current- or never-users (RR 0.00).

The higher rates of CKD-related endpoints in the EC nonusers than in the EC-users were consistent with imbalances in non-EC covariates that are known risk factors for CKD, such as older age and higher rates of diabetes, hypertension and obesity. Additionally, there was a higher rate of CKD-related endpoints in CC former users than in CC current and never users, and this was true for both EC nonusers and EC users.

3.4. Step III: Population-Weighted Data

Population-weighted adjustment is a standard practice for NHANES data, to ensure the findings are generalizable to the broader U.S. population and was used by Li *et al.* It should be noted that this adjustment does not remove all sources of bias, including biases associated with increased as well as decreased risk. While population-weighted data accounted for NHANES oversampling of racial/ethnic minorities, the increased prevalence of non-Hispanic white individuals was narrowed but still persisted for EC users who were CC current and former users (see Table S1, population-weighted data, unadjusted for covariates). In the EC groups, age remained younger, male sex remained more common, and rates of diabetes, hypertension and obesity remained lower than those in the non-EC cohorts. The former CC users had stopped smoking 18.7 years previously in the non-EC group, whereas the EC group had stopped CC use more recently (4.0 ± 5.6 years, indicating many recent CC users).

An attempt was made to replicate the adjusted analyses by Li *et al.* (using the broader definition, Table S2), using weighted, multivariable logistic regression models between CKD and EC use in the entire analytic sample across all smoking statuses. However, the significant effects of EC on CKD could not be replicated (all three models *p*s > 0.05). Instead, when segmented by CC use, the OR of CKD was lower in each of the EC use groups than in the comparable nonuse groups (Table 2). Critically, while p values can be derived, the low number of harm events limits the statistical reliability of the analysis (see also Table S1 for population-weighted data, segmented by CC use status).

Table 2. Univariate associations between current ENDS use and CKD* prevalence.

CC use segment	OR [CI] (EC users vs. EC nonusers)	P value	Number of EC CKD events* in the raw data sample
CC current-users	0.49 [0.12 - 2.05]	0.312	n = 3
CC former-users	0.82 [0.33 - 2.06]	0.659	n = 13
CC never-users	0.02 [0.00 - 0.18]	0.001**	n = 1

NHANES 2017-2020 unadjusted, population-weighted data. *CKD is defined via the broader definition of Li *et al.* (2025). **EC users have significantly lower odds of CKD vs. EC nonusers, but n = 1 harm event in the EC user segment renders this statistic unreliable.

3.5. Step IV: Matched Case-Control Samples

To mitigate the imbalances in covariates between cohorts in the raw data (Table 1), current-, former-, and never-smoking EC users were matched to up to 5 closely matched EC nonusers to serve as a case-control sample. A total of 194 EC users were matched to 909 EC nonusers; their characteristics are summarized in Table 3 (see also Table S3 for segmentation by CC use status and Table S4 for comparisons of unweighted and population-weighted data).

Table 3. Matched and population-weighted case—control samples.

Characteristic		Matched case—control	
		EC nonuse	EC use
Sample size (unweighted)	N	909	194
Age (years)	Weighted mean (SD)	35.8 (14.3)	34.2 (14.4)
Male (% of column segment)	Weighted %	59.3%	62.8%
Non-Hispanic White	Weighted %	70.1%	75.9%
Diabetes diagnosis or medication	Weighted %	6.8%	4.6%
BMI ≥ 30 kg/m^2	Weighted %	37.0%	32.2%
BP, Systolic (mm Hg)	Weighted mean (SD)	117.2 (13.6)	118.3 (13.6)
BP ≥140 mmHg or antihypertensive medication	Weighted %	18.7%	18.7%
Current CC use (%)	Weighted %	42.6%	36.4%
Former CC use (%)	Weighted %	35.1%	44.4%
Never CC use (%)	Weighted %	22.4%	19.3%
Duration of regular CC smoking (years, in current and former CC users)	Weighted mean (SD)	19.8 (13.9)	18.3 (14.0)
Current CPD (years, in current CC users)	Weighted mean (SD)	12.7 (8.6)	11.2 (9.8)
Time quit CC (years, in former CC users)	Weighted mean (SD)	5.5 (7.0)	4.0 (5.6)
EC use every day (5/5 days)	Weighted %	N/A	63.9%
Cotinine Serum (LBXCOT; ng/ml)	Weighted mean (SD)	110.9 (155.4)	211.8 (151.8)
LBXCOT ≥ 10	Weighted %	47.7%	88.5%

Continued

Albumin/Creatinine (URDACT, unitless)			
URDACT < 30	Weighted %	93.1%	91.0%
URDACT 30 - 299	Weighted %	5.9%	8.8%
URDACT ≥ 300*	**Weighted %**	**1.0%**	**0.2%**
eGFR (mL/min/1.73m^2)			
eGFR < 60	Weighted %	0.9%	0.7%
eGFR < 60 or URDACT ≥ 30**	**Weighted %**	**7.4%**	**9.3%**
***CKD (narrower definition of Li *et al.*)**	**Unadjusted RR**	***Ref***	**0.17*****
****CKD (broader definition of Li *et al.*)**	**Unadjusted RR**	***Ref***	**1.26*****

The estimates refer to weighted percentages for categorical variables and weighted means (weighted SDs) for continuous variables. LBXCOT and URDACT are NHANES variables representing cotinine serum levels and the albumin/creatinine ratio in urine, respectively. ***RR (relative risk) calculated on the basis of the prevalence of CKD among EC users divided by the prevalence of CKD among EC nonusers. No formal modeling analysis was conducted due to the limited sample size.

In the matched controls, according to the definitions of Li *et al.*, the RR for CKD was lower for the narrower definition (0.17) but higher for the broader definition (1.26) for EC users than for EC nonusers. According to the KDIGO Heat Map definition of the risk of CKD progression, morbidity or mortality, which is tailored to screening and early detection of CKD, there was no apparent difference between EC users and nonusers. In the EC use cohort, 90.7% of the participants were considered low risk, 8.7% were considered mild to moderate risk, and 0.6% were considered high risk, with no participants in the very high or highest risk groups. In the EC nonuse cohort, 92.6% were considered low risk, 5.9% were considered mild to moderate risk, and 1.5% were considered high, very high, or highest risk (see Figure 4).

3.6. Technical Note

As discussed in the Methods, in 2019 NHANES stopped collecting 30-day EC use and instead only collected 5-day EC use data. Therefore, we used 5-day EC use data as an indicator of EC use frequency in this study. Because the 2017-18 questionnaire asked about both 5-day and 30-day use, it provided a unique opportunity to test the correlation between these databases as well as the reliability of self-reporting of tobacco use. As shown in Supplemental Materials II, the correlation between the two metrics was good but not perfect. Among past 30-day users, past 5-day and 30-day use frequencies were significantly correlated ($r = 0.7840$, $p < 0.001$). Use for 4 - 5, 2 - 3, and 1 of the past 5 days translated to ~24 - 25, ~7 - 10 and ~4 of past 30 days, respectively. Notably, 17% of past 5-day users also reported no use in the past 30 days, and 20% or more who claimed use every day of the past 30 also claimed less than 4 days of use in the past 5 days. These inconsistencies highlight the imprecisions inherent in self-reporting of tobacco use in NHANES (see Tables S5-S7).

A. EC Non-Users (N=909, Matched)

	A1 (<30)	*A2 (30-299)*	*A3 (≥300)*
G1 (GFR ≥90)	667 **(75.99%)**	47 **(4.74%)**	5 **(0.62%)***
G2 (60-90)	152 **(16.63%)**	14 **(0.85%)**	4 **(0.23%)**
G3a (45-60)	3 **(0.30%)**	5 **(0.20%)**	1 **(0.03%)**
G3b (30-45)	3 **(0.15%)**	2 **(0.05%)**	0 **(0.00%)**
G4 (15-30)	0 **(0.00%)**	2 **(0.08%)**	3 **(0.09%)**
G5 (<15)	0 **(0.00%)**	0 **(0.00%)**	1 **(0.03%)**

**Unweighted N (Weighted %)*

B. EC Users (N=194, Matched)

	A1 (<30)	*A2 (30-299)*	*A3 (≥300)*
G1 (GFR ≥90)	145 **(77.03%)**	11 **(6.65%)**	0 **(0.00%)***
G2 (60-90)	32 **(13.69%)**	3 **(1.78%)**	1 **(0.17%)**
G3a (45-60)	1 **(0.28%)**	1 **(0.39%)**	0 **(0.00%)**
G3b (30-45)	0 **(0.00%)**	0 **(0.00%)**	0 **(0.00%)**
G4 (15-30)	0 **(0.00%)**	0 **(0.00%)**	0 **(0.00%)**
G5 (<15)	0 **(0.00%)**	0 **(0.00%)**	0 **(0.00%)**

**Unweighted N (Weighted %)*

C. CKD Risk Stratification

	Unweighted		***Weighted***	
EC Use?	*No*	*Yes*	***No***	***Yes***
Low risk	90.10%	91.23%	**92.62%**	**90.72%**
Mild to moderate risk	7.04%	7.73%	**5.89%**	**8.71%**
High risk	1.87%	1.03%	**1.20%**	**0.56%**
Very high risk	0.55%	0.00%	**0.16%**	**0.00%**
Highest risk	0.44%	0.00%	**0.12%**	**0.00%**

D. CKD Relative Risk**

	Unweighted	***Weighted***
Low risk	1.01	**0.98**
Any increased risk	0.98	**1.26**
High to highest risk	0.36	**0.38**

***EC Users vs. Non-Users*

(Panel A) CKD risk, EC nonusers. (Panel B) CKD risk, EC users. (Panel C) CKD risk, EC users vs. nonusers, stratified by severity of risk. Risk of progression, morbidity and mortality per the CKD Heat Map[4].

Figure 4. CKD risk (matched, covariate-adjusted and population-weighted samples).

4. Discussion

In this replication study, we did not find evidence for an association of EC use with CKD risk across 3 markers (the narrow and broad endpoints of Li *et al.* and the CKD Heat Map). Cross-sectional studies use modeling approaches to account for any imbalances in covariates. In the present study, precise characterization of exposure and segmentation of CC use were critical to minimize confounding between CC and EC use [3].

This replication study was subject to several limitations. First, chronic kidney disease diagnosis requires persistent aberrant eGFR or urine albumin readings for 3 months to rule out acute, reversible conditions, such as transient infections, but the endpoints here were limited to a single acute timepoint [5]. Next, the only EC use measure available in NHANES 2017-2020 was past 5-day use, without duration of use, or 30-day use information. Therefore, dose–response analyses are best addressed via PATH or other databases, which provide more precise measurements of EC use than NHANES does. The lack of tracking of EC duration of use meant that there was no means to determine which came first, the harm event, or EC use. Both the time of diagnosis and the time of starting regular EC use are necessary to establish causality. Finally, there was a minimal number of harm events in the EC group, meaning that sensitivity analyses were not valid in this dataset.

We could not replicate the results of Li *et al.* and noted the following imprecision and deviations from best practices in their analysis:

1) Descriptive data for CKD prevalence were not published by the authors. While the underlying dataset was available from NHANES, the number of calculations and exclusions needed to derive the analysis data indicates that a new dataset was generated. It is central in every cross-sectional study to be able to transparently follow how the raw data were transformed into adjusted odds ratios.

2) The present analysis resulted in a retained analytic sample size of n = 7,139, which was much larger than Li *et al.*'s sample size of n = 872 (n = 684 EC nonusers and n = 188 EC users). One potential explanation for this discrepancy might be failure to account for skip patterns in the survey: some questions are asked in series, where a second question is asked depending on the answer of the first question. Nonanswer to the second question (e.g., current smoking status) is not the same as missing or incomplete data if it is answered in the first question (*i.e.*, never-established smoking). The present replication study carefully accounted for skip patterns, and thus retained an analytic sample that was over eight times larger than the sample of Li *et al.*

3) In unadjusted data, Li *et al.* reported a fourfold higher rate of CKD in EC users than the rate reported in the present analysis but reported a rate in EC nonusers similar to that reported in the present study. In EC nonusers, a CKD rate of 18.6% was reported by Li *et al.* (using their broader definition), and the present analysis reported a similar rate of 18.4%. In EC users, Li *et al.* reported a rate of 33.5%, for a relative risk (RR) of 1.82, whereas we observed a rate of 8.4%, for an RR of 0.46 (see **Table 3** from Li *et al.* and **Table 1** from the present study). We do not have an explanation for how Li *et al.* found so many cases of CKD in the EC user unadjusted data, and believe it may indicate a major error in their analysis.

4) Li *et al.* reported that of 188 EC users, 40.4% used ECs 3 or more days per week, with a minority (the 75th percentile) representing 4 or more days of use per week. In contrast, we observed that 53% of the 203 EC users used them every day of the past 5 days (see **Table 3** from Li *et al.* and **Table 1** from the present study).

5) Li *et al.* reported that granular data were not available about CC use history and consequently omitted critical variables, including years of CC use, former CC use, time quit and CPD; however, these data are readily available (and were included in the present analysis).

6) Because smoking and vaping use patterns are not independent, it is crucial to segment current, former, and never smokers separately in the EC group (and comparatively in the non-EC group) to minimize confounding. As lingering health effects from prior CC use could be misattributed to EC use, EC users who have switched from former smoking should most precisely be compared with former smokers with a similar duration of CC smoking and time quit. Likewise, EC users who dual-use CCs should be compared with exclusive CC smokers who have a similar duration of CC smoking (3). In the present analysis, we more precisely segmented EC users, and demonstrated that frequent EC use was concentrated among older, former long-term smokers with more comorbidities; this further calls the results of Li at al into question, as they did not evaluate this "reverse causality" confounding relationship.

7) Li *et al.* used crude definitions of CKD to obtain binary (yes/no) metrics (see Methods). In trying to replicate the sensitivity analysis of Li *et al.* involving the more stringent definition of CKD, we observed that the EC group had only n = 1 harm event (urine/creatinine ratio > 300 mg/g), rendering the analysis invalid. As a statistical best practice, cross-sectional studies should include only cohorts with a ratio of at least 10 harm events per adjustment variable in the regression model[3]. Furthermore, the CKD Heat Map provides more precise gradations and represents risk more comprehensively, such as the risk of progression to CKD, rather than a definitive diagnosis in the context of the general population, such as NHANES [4].

8) Li *et al.* reported a dose–response relationship between the frequency of EC use and CKD risk. However, this is likely explained by confounding, not a true dose–response effect, as frequent EC use was concentrated within formerly smoking EC users (54/65 = 83%) as opposed to EC users who currently (32/79 = 41%) or never smoked (17/50 = 34%). These former smokers were older and more likely to have comorbidities (**Table 1**).

9) Finally, CKD is, by definition, a chronic condition. The diagnosis of CKD requires sustained aberrant readings for 3 months to exclude transient albuminuria associated with events unrelated to CKD (e.g., infection, fever, vigorous exercise) or acute kidney injury that may be reversed in the near future. Furthermore, without information about the timing of CKD onset vs. the duration of EC use, establishing causality is not possible. In particular, the timing of the onset of CKD and other comorbidities is necessary to identify people who may have switched from CCs to ECs because they were experiencing smoking-related health effects (reverse-causality) and to perform a sensitivity analysis on the inclusion of this population.

This replication study is instructive because it provides examples of common issues that should be considered for more precise and accurate design and analysis of cross-sectional studies of nicotine and tobacco use[3]. For instance, it underscores the potential for errors during the transformation of raw data into population-weighted data. Recent analyses of the NHANES database by authors associated with Research Update have included four studies reporting sample sizes that appear inconsistent with the dataset. To date, two papers have been corrected through retraction by an editorial board; the second retraction followed an expose in *Science*[1] [6]-[9]. Additionally, a widely cited meta-analysis (Glantz *et al.*, 2024) revealed that one of its key conclusions—that ECs are not associated with lower stroke risk than CCs—was dependent on the validity of the most recently retracted study [9] [10].

A second common error is the lack of sufficient segmentation (current vs. former vs. never CC use) to prevent confounding due to the nonindependence of EC and CC use patterns. This study also highlights the need for NHANES to include

[1]Patel, U., Patel, N., Khurana, M., Parulekar, A., Patel, A., Ortiz, J., *et al.* (2022) Retracted: Effect Comparison of E-Cigarette and Traditional Smoking and Association with Stroke—A Cross-Sectional Study of NHANES. Neurology International, 14, 441-452. https://doi.org/10.3390/neurolint14020037

more comprehensive nicotine product use metrics (including duration of use and past 30-day use) in future waves to improve the precision and accuracy of subsequent analyses. Without these data, it is impossible to determine which came first, the harm event, or the start of EC use. Finally, this replication study highlights the importance of transparent and comprehensive disclosure of analyses of cross-sectional studies, providing clear tracking of the transformation from raw data to final adjusted odds ratios. This can help prevent statistically unreliable practices such as performing sensitivity analyses on an insufficient number of harm events and can identify and mitigate potential confounders that might otherwise impact study accuracy. Complete disclosure in the text and supplemental information provides visibility into the exact methods used by the authors and any strengths and limitations of the analysis.

In closing, this replication study highlights how precise segmentation and characterization of exposure to all tobacco products is critical for accurate analysis of cross-sectional studies and suggests metrics for incorporation into future waves of NHANES. The results revealed, within the limitations of the NHANES data set, that frequent EC use was associated with smoking cessation, and suggest that with respect to CKD, electronic cigarettes may serve as a risk reduced alternative when used instead of smoking cigarettes. The important question of whether and under which circumstances nicotine product use induces or reduces the risk of tobacco-related diseases remains relevant and should continue to be studied via precise and accurate methodologies.

5. Data Availability

The NHANES data analyzed in this replication study are publicly available at https://wwwn.cdc.gov/nchs/nhanes/continuousnhanes/default.aspx?Cycle=2017-2020. Additional analyses performed by the authors are available upon reasonable request.

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A preprint for this publication was posted on medRxiv [11]. The corresponding authors of the original study were notified on October 13, 2025, and they were encouraged to provide feedback.

Author Contributions Statement

G.C. wrote the initial draft and generated the figures. G.C., S.K. and A.S. each contributed to the writing, editing and review of the manuscript. S.K. was the lead for the analysis of NHANES data. G.C., S.K. and A.S. each contributed to the review of the data analysis. All the authors have read and approved the manuscript.

Additional Information

Ethics Approval and Consent to Participate

This research was conducted in accordance with the Declaration of Helsinki and

the Belmont Report. IRB review and further consent agreements (beyond those already secured by the CDC in performing the NHANES survey) were not applicable because only publicly available deidentified NHANES data were used (exempt under the U.S. Office of Human Research Protections requirement 45 CFR 46.104(d)(2)), and the study was performed in accordance with the CDC Data User Agreement.

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Competing Interests

G.C. is a salaried employee of the Rose Research Center (RRC), an independent contract research organization that performs studies pertaining to smoking cessation and tobacco harm reduction. The founder of the RRC, Dr. Jed Rose, invented the nicotine patch and performed foundational research leading to varenicline/Chantix. Research support for other projects: National Institute on Drug Abuse; Global Action to End Smoking, Inc. (formerly Foundation for a Smoke-Free World, Inc.), a US nonprofit 501(c)(3) private foundation; Nicotine BRST LLC; JUUL Labs; Altria; Embera Neurotherapeutics, Inc.; Otsuka Pharmaceutical; Swedish Match, Philip Morris International. G.C. was previously a Principal Scientist at JUUL Labs. He was also employed at Nektar Therapeutics, whose pipeline included an inhaled NRT. Stock holdings in Qnovia, a developer of an inhaled NRT, and JUUL Labs.

A.S. and S.K. are employees of Pinney Associates (PA), which consults to Juul Labs, Inc. on nicotine vapor products to advance tobacco harm reduction. A.S. also serves on the advisory board of the Global Forum on Nicotine (GFN) in exchange for travel support to the GFN annual conference and a small honorarium. In addition, in the past 3 years, PA has consulted to Philip Morris International (PMI) solely on US regulatory pathways for non-combustible, non-tobacco, nicotine products. PA does not consult on combustible tobacco products. In the past 3 years, A.S. also consulted on behavioral science to the Center of Excellence for the Acceleration of Harm Reduction (CoEHAR) through ECLAT Srl., which received funding from the Global Action to End Smoking (GA).

Conflicts of Interest

This study was not funded or commissioned by any entities external to RRC or Pinney Associates, and no external entities had any role in or oversight of this work. The opinions expressed by G.C. reflect his personal opinions.

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Supplemental Materials I

Table S1. Population-weighted data, NHANES 2017-2020.

Characteristic		CC Current Use (N = 1407)		CC Former Use (N = 1856)		CC Never Use (N = 4846)	
		EC Non-Use	EC Use	EC Non-Use	EC Use	EC Non-Use	EC Use
Sample size (% of all EC users or nonusers)	**N (%)**	**1328 (16.8%)**	**79 (38.9%)**	**1788 (22.6%)**	**68 (33.5%)**	**4790 (60.6%)**	**56 (27.6%)**
Age (years)	Mean (SD)	44.5 (15.1)	39.3 (13.7)	54.6 (16.1)	35.2 (14.9)	45.9 (17.9)	23.0 (6.1)
Male (% of column segment)	N (%)	53.4%	51.7%	58.1%	71.2%	42.2%	70.8%
Non-Hispanic White	N (%)	62.2%	79.5%	72.2%	80.7%	58.4%	59.1%
Diabetes diagnosis or medication	N (%)	10.6%	3.6%	17.7%	6.8%	10.6%	0.0%
BMI ≥ 30 kg/m^2	N (%)	35.5%	34.4%	47.7%	36.3%	41.5%	12.7%
BP, systolic (mm Hg)	N (%)	122.2	116.8	124.8	120.7	120.3	115.5
BP ≥140 mm Hg or antihypertensive medication	N (%)	29.8%	19.3%	39.3%	24.5%	26.8%	4.5%
Duration of regular CC smoking (years)	Mean (SD)	26.9 (15.1)	23.5 (14.0)	19.0 (13.4)	14.2 (12.6)	N/A	N/A
Current CPD	Mean (SD)	11.9 (8.3)	10.8 (9.5)	N/A	N/A	N/A	N/A
Time quit CC (years)	Mean (SD)	N/A	N/A	18.7 (15.1)	4.0 (5.6)	N/A	N/A
EC use every day (5/5 days)	N (%)	N/A	46.2%	N/A	84.5%	N/A	48.0%
Cotinine Serum (LBXCOT; ng/ml)	Mean (SD)	226.8 (148.2)	219.2 (127.0)	26.8 (103.2)	247.7 (162.7)	7.8 (55.5)	100.0 (104.5)
LBXCOT ≥ 10	N (%)	93.8%	96.6%	12.7%	90.6%	4.7%	68.5%
Albumin/Creatinine (URDACT, unitless)							
URDACT < 30	N (%)	90.2%	93.8%	88.8%	85.9%	90.1%	99.7%
URDACT 30 - 299	N (%)	7.9%	6.2%	9.0%	13.7%	8.5%	0.3%
URDACT ≥ 300*	**N (%)**	**1.9%**	**0.0%**	**2.2%**	**0.4%**	**1.4%**	**0.0%**
eGFR (mL/min/1.73m^2)							
eGFR < 60	N (%)	3.2%	0.0%	9.2%	1.5%	4.7%	0.0%
eGFR < 60 or URDACT ≥ 30**	**N (%)**	**12.0%**	**6.2%**	**17.4%**	**14.7%**	**13.0%**	**0.3%**
***CKD (narrower definition of Li *et al.*)**	**Unadjusted RR**	***Ref***	**0.00**	***Ref***	**0.18**	***Ref***	**0.00**
****CKD (broader definition of Li *et al.*)**	**Unadjusted RR**	***Ref***	**0.52**	***Ref***	**0.84**	***Ref***	**0.02**

CC: combusted cigarettes; EC: e-cigarettes; CC Current Use: at least 100 lifetime CCs (established use) and use in the past 30 days (current established use); CC Former Use: former established use; CC Never Use: never established use; EC use: use in the past 5 days. BP: systolic blood pressure; BMI: body mass index; CPD: cigarettes per day; CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate (see Methods and Figure 1).

Table S2. Replication of Li *et al.*, using non case-control sample before matching (unbalanced for CC current and former use history).

Statistical Model	Adjusted for*	OR [CI]	P-value
Model 1	Age, gender, race	1.32 (0.56 - 3.13)	0.508
Model 2	Model 1 + BMI	1.33 (0.56 - 3.19)	0.497
Model 3	Model 2 + diabetes, hypertension, current smoking	1.40 (0.58 - 3.41)	0.431

OR (odds ratio); CI (confidence interval) CC (combustible cigarettes). *OR adjustments: Age, BMI: continuous variables; diabetes, hypertension: binary variables; current smoking: modified the smoking status variable into current vs. former or never smoking.

Table S3. Matched and population-weighted case-control samples (segmented by CC and EC use).

Characteristic		CC Current Use (N = 446)		CC Former Use (N = 365)		CC Never Use (N = 292)	
		EC Non-Use	EC Use	EC Non-Use	EC Use	EC Non-Use	EC Use
Sample size (% of all EC users or nonusers)	**N (unweighted %)**	**371 (40.8%)**	**75 (38.7%)**	**300 (33.0%)**	**65 (33.5%)**	**238 (26.2%)**	**54 (27.8%)**
Age (years)	Weighted mean (SD)	39.0 (13.7)	38.6 (13.7)	39.8 (14.2)	35.4 (15.0)	23.5 (6.8)	23.1 (6.2)
Male (% of column segment)	Unweighted N (weighted %)	215 (52.2%)	36 (49.8%)	179 (60.7%)	41 (70.4%)	156 (70.6%)	37 (69.6%)
Non-Hispanic White	Unweighted N (weighted %)	218 (76.2%)	44 (77.8%)	115 (65.3%)	39 (80.7%)	109 (66.0%)	25 (61.4%)
Diabetes diagnosis or medication	Unweighted N (weighted %)	25 (5.8%)	5 (4.0%)	43 (12.2%)	7 (7.0%)	0 (0.0%)	0 (0.0%)
BMI ≥ 30 kg/m^2	Unweighted N (weighted %)	134 (35.6%)	30 (38.0%)	150 (51.4%)	28 (35.8%)	44 (17.0%)	9 (13.2%)
BP, systolic (mm Hg)	Weighted mean (SD)	117.8 (13.7)	116.8 (14.1)	119.2 (14.1)	120.7 (14.1)	113.2 (12.1)	115.5 (10.6)
BP ≥ 140 mm Hg or antihypertensive medication	Unweighted N (weighted %)	83 (22.1%)	14 (19.3%)	92 (23.7%)	17 (24.5%)	5 (4.3%)	4 (4.5%)
Duration of regular CC smoking (years)	Unweighted N (weighted %)	22.2 (14.4)	23.1 (14.2)	16.9 (12.6)	14.4 (12.6)	N/A	N/A
Current CPD	Unweighted N (weighted %)	12.7 (8.6)	11.2 (9.8)	N/A	N/A	N/A	N/A
Time quit CC (years)	Unweighted N (weighted %)	N/A	N/A	5.5 (7.0)	4.0 (5.6)	N/A	N/A
EC use every day (5/5 days)	Weighted mean (SD)	N/A	30 (47.4%)	N/A	53 (84.1%)	N/A	19 (48.4%)
Cotinine Serum (LBXCOT; ng/ml)	Unweighted N (weighted %)	228.8 (149.0)	227.9 (130.0)	34.1 (106.2)	248.0 (164.5)	6.8 (38.6)	98.1 (99.8)
LBXCOT ≥ 10	N (%)	349 (92.1%)	71 (96.2%)	67 (19.2%)	58 (90.3%)	23 (7.8%)	36 (69.6%)
Albumin/Creatinine (URDACT, unitless)							
URDACT < 30	N (%)	335 (93.0%)	72 (93.1%)	268 (92.7%)	53 (85.5%)	222 (93.8%)	53 (99.7%)
URDACT 30-299	N (%)	32 (5.8%)	3 (6.9%)	23 (6.1%)	11 (14.1%)	15 (5.7%)	1 (0.3%)

Continued

URDACT ≥ 300*	**N (%)**	**4 (1.1%)**	**0 (0.0%)**	**9 (1.2%)**	**1 (0.4%)**	**1 (0.5%)**	**0 (0.0%)**
eGFR (mL/min/1.73 m^2)							
eGFR < 60	N (%)	4 (0.5%)	0 (0.0%)	16 (2.1%)	2 (1.5%)	0 (0.0%)	0 (0.0%)
eGFR < 60 or URDACT ≥ 30**	**N (%)**	**37 (7.2%)**	**3 (6.9%)**	**37 (8.4%)**	**13 (15.1%)**	**16 (6.2%)**	**1 (0.3%)**
***CKD (narrower definition of Li *et al.*)**	**Unadjusted RR*****	***Ref***	**0.00**	***Ref***	**0.33**	***Ref***	**0.00**
****CKD (broader definition of Li *et al.*)**	**Unadjusted RR*****	***Ref***	**0.96**	***Ref***	**1.80**	***Ref***	**0.05**

***RR calculated based on the prevalence of CKD among EC users divided by the prevalence of CKD among EC nonusers. No formal modeling analysis was conducted due to the limited sample size.

Table S4. Matched, population-weighted case-control samples (unweighted sample sizes are also shown for comparative purposes)

Characteristic		Matched Case-Control	
		EC Non-Use	EC Use
Sample size (% of all EC users or nonusers)	N (%)	909	194
Age (years)	Weighted mean (SD)	35.8 (14.3)	34.2 (14.4)
Male (% of column segment)	Unweighted N (weighted %)	550 (59.3%)	114 (62.8%)
Non-Hispanic White	Unweighted N (weighted %)	442 (70.1%)	108 (75.9%)
Diabetes diagnosis or medication	Unweighted N (weighted %)	68 (6.8%)	12 (4.6%)
BMI ≥ 30 kg/m^2	Unweighted N (weighted %)	328 (37.0%)	67 (32.2%)
BP, systolic (mm Hg)	Weighted mean (SD)	117.2 (13.6)	118.3 (13.6)
BP ≥ 140 mm Hg or antihypertensive medication	Unweighted N (weighted %)	180 (18.7%)	35 (18.7%)
Current CC use (%)	Unweighted N (weighted %)	371 (42.6%)	75 (36.4%)
Former CC use (%)	Unweighted N (weighted %)	300 (35.1%)	65 (44.4%)
Never CC use (%)	Unweighted N (weighted %)	238 (22.4%)	54 (19.3%)
Duration of regular CC smoking (years)	Unweighted N (weighted %)	19.8 (13.9)	18.3 (14.0)
Current CPD	Unweighted N (weighted %)	12.7 (8.6)	11.2 (9.8)
Time quit CC (years)	Unweighted N (weighted %)	5.5 (7.0)	4.0 (5.6)
EC use every day (5/5 days)	Weighted mean (SD)	N/A	102 (63.9%)
Cotinine Serum (LBXCOT; ng/ml)	Unweighted N (weighted %)	110.9 (155.4)	211.8 (151.8)
LBXCOT ≥ 10	N (%)	439 (47.7%)	165 (88.5%)
Albumin/Creatinine (URDACT, unitless)			
URDACT < 30	N (%)	825 (93.1%)	178 (91.0%)
URDACT 30-299	N (%)	70 (5.9%)	15 (8.8%)
URDACT ≥ 300*	**N (%)**	**14 (1.0%)**	**1 (0.2%)**
eGFR (mL/min/1.73m^2)			
eGFR < 60	N (%)	20 (0.9%)	2 (0.7%)

Continued

eGFR < 60 or URDACT ≥ 30**	**N (%)**	**90 (7.4%)**	**17 (9.3%)**
***CKD (narrower definition of Li *et al.*)**	**Unadjusted RR*****	***Ref***	**0.17***
****CKD (broader definition of Li *et al.*)**	**Unadjusted RR*****	***Ref***	**1.26***

Note: estimates refer to unweighted N (weighted %) for categorical variables and the weighted mean (weighted SD) for continuous variables. ***Calculated based on the prevalence of CKD among EC users divided by the prevalence of CKD among EC nonusers. No formal modeling analysis was conducted due to the limited sample size.

Supplemental Materials II

Association of electronic cigarette use with chronic kidney disease in NHANES 2017-2020: A cross-sectional replication study

Supplemental Materials II: 5-day vs. 30-day self-reported ENDS use, NHANES 2017-2018

Methods

A total of 9254 participants were recruited for NHANES 17-18 data collection. Past 30-day and past 5-day ENDS use status were available for 5532 participants. The binary measures of past 30- and 5-day, as well as the use frequency were analyzed within-participant to assess any inconsistencies.

Results

Out of 5532 participants, 290 reported past 30-day use (unweighted: 5.2%; weighted: 6.4%), while 103 reported past 5-day use (unweighted: 1.9%; weighted: 2.4%, Figure S1). However, of these past 5-day users, 17 of the 103 also reported that they had not used ENDS in the past 30 days (unweighted: 16.5%; weighted: 17.5%), which is self-contradictory. Despite this inconsistency, past 30- and 5-day use were moderately correlated (phi coefficient = 0.48).

		Past 5-day EC users	
	Past 5-day use / ***Past 30-day use***	***No***	***Yes***
Past 30-day EC users	***No***	**n = 5,225** (96.2% / 95.4%)*	**n = 17** (16.5% / 17.5%)
	Yes	**n = 204** (3.8% / 4.6%)	**n = 86** (83.5% / 82.5%)
	Total	**n = 5,429** (100% / 100%)	**n = 103** (100% / 100%)

*Unweighted N, (unweighted column % / weighted column %)

Figure S1. Cross-tabulation between past 30-day and past 5-day use.

To investigate the apparent inconsistency further, we examined participants' ENDS use frequencies in the past 5 and 30 days (Figure S2). Among past 30-day users, past 5-day and 30-day use frequencies were significantly correlated ($r = 0.7840$, $p < 0.001$). Past 5-day use appears to cluster in predictive value for 30-day use, as those reporting 4+ day use in the past 5 days were estimated to have used 24+ days in the past 30 days. However, internal inconsistencies continued to emerge, such as all 30-day users reporting fewer than all 5-day use. Table S5 summarizes the readily identifiable instances of temporal contradictions.

Conclusion

In NHANES, the past 5-day and past 30-day measures demonstrated an expected correlation, suggesting that either metric would allow a reasonably accurate approximation of ENDS use behavior when only one is available. Nonetheless, the presence of noticeable inconsistencies between the two timeframes introduces a substantial uncertainty. Future iterations of NHANES would benefit from collecting both 5-day and 30-day measures as each represents distinct aspects of recent ENDS use behavior. Furthermore, an embedded form of internal quality control may be able to detect and resolve such inconsistencies in real time, enhancing data quality and confidence in the insights they may generate.

Past 5-day EC users (n=103)

Past 30-day EC users (n=289)	Past 5-day use / Past 30-day use	0 days	1 day	2 days	3 days	4 days	5 days
	0 days	n=5,225	7	4	3	0	3
	1-4 days	149	6	3	4	0	3
	5-9 days	19	2	2	3	0	0
	10-14 days	9	3	1	0	0	1
	15-19 days	10	1	1	2	1	3
	20-24 days	4	0	2	0	2	2
	25-29 days	1	0	0	0	1	1
	30 days	11	0	2	1	3	36
	Unweighted mean (days/30d)	**0.2**	**3.7**	**9.7**	**6.5**	**24.2**	**24.7**
	Weighted mean (days/30d)	**0.2**	**2.7**	**7.3**	**6.0**	**26.2**	**25.1**

Figure S2. Past 5-day patterns of use among past 30-day ENDS users.

Table S5. Temporal inconsistencies between past 5-day and 30-day ENDS use.

Type of Inconsistency	Frequencies	Unweighted %	Weighted %
Past 5-day user reported no past 30-day use	17/103	16.5%	17.5%
Past 30-day non-user reported past 5-day use	17/5242	0.3%	0.4%
Past 30/30-day users used < 5/5 days	17/53	32.1%	26.6%
Past 30/30-day users used < 4/5 days	14/53	26.0%	19.9%
Past 20+/30-day users used 0/5 days	16/66	24.2%	21.7%