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Prevalence of Cigarette Smoking among Patients with Different Histologic Types of Kidney Cancer

Ted Gansler¹, Stacey A. Fedewa¹, W. Dana Flanders², Lori A. Pollack³, David A. Siegel³, Ahmedin Jemal¹

¹Intramural Research, American Cancer Society, Atlanta, Georgia.

²Departments of Biostatistics and Epidemiology, Rollins School of Public Health, Emory University, Atlanta, Georgia.

³Division of Cancer Prevention and Control, Centers for Disease Control and Prevention, Atlanta, Georgia.

Abstract

Background: Cigarette smoking is causally linked to renal cell carcinoma (RCC). However, associations for individual RCC histologies are not well described. Newly available data on tobacco use from population-based cancer registries allow characterization of associations with individual RCC types.

Methods: We analyzed data for 30,282 RCC cases from 8 states that collected tobacco use information for a National Program of Cancer Registry project. We compared the prevalence and adjusted prevalence ratios (aPR) of cigarette smoking (current vs. never, former vs. never) among individuals diagnosed between 2011 and 2016 with clear cell RCC, papillary RCC, chromophobe RCC, renal collecting duct/medullary carcinoma, cyst-associated RCC, and unclassified RCC.

Corresponding Author: Ted Gansler, American Cancer Society, 250 Williams Street, Atlanta, GA 30303-1002. Phone: 321-613-2182; ted.gansler@cancer.org.

Authors' Contributions

Conception and design: T. Gansler, S.A. Fedewa, L.A. Pollack

Development of methodology: T. Gansler, L.A. Pollack, D.A. Siegel

Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): L.A. Pollack

Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): T. Gansler, S.A. Fedewa, W.D. Flanders, L.A. Pollack, D.A. Siegel, A. Jemal

Writing, review, and/or revision of the manuscript: T. Gansler, S.A. Fedewa, W.D. Flanders, L.A. Pollack, D.A. Siegel, A. Jemal

Study supervision: L.A. Pollack

Other (interpretation of data): D.A. Siegel

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Disclosure of Potential Conflicts of Interest

W.D. Flanders is an owner of Epidemiologic Research & Methods. No potential conflicts of interest were disclosed by the other authors.

Results: Of 30,282 patients with RCC, 50.2% were current or former cigarette smokers. By histology, proportions of current or former smokers ranged from 38% in patients with chromophobe carcinoma to 61.9% in those with collecting duct/medullary carcinoma. The aPRs (with the most common histology, clear cell RCC, as referent group) for current and former cigarette smoking among chromophobe RCC cases (4.9% of our analytic sample) were 0.58 [95% confidence interval (CI), 0.50–0.67] and 0.88 (95% CI, 0.81–0.95), respectively. Other aPRs were slightly increased (papillary RCC and unclassified RCC, current smoking only), slightly decreased (unclassified RCC, former smoking only), or not significantly different from 1.0 (collecting duct/medullary carcinoma and cyst-associated RCC).

Conclusions: Compared with other RCC histologic types, chromophobe RCC has a weaker (if any) association with smoking.

Impact: This study shows the value of population-based cancer registries' collection of smoking data, especially for epidemiologic investigation of rare cancers.

Introduction

Cigarette smoking has been causally linked to cancers of the kidney and renal pelvis. It is estimated that cigarette smoking is responsible for approximately 17.4% of kidney, renal pelvis, and ureter cancer cases in the United States (1). According to a recent meta-analysis of 24 studies, the risk of developing renal cell carcinoma (RCC), the most common type of kidney cancer, was 36% higher in current smokers and 16% higher in former smokers compared with the risk in never smokers (2).

The association of smoking with the development of individual RCC histologic types, however, has not been well characterized. Two previous studies have suggested that incidence of chromophobe RCC is less impacted by smoking, if at all (3, 4). Furthermore, no studies, to our knowledge, specifically examined the associations of smoking with renal collecting duct carcinoma, renal medullary carcinoma, and cyst-associated RCC. Because these cancers are uncommon, there are challenges to using existing prospective cohorts or even pooled cohort data to address this question. Supplementing large population-based registries, such the Centers for Disease Control and Prevention's (CDC's) National Program of Cancer Registries (NPCR) with information about common exposures represents a novel approach to studying associations of these risk factors with rare cancers.

Risk factor exposures, including tobacco use, are not routinely collected by cancer registries in the United States. As part of a special study, however, 10 of the CDC's NPCR registries have been abstracting smoking history from medical records of patients with cancer diagnosed since 2011. A recent evaluation by Siegel and colleagues showed the capture of tobacco use to be at an acceptable level of completeness for use in epidemiology (5, 6). Herein, we examine whether the prevalence of cigarette smoking differs among individuals diagnosed between 2011 and 2016 with clear cell RCC, papillary RCC, chromophobe RCC, unclassified RCC, renal collecting duct or medullary carcinoma, and cyst-associated RCC. This work was undertaken to focus further exploration into the etiologic heterogeneity of renal malignancy, and as an example of the value of including exposure information in cancer registry data.

Materials and Methods

Study participants

Data were collected from the Enhancing Cancer Registry Data for Comparative Effectiveness Research (CER) Project, which was supported through the CDC's NPCR program. The following population-based cancer registries of the NPCR program participated in the CER project, covering the following geographic areas: Alaska, Colorado, Idaho, Louisiana, New Hampshire, North Carolina, Rhode Island, and Texas, as well as 13 counties of the Sacramento region of California and 5 metropolitan counties of Miami in Florida (5, 6). This project was approved by the CDC institutional review board and conducted in accordance with the United States Common Rule. Patient consent was not required because the data were deidentified before they were submitted to the CDC.

Inclusion and exclusion

Cases of first and subsequent histologically confirmed malignant renal parenchymal (ICD-10 code C64.9) neoplasms diagnosed from 2011 through 2016 were selected from the 10 state registries with enhanced tobacco use data collection. We included a limited number of histologic categories based on International Classification of Diseases for Oncology, third edition (ICDO-3) codes (7): clear cell RCC (8310), papillary RCC (8050, 8260), chromophobe RCC (8317), unclassified RCC (8312), renal collecting duct carcinoma or renal medullary carcinoma (8319, 8510), and cyst-associated RCC (8316). Other histologies were excluded because they were too rare for sufficiently precise analyses even in this large dataset. Although renal collecting duct carcinoma (carcinoma of the collecting ducts of Bellini) and renal medullary carcinoma are defined individually in the 2004 World Health Organization (WHO) classification, they are considered together in this study because the WHO assigned the same ICDO-3 code to both entities (8). Although 8319 is the recommended code for renal medullary carcinoma, we also included cases coded as 8510 (medullary carcinoma, NOS) because this code is very unlikely to have been used for any other renal malignancy and because this inclusion increased the number of cases of this entity by approximately 21%.

We excluded cases that were coded as sarcomatoid RCC (8318) because the 2004 and 2016 WHO classifications do not consider sarcomatoid RCC as a specific type of RCC, but instead as a secondary change that can occur in RCC with various histologic types (for example, clear cell RCC with focal sarcomatoid change). Similarly, cases coded as granular RCC (8320) were excluded because this is considered an obsolete diagnosis and is not included in the 2004 and 2016 WHO classifications (8, 9). Patients younger than 30 years were excluded because of few cases in this group and because it is unlikely that their cancers would have been attributable to cigarette smoking. The latency for most carcinogens is a period of decades and including cases with shorter times since their initial exposure would bias measures of association toward the null (10, 11). To limit the impact of nonresponse bias possibly associated with smoking status (i.e., more complete data for smokers than nonsmokers) we examined the completeness of smoking data from each registry during each year from 2011–2016 and only included cases from registry-year combinations having at least 75% completeness. Two of the ten registries did not meet this requirement during any

of these years. One registry met this requirement for 2016 only, 1 did for 2015–2016, 1 did for 2014 and 2016, 1 did for 2014–2016, 2 did for 2012–2016, and 2 did for 2011–2016. Cases with missing data regarding cigarette smoking were also excluded.

Of the initial 109,436 cases of renal parenchymal malignancy recorded in the 10 registries during 2011–2016, 87,685 remained after exclusions of cancers not histologically confirmed, cancers with histologies other than those noted above, and patients younger than 30 years. After an additional 52,493 cases were excluded because they were from registry-year combinations with <75% completeness of cigarette smoking data, and an additional 4,910 were excluded because of individual-level missing data on cigarette smoking status, 30,282 participants remained in the analytic sample (Fig. 1).

Outcome and independent variables

The primary outcome was histologic type of renal malignancy.

The main independent variable was cigarette smoking status at diagnosis, abstracted from information documented in the medical records and coded by registrars according to a standard protocol (5) as current, former (initial abstraction distinguished 3 categories—cessation within 1 year of diagnosis, cessation before that time, and unknown time since cessation—which were combined for this study), or never. Additional independent variables included year of diagnosis; patient age, sex, and race/ethnicity (Non-Hispanic White, Non-Hispanic Black, Non-Hispanic American Indian/Alaska Native, Non-Hispanic Asian Pacific Islander, Hispanic, and Non-Hispanic Other/Unknown).

Data analysis

Records for patients diagnosed with cancer of the kidney, renal pelvis, or ureters from 2011 through 2016 were extracted from records of the 10 participating registries using SEER*Stat version 8.3.2 (<https://seer.cancer.gov/seerstat/>). We refined the case selection and performed bivariate statistical analyses with SPSS Statistics version 24. χ^2 tests and the corresponding two-tailed *P* values with a significance level at 0.05 were used to examine potential associations of RCC histology with the independent variables noted above. Prevalence ratios (PR) of former and current smoking and 95% confidence intervals (CI) were computed for papillary RCC, chromophobe RCC, cyst-associated RCC, renal collecting duct/medullary carcinoma, and unclassified RCC cases relative to clear cell RCC (the most common RCC histology) in separate log-binomial models for each of these histologies, using SAS, version 9.3. Adjusted prevalence ratios (aPR) were estimated and accounted for patient age, sex, and race/ethnicity. To account for potential clustering of these patient sociodemographic characteristics within a state, we conducted a sensitivity analysis using multilevel log-binomial models accounting for state as a variable as well as clustering within states.

In bias analyses, we examined the potential impact of missing cigarette smoking status on results by varying the probability of current and former cigarette smoking according to histology. For example, 13% of chromophobe cases were missing cigarette smoking status and in the bias analyses, we assigned proportions (0 to 1 by 0.05 increments) that these 13% missing were indeed current smokers. If 50% of those missing smoking data were in

fact current smokers, the observed percentage (9%) increased to 10%. The same process was repeated for clear cell cases (the referent group) and resultant unadjusted PRs were computed.

Results

Study participants and characteristics, 2011–2016

Supplementary Table S1 shows the demographic and clinical characteristics of individuals who were included or excluded based on the criteria of 75% or greater completeness of cigarette smoking data for state and year combinations, and availability of individual-level cigarette smoking information (among cases from state-year combinations with completeness 75%). Between 2011 and 2016, the percentage of cases excluded decreased from 75.2% to 31.8% as more states met the 75% threshold. The distribution of cases by demographic and clinical characteristics between included and excluded groups were generally similar except that the proportions of Hispanics and Asians are higher, and the proportion of whites is lower in the excluded group compared to the included group. The demographic and clinical characteristics of groups with and without individual-level smoking information are generally similar except that the proportion of unclassified RCC is higher in the group without individual-level information compared to those with individual-level information.

Characteristics of the analytic sample are summarized in Table 1. More than three fourths (77.7%) were ages 50–79, 63.7% were male, and 70.9% were non-Hispanic whites. Compared with younger individuals, those older than 60 years were more likely to be former smokers and less likely to be current smokers. Females were much more likely than males to be never smokers. In comparison with non-Hispanic white and non-Hispanic black participants, non-Hispanic Asians/Pacific Islanders, and Hispanics were more likely to be never smokers and non-Hispanic American Indians/Alaska Natives were less likely. The number of cases meeting all inclusion criteria increased steadily over time from 2,881 during 2011 to 9,040 during 2016.

Bivariate associations of demographic factors and cigarette smoking with kidney cancer histology

Overall, a majority (58.9%) of included kidney cancers were clear cell histology. Unclassified, papillary, and chromophobe RCC comprised 21.5%, 13.9%, and 4.9%, respectively, with cyst-associated RCC and collecting duct/medullary cancers representing less than 1%, together (Table 2).

The most noteworthy component of the statistically significant ($P < 0.001$) association of cigarette smoking and histology concerned chromophobe carcinomas, in which the percentage of never smokers among cases was the highest (62.0%) and the percentages of current and former smokers were the lowest (10.4% and 27.6%, respectively) of all histologic types. The percentages of never smokers for the other histologies ranged from 38.1% (collecting duct/medullary carcinomas) to 50.4% (unclassified RCC).

Differences in the proportions of various kidney cancer histologies by diagnosis year were relatively small but were statistically significant ($P < 0.001$) because of the very large sample size. There were significant ($P < 0.001$) associations with age at diagnosis, with percentages of clear cell RCC and especially chromophobe RCC inversely associated with age. Although more males than females were diagnosed with all histologic types (shown as column percentages in Table 2), their distribution varied significantly by sex ($P < 0.001$). Clear cell and especially chromophobe types were noteworthy in that they comprised a substantially higher percentage of cases among females than among males (row percentages in Table 2). Race/ethnicity was also significantly associated with histology ($P < 0.001$), with the most notable result being a particularly high proportion of papillary cancers (32.4%) and low proportion of clear cell cancers (39.6%) among non-Hispanic blacks.

Independent associations of demographic factors and cigarette smoking with kidney cancer histology

The aPRs for current and former smoking (determined in separate models) among persons diagnosed with chromophobe RCC (with clear cell RCC as the referent group) were 0.58 (95% CI, 0.50–0.67) and 0.88 (95% CI, 0.81–0.95), respectively (Table 3). Relative to clear cell RCC, the aPRs for unclassified RCC were 1.10 (95% CI, 1.04–1.17) for current smoking and 0.93 (95% CI, 0.89–0.97) for former smoking. The aPRs for papillary RCC cases were 1.12 (95% CI, 1.04–1.20) for current smoking and 0.97 (95% CI, 0.92–1.01) for former smoking. Thus, chromophobe RCC was the only histology with statistically significant aPRs for current and former smoking that were both in the same direction, that is, lower than 1.0, indicating a weaker association with smoking relative to clear cell RCC.

A sensitivity analysis (Supplementary Table S2) using multilevel log-binomial models to account for potential clustering of patient sociodemographic characteristics within a state yielded results that were nearly identical to those shown in Table 3.

Bias analysis

As shown in Supplementary Table S3, nondifferential selection did not account for the observed PRs. The differential classification of cigarette smoking/missing would have to be extreme to drive the observed point estimates to the null. For example, if all of the 13% of chromophobe cases with missing cigarette smoking information were current smokers and all of the 13% of clear cell RCC cases were nonsmokers, the prevalence ratio of current smoking for chromophobe RCC would still be less than 1.

Discussion

In this study of kidney cancer cases from 10 state cancer registries that expanded collection of tobacco use information as part of a pilot project of the CDC, there were prominent differences in cigarette smoking status between patients with chromophobe cancers and those with other kidney cancer histologies. Although never smokers comprised between 21.8% and 50.4% of other histologic categories, 62.0% of patients with chromophobe cancers were never smokers. Comparisons of logistic models for the adjusted associations of cigarette smoking status with kidney cancer histology (relative to clear cell RCC) confirm

significant differences by histology, with chromophobe RCC having an aPR for current smoking of 0.58 (95% CI, 0.50–0.67). This result indicates that compared to never smokers, current cigarette smokers are less likely to have chromophobe RCC than clear cell RCC and is in agreement with the significantly lower prevalence of smoking among patients with chromophobe RCC relative to other kidney cancer histologies reported by Patel and colleagues and in one of the 2 datasets analyzed by Purdue and colleagues (3, 4).

Purdue and colleagues analyzed data from 2 RCC case–control studies with a total of 2,314 cases. In their combined case–control analysis, smoking was not significantly associated with odds of developing any of the RCC types they examined (clear cell, papillary, chromophobe, other/NOS). When they analyzed data from the U.S. and European studies separately, the former (but not the latter) demonstrated this association for all types except chromophobe RCC. Moreover, their case-only analysis indicated that smoking prevalence was significantly lower among cases with chromophobe RCC than among those with clear cell RCC (4). In a second case–control study that included 705 cases of nonfamilial RCC, Patel and colleagues reported that the prevalence of current smoking was lower in patients diagnosed with chromophobe RCC (6%) than among those with clear cell (23%) or papillary (26%) RCC or even benign renal lesions (14%), and that current smoking was significantly associated with clear cell and papillary RCC, but not chromophobe RCC (relative to benign lesions) in multivariable analyses (3).

The agreement of this study with two prior reports supports the quality of smoking data recorded in this CDC NPCR pilot study (5), and the value of recording selected exposure information in cancer registries.

One obvious strength of this study is the very large number of cases (nearly 10-fold more than any of the previous studies of smoking and chromophobe RCC). The main limitation is the incompleteness of data abstracted from patient medical records regarding smoking status. However, despite this information being available from 56,303 of 87,685 (64.2%) of cases overall, we addressed this challenge by including cases only from registry-year combinations with relatively good levels of completeness (at least 75%) so that completeness of cigarette smoking information in the analytic sample was 86.0%. Two bias analyses (one each for current and former smoking) in which the 13% of chromophobe and clear cell RCC cases missing smoking information were assumed in varying proportions to be smokers or nonsmokers showed that this extent of data incompleteness is very unlikely to have substantively influenced our results. Even when smoking data were available, their level of detail was limited, and accuracy was uncertain. Because abstraction of smoking status was based on medical records, it was not possible to assure that all clinicians applied consistent definitions, such as having smoked at least 100 cigarettes to distinguish never smokers from current or former cigarette smokers. Although details such as pack-years of exposure would have been interesting, qualitative classification of smoking was sufficient to support our conclusions. Self-report of smoking status tends to underestimate actual smoking (12) and may not be updated frequently enough to reflect recent cessation. However, self-reported current smoking status among adults correlates very highly with cotinine levels (13). Furthermore, differential misclassification of smoking status according

to RCC histology seems highly improbable, and nondifferential misclassification resulting from very recent cessation is not likely to have substantially influenced our results.

Another limitation is that this data set does not include cancer-free controls. Although we demonstrated heterogeneity of cigarette smoking status by RCC histology, we could not compare smoking history among RCC cases and controls and therefore could not calculate odds ratios for smoking and each histologic type of RCC. Finally, although it would have been ideal to include covariates such as preexisting nonneoplastic kidney disease and family history of RCC that were not available in this dataset, it seems unlikely that this information would have changed the main conclusion of this study.

In addition to showing that the association of cigarette smoking and RCC risk varies according to RCC histology, with chromophobe RCC differing from other histologies regarding that association, this study more broadly illustrates the value of abstraction by cancer registries of information regarding common exposures such as smoking. Prospective cohort studies can provide reliable information regarding relative risks and attributable fractions for associations of common exposures and common cancer sites (including common histologic types) but are intrinsically limited in their utility for studying rare outcomes. A case–control design is better suited for investigation of rare outcomes, but such studies may require collaboration of multiple large centers to identify enough cases and require allocation of resources specifically for identifying these patients and/or their records. Although cases for a case–control study can also be identified from registry data, this strategy often requires substantial effort, time, and expense for obtaining exposure data. Including some exposure data during case abstraction by cancer registries (even if detail and completeness of exposure information are not optimal) may be very useful for generating hypotheses about associations of these exposures with rare cancers. For example, our conclusion that chromophobe RCC is not strongly associated with smoking might justify larger case–control studies of that question, as well as more intensive examination of other exposures and inherited predispositions; recognizing the need to account for a larger population attributable fraction for this uncommon malignancy would be a valuable step toward reducing its incidence and/or mortality.

The availability of electronic health records using standardized formatting and advances in artificial intelligence has the potential to make automated abstracting of some exposure data from medical records to enhance cancer surveillance increasingly feasible. This study shows that as these advances become more common, registry data may be valuable for exploratory studies of cancer etiology.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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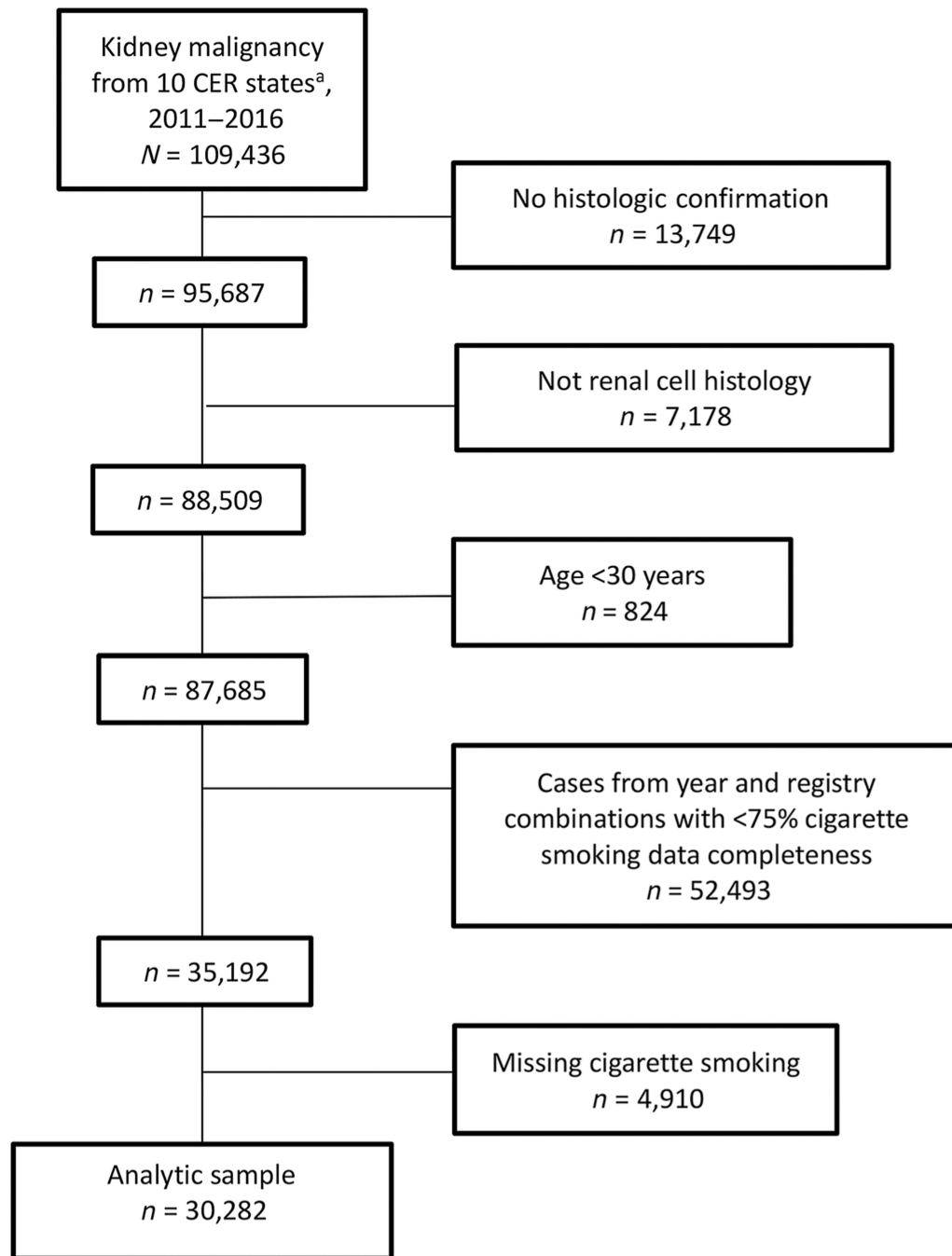


Figure 1. Exclusion criteria for analysis, excluding cases from year and registry combinations with <75% cigarette smoking data complete. ^a Refers to 10 states participating in the Enhancing Cancer Registry Data for Comparative Effectiveness Research Project, which was supported through the CDC's NPCR program.

Table 1.

Demographic characteristics of study participants in analytic sample, by cigarette smoking status.

	Cigarette smoking status			
	Never <i>N</i> (Row%) [Column%]	Current <i>N</i> (Row%) [Column%]	Former <i>N</i> (Row%) [Column%]	Total <i>N</i> (Row%) [Column%]
Diagnosis year ^a				
2011	1,527 (45.2) [10.1]	500 (14.8) [9.4]	854 (25.3) [8.6]	2,881 (100.0) [9.5]
2012	1,763 (42.0) [11.7]	672 (16.0) [12.7]	1,106 (26.4) [11.2]	3,541 (100.0) [11.7]
2013	1,802 (42.9) [12.0]	642 (15.3) [12.1]	1,163 (27.7) [11.7]	3,607 (100.0) [11.9]
2014	2,682 (42.8) [17.8]	991 (15.8) [18.7]	1,840 (29.3) [18.6]	5,513 (100.0) [18.2]
2015	2,729 (42.7) [18.1]	977 (15.3) [18.4]	1,944 (31.2) [20.1]	5,700 (100.0) [18.8]
2016	4,563 (42.4) [30.3]	1,527 (14.2) [28.8]	2,950 (27.4) [29.8]	9,040 (100.0) [29.9]
Age ^d				
30–39	607 (47.2) [4.0]	342 (26.6) [6.4]	200 (15.5) [2.0]	1,149 (100.0) [3.8]
40–49	1,753 (46.8) [11.6]	845 (22.6) [15.9]	680 (18.2) [6.9]	3,278 (100.0) [10.8]
50–59	3,429 (42.6) [22.8]	1,693 (21.0) [31.9]	1,832 (22.7) [18.5]	6,954 (100.0) [23.0]
60–69	4,659 (40.7) [30.9]	1,656 (14.5) [31.2]	3,414 (29.8) [34.5]	9,729 (100.0) [32.1]
70–79	3,371 (42.6) [22.4]	658 (8.3) [12.4]	2,803 (35.4) [28.3]	6,832 (100.0) [22.6]
80+	1,247 (45.4) [8.3]	115 (4.2) [2.2]	978 (35.6) [9.9]	2,340 (100.0) [7.7]
Sex ^d				
Female	6,387 (51.1) [42.4]	1,673 (13.4) [31.5]	2,941 (23.5) [29.7]	11,001 (100.0) [36.3]
Male	8,679 (38.3) [57.6]	3,636 (16.0) [68.5]	6,966 (30.7) [70.3]	19,281 (100.0) [63.7]
Race/ethnicity ^{a,b}				
NH White	10,119 (40.8) [67.2]	3,856 (15.5) [72.6]	7,499 (30.2) [75.7]	21,474 (100.0) [70.9]
NH Black	2,062 (45.6) [13.7]	752 (16.6) [14.2]	1,073 (23.7) [10.8]	3,887 (100.0) [12.8]
NH American Indian/Alaska Native	72 (30.4) [0.5]	73 (30.8) [1.4]	64 (27.0) [0.6]	209 (100.0) [0.7]
NH Asian/Pacific Islander	166 (58.2) [1.1]	22 (7.7) [0.4]	61 (21.4) [0.6]	249 (100.0) [0.8]
Hispanic	2,540 (50.0) [16.9]	580 (11.4) [10.9]	1,148 (22.6) [11.6]	4,268 (100.0) [14.1]
Other/unknown	107 (43.0) [0.7]	26 (10.4) [0.5]	62 (24.9) [0.6]	195 (100.0) [0.6]
Total	15,066 (42.8) [100.0]	5,309 (15.1) [100.0]	9,907 (28.2) [100.0]	30,282 (100.0) [100.0]

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$P < 0.001$

^aHispanic category includes all cases designating Hispanic ethnicity, regardless of race. All other categories are non-Hispanic (NH).

Table 2.

Associations of cigarette smoking and demographic characteristics with renal cell carcinoma histologic types, data only from year and NPCR registry combinations with <25% cigarette smoking data missing, and from cases with available individual-level cigarette smoking information.

	N (Row%) [Column%]						
	Papillary	Chromophobe	Clear cell	Cyst-associated	Collecting duct/medullary	Renal cell, unclassified	Total
Diagnosis year ^a							
2011–2012	879 (13.7) [20.8]	280 (4.4) [18.7]	3,572 (55.6) [20.0]	29 (0.5) [21.5]	16 (0.2) [25.8]	1,646 (25.6) [25.2]	6,422 (100) [21.2]
2013–2014	1,261 (13.8) [29.9]	468 (5.1) [31.3]	5,346 (58.6) [30.0]	49 (0.5) [36.3]	18 (0.2) [28.6]	1,978 (21.7) [30.3]	9,120 (100) [30.1]
2015–2016	2,078 (14.1) [49.3]	746 (5.1) [49.9]	8,931 (60.6) [50.0]	57 (0.4) [42.2]	29 (0.2) [46.0]	2,899 (19.7) [44.4]	14,740 (100) [48.7]
Age ^d							
30–49	498 (11.2) [11.8]	306 (6.9) [20.5]	2,760 (62.3) [15.5]	24 (0.5) [17.8]	17 (0.4) [27.0]	822 (18.6) [12.6]	4,427 (100) [14.6]
50–69	2,401 (14.4) [56.9]	768 (4.6) [51.4]	9,990 (59.9) [56.0]	84 (0.5) [62.2]	25 (0.1) [39.7]	3,415 (20.5) [52.4]	16,683 (100) [55.1]
70+	1,319 (14.4) [31.3]	420 (4.6) [28.1]	5,099 (55.6) [28.6]	27 (0.3) [20.0]	21 (0.2) [33.3]	2,286 (24.9) [35.0]	9,172 (100) [30.3]
Sex ^d							
Female	1,031 (9.4) [24.4]	648 (5.9) [43.4]	6,814 (61.9) [38.2]	60 (0.5) [44.4]	14 (0.1) [22.2]	2,434 (22.1) [37.3]	11,011 (100) [36.3]
Male	3,187 (16.5) [75.6]	846 (4.4) [56.6]	11,035 (57.2) [61.8]	75 (0.4) [55.6]	49 (0.3) [77.8]	4,089 (21.2) [62.7]	19,281 (100) [63.7]
Race/ethnicity ^{a,b,c}							
NH White	2,506 (11.7) [59.4]	1,001 (4.7) [67.0]	13,385 (62.3) [75.0]	79 (0.4) [58.5]	33 (0.2) [52.4]	4,470 (20.8) [68.5]	21,474 (100) [70.9]
NH Black	1,258 (32.4) [29.8]	223 (5.7) [14.9]	1,541 (39.6) [8.6]	42 (1.1) [31.1]	19 (0.5) [30.2]	804 (20.7) [12.3]	3,887 (100) [12.8]
NH American Indian/Alaska Native	24 (11.5) [0.6]	6 (2.9) [0.4]	155 (74.2) [0.9]			22 (10.5) [0.3]	209 (100) [0.7]
NH Asian/Pacific Islander	32 (12.9) [0.8]	18 (7.2) [1.2]	151 (60.6) [0.8]			47 (18.9) [0.7]	249 (100) [0.8]
Hispanic	371 (8.7) [8.8]	228 (5.3) [15.3]	2,508 (58.8) [14.1]			1,139 (26.7) [17.5]	4,268 (100) [14.1]
Other/unknown	27 (13.8) [0.6]	18 (9.2) [1.2]	109 (55.9) [0.6]			41 (21.0) [0.6]	195 (100) [0.6]
All except NH White and NH Black				14 (0.3) [10.4]	11 (0.2) [17.5]		
Cigarette smoking ^a							
Never	1,987 (13.2) [47.1]	927 (6.2) [62.0]	8,773 (58.2) [49.2]	65 (0.4) [48.1]	24 (0.2) [38.1]	3,290 (21.8) [50.4]	15,066 (100) [49.8]
Former	1,409 (14.2) [33.4]	412 (4.2) [27.6]	5,948 (60.0) [33.3]	41 (0.4) [30.4]	26 (0.3) [41.3]	2,071 (20.9) [31.7]	9,907 (100) [32.7]
Current	822 (15.5) [19.5]	155 (2.9) [10.4]	3,128 (58.9) [17.5]	29 (0.5) [21.5]	13 (0.2) [20.6]	1,162 (21.9) [17.8]	5,309 (100) [17.5]

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<i>N</i> (Row%) [Column%]							
	Papillary	Chromophobe	Clear cell	Cyst-associated	Collecting duct/medullary	Renal cell, unclassified	Total
Total	4,218 (13.9) [100]	1494 (4.9) [100]	17,849 (58.9) [100]	135 (0.4) [100]	63 (0.2) [100]	6,523 (21.5) [100]	30,282 (100) [100]

^a $P < 0.001$ ^b Hispanic category includes all cases designating Hispanic ethnicity, regardless of race. All other categories are non-Hispanic (NH).^c American Indian and Alaska Native, Asian Pacific Islander, Hispanic, and Other/Unknown categories were combined as "All except NH White and NH Black" because of small numbers in some cells. The NPCR data use agreement does not permit reporting any cells with <6 cases.

Table 3.

Adjusted^a associations of current and former smoking and demographic factors with kidney cancer histology, data only from year and registry combinations with <25% cigarette smoking data missing.

Histology ^c	Adjusted ^a prevalence ratio relative to clear cell ^b (95% CI; P)		
	Current cigarette smokers	Former cigarette smokers	Never smokers
Papillary	1.12 (1.04–1.20) [0.002]	0.97 (0.92–1.01) [0.166]	Referent
Chromophobe	0.58 (0.50–0.67) [<0.001]	0.88 (0.81–0.95) [0.002]	Referent
Cyst-associated	1.17 (0.86–1.60) [0.326]	0.98 (0.76–1.26) [0.880]	Referent
Collecting duct/medullary	1.09 (0.68–1.73) [0.723]	1.25 (0.95–1.65) [0.107]	Referent
Unclassified	1.10 (1.04–1.17) [0.001]	0.93 (0.89–0.97) [<0.001]	Referent

^aAdjusted for age, sex, and race/ethnicity.

^bClear cell RCC was chosen as the referent histologic category because it is the most common.

^cThis table contains results from individual models for papillary RCC, chromophobe RCC, cyst-associated RCC, collecting duct/medullary carcinoma, and unclassified RCC.