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Occupational Exposures and Chronic Kidney Disease: Possible associations with endotoxin and ultrafine particles

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Abstract

Background—Chronic kidney disease (CKD) carries a high public health burden yet there is limited research on occupational factors, which are examined in this retrospective case-control study.

Methods—Newly diagnosed cases of CKD (n=547) and controls (n=508) from North Carolina provided detailed work histories in telephone interviews. Unconditional logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs).

Results—There was heterogeneity in the association of CKD and agricultural work, with crop production associated with increased risk and work with livestock associated with decreased risk. Work with cutting/cooling/lubricating oils was associated with a reduced risk. CKD risk was increased for working in dusty conditions.

Conclusions—CKD risk was reduced in subjects with occupational exposures previously reported to involve endotoxin exposure. Further, exposure to dusty conditions was consistently associated with increased risk of glomerulonephritis across industry, suggesting that research on CKD and ultrafine particulates is needed.

Keywords

kidney disease; occupational exposures; heavy metals; silica; particulates; nephritis

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Author contributions:

TRS: Drafted the manuscript and performed statistical analyses

DPS: Designed study, collected data, and provided feedback of analyses

CGP: Enhanced background and discussion sections

KMA: Provided oversight of analyses and critical revision of manuscript

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INTRODUCTION

There is increasing interest in occupational risk factors for chronic kidney disease (CKD). This stems from observations of elevated CKD prevalence in low- and middle-income countries, particularly in rural agricultural communities such as El Salvador, Nicaragua, India, and Sri Lanka [Almaguer, et al., 2014], where the predominant risk factors observed in the US (e.g., obesity, diabetes, and hypertension) are typically absent in patients and environmental and occupation exposures are hypothesized to play a larger role [Soderland, et al., 2010, Weiner, et al., 2013]. The impact of occupational risk factors on CKD in the US requires greater understanding as well, where it has been estimated that nearly 4 million Americans are exposed to known or suspected nephrotoxins in the workplace [Landrigan, et al., 1984].

Approximately 11.5% of US adults have CKD [Levey, et al., 2009], and its prevalence is increasing in the US [Coresh, et al., 2007] and in many other countries [Bello, et al., 2005, Nwankwo, et al., 2005]. Overall Medicare expenditures for CKD reached \$41 billion in 2010 according to the US Renal Data System [US Renal Data System]. The percentage of CKD deaths in the US thought to be attributable to occupational exposures was 8.2 to 14.5%, based on exposure to silica, solvents, and metals, the most well-recognized occupational risk factors for CKD [Steenland, et al., 2003]. Occupational factors may be modifiable. Therefore, a greater understanding of occupational causes of kidney disease can prevent CKD morbidity and mortality.

In epidemiologic studies, identification of workplace risk factors can come from linking large occupational cohorts with limited, specific exposures to death registries to see whether exposed workers were more likely to die from the disease of interest. Alternatively, a case-control design, in which the experiences of diseased and non-diseased subjects are compared, provides a means to potentially examine a wider range of past occupations and exposures. To our knowledge, no prior case-control study of incident CKD in the US has examined full occupational histories. Such a study can identify novel etiologic factors or add information to known or suspected ones.

In this analysis, we examined a range of occupational exposures and a history of having worked in specific industries in a well-characterized case-control study with a diverse sample from North Carolina to identify occupational factors associated with CKD risk overall and within subtypes of CKD.

MATERIALS AND METHODS

Study population

This case-control study of incident CKD has been described in detail elsewhere [Sandler, et al., 1989]. Briefly, patients with a first diagnosis of CKD were identified from four North Carolina medical centers (1980-82). Eligible patients were between 30 and 79 years of age, residents of North Carolina, and had one of the following *International Classification of Diseases* (Ninth Edition) codes: 403, 404, 582, 583, 585, 586, 587, 590.0, 590.8, or 593.9. A

new, sustained elevation of serum creatinine (2 measurements >1.5 mg/dL) was also required. Ten percent of case records were independently reviewed, with 93% concordance [Vupputuri and Sandler, 2003]. Patients were excluded for preexisting renal disease, systemic or familial conditions with known effects on the kidney, and external causes of kidney disease. Cases were classified as hypertensive nephrosclerosis (19%), diabetic nephropathy (19%), glomerulonephritis (13%), or interstitial nephritis (19%). Cases with insufficient clinical evaluations or advanced and unclassifiable disease were categorized as renal insufficiency (22%) or end-stage renal disease (ESRD) (7%).

Potential control subjects were identified through random digit dialing (<65 years of age) and Health Care Financing Administration Medicare listings (65 years of age). Controls were residents of North Carolina and frequency-matched to cases by age (± 5 years), sex, race, and proximity to study hospitals.

Of 4,268 potential cases, reasons for not meeting eligibility criteria were preexisting renal disease (n=1,467), missing age or residence information (n=599), not meeting clinical criteria above (n=697), and renal failure due to extrarenal causes (n=796), as detailed earlier [Sandler, et al., 1989]. There were 709 cases who met inclusion criteria. Among 607 contacted, 554 (91%) agreed to participate, an overall response rate of 78%. Contact was made with 608 of 717 potential controls. 520 (86%) agreed to participate, for an overall response rate of 73%. Four controls reporting a history of CKD were excluded.

Telephone interviews were conducted with case and control subjects and proxy respondents were allowed for respondents unable to participate directly (for 299 cases and 50 controls). Interviewers were given no information regarding case/control status. Interviews covered demographic characteristics, personal and family medical history, medication use, and occupational history and exposure to potentially toxic chemicals. Subjects were asked to self-report race, with possible response categories of White (non-Hispanic), Black (non-Hispanic), Hispanic, American Indian/Alaskan Native, and Asian/Pacific Islander. Only 27 cases reported a race/ethnicity category other than Black or White, too few for meaningful analysis. Given the potential for differences in other CKD risk factors by race, these subjects were excluded. The present analysis was thus restricted to those self-identifying their race as Black (244 cases, 231 controls) or White (303 cases, 277 controls).

For jobs held 2 years, subjects were asked whether full- or part-time, work duration, and whether they had exposure to “solvents, degreasers, or other cleaning agents”, “metal particles, dusts, chips, or fumes”, “sand or silica”, or “other dusty conditions” on the job. In addition, questions asked about work in specific industries (furniture manufacturing, textile or clothing manufacturing, dry cleaning, battery plant, auto mechanics or repair, smelting, lead, or other metal industry, and paint manufacturing). Subjects were asked if ever exposed to specific organic solvents (e.g., cutting/lubricating/cooling oils, benzene, toluene, tetrachloroethylene, or turpentine), metal fumes or particles (from working with lead, cadmium, or other metals), or other materials of interest (including sand or silica, lead paint, car radiators or batteries, and either chloroform, ether, formaldehyde, or other solvents/metals not listed) 5 times in a year. For each exposure, information on duration and

frequency of use as well as whether exposure was occupational or nonoccupational (“hobby or around the house”) were requested.

Data Analysis

We compared the distribution of demographic characteristics and potential CKD risk factors including education, body mass index (BMI), analgesic use, and cola consumption for cases and controls using unconditional logistic regression, adjusting for matching factors age (continuous), race (Black, White), and sex. We used unconditional logistic regression to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for the association between CKD and ever employed in a specific industry or exposure to various substances, controlling for matching factors plus education (<8, 8 to 11, >11 years), BMI (<20, 20 to <25, 25 to <27, and ≥27 kg/m²), analgesic use (never, occasionally, weekly, daily), and cola consumption (0, >0 to <7, 7 to <14, 14 to <21, ≥21 glasses/week), covariates found to be confounders or risk factors for CKD in this study population [Saldana, et al., 2007, Sandler, et al., 1989, Vupputuri and Sandler, 2003].

Jobs held for ≥2 years were classified by industry, in accordance with the US Census of Industries and Occupations [US Census Bureau]. We restricted analysis to industries for which ≥20 subjects reported employment and ≥5 subjects were represented in each joint exposure-disease category (e.g., in 2×2 table). We assessed exposure-response for 0-2 (referent), 2-5, and >5 years of employment with trend tests using an ordinal variable with mean duration of each exposure category.

We also estimated the association between CKD and exposure to specific substances such as solvents, sand or silica, metals, or dusty conditions while working in individual industries. To combine information on industry and specific exposures, subjects were categorized into groups: never worked in the industry (referent), worked in the industry but not exposed to substance, and worked in the industry and exposed to substance of interest.

Polytomous logistic regression was used to estimate the association between CKD subtypes and specific classes of exposure (dusty conditions, sand or silica, solvents and cleaning agents, and metal particles, chips, or fumes), regardless of industry. Analyses stratified by race, sex, history of hypertension, or analgesic use (never/occasionally, weekly/daily; never/occasionally/weekly, daily) were performed to assess effect modification. Analyses were repeated excluding proxy respondents to examine their impact. Statistical analysis was performed using SAS software, version 9.1 (Cary, NC).

RESULTS

Participants had a mean age of 62 years and slightly more than half were male (56%) and White (55%) (Table I). Compared to controls, CKD cases had less education, higher BMI, and consumed more analgesic medicines and cola beverages.

Subjects reported holding jobs ≥2 years in 96 different industries. Of these, 24 had ≥5 cases and 5 controls who had worked in that industry. There were null associations for industries where employees most likely worked in an office setting (e.g., religious organizations,

colleges/universities, elementary/secondary schools), food services (e.g., restaurants/grocery), health care (e.g., hospitals/nursing services), and retail stores (data not shown).

We present results for selected industries for which sufficient power existed to examine a dose-response relationship (Table II). Those who worked ≥ 2 years in agricultural crop production had a higher odds of CKD compared to those who did not (odds ratio (OR) 1.56, 95% confidence interval (CI) 1.08-2.26). The odds of CKD appeared to increase with increasing duration in crop production (OR_{2-5 yrs} 1.21, 95% CI 0.53-2.76; OR_{>5 yrs} 1.60, 95% CI 1.04-2.48; $p_{\text{trend}}=0.035$). Conversely, working in agricultural livestock production was associated with a decreased odds of CKD (OR 0.31, 95% CI 0.16-0.61), regardless of duration. Furniture and fixture manufacturing was also associated with an elevated odds of CKD (OR 1.58, 95% CI 0.90-2.75). The association was strongest for having worked >5 years (OR 1.94, 95% CI 0.95-3.95). There was no apparent increased CKD risk with ever working in construction, knitting mills, yarn/thread/fabric mills, or laundry, dry cleaning, and garment services. Analyses stratified by race, gender, and history of hypertension did not show consistent differences between groups and data became too sparse to analyze when stratified by analgesic use (data not shown).

To examine specific industries more closely, we investigated whether there were relationships between CKD and specific substances or conditions in the industry (Table III). The odds ratio for the overall association between CKD and working in any job with dusty conditions for ≥ 2 years was 1.32 (95% CI 1.00-1.74). Associations with CKD were seen for exposure to dusty conditions in agricultural crop production (OR 2.46, 95% CI 1.43-4.22) and furniture and fixture manufacturing (OR 2.31, 95% CI 1.08-4.93). There was no association between construction work in dusty conditions overall (OR 1.22, 95% CI 0.60-2.48), but when subjects specifically reported work with sand or silica, the association appeared elevated albeit with few exposed controls (OR 2.65, 95% CI 0.90-7.75). There was no overall association between CKD and exposure to solvents, degreasers, or other cleaning agents in jobs lasting ≥ 2 years. Though based on small numbers, work in furniture and fixture manufacturing with exposure to solvents was associated with a two-fold increased odds of CKD (OR 2.26, 95% CI 0.79-6.47) as was work in the laundry, dry cleaning and garment service industry with exposure to solvents (OR 3.29, 95% CI 0.64-17.29).

Next, we examined the relation between subtypes of CKD and reporting dusty conditions, sand or silica exposure, metal particles, or use of solvents, degreasers, and cleaning agents in any job held for ≥ 2 years, regardless of industry (Table IV). Work in dusty conditions was most strongly associated with glomerulonephritis (OR 2.19, 95% CI 1.25-3.86). Odds of both hypertensive nephrosclerosis and ESRD were increased in dusty conditions approximately 1.5-fold (OR 1.52, 95% CI 0.95-2.45; OR 1.57, 95% CI 0.73-3.53, respectively). Sand or silica exposure was also associated with increased glomerulonephritis risk (OR 3.51, 95% CI 1.29-9.57). No increased odds of CKD subtypes was observed for exposure to metal particles, dusts, chips, or fumes.

Lastly, we examined the relationship between CKD and selected self-reported occupational exposures (Table V). Cutting, cooling, and lubricating oils were associated with a reduced risk of CKD (OR 0.55, 95% CI 0.36-0.83). Conversely, there was a four-fold increase in the

odds of CKD (OR 4.13, 95% CI 1.13-15.17) associated with use of gasoline as a solvent or cleaning agent. General occupational exposure to sand or silica was associated with increased odds of CKD, consistent with what we found based on job histories. No increase in CKD was observed in subjects exposed to lead fumes or particles (OR 1.04, 95% CI 0.47-2.30).

Overall, results did not change substantially when re-analyzed excluding proxy respondents. One exception may be benzene, where the direction of the association changed though the confidence intervals were consistent (OR 0.79, 95% CI 0.44-1.43). For illustration, results for reporting of specific agents, such as solvents and other agents are shown as online Supporting Information in Supplemental Table I).

DISCUSSION

We observed an elevated CKD risk with dusty conditions across industries and reduced CKD risk in industries that involve exposure to endotoxin, suggesting that these types of exposures may not be fully appreciated as factors in occupationally related CKD. Regarding specific industries associated with an elevated CKD risk, a nearly two-fold increased odds of CKD was observed among those who reported work in furniture and fixture manufacturing, and there was a trend in increasing odds of CKD with increasing years worked in agricultural production. Examination of specific agents used at work found that an increased odds of CKD was also observed for working with solvents, degreasers, or other cleaning agents, as well as sand or silica, and for dusty conditions. The risk of glomerulonephritis was doubled for those who reported working in dusty conditions and more than tripled for those who worked with sand or silica. Interestingly, reduced odds of CKD were observed for work in agricultural production of livestock and exposure to cutting, lubricating, and cooling oils, activities that may involve exposure to endotoxin.

The association with dusty conditions was observed overall and for specific industries. The classification “dusty conditions” is non-specific and may reflect different underlying materials in different industries. In particular, silica may be components of dust in some of these industries. Silica has been reported at ambient levels in US cities, but silica can also be created during industrial processes [World Health Organization, 2000]. In North Carolina, farming activities have been reported to influence silica exposure [Archer, et al., 2002, Parks, et al., 1999, Parks, et al., 2003]. The relationship between silica exposure and CKD has been documented previously in a number of studies [Boujemaa, et al., 1994, Calvert, et al., 1997, Carta, et al., 2001, Cherry, et al., 2013, Gregorini, et al., 1993, Hotz, et al., 1995, McDonald, et al., 2001, McDonald, et al., 2005, Ng, et al., 1993, Nuyts, et al., 1995, Parks, et al., 1999, Rapiti, et al., 1999, Steenland, et al., 1990, Steenland, et al., 1992, Steenland, et al., 2002, Steenland, et al., 2001]. Both the National Institute for Occupational Safety and Health and the World Health Organization have recognized the growing evidence for a relationship between crystalline silica and renal diseases [Centers for Disease Control and Prevention, 2002, World Health Organization, 2000]. Damage is thought to occur via inflammatory processes due to the accumulation of antibody-antigen complexes filtered by the glomerulus [Parks, et al., 1999]. Alternatively, kidney damage may follow initiation of

an auto-immune reaction [Calvert, et al., 1997], or even from nephrotoxicity when silica particles directly come into contact with the kidney [Steenland, 2005].

Although much research has come from silica, the consistency of the dusty conditions finding across industries indicates that greater investigation into this type of exposure is warranted. Airborne ultrafine particles may be important more generally as they are known to translocate the lung via fluid dynamics and enter the bloodstream [Miserocchi, et al., 2008, Shannahan, et al., 2012]. In the bloodstream, these substances may be filtered by the kidney which also metabolize substances to potentially more toxic forms to enable their excretion [Pfaller and Gstraunthaler, 1998]. For workers with long-term, low levels of potentially harmful exposures, they may cause gradual, irreversible damage to the organ, potentially leading to CKD. Further, the translocation of foreign particles into the bloodstream, may initiate a systemic immunologic response, consistent with auto-immune disease which may damage the kidney. This has been reported for asbestos exposure [Pfau, et al., 2008].

Inverse associations for CKD were observed for those who had worked in industries that have previously reported having endotoxin exposure, including agricultural production of livestock and industries that used cutting, lubricating, cooling oils. Endotoxin, produced by Gram-negative bacteria, is found on organic material, such as animal waste. Cutting, lubricating, and cooling oils, which facilitate the cutting and grinding of metals, may be water-based fluids which allow bacterial growth and therefore the presence of endotoxin [Friesen, et al., 2011]. In murine models comparing mice with chronic renal disease, those receiving plasmacytoid dendritic cells (pDCs - found in both human and mouse kidney) pretreated with lipopolysaccharide (LPS, a purified form of endotoxin), exhibited reduced glomerulosclerosis, tubulointerstitial injury, and interstitial fibrosis, and improved renal function compared with mice transferred naïve pDCs [Zheng, et al., 2012]. The authors suggested that the protective mechanism may involve suppressing proinflammation cytokines in renal macrophages. Occupational cohorts with quantitative estimates of endotoxin exposure exist and are ideal studies in which to study the hypothesis proposed here.

In our results, occupational solvent use overall was associated with glomerulonephritis but not the general classification of CKD. Further, many of the individual solvents we investigated were not associated with CKD overall. We did observe an elevated risk in the furniture and fixture manufacturing, an industry which uses various solvents including toluene. Occupational exposure to toluene has been associated with biomarkers indicating renal glomerular and tubular lesions [Gonzalez-Yebra, et al., 2006, Lauwerys, et al., 1985]. Workers may not always know which specific substances are in solvent mixtures they are exposed to, and we did not have enough subjects specifically reporting toluene or other solvents to study them in depth. As for other solvents across the study population, only self-reported use of gasoline as a solvent or cleaning agent was associated with an increased risk of CKD based on 12 exposed cases and 3 exposed controls. Although an association between CKD and gasoline has been reported in prior studies [Jacob, et al., 2007, Radican, et al., 2006], our finding could be due to other correlated exposures (e.g., via automotive repair), or tetraethyl lead, a common gasoline additive at the time of the study. Lead can

damage kidney tubule epithelial cells directly by triggering oxidative stress, apoptosis, and necrosis [Nolan and Shaikh, 1992, Sabolic, 2006, Steenland, et al., 1990]. In addition, chronic lead exposure is associated with the development of hypertension and saturnine gout, both of which are risk factors for CKD [Nolan and Shaikh, 1992]. Lead has been associated with kidney damage and ESRD [Chowdhury, et al., 2014, Meyer, et al., 1984, Steenland, et al., 1990]. Previous studies of solvents focused specifically on glomerulonephritis or ESRD (which includes glomerulonephritis but also other causes). In our study only 13% of cases had glomerulonephritis and 7% were classified as ESRD.

Self-reported lead exposure was not associated with CKD in our study. Numerous studies have found associations between lead and CKD or biomarkers of kidney dysfunction [Ehrlich, et al., 1998, Garcon, et al., 2004, Muntner, et al., 2003, Muntner, et al., 2005, Staessen, et al., 1992, Tsaih, et al., 2004, Wang, et al., 2002, Weaver, et al., 2009]. The lack of association could be due to small numbers with lead exposure, insufficient numbers with specific disease subtypes or poor reporting of exposure in response to the question, which asked about having been exposed to lead fumes or particles 5 times a year. On the other hand, we previously reported an association in this study population with moonshine consumption which is a non-occupational source of lead exposure [Vupputuri and Sandler, 2003].

A strength of this study was that subjects were asked to report all jobs (and industries) they had worked for 2 years, along with self-reported exposure data for each job. The questionnaire covered many classes of potentially nephrotoxic agents and, for each job, allowed the exploration of which class was relevant in a particular industry. We also asked about ever employment in specific jobs or industries and results were similar (data not shown). The study included data on a large number of potential confounders, including medical history, medication use, and dietary factors. This is important because industry-based studies often lack data on important confounders. Prior reports using data from this study found that while analgesic use [Sandler, et al., 1989], BMI [Vupputuri and Sandler, 2003], and cola consumption [Saldana, et al., 2007] were associated with CKD, smoking was not [Vupputuri and Sandler, 2003]. We controlled for BMI, analgesics, and cola consumption as well as education as a marker for socioeconomic status. This may not perfectly reflect the full range of factors that socioeconomic status represents and it is possible that residual confounding by socioeconomic status remains after controlling for education.

Limitations include lack of validation of self-reported exposures and job history. Non-differential exposure misclassification may underestimate true underlying effects. Recall bias, though possible, is not likely because associations between kidney disease and occupational exposures were not widely known at the time of the study. Studies have shown reasonable accuracy in proxy respondents' reporting of occupational histories and lower accuracy in the reporting of specific exposures [Colt, et al., 2001, Lerchen and Samet, 1986, Soll-Johanning and Hannerz, 2002]. In our analyses, excluding proxies did not change observed associations.

Our study lacked power to detect CKD associated with some exposures of interest. Low numbers of exposed subjects precluded several analyses and meant that caution is required in interpreting results. In addition, few cases had biopsy-proven diagnoses, increasing opportunity for disease misclassification and potentially a bias to the null. If biopsies were more likely to occur based on socioeconomic status, occupation, or specific exposures, detection bias may influence the results for specific disease subtypes.

The primary advantage of this study is that it allowed us to examine patterns of CKD across industries. In so doing, we were able to pool similar exposures across industries and identify two associations that may be unrecognized. This has led us to identify a need for research into respirable ultrafine particles more generally as well as the influence of endotoxin exposure on CKD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table I

Selected characteristics of chronic kidney disease cases and controls in North Carolina

Characteristic ^a	Cases (N=547)		Controls (N=508)		p-value ^b
	N	%	N	%	
Mean age, years (SD)	63.1	(12.0)	61.7	(12.1)	-
Sex					
Male	306	55.9	285	56.1	-
Female	241	44.1	223	43.9	
Race					
Black	244	44.6	231	45.5	-
White	303	55.4	277	54.5	
Education, years					
<8	203	37.7	126	25.0	<0.001
8-11	160	29.7	144	28.5	
11	176	16.7	235	46.5	
BMI, kg/m ²					
<20	21	3.9	33	6.6	<0.001
20 to <25	198	36.8	227	45.2	
25 to <27	99	18.4	98	19.5	
27	220	40.9	144	28.7	
Analgesic use					
Never	63	11.5	58	11.4	<0.001
Occasionally	199	36.3	281	55.3	
Weekly	142	26.0	114	22.4	
Daily	88	16.1	28	5.5	
Cola consumption, glasses/week					
Never	100	19.2	139	28.4	<0.001
>0 to <7	162	31.0	161	32.9	
7 to <14	125	24.0	103	21.0	
14 to <21	80	15.3	56	11.4	
21	55	10.5	31	6.3	

^aData missing on education (8 cases, 3 controls), analgesic use (9 cases, 6 controls), cola consumption (25 cases, 18 controls).^bControlling for matching factors age, sex, and race.

Table II

Association between chronic kidney disease and working in specific industries in North Carolina

Industry ^a	Ever worked, duration worked in industry ^b	Cases N (%)	Controls N (%)	OR ^c	95% CI ^d
Agricultural production-crops	Never	371 (77.0)	397 (86.5)	1.00	Referent
	Ever	111 (23.0)	62 (13.5)	1.56	1.08-2.26
	2 to 5 yrs	14 (2.9)	11 (2.4)	1.21	0.53-2.76
	>5 yrs	76 (15.8)	41 (8.9)	1.60	1.04-2.48
	Trend			p=0.035	
Agricultural production-livestock	Never	467 (96.9)	426 (92.8)	1.00	Referent
	Ever	15 (3.1)	33 (7.2)	0.31	0.16-0.61
	2 to 5 yrs	3 (0.6)	7 (1.5)	0.28	0.07-1.15
	>5 yrs	10 (2.1)	22 (4.8)	0.30	0.14-0.67
	Trend			p=0.001	
Construction	Never	439 (91.1)	416 (90.6)	1.00	Referent
	Ever	43 (8.9)	43 (9.4)	0.86	0.53-1.38
	2 to 5 yrs	15 (3.1)	11 (2.4)	1.28	0.56-2.90
	>5 yrs	24 (5.0)	27 (5.9)	0.73	0.39-1.29
	Trend			p=0.267	
Knitting mills	Never	452 (93.8)	425 (92.6)	1.00	Referent
	Ever	30 (6.2)	34 (7.4)	0.75	0.44-1.28
	2 to 5 yrs	8 (1.7)	10 (2.2)	0.62	0.23-1.64
	>5 yrs	17 (3.5)	24 (5.2)	0.65	0.34-1.26
	Trend			p=0.187	
Yarn, thread, and fabric mills	Never	420 (87.1)	411 (89.5)	1.00	Referent
	Ever	62 (12.9)	48 (10.5)	1.13	0.74-1.71
	2 to 5 yrs	16 (3.3)	14 (3.1)	1.05	0.50-2.22
	>5 yrs	44 (9.1)	29 (6.3)	1.26	0.76-2.10
	Trend			p=0.365	
Furniture and fixture manufacturing	Never	441 (91.5)	437 (95.2)	1.00	Referent
	Ever	41 (8.5)	22 (4.8)	1.58	0.90-2.75
	2 to 5 yrs	8 (1.7)	8 (0.8)	0.96	0.35-2.65
	>5 yrs	28 (5.8)	12 (2.6)	1.94	0.95-3.95
	Trend			p=0.072	
Laundry, cleaning, and garment services	Never	466 (96.7)	447 (97.4)	1.00	Referent
	Ever	16 (3.3)	12 (2.6)	1.09	0.49-2.41
	2 to 5 yrs	7 (1.5)	4 (0.9)	1.57	0.43-5.71
	>5 yrs	7 (1.5)	6 (1.3)	0.92	0.29-2.87
	Trend			p=0.950	

^a Industry groupings correspond to the following US Census of Industries and Occupations. codes (1980): 10-Agricultural crop production; 60-Construction; 132-Knitting mills; 142-Yarn, thread, and fabric mills; 242-Furniture and fixture manufacturing; 771-Laundry, cleaning, and garment services.

^b Data missing on duration worked in agricultural crop production (21 cases), construction (4 cases, 5 controls), knitting mills (5 cases), yarn, thread, and fabric mills (2 cases, 5 controls), furniture and fixture manufacturing (5 cases, 2 controls), and laundry, cleaning, and garment services (2 cases, 2 controls).

^c Odds ratio, adjusting for age, race, sex, education, BMI, analgesic use, and cola consumption.

^d Confidence interval.

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Table III

Association of chronic kidney disease and exposure to selected materials while working in specific industries

Industry	Employment in industry/exposure	Dusty conditions		Solvents, degreasers, other cleaning agents			
		Cases N (%)	Controls N (%)	OR ^a	95% CI ^b	Cases N (%)	Controls N (%)
Any	Employed/unexposed	227 (47.1)	261 (56.9)	1.00	Referent	339 (70.3)	329 (71.7)
	Employed/exposed	255 (52.9)	198 (43.1)	1.32	1.00-1.74	143 (29.7)	130 (28.3)
	None/-	371 (77.0)	397 (86.5)	1.00	Referent	371 (77.0)	397 (86.5)
Agricultural production-crops	Employed/unexposed	50 (10.4)	41 (8.9)	1.10	0.69-1.74	97 (20.1)	54 (11.8)
	Employed/exposed	61 (12.6)	21 (4.6)	2.46	1.43-4.22	14 (2.9)	8 (1.7)
	None/-	439 (46.7)	416 (44.2)	1.00	Referent	-	-
Construction	Employed/unexposed	22 (2.3)	28 (3.0)	0.67	0.36-1.23	-	-
	Employed/exposed	21 (2.2)	15 (1.6)	1.22	0.60-2.48	-	-
	None/-	439 (91.1)	416 (90.6)	1.00	Referent	-	-
Construction (sand or silica)	Employed/unexposed	29 (6.0)	38 (8.3)	0.64	0.38-1.10	-	-
	Employed/exposed	14 (2.9)	5 (1.1)	2.65	0.90-7.75	-	-
	None/-	452 (93.8)	425 (92.6)	1.00	Referent	-	-
Knitting mills	Employed/unexposed	13 (2.7)	24 (5.2)	0.47	0.23-0.96	-	-
	Employed/exposed	17 (3.5)	10 (2.2)	1.42	0.62-3.24	-	-
	None/-	420 (87.1)	411 (89.5)	1.00	Referent	-	-
Yarn, fabric, and thread mills	Employed/unexposed	21 (4.4)	24 (5.2)	0.87	0.47-1.61	-	-
	Employed/exposed	41 (8.5)	24 (5.2)	1.37	0.80-2.35	-	-
	None/-	441 (91.5)	437 (95.2)	1.00	Referent	441 (91.5)	437 (95.2)
Furniture and fixture manufacturing	Employed/unexposed	13 (2.7)	12 (2.6)	0.95	0.42-2.17	27 (5.6)	17 (3.7)
	Employed/exposed	28 (5.8)	10 (2.2)	2.31	1.08-4.93	14 (2.9)	5 (1.1)
	None/-	466 (96.7)	447 (97.4)	1.00	Referent	466 (96.7)	447 (97.4)
Laundry, dry cleaning, and garment services	Employed/unexposed	14 (2.9)	11 (12.4)	1.01	0.44-2.32	10 (2.1)	10 (2.2)
	Employed/exposed	2 (0.4)	1 (0.2)	2.09	0.17-25.95	6 (1.2)	2 (0.4)

^aOdds ratio, adjusting for age, race, sex, education, BMI, analgesic use, and cola consumption.

^bConfidence interval.

Table IV

Relationship between chronic kidney disease subtypes and exposure to occupational agents in any jobs held for two or more years

Disease subtype	Dusty conditions	Sand or silica	Solvents, degreasers, and cleaning agents	Metal particles, dusts, chips, or fumes
Controls, n=459				
% Exposed	56.9	2.6	28.3	17.9
Hypertensive Nephrosclerosis, n=93				
% Exposed	53.8	3.2	23.6	11.8
OR ^a (95% CI) ^b	1.52 (0.95-2.45)	1.47 (0.39-5.57)	0.89 (0.51-1.56)	0.73 (0.36-1.48)
Diabetic Nephropathy, n=94				
% Exposed	47.9	4.2	31.9	17.0
OR ^a (95% CI)	1.16 (0.73-1.86)	1.96 (0.59-6.49)	1.11 (0.66-1.87)	0.99 (0.53-1.87)
Glomerulonephritis, n=65				
% Exposed	66.1	10.8	44.6	23.1
OR ^a (95% CI)	2.19 (1.25-3.86)	3.51 (1.29-9.57)	1.62 (0.92-2.86)	1.06 (0.55-2.03)
Interstitial Nephritis, n=93				
% Exposed	47.3	3.2	23.6	14.0
OR ^a (95% CI)	1.00 (0.62-1.61)	1.33 (0.35-5.02)	0.77 (0.44-1.36)	0.77 (0.39-1.52)
ESRD, n=32				
% Exposed	56.2	3.1	34.4	12.5
OR ^a (95% CI)	1.57 (0.73-3.53)	0.97 (0.12-8.15)	1.34 (0.59-3.04)	0.66 (0.21-2.03)
Renal Insufficiency, n=105				
% Exposed	52.4	5.7	27.6	19.0
OR ^a (95% CI)	1.11 (0.70-1.76)	1.84 (0.63-5.38)	0.95 (0.57-1.61)	1.02 (0.56-1.85)

^a Polytomous regression models adjusted for age, race, sex, education, BMI, analgesic use, and cola consumption; four polytomous models were generated, one for each exposure of interest.

^b Confidence interval.

Table V

Relationship between chronic kidney disease and exposure to selected solvents and other agents

Exposure type	Specific agent		Cases N (%)	Controls N (%)	OR ^a	95% CI ^b
Solvents and cleaning agents	Cutting, lubricating, cooling oils	Never	483 (89)	425 (83)	1.00	Referent
		Ever	62 (11)	88 (17)	0.55	0.36-0.83
	Benzene	Never	468 (94.9)	443 (93.7)	1.00	Referent
		Ever	23 (5.1)	30 (6.3)	0.79	0.44-1.43
	Carbon tetrachloride	Never	485 (98.4)	454 (96.4)	1.00	Referent
		Ever	8 (1.6)	17 (3.6)	0.59	0.25-1.43
	Turpentine	Never	439 (88.5)	415 (88.7)	1.00	Referent
		Ever	57 (11.5)	58 (11.3)	0.88	0.58-1.33
	Ethylene glycol	Never	492 (99.0)	461 (98.3)	1.00	Referent
		Ever	5 (1.0)	8 (1.7)	0.69	0.22-2.20
	Gasoline	Never	464 (97.5)	459 (99.4)	1.00	Referent
		Ever	12 (2.5)	3 (0.6)	4.13	1.13-15.17
Other agents	Sand or silica	Never	463 (94.9)	447 (97.0)	1.00	Referent
		Ever	25 (5.1)	14 (3.0)	1.70	0.84-3.44
	Lead	Never	461 (93.9)	435 (92.6)	1.00	Referent
		Ever	30 (6.1)	35 (7.4)	1.04	0.47-2.30

^a Adjusting for age, race, sex, education, BMI, analgesic use, and cola consumption.^b Confidence interval.