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Occupational particle exposure and chronic kidney disease: a cohort study in Swedish construction workers

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ABSTRACT

Objectives Increasing epidemiological and experimental evidence suggests that particle exposure is an environmental risk factor for chronic kidney disease (CKD). However, only a few case–control studies have investigated this association in an occupational setting. Hence, our objective was to investigate associations between particle exposure and CKD in a large cohort of Swedish construction workers.

Methods We performed a retrospective cohort study in the Swedish Construction Workers' Cohort, recruited 1971–1993 (n=286 089). A job-exposure matrix was used to identify workers exposed to nine different particulate exposures, which were combined into three main categories (inorganic dust and fumes, wood dust and fibres). Incident CKD and start of renal replacement therapy (RRT) were obtained from validated national registries until 2021 and analysed using adjusted Cox proportional hazards models.

Results Exposure to inorganic dust and fumes was associated with an increased risk of CKD and RRT during working age (adjusted HR for CKD at age <65 years 1.15, 95% CI 1.05 to 1.26). The elevated risk did not persist after retirement age. Exposure to cement dust, concrete dust and diesel exhaust was associated with CKD. Elevated HRs were also found for quartz dust and welding fumes.

Conclusions Workers exposed to inorganic particles seem to be at elevated risk of CKD and RRT. Our results are in line with previous evidence of renal effects of ambient air pollution and warrant further efforts to reduce occupational and ambient particle exposure.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Increasing evidence suggests an association between ambient air pollution and chronic kidney disease, however, this has not been exhaustively investigated in an occupational setting.

WHAT THIS STUDY ADDS

⇒ In a large cohort of construction workers, we find evidence for an association between particle exposure and an increased risk of kidney disease during working age.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our findings emphasise the need to consider kidney disease in risk assessments and warrant efforts to reduce both occupational and ambient particle exposure.

INTRODUCTION

Chronic kidney disease (CKD) represents a large and growing share of the global burden of disease.[1 2] CKD also constitutes a well-established, independent risk factor for all-cause mortality and foremost cardiovascular disease.[3 4] A growing number of epidemiological studies report associations between ambient air pollution and incident CKD.[5 6] Investigations of the potential biological mechanisms of particle exposure have indicated proinflammatory effects, tubulointerstitial injury, microvascular and endothelial dysfunction, morphological changes in renal tissue and decreases in renal cell viability associated with subchronic exposure to ambient particle matter in rodent models.[7–10]

Particle exposure has been shown to cause a higher risk of cardiovascular events in both ambient[11 12] and occupational[13–16] settings. While uncertainty remains regarding the underlying biological pathways, this association is usually attributed to a systemic inflammatory reaction, translocation of particles through the blood stream and autonomic nervous dysregulation.[17 18] Because of the large pathomechanistic overlap between cardiovascular and renal diseases, for example, endothelial dysfunction, inflammation, hypertension and renin–angiotensin system overactivation,[19 20] similar pathways may also contribute to an increased risk of CKD.

Occupational particle exposure consists of a heterogeneous mixture of particles of different origins, including combustion, mineral dust and metal fumes, and usually involves substantially higher concentrations than in ambient settings.[21] Most studies on occupational particle exposure and CKD have focused on silica[22–26] while the risk of CKD among workers exposed to dust in general or welding fumes has previously only been investigated in a few case–control studies.[27 28] Hence, there is a need for adequately powered cohort studies of the association between occupational particle exposure and CKD. The aim of this study was to investigate this among Swedish construction workers. We hypothesised that, if the association

between ambient air pollution and CKD is causal, workers with occupational exposure to particles would also be subject to an elevated risk of CKD.

METHODS

We performed a retrospective cohort analysis of the association between occupational exposure to particles and incident CKD and the need for renal replacement therapy (RRT) in the Swedish Construction Workers' cohort (Bygghälsokohorten).

Study population

From the 1960s to 1993, the Construction Industry's Organization for Working Environment (Bygghälsan) offered free regular medical exams to Swedish construction workers. The participation rate was high, approximately 80%.[29] From 1971, information on participants' occupational category and some health data were recorded in a digital registry. We included all workers examined from 1971 to 1993 for whom information on occupational title had been collected at a baseline exam (missing for 11% of the original cohort). We excluded female workers (5%), as few were employed in the occupational settings included in the study, and workers <15 or >65 years old at the first recorded health examination (5%). We also excluded individuals for whom no smoking or anthropometry data were available (8%), office workers (5%) and individuals with reused personal identification numbers (0.07%). Out of the original cohort (n=389 132), we thus included 286 089 workers (74% of full cohort, online supplemental table S1).

Information on participants' health status (height, weight, smoking habits and blood pressure) was obtained from the first recorded examination. Questionnaire data on cigarette, cigar and pipe smoking were obtained until 1974 and after 1978 (questions on smoking habits were not included in exams 1975–June 1978). Data from the first recorded examination were used for smoking status (never-smoker, former smoker or current smoker) and smoking intensity. For current smokers, we categorised combined tobacco smoking intensity as light (equivalent to 0–14 cigarettes per day), medium (equivalent to 15–24 cigarettes per day) or heavy (equivalent to ≥25 cigarettes per day). Body mass index (BMI) was categorised as non-overweight (<25), overweight (25–30) or obese (≥30). In case of missing smoking or anthropometry data at the first examination, data from a subsequent examination were used if available; otherwise, these data were coded as missing. Information on immigration and emigration as well as employment and civil status was obtained from Statistics Sweden.

Exposure assessment

A job-exposure matrix (JEM) was developed for the Swedish Construction Workers' cohort as previously described.[30] Exposure assessment in the JEM was based on a series of site visits by trained occupational hygienists during 1971–1977.[31] Participants were initially classified into 214 job codes, which after 1985 were reduced to 90 job codes with similar exposures. From the original JEM, we identified nine particle exposures (cement dust, concrete dust, quartz dust (crystalline silica), welding fumes, diesel exhaust, asphalt fumes, wood dust, asbestos and man-made mineral fibres (MMMF)). For each job code, selected exposures were assessed and graded on a relative scale from 0 to 5, where 0 referred to no exposure and grades 3–5 corresponded to exposure above the occupational exposure limit (OEL) at the time of the construction of the original JEM (online supplemental table S2). In the absence of an OEL, the threshold for grade 3 was set to levels considered the maximum acceptable at the time.[32] Exposure to diesel exhaust was assessed based on the OEL for nitrogen dioxide. Since very few jobs were considered highly exposed to diesel exhaust, a 0.5 grade was retrospectively added to better identify low-exposed participants.[30] In the exposure–response analyses, grade 1 was considered low exposure, and grades 2 and above were considered high exposure. For diesel exhaust, grade 0.5 was considered low exposure and grades 1 and above were considered high exposure. Each participant was assigned a job code and exposure at the time of entry into the cohort.

We created three major exposure categories to separate wood dust and fibres from inorganic particles. Thus, the first category, named inorganic dust and fumes, included workers exposed to cement dust, concrete dust, quartz dust, welding fumes, diesel exhaust or asphalt fumes. The second category included workers exposed to wood dust, and the third category included workers exposed to fibres (MMMF or asbestos). These three exposure categories were all dichotomous. Participants with no occupational exposure to particles (ie, any of the nine above) were classified as unexposed and used as the reference group in the statistical analyses. Some cohort participants were assigned to more than one exposure category. Lastly, we analysed associations with each of the nine original particle exposures separately (unexposed vs any exposure).

Chronic kidney disease

Individuals in the Swedish Construction Workers' cohort were linked to the Swedish National Patient Register, the Swedish Renal Registry and the Cause-of-death Register using individual personal identification numbers. Dates and underlying causes of death were obtained from the Cause-of-death Register from 1971 to 2021, and dates and diagnoses were obtained from the National Patient Register for in-patient care from 1971 to 2022. Dates and diagnoses for hospital-based outpatient care were obtained from 2001 to 2022. In a previous review of patient files, we have shown that renal diagnoses in the Swedish National Patient Register have high validity, finding that 94% of patients had a correct CKD diagnosis.[33] Date of start of RRT, including dialysis and renal transplantation, was obtained from the Swedish Renal Registry from 1991 to 2020.

The primary endpoint was incident CKD (International Classification of Diseases, ICD-8: 582, 792; ICD-9: 585; ICD-10: N18). Date of first CKD diagnosis was obtained from the National Patient Register for inpatient and outpatient care. If a participant had died with CKD as the main underlying cause of death, but without previous records of a CKD diagnosis, the date of death was used as the incidence date. The secondary endpoint was start of RRT. Starting date of RRT was obtained both from the National Patient Register (ICD-8: Y29,01; ICD-9: V56, V45B, V42A; ICD-10: Z49, Z99.2, Z94.0) and from the Swedish Renal Registry, and the earliest of these two used as the incidence date. Lastly, we explored associations with the three main aetiologies of CKD: diabetic nephropathy (ICD-8: 250,04; ICD-9: 250D; ICD-10: E10.2, E11.2, E13.2, E14.2), hypertensive nephropathy (ICD-8: 403,99, 404,99, 584; ICD-9: 403, 404, 587; ICD-10: I12, I13) and chronic glomerulonephritis (ICD-8: 582; ICD-9: 582; ICD-10: N03), all obtained from the National Patient Register.

Statistical analysis

We estimated multivariable Cox proportional hazards models, with calendar year on the time axis. Starting date for accrual

of person-years was the first recorded health examination (ie, between 1971 and 1993), the first year for which the participant's county of residence had complete and continuous coverage in the National Patient Register for in-patient care (ie, between 1964 and 1987) or age 30 years, whichever occurred the latest. Participants were censored on 31 December 2021 or at the event, emigration, death, age 90 years or diagnosis of hereditary nephropathy (ICD-8: 753; ICD-9: 753; ICD-10: N07).

To account for different associations between exposure and outcomes during working life and after retirement (ie, before vs after age 65), we allowed for different HRs by including as separate terms both exposure and exposure interacted with an older-than-65 dummy indicator (Wald CIs for the older-than-65-year group were calculated from the variances and covariances). Initial analyses without stratification for age did not fulfil the proportional hazards assumption. To account for the non-linear trends in baseline CKD incidence over age and CKD diagnostics over time, we adjusted for the interaction between natural splines for calendar year and age. This effectively allowed the relationship between age and disease risk to change with calendar time.

The models were adjusted using three different sets of covariates (a directed acyclic graph is presented in online supplemental figure S1). The crude model included only the interaction between age and calendar year, in addition to the exposure term and the interaction between exposure and the older-than-65-year indicator. In the main model, we added baseline covariates describing smoking status and intensity and BMI. Thus, the main model was $h\ (t)=h_0\ (t)\times exp(\beta_1\ [exposure]+\beta_2\ [exposure:\ age \geq 65]+\beta_3\ [ns(age_t):\ ns(year_t)]+\beta_4\ [smoking\ status]+\beta_5\ [smoking\ intensity]+\beta_6\ [BMI])$, where h signifies the hazard function, h_0 the baseline hazard, t the calendar year (ie, the time axis) and *ns* a natural spline function with four df. To estimate the direct effect (ie, not mediated by type 2 diabetes or hypertension) we created an extended model where we added the diagnosed type 2 diabetes mellitus (ICD-8 and ICD-9: 250; ICD-10: E10–E14) and hypertension (ICD-8: 400–404; ICD-9: 401–404; ICD-10: I10–I14) as binary, time-varying variables, both obtained from the National Patient Register.

We performed a number of sensitivity analyses to assess the robustness of model assumptions. We probed the model specification by performing analyses in the main model without BMI, as it could be considered a mediator, and in the main model including adjustment for geographic region of recruitment. However, since only 1.5% of participants were of non-Nordic origin, we did not stratify results on immigration status. We also ran the main analyses with age on the time axis, adjusting for age and calendar year using a spline interaction term, as above. Associations between the nine particle exposures and disease were investigated both in separate regression models and in a joint ('multipollutant') model. To assess the role of quartz dust exposure, we performed analyses restricted to workers with no recorded quartz dust exposure. Lastly, we investigated if the workers stayed in the construction industry and in the same job.

All analyses were performed in R 4.1.[34] Cox proportional hazards models were fit using the 'coxph' function from the Survival package.[35] The proportional hazards assumption was checked using tests for a null slope in the Schoenfeld residuals, using the 'cox.zph' function.

RESULTS

Most participants were enrolled during the 1970s. Characteristics of study participants at enrolment are presented in table 1. Mean age at first recorded health examination was 34 years and differed between job titles but was similar across the three major exposure categories. 95% of the participants were born in Sweden and the majority (71%) of the immigrated participants were born in another Nordic country. On average, cohort participants took part in three recorded medical exams, with 37% taking part only once. As expected, participants were stable within their occupations and within the construction industry (online supplemental figures S2–S4). For instance, among participants recruited in 1985 or later who were alive 25 years after enrolment, 61% were at that time still employed in the construction industry and only 23% had left the construction industry for work in other sectors.

Just over half of the participants (158 210 participants, 55%) were exposed to inorganic dust or fumes while 19 650 (6.9%) were exposed to wood dust and 22 820 (8.0%) to fibres. A little more than one-third of the cohort participants (105 149, 37%) were considered not exposed to any of the nine particle exposures. Participants included in the three major exposure categories were similar on all potential confounders, except for a slightly higher percentage of smokers among participants exposed to inorganic dust and fumes (43%) and fibres (44%), compared with unexposed participants (37%) and participants exposed to wood dust (36%).

The number of cohort participants with occupational exposure to particles is presented in table 2, distributed across the nine different particle exposures. Concrete dust was the most common form of particle exposure with 110 185 exposed participants (38%), followed by quartz dust, to which 58 458 (20%) were exposed. No single occupational title dominated among unexposed participants, among participants exposed to inorganic dust or fumes, or among participants exposed to fibres, while participants exposed to wood dust were either carpenters or flooring installers (online supplemental table S3).

We identified 10 194 cases of CKD over 8 019 608 person-years and 2025 cases of RRT over 8 053 024 person-years between the ages 30 and 90 years. Thus, the incidence of CKD

Table 1 Characteristics at enrolment for the included participants, for all participants and per exposure category

	All	Unexposed	Inorganic dust and fumes	Wood dust	Fibres
N	286 089	105 149	158 210	19 650	22 820
Age, mean (SD)	34 (13)	32 (12)	35 (13)	33 (13)	32 (13)
Current smokers, per cent	40	37	43	36	44
Heavy smokers*, per cent	6.3	6.2	6.6	4.7	6.4
Enrolment year, median (SD)	1976 (7)	1977 (7)	1976 (7)	1978 (7)	1977 (6)
BMI, mean (SD)	24.1 (3.1)	23.9 (3.0)	24.3 (3.2)	23.8 (2.9)	23.8 (3.1)
Syst. BP, mean (SD) (mm Hg)	133 (27)	132 (25)	134 (27)	133 (33)	133 (25)

*Corresponding to combined cigarette, cigar and pipe smoking equivalent to ≥25 cigarettes per day. Note that some individuals are included in multiple exposure categories.
BMI, body mass index; Syst. BP, systolic blood pressure.

Table 2 Number of cohort participants distributed across the nine different particle exposures

	Unexposed	Exposed
Inorganic dust and fumes		
Cement dust	261 960	24 129
Concrete dust	175 904	110 185
Quartz dust	227 604	58 485
Welding fumes	257 974	28 115
Diesel exhaust	247 478	38 611
Asphalt fumes	280 541	5 548
Wood dust		
Wood dust	266 439	19 650
Fibres		
Asbestos	273 207	22 613
MMMF	263 476	12 882

MMMF, man-made mineral fibres.

was 127 cases per 100 000 person-years and of RRT 25 cases per 100 000 person-years. The number of cases, person-years and incidence rates for each exposure group, outcome and age stratum are presented in online supplemental table S4. The average follow-up time was 27.5 years for CKD and 27.6 years for RRT. During the follow-up for CKD, 87 694 participants were diagnosed with hypertension and 35 380 with diabetes mellitus.

Exposure to inorganic dust and fumes was associated with a higher risk of both CKD (adjusted HR 1.15, 95% CI 1.05 to 1.26) and RRT during working age while associations at ages ≥65 years were null (table 3). Results from analyses not stratified on age are presented in online supplemental table S5, but tests of null slope in the Shoenfeld residuals indicated that these analyses did not fulfil the proportional hazards assumption. Results from analyses with age on the time axis were very similar to results using calendar year on the time axis (online supplemental table S6). Adjustment for comorbidities (ie, hypertension and diabetes mellitus, our extended model) affected the estimates only marginally. The associations were robust to the exclusion of participants classified as exposed to quartz (table 4). Estimates were slightly stronger in sensitivity analyses without adjustment for BMI while additional adjustment for geographical region had no effect on the estimates (online supplemental table S7). Estimates for CKD and RRT were highly congruent. Associations with exposure to wood dust and fibres were null or slightly in the opposite direction.

Exploring associations with the three main aetiologies of CKD, we found indications of an association between inorganic dust and fumes exposure and both chronic glomerulonephritis and hypertensive nephropathy during working age, although all CIs overlapped the null while there were no consistent associations with diabetic nephropathy (table 5, number of cases and person-years for these analyses are presented in online supplemental table S8). The smaller number of cases limited the interpretability of the estimates for exposure to wood dust and fibres. In separate analyses for each of the nine particulate exposures, we found associations with exposure to cement dust, concrete dust and diesel exhaust (online supplemental table S9). The HR for quartz dust was elevated for both CKD and RRT but CIs overlapped the null. Results from the combined regression ('multipollutant') model including all nine particle exposures were similar but with larger CIs (online supplemental table S10). Results from the exposure–response analysis indicated tentative exposure–response patterns during working age for cement dust and concrete dust for CKD, and for quartz dust for RRT, but

Table 3 Adjusted HRs for chronic kidney disease (CKD) and renal replacement therapy (RRT)

	Exposure	Covariate model	Adjusted HRs (95% CI) Age <65 years	Age ≥65 years
CKD	Inorganic dust and fumes	Crude*	1.22 (1.11 to 1.33)	1.04 (1.00 to 1.09)
		Main†	1.15 (1.05 to 1.26)	1.01 (0.97 to 1.06)
		Extended‡	1.14 (1.04 to 1.25)	1.02 (0.98 to 1.07)
	Wood dust	Crude*	0.85 (0.68 to 1.05)	0.94 (0.86 to 1.04)
		Main†	0.85 (0.68 to 1.05)	0.99 (0.90 to 1.09)
		Extended‡	0.84 (0.68 to 1.05)	1.00 (0.90 to 1.10)
	Fibres	Crude*	1.05 (0.88 to 1.26)	0.94 (0.86 to 1.03)
		Main†	1.01 (0.85 to 1.21)	0.93 (0.85 to 1.02)
		Extended‡	0.99 (0.83 to 1.19)	0.93 (0.85 to 1.02)
RRT	Inorganic dust and fumes	Crude*	1.22 (1.06 to 1.40)	1.03 (0.92 to 1.16)
		Main†	1.17 (1.01 to 1.34)	1.00 (0.89 to 1.12)
		Extended‡	1.16 (1.01 to 1.33)	1.01 (0.90 to 1.13)
	Wood dust	Crude*	0.85 (0.61 to 1.18)	0.73 (0.55 to 0.97)
		Main†	0.85 (0.61 to 1.19)	0.77 (0.58 to 1.02)
		Extended‡	0.85 (0.61 to 1.19)	0.78 (0.59 to 1.03)
	Fibres	Crude*	1.02 (0.77 to 1.34)	0.92 (0.72 to 1.17)
		Main†	0.99 (0.75 to 1.30)	0.91 (0.72 to 1.16)
		Extended‡	0.97 (0.74 to 1.28)	0.92 (0.72 to 1.17)

*The crude model included only adjustment for age.
†The main model also included smoking status, smoking intensity and BMI.
‡The extended model also included diagnosed diabetes and hypertension.
BMI, body mass index; CKD, chronic kidney disease; RRT, renal replacement therapy.

Table 4 Adjusted HRs (main covariate model) for exposure to inorganic dusts and fumes, for CKD, restricted to participants without quartz dust exposure

	Adjusted* HR (95% CI) Age <65 years	Age ≥65 years
CKD	1.17 (1.06 to 1.30)	1.02 (0.97 to 1.08)
RRT	1.17 (1.00 to 1.37)	1.01 (0.88 to 1.15)

*The main model included adjustment for age, smoking status, smoking intensity and BMI.
BMI, body mass index; CKD, chronic kidney disease; RRT, renal replacement therapy.

Table 5 Adjusted HRs (main model) for cGN, DN and HN, stratified by attained age

	Exposure	Adjusted* HR (95% CI) Age <65 years	Age ≥65 years
cGN	Inorganic dust and fumes	1.13 (0.95 to 1.35)	1.07 (0.84 to 1.37)
	Wood dust	0.75 (0.49 to 1.15)	1.10 (0.65 to 1.86)
	Fibre	1.07 (0.76 to 1.49)	1.08 (0.66 to 1.76)
DN	Inorganic dust and fumes	1.04 (0.91 to 1.19)	1.08 (0.97 to 1.20)
	Wood dust	1.02 (0.76 to 1.37)	0.78 (0.60 to 1.03)
	Fibre	1.00 (0.77 to 1.29)	1.02 (0.82 to 1.27)
HN	Inorganic dust and fumes	1.13 (0.97 to 1.32)	1.06 (0.95 to 1.18)
	Wood dust	0.86 (0.59 to 1.27)	0.92 (0.72 to 1.18)
	Fibre	1.04 (0.76 to 1.42)	0.95 (0.76 to 1.19)

*The main model included adjustment for age, smoking status, smoking intensity and BMI.
BMI, body mass index; cGN, chronic glomerulonephritis; DN, diabetic nephropathy; HN, hypertensive nephropathy.

no consistent associations after retirement (online supplemental table S11).

DISCUSSION

In this cohort of Swedish construction workers, we found consistent associations between occupational exposure to inorganic dust and fumes and an increased risk of CKD and RRT after adjustment for smoking, BMI and comorbidities during working age (age <65 years). Associations seemed to be driven primarily by exposure to diesel exhaust, cement dust and concrete dust and were robust to exclusion of quartz-exposed individuals. The results confirm our hypothesis and provide evidence of an elevated risk of CKD for construction workers with long-term occupational exposure to inorganic dust and fumes.

Our results are consistent with the limited number of previous studies in occupational settings. The case–control study by Sponholtz *et al*[28] reported associations between having worked in dusty conditions in agricultural crop production and both CKD and end-stage renal disease. For workers in the construction industry, they reported elevated but statistically non-significant associations (OR 1.22, 95%CI 0.60, 2.48), which are roughly compatible with our estimates. Likewise, Nuyts *et al*[27] found associations between multiple forms of dust, including welding fumes and chronic renal failure.

The elevated risk of renal disease following exposure was not sustained at older ages (≥65 years). This indicates that elevated risk incurred by particle exposure attenuates after exposure cessation. Of the three main aetiologies (chronic glomerulonephritis, diabetic nephropathy and hypertensive nephropathy) chronic glomerulonephritis and hypertensive nephropathy showed elevated estimates, although the smaller number of cases of chronic glomerulonephritis resulted in wider confidence intervals including the null. This is similar to findings by Sponholtz *et al*,[28] who for workers in generally dusty conditions reported the strongest association with glomerulonephritis, a tentative association with hypertensive nephropathy and a weak or null association with diabetic nephropathy.

Analyses of associations with the nine particle exposures showed positive associations for exposure to cement dust, concrete dust, diesel exhaust and possibly quartz dust (online supplemental table S9). For cement and concrete dusts, we also observed indications of exposure–response patterns with CKD (online supplemental table S11). The elevated HRs for exposure to diesel exhaust are of particular interest in relation to previously reported associations with ambient air pollution.[36–38] This indicates that silica is not the sole factor driving associations between dust exposure and CKD. This is also supported by the robustness of the overall associations between inorganic dust and fumes and CKD to exclusion of the participants exposed to quartz dust. The similarity of point estimates for quartz and other inorganic dust is reminiscent of findings for rheumatological diseases in the same cohort.[39]

The primary strength of this study is the very large, socioeconomically homogeneous cohort with a long follow-up time, as well as the high quality and coverage of outcome data from national registries and including outpatient care for most of the follow-up period. Another strength is the externally assessed exposure metric obtained through a previously established JEM, which precludes recall bias. Misclassification of the outcome is unlikely, because of the high validity of CKD diagnoses from the Swedish National Patient Register.[33] The use of national registries allowed us to assume complete information for non-emigrated participants, although the increase in knowledge and awareness of CKD over the study period means that there is a higher risk of delayed or missed diagnoses in the earlier periods. However, the effect of missed outcomes should be non-differential and partially remedied through supplementing the CKD endpoint with cause-of-death data and adjustment for calendar year in the regression models. Contributing to this risk of delayed or missed cases was our inability to include diagnoses from primary care, where non-complicated early CKD is increasingly treated, as there is no national register for primary care diagnoses in Sweden. Unfortunately, the registry-based outcome meant that we did not have access to other renal measures, such as creatinine, eGFR or albuminuria. Although it is possible to include CKD staging in ICD-10 diagnoses, this information was available only for a small minority of the cases. On the other hand, the registry-based outcome enabled separate analyses of RRT initiation, as well as the possibility to explore the three main aetiologies of CKD.

Our main limitation as an observational study is that we cannot fully exclude effects from other exposures associated with occupation (eg, most unexposed workers were foremen or electricians, online supplemental table S3). However, as both the unexposed and exposed groups were construction workers, it is reasonable to believe that lifestyle factors were similar in both the exposed and unexposed groups, thus being unlikely to account for the associations we report. Furthermore, inherent in using a JEM for exposure assessment is a risk of exposure misclassification. Similarly, it is likely that exposure has decreased over time, which would not be captured by the JEM. This is unlikely to have changed the contrast between exposed and unexposed qualitatively; however, it precludes direct translation of our risk estimates to certain exposure concentrations and complicates interpretation of the exposure–response analyses. Therefore, the exposure–response analyses should be interpreted with caution due to uncertainty in the graded exposure assessment. Another important limitation is that we were unable to assess exposure duration. However, workers in the Swedish construction industry are known to stay within the same occupation for a long time,[32] which our data also corroborated (online supplemental figures S2–S4). It is likely that misclassification of levels and duration of particle exposure is non-differential, as very few participants had developed CKD at the time of occupational coding and exposure assessment. Consequently, associations between particle exposure and risk of CKD may well be stronger than shown in table 3. Another limitation is that workers were not unexposed at enrolment, which could theoretically mean both that exposure may already have affected participant data obtained at enrolment and that there might be a selection of survivors. The former is unlikely to have affected the covariates (sex, smoking and BMI) included in our analyses, and the latter is likely negligible due to the rarity of CKD below 30 years of age. Lastly, data on smoking habits and BMI were missing for a large number of participants, as questions on smoking habits were not included in examinations 1975–1978. However, almost all of these data could be recovered from subsequent visits, which limits the risk of selection bias. Although workers exposed to inorganic dust and fumes were more often smokers and had slightly higher BMI (table 1), differences were small and adjustment of the regression models had little effect on the estimates, making major confounding of our results unlikely.

CONCLUSIONS

In this large cohort study of Swedish construction workers, long-term occupational exposure to inorganic particles was associated with both incident CKD and need for RRT during working age. Our results indicate that renal effects of particle exposure are not solely driven by silica exposure, adding to the growing body of evidence for a causal relationship between exposure to particle matter and CKD. Considering the substantial disease burden and costly treatment of CKD, this has large implications for public health and warrants further efforts to reduce occupational and ambient particle exposure.

Correction notice This article has been corrected since it was published. Licence updated to CC BY on 1st August 2024.

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Contributors LS conceptualised the study and acquired funding for the study. KKE, EMA and LS developed the analytical protocol. KKE conducted the statistical analyses and wrote the first draft. EMA, MA, LB, AC, SJ, FH, NM, KT and LS provided expertise and critical revisions during manuscript preparation. LS is the guarantor of this study. All authors approved the final manuscript.

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Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by Swedish Ethical Review Authority (Dnr 2021-02326). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available. All data used in this study were obtained from the Swedish Construction Workers' Cohort (Umeå University), Statistics Sweden, and the National Board of Health and Welfare.

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REFERENCES

1 Jha V, Garcia-Garcia G, Iseki K, *et al*. Chronic kidney disease: global dimension and perspectives. *Lancet* 2013;382:260–72.
2 Murray CJL, Aravkin AY, Zheng P, *et al*. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the global burden of disease study 2019. *Lancet* 2020;396:1223–49.
3 Gansevoort RT, Correa-Rotter R, Hemmelgarn BR, *et al*. Chronic kidney disease and cardiovascular risk: epidemiology, mechanisms, and prevention. *Lancet* 2013;382:339–52.
4 Matsushita K, Astor BC, Woodward M, *et al*. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. *Lancet* 2010;375:2073–81.
5 Rasking L, Vanbrabant K, Bové H, *et al*. Adverse effects of fine particulate matter on human kidney functioning: a systematic review. *Environ Health* 2022;21:24.
6 Ye JJ, Wang SS, Fang Y, *et al*. Ambient air pollution exposure and risk of chronic kidney disease: a systematic review of the literature and meta-analysis. *Environ Res* 2021;195:110867.
7 Yan Y-H, C-K Chou C, Wang J-S, *et al*. Subchronic effects of inhaled ambient particulate matter on glucose homeostasis and target organ damage in a type 1 diabetic rat model. *Toxicol Appl Pharmacol* 2014;281:211–20.
8 Aztatzi-Aguilar OG, Uribe-Ramírez M, Narváez-Morales J, *et al*. Early kidney damage induced by subchronic exposure to PM2.5 in rats. *Part Fibre Toxicol* 2016;13.
9 Tavera Busso I, Mateos AC, Juncos LI, *et al*. Kidney damage induced by sub-chronic fine particulate matter exposure. *Environ Int* 2018;121:635–42.
10 Hsu Y-H, Chuang H-C, Lee Y-H, *et al*. Traffic-related particulate matter exposure induces nephrotoxicity in vitro and in vivo. *Free Radic Biol Med* 2019;135:235–44.
11 Brook RD, Rajagopalan S, Pope CA III, *et al*. Particulate matter air pollution and cardiovascular disease. *Circulation* 2010;121:2331–78.
12 Bevan GH, Al-Kindi SG, Brook RD, *et al*. Ambient air pollution and atherosclerosis. *ATVB* 2021;41:628–37.
13 Torén K, Bergdahl IA, Nilsson T, *et al*. Occupational exposure to particulate air pollution and mortality due to ischaemic heart disease and cerebrovascular disease. *Occup Environ Med* 2007;64:515–9.
14 Mocevic E, Kristiansen P, Bonde JP. Risk of ischemic heart disease following occupational exposure to welding fumes: a systematic review with meta-analysis. *Int Arch Occup Environ Health* 2015;88:259–72.
15 Liu K, Mu M, Fang K, *et al*. Occupational exposure to silica and risk of heart disease: A systematic review with meta-analysis. *BMJ Open* 2020;10:e029653.
16 Gustavsson P, Plato N, Hallqvist J, *et al*. A population-based case-referent study of myocardial infarction and occupational exposure to motor exhaust, other combustion products. *Epidemiology* 2001;12:222–8.
17 Fiordelisi A, Piscitelli P, Trimarco B, *et al*. The mechanisms of air pollution and particulate matter in cardiovascular diseases. *Heart Fail Rev* 2017;22:337–47.
18 Rajagopalan S, Al-Kindi SG, Brook RD. Air pollution and cardiovascular disease: JACC state-of-the-art review. *J Am Coll Cardiol* 2018;72:2054–70.
19 Schefold JC, Filippatos G, Hasenfuss G, *et al*. Heart failure and kidney Dysfuction. *Nat Rev Nephrol* 2016;12:610–23.
20 Amann K, Wanner C, Ritz E. Cross-talk between the kidney and the cardiovascular system. *J Am Soc Nephrol* 2006;17:2112–9.
21 Viitanen AK, Uuksulainen S, Koivisto AJ, *et al*. Workplace measurements of Ultrafine particles-a literature review. *Ann Work Expo Health* 2017;61:749–58.
22 Möhner M, Pohrt A, Gellissen J. Occupational exposure to Respirable crystalline silica and chronic non-malignant renal disease: systematic review and meta-analysis. *Int Arch Occup Environ Health* 2017;90:555–74.
23 Vupputuri S, Parks CG, Nylander-French LA, *et al*. Occupational silica exposure and chronic kidney disease. *Renal Failure* 2012;34:40–6.
24 Steenland NK, Thun MJ, Ferguson CW, *et al*. Occupational and other exposures associated with male end-stage renal disease: a case/control study. *Am J Public Health* 1990;80:153–7.
25 Rapiti E, Sperati A, Miceli M, *et al*. End stage renal disease among ceramic workers exposed to silica. *Occup Environ Med* 1999;56:559–61.
26 Archer JD, Cooper GS, Reist PC, *et al*. Exposure to respirable crystalline silica in Eastern North Carolina farm workers. *AIHA J (Fairfax, Va)* 2002;63:750–5.
27 Nuyts GD, D'Haese PC, Elseviers MM, *et al*. New occupational risk factors for chronic renal failure. *Lancet* 1995;346:7–11.
28 Sponholtz TR, Sandler DP, Parks CG, *et al*. Occupational exposures and chronic kidney disease: possible associations with endotoxin and Ultrafine particles. *Am J Ind Med* 2016;59:1–11.
29 Stattin M, Järvholm B. Occupation, work environment, and disability pension: a prospective study of construction workers. *Scand J Public Health* 2005;33:84–90.
30 Lee WJ, Baris D, Järvholm B, *et al*. Multiple myeloma and diesel and other occupational exposures in Swedish construction workers. *Int J Cancer* 2003;107:134–8.
31 Bygghälsan, environmental descriptions of occupations with the construction industry [in Swedish]. Bygghälsan; 1977.
32 Bergdahl IA, Torén K, Eriksson K, *et al*. Increased mortality in COPD among construction workers exposed to inorganic dust. *Eur Respir J* 2004;23:402–6.
33 Harari F, Sallsten G, Christensson A, *et al*. Blood lead levels and decreased kidney function in a population-based cohort. *Am J Kidney Dis* 2018;72:381–9.
34 R Core Team. R: A language and environment for statistical computing. 2021. Available: https://www.r-project.org/
35 Therneau TM, Grambsch PM. *Modeling survival data: extending the {C}ox model*. Springer, New York, 2000.
36 Blum MF, Surapaneni A, Stewart JD, *et al*. Particulate matter and albuminuria, glomerular filtration rate, and incident CKD. *Clin J Am Soc Nephrol* 2020;15:311–9.
37 Xu Y, Andersson EM, Krage Carlsen H, *et al*. Associations between long-term exposure to low-level air pollution and risk of chronic kidney disease—findings from the Malmö diet and cancer cohort. *Environ Int* 2022;160:107085.
38 Bowe B, Xie Y, Li T, *et al*. Particulate matter air pollution and the risk of incident CKD and progression to ESRD. *J Am Soc Nephrol* 2018;29:218–30.
39 Blanc PD, Järvholm B, Torén K. Prospective risk of rheumatologic disease associated with occupational exposure in a cohort of male construction workers. *Am J Med* 2015;128:1094–101.