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Fine particulate matter and incident coronary heart disease events up to 10 years of follow-up among *Deepwater Horizon* oil spill workers

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Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Abstract

Background: During the 2010 *Deepwater Horizon* (*DWH*) disaster, *in-situ* burning and flaring were conducted to remove oil from the water. Workers near combustion sites were potentially exposed to burning-related fine particulate matter ($PM_{2.5}$). Exposure to $PM_{2.5}$ has been linked to increased risk of coronary heart disease (CHD), but no study has examined the relationship among oil spill workers.

Objectives: To investigate the association between estimated $PM_{2.5}$ from burning/flaring of oil/gas and CHD risk among the *DWH* oil spill workers.

Methods: We included workers who participated in response and cleanup activities on the water during the *DWH* disaster (N=9,091). $PM_{2.5}$ exposures were estimated using a job-exposure matrix that linked modelled $PM_{2.5}$ concentrations to detailed *DWH* spill work histories provided by participants. We ascertained CHD events as the first self-reported physician-diagnosed CHD or a fatal CHD event that occurred after each worker's last day of burning exposure. We estimated hazard ratios (HR) and 95% confidence intervals (95%CI) for the associations between categories of average or cumulative daily maximum $PM_{2.5}$ exposure (versus a referent category of water workers not near controlled burning) and subsequent CHD. We assessed exposure-response trends by examining continuous exposure parameters in models.

Results: We observed increased CHD hazard among workers with higher levels of average daily maximum exposure (low vs. referent: HR=1.26, 95% CI: 0.93, 1.70; high vs. referent: HR=2.11, 95% CI: 1.08, 4.12; per 10 $\mu g/m^3$ increase: HR=1.10, 95% CI: 1.02, 1.19). We also observed suggestively elevated HRs among workers with higher cumulative daily maximum exposure (low vs. referent: HR=1.19, 95% CI: 0.68, 2.08; medium vs. referent: HR=1.38, 95% CI: 0.88, 2.16; high vs. referent: HR=1.44, 95% CI: 0.96, 2.14; per 100 $\mu g/m^3$-d increase: HR=1.03, 95% CI: 1.00, 1.05).

Conclusions: Among oil spill workers, exposure to $PM_{2.5}$ from flaring/burning of oil/gas was associated with increased risk of CHD.

Keywords

$PM_{2.5}$; particulate matter; air pollution; coronary heart disease; myocardial infarction; oil spill

Introduction

The *Deepwater Horizon* (*DWH*) disaster in April 2010 resulted in the largest marine oil spill in U.S. history (National Commission on the BP Deepwater Horizon Oil Spill and Offshore Drilling 2011). Following the disaster, an extensive oil spill response and cleanup (OSRC) effort was launched to contain the spill and remove crude oil from the environment (National Commission on the BP Deepwater Horizon Oil Spill and Offshore Drilling 2011). Controlled burning was employed as a spill remediation method and played an important role in efficiently removing oil from the sea surface (U.S. Coast Guard 2011). Two controlled burning activities took place: 1) flaring of oil/natural gas on vessels, and 2) *in situ* burning of oil in the offshore area (U.S. Coast Guard 2011). The term "controlled burning" will henceforth refer to both of these activities. Between May 17, 2010 and July 16, 2010, two drilling rigs and a production/offloading vessel collected crude oil at the wellhead and flared onboard either the oil/gas mixture or the natural gas separated from the oil (U.S. Coast Guard 2011). While flaring occurred almost continuously in the two months, *in situ* burning was conducted only on certain days and hours when weather conditions were suitable (Allen et al. 2011). From April 28, 2010 to July 19, 2010, the *in situ* burn (ISB) taskforce attempted 411 burns offshore, which resulted in the removal of ~5% of the total discharged oil (Allen et al. 2011; Ramseur 2010). Almost all controlled burning activities were complete by July 15, 2010.

Both flaring and *in situ* burning generated substantial particulate and gaseous emissions that could have been inhaled by workers near sites of burning. One emission of particular concern was fine particulate matter, particles with aerodynamic diameter of 2.5 microns or less ($PM_{2.5}$), which are regarded by health professionals as the main toxicant to monitor and investigate in controlled burns (Barnea 2011). $PM_{2.5}$ is a universal air pollutant and one of six criteria pollutants whose outdoor levels are regulated by the U.S. Environmental Protection Agency (EPA) for their harmful effects on human health and the environment (Batavia 1991). During the *DWH* disaster, the U.S. federal agencies collected several ISB plume samples to monitor the air pollutants present. Laboratory analyses of the samples showed high levels of particulate matter and its components (soot particles, black carbon, dioxins) (Aurell and Gullett 2010; Gullett et al. 2016; Perring et al. 2011), demonstrating the potential inhalation hazards workers near the ISB might have encountered. Based on a Gaussian plume dispersion model and self-reported OSRC work histories, personal $PM_{2.5}$ estimates from controlled burning of oil/gas have been developed for *DWH* oil spill workers (Pratt et al. 2022), providing an opportunity to study the health impacts of this exposure (Chen et al. 2022; Kwok et al. 2022).

A link between short-term $PM_{2.5}$ exposure and coronary heart disease (CHD) has been documented in numerous studies of ambient air pollution. Studies have associated hospitalizations and emergency department visits due to CHD with $PM_{2.5}$ concentrations on the same day or a few days before (Dominici et al. 2006; Hsu et al. 2017; Talbott et al. 2014), but few have explored the *persistent* effect of a relatively short-term $PM_{2.5}$ exposure. In studies of *DWH* oil spill workers, elevated risk of CHD up to 5 years after the spill has been observed among workers with higher exposure to maximum levels of total petroleum hydrocarbons (THC) and with longer duration of work (Strelitz et al. 2019a; Strelitz et al.

2019b). No apparent association was found for a crude self-reported measure of controlled burning exposure (yes/no), possibly because of misclassification in the exposure (Strelitz et al. 2018). The purpose of the present study is to assess the relationship between quantitative estimates of $PM_{2.5}$ concentrations from controlled burning of oil/gas and CHD risk among *DWH* oil spill workers up to 10 years after the spill.

Methods

Study population

The Gulf Long-Term Follow-up Study (GuLF Study) is a prospective study of 32,609 participants (ages 21 years and older) who either worked on the *DWH* oil spill cleanup (workers) or completed safety training but were not hired (non-workers) (Engel et al. 2017; Kwok et al. 2017). Between March 2011 and May 2013, computer-assisted telephone interviews were conducted to enroll participants and obtain information on socio-demographics, lifestyle, health, and *DWH* spill work histories. Since enrollment, two rounds of follow-up interviews (May 2013-April 2016 and November 2017-July 2021) have been conducted to ascertain changes in health status since the previous interview. We excluded from analysis 999 Vietnamese-speaking participants who completed an abbreviated enrollment interview that did not collect complete *DWH* oil spill work histories needed to assign exposure estimates. Among the remaining 31,609 participants, 21,256 (67%) and 14,187 (45%) completed the first and second follow-up interviews, respectively, although response rates were over 88% in both follow-ups among those who could be reached by phone or mail.

For all analyses, we restricted the study population to the 24,375 workers, because burning-related $PM_{2.5}$ exposures were not estimated for non-workers. We excluded 35 workers who did not respond to questions on CHD diagnoses in any of the interviews and excluded 740 workers who reported a CHD diagnosis before the start of follow-up for incident CHD events. Of the remaining 23,600 workers, we restricted our analysis to the 21,254 workers who worked at least one day between May 15 and July 15, 2010, the period in which the majority of flaring and ISB occurred. We further restricted our main analysis to the 9,482 workers who conducted any OSRC work on water (i.e. water workers). Land workers were excluded from the analysis because they were additionally exposed to engine emissions from vehicles and land equipment, but we lacked information to estimate this background exposure. Finally, we removed 391 workers with missing covariates, leaving a final analytical sample of 9,091 participants (Figure S1). Workers were followed from the date after their last day of burning exposure (i.e. the date after either their last day of OSRC work or July 15, 2010, whichever occurred first).

All participants provided informed consent. The study was approved by the Institutional Review Board (IRB) of the National Institute of Environmental Health Sciences and is now overseen by the combined National Institute of Health IRB.

PM$_{2.5}$ exposure assessment

The method for developing PM$_{2.5}$ exposure estimates for workers in the GuLF Study has been described elsewhere (Pratt et al. 2022). While working on water, workers were potentially exposed to PM$_{2.5}$ emissions from flaring, *in situ* burning, and water vessel engines. Air concentration estimates were developed to reflect emissions from controlled burning but did not account for vessel emissions due to uncertainties in the locations of workers and vessels.

For the controlled burning period of May 15 - July 15, 2010, study researchers estimated PM$_{2.5}$ emissions at the flaring and ISBs sources based on amount of oil/gas burned, emission factors, and duration of combustion. These data, along with meteorological data and source characterizations were incorporated into AERMOD (Cimorelli et al. 2005), a Gaussian air dispersion model, to estimate hourly PM$_{2.5}$ air concentrations at 3,960 geospatial model receptors on days with controlled burning. From the hourly concentrations, two daily concentrations were calculated at each receptor: the highest 1-hour (maximum 1-hour) and the higher of two 12-hour (0:00–11:59 and 12:00–23:59) (maximum 12-hour) concentrations.

Study researchers created exposure groups based primarily on work areas in the Gulf: hot zone (1 nautical mile (nmi) radius around the wellhead), source (>1 and 5 nmi radius around the wellhead), offshore (>5 nmi from the wellhead to >3 nmi from shore), near shore (3 nmi from shore), and land. Those who performed OSRC work in the offshore area were further divided by self-reported job/activity into ISB workers and non-ISB workers, since the former group were expected to have been exposed to higher PM$_{2.5}$ concentrations from directly participating in the ISB burning. To develop summary statistics by work area, offshore, nearshore, and land areas were delineated by 10×10 nmi grid squares, and the hot zone and source areas were delineated by a finer grid of 1×1 nmi squares inside the 10×10 nmi square containing the wellsite. For ISB workers, daily concentration was estimated by 1) averaging concentrations (either maximum 1 or 12-hour) for all receptors within each square that contained an ISB on each burn day, 2) averaging all grid square estimates with an ISB on a given day in step 1 to generate a daily estimate, and 3) averaging the estimates in step 2 across all days with ISBs (N=30). For all the other exposure groups (work areas), the average concentrations were calculated by averaging the daily maximum 1- and 12-hour concentrations of the receptors located within a work area (the work areas defined by a spatial map provided in the supplementary materials of Pratt et al. (2022)) and then averaging the daily average work-area concentrations over all days with controlled burning (N=57).

Each worker was matched to the appropriate exposure group based on the detailed *DWH* spill work histories that they reported in a structured interview at enrollment and assigned the average concentration estimate corresponding to their exposure group. We refer to these concentration estimates as exposures, although these exposure estimates were ambient air concentrations estimates rather than personal exposure estimates. Participants who worked in multiple locations and/or performed multiple activities were matched to the exposure group with the highest estimate. In addition to the average exposure, study researchers also created a cumulative exposure metric by multiplying each worker's average exposure by

his/her duration of work adjusted for the number of burn days in the controlled burning period to reflect the participant's total $PM_{2.5}$ burden. A total of four exposure variables were created from the two exposure metrics (average and cumulative exposures) and the two daily concentration values (maximum 1-hour and maximum 12-hour). Because exposure estimates using the maximum 1-hour daily and the maximum 12-hour average daily concentrations had nearly identical distributions (Pearson r>0.99), we chose to examine only the average maximum 12-h exposure (mg/m^3) and the cumulative maximum 12-h exposure (mg/m^3-day) (henceforth, average daily maximum and cumulative daily maximum exposures) in all analyses.

Outcome assessment

The outcome of interest was the first occurrence of a CHD event after the last day each worker was exposed to controlled burning. CHD was defined as either a self-reported physician diagnosis of CHD or an International Classification of Disease (ICD)-coded fatal CHD event. CHD was self-reported at the enrollment interview and in each of the two follow-up interviews. Participants were asked if a doctor had ever told them that they 1) had a myocardial infarction (MI) or 2) had blockage in the arteries of the heart. Those who responded "yes" were asked to provide the month and year of, or the age at, the event. Participants who reported having either of the two diagnoses were classified as non-fatal CHD cases. Fatal CHD events were ascertained by linking the GuLF Study with the National Death Index through December 31, 2019. We identified deaths with ischemic heart disease (ICD-10 code I20-I25) as the underlying cause. The risk period for CHD began on the date after each worker's last day of burning exposure and ended at the first of CHD event, death from other causes, withdrawal from the study, or end of follow-up (December 31, 2019).

Statistical modeling

We used Cox proportional hazards models (Cox 1972) to estimate hazard ratios (HRs) for the first incident CHD event associated with $PM_{2.5}$ exposure from controlled burning. For both average and cumulative daily maximum $PM_{2.5}$ exposures, we created a referent group by combining nearshore and non-ISB offshore workers, whose exposures were substantially lower than those of the other water workers (Table S1). For average daily maximum exposure, we collapsed ISB workers (10.4 $\mu g/m^3$) and source/hot zone workers (28.7 $\mu g/m^3$) due to the small number of workers in the ISB group (N=41). The recoded average daily maximum exposure measure examined in the models had three levels: referent (0.8 $\mu g/m^3$), low (10.4–28.7 $\mu g/m^3$), and high (96.9 $\mu g/m^3$, concentration assigned to hot zone workers). Because the cumulative daily maximum exposure had greater exposure variability (due to varying work durations among workers) than the average daily maximum exposure, we examined this measure by categorizing the non-referent group (i.e. ISB, source/hot zone, and hot zone workers) into tertiles based on the cumulative daily maximum exposure and examining the tertiles along with the referent group as a four-level categorical measure: the referent group (<10 $\mu g/m^3$-days), low (10–679 $\mu g/m^3$-days), medium (689–1378 $\mu g/m^3$-days), and high (1406–4071 $\mu g/m^3$-days). Because of tied values at the tertile cutoffs (Figure S2), the tertiles are not equally sized. In addition to the categorical exposure models, we

also examined continuous versions of average (per 10 μg/m^3 increase) and cumulative daily maximum exposures (per 100 μg/m^3-day increase) in separate models.

We accounted for confounding using inverse probability (IP) of exposure weighting (Cole and Hernan 2004). Covariates included in the weighting model comprised the minimally sufficient adjustment set and predictors of the outcome, as identified from a directed acyclic graph (Brookhart et al. 2006; Greenland et al. 1999; Textor et al. 2016) (Figure S3). We obtained stabilized exposure weights by fitting a multinomial logistic regression model for the exposure with respect to selected covariates. All covariates were ascertained at enrollment and included the following: age (in years: 20–29, 30–39, 40–49, 50–59, 60), sex (male; female), self-reported race (White; Black; other/multi-racial ("American Indian or Alaskan Native", "Asian", "Native Hawaiian or Pacific Islander", "other races")), Hispanic ethnicity (Hispanic; non-Hispanic), cigarette smoking status (current heavy (20 cigarettes/ day); current light (<20 cigarettes/day); former; never), highest educational attainment (less than high school; high school diploma or general equivalency diploma; some college or 2-year degree; 4-year college graduate or more), body mass index (BMI; in kg/m^2: underweight or normal [<25], overweight [25-<30], obese I [30-<35], obese II 35]), previous oil spill cleanup experience (yes; no), previous oil industry experience (yes; no), pre-cleanup diabetes diagnosis (yes; no), and residential proximity to the spill (living in a coastal county directly affected by the spill or a county adjacent to the impacted counties; living in a Gulf state further from the spill; living in a non-Gulf state).

To account for informative censoring due to loss to follow-up, we used IP-censoring weighting (Hernán et al. 2004; Howe et al. 2016). Participants were considered censored if they 1) did not complete a follow-up interview or completed the first but not the second interview and 2) had not experienced a CHD event prior to being lost to follow-up. We obtained stabilized censoring weights by modelling censoring as a function of its predictors in a pooled logistic regression. Covariates in the IP-censoring weights were determined from a causal diagram and included the following: PM$_{2.5}$ exposure, age, sex, race, Hispanic ethnicity, cigarette smoking, highest educational attainment, previous oil spill cleanup experience, and residential proximity to the spill. The finalized weights applied to the models were the product of the IP-exposure and the IP-censoring weights. Cox proportional hazards models with a robust variance estimator were fitted to estimate HRs and 95% confidence intervals (CIs).

We conducted a number of sensitivity analyses. First, we examined non-fatal cases as the outcome (i.e., excluding fatal cases). We could not examine fatal CHD alone as the outcome because the number of fatal cases was small (N=29). We also conducted analyses using an alternative definition of CHD-related deaths based on ischemic heart disease as either a *contributing* or *underlying* cause rather than only the *underlying* cause of death. Because CHD deaths that occurred after the start of OSRC work and prior to cohort enrollment could not be identified, we explored the impact of starting the risk period at study enrollment, rather than the date after the last day of burning exposure, which led to the exclusion of 108 non-fatal CHD cases. In addition, we adjusted for self-reported pre-exposure hypertension by including it in the IP-exposure weights to see if results differed. We did not account for this covariate in the main analysis because *pre-exposure* hypertension was not associated

with crude oil exposures and we were concerned about the accuracy of self-reports in ascertaining hypertension (Gonçalves et al. 2018). Furthermore, we examined associations in the subset of workers without a pre-exposure hypertension diagnosis. We were not able to examine associations in participants with a prevalent hypertension diagnosis because of small number of cases in this subgroup. Because volatile components of the crude oil may also be related to cardiovascular disease (Denic-Roberts et al. 2022; Strelitz et al. 2019b), we accounted for potential co-pollutant confounding by adjusting for cumulative THC exposure to see if results differed. Exposure to THC was estimated via a job-exposure matrix based on personal air sample measurements and *DWH* spill work histories provided by participants (Stewart et al. 2022). To explore the potential bias from mis-recalling the date of CHD diagnosis among participants who reported a non-fatal CHD event, we performed an exploratory analysis that coarsened the time interval in which events were identified so that CHD events were tallied every 4 months instead of every month.

In addition to controlled burning exposures, OSRC workers were also exposed to $PM_{2.5}$ from engine emissions, which were not examined in the study. Compared to $PM_{2.5}$ concentrations from controlled burning, $PM_{2.5}$ estimates from vessel engine emissions contained much greater uncertainty because the exact numbers, locations, and characteristics of the vessels are not precisely known. To explore the impact of not being able to account for this uncertain co-exposure, we performed a sub-analysis that excluded non-ISB offshore workers, the group with the largest potential vessel exhaust exposure variability, to see if results differed. In another sensitivity analysis, we included land workers as an additional exposure category for comparison with the referent group to explore the potential bias from excluding the land workers in our main analysis. All analyses were performed using SAS, version 9.4 (SAS Institute Inc., Cary, NC, USA). An alpha level of 0.05 was considered statistically significant for all analyses.

Results

Compared to the full analytical sample (N=9,091), those who completed the first (N=6,204) or second (N=4,251) follow-up interviews tended to be older, female, White, and former or never smokers (Table 1). They were also more likely to have graduated from college and to reside in a non-Gulf state. There were no substantive differences in the other characteristics. During a median follow-up of 59 months (range: 1–115 months), 372 out of 9,091 workers had an incident CHD event that occurred after the end of OSRC work. This included 343 cases of non-fatal CHD and 29 fatal CHD events without a history of reported CHD. Over 90% of cases occurred among participants who were 40 years or older at enrollment. The number of cases that occurred in the first 2, 4, and 6 years of follow-up were 128 (34.4%), 210 (56.5%), and 276 (74.2%), respectively.

Compared to workers in the referent group, we observed increased risks of CHD among workers with higher *average* daily maximum exposure (low vs. referent: HR=1.26, 95% CI: 0.93, 1.70; high vs. referent: HR=2.11, 95% CI: 1.08, 4.12) (Table 2). We also saw a significantly elevated HR in the analysis with continuous exposure (per 10 μg/m³ increase: HR = 1.10, 95%CI: 1.02, 1.19). When examining *cumulative* daily maximum exposure, we observed elevated HRs among workers in higher exposure categories compared to

the referent group (low vs. referent: HR=1.19, 95% CI: 0.68, 2.08; medium vs. referent: HR=1.38, 95% CI: 0.88, 2.16; high vs. referent: HR=1.44, 95% CI: 0.96, 2.14). Analysis of continuous exposure showed a marginally significant association with CHD risk (per 100 μg/m^3-day increase: HR = 1.03, 95%CI: 1.00, 1.05). In analyses without censoring weights, we observed slightly stronger effect estimates (Table 2). The mean and range of the stabilized IP weights for the exposures are shown in Table S2.

When we restricted the outcome to non-fatal CHD, we observed similar associations (Table 3). The sensitivity analysis that identified fatal events as deaths with CHD as either a *contributing* or *underlying* cause of death produced minimal differences in the observed associations (Table S3). In an analysis where we started the risk period at time of enrollment instead of at the end of controlled burning exposure, workers in the highest exposure categories of average and cumulative exposure were at similarly increased risk of CHD as that in the main analysis, although risk in the medium cumulative exposure category was no longer elevated (Table S4). When we accounted for pre-exposure hypertension in the model, we observed similar associations, although risk among workers in the medium cumulative exposure category was somewhat attenuated, possibly because a disproportionate number of individuals in this exposure category were missing hypertension data (Table S5). Associations were somewhat weaker in the subgroup analysis among workers without a pre-exposure hypertension diagnosis; however, confidence intervals were wide (Table S6). When we adjusted in the model for cumulative THC exposure, which was poorly/moderately correlated with average and cumulative daily maximum PM$_{2.5}$ exposures (Pearson *r*=0.26–0.28), the observed effect estimate in the medium cumulative exposure group was attenuated, although findings in the high categories of both exposure metrics were not substantively different (Table S7). Results were similar when we excluded non-ISB offshore workers from the analytical sample (Table S8) or when we expanded the study population to include land workers as a separate exposure group (Table S9). When we coarsened the time interval in which CHD events were identified, which did not change the *number* of events, to explore the potential impact of mis-recalling the date of CHD diagnosis (for a few months), we observed similar associations (Table S10).

Discussion

In this study, we examined the relationship between exposure to PM$_{2.5}$ from controlled burning of oil/gas and risk of CHD among oil spill workers up to ten years after the *DWH* disaster. We observed elevated effect estimates in the upper categories of both average and cumulative exposure. Notably, those in the high average exposure category had 2.1 times the hazard of CHD compared to the referent group, which is close to the increase in CHD risk among men from smoking 20 cigarettes per day (RR=2.27) reported in a meta-analysis (Hackshaw et al. 2018). These results suggest that exposure to high levels of PM$_{2.5}$ from controlled burning of crude oil and gas for a relatively short period (days to weeks) could increase workers' risk of CHD events several years after the exposure.

In our study population, the average daily maximum exposure that workers experienced varied significantly across exposure groups (Pratt et al. 2020). The levels of PM$_{2.5}$ assigned to the ISB and source/hot zone workers, which were in the range of 10–29 μg/m^3, are similar

to concentrations observed in air pollution studies conducted in developed countries (Host et al. 2008; Michikawa et al. 2019; Zanobetti and Schwartz 2009). In contrast, workers in the hot zone were exposed to a $PM_{2.5}$ level (97 μg/m^3) on par with those measured in urban areas of developing countries (Chen et al. 2017; Krishna et al. 2021) and substantially greater than the U.S. EPA National Ambient Air Quality Standard for $PM_{2.5}$ for the general population (24-hr average of 35 μg/m^3) (Batavia 1991).

The relationship between short-term $PM_{2.5}$ exposure and CHD has been examined extensively in ambient air pollution studies. A recent review by the U.S. EPA (2020) has implicated short-term $PM_{2.5}$ exposure as a major contributor to CHD. The strongest evidence came from several multi-city studies of emergency department visits and hospitalizations due to CHD in the US (Haley et al. 2009; Hsu et al. 2017; Kloog et al. 2014; Talbott et al. 2014) and other countries (Barnett et al. 2006; Host et al. 2008; Weichenthal et al. 2016), with supplemental evidence also linking this exposure to CHD mortality (Chen et al. 2017; Dabass et al. 2016; Michikawa et al. 2019). Short-term $PM_{2.5}$ exposure has also been associated with MI, as shown in a recent meta-analysis (Farhadi et al. 2020). Unlike these studies, which examined CHD events on the same day of, or within days after, $PM_{2.5}$ exposure, our study focused on *longer-term* risk; we were underpowered to examine the acute effect of exposure because only 8 non-fatal CHD events occurred within a month of exposure and we lacked data on fatal CHD events prior to study enrollment. Although our study generally agreed with these ambient air pollution studies in identifying a positive association between $PM_{2.5}$ exposure and CHD risk, the chemical composition of the $PM_{2.5}$ experienced by OSRC workers in the *DWH* disaster likely differed from that examined in the studies above due to differences in emission sources and environmental factors. While the $PM_{2.5}$ in our study originated primarily from controlled burning of oil and gas and to a smaller extent, from engine emissions, $PM_{2.5}$ detected in urban areas tends to come from automobile exhaust and other industrial and residential sources (Cheng et al. 2016). Different constituents of $PM_{2.5}$ have been associated with varying health effects, as discussed in a review (Yang et al. 2019).

Despite the lack of ambient air pollution studies that have assessed long-term cardiovascular effects following a transient $PM_{2.5}$ exposure, a few occupational studies have found persistent cardiovascular effects among workers exposed to air pollutants. In an analysis of workers who participated in the *Hebei Spirit* oil spill cleanup, longer duration of cleanup work was associated with higher risk of self-reported angina or MI up to 10 years after the spill, although controlled burning was not used as an oil mitigation method in this spill (Lee et al. 2020). Previous analyses in the same cohort of *DWH* OSRC workers showed elevated risk of CHD/MI several years after oil spill work (Strelitz et al. 2018; Strelitz et al. 2019a; Strelitz et al. 2019b). Specifically, risk of CHD was higher among workers with higher maximum THC inhalation exposure (as estimated with an earlier ordinal exposure metric) and longer duration of OSRC work. In contrast, no association was found between a crude measure of controlled burning exposure (yes/no) and risk of CHD three years after the spill, possibly because of imprecision in the exposure measurement or too few events among the exposed group to detect an association (Strelitz et al. 2018). With the more recently developed quantitative $PM_{2.5}$ estimates and a longer follow-up time, we observed positive associations of CHD risk with average and cumulative daily maximum $PM_{2.5}$ exposures,

which remained elevated after accounting for co-exposure to THC. Persistently elevated risk of cardiovascular diagnosis (CHD, MI, stroke, or congestive heart failure) has also been reported among responders to the 2001 World Trade Center disaster who were exposed to the dust cloud (Sloan et al. 2021); however, most of the dust particles in the disaster differed in important ways from the $PM_{2.5}$ experienced by the *DWH* oil spill workers, including the particle size and composition (Lippmann et al. 2015).

In our analysis, CHD deaths that occurred among OSRC workers before study enrollment could not be identified because enrollment was contingent upon survival. If $PM_{2.5}$-induced CHD deaths occurred more frequently in the pre-enrollment period, then our results might have underestimated the true HRs. However, given the relatively short span between exposure and enrollment (median duration: 1.6 years) and the overall small number of CHD deaths (N=29) that occurred during the entire follow-up, we do not expect that results would be substantively different had we been able to identify cases that occurred during this immortal time. In a sub-analysis, we examined non-fatal CHD as the outcome, for which there was less immortal time bias, and observed similar associations. In another analysis, we explored the impact of starting the risk period at each worker's date of enrollment in the cohort, which led to the exclusion of 108 self-reported CHD cases between exposure and enrollment. We observed similar risks among workers in the high exposure categories, but effect estimates were attenuated in the low average exposure and medium cumulative exposure categories, possibly because a higher proportion of these workers had incident non-fatal CHD events prior to enrollment: Approximately 1.67% and 1.99% of workers in the low average exposure and medium cumulative exposure categories, respectively, had an incident CHD event before enrollment, compared to 1.32% in the referent group.

Although understanding of the mechanisms underlying the association between $PM_{2.5}$ and CHD is still evolving, two potential biological pathways have been proposed. The first pathway begins when $PM_{2.5}$ in the respiratory tract activates reactive oxygen species, inducing oxidative stress and inflammation in the circulatory system (Brook et al. 2004). The inflammatory responses can stimulate the systemic release of pro-inflammatory proteins, which increases the potential for thrombosis and risk of CHD (Hajat et al. 2015; Hennig et al. 2014). PM-induced inflammation can also impair vascular function (Kampfrath et al. 2011; Lawal et al. 2016), which may lead to rupture of existing plaques and trigger an acute CHD event (Gutiérrez et al. 2013). Alternatively, $PM_{2.5}$ can increase the risk of CHD by modulating the autonomic nervous system and stimulating sympathetic activity, resulting in increased blood pressure and decreased heart rate variability (U.S. EPA 2020). Elevated blood pressure can promote CHD by contributing to atherosclerotic progression and/or destabilizing existing plaques (Escobar 2002). Both hypertension and decreased heart rate variability have been linked to cardiac arrhythmias (Ferrari and Fox 2016; Lip et al. 2017), which can lead to myocardial ischemia and exacerbate CHD (Liang and Wang 2021). Consistent with this mechanism, one study of the *DWH* workers has associated burning exposure with a modest increase in risk of hypertension detected within 3 years of the spill (Kwok et al. 2022), and another study of Coast Guard responders who participated in the *DWH* spill cleanup has observed an increased prevalence of sudden heartbeat changes (arrythmias) among workers reporting ever being in the vicinity of burning oil (Denic-Roberts et al. 2022). In our sub-analysis restricted to workers without

pre-exposure hypertension, we observed somewhat weaker associations between $PM_{2.5}$ and CHD, which suggests that risk may be higher among people with pre-existing hypertension; however, the literature on the impact of prevalent hypertension on the relationship between $PM_{2.5}$ and CHD is mixed (U.S. EPA 2020). Together, current mechanistic understanding supports the plausibility of the observed cardiovascular effects of exposure to $PM_{2.5}$.

One major strength of our study is the development of quantitative $PM_{2.5}$ estimates from a well-established air dispersion model (AERMOD) and detailed *DWH* spill work histories provided by participants. Because controlled burning had not been adopted as a major mitigation technique in previous oil spills, these exposure estimates allowed us to examine, for the first time, the relationship between CHD and $PM_{2.5}$ exposure from this unique emission source. Moreover, while most air pollution literature has assessed acute CHD events following a transient $PM_{2.5}$ exposure, the extensive follow-up time of this cohort provided an opportunity to investigate the *long-term* cardiovascular impact of a relatively short-term $PM_{2.5}$ exposure. Another strength of the study is the differences in average daily exposure among study participants, which allowed us to examine the exposure-response trend across a wide range of exposure levels. To account for potential informative censoring from participants who did not respond to the follow-up interviews, we performed an IP-censoring weighted analysis and found only slightly attenuated results compared to the unweighted analysis. This provides some reassurance that our results are robust to non-response bias. Lastly, the availability of participant-level data on many important covariates (e.g. cigarette smoking, education, previous oil industry experience, and co-exposure to THC) allowed us to account for important confounders of the association and obtain more accurate effect estimates.

Our study also has limitations. One limitation is potential misclassification of the outcome, as we could not obtain medical records from participants to confirm their CHD diagnosis, and death certificates may be inaccurate in identifying the true cause of death. Previous studies have found moderate to high sensitivity (0.78–0.98) and specificity (0.72–1.0) of self-reported MI and of death certificate diagnosis of CHD (Barr et al. 2009; Coady et al. 2001; Eliassen et al. 2016; Folsom et al. 1987; Fourrier-Réglat et al. 2010; Goraya et al. 2000; Lloyd-Jones et al. 1998; Machón et al. 2013; Okura et al. 2004; Yamagishi et al. 2009), and identified older age as a predictor of poorer accuracy (Lloyd-Jones et al. 1998; Okura et al. 2004; Olubowale et al. 2017; Yamagishi et al. 2009). Compared to populations examined in these validation studies, the GuLF Study participants were younger at enrollment, so we expect a lower degree of outcome misclassification in our population. When reporting CHD diagnoses, some participants may have recalled the wrong dates of diagnosis, resulting in measurement error in event time. To explore its potential impact, we performed an exploratory analysis that coarsened the time interval in which events were identified (i.e. tallied CHD events every 4 months instead of every month) and observed similar associations. This indicates that our analysis was robust to measurement error of at least a few months in recall time.

Second, although the quantitative $PM_{2.5}$ estimates were an improvement over the crude surrogates of inhalation exposures examined in previous oil spill studies, they were likely to contain measurement error. The dispersion model estimates were based on emission

factors from published studies informed by photographs and videos of the controlled burning. Furthermore, the estimates are ambient air concentrations, rather than personal exposures. To assign average exposures to participants, we created exposure groups based primarily on work areas and participation in *in situ* burning; however, within the same work area, air concentrations, and thus workers' exposures, could have differed depending on their proximity to the burning sites and whether ISBs occurred during their work shift. Because we did not have the exact location of most workers on a daily basis, we created spatiotemporal averages across Gulf areas to reflect the average daily maximum exposure levels that workers could have encountered during the controlled burning period. It is possible that the measurement error might have biased our analysis of continuous exposures, but we do not expect it to have substantively changed results of the categorical exposure analysis. Also, because we did not have sufficient detail on the time spent in each location/ activity for some participants who performed OSRC work in multiple locations/activities during the controlled burning period, we assigned these workers the highest exposure among those locations/activities. This approach might have conservatively overestimated exposures for some workers.

Third, because our goal was to assess the cardiovascular effects of $PM_{2.5}$ exposure from controlled burning to inform decisions on using this oil mitigation method in future spills and because we lacked the necessary data to estimate exposures from vessel engine exhaust, the $PM_{2.5}$ estimates reflected only exposure from ISBs and flaring and did not capture background exposures from engine exhaust (Pratt et al. 2020). In our main analysis, we decided *a priori* to restrict our study population to water workers, who likely shared the same approximate level of background exposure from water vessel engine, and excluded land workers who were exposed to different background sources of $PM_{2.5}$ emission (i.e. vehicles and land equipment). In a sensitivity analysis in which we included land workers in the analysis, we observed no difference in risk of CHD between land workers and the referent group, which suggests that co-exposure to the different source of background $PM_{2.5}$ alone did not produce a noticeable difference in workers' risk of CHD. In another sensitivity analysis in which we excluded the water worker group with the highest potential variability in exposure from vessel engine exhaust (i.e. the non-ISB offshore group), we observed associations similar to those in the main analysis.

Fourth, there could be bias from unmeasured confounders or imperfect measurement of existing covariates in the models. We were unable to account for co-exposure to all other occupational exposures from the OSRC activities, such as chemicals dispersants (U.S. Coast Guard 2011) and other gaseous pollutants generated by the controlled burning (Middlebrook et al. 2012). In a sensitivity analysis, we accounted for an important co-pollutant, THC and found attenuated effect estimate among workers with medium cumulative $PM_{2.5}$ exposure but similar effect estimates in other exposure categories. Because prior oil spill or oil industry experience may have influenced workers' assignment to specific clean-up jobs/tasks (Stewart et al. 2022), we adjusted for self-reported prior work in the oil industry and oil spill cleanups to reduce confounding; however, we were not able to account for other factors (e.g. physical fitness) that might have influenced workers' job assignment. There could also be confounding if workers' baseline health at the time of the spill affected their duration of work (and thus, possibly their cumulative $PM_{2.5}$ exposure) and was related to

their future risk of CHD. We adjusted for several indicators of baseline health (self-reported BMI, pre-exposure diabetes, pre-exposure hypertension, smoking) to reduce this potential bias, but there could be measurement error in some of these self-reported health indicators. We used self-reported race, ethnicity, and education as proxies for the downstream effects of socioeconomic disparities, acknowledging that these variables might not fully capture the socioeconomic effects (e.g. healthy food access, neighborhood air quality) that may influence risk of CHD (Hajat et al. 2013; Larson et al. 2009).

In this study, we identified a positive association between controlled burning-related $PM_{2.5}$ exposure and CHD risk among oil spill workers up to 10 years after the spill. We observed evidence of monotonic exposure-response trends and clinically meaningful increases in CHD risk among workers in the higher exposure categories. To our knowledge, our study is the first to evaluate such association among oil spill workers, and the results provide important insights for those considering controlled burning as a mitigation method for future oil spills. Our study is also among the few to demonstrate a persistent relationship between short-term particulate exposure and CHD risk. Additional research is needed in other populations and settings to confirm these study findings.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments:

Abbreviations:

BMI	body mass index
CHD	coronary heart disease
CI	confidence interval
DWH	Deepwater Horizon
EMM	effect measure modification
EPA	Environmental Protection Agency
HR	hazard ratio
IP	inverse probability
ISB	*in situ* burn
MI	myocardial infarction

OSRC	oil spill response and cleanup
PM$_{2.5}$	fine particulate matter
THC	total hydrocarbons

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Highlights

- In the *Deepwater Horizon* disaster, controlled burning of oil/gas produced $PM_{2.5}$.

- Many oil spill workers were exposed to $PM_{2.5}$ levels above the EPA's daily standard.

- $PM_{2.5}$ exposure was linked to higher risk of coronary heart disease among workers.

- Increase in heart disease risk persisted up to 10 years after the burning exposure.

Table 1.

Characteristics of *DWH* oil spill water workers who responded to the enrollment, first follow-up, and second follow-up interviews, respectively

Characteristic	Enrollment (n=9,091)	1st Follow-up (n=6,204)	2nd Follow-up (n=4,251)
	n (%)	*n* (%)	*n* (%)
Age at enrollment (y)			
20–29	2093 (23.0)	1237(19.9)	797(18.8)
30–39	2244 (24.7)	1441 (23.2)	941 (22.1)
40–19	2231 (24.5)	1556 (25.1)	1097 (25.8)
50–59	1766(19.4)	1366 (22.0)	960 (22.6)
>=60	757(8.3)	604 (9.7)	456(10.7)
Gender			
Male	8229 (90.5)	5555 (89.5)	3780 (88.9)
Female	862 (9.5)	649 (10.5)	471 (11.1)
Race			
White	6548 (72.0)	4511 (72.7)	3237 (76.2)
Black	1562(17.2)	1030(16.6)	611 (14.4)
Other	981 (10.8)	663 (10.7)	403 (9.5)
Hispanic ethnicity			
No	8490 (93.4)	5809 (93.6)	4017(94.5)
Yes	601 (6.6)	395 (6.4)	234 (5.5)
Highest educational attainment			
Less than high school	1674(18.4)	1078 (17.4)	583(13.7)
High school diploma/GED	2839(31.2)	1838(29.6)	1189 (28.0)
Some college/2-year degree	2822 (31.0)	1942 (31.3)	1381 (32.5)
4-year college graduate or more	1756(19.3)	1346 (21.7)	1098 (25.8)
Weight classification			
Underweight or normal (BMI <25)	2390 (26.3)	1609 (25.9)	1037 (24.4)
Overweight (25 ≤ BMI < 30)	3887 (42.8)	2638 (42.5)	1874(44.1)
Obese I (30 ≤ BMI < 35)	1849 (20.3)	1275 (20.6)	875 (20.6)
Obese II (BMI ≥ 35)	965 (10.6)	682 (11.0)	465 (10.9)
Reported pre-cleanup diabetes diagnosis			

Characteristic	Enrollment (n=9,091)	1st Follow-up (n=6,204)	2nd Follow-up (n=4,251)
	n (%)	n (%)	n (%)
No	8751 (96.3)	5956 (96.0)	4086 (96.1)
Yes	340 (3.7)	248 (4.0)	165 (3.9)
Reported pre-spill hypertension diagnosis			
Missing	150(1.7)	102(1.6)	68(1.6)
No	7532 (82.9)	5069(81.7)	3462 (81.4)
Yes	1409(15.5)	1033 (16.7)	721 (17.0)
Smoking status			
Current heavy smoker (20 cigarettes/d)	1102(12.1)	691 (11.1)	383 (9.0)
Current light smoker (< 20 cigarettes/d)	1887 (20.8)	1206(19.4)	739(17.4)
Former smoker	2013 (22.1)	1426 (23.0)	1028 (24.2)
Never smoked	4089 (45.0)	2881 (46.4)	2101 (49.4)
Residential county proximity to Gulf of Mexico [a]			
Direct or indirect contact	5716 (62.9)	3810(61.4)	2489 (58.6)
Other Gulf state residence	1696(18.7)	1124(18.1)	764(18.0)
Non-Gulf state residence	1679(18.5)	1270 (20.5)	998 (23.5)
Previous oil spill cleanup work			
No	7813 (85.9)	5264 (84.9)	3577(84.1)
Yes	1278(14.1)	940 (15.2)	674(15.9)
Previous oil industry experience			
No	7294 (80.2)	4952 (79.8)	3395 (79.9)
Yes	1797(19.8)	1252 (20.2)	856 (20.1)

Abbreviations: *DWH, Deepwater Horizon*; GED, General Equivalency Diploma; BMI, body mass index

[a] Direct proximity is defined as living in a county directly adjacent to the Gulf of Mexico; indirect is defined as living in a county adjacent to coastal counties

Table 2.

Association between PM$_{2.5}$ exposure and incident CHD events among *DWH* disaster oil spill water workers, 2010–2019 (N=9,091).

PM$_{2.5}$ Exposure	Total Cases (n=372)	Total N (n=9,091)	No censoring weights[a]		IP-censoring weighted[a,b]	
			HR (95% CI)	p-value	HR (95% CI)	p-value
Average exposure						
Referent[c]	293	7111	Referent		Referent	
Low	64	1672	1.29 (0.96, 1.74)	0.10	1.26 (0.93, 1.70)	0.13
High	15	308	2.17 (1.12, 4.20)	0.02	2.11 (1.08, 4.12)	0.03
Per 10 µg/m^3 increase			1.11 (1.03, 1.19)	0.01	1.10 (1.02, 1.19)	0.01
Cumulative exposure						
Referent[c]	293	7111	Referent		Referent	
Low	20	589	1.21 (0.69, 2.10)	0.50	1.19 (0.68, 2.08)	0.54
Medium	26	603	1.37 (0.87, 2.17)	0.18	1.38 (0.88, 2.16)	0.16
High	33	788	1.53 (1.03, 2.29)	0.04	1.44 (0.96, 2.14)	0.08
Per 100 µg/m^3-d increase			1.03 (1.00, 1.05)	0.05	1.03 (1.00, 1.05)	0.06

Abbreviations: CHD, coronary heart disease; *DWH, Deepwater Horizon*; HR, hazard ratio; CI, confidence interval

[a] Models accounted for age, gender, race, ethnicity, weight class, smoking, pre-cleanup diabetes, education, residential proximity to the Gulf of Mexico, previous oil spill cleanup work, and previous oil industry experience

[b] Censoring weights accounted for exposure, age, gender, race, ethnicity, weight class, smoking, pre-cleanup diabetes, education, residential proximity to the Gulf of Mexico, previous oil spill cleanup work, and previous oil industry experience

[c] The referent group consisted of nearshore workers and offshore workers who did not work on *in situ* burns.

Table 3.

Association between PM$_{2.5}$ exposure and incident non-fatal CHD among *DWH* disaster oil spill workers, 2010–2019 (N=9,091).

PM$_{2.5}$ Exposure	Total Cases (n=343)	Total N (n=9,091)	HR (95% CI)[a]	p-value
Average exposure				
Referent[b]	270	7111	Referent	
Low	61	1672	1.31 (0.96, 1.79)	0.09
High	14	308	2.21 (1.10, 4.45)	0.03
Per 10 μg/m³ increase			1.11 (1.03, 1.20)	0.01
Cumulative exposure				
Referent[b]	270	7111	Referent	
Low	19	589	1.18 (0.65, 2.15)	0.58
Medium	26	603	1.53 (0.97, 2.39)	0.07
High	30	788	1.48 (0.97, 2.25)	0.07
Per 100 μg/m³-d increase			1.03 (1.00, 1.06)	0.04

Abbreviations: CHD, coronary heart disease; *DWH, Deepwater Horizon*; HR, hazard ratio; CI, confidence interval

[a] Models accounted for age, gender, race, ethnicity, weight class, smoking, pre-cleanup diabetes, education, residential proximity to the Gulf of Mexico, previous oil spill cleanup work, and previous oil industry experience

[b] The referent group consisted of nearshore workers and offshore workers who did not work on *in situ* burns.