



Association of Occupational Exposure to Inhaled Agents in Operating Rooms With Incidence of Chronic Obstructive Pulmonary Disease Among US Female Nurses

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Abstract

IMPORTANCE Employment in operating rooms (ORs) may involve exposure to several inhaled agents, including surgical smoke and disinfectants, which are associated with adverse respiratory health effects. However, the association of long-term employment in ORs and chronic obstructive pulmonary disease (COPD) remains unknown.

OBJECTIVE To examine the association of working in an OR with incidence of COPD among female nurses in the US.

DESIGN, SETTING, AND PARTICIPANTS This cohort study used data from the Nurses' Health Study for US female registered nurses who provided information on questionnaires regarding OR employment history in 1984 and job type in 1982 and who had no history of COPD in 1984 (baseline). Data analyses were conducted from April 1, 2020, to January 31, 2021.

EXPOSURES Duration of nursing in the OR and job type.

MAIN OUTCOMES AND MEASURES The associations of any employment as an OR nurse, duration of employment, and duration and job type with incidence of self-reported, physician-diagnosed COPD. Hazard ratios (HRs) and 95% CIs were estimated using Cox proportional hazards regression models stratified by age and calendar year. Models were adjusted for covariates, with model 1 adjusting for age, model 2 also adjusting for cigarette smoking status and pack-year of smoking, and model 3 also adjusting for race and ethnicity, US Census region, and body mass index.

RESULTS Among 75 011 female nurses included in the analyses, the mean (SD) age at baseline was 50.5 (7.2) years; 29% had a history of employment in an OR, and 3% had 15 or more years of OR experience. In model 3, employment in an OR for 15 or more years was associated with a 46% increased risk of developing COPD compared with no history of OR employment (HR, 1.46; 95% CI, 1.10-1.93). Compared with nurses who never worked in an OR and had an administrative or nursing education function or a nonnursing job in 1982, the risk of developing COPD was greater among nurses who provided outpatient care (HR, 1.24; 95% CI, 1.04-1.47) and nurses employed in inpatient units (HR, 1.31; 95% CI, 1.07-1.59) who had no history of OR employment and was 69% greater among nurses with OR experience of 15 years or more (HR, 1.69; 95% CI, 1.25-2.28).

CONCLUSIONS AND RELEVANCE In this cohort study, OR employment of 15 years or more was associated with an increased risk of developing COPD among female nurses. Additional studies with more recent and direct environmental monitoring data of multiple occupational exposures are needed to assess the relative role of exposure to surgical smoke and disinfectants in the observed association.

JAMA Network Open. 2021;4(9):e2125749. doi:10.1001/jamanetworkopen.2021.25749

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Key Points

Question Is there an association between a history of operating room (OR) employment, as proxy for exposure to inhaled agents such as surgical smoke and disinfectants, and incidence of chronic obstructive pulmonary disease among female nurses in the US?

Findings In this cohort study of 75 011 US female nurses, nurses with 15 or more years of OR employment had a 69% greater risk of developing chronic obstructive pulmonary disease compared with those who never worked in an OR and had an administrative or nursing education function or nonnursing job.

Meaning These findings suggest that exposure to inhaled agents in the OR may be associated with independent health risks to the respiratory system.

+ Supplemental content

Author affiliations and article information are listed at the end of this article.

Introduction

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide^{1,2} and in the US.³ Although tobacco smoking is the primary factor associated with COPD, increasing evidence suggests that occupational exposure is another important contributor to the burden of disease.⁴⁻⁶ Health care is among the largest sectors in the US economy, with more than 18 million individuals employed, and nearly 80% are women.⁷ Disinfectants and surgical smoke, a visible acrid gaseous by-product from laser tissue ablation, electrocautery, and ultrasonic scalpel tissue dissection, are among the widely studied hazardous chemicals that are present in health care settings.⁸

Disinfectants used in health care settings contain a large variety of active ingredients, such as formaldehyde, hypochlorite, hydrogen peroxide, glutaraldehyde, all of which are capable of causing injury to the airway epithelium and oxidative stress and may be associated with neutrophilic inflammation.⁹⁻¹¹ Surgical smoke consists of carbon monoxide, polyaromatic hydrocarbons, nitriles, fatty acids, phenols, benzene, hydrogen cyanide, formaldehyde, viable and nonviable cellular materials, viruses, and bacteria¹²⁻¹⁴ and has been shown to induce inflammatory pulmonary changes in animals after repeated exposure and to have mutagenic potential in laboratory and animal studies.^{9,15-24} Many studies^{10,11,25-27} have documented increased incidence or prevalence of asthma or respiratory symptoms associated with exposure to disinfectants among individuals with different occupations, although these studies largely focused on asthma.

The level of exposure to disinfectants tends to vary by specific job types. Previous studies have suggested that operating room (OR) nurses have the highest level of self-reported disinfectant use,^{25,28} followed by nurses employed in emergency departments or inpatient units.¹⁰ In addition to disinfectant exposure, OR nurses are also exposed to surgical smoke, another respiratory irritant that has been shown to be associated with acute respiratory toxicity.²⁹⁻³² Despite studies showing irritant properties of chemicals contained in disinfectants and surgical smoke,^{33,34} the association of long-term employment in an OR (and prolonged exposure to these respiratory irritants) with COPD remains unknown.

Investigations of the long-term potential health risks of exposure to surgical smoke and disinfectants are rare because of the inherent challenges to obtaining valid estimates of exposure to surgical smoke over extended periods in a large population cohort. Using the duration of operating room nursing (ORN) as a proxy for cumulative surgical smoke exposure, Gates et al³⁵ found no association of ORN with lung cancer prospectively assessed for a maximum 16 years of follow-up among a cohort of US nurses. Other studies have used nursing job type (eg, education or administration, outpatient care or other nursing role, emergency department or inpatient care, and OR) as a proxy for disinfectant exposure levels to assess asthma control and risk of developing COPD.^{5,36}

To our knowledge, the association of OR employment history with COPD has not been investigated in a large population. Using data from the Nurses' Health Study (NHS), a large prospective cohort study of US female nurses, we assessed the association of OR employment with COPD by incorporating both duration of ORN and job type to proxy potential exposure to disinfectants and surgical smoke. We hypothesized that, independent of cigarette smoking and other important confounders, nurses with any history of employment in an OR would be more likely to develop COPD compared with those with no OR employment history.

Methods

Population

This cohort study used data from the NHS, an ongoing prospective study of US female registered nurses that was initiated in 1976. Study participants complete follow-up questionnaires every 2 years regarding risk factors for diseases and health outcomes. The present study included 95 483

respondents who returned questionnaires in 1982 and 1984. The institutional review boards of the Brigham and Women's Hospital and Harvard T.H. Chan School of Public Health approved the NHS protocol, and written informed consent was obtained from all participants. The present study was conducted according to the ethical guidelines of Brigham and Women's Hospital and approved by the Boston University Medical Center institutional review board. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline. Analyses were conducted from April 1, 2020, to January 31, 2021.

Operating room employment history was evaluated in 1984, which was defined as the baseline for the study. Questionnaire-based data collection was conducted biennially thereafter; follow-up was censored by the year 2000 when the supplemental COPD questionnaires were sent to every woman who reported a physician's diagnosis of emphysema or chronic bronchitis to validate the self-reported measure. We excluded 16 566 respondents with missing information on job type in 1982 and missing information on OR employment history in 1984. We further excluded 3168 individuals who reported a history of COPD in 1984 (baseline for the current analysis), in addition to 738 respondents who were lost to follow-up immediately after baseline (1984). The resultant analytic sample for primary analyses was 75 011 female nurses (eFigure in the Supplement).

Assessment of Exposure

Nurses were asked in 1982 to report their current employment status (nursing education, outpatient care or community nursing, inpatient staff nursing, OR nursing, other nursing, nonnursing employment, or homemaker) and in 1984 for the total number of years of regular work in an OR (none, <1 year, 1-4 years, 5-9 years, 10-14 years, and ≥ 15 years). The primary exposure of interest was the duration of ORN reported in 1984, considered a proxy measure for the duration of exposure to surgical smoke³⁵ and duration of high-level exposure to disinfectants.²⁵ Based on the examination of the distribution of the duration of ORN, we used the following categories to ensure sufficient numbers of observation and incident cases in each category: (1) never, (2) less than 5 years, (3) 5 to 14 years, and (4) 15 years or longer.

We further divided the group of respondents who never worked in an OR by their job type as reported in 1982 to capture the potential exposure to disinfectants and surgical smoke in nursing jobs other than ORN: (1) no ORN employment and employment in administration, nurse education, or nonnursing job (hypothesis: no or low exposure to disinfectants, no exposure to surgical smoke); (2) no ORN employment and employment in outpatient care or other nursing job (hypothesis: medium exposure to disinfectants, no exposure to surgical smoke); (3) no ORN employment and employment in emergency department or inpatient unit (hypothesis: medium to high exposure to disinfectants, no exposure to surgical smoke); (4) ORN employment for less than 5 years (hypothesis: low to medium exposure to disinfectants and surgical smoke); (5) ORN employment for 5 to 14 years (hypothesis: medium to high exposure to disinfectants and surgical smoke); and (6) ORN employment for 15 or more years (hypothesis: high exposure to disinfectants and surgical smoke).²⁵

Respiratory Conditions

Supplemental COPD questionnaires were sent to every participant who reported a physician's diagnosis of emphysema or chronic bronchitis (on biennial questionnaires) in 1998 and in 2000. The specific questionnaire included, among other data, information confirming a physician's diagnosis of emphysema, chronic bronchitis, or COPD; the dates of symptom onset and diagnosis; and the tests performed to confirm the diagnosis or symptoms consistent with a diagnosis of chronic bronchitis. Self-reported COPD events were defined as those described by participants who previously reported physician-diagnosed chronic bronchitis or emphysema on the original main questionnaire (1988-1996) and answered positively to physician-diagnosed chronic bronchitis, physician-diagnosed emphysema, or physician-diagnosed COPD on supplemental COPD questionnaires (1998, 2000, or both 1998 and 2000).

We also considered a more stringent case definition in a sensitivity analysis when self-reported COPD events during follow-up were additionally confirmed by a diagnostic test (eg, pulmonary function testing, chest radiography, or chest computed tomography) based on information obtained in the 1998 or 2000 supplemental questionnaire. These epidemiologic definitions were validated in a random sample of COPD events in the NHS.³⁷

Covariates

Data on race and ethnicity were combined to classify respondents as non-Hispanic White and other (non-Hispanic Black, Hispanic, and non-Hispanic other). Other measures included age (continuous), census region (New England, Mid-Atlantic, East North Central, South Atlantic, West Central, and Pacific), smoking status (never, former, or current), pack-years, pack-years squared, and body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) (<20.0, 20.0 to 24.9, 25.0 to 29.9, and ≥ 30.0). Time-constant covariates (race and ethnicity, US Census region) were assessed at baseline (1984), and BMI, smoking status, and pack-years were handled as time-varying covariates and updated during follow-up.

Statistical Analysis

Hazard ratios (HRs) and 95% CIs were estimated using Cox proportional hazards regression models. All models were stratified by age and calendar year. Respondents contributed follow-up time from baseline (1984) to the time at which a diagnosis of COPD was made, loss to follow-up, death, or 2000 (the end of follow-up), whichever came first. We examined the association between exposure and COPD with sequential adjustment for covariates. In the first model, we adjusted for age only; in the second model, we additionally adjusted for cigarette smoking status and pack-years of smoking; and in the third model, we additionally adjusted for race and ethnicity, census region, and BMI. Missing data on smoking status (missing for 0.2% of participants), pack-years (0.2%), and BMI (4.9%) were assigned to a separate category in the analyses. All statistical analyses were conducted using SAS, version 9.4 (SAS Institute Inc). All *P* values were based on 2-sided tests and were considered statistically significant at $P < .05$.

Auxiliary analyses were conducted to assess the robustness of the results. First, we excluded participants who reported a COPD diagnosis within 4 years from baseline ($n = 1506$). Second, we excluded respondents with a self-reported history of chronic diseases, including cancer, heart disease, or diabetes at baseline ($n = 8205$). Third, we further adjusted for time-varying physical activity (metabolic equivalent of task expressed as number of hours per week; quintiles) and dietary quality (as determined by Alternative Healthy Eating Index 2010³⁸; quintiles), secondhand smoke exposure (yes or no) measured in 1982, and for married nurses, spouse's highest educational attainment (high school, college, or graduate degree) measured in 1992 as a proxy for socioeconomic status. Fourth, we performed stratified analyses by smoking status (never, former, or current). Finally, we repeated the analyses using a more stringent case definition.

Results

Among 75 011 women included in the analysis, the mean (SD) age at baseline (1984) was 50.5 (7.2) years; 72 709 (96.9%) identified as non-Hispanic White, and 2302 (3.1%) identified as other; 44.9% reported never smoking, and 13.4% had obesity (**Table 1**). Among the participants, 71% never worked in an OR and 3% reported 15 or more years of OR employment. Respondents with longer OR employment histories were less likely to be non-Hispanic White (≥ 15 y employment vs none: 2270 of 2381 [95.3%] vs 51 913 of 53 433 [97.2%]), were less likely to have reported never smoking (≥ 15 y employment vs none: 1019 of 2375 [42.9%] vs 24 525 of 53 341 [46.0%]), and were more likely have obesity (≥ 15 y employment vs none: 333 of 2251 [14.8%] vs 6697 of 50 788 [13.2%]).

Association Between OR Employment and COPD

During the follow-up period from 1984 to 2000, 1091 incident events of COPD were reported (Figure). The Kaplan-Meier curve showed higher incident rates of COPD associated with longer OR employment history, although the unadjusted incident rates of COPD among nurses reporting less than 5 years and 5 to 14 years of ORN employment history were similar. In model 1, any employment

Table 1. Baseline Characteristics of US Female Nurse Respondents to the 1984 Questionnaire of the Nurses' Health Study by Cumulative Operating Room Employment Duration

Variables	Nurse respondents				
	Total (N = 75 011)	None (n = 53 433 [71%])	<5 y (n = 15 319 [20%])	5-14 y (n = 3878 [6%])	≥15 y (n = 2381 [3%])
Age, mean (SD), y	50.5 (7.2)	50.0 (7.2)	51.7 (6.9)	50.6 (7.1)	51.5 (6.7)
Race and ethnicity, No. (%)					
Non-Hispanic White	72 709 (96.9)	51 913 (97.2)	14 788 (95.5)	3738 (96.4)	2270 (95.3)
Other ^a	2302 (3.1)	1520 (2.8)	531 (4.5)	140 (3.6)	111 (4.7)
Census region, No. (%)					
New England	10 846 (14.5)	7995 (15.0)	2030 (13.3)	508 (13.1)	313 (13.2)
Mid-Atlantic	32 579 (43.4)	23 815 (44.6)	6330 (41.3)	1536 (39.6)	898 (37.7)
East North Central	14 397 (19.2)	10 097 (18.9)	2974 (19.4)	825 (21.3)	501 (21.0)
South Atlantic	4357 (5.8)	3100 (5.8)	837 (5.7)	239 (6.2)	145 (6.1)
West Central	3515 (4.7)	2083 (3.9)	1006 (6.6)	261 (6.7)	165 (6.9)
Pacific	9317 (12.4)	6343 (11.9)	2106 (13.8)	509 (13.1)	359 (15.1)
Smoking status, No. (%) ^b					
Never	33 585 (44.9)	24 525 (46.0)	6507 (42.6)	1534 (39.6)	1019 (42.9)
Former	23 890 (31.9)	16 825 (31.5)	5063 (33.1)	1300 (33.6)	702 (29.6)
Current	17 392 (23.2)	11 991 (22.5)	3711 (24.3)	1036 (26.8)	654 (27.5)
Pack-years among ever smokers, mean (SD) ^c	21.7 (17.9)	21.3 (17.8)	22.7 (18.4)	22.5 (17.8)	22.6 (17.5)
BMI, No. (%) ^d					
<20.0	5471 (7.7)	3832 (7.7)	163 (7.4)	1376 (8.1)	163 (7.2)
20.0-24.9	37 067 (51.9)	26 729 (52.5)	1102 (50.8)	9236 (50.0)	1102 (49.0)
25.0-29.9	19 249 (27.0)	13 530 (26.6)	653 (27.8)	5066 (27.8)	653 (29.0)
≥30.0	9582 (13.4)	6697 (13.2)	333 (14.0)	2522 (14.2)	333 (14.8)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); ORN, operating room nursing.

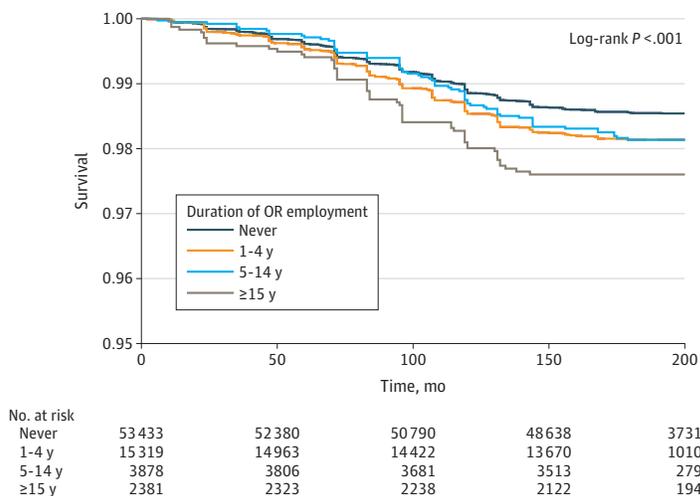
^a Other included Non-Hispanic Black, Hispanic, and non-Hispanic other.

^b Data were missing for 144 respondents (0.2%).

^c Data were missing for 140 respondents (0.2%).

^d Data were missing for 3642 respondents (4.9%).

Figure. Kaplan-Meier Curve of Survival by Cumulative Operating Room (OR) Employment Duration Among US Female Nurses



in an OR was associated with a 16% increased risk of developing COPD compared with no employment in an OR (HR, 1.16; 95% CI, 1.02-1.31) (Table 2). There was no association in models 2 (HR, 1.10; 95% CI, 0.97-1.25) and 3 (HR, 1.10; 95% CI, 0.97-1.25). When the duration of ORN employment was examined, compared with those with no history of ORN employment, those who reported 15 or more years of exposure had the greatest risk of COPD in model 3 (HR, 1.46; 95% CI, 1.10-1.93); a significant trend was observed as the years of OR employment increased, although there was only an association for 15 or more years of employment (<5 years: HR, 1.05 [95% CI, 0.90-1.21]; 5 to 14 years: HR, 1.08 [95% CI, 0.83-1.40]) ($P = .03$ for trend).

We further divided the group of nurses with no prior OR employment into 3 groups based on job type in 1982 (Table 3). Compared with working in administration, nursing education, or a nonnursing job, employment in an outpatient or community nurse setting was associated with a higher incidence of COPD in model 3 (HR, 1.24; 95% CI, 1.04-1.47). A positive association was also observed for employment in an inpatient unit or emergency department (HR, 1.31; 95% CI, 1.07-1.59). The strongest association was observed among nurses who reported 15 or more years of OR employment (HR, 1.69; 95% CI, 1.25-2.28).

Table 2. Hazard Ratios for the Association of Operating Room Employment Duration With Risk of COPD Among US Female Nurses in the Nurses' Health Study in 1984

Exposure	Events, No.	Person-years	Model 1 ^a		Model 2 ^b		Model 3 ^c	
			Hazard ratio (95% CI)	P value for trend	Hazard ratio (95% CI)	P value for trend	Hazard ratio (95% CI)	P value for trend
ORN employment status								
Never	723	771 374	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA
Ever	368	308 578	1.16 (1.02-1.31)	NA	1.10 (0.97-1.25)	NA	1.10 (0.97-1.25)	NA
ORN employment duration								
Never	723	771 374	1 [Reference]		1 [Reference]		1 [Reference]	
<5 y	251	219 485	1.10 (0.95-1.27)	.003	1.05 (0.91-1.21)	.03	1.05 (0.90-1.21)	.03
5-14 y	64	55 362	1.20 (0.93-1.55)		1.09 (0.84-1.41)		1.08 (0.83-1.40)	
≥15 y	53	33 731	1.49 (1.13-1.97)		1.45 (1.09-1.92)		1.46 (1.10-1.93)	

Abbreviations: COPD, chronic obstructive pulmonary disease; NA, not applicable; ORN, operating room nursing.

^a Adjusted for age (continuous).

^b Adjusted for age (continuous), smoking status (never, former, or current), pack-years, and pack-years squared.

^c Adjusted for age (continuous), smoking status (never, former, or current), pack-years, and pack-years squared, race and ethnicity (non-Hispanic White, other), census region (New England, Mid-Atlantic, East North Central, South Atlantic, West Central, and Pacific), and body mass index (calculated as weight in kilograms divided by height in meters squared) (<20.0, 20.0 to 24.9, 25.0 to 29.9, and ≥30.0).

Table 3. Hazard Ratios for the Association of Cumulative Operating Room Employment Duration and Job Type With COPD Among US Female Nurses in the Nurses' Health Study in 1984

ORN employment status and duration	Events, No.	Person-years	Model 1 ^a		Model 2 ^b		Model 3 ^c	
			Hazard ratio (95% CI)	P value for trend	Hazard ratio (95% CI)	P value for trend	Hazard ratio (95% CI)	P value for trend
Never, administrative or nonnursing	249	281 033	1 [Reference]		1 [Reference]		1 [Reference]	
Never, outpatient care	291	303 253	1.18 (1.00-1.40)		1.23 (1.03-1.46)		1.24 (1.04-1.47)	
Never, inpatient care	183	187 088	1.28 (1.06-1.55)	<.001	1.30 (1.07-1.58)	.003	1.31 (1.07-1.59)	.003
Ever, <5 y	251	219 485	1.24 (1.04-1.48)		1.21 (1.01-1.44)		1.21 (1.01-1.45)	
Ever, 5-14 y	64	55 362	1.36 (1.03-1.79)		1.25 (0.95-1.65)		1.25 (0.95-1.65)	
Ever, ≥15 y	53	33 731	1.69 (1.25-2.28)		1.67 (1.24-2.25)		1.69 (1.25-2.28)	

Abbreviations: COPD, chronic obstructive pulmonary disease; ORN, operating room nursing.

^a Adjusted for age (continuous).

^b Adjusted for age (continuous), smoking status (never, former, or current), pack-years, and pack-years squared.

^c Adjusted for age (continuous), smoking status (never, former, or current), pack-years, and pack-years squared, race and ethnicity (non-Hispanic White, other), census region (New England, Mid-Atlantic, East North Central, South Atlantic, West Central, and Pacific), and body mass index (calculated as weight in kilograms divided by height in meters squared) (<20.0, 20.0 to 24.9, 25.0 to 29.9, and ≥30.0).

Sensitivity Analysis

Similar results were observed when participants who developed COPD within 4 years from baseline were excluded; when further adjusting for physical activity, diet quality, secondhand smoke exposure, and spouse's educational level; when observations with missing data on covariates were excluded; and when respondents with a history of chronic diseases were excluded (eTables 1 and 2 in the Supplement). There was no association between OR employment and COPD among participants who were currently smoking cigarettes. The HRs were greater than in the main analyses for former smoking status, although the association was not significant for 5 to 14 years of OR experience, and the association of 15 or more years of OR experience was stronger than in the main analyses for never smoking status (HR, 1.97; 95% CI, 1.01-3.84 vs HR, 1.69; 95% CI, 1.25-2.28). With use of a more stringent definition of COPD, the overall patterns of results were similar (eg, nurses with any OR employment had a 9% greater risk of developing of COPD than nurses with no OR employment, but the result was not significant [HR, 1.09; 95% CI, 0.94-1.26]), and a few coefficients were no longer significant at $P < .05$ level, potentially owing to fewer incident events.

Discussion

In this large prospective cohort study, long-term OR employment was associated with an increased risk of incident COPD. The results were robust to additional model specifications to mitigate residual confounding by smoking, chronic disease, and other characteristics.

Building on the studies of respiratory effect of disinfectant exposure,^{5,39} we hypothesized that the potential risks associated with different nursing jobs would reflect exposure to disinfectants and/or surgical smoke. We found that long-term (≥ 15 years) OR employment (exposure to both surgical smoke and disinfectants) was associated with a 69% increased risk of COPD compared with 31% increased risk among those who never worked in an OR but were currently employed in an emergency department or an inpatient unit (exposure to disinfectants but no or little exposure to surgical smoke). This difference may be explained by a synergistic effect of surgical smoke and disinfectant exposure or a higher level of exposure to surgical smoke and/or disinfectants in this particular type of nursing job.

In the NHS II,⁵ a related cohort study of US nurses, occupational exposure to cleaning products and disinfectants was associated with increased risk of developing COPD, and consistent results have been observed among occupational cleaners.^{40,41} A few studies that compared the mutagenicity and toxicity of surgical smoke with those of cigarette smoke have suggested that laser irradiation or electrocauterization of 1 g of tissue could equate to exposure to 3 to 6 cigarettes,⁴² and the mutagenic equivalent of average daily surgical smoke produced may be as high as exposure to 27 to 30 cigarettes.³⁴ Another study found significantly lower concentrations of the most commonly detected carcinogenic and irritant hydrocarbons in surgical smoke than in cigarette smoke.⁴³ Although these comparisons may be influenced by the particular surgical technology involved, tissue samples used for smoke generation and toxicity analysis, and environmental dispersion of smoke, they underscore the potential adverse effects associated with long-term exposure to surgical smoke.⁴⁴

Few studies have assessed the association of disinfectant exposure with COPD risk, and the role of occupational exposure to surgical smoke in COPD pathogenesis has, to our knowledge, never been investigated in a population study. The findings of the present study are consistent with clinical evidence and represent an early attempt to assess the implications of occupational exposure to disinfectants and surgical smoke.

Strengths and Limitations

This study has several strengths, including the large sample size, prospective follow-up, and a validated measure of COPD diagnosis. This study also has limitations. The cumulative OR experience was only assessed in 1984, which reflects working conditions in ORs several decades ago. The

surgical technology and protective equipment in an OR environment, as well as types of respiratory irritants and intensity of exposure, have evolved over time. However, we believe that the findings are still relevant to current working conditions for a few reasons. First, use of disinfectants to prevent health care-associated infections has increased.⁴⁵ Although more recent cleaning and disinfecting products may be associated with fewer health hazards, evidence regarding the health effects of these products is limited.⁴⁵ The association between occupational disinfectant exposure and respiratory disease was observed with data from 1991 in the European Community Respiratory Health Survey⁴⁶ and with exposure assessed from 2009 to 2013 in the NHS II.⁵ Second, there is little evidence that the hazard of surgical smoke has been reduced. Smoke-generating minimally invasive surgery has been performed in an increasingly diverse array of contexts and is now considered the standard of care for a wide spectrum of general surgical procedures.^{12,47,48} Despite the improved filtering efficiency, contemporary high-performing masks commonly used in health care settings (eg, N95 masks) may not filter ultrafine particles (which can be as small as 10 nm) in surgical smoke.⁴⁴ Given the limitation of passive protective equipment, professional and governmental organizations⁴⁹ have recommended that local exhaust ventilation be consistently used to protect health care workers⁵⁰; however, the prevalence of the widely recommended engineering control has remained low.¹² In a recent study, only 14% of perioperative personnel reported that local exhaust ventilation was always used during electrosurgery.⁴⁹

In addition, a few other limitations should be noted. First, we used OR employment history as a proxy for both surgical smoke exposure and disinfectant exposure and could not separate the roles of the 2 types of exposure in the analyses. Moreover, the results may have been affected by other related and competing respiratory irritants, such as formaldehyde⁵¹ and exhaled anesthesia such as isoflurane.⁵² Although we attempted to capture a gradient exposure to both sources of respiratory irritants, direct measures were not available. Future studies should incorporate more detailed direct environmental monitoring data of multiple occupational exposures. Third, employment status was not available in 1984; using employment status in 1982 may have resulted in misclassification. However, given that the incident events were assessed after baseline, any misclassification may have been nondifferential and would likely have weakened the associations. Fourth, OR employment status was not available during the follow-up period, precluding the possibility of updating exposure.

Conclusions

In this large prospective cohort study of US female nurses, OR employment for 15 or more years assessed in 1984 was associated with an increased risk of incident COPD over 16 years of follow-up. Additional studies with more recent and direct environmental monitoring data of multiple occupational exposures appear to be needed to examine the contributions of exposure to surgical smoke and disinfectants to the risk of developing COPD.

ARTICLE INFORMATION

Accepted for Publication: July 16, 2021.

Published: September 20, 2021. doi:10.1001/jamanetworkopen.2021.25749

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Author Contributions: Drs Xie and Stokes had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Xie, Stokes.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Xie, Dumas.

Obtained funding: Camargo, Stokes.

Administrative, technical, or material support: Xie, Boggs, Camargo, Stokes.

Supervision: Camargo, Stokes.

Conflict of Interest Disclosures: Ms Boggs reported receiving grants from the Centers for Disease Control and Prevention during the conduct of the study. Dr Camargo reported receiving grants from the National Institutes of Health and the Centers for Disease Control and Prevention during the conduct of the study. Dr Stokes reported receiving grants from Ethicon, Inc and Swiss Re during the conduct of the study. No other disclosures were reported.

Funding/Support: This analysis was supported in part by research grants UM1 CA-186107 (NHS cohort infrastructure grant), R01 HL-063841 (Dr Camargo), R21 AI-052338 (Dr Camargo), and R01 OH-101359 (Dr Camargo) from the National Institutes of Health and by an analysis grant from Ethicon Inc (Dr Stokes).

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of the study sponsors.

Additional Contributions: The underlying Nurses' Health Study is coordinated at the Channing Division of Network Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts. We thank Gary Chase, BS, the senior project manager of the Nurses' Health Studies, and other staff for their valuable contributions. Mr Chase and the other staff members did not receive any compensation from the current research.

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SUPPLEMENT.

eTable 1. Association of Operating Room Employment History with COPD Among US Nurses, Sensitivity Checks

eTable 2. Association of Operating Room Employment with COPD by Employment Years and Job Type, Sensitivity Checks

eFigure. Selection of Study Participants From NHS