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Impact of Occupational Exposure to Disinfectant or Cleaning Agents on Asthma

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ABSTRACT

Project Title: Impact of Occupational Exposure to Disinfectant or Cleaning Agents on Asthma

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Recent efforts to prevent healthcare-associated infections have led to increased use of disinfectants and cleaning agents. Studies suggest that occupational groups with regular exposure to these agents (e.g., health care workers) are at increased risk of asthma. However, the actual role of these common agents on the development and clinical course of asthma, and the specific agents and tasks involved, is largely unknown. The overall aim of the project was to address this knowledge gap in the Nurses' Health Study II, an ongoing prospective cohort study of 116,430 registered nurses, aged 24-44 years at baseline in 1989. Over the first 26 years, we observed ~14,000 incident cases of doctor-diagnosed asthma among ~22,000 nurses with a lifetime history of asthma. In 2009, 2011 and 2013, we asked all nurses about their job types and self-reported exposure to disinfectant or cleaning agents (~35% of nurses were exposed weekly). In this project, we enhanced assessment of both the exposure and outcome through supplementary questionnaires during 2014-2017. All nurses with asthma were sent questionnaires with validated questions on occupational exposures and asthma control (as defined by the 2007 NIH guidelines). The supplementary occupational questionnaire also was sent to a random sample of nurses without asthma (n=12,192); exposure data from this non-asthmatic group was used to create job exposure matrices (JEM) and task exposure matrices (TEM) that were applied to the entire cohort to better estimate exposure to specific agents. The enhanced data improved statistical power and permitted identification of specific agents that are most closely linked with asthma. The project had three specific aims. First, we used cohort data from 1989-2011 to determine the association between occupational exposure and incident asthma. We evaluated the "healthy worker effect" by examining job changes in relation to asthma status. Second, we performed a cross-sectional study (2014) to determine the association between occupational exposure and asthma control. Third, we conducted a prospective study to determine the association between occupational exposure and incident asthma (2009-2015, n~370 cases). In the final year, we also performed preliminary work on the relation of occupational exposure to risk of incident COPD (2009-2015, n~582 cases). Although occupational exposure to disinfectant or cleaning agents was not associated with incident asthma in late-career nurses, it was associated with worse asthma control. Moreover, preliminary work suggested, for the first time, that occupational exposure to disinfectant or cleaning agents was associated with incident chronic obstructive pulmonary disease (COPD). In summary, this innovative project determined the relation of a common occupational exposure among nurses to risk of adult-onset asthma and poor asthma control. The project provided a unique opportunity, in a large occupational cohort, to test several novel hypotheses about occupational exposures to disinfectant or cleaning agents and their impact on asthma – and to begin to study the role of occupational exposures on risk of developing COPD. The study results could have a major public health impact on the well-being of health care workers, cleaners, and others who are regularly exposed to disinfectant or cleaning agents.

SECTION 1

Significant or Key Findings: The project successfully addressed all aims, with publication of multiple scientific manuscripts and presentations at multiple international meetings. Additional manuscripts are currently under peer review. Taking each of the Aims in turn:

- 1. Cohort study (1989-2013): To determine the association between occupational exposure and incident asthma.** Nurses reported job type in 1989, and they reported job types held over the 20-year period in 2009. *Hypothesis 1a:* Women in job types with higher levels of exposure (e.g., operating room [OR] nurses) have a higher asthma incidence than women in non-exposed groups (e.g., administration). We will evaluate the magnitude of a potential “healthy worker” effect by considering changes in job type, per asthma status at the time of each job, with an interest in women working in the OR. *Hypothesis 1b:* Women in job types with higher self-reported recent use of disinfectants and sprays have a higher 4-year incidence of asthma (2007-2013).

The “healthy worker” effect was stronger than we anticipated and the original analysis plan was discarded. Instead, we focused on whether asthma history influences job choices among nurses, a topic that was largely unknown. Briefly, we found that asthma history was associated with baseline job type and subsequent job changes among nurses (Dumas et al, *Occup Environ Med* 2014). We believe that this may partly reflect avoidance of tasks involving disinfectant use, and may introduce bias in cross-sectional studies on disinfectant exposure and asthma in nurses.

- 2. Cross-sectional study (2014): To determine the association between occupational exposure and asthma severity and control.** This aim will use enhanced data concerning occupational exposure (based on self-report and exposures patterns evaluated by principal component analysis [PCA], job-exposure matrix [JEM] and task-exposure matrix [TEM]) and asthma (based on a supplemental asthma questionnaire). *Hypothesis 2:* Higher levels of the enhanced exposure are associated with worse asthma severity and control.

We successfully created the JEM/TEM (or JTEM) and described this innovation in the scientific literature (Quinot et al, *Occup Environ Med* 2017). Briefly, we found that the JTEM may provide more accurate estimates than the JEM, especially for nursing jobs with heterogeneous tasks. We concluded that use of the JTEM is likely to reduce exposure misclassification. We posted the article and relevant materials online to promote further dissemination of this new tool: <http://nhs2item.org>.

We next addressed the role of occupational exposure with asthma severity/control (Dumas et al, *Eur Respir J* 2017). Briefly, we found that use of several disinfectants was associated with poor asthma control. Our findings suggested targets for future efforts to prevent worsening of asthma control in healthcare workers.

We extended this result by looking at another novel exposure: self-reported washing of arms/hands with disinfectants (Dumas et al, *Occup Environ Med* 2018). Briefly, frequency of hand/arm hygiene tasks in nurses was associated with poor asthma control. We believe that the results suggest an adverse effect of products used for surgical hand/arm antisepsis, and that this new potential occupational risk factor for asthma warrants further study.

- 3. Cohort study (2009-2015): To determine the prospective association between occupational exposure and incident asthma.** Exposure assessment will be based on the 2009 and 2011 NHSII main questionnaires, enhanced by the nurse-specific JEM and TEM. The enhanced data will improve statistical power and allow identification of the specific agents that are most closely linked with asthma risk. *Hypothesis 3:* Higher levels of the enhanced exposure are associated with higher 6-year incidence of asthma (2009-2015).

Briefly, no association was observed between exposure to disinfectants and asthma incidence in a population of late-career nurses (Dumas et al, manuscript under review). Nevertheless, we believe that a potential role of disinfectant exposures in asthma development warrants further study among healthcare workers at earlier career stage.

In addition to the three aims, we completed a spin-off paper on the determinants of disinfectant use among nurses in U.S. Healthcare facilities (Dumas et al, *Am J Ind Med* 2017). Briefly, we found that disinfectant use was more common among nurses working in smaller hospitals, possibly because they perform more diverse tasks. Variations in spray use by hospital size and region suggest additional targets for future efforts to prevent occupational asthma.

Lastly, in another spin-off paper, we investigated the role of occupational exposure to disinfectant or cleaning agents and the development of COPD (Dumas et al, manuscript under review). Briefly, the results support a prospective association between occupational exposure to disinfectants and higher COPD incidence in nurses. We believe that this novel hypothesis merits further investigation.

Translation of Findings: Our findings support improvement of safety programs in healthcare settings targeted to workers with asthma. We found that among nurses with asthma, occupational exposure to a wide range of disinfectants and cleaning agents was associated with poor asthma control. Our work suggests adverse effects of high-level disinfectants used on critical/semi-critical items (aldehydes, bleach and hydrogen peroxide), products used to clean items before disinfection or sterilization (enzymatic cleaners), and products used for surgical hand/arm antisepsis. Apart from the active ingredients, we found that use of sprays was associated with poor asthma control. The use of respiratory protection devices when handling disinfectants was limited and we could not determine whether use of respiratory protection devices had an impact on the association between disinfectant use and asthma control.

In addition, our work may help preventing the development of chronic respiratory diseases among healthcare workers. Although we did not observe increased risk of incident asthma associated with use of disinfectants / cleaning agents in late career nurses, preliminary results suggest their potential impact on COPD development. This novel important finding merits further investigation.

Overall, our research highlights the urgency of integrating occupational health considerations in guidelines for cleaning and disinfection in healthcare.

Research Outcomes/Impact: Our research has important potential outcomes as findings can guide improvement in occupational safety and health of millions of healthcare workers. They suggest targets for future efforts to improve asthma management, by integrating occupational health considerations in guidelines for cleaning/disinfection in healthcare. The development of new approaches to maintain infection control standards in healthcare settings may be needed. Because a wide range of chemical disinfectants/cleaning agents were associated with poor respiratory outcomes, our results support the investigation of emerging nonchemical technologies for disinfection (e.g. steam, ultraviolet light) as an alternative to chemical disinfection and further research on green cleaning. Our findings also suggest that reducing the use of sprays may help improving respiratory health among healthcare workers.

Preliminary findings also suggest an impact of exposure to disinfectants and cleaning agents on a broader range of respiratory outcome, in particular on COPD development. This should guide the development of research to investigate this novel hypothesis.

SECTION 2**1. Scientific Report**

a. Background: Growing evidence suggests a deleterious role of disinfectant and cleaning agents on asthma. Given the frequency with which these common agents are used in healthcare settings, occupational exposure could have an important public health impact. For this R01 project, we generated hypotheses regarding the deleterious role of surface and instrument disinfection, cleaning sprays, bleach and ammonia, in asthma. We also proposed to use generate JEMs and TEMs for exposure assessment since specific population-based JEMs and TEMs have been shown to be appropriate methods to assess occupational exposure in large-scale epidemiological surveys. Moreover, we proposed that the intensity and duration of exposure to sensitizers and irritants, which have been evaluated in few studies, are important predictors of occupational asthma. We took advantage of a unique opportunity to test all of these hypotheses in the Nurses' Health Study II (NHSII), an ongoing cohort of >116,000 registered nurses in whom specific hospital worksites and use of disinfectants can be assessed and in whom asthma incidence is being followed. We believed that findings from this longitudinal study of >116,000 nurses could clarify the impact of this common occupational exposure on asthma.

b. Specific Aims: The Specific Aims were based on three inter-related studies, each with its own Aim and the opportunity to test specific hypotheses. The October 2012 U.S. government shut-down and subsequent budget problems significantly delayed the start of the R01 project from 12/1/12 (proposed) to 9/1/13 (actual). Accordingly, all dates in the original grant application are incorrect. Although this delay created logistical challenges, it also created opportunities, such as increased duration of follow-up. Regardless, the basic aims were unchanged:

Aim 1. Cohort study (1989-2013): To determine the association between occupational exposure and incident asthma. Nurses reported job type in 1989, and they reported job types held over the 20-year period in 2009. Hypothesis 1a: Women in job types with higher levels of exposure (e.g., operating room [OR] nurses) have a higher asthma incidence than women in non-exposed groups (e.g., administration). We will evaluate the magnitude of a potential "healthy worker" effect by considering changes in job type, per asthma status at the time of each job, with an interest in women working in the OR. Hypothesis 1b: Women in job types with higher self-reported recent use of disinfectants and sprays have a higher 4-year incidence of asthma (2007-2013).

Aim 2. Cross-sectional study (2014): To determine the association between occupational exposure and asthma severity and control. This aim will use enhanced data concerning occupational exposure (based on self-report and exposures patterns evaluated by principal component analysis [PCA], job-exposure matrix [JEM] and task-exposure matrix [TEM]) and asthma (based on a supplemental asthma questionnaire). Hypothesis 2: Higher levels of the enhanced exposure are associated with worse asthma severity and control.

Aim3. Cohort study (2009-2015): To determine the prospective association between occupational exposure and incident asthma. Exposure assessment will be based on the 2009 and 2011 NHSII main questionnaires, enhanced by the nurse-specific JEM and TEM. The enhanced data will improve statistical power and allow identification of the specific agents that are most closely linked with asthma risk. Hypothesis 3: Higher levels of the enhanced exposure are associated with higher 6-year incidence of asthma (2009-2015).

c. Methodology:

Population: The NHSII began in 1989 when 116 430 female registered nurses from 15 US states, aged 25–44 years, completed a questionnaire on their medical history and lifestyle characteristics. Follow-up

questionnaires have been sent every 2 years since. In 2014, we initiated a nested case–control study on asthma. 18,096 participants who ever reported physician-diagnosed asthma in biennial questionnaires were invited to complete a supplemental questionnaire on asthma (response rate 80%); those who were in a nursing job in 2011 were also invited to complete a questionnaire on occupational exposures. In addition, a random sample of 12 192 non-asthmatic nurses (who were still in a nursing job at the time of the 2011 follow-up questionnaire) were invited to complete a questionnaire on occupational exposures (response rate 91%). Non-asthmatic nurses were selected among all types of nursing jobs and an additional sample of nurses (enriched sample) was selected among operating room (OR), emergency room (ER) and intensive care unit (ICU) nurses to enrich the sample of less frequent nursing jobs with expected high exposure levels.

Occupational exposure in the biennial questionnaire: Data on work status and type of nursing job were collected at baseline (1989) and in follow-up questionnaires in 1993, 1997, 2001, 2009, 2011, and 2013 with the question “Which best describes your current employment status”. In 1989, options included nursing in inpatient or Emergency Room (ER), Operating Room (OR), outpatient or community; nursing education; nursing administration; other nursing; non-nursing employment; or fulltime homemaker. Other options were included in follow-up questionnaires (e.g., Intensive Care Unit [ICU], disabled, retired, other). In 2009, 2011, and 2013 a general question regarding the frequency (days/week) of use of disinfectants at work have been added: « Thinking about your current job and the use of disinfectants (such as ethylene oxide, hydrogen peroxide, orthophthalaldehyde, formaldehyde, glutaraldehyde and bleach): (a) On how many days per week, on average, do you clean medical instruments with disinfectants? (b) On how many days per week, on average, do you clean surfaces (like floors, tables) at work with disinfectants? (never, <1 day/week, 1-3 days/week, 4-7 days/week) ».

In 2011 and 2013, specific questions were asked about the use of sprays: “In your current job, on how many days per week, on average, do you use spray or aerosol products? (never, <1 day/week, 1-3 days/week, 4-7 days/week)”. Those who reported weekly use of sprays were asked to report tasks where they used sprays (patient care; instrument cleaning or disinfection; surface cleaning or disinfection; air-refreshing; other).

Exposure to specific disinfectants and cleaning products: The occupational questionnaire used in our study was adapted to U.S. context from questionnaires used in European studies (European Community Respiratory Health Survey and Epidemiological study on the Genetics and Environment of Asthma, with additions of relevant tasks based on results from a study of asthma among healthcare workers in Texas. Information on general disinfection tasks (frequency of use of disinfectants to clean surfaces/medical instruments and use of sprays) was collected in the occupational questionnaire. In addition, questions were asked about the frequency of use (‘On how many days per week do you use the following disinfectants at work?’) of 14 specific disinfectants (eg, glutaraldehyde, bleach, quats). Participants who did not know the active compound in the products they use could fill in the brand name instead; we searched the corresponding safety data sheets to determine the products’ compounds and re-evaluated the nurses’ exposure accordingly.

We developed a job-exposure matrix (JEM) and a job-task-exposure matrix (JTEM) to evaluate exposure to seven major disinfectants/cleaning products (formaldehyde, glutaraldehyde, hypochlorite bleach, hydrogen peroxide, alcohol, quats, and enzymatic cleaners). The development of the JTEM was based on the responses to the questions described above in a population of 9,073 nurses without asthma. We generated the JTEM based on the percentage of participants reporting exposure to a given disinfectant for a given nursing job and task category. The “job-task” axis of the JTEM included the 24 possible combinations of 8 types of nursing jobs by 3 categories of cleaning tasks (surfaces only, at least instruments, none). Specific cut-offs were defined to classify exposure in “low”, “medium” and “high” levels for each disinfectant, in a given job or job-task combination. We also created a JEM to evaluate exposure to specific disinfectants. With the JEM, exposure level was assigned based on type

of nursing job, without taking into account tasks.) The JEM and JTEM were applied to the entire cohort to better estimate exposure to specific agents.

Because of their lower exposure prevalence, eight other products (ortho-phthalaldehyde, peracetic acid, acetic acid, ammonia, phenolics, ethylene oxide, chloramine T and “green” products) could be evaluated only by self-report.

In the occupational questionnaire, nurses were also asked about the daily frequency of hand/arm hygiene tasks involving disinfectants (ie, nurses were specifically asked not to include tasks only involving use of soap): ‘In your current job, how many times per day, on average, do you ...’: ‘wash/scrub your hands with disinfectants or hand sanitizers’, to evaluate frequency of hand hygiene tasks; and ‘wash/scrub your arms with disinfecting products’.

Survey of hospital infection control department: In order to obtain additional information regarding the disinfectants and cleaning products used in the hospitals where NHSII nurses worked, we addressed a 2-page survey to infection control departments of the 16 hospitals where ≥ 10 nurses worked. We received responses from 8 hospitals where a total of 177 NHSII nurses worked. Responses from infection control departments and nurses were compared qualitatively, in particular regarding the ingredients of the products used by nurses for cleaning/ disinfection tasks.

Asthma: Participants who reported asthma in biennial questionnaires were categorized on the basis of supplemental asthma questionnaires according to validated case definitions. To define asthma cases, we selected participants who reiterated on the supplemental questionnaire that a physician had diagnosed her as having asthma and who reported use of any asthma medication in the past year. Among all asthma cases, asthma control was defined using the Asthma Control Test (ACT) score (range 5–25), based on five questions on activity limitations, frequency of symptoms and frequency of use of quick-relief medication in the past 4 weeks. Incident cases of physician-diagnosed asthma were identified from 2009 to 2015.

Analyses: Associations between exposure to disinfectants and asthma control were evaluated either by logistic regressions (asthma control) or Cox proportional hazard models (asthma incidence). Asthma control was classified into four categories based on ACT score (25: controlled; 20–24: partly controlled; 16–19: poorly controlled; ≤ 15 : very poorly controlled) and considered either as a categorical variable or as an ordinal variable. Asthma incidence was studied as a dichotomous variable. Disinfection tasks were studied using dichotomous variables (task performed 1–3 or 4–7 versus never or < 1 day(s) per week). Exposure to specific disinfectants according to the JTEM was studied using three-level variables (low, medium or high exposure level). Analyses were adjusted for age, smoking status, body mass index (BMI), race (White versus other) and ethnicity (Hispanic versus other).

d. Results: Over the 4-year R01 grant, we successfully addressed all of original aims and hypotheses, and also performed two spin-off projects on: 1) the determinants of disinfectant use among nurses in U.S. healthcare facilities, and 2) the prospective association between occupational exposure to disinfectants and incident COPD. We summarize all of these results below.

Aim 1. Cohort study (1989-2013): To determine the association between occupational exposure and incident asthma. The “healthy worker” effect was stronger than we anticipated and the original analysis plan was discarded. Instead, we focused on whether asthma history influences job choices among nurses, a topic that was largely unknown. Briefly, we found that asthma history was associated with baseline job type and subsequent job changes among nurses (Dumas et al, *Occup Environ Med* 2014). We believe that this may partly reflect avoidance of tasks involving disinfectant use, and may introduce bias in cross-sectional studies on disinfectant exposure and asthma in nurses.

Aim 2. Cross-sectional study (2014): To determine the association between occupational exposure and asthma severity and control. We successfully created the JEM/TEM (or JTEM) and

described this innovation in the scientific literature (Quinot et al, *Occup Environ Med* 2017). Briefly, we found that the JTEM may provide more accurate estimates than the JEM, especially for nursing jobs with heterogeneous tasks. We concluded that use of the JTEM is likely to reduce exposure misclassification. We posted the article and relevant materials online to promote further dissemination of this new tool: <http://nhs2jtem.org>.

We next addressed the role of occupational exposure with asthma severity/control (Dumas et al, *Eur Respir J* 2017). Briefly, we found that use of several disinfectants was associated with poor asthma control. Our findings suggested targets for future efforts to prevent worsening of asthma control in healthcare workers.

We extended this result by looking at another novel exposure: self-reported washing of arms/hands with disinfectants (Dumas et al, *Occup Environ Med* 2018). Briefly, frequency of hand/arm hygiene tasks in nurses was associated with poor asthma control. We believe that the results suggest an adverse effect of products used for surgical hand/arm antisepsis, and that this new potential occupational risk factor for asthma warrants further study.

Aim 3. Cohort study (2009-2015): To determine the prospective association between occupational exposure and incident asthma. We performed the analyses for this third Aim during the final year of the project and the results are not yet published (Dumas et al, manuscript under review). For this reason, we present additional detail herein. Analyses included 61,538 participants who were still in a nursing job and with no history of asthma in 2009 (baseline; mean age: 55 years). During 277,742 person-years of follow-up from 2009 to 2015, 370 nurses reported incident physician-diagnosed asthma. Occupational exposure was evaluated by questionnaire and the JTEM. Weekly use of disinfectants to clean surfaces only (23% exposed) or to clean medical instruments (19% exposed) was not associated with incident asthma (adjusted hazard ratio [95% CI] for surfaces, 1.12 [0.87-1.43]; for instruments, 1.13 [0.87-1.48]). No association was observed between high level exposure to specific disinfectants/cleaning products evaluated by the JTEM (formaldehyde, glutaraldehyde, bleach, hydrogen peroxide, alcohol quats or enzymatic cleaners) and asthma incidence (Table 1). In conclusion, no association was observed between exposure to disinfectants and asthma incidence in a population of late-career nurses. A potential role of disinfectant exposures in asthma development warrants further study among healthcare workers at earlier career stage.

Table 1. Prospective associations between exposure to specific disinfectants/cleaning products evaluated by the JTEM and asthma incidence in US female nurses

	Person-years	No. of cases	Multivariable-adjusted HR	
			HR	95% CI
Formaldehyde	25,029	32	0.97	0.67-1.40
Glutaraldehyde	79,151	108	1.12	0.88-1.41
Hypochlorite bleach	76,749	109	1.07	0.84-1.36
Hydrogen peroxide	88,052	117	1.06	0.84-1.34
Alcohol	95,332	142	1.14	0.91-1.42
Quats	96,781	124	1.00	0.79-1.26
Enzymatic cleaners	40,992	52	0.97	0.72-1.30

Abbreviations: HR, hazard ratio; CI, confidence interval; JTEM – Job-Task-Exposure Matrix.

Multivariable models were adjusted for age, race, ethnicity, smoking status and body mass index.

Exposure to disinfectants/cleaning products was evaluated at the questionnaire cycle before time of diagnosis. Associations presented compare high exposure level vs. low exposure level, for each product. No association was observed when comparing medium vs. low exposure level.

In addition to the three aims, we completed a spin-off paper on the determinants of disinfectant use among nurses in U.S. Healthcare facilities (Dumas et al, *Am J Ind Med* 2017). Briefly, we found that disinfectant use was more common among nurses working in smaller hospitals, possibly because they perform more diverse tasks. Variations in spray use by hospital size and region suggest additional targets for future efforts to prevent occupational asthma.

Lastly, given the close relation between asthma and COPD in adults, we also investigated the **prospective association between occupational exposure to disinfectants and incident COPD**, (Dumas et al, manuscript under review). Because these results are not yet published, we present additional detail herein. Analyses included 73,262 participants who were still in a nursing job and with no history of COPD in 2009 (baseline; mean age: 55 years). During 368,145 person-years of follow-up, from 2009 to 2015, 582 nurses reported incident physician-diagnosed COPD. Occupational exposure was evaluated by questionnaire and the JTEM. Weekly use of disinfectants to clean surfaces only (23% exposed) and to clean medical instruments (19% exposed) was associated with incident COPD, with adjusted hazard ratio (aHR) [95%CI] of 1.38 [1.13-1.68] and 1.31 [1.06-1.61], respectively. High level exposure to several specific disinfectants evaluated by the JTEM (glutaraldehyde, bleach, hydrogen peroxide, alcohol and quats) were significantly ($p < 0.05$) associated with incident COPD, with aHRs ranging from 1.25 to 1.36 (table 2). Associations between use of disinfectants and COPD incidence were not modified by smoking or asthma status. In conclusion, results support a prospective association between occupational exposure to disinfectants and higher COPD incidence in nurses. This novel hypothesis merits further investigation.

Table 2. Prospective associations between exposure to specific disinfectants/cleaning products evaluated by the JTEM and COPD incidence in US female nurses

	Person-years	No. of cases	Multivariable-adjusted HR	
			HR	95% CI
Formaldehyde	38,056	62	1.20	0.92-1.57
Glutaraldehyde	125,281	192	1.25	1.04-1.51
Hypochlorite bleach	127,879	215	1.36	1.12-1.64
Hydrogen peroxide	141,504	229	1.29	1.08-1.54
Alcohol	150,512	245	1.32	1.10-1.59
Quats	142,722	233	1.33	1.11-1.60
Enzymatic cleaners	69,447	97	1.05	0.83-1.31

Abbreviations: HR, hazard ratio; CI, confidence interval; JTEM – Job-Task-Exposure Matrix.

Results in bold are statistically significant. Multivariable models were adjusted for age, smoking status and pack-years (continuous), race, ethnicity and body mass index.

Exposure evaluated as the highest exposure level at any of the questionnaire cycles before time of diagnosis. Associations presented compare high exposure level vs. low exposure level, for each product. No association was observed when comparing medium vs. low exposure level, except for glutaraldehyde (adjusted HR: 1.50, 95% CI: 1.18-1.90).

e. Discussion: Our findings support improvement of safety programs in healthcare settings targeted to workers with asthma. We found that among nurses with asthma, occupational exposure to a wide range of disinfectants and cleaning agents was associated with poor asthma control. In particular, our work suggests adverse effects of high-level disinfectants used on critical or semicritical items (aldehydes, hypochlorite bleach and hydrogen peroxide), products used to clean items before high-level disinfection or sterilisation (enzymatic cleaners), and products used for surgical hand/arm antisepsis. Apart from the active ingredients, we found that use of sprays was associated with poor asthma control. The use of respiratory protection devices when handling disinfectants was limited and we could not determine whether use of respiratory protection devices had an impact on the association between disinfectant use and asthma control.

In addition, our work may help preventing the development of chronic respiratory diseases among healthcare workers. Although we did not observe increased risk of incident asthma associated with use of disinfectants / cleaning agents in late career nurses, preliminary results suggest their potential impact on COPD development. This novel important finding merits further investigation.

Overall, our research highlights the urgency of integrating occupational health considerations in guidelines for cleaning and disinfection in healthcare.

Regarding the overall impact of the project, our research has important potential outcomes as findings can guide future improvement in occupational safety and health of millions of healthcare workers. They suggest targets for future efforts to improve asthma management, by integrating occupational health considerations in guidelines for cleaning and disinfection in healthcare. The development of new approaches to maintain infection control standards in healthcare settings may be needed. Because a wide range of chemical disinfectants / cleaning agents were associated with poor respiratory outcomes, our results support the investigation of emerging nonchemical technologies for disinfection (e.g. steam, ultraviolet light) as a potential alternative to chemical disinfection and further research on green cleaning, integrating health risk reduction among the products' standards. Our findings also suggest that reducing the use of products in spray form may help improving respiratory health among healthcare workers.

Lastly, preliminary findings also suggest an impact of exposure to disinfectants and cleaning agents on a broader range of respiratory outcome, in particular on COPD development. This should guide the development of research to investigate this novel hypothesis.

f. Conclusion: This R01 project, for the first time, determined the relation of a common occupational exposure among nurses to risk of adult-onset asthma and poor asthma control. The project provided a unique opportunity, in a large occupational cohort, to test several novel hypotheses about occupational exposures to disinfectant or cleaning agents and their impact on asthma. Although occupational exposure to disinfectant or cleaning agents was not associated with incident asthma in late-career nurses, it was associated with worse asthma control. Moreover, preliminary work suggested that occupational exposure was associated incident COPD. The study results could have a major public health impact on the well-being of health care workers, cleaners, and others who are regularly exposed to disinfectant or cleaning agents.

2. Publications

a. Original Research Publications

1. Dumas O, Varraso R, Boggs KM, Descatha A, Henneberger PK, Quinot C, Speizer FE, Zock JP, Le Moual N, Camargo CA Jr: [2018] Association of Hand and Arm Disinfection with Asthma Control in US nurses. *Occup Environ Med* 75:378-381.
PMID: 29475850. PMCID: [PMC5899017](#) [Available on 2019-05-01]
2. Dumas, O, Wiley AS, Quinot C, Varraso R, Zock, JP, Henneberger PK, Speizer FE, Le Moual N, Camargo CA Jr: [2017] Occupational Exposure to Disinfectants and Asthma Control in U.S. Nurses. *Eur Respir J* 50(4): pii: 1700237.
PMID: 28982772. PMCID: [PMC5702691](#) [Available on 2018-10-05]
3. Dumas O, Wiley AS, Henneberger PK, Speizer FE, Zock JP, Varraso R, Le Moual N, Boggs KM, Camargo CA Jr: [2017] Determinants of Disinfectant Use among Nurses in U.S. Healthcare Facilities. *Am J Ind Med* 60: 131-140.
PMID: 27862135. PMCID: [PMC5154899](#)

4. Quinot C, Dumas O, Henneberger PK, Varraso R, Wiley AS, Speizer FE, Goldberg M, Zock JP, Camargo CA Jr, Le Moual N: [2017]. Development of a Job-Task-Exposure Matrix to Assess Occupational Exposure to Disinfectants among US Nurses. *Occup Environ Med* 74: 130-137. PMID: 27566782. PMCID: [PMC5237395](#)
5. Dumas O, Varraso R, Zock JP, Henneberger PK, Speizer FE, Wiley AS, Le Moual N, Camargo CA Jr: [2015] Asthma History, Job Type, and Job Changes among U.S. Nurses. *Occup Environ Med* 72:482-488. PMID: 25713153. PMCID: [PMC4472505](#)

b. Abstract Presentations

1. Dumas O, Varraso R, Boggs KM, Quinot C, Zock JP, Henneberger PK, Speizer FE, Le Moual N, Camargo CA Jr: [2017] Occupational Exposure to Disinfectants and COPD Incidence in US Nurses: A Prospective Cohort Study [abstract]. Presented at the European Respiratory Society International Congress (Milan, Italy; September 9-13, 2017). Oral presentation.
2. Dumas O, Varraso R, Boggs KM, Henneberger PK, Quinot C, Speizer FE, Zock JP, Le Moual N, Camargo CA Jr: [2016]. Hand Hygiene and Asthma Control in U.S. Nurses: A New Risk Factor for Work-related Asthma? Presented at Epidemiology in Occupational Health Meeting (Barcelona, Spain; September 4-7, 2016). Oral presentation.
3. Dumas O, Wiley AS, Henneberger PK, Speizer FE, Zock JP, Varraso R, Le Moual N, Boggs K, Camargo CA Jr: [2016] Variations in Disinfectants Used by Nurses in US Healthcare Facilities. Presented at American Thoracic Society International Congress (San Francisco, CA; May 13-18, 2016). Poster presentation.
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6. Dumas O, Varraso R, Zock JP, Henneberger PK, Speizer FE, Wiley AS, Le Moual N, Camargo CA Jr. Asthma History, Job Type, and Job Changes among U.S. Nurses. Presented at European Respiratory Society International Congress (Munich, Germany; September 6-10, 2014). Oral presentation.

Targeted/Planned Enrollment Table

Study Title: Impact of Occupational Exposure to Disinfectant or Cleaning Agents on Asthma

Total Planned Enrollment: Ongoing cohort study (n=116,678 women enrolled in 1989)

TARGETED/PLANNED ENROLLMENT: Number of Subjects			
Ethnic Category	Sex/Gender		
	Females	Males	Total
Hispanic or Latino	1,874	0	1,874
Not Hispanic or Latino	114,804	0	114,804
Ethnic Category: Total of All Subjects *	116,678	0	116,678
Racial Categories			
American Indian/Alaska Native	0	0	0
Asian	2,408	0	2,408
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2,206	0	2,206
White	112,064	0	112,064
Racial Categories: Total of All Subjects *	116,678	0	116,678

* The "Ethnic Category: Total of All Subjects" must be equal to the "Racial Categories: Total of All Subjects."

Inclusion of Women and Minorities

The study involved women in the Nurses Health Study II (NHSII), an ongoing cohort of >116,000 nurses. Women in the NHSII cohort were recruited in 1989, and no exclusions were made on race/ethnicity when establishing the cohort. Registered nurses at that time were predominately White, and the race/ethnic breakdown corresponds to that of women entering nursing in the preceding decades as reported in the National Nursing Survey. The occupational selection was made to increase the cost-effectiveness of the study and to improve internal validity by drawing on the training of the participants and their ability to provide accurate information on both exposures and outcome. The cohort provides a unique opportunity for research on occupational exposures and their impact on asthma. The Targeted/Planned Enrollment Form provides estimates of total study enrollment by sex and race/ethnicity.

Inclusion of Children

The study – on occupational exposures and risk of adult-onset asthma – involves women in the ongoing Nurses' Health Study II. The proposed study does not include children.