

Online supplement

Occupational exposure to disinfectants and asthma control in U.S. nurses

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Asthma Control Test (ACT) score

The ACT score was based on responses to the five questions, each scored using a 5-point scale (1: poor control to 5: good control). Scores for each question are then summed to give the ACT score (range 5-25). The questions were: “In the past 4 weeks, how much of the time did your asthma keep you from getting as much done at work, school or at home?” (“All of the time” to “None of the time”); “During the past 4 weeks, how often have you had shortness of breath?” (“More than once a day” to “Not at all”); “During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?” (“4 or more nights a week” to “Not at all”); “During the past 4 weeks, how often have you used your β -agonist inhaler (e.g., albuterol) for symptom control? (Please do not count prevention of exercise-induced bronchospasm)?” (“3 or more times per day” to “Not at all”); and “How would you rate your asthma control during the past 4 weeks?” (“Not controlled at all” to “Completely controlled”).

Occupational exposure

The occupational questionnaire used in our study was adapted to U.S. context from questionnaires used in European studies (European Community Respiratory Health Survey [E1] and Epidemiological study on the Genetics and Environment of Asthma [E2], with additions of relevant tasks based on results from a study of asthma among healthcare workers in Texas.

Job type and tasks

Current nursing job type was evaluated using the question “Which best describes your current employment status?”, in 8 categories: nursing in the emergency room (3%), operating room (5%), intensive care unit (4%), other inpatient nurse (13%), outpatient or community (28%), other hospital nursing (10%), nursing outside hospital (18%) and nursing education or

administration (19%). The two main questions regarding the frequency (days/week) of disinfection tasks were: « 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) ».

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).

Specific disinfectants

Exposure to seven major disinfectants/cleaning products was evaluated by the JTEM (formaldehyde, glutaraldehyde, hypochlorite bleach, hydrogen peroxide, alcohol, quats, and enzymatic cleaners), as described in detail below. Because of their lower exposure prevalence, eight other products (ortho-phtalaldehyde, peracetic acid, acetic acid, ammonia, phenolics, ethylene oxide, chloramine T and “green” products) could be evaluated only by self-report [E3], using questions about the frequency of use (“On how many days per week do you use the following disinfectants at work?”) of the specific disinfectants in the occupation questionnaire. 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. Associations of these eight products with asthma control are presented in supplementary Table E6.

Job-task exposure matrix (JTEM)

The development of the JTEM has been described in detail elsewhere.[E1] Briefly, it used the responses to the questions described above in a population of 9,073 nurses without asthma, drawn from the Nurses' Health Study II. 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.

Given the way the JTEM was designed, "high level" of exposure should be understood as higher probability of frequent (weekly) exposure. As cut-off chosen were disinfectant-specific, and were relative to the average level of use within each job/tasks, "high level" is disinfectant specific (eg, "high" level of glutaraldehyde does not compare to "high" level of exposure to alcohol in terms of intensity, frequency or concentration of exposure).

As reported previously [E3], we also created a job-exposure matrix (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. However, we expected that assigning exposure level to many cleaning/disinfecting products based on jobs only may lead to non-differential misclassification of exposure and drive estimates of associations with health outcomes toward the null [E2–E4]. Consistently with this assumption, we did not observe any association between exposures evaluated by the JEM and asthma control (results not shown). The fact that associations with asthma control were observed with the JTEM (more precise

exposure estimates) and not the JEM further strengthens the evidence for a specific role of exposure to disinfectants – as compared to other potential work-related exposures among nurses – in asthma outcomes.

References

- E1. Mirabelli MC, Zock JP, Plana E, Antó JM, Benke G, Blanc PD, Dahlman-Hoglund A, Jarvis DL, Kromhout H, Lillienberg L, Norback D, Olivieri M, Radon K, Sunyer J, Torén K, van Sprundel M, Villani S, Kogevinas M. Occupational risk factors for asthma among nurses and related healthcare professionals in an international study. *Occup Env. Med* 2007; 64: 474–479.
- E2. Donnay C, Denis MA, Magis R, Fevotte J, Massin N, Dumas O, Pin I, Choudat D, Kauffmann F, Le Moual N. Under-estimation of self-reported occupational exposure by questionnaire in hospital workers. *Occup Env. Med* 2011; 68: 611–617.
- E3. Quinot C, Dumas O, Henneberger PK, Varraso R, Wiley AS, Speizer FE, Golberg M, Zock J-P, Camargo CJ, Le Moual N. Development of a job-task-exposure matrix to assess occupational exposure to disinfectants among US nurses. *Occup Env. Med* 2017; 74: 130–137.
- E4. Delclos GL, Gimeno D, Arif AA, Benavides FG, Zock JP. Occupational exposures and asthma in health-care workers: comparison of self-reports with a workplace-specific job exposure matrix. *Am J Epidemiol* 2009; 169: 581–587.

Table E1. Associations between self-reported use of different types of sprays and asthma control

	Asthma Control Test score							P trend
	25		20-24		≤19			
	n	%	OR*	%	OR* (95% CI)	%	OR* (95% CI)	
Weekly use of sprays								
No (ref.)	3,301	33	1	50	1	17	1	
For surface cleaning/disinfection	529	28	1	50	1.15 (0.92-1.43)	22	1.47 (1.13-1.91)	0.02
For instrument cleaning/disinfection	166	27	1	52	1.27 (0.88-1.85)	21	1.47 (0.93-2.32)	0.09
For patient care	227	22	1	56	1.64 (1.17-2.30)	21	1.76 (1.17-2.66)	0.005
Air-refreshing sprays	382	26	1	51	1.26 (0.97-1.62)	23	1.56 (1.14-2.12)	0.004

* Adjusted for age, smoking status, body mass index, race and ethnicity. OR – odds ratio; CI – confidence interval; NHS II: Nurses' Health Study II.

Table E2. Associations between self-reported frequency of cleaning/disinfection tasks and asthma control

	Asthma Control Test score							P trend
	25		20-24		≤19			
	n	%	OR*	%	OR* (95% CI)	%	OR* (95% CI)	
Use of disinfectant to clean surfaces								
Never (ref.)	1,396	34	1	48	1	19	1	
<1 day/week	783	30	1	52	1.21 (0.99-1.48)	18	1.09 (0.94-1.41)	0.32
1-3 days/week	1,082	33	1	49	1.04 (0.87-1.25)	18	0.98 (0.78-1.24)	0.98
4-7 days/week	811	28	1	52	1.30 (1.06-1.59)	20	1.25 (0.96-1.61)	0.03
Use of disinfectant to clean instruments								
Never	2,803	33	1	49	1	18	1	
<1 day/week	496	29	1	53	1.26 (1.01-1.57)	18	1.16 (0.87-1.56)	0.16
1-3 days/week	493	30	1	47	1.07 (0.86-1.34)	23	1.51 (1.15-1.99)	0.005
4-7 days/week	276	25	1	53	1.49 (1.09-2.00)	22	1.71 (1.18-2.47)	0.003
Use of sprays†								
Never	2,469	34	1	49	1	17	1	
<1 day/week	832	28	1	52	1.26 (1.05-1.51)	20	1.37 (1.08-1.73)	0.005
1-3 days/week	484	28	1	50	1.25 (0.99-1.57)	22	1.57 (1.18-2.08)	0.002
4-7 days/week	282	29	1	47	1.12 (0.84-1.49)	23	1.59 (1.13-2.25)	0.01

* Adjusted for age, smoking status, body mass index, race and ethnicity. OR – odds ratio; CI – confidence interval; NHS II: Nurses' Health Study II. †Use of spray for patient care, instrument cleaning or disinfection, surface cleaning or disinfection, air-refreshing or other.

Table E3. Associations between self-reported use of disinfectants in 2013 NHSII main questionnaire and asthma control in 2014 asthma supplemental questionnaire (n=3,913)

	Asthma Control Test score									P trend
	25		20-24		16-19		≤15			
	n	%	OR*	%	OR* (95% CI)	%	OR* (95% CI)	%	OR* (95% CI)	
Weekly use of disinfectant										
To clean surfaces										
No	2,212	34	1	49	1	11	1	6	1	
Yes	1,638	30	1	50	1.16 (1.00-1.34)	13	1.18 (0.94-1.47)	7	1.30 (0.98-1.71)	0.02
To clean instruments										
No	3,186	33	1	50	1	11	1	6	1	
Yes	665	29	1	49	1.07 (0.88-1.31)	14	1.37 (1.04-1.82)	8	1.52 (1.08-2.13)	0.006
Surface and/or instruments										
None	2,108	34	1	49	1	11	1	6	1	
Surface only	1,072	31	1	52	1.17 (0.99-1.39)	11	1.02 (0.78-1.32)	6	1.15 (0.83-1.60)	0.31
Instruments	665	29	1	49	1.14 (0.93-1.39)	14	1.39 (1.04-1.85)	8	1.60 (1.11-2.29)	0.003
Weekly use of sprays										
Any spray										
No	3,177	33	1	49	1	12	1	6	1	
Yes	664	29	1	51	1.12 (0.93-1.36)	12	1.08 (0.81-1.44)	8	1.27 (0.89-1.81)	0.21
Sprays for disinfection	498	29	1	50	1.13 (0.90-1.41)	13	1.14 (0.83-1.59)	8	1.49 (1.02-2.18)	0.08
Sprays for instrument disinfection	154	29	1	48	1.05 (0.72-1.54)	16	1.48 (0.89-2.45)	7	1.23 (0.62-2.43)	0.22

* Adjusted for age, smoking status, body mass index, race and ethnicity. OR – odds ratio; CI – confidence interval; NHS II: Nurses’ Health Study II.

Table E4. Associations between self-reported cleaning/disinfection tasks and asthma control, using a more stringent asthma definition‡ (n=2,946)

	Asthma Control Test score									P trend
	25 (ref.)		20-24		16-19		≤15			
	n	%	OR*	%	OR* (95% CI)	%	OR* (95% CI)	%	OR* (95% CI)	
Weekly use of disinfectant										
To clean surfaces										
No (ref.)	1,585	28	1	50	1	14	1	8	1	
Yes	1,339	26	1	52	1.12 (0.94-1.34)	13	1.01 (0.79-1.29)	9	1.28 (0.96-1.72)	0.24
To clean instruments										
No (ref.)	2,377	28	1	51	1	14	1	7	1	
Yes	543	23	1	21	1.18 (0.94-1.50)	15	1.30 (0.95-1.77)	11	1.84 (1.29-2.60)	0.002
Surface and/or instruments										
None (ref.)	1,510	29	1	50	1	14	1	7	1	
Surface only	872	27	1	53	1.13 (0.92-1.37)	13	0.91 (0.68-1.20)	8	1.05 (0.74-1.49)	0.97
Instruments	543	23	1	51	1.25 (0.98-1.59)	15	1.25 (0.90-1.74)	12	1.87 (1.29-2.71)	0.003
Weekly use of sprays†										
No (ref.)	2,379	28	1	51	1	13	1	8	1	
Yes	541	23	1	50	1.15 (0.91-1.46)	16	1.42 (1.04-1.93)	10	1.43 (0.99-2.05)	0.01

* OR from multinomial logistic regressions, adjusted for age, smoking status, body mass index, race and ethnicity. †Use of spray for patient care, instrument cleaning or disinfection, surface cleaning or disinfection, air-refreshing or other. All exposure variables had <1% missing values. OR – odds ratio; CI – confidence interval; JTEM – Job-Task-Exposure Matrix. ‡ In addition to asthma case definition used in main analyses, participants had to report use of a prescribed long-term preventive medication (ie, inhaled corticosteroids, cromolyn sodium, nedocromil, salmeterol, theophylline) in the past year.

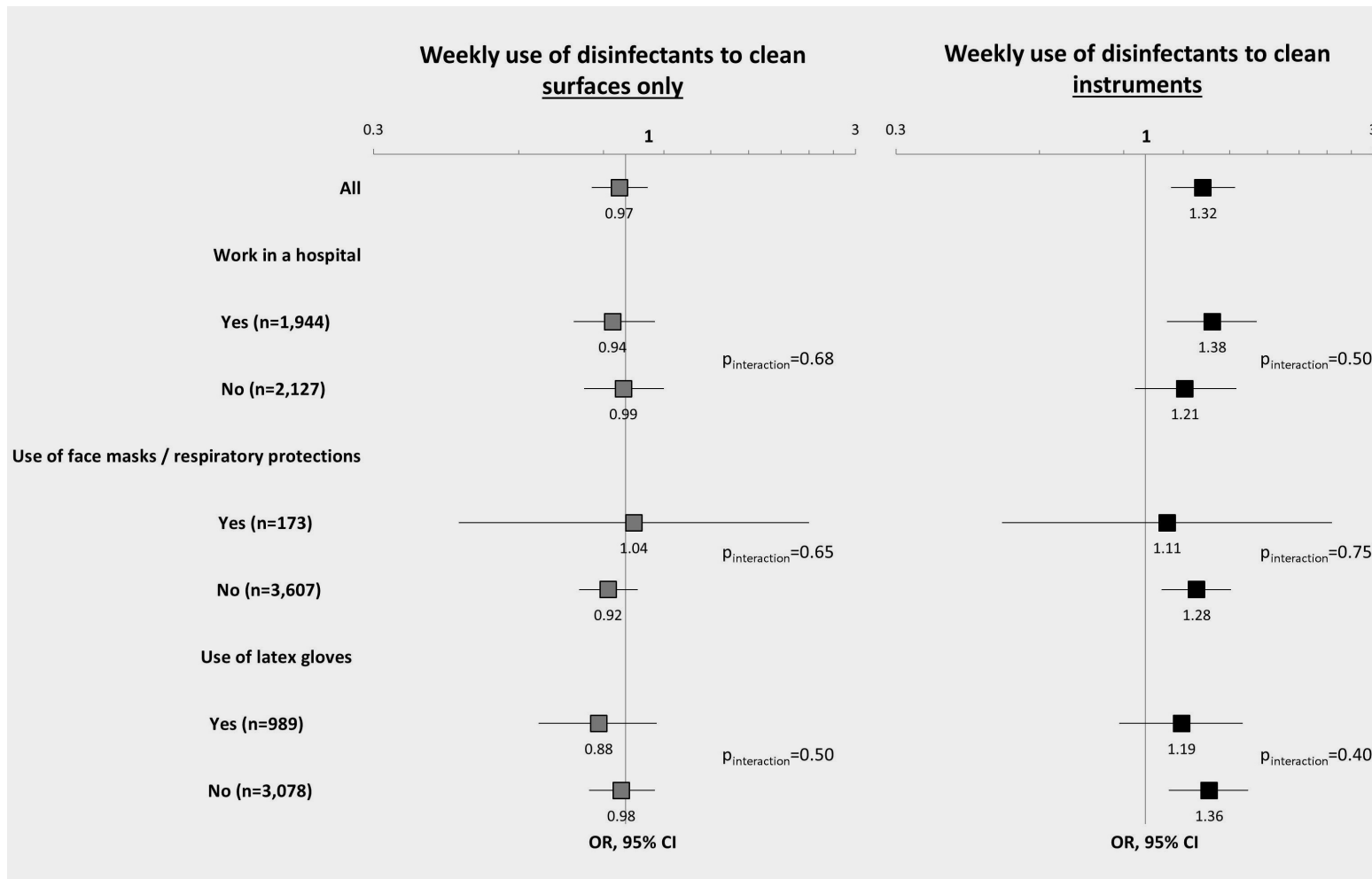


Figure E1. Associations between self-reported cleaning/disinfection tasks and asthma control, according to workplace characteristics (hospital vs. no), self-reported use of respiratory protections during work with disinfectants, and self-reported use of latex gloves. Results are presented as odds ratio (OR) and 95% confidence intervals (CI) for a decrease in Asthma Control Test score category (25: controlled; 20-24: partly controlled; 16-19: poorly controlled; ≤ 15 : very poorly controlled), analyzed as an ordinal variable (ordinal logistic regression), and adjusted for age, smoking status, body mass index, race and ethnicity.

Table E5. Associations between exposure to specific disinfectants evaluated by JTEM and asthma control categories

Specific products	Exposure level	n	Asthma Control Test score								P trend
			25		20-24		16-19		≤15		
			%	OR*	%	OR* (95% CI)	%	OR* (95% CI)	%	OR* (95% CI)	
Formaldehyde	Low	3,627	32	1	50	1	12	1	6	1	
	Medium	177	30	1	48	1.05 (0.74 - 1.49)	14	1.29 (0.78-2.11)	8	1.41 (0.77-2.60)	0.24
	High	268	27	1	50	1.23 (0.91 - 1.65)	15	1.56 (1.04-2.35)	8	1.55 (0.93-2.59)	0.02
Glutaraldehyde	Low	2,193	33	1	49	1	12	1	6	1	
	Medium	604	33	1	51	1.04 (0.85 - 1.27)	11	0.82 (0.59-1.12)	5	0.79 (0.51-1.22)	0.31
	High	1,275	30	1	50	1.14 (0.97 - 1.34)	12	1.09 (0.86-1.38)	8	1.54 (1.15-2.06)	0.02
Hypochlorite bleach	Low	1,884	33	1	49	1	12	1	6	1	
	Medium	981	31	1	52	1.15 (0.97 - 1.38)	11	0.95 (0.72-1.24)	6	1.09 (0.77-1.55)	0.61
	High	1,207	30	1	49	1.12 (0.95 - 1.32)	12	1.12 (0.88-1.44)	8	1.55 (1.14-2.10)	0.02
Hydrogen peroxide	Low	2,032	33	1	49	1	12	1	6	1	
	Medium	691	33	1	53	1.04 (0.86 - 1.27)	9	0.74 (0.54-1.02)	5	0.76 (0.50-1.15)	0.16
	High	1,349	30	1	49	1.08 (0.92 - 1.27)	13	1.16 (0.92-1.47)	8	1.55 (1.16-2.07)	0.01
Alcohol	Low	1,884	33	1	49	1	12	1	6	1	
	Medium	597	31	1	49	1.11 (0.89 - 1.37)	13	1.12 (0.82-1.53)	7	1.39 (0.94-2.05)	0.14
	High	1,591	31	1	51	1.14 (0.98 - 1.33)	11	1.02 (0.81-1.28)	7	1.32 (0.99-1.77)	0.12
Quats	Low	1,884	33	1	49	1	12	1	6	1	
	Medium	640	30	1	50	1.13 (0.92 - 1.40)	12	1.10 (0.81-1.50)	8	1.43 (0.97-2.08)	0.10
	High	1,548	30	1	51	1.13 (0.97 - 1.32)	12	1.02 (0.81-1.29)	7	1.31 (0.97-1.75)	0.14
Enzymatic cleaners	Low	3,271	32	1	50	1	12	1	6	1	
	Medium	230	31	1	45	0.92 (0.67 - 1.26)	15	1.39 (0.91-2.12)	8	1.43 (0.84-2.43)	0.14
	High	571	28	1	49	1.14 (0.92 - 1.40)	14	1.39 (1.03-1.88)	9	1.87 (1.32-2.66)	0.001

* Adjusted for age, smoking status, body mass index, race and ethnicity. OR – odds ratio; CI – confidence interval; JTEM – Job-Task-Exposure Matrix.

Table E6. Associations between self-reported use of specific disinfectants/cleaning products and asthma control (exposures not evaluated by JTEM)

Specific products	Frequency of use	n	Asthma Control Test score						
			25 (ref.)	20-24		≤19		P trend	
			%	OR*	%	OR* (95% CI)	%		OR* (95% CI)
Ortho-phtalaldehyde	<1 day/week (ref.)	3,652	31	1	50	1	19	1	-
	1-3 days/week	129	32	1	50	0.86 (0.57-1.30)	18	0.75 (0.44-1.28)	0.32
	4-7 days/week	49	16	1	61	2.41 (1.04-5.59)	23	2.00 (0.76-5.27)	0.19
“Green” products	<1 day/week (ref.)	3,596	32	1	49	1	19	1	
	1-3 days/week	145	28	1	51	1.10 (0.74-1.63)	21	1.17 (0.72-1.91)	0.51
	4-7 days/week	60	20	1	53	1.76 (0.90-3.45)	27	2.28 (1.06-4.92)	0.03
Peracetic acid	<1 day/week (ref.)	3,801	32	1	50	1	18	1	-
	≥1 day/week	35	31	1	46	0.89 (0.41-1.95)	23	1.07 (0.42-2.71)	0.90
Acetic acid	<1 day/week (ref.)	3,762	32	1	50	1	18	1	
	≥1 day/week	101	25	1	48	1.14 (0.70-1.85)	27	1.46 (0.83-2.58)	0.18
Ammonia	<1 day/week (ref.)	3,820	31	1	50	1	19	1	
	≥1 day/week	48	17	1	54	2.11 (0.95-4.69)	29	2.81 (1.15-6.89)	0.02
Phenolics	<1 day/week (ref.)	3,784	32	1	50	1	18	1	
	≥1 day/week	73	26	1	51	1.17 (0.66-2.06)	23	1.42 (0.72-2.78)	0.30
Ethylene oxide†	<1 day/week (ref.)	3,890	-	-	-	-	-	-	-
	≥1 day/week	24	-	-	-	-	-	-	-
Chloramine T†	<1 day/week (ref.)	3,865	-	-	-	-	-	-	-
	≥1 day/week	7	-	-	-	-	-	-	-

*OR from multinomial logistic regression, adjusted for age, smoking status, body mass index, race, ethnicity, and exposure to other disinfectants evaluated by JTEM (combination presented in Table 4). Exposures were studied as 3-category variables (<1, 1-3, 4-7 days/week) when there was at least 30 participants in each category, and as 2-category variables (<1 vs ≥ 1 day/week) otherwise. Asthma control was studied as a 3-category variable (25: controlled; 20-24: partly controlled; ≤19: poorly to very poorly controlled). †Analyses were not performed for ethylene oxide and chloramine T as less than 30 participants reported using these products weekly. OR – odds ratio; CI – confidence interval; JTEM – Job-Task-Exposure Matrix.