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OEM Online First, published on February 23, 2018 as 10.1136/oemed-2017-104740

SHORT REPORT

Association of hand and arm disinfection with asthma control in US nurses

Orianne Dumas,[1,2] Raphäelle Varraso,[1,2] Krislyn M Boggs,[3] Alexis Descatha,[1,2,4] Paul K Henneberger,[5] Catherine Quinot,[1,2] Frank E Speizer,[3] Jan-Paul Zock,[6,7,8] Nicole Le Moual,[1,2] Carlos A Camargo Jr[3,9]

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/oemed-2017-104740).

For numbered affiliations see end of article.

Correspondence to
Dr Orianne Dumas, INSERM, U1168, VIMA: Aging and chronic diseases, Epidemiological and public health approaches, Villejuif 94807, France; orianne.dumas@inserm.fr

Received 28 August 2017
Revised 23 January 2018
Accepted 4 February 2018

ABSTRACT

Objectives To investigate the association between occupational exposure to disinfectants/antiseptics used for hand hygiene and asthma control in nurses.

Methods In 2014, we invited female nurses with asthma drawn from the Nurses' Health Study II to complete two supplemental questionnaires on their occupation and asthma (cross-sectional study, response rate: 80%). Among 4055 nurses (mean age: 59 years) with physician-diagnosed asthma and asthma medication use in the past year, we examined asthma control, as defined by the Asthma Control Test (ACT). Nurses were asked about the daily frequency of hand hygiene tasks: 'wash/scrub hands with disinfectants/hand sanitizers' (hand hygiene) and 'wash/scrub arms with disinfecting products' (surrogate of surgical hand/arm antisepsis). Analyses were adjusted for age, race, ethnicity, smoking status and body mass index.

Results Nurses with partly controlled asthma (ACT: 20–24, 50%) and poorly controlled asthma (ACT ≤19, 18%) were compared with nurses with controlled asthma (ACT=25, 32%). In separate models, both hand and arm hygiene were associated with poorly controlled asthma. After mutual adjustment, only arm hygiene was associated with poorly controlled asthma: OR (95% CI) for <1 time/day, 1.38 (1.06 to 1.80); ≥1 time/day, 1.96 (1.52 to 2.51), versus never. We observed a consistent dose–response relationship between frequency of arm hygiene tasks (never to >10 times/day) and poor asthma control. Associations persisted after further adjustment for surfaces/instruments disinfection tasks.

Conclusions Frequency of hand/arm hygiene tasks in nurses was associated with poor asthma control. The results suggest an adverse effect of products used for surgical hand/arm antisepsis. This potential new occupational risk factor for asthma warrants further study.

Key messages

What is already known about this subject?

- Healthcare workers have an increased risk of asthma, partly attributed to agents used for cleaning/disinfection of surfaces and medical instruments.
- However, little is known regarding the potential respiratory risks associated with disinfectants/antiseptics used for hand hygiene.

What are the new findings?

- In a cross-sectional study of more than 4000 US nurses with asthma, we found that frequency of hand and arm hygiene tasks was associated with poor asthma control.
- The results suggest an adverse effect of products used for surgical hand/arm antisepsis.

How might this impact on policy or clinical practice in the foreseeable future?

- If our findings are confirmed, some hand/arm hygiene tasks and the identified hygiene products would need to be added to current strategies of occupational illness prevention among healthcare workers.

INTRODUCTION

Healthcare workers have an increased risk of asthma, partly attributed to exposure to cleaning products and disinfectants.[1 2] Exposure to several agents used for cleaning/disinfection of surfaces and medical instruments (eg, bleach, hydrogen peroxide, aldehydes and quaternary ammonium compounds) has been associated with increased risk of asthma and poor asthma control.[1–3]

Hand hygiene practices in healthcare workers also involve chemical exposures. In hospitals, employees wash their hands 5–30 times per shift.[4] Products used for hand hygiene in US healthcare are most often alcohol-based solutions.[4 5] For surgical personnel, hand antisepsis further involves washing/scrubbing their hands and forearms with water-based or alcohol-based preparations generally containing chlorhexidine or povidone iodine.[4 6 7]

The irritant and allergenic properties of antiseptic agents have been well examined in relation to skin disorders.[6] In contrast, little is known regarding the potential respiratory risks associated with hand hygiene practices among healthcare workers. To address this question, we aimed to study the association between occupational exposures related to hand hygiene practices and asthma control in a large cohort of US female nurses.

METHODS

The Nurses' Health Study II (NHSII) began in 1989 with the inclusion of 116 430 female registered nurses from 15 US states, aged 25–44 years. Follow-up questionnaires have been sent every 2 years since. In 2014–2015, all nurses who ever reported physician-diagnosed asthma in biennial

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To cite: Dumas O, Varraso R, Boggs KM, *et al*. *Occup Environ Med* Epub ahead of print: [please include Day Month Year]. doi:10.1136/oemed-2017-104740

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questionnaires (1991–2015) and who recently returned a biennial questionnaire (2013 or 2015) were invited to complete two questionnaires, on their current occupation and on asthma (response rate: 80%). Details of data collection have been published elsewhere.[3] .

Based on the asthma questionnaire, we selected participants who reiterated that a physician had diagnosed her as having asthma, and who reported use of asthma medication in the past year (asthma case definition). Asthma control was defined by the Asthma Control Test (ACT), based on activity limitations, frequency of symptoms and frequency of use of quick-relief medication in the past 4 weeks.[8]

In the occupational questionnaire, nurses were 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' (later referred to as 'hand hygiene'), to evaluate frequency of hand hygiene tasks; and 'wash/scrub your arms with disinfecting products' (later referred to as 'arm hygiene'), a surrogate to evaluate frequency of surgical hand/arm antisepsis.[4] Exposure to other disinfectants, that is, used to clean surfaces/instruments, was evaluated by questionnaire and by a job-task-exposure matrix (JTEM).[9]

Associations between the frequency of hand and arm hygiene and asthma control were evaluated by multinomial logistic regressions adjusted for age, race, ethnicity, smoking status and body mass index (BMI). Observations with missing values for covariates (all <1%) were excluded from multivariable analyses. Separate models were first used for each of the exposures of interest (hand/arm hygiene); then the two variables were entered in the same model for mutual adjustment. Additional models were further adjusted for exposure to disinfectants to clean surfaces/instruments. A two-sided $P<0.05$ was considered statistically significant. Analyses were run using SAS V.9 (SAS Institute, Cary, North Carolina, USA).

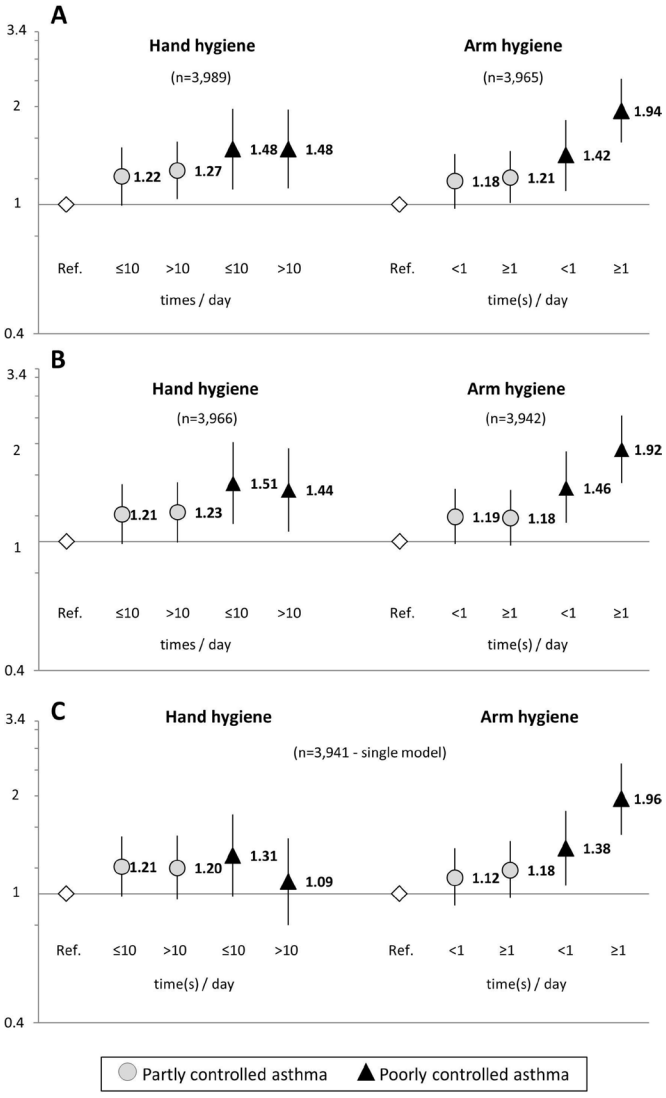


Figure 1 Associations of hand and arm hygiene with asthma control: (A) separate models for hand and arm hygiene; (B) separate models for hand and arm hygiene, with adjustment for self-reported weekly use of disinfectants to clean surfaces/instruments (no, surfaces only, instruments) and (C) hand and arm hygiene entered in the same model for mutual adjustment. Multinomial logistic regressions, adjusted for age, smoking status in 2013, body mass index in 2013, race and ethnicity. The results are presented as OR and 95% CIs (lines). Reference category was 'never' for hand/arm hygiene and 'controlled asthma' for asthma control.

RESULTS

Among 4237 nurses who returned both questionnaires on asthma and occupation, and who met our asthma case definition, participants with missing data for ACT (n=135) or for hand and arm hygiene tasks (n=47) were excluded. This yielded an analytic sample of 4055 women. Participants were on average 59 years of age, 94% were white, 2% were Hispanic, 42% were obese (BMI ≥30 kg/m^2), 4% were current smokers and 29% were ex-smokers.

Reported frequency of hand hygiene tasks (never, 15%; <1 time/day, 4%; 1–3 times/day, 11%; 4–10 times/day, 24% and >10 times/day, 46%—n=4031) was higher than frequency of arm hygiene (never, 62%; <1 time/day, 17%; 1–3 times/day, 12%; 4–10 times/day, 5% and >10 times/day, 4%—n=4006). Thus, different cut-offs were chosen to classify exposure variables into three categories for hand hygiene (never, 15%; ≤10 times/day, 39% and >10 times/day, 46%) and arm hygiene (never, 62%; <1 time/day, 17% and ≥1 time/day, 21%). Among nurses who reported arm hygiene tasks ≥1 time/day, 78% reported hand hygiene tasks >10 times/day; among those who reported hand hygiene >10 times/day, 35% reported arm hygiene ≥1 time/day (online supplementary table E1).

In main analyses, nurses with partly controlled asthma (ACT 20–24, 50%) and poorly controlled asthma (ACT ≤19, 18%) were compared with nurses with controlled asthma (ACT=25, 32%). When using separate models for the two exposure variables, both hand hygiene (>10 times/day *vs* never) and arm hygiene (≥1 time/day *vs* never) were associated with partly and poorly controlled asthma (figure 1A). The results were consistent when examining more detailed categories of asthma control (online supplementary table E2). Moreover, similar associations persisted after further adjustment for other disinfection tasks: self-reported use of disinfectants to clean surfaces or medical instruments (figure 1B; and online supplementary table E3) or exposure to specific disinfectants evaluated by a JTEM (online supplementary table E4).

However, after mutual adjustment (figure 1C), only arm hygiene was associated with poorly controlled asthma: OR (95% CI) for <1 time/day versus never, 1.38 (1.06 to 1.80); and for ≥1 time/day versus never, 1.96 (1.52 to 2.51). Furthermore, among nurses who reported never doing arm hygiene

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tasks (n=2443), no association was observed between hand hygiene and poor asthma control (>10 times/day versus never, 1.10 (0.79 to 1.53)). In contrast, among nurses who reported infrequent hand hygiene (never or ≤10 times/day, n=2119), arm hygiene was associated with poorly controlled asthma (≥1 time/day versus never, 2.59 (1.65 to 4.07)). Finally, when examining exposure frequency using more detailed categories (online supplementary figure E1), we observed a consistent dose–response relationship between frequency of arm hygiene tasks (never to >10 times/day) and poor asthma control. This clear trend was not observed for hand hygiene.

The findings were confirmed for arm hygiene in sensitivity analyses using a more stringent asthma definition based on medication (online supplementary figure E2) and in models with further adjustment for nursing job types, household income or husband's education (not shown). Moreover, the associations between hand and arm hygiene and poor asthma control were similar in participants with or without allergy (defined by report of ever having had hay fever, seasonal allergy or allergic rhinitis; $p_{interaction}$ for hand hygiene: 0.32; for arm hygiene: 0.29).

DISCUSSION

In a study of 4055 nurses with asthma, increased frequency of hand/arm hygiene tasks was associated with poor asthma control. The strongest evidence was found for an association between arm hygiene, a surrogate of surgical hand/arm antisepsis, and poor asthma control. This association remained statistically significant after adjustment for other disinfectant exposures and general hand hygiene tasks. It was further supported by a clear dose–response relationship across categories of arm hygiene tasks frequency.

To our knowledge, we are the first to report an association between hand hygiene tasks and adverse respiratory outcomes in healthcare workers. We used a validated asthma definition in this large population of nurses,[10] and a standardised, validated and commonly used measure of asthma control (ACT) which integrates several domains of the disease (symptoms, use of rescue therapy, sleep disorders and activity limitations).[8] The main exposures of interest were evaluated by questionnaire. To reduce potential misclassification bias, we asked about frequency of hand hygiene tasks rather than use of specific agents (eg, chlorhexidine), which may not be known by the nurses. Nonetheless, our results may be subject to differential misclassification bias (ie, differential recall of exposure according to asthma control[11]). Although such bias cannot be completely ruled out, it would probably affect both exposures of interest similarly and lead to spurious associations for both hand and arm hygiene; however, after mutual adjustment, only frequency of arm hygiene was associated with poor asthma control. This pattern of associations is consistent with the hypothesis of an effect of agents specifically used for surgical hand/arm antisepsis, rather than regular hand hygiene products (alcohols). Latex exposure may be a cause of occupational asthma in healthcare workers. However, preventive efforts in the past decade, such as reduction in the use of powdered latex gloves, have led to a reduction of occupational asthma cases due to latex.[12] As reported earlier,[3] the use of latex gloves was not associated with poor asthma control in NHSII nurses and is unlikely a confounder in the current study.

Limitations of the current study include its cross-sectional design and the absence of information regarding the specific agents used for hand/arm hygiene tasks or test for sensitisation to workplace agents. We are thus limited in drawing conclusions regarding potential agent(s) responsible for the observed association. However, chlorhexidine and povidone iodine are currently the agents the most commonly used for surgical hand/arm antisepsis.[7] Moreover, in a survey of a sample of the hospitals where NHSII nurses work, a chlorhexidine solution was used for surgical hand/arm antisepsis in seven out of eight hospitals surveyed.[13] Chlorhexidine is a skin sensitiser[6] and cases of occupational asthma or occupational airway allergy due to chlorhexidine have been reported in nurses.[14] Povidone iodine also has been involved in skin allergies, although such cases are thought to be rare.[6] Beside allergenic potential, chlorhexidine and povidone iodine have well-documented skin irritation properties[6] and may also cause airway irritation.[15] Thus, mechanisms for a potential impact of antiseptic agents on respiratory health may include both sensitisation and irritation, either through the dermal or inhalation route of exposure.[16]

In conclusion, increased frequency of hand and arm hygiene tasks in nurses was associated with poor asthma control. The results suggest a role of products used for surgical hand/arm antisepsis, but not of common hand hygiene tasks. The potential respiratory risks of products used for hand hygiene merit further investigation, to confirm our results and to clarify the putative agents and mechanisms. If our findings are confirmed, hand hygiene tasks (and the identified hygiene products) would need to be added to current strategies of occupational illness prevention among healthcare workers, which may require the development of new approaches to maintain infection control standards in healthcare settings.[17]

Author affiliations
[1]INSERM, U1168, VIMA: Aging and chronic diseases, Epidemiological and public health approaches, F-94807, Villejuif, France
[2]Univ Versailles Saint-Quentin-en-Yvelines, UMR-S 1168, F-78180, Montigny le Bretonneux, France
[3]Channing Division of Network Medicine, Department of Medicine, Brigham & Women's Hospital and Harvard Medical School, Boston, Massachusetts, USA
[4]AP-HP UVSQ, Occupational Health Unit/Population-Based Epidemiological Cohorts Unit, UMS 011, University Hospital of Poincaré, Garches, France
[5]Respiratory Health Division, National Institute for Occupational Safety and Health, Morgantown, West Virginia, USA
[6]ISGlobal, Centre for Research in Environmental Epidemiology, Barcelona, Spain
[7]Universitat Pompeu Fabra (UPF), Barcelona, Spain
[8]CIBER Epidemiología y Salud Pública (CIBERESP), Madrid, Spain
[9]Department of Emergency Medicine, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, USA

Acknowledgements The Nurses' Health Study II (NHSII) is coordinated at the Channing Division of Network Medicine, Brigham and Women's Hospital, Boston, Massachusetts, USA. We would like to thank the participants and staff of the NHSII for their valuable contributions. In particular, we would like to thank Aleta Wiley, Lisa Abramovitz, Charlotte Marsh, Chidiogo Onwuakor and Christina Staffiere for their help with data cleaning and management. We also thank Francine Kauffmann for her participation in the study conception. ISGlobal is a member of the CERCA Programme, Generalitat de Catalunya.

Contributors OD contributed to the study conception, the acquisition, analysis and interpretation of the data and primary manuscript preparation. RV, AD, PKH, CQ and J-PZ were involved in the data interpretation and critical revision of the manuscript. KMB and FES contributed to the acquisition and interpretation of the data and critical revision of the manuscript. NLM contributed to the study conception, data interpretation and critical revision of the manuscript. CAC participated in the study conception, acquisition of the data, data interpretation and critical revision of the manuscript. All authors approved the final version of the manuscript and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding Centers for Disease Control and Prevention R01 OH-10359; National Institutes of Health UM1 CA176726. The research leading to these results has received funding from the People Program (Marie Curie Actions) of the European Union's Seventh Framework Program (FP7/2007-2013) under REA grant agreement n. PCOFUND-GA-2013-609102, through the PRESTIGE programme coordinated by Campus France.

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Disclaimer The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health.

Competing interests None declared.

Patient consent Obtained.

Ethics approval This investigation was approved by the institutional review board at the Brigham and Women's Hospital (Boston, Massachusetts, USA)

Provenance and peer review Not commissioned; externally peer reviewed.

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Occup Environ Med published online February 23, 2018

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Online supplement

Association of hand and arm disinfection with asthma control in U.S. nurses

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Table E1. Characteristics of the participants according to frequency of hand and arm hygiene tasks

	Hand hygiene (n=4,031)			Arm hygiene (n=4,006)		
	Never	≤10 times/day	>10 times/day	Never	<1 time/day	≥1 times/day
%	15	39	46	62	17	21
Age, m (sd)	59.0 (4.5)	59.0 (4.3)	58.3 (4.2)	58.8 (4.4)	58.4 (4.2)	58.4 (4.3)
Race (non white), %	5	5	7	5	6	6
Ethnicity (Hispanic), %	3	2	2	2	2	2
Smoking status, %						
Never smoker	68	67	67	68	68	64
Ex-smoker	29	30	29	29	28	31
Current smoker	3	3	4	3	4	5
BMI, %						
<25 kg/m2	31	28	28	29	30	23
25-29.9 kg/m2	28	31	29	30	30	29
≥ 30 kg/m2	41	41	43	41	40	48
Hand hygiene, %						
Never	-	-	-	24	1	0
≤10 times/day	-	-	-	45	38	22
>10 times/day	-	-	-	31	61	78
Arm hygiene, %						
Never	98	71	42	-	-	-
<1 time/day	1	17	23	-	-	-
≥1 times/day	0	12	35	-	-	-
Surface and/or instruments disinfection*, %						
None	74	64	32	60	44	27
Surface only	17	26	39	27	37	36
Instruments	9	10	29	13	19	37
Job type†, %						
ER	1	1	4	2	3	5
OR	1	4	7	2	6	12
ICU	0	1	9	2	4	12
Other inpatient nurse	4	7	21	10	17	21
Nursing in education or administration	27	26	10	22	16	9
Outpatient or community	30	28	27	31	28	19
Other hospital nursing	6	10	11	10	10	10
Nursing outside hospital	29	22	11	21	17	12

BMI – Body Mass Index; ER - emergency room; ICU - intensive care unit; OR - operating room. * Self-reported weekly use of disinfectants to clean surfaces/instruments. † Evaluated by questionnaire ("Which best describes your current employment status?")

Table E2. Associations of hand and arm hygiene with asthma control, using more detailed categories of asthma control

	Partly controlled asthma (ACT=20-24)	Poorly controlled asthma (ACT=16-19)	Very poorly controlled asthma (ACT≤15)	p_{trend}
	OR (95% CI)	OR (95% CI)	OR (95% CI)	
Hand hygiene (n=3,989)				
Never	1	1	1	
≤10 times/day	1.22 (0.99-1.50)	1.32 (0.96-1.82)	1.96 (1.21-3.18)	0.005
>10 times/day	1.27 (1.04-1.56)	1.22 (0.89-1.67)	2.28 (1.42-3.66)	0.002
Arm hygiene (n=3,965)				
Never	1	1	1	
<1 time/day	1.18 (0.97-1.43)	1.37 (1.03-1.82)	1.52 (1.05-2.21)	0.007
≥1 times/day	1.21 (1.01-1.46)	1.69 (1.30-2.19)	2.47 (1.80-3.37)	<0.001

ACT, Asthma Control Test score. * Reference category: Controlled asthma (Asthma Control Test score = 25). All models were adjusted for age, smoking status in 2013, body mass index in 2013, race and ethnicity. Separate models were used for hand and arm hygiene. Observations with missing values for covariates (smoking status, body mass index, exposure to surface/instrument disinfectants: all <1%) were excluded from multivariable analyses.

Table E3. Associations of hand and arm hygiene with asthma control, with further adjustment for self-reported use of surface and/or instrument disinfectants

	Partly controlled asthma (ACT=20-24)	Poorly controlled asthma (ACT=16-19)	Very poorly controlled asthma (ACT≤15)	p_{trend}
	OR (95% CI)	OR (95% CI)	OR (95% CI)	
Model 1†, n=3,966				
Hand hygiene				
Never	1	1	1	
≤10 times/day	1.21 (0.98-1.50)	1.37 (0.99-1.89)	1.93 (1.19-3.14)	0.004
>10 times/day	1.23 (0.99-1.53)	1.22 (0.87-1.71)	2.06 (1.27-3.37)	0.01
Surface and/or instruments				
None	1	1	1	
Surface only	1.02 (0.86-1.21)	0.83 (0.64-1.08)	0.92 (0.66-1.29)	0.38
Instruments	1.13 (0.92-1.39)	1.26 (0.94-1.70)	1.63 (1.14-2.35)	0.01
Model 2‡, n=3,942				
Arm hygiene				
Never	1	1	1	
<1 time/day	1.19 (0.98-1.45)	1.43 (1.07-1.92)	1.54 (1.05-2.24)	0.004
≥1 times/day	1.18 (0.97-1.44)	1.72 (1.31-2.27)	2.31 (1.66-3.21)	<0.001
Surface and/or instruments				
None	1	1	1	
Surface only	1.01 (0.86-1.19)	0.77 (0.60-0.99)	0.88 (0.63-1.22)	0.17
Instruments	1.12 (0.91-1.34)	1.08 (0.81-1.45)	1.41 (0.99-2.02)	0.09

ACT, Asthma Control Test score. * Reference category: Controlled asthma (Asthma Control Test score = 25). All models were adjusted for age, smoking status in 2013, body mass index in 2013, race and ethnicity. †Model 1 including hand hygiene and self-reported weekly use of disinfectants to clean surfaces/instruments. ‡Model 2 including arm hygiene and self-reported weekly use of disinfectants to clean surfaces/instruments. Observations with missing values for covariates (smoking status, body mass index, exposure to surface/instrument disinfectants: all <1%) were excluded from multivariable analyses.

Table E4. Associations of hand and arm hygiene with asthma control, with further adjustment for exposure to specific products evaluated by a job-task-exposure matrix

	Partly controlled asthma (ACT=20-24)	Poorly controlled asthma (ACT=16-19)	Very poorly controlled asthma (ACT≤15)	p_{trend}
	OR (95% CI)	OR (95% CI)	OR (95% CI)	
Model 1†, n=3,966				
Hand hygiene				
Never	1	1	1	
≤10 times/day	1.22 (0.99-1.51)	1.35 (0.98-1.87)	1.89 (1.17-3.07)	0.004
>10 times/day	1.26 (1.01-1.55)	1.19 (0.86-1.65)	1.97 (1.21-3.20)	0.01
JTEM exposure combinations				
No high level exposure	1	1	1	
1): high exposure level to bleach or hydrogen peroxide	0.87 (0.70-1.08)	0.91 (0.65-1.26)	1.08 (0.71-1.65)	0.62
2): high exposure level to formaldehyde or glutaraldehyde	0.96 (0.75-1.22)	0.90 (0.62-1.31)	0.99 (0.61-1.62)	0.67
3): 1) + 2)	1.09 (0.82-1.45)	1.14 (0.75-1.74)	1.63 (1.01-2.64)	0.11
4): 1) + 2) + high exposure level to enzymatic cleaners§	1.07 (0.86-1.34)	1.32 (0.96-1.82)	1.78 (1.21-2.62)	0.01
Model 2‡, n=3,942				
Arm hygiene				
Never	1	1	1	
<1 time/day	1.20 (0.99-1.46)	1.41 (1.06-1.89)	1.50 (1.03-1.46)	0.005
≥1 times/day	1.20 (0.98-1.46)	1.69 (1.28-2.23)	2.23 (1.60-3.11)	<0.001
JTEM exposure combinations				
No high level exposure	1	1	1	
1): high exposure level to bleach or hydrogen peroxide	0.85 (0.69-1.06)	0.86 (0.62-1.19)	1.04 (0.68-1.57)	0.43
2): high exposure level to formaldehyde or glutaraldehyde	0.96 (0.75-1.22)	0.85 (0.58-1.23)	0.97 (0.60-1.58)	0.53
3): 1) + 2)	1.06 (0.80-1.40)	0.95 (0.62-1.42)	1.29 (0.80-2.09)	0.56
4): 1) + 2) + high exposure level to enzymatic cleaners§	1.06 (0.85-1.33)	1.16 (0.84-1.60)	1.57 (1.07-2.31)	0.07

ACT, Asthma Control Test score; JTEM, job-task-exposure matrix. * Reference category: Controlled asthma (Asthma Control Test score = 25). All models were adjusted for age, smoking status in 2013, body mass index in 2013, race and ethnicity. †Model 1 including hand hygiene and exposure to combinations of specific disinfectants/cleaning products evaluated by the JTEM. ‡Model 2 including arm hygiene and exposure to combinations of specific disinfectants/cleaning products evaluated by the JTEM. Observations with missing values for covariates (smoking status, body mass index, exposure to surface/instrument disinfectants: all <1%) were excluded from multivariable analyses.

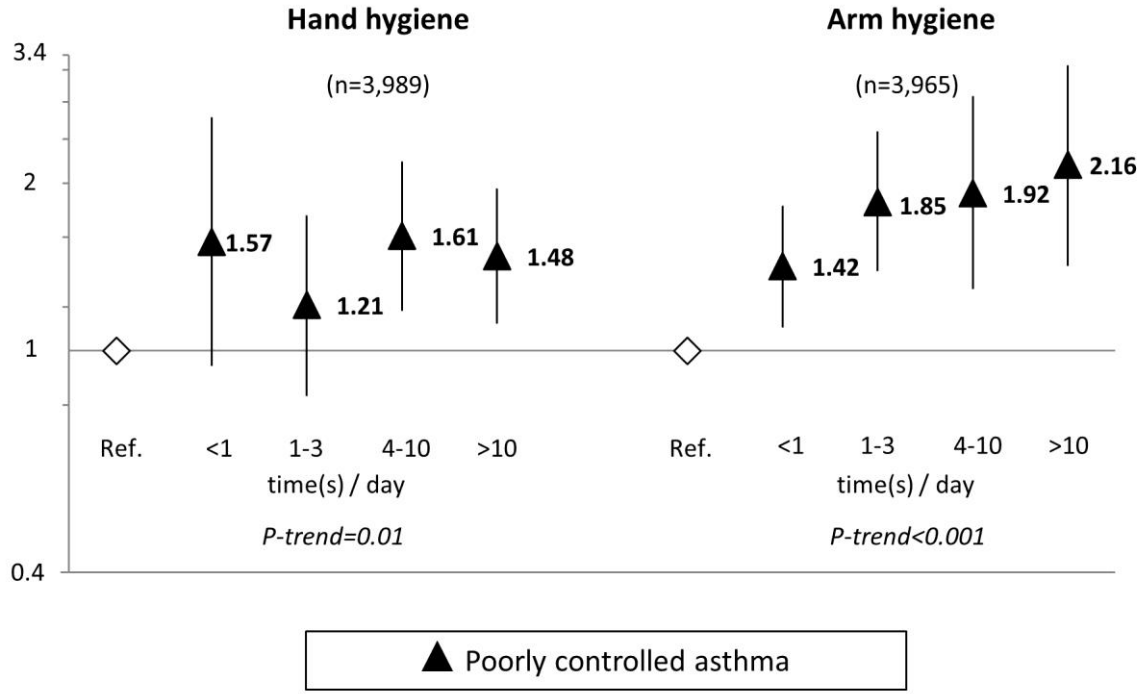


Figure E1. Associations of hand and arm hygiene with poor asthma control (*vs.* controlled) using detailed categories of hand and arm hygiene tasks frequency to examine dose-response relationships.
Multinomial logistic regressions, adjusted for age, smoking status in 2013, body mass index in 2013, race and ethnicity. Reference category for hand and arm hygiene: "never".

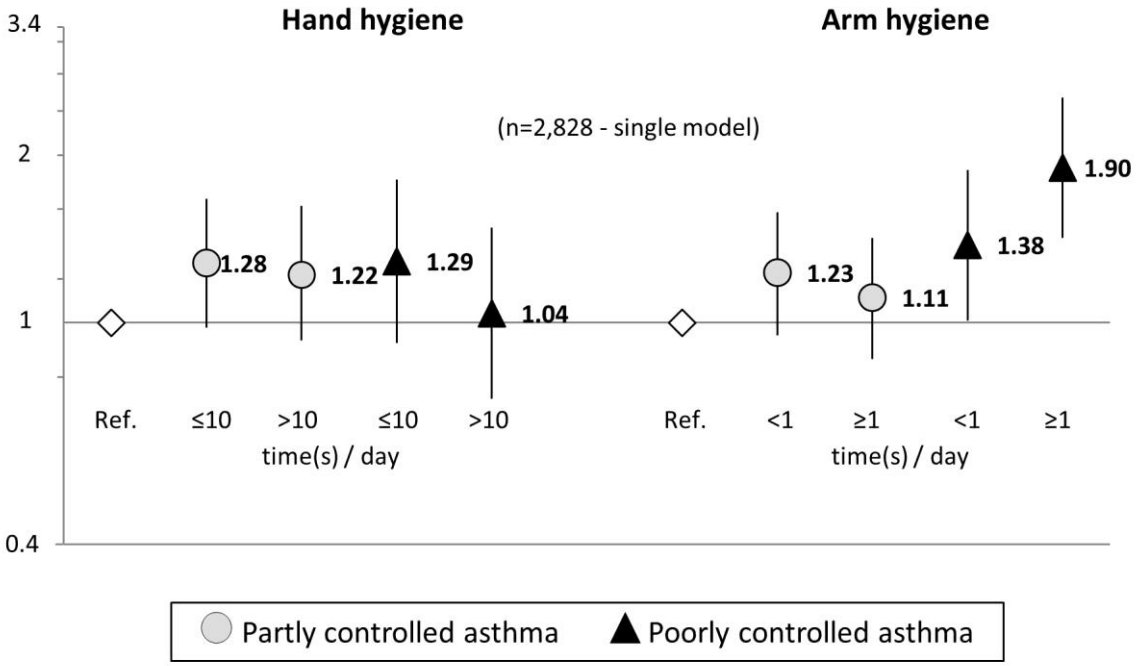


Figure E2. Associations of hand and arm hygiene with asthma control using a more stringent asthma definition.
Asthma definition: in addition to asthma case definition used in main analyses, participants had to report use of a prescribed long-term preventive medication (ie, inhaled corticosteroids, cromolyn sodium, nedocromil, salmeterol, theophylline) in the past year. Hand and arm hygiene were entered in the same model for mutual adjustment. Multinomial logistic regressions, adjusted for age, smoking status in 2013, body mass index in 2013, race and ethnicity. Reference category was "never" for hand/arm hygiene and "controlled asthma" for asthma control.