Original research

Occupational risk factors and exposure–response relationships for airway disease among health workers exposed to cleaning agents in tertiary hospitals

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ABSTRACT

Objectives This study investigated occupational risk factors and exposure–response relationships for airway disease among health workers (HWs) exposed to cleaning agents in two tertiary hospitals in South Africa and Tanzania.

Methods In this cross-sectional study, 697 participants completed questionnaire interviews while 654 underwent fractional exhaled nitric oxide (FeNO) testing. Asthma Symptom Score (ASS) was computed based on the sum of answers to five questions on asthma-related symptoms in the past 12 months. For exposure–response analyses, cleaning agent-related self-reported exposure variables were categorised into three levels (cleaning product not used; use of a cleaning product for up to 99 min per week and use of a cleaning product for ≥100 min per week).

Results Asthma-related outcomes (ASS and FeNO) demonstrated positive associations with medical instrument cleaning agents (orthophthalaldehyde and enzymatic cleaners) and tasks (instruments precleaning and changing sterilisation solutions) as well as patient care activities (disinfection prior to procedures and disinfecting wounds). A particularly pronounced dose–response relationship was observed between work-related ocular-nasal symptoms and medical instrument cleaning agents (orthophthalaldehyde, glutaraldehyde, enzymatic cleaners, alcohols and bleach) (OR range: 2.37–4.56) and tasks (OR range: 2.92–4.44). A strong association was also observed between ASS and use of sprays for fixed surface cleaning (mean ratio 2.81; 95% CI 1.41 to 5.59).

Conclusions Specific agents for medical instrument disinfection for example, orthophthalaldehyde and enzymatic cleaners, patient care activities and use of sprays are important occupational risk factors for airway disease among HWs.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The association between asthma and exposure to cleaning agents in healthcare settings is well recognised. However, limited information exists regarding the exposure–response relationships between the frequency of exposure to specific cleaning agents and airway disease. This study investigated the association between exposure to specific cleaning agents, associated tasks and duration of use and their relationship with airway disease in health workers employed in tertiary hospitals.

WHAT THIS STUDY ADDS

⇒ Certain medical instrument cleaning agents (including orthophthalaldehyde and enzymatic cleaners), tasks (precleaning of medical instruments and changing sterilisation solutions), patient care activities (disinfection prior to procedures and cleaning/disinfecting wounds) and use of sprays for fixed surface cleaning were important occupational risk factors for airway disease in healthcare settings. In addition, a positive dose–response relationship was demonstrated between work-related ocular-nasal symptoms and medical instrument cleaning agents as well as tasks.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ There is a need to establish disinfectant chemical oversight committees in health facilities, which comprise occupational health, infection prevention and control personnel, as well procurement staff to better manage selection and use of cleaning agents in order to promote an integrated approach towards prevention of both work-related diseases and healthcare associated infections.

INTRODUCTION

Previous studies have demonstrated an association between asthma or respiratory symptoms and exposure to broad categories of cleaning-related exposures in healthcare settings.[1] However, few studies have identified the specific cleaning agents responsible for asthma and other health outcomes.[2–4] Products used for medical instrument cleaning and disinfection such as glutaraldehyde, orthophthalaldehyde (OPA) and quaternary ammonium compounds (QACs) have been implicated in the causation and exacerbation of work-related asthma (WRA) and upper airway outcomes such as rhinitis.[4–7] Arif and Delclos demonstrated exposure–response relationships for work-exacerbated asthma in health workers (HWs) that used disinfectants for medical instrument disinfection (glutaraldehyde/OPA, formalin/formaldehyde,

chloramines and ethylene oxide).[3] In recent years, there has been an increase in the use of enzymatic cleaners for precleaning of medical instruments prior to high-level disinfection.[8 9] Two studies reported cases of occupational asthma and rhinitis among HWs using enzymatic cleaners.[9 10] Other agents such as hydrogen peroxide and a mixture of hydrogen peroxide, peracetic acid and acetic used for high-level disinfection of medical instruments have also been linked to respiratory and ocular-nasal symptoms.[11 12]

Several studies have reported an association between asthma and fixed surface cleaning products such as ammonia and bleach.[1–4 7 13 14] A Spanish study of cleaning workers employed in various settings including hospitals, reported an increased risk of asthma symptoms in workers that used hydrochloric acid, degreasers, air fresheners or ammonia in the last year.[13] Dumas *et al*[4] also demonstrated an association between poor asthma control and exposure to hypochlorite bleach among nurses in the USA. Prior to this, a US study also demonstrated exposure–response relationships between WRA symptoms (WRAS) and use of cleaning agents for fixed surfaces cleaning/disinfection.[3] Other earlier studies demonstrated dose–response relationships between asthma and use of bleach in Spanish domestic cleaners as well as with frequency and types of cleaning sprays used.[15 16]

In order to adhere to strict infection prevention standards in healthcare settings, HWs frequently wash and sanitise their hands, using products such as alcohols, chlorhexidine and povidone iodine.[17–19] Chlorhexidine is well known for its sensitising and irritating properties to both airways and skin.[17–19] Previous studies have reported cases of occupational asthma and dermatitis due to chlorhexidine.[17–19] Alcohols are also potential respiratory and skin irritants. Povidone iodine is a well-known skin irritant but its sensitising properties have not been well characterised.[20] Aside from the type of products associated with adverse respiratory health effects, Dumas *et al* have also reported that poor asthma control was positively associated with increased frequency of hand hygiene practices among US nurses, with clear dose–response relationship demonstrated for surgical hand/arm hygiene.[19]

Patient care activities performed by nurses often include the use of adhesives and adhesive removers, particularly in surgical and intensive care units.[5 8] A US study[5] found an almost twofold increased odds of asthma in nursing professionals exposed to adhesives, adhesive removers and/or solvents.[5] Alcohols, chlorhexidine and povidone iodine commonly used for disinfection of wounds and patients' skin before various medical procedures are also known to have irritant or allergenic properties.[20]

There is limited information on the specific cleaning agents and tasks associated with airway disease in African settings. Furthermore, very limited information exists regarding exposure–response relationships between the frequency of exposure to specific cleaning agents (such as OPA) and airway disease. The aim of this study was to examine the association between exposure to specific cleaning agents, associated tasks as well as duration of use and their relationship with airway disease in HWs. It was hypothesised that exposure to specific cleaning agents and tasks is a risk factor for asthma symptoms, work-related respiratory symptoms and airway inflammation.

METHODS

Study design, population and sampling

A cross-sectional study of 699 HWs was conducted in two large tertiary academic hospitals (346 from a South Africa hospital (SAH) and 353 from Tanzanian hospital (TAH)) during the period July 2014–March 2015 for the SAH and between September 2017 and March 2018 for the TAH. All permanently employed HWs in selected departments that regularly used cleaning agents constituted the sampling frame of the study, as previously described.[21–23] Study participants were selected from these departments using stratified random sampling according to job title, choosing up to five HWs from each department. The combined overall response rate across the two hospitals was 53% as previously reported.[22]

Questionnaire

A total of 697 participants completed the questionnaire interviews (344 from SAH and 353 from TAH). Each participant answered a modified questionnaire for the investigation of asthma as contained in the Protocol for the European Community Respiratory Health Survey II. The study questionnaire also included validated questions from the NIOSH-specific questionnaire for cleaning agents in the healthcare setting.[24] The questionnaire was administered by trained interviewers in English for South African HWs (SAHWs) and in Swahili language for Tanzanian HWs. The translated Swahili questionnaire was back-translated to ensure validity and repeatability.

Fractional exhaled nitric oxide

A total of 654 participants performed fractional exhaled nitric oxide (FeNO) tests (334 from SAH and 320 from TAH). A handheld portable exhaled nitric oxide sampling device (NIOX MINO Airway Inflammation Monitor (NIOX MINO); Aerocrine AB, Solna, Sweden) was used according to the manufacturer's instructions. Two technically adequate measurements were performed in line with the current American Thoracic Society/European Respiratory Society recommendations.[25] A third effort was performed if the difference between the first two measurements was more than 10 ppb. In cases where a third measurement was conducted—the average of all three measurements was used.

Immunological assessment

Blood samples were collected from 682 participants. Atopy was determined by the Phadiatop test. The quantification of specific IgE antibodies to common aero-allergens (Phadiatop) and recombinant natural rubber latex (NRL) components (Hevea brasiliensis—Hev b5, Hev b6.02) was performed using the UniCAP system (Phadia Laboratory Systems, ThermoFisher Scientific). A value of ≥0.35 KU/L was considered a positive test. Further details are provided elsewhere.[21 22]

Operational definitions of asthma-related outcomes and occupational risk factors

An Asthma Symptom Score (ASS) was computed based on the sum of answers (0=no, 1=yes) to five questions reported in the past 12 months. The questions included the presence of shortness of breath while wheezing; being woken up with chest tightness; an attack of shortness of breath at rest; an attack of shortness of breath after exercise; and being woken up by an attack of shortness of breath, as has been described in previous studies.[13 26] A binary variable was created from these five asthma-related symptoms (≥ 2 symptoms vs 0–1 symptom). Having ≥2 asthma-related symptoms was considered to being 'more symptomatic' with higher probability of asthma and 0–1 symptom as being 'less symptomatic'.

Participants were considered to have work-related ocular-nasal symptoms (WRONS) if they experienced sneezing/itchy/runny nose or red/itchy/watery eyes at work in the past 12 months that improved when away from work or worsened on return to work; and WRAS if they experienced chest tightness, wheezing or shortness of breath at work in the past 12 months that improved when away from work or worsened on return to work. In addition to FeNO being analysed as a continuous variable, a categorical

variable (FeNO≥50 ppb) was also computed to gain more specificity for probable asthma in the analysis.[27] Individuals with atopy were defined as having a positive Phadiatop test.

Information on occupational risk factors was obtained from the questionnaire, which had detailed information on the use of cleaning agents and related tasks in the past 12 months.[24] More information regarding exposure assessment is provided in online supplemental table S1 and S2 and further details are contained in our recent article.[23] Four major categories of cleaning-related tasks were considered, that is, medical instrument cleaning and disinfection, fixed surface cleaning and disinfection, specimen preparation and patients' skin/wound cleaning and disinfection. For each cleaning agent, frequency of use per week was calculated by multiplying duration of use per day and number of days used per week. Similarly, for each cleaning task, frequency of task performance per week was calculated by multiplying duration of the task, the number of times the task was performed per day and number of days the task was performed per week. For exposure–response analyses, cleaning-related predictor variables were categorised into three levels (cleaning product not used, use of a cleaning product for up to 99 min per week and use of a cleaning product for ≥100 min per week). These cut-off numbers were chosen after initially studying the distribution of the data based on duration and frequency of exposure of the participants. These cut-offs were considered the best fit and appropriate to use across all cleaning agents used and tasks performed.

Statistical analysis

All data analyses were performed using statistical software STATA V.14 (StataCorp). Multivariate logistic and linear saturated regression models adjusting for atopy, gender, smoking, age, study site and allergic sensitisation to NRL were used to evaluate the association between asthma-related outcomes (and other relevant clinical endpoints) and specific cleaning agents and tasks. Regression models adjusting for atopy, gender and smoking are included as online supplemental tables S3–S7. For linear regression analyses, log transformed values of FeNO were used and reported as geometric mean (GM) ratios with 95% CIs. A negative binomial regression analysis was used to explore the association between ASS (a count outcome variable) and cleaning-related risk factors. The results of the negative binomial regression models were reported as mean ratios with 95% CIs.

RESULTS

Demographic characteristics of HWs in the two tertiary hospitals

Females comprised the majority (77%) of the study participants (table 1). The median age was 42 years (IQR: 32–51 years). South African HWs were significantly older, with a higher median body mass index, and a higher prevalence of cigarette smoking compared with their counterparts. Atopy was higher (47%) in South African HWs (p=0.047). The prevalence of allergic sensitisation to NRL (Hev b5 or Hev b6.02) was 2%, with no significant differences between the two hospitals.

Respiratory symptoms and airway inflammation associated with medical instrument cleaning and disinfection

The presence of WRONS in the past 12 months was positively associated with increased duration (≥100 min/week) of use of OPA, glutaraldehyde, enzymatic cleaners, alcohols or bleach (table 2). Similarly, increased duration (≥100 min/week) of tasks such as manual disinfection of instruments (OR 2.92; 95% CI 1.33 to 6.41) and changing sterilisation solutions (OR 4.44; 95% CI 1.70 to 11.62) were also significantly associated with WRONS (table 3). An increased odd of WRAS in the past 12 months was also observed with hydrogen peroxide (OR 3.69;

Table 1 Demographic characteristics of health workers in the two tertiary hospitals

Demographic characteristics	Overall	SAH n (%)	TAH n (%)	P value (χ^2 test)
Participants (n)	**697**	**344**	**353**	
Age (years) (median (IQR))	42 (32–51)	46 (33–51)	39 (31–51)	0.009*
Gender (%F:M)	77:23	84:16	71:29	<0.001
BMI (median (IQR))	29 (26–34)	31 (27–37)	28 (25–32)	<0.001*
Smoking status: n (%)				<0.001
Current smokers	42 (6)	40 (12)	2 (1)	
Ex-smokers	48 (7)	48 (14)	0 (0)	
Never smokers	607 (87)	256 (74)	351 (99)	
Job title: n (%)				<0.001
Registered nurse	283 (41)	132 (38)	151 (43)	
Nurse assistant/health attendant	168 (24)	59 (17)	109 (31)	
Enrolled nurse	75 (11)	48 (14)	27 (8)	
Cleaner	85 (12)	45 (13)	40 (11)	
Clerk	38 (5)	13 (4)	25 (7)	
Technician	34 (5)	33 (10)	1 (0)	
Porter	14 (2)	14 (4)	0 (0)	
Total years in healthcare industry (median (IQR))	14 (6–28)	20 (8–28)	11 (4–27)	<0.001*
Family history of allergy	353 (51)	219 (64)	134 (38)	<0.001
Atopy (positive phadiatop test)	296 (43)	160 (47)	136 (40)	0.047
Allergic sensitisation to latex (Hev b5 or Hev b6.02)	11 (2)	7 (2)	4 (1)	0.352
Latex Hev b5	3 (0)	3 (1)	0 (0)	0.122†
Latex Hev b6.02	8 (1)	4 (1)	4 (1)	1.000†

*Wilcoxon sum rank test.
†Fisher's exact test.
BMI, body mass index; F, female; M, male; SAH, South African hospital; TAH, Tanzanian hospital.

Table 2 Respiratory symptoms and airway inflammation associated with specific medical instrument cleaning and disinfection agents in tertiary hospital health workers

	n (%)	Asthma symptom score†	Asthma symptom score (≥2 vs 0–1)	WRONS	WRAS	FeNO, ppb‡ (n=654)	FeNO≥50 ppb (n=654)
Prevalence (%) (n=697)			91 (13)	109 (16)	48 (7)		41 (6)
Medical instruments cleaning and disinfection	301 (43)	1.11 (0.83 to 1.48)	1.04 (0.65 to 1.65)	1.30 (0.85 to 1.97)	0.76 (0.41 to 1.41)	1.05 (0.95 to 1.15)	1.42 (0.73 to 2.77)
Orthophthalaldehyde							
Yes versus no	113 (16)	1.00 (0.68 to 1.47)	0.81 (0.43 to 1.54)	1.66 (0.98 to 2.81)	0.82 (0.33 to 2.01)	1.05 (0.93 to 1.20)	**2.60 (1.22 to 5.55)***
0 min/week	584 (86)	1	1	1	1	1	1
1–99 min/week	64 (10)	1.16 (0.72 to 1.86)	1.06 (0.50 to 2.26)	1.12 (0.54 to 2.34)	0.72 (0.21 to 2.47)	1.12 (0.95 to 1.32)	**3.35 (1.42 to 7.92)****
≥100 min/week	30 (4)	1.10 (0.56 to 2.16)	0.73 (0.21 to 2.52)	**3.40 (1.46 to 7.48)****	1.54 (0.44 to 5.45)	0.97 (0.78 to 1.22)	0.79 (0.10 to 6.15)
Glutaraldehyde							
Yes versus no	49 (7)	1.33 (0.74 to 2.38)	1.36 (0.55 to 3.35)	1.20 (0.56 to 2.57)	0.88 (0.29 to 2.66)	1.00 (0.82 to 1.21)	1.23 (0.34 to 4.48)
0 min/week	648 (94)	1	1	1	1	1	1
1–99 min/week	28 (4)	1.47 (0.72 to 3.01)	1.35 (0.43 to 4.25)	0.57 (0.17 to 1.95)	0.79 (0.18 to 3.57)	1.03 (0.81 to 1.31)	1.59 (0.34 to 7.50)
≥100 min/week	16 (2)	1.05 (0.36 to 3.09)	1.27 (0.27 to 6.03)	**3.69 (1.30 to 10.45)***	1.45 (0.30 to 6.95)	1.02 (0.73 to 1.41)	1.12 (0.13 to 9.35)
Enzymatic cleaners							
Yes versus no	113 (16)	1.10 (0.76 to 1.60)	1.12 (0.62 to 2.03)	1.27 (0.74 to 2.19)	1.50 (0.71 to 3.17)	1.09 (0.96 to 1.23)	2.09 (0.98 to 4.48)
0 min/week	584 (87)	1	1	1	1	1	1
1–99 min/week	46 (7)	1.46 (0.87 to 2.47)	1.70 (0.76 to 3.78)	0.72 (0.27 to 1.91)	2.05 (0.74 to 5.71)	1.09 (0.90 to 1.32)	**3.37 (1.30 to 8.71)***
≥100 min/week	43 (6)	1.09 (0.60 to 1.98)	0.92 (0.34 to 2.45)	**2.57 (1.27 to 5.18)****	1.09 (0.31 to 3.76)	1.02 (0.84 to 1.24)	1.07 (0.24 to 4.80)
Chlorhexidine							
Yes versus no	84 (12)	1.00 (0.64 to 1.54)	0.65 (0.32 to 1.35)	0.81 (0.38 to 1.73)	0.76 (0.24 to 2.37)	**1.19 (1.02 to 1.38)***	1.87 (0.73 to 4.80)
0 min/week	613 (91)	1	1	1	1	1	1
1–99 min/week	44 (7)	1.10 (0.63 to 1.94)	0.48 (0.16 to 1.45)	0.79 (0.29 to 2.15)	NC	**1.24 (1.03 to 1.51)***	2.47 (0.79 to 7.70)
≥100 min/week	13 (2)	1.23 (0.48 to 3.15)	0.71 (0.15 to 3.39)	1.84 (0.48 to 7.12)	1.16 (0.14 to 9.77)	1.03 (0.74 to 1.43)	NC
Quaternary ammonium compounds							
Yes versus no	26 (4)	0.88 (0.43 to 1.82)	1.30 (0.45 to 3.72)	1.04 (0.33 to 3.26)	2.70 (0.71 to 10.23)	1.11 (0.87 to 1.41)	2.44 (0.64 to 9.34)
0 min/week	671 (97)	1	1	1	1	1	1
1–99 min/week	15 (2)	0.69 (0.25 to 1.94)	0.91 (0.19 to 4.36)	0.40 (0.05 to 3.18)	NC	1.15 (0.84 to 1.58)	**4.63 (1.11 to 19.26)***
≥100 min/week	3 (1)	NC	NC	NC	NC	NC	NC
Hydrogen peroxide							
Yes versus no	40 (6)	1.30 (0.73 to 2.31)	1.47 (0.61 to 3.55)	1.77 (0.80 to 3.89)	**3.69 (1.49 to 9.18)****	1.06 (0.87 to 1.30)	2.19 (0.76 to 6.33)
0 min/week	657 (95)	1	1	1	1	1	1
1–99 min/week	27 (4)	1.48 (0.76 to 2.89)	1.92 (0.72 to 5.15)	2.19 (0.87 to 5.50)	**3.64 (1.25 to 10.58)***	1.06 (0.82 to 1.36)	1.53 (0.40 to 5.87)
≥100 min/week	7 (1)	NC	NC	NC	NC	NC	NC
Alcohols							
Yes versus no	104 (15)	0.86 (0.57 to 1.30)	0.84 (0.43 to 1.63)	1.09 (0.61 to 1.94)	0.83 (0.34 to 2.02)	0.99 (0.87 to 1.13)	1.39 (0.60 to 3.18)
0 min/week	593 (88)	1	1	1	1	1	1
1–99 min/week	64 (10)	0.99 (0.60 to 1.62)	1.13 (0.52 to 2.43)	0.56 (0.23 to 1.34)	0.86 (0.29 to 2.53)	1.00 (0.85 to 1.17)	1.73 (0.67 to 4.48)
≥100 min/week	16 (2)	1.01 (0.41 to 2.52)	0.91 (0.20 to 4.17)	**4.56 (1.62 to 12.83)****	0.87 (0.11 to 6.91)	1.21 (0.89 to 1.63)	1.27 (0.16 to 10.37)
Bleach							
Yes versus no	204 (29)	1.01 (0.72 to 1.39)	0.94 (0.55 to 1.62)	1.12 (0.70 to 1.78)	0.65 (0.32 to 1.33)	0.94 (0.84 to 1.05)	0.81 (0.37 to 1.75)
0 min/week	493 (75)	1	1	1	1	1	1

continued

Table 2 continued

	n (%)	Asthma symptom score†	Asthma symptom score (≥2 vs 0–1)	WRONS	WRAS	FeNO, ppb‡ (n=654)	FeNO≥50 ppb (n=654)
1–99 min/week	89 (14)	1.00 (0.65 to 1.54)	0.86 (0.41 to 1.79)	0.69 (0.34 to 1.42)	0.24 (0.06 to 1.03)	0.97 (0.83 to 1.12)	0.72 (0.24 to 2.17)
≥100 min/week	75 (11)	1.05 (0.64 to 1.73)	0.91 (0.39 to 2.11)	**2.37 (1.30 to 4.34)****	1.16 (0.49 to 2.75)	0.95 (0.81 to 1.11)	0.88 (0.28 to 2.78)

Data are presented as OR (95% CI), unless otherwise indicated.
Adjusted for atopy, gender, smoking, age, study site and allergic sensitisation to natural rubber latex.
Bold values denote statistical significance at p<0.05 level.
*p<0.05, **p<0.01.
†Mean ratio (95% CI).
‡Geometric mean ratio (95% CI).
FeNO, fractional exhaled nitric oxide; NC, not calculable; WRAS, work-related asthma symptoms; WRONS, work-related ocular-nasal symptoms.

95% CI 1.49 to 9.18) usage for medical instrument disinfection. Furthermore, increasing ASS was also associated with precleaning of instruments for removal of gross contaminants (mean ratio—MR 1.35; 95% CI 1.00 to 1.84) and changing sterilisation solutions (MR 1.38; 95% CI 1.00 to 1.92).

Increasing FeNO levels were weakly associated with use of chlorhexidine (GM ratio 1.24; 95% CI 1.03 to 1.51). However, stronger associations were observed for FeNO≥50 ppb in HWs that used QACs (OR 4.63; 95% CI 1.11 to 19.26), enzymatic cleaners (OR 3.37; 95% CI 1.30 to 8.71) and OPA (OR 3.35; 95% CI 1.42 to 7.92) between 1 and 99 min per week. Furthermore, increasing FeNO was also positively associated with HWs involved in precleaning of medical instruments to remove gross contaminants.

Respiratory symptoms and airway inflammation associated with cleaning and disinfection of fixed surfaces

A higher ASS (MR 1.46; 95% CI 1.00 to 2.13) was observed for HWs that used bleach for fixed surface cleaning and disinfection for duration between 1 and 99 min per week (table 4). The use of chemical products containing ammonia was associated with being more symptomatic (≥2 asthma-related symptoms) (OR 2.27; 95% CI 0.89 to 5.84), although not statistically significant. More symptomatic (≥2 asthma-related symptoms) HWs were more likely to use sprays rather than wipes (OR 5.01; 95% CI 1.80 to 13.91) for cleaning and disinfection of fixed surfaces. Further information is provided in online supplemental table S8.

Respiratory symptoms and airway inflammation associated with specimen preparation products

A higher ASS (MR 1.49; 95% CI 1.03 to 2.16) was observed for HWs that used formalin (10%) solution to prepare specimens for up to 99 min per week (table 4). The presence of WRONS in the past 12 months was positively associated with the use of alcohol-based cytological fixative spray (OR 2.72; 95% CI 1.05 to 7.07). Furthermore, HWs with increasing FeNO levels were also more likely to use formalin (10%) solution (GM ratio 1.17; 95% CI 1.03 to 1.34) for tissue fixation and alcohol-based cytological fixative spray (GM ratio 1.36; 95% CI 1.01 to 1.83) for up to 99 min per week.

Respiratory symptoms and airway inflammation associated with patients' skin/wound cleaning and disinfection

HWs that were more symptomatic (ASS≥2) were more likely to perform patient care activities such as disinfecting patient's skin prior to a procedure (OR 2.46; 95% CI 1.19 to 5.09) or cleaning and disinfection of wounds (OR 3.14; 95% CI 1.17 to 8.41) (table 5). This relationship showed a clear dose–response trend among HWs that performed patient care activities for ≥100 min per week, in that they had higher odds of being more symptomatic. A strong association was also observed between the presence of WRONS among HWs involved in disinfecting patient skin areas prior to procedures (OR 2.23; 95% CI 1.15 to 4.31), cleaning and disinfection of wounds (OR 2.69; 95% CI 1.03 to 7.01) and those that used adhesives (OR 2.41; 95% CI 1.00 to 5.82) as well as between WRAS and applying wound dressings (OR 4.17; 95% CI 1.19 to 14.64). Weak exposure–response relationships were observed for increasing FeNO levels among HWs that performed disinfection of patient skin prior to procedures and cleaning and disinfection of wounds.

Table 3 Respiratory symptoms and airway inflammation associated with specific medical instrument cleaning and disinfection tasks in tertiary hospital health workers

	n (%)	Asthma symptom score†	Asthma symptom score (≥2 vs 0–1)	WRONS	WRAS	FeNO, ppb‡ (n=654)	FeNO≥50 ppb (n=654)
Prevalence (%) (n=697)			91 (13)	109 (16)	48 (7)		41 (6)
Medical instruments cleaning and disinfection	301 (43)						
Medical instruments cleaning and disinfecting tasks§	331 (48)	1.14 (0.84 to 1.55)	1.14 (0.71 to 1.84)	1.24 (0.79 to 1.94)	1.01 (0.54 to 1.89)	1.07 (0.97 to 1.18)	1.49 (0.74 to 3.01)
Manually disassembling instruments, removing/flushing gross contaminants							
Yes versus no	201 (29)	1.35 (1.00 to 1.84)	1.26 (0.77 to 2.04)	1.13 (0.71 to 1.79)	1.16 (0.60 to 2.22)	**1.12 (1.01 to 1.25)***	1.74 (0.86 to 3.50)
0 min/week	496 (71)	1	1	1	1	1	1
1–99 min/week	133 (19)	1.40 (0.98 to 1.99)	1.36 (0.78 to 2.35)	0.82 (0.46 to 1.47)	1.23 (0.58 to 2.63)	**1.15 (1.02 to 1.30)***	2.00 (0.91 to 4.38)
≥100 min/week	68 (10)	1.27 (0.80 to 2.03)	1.07 (0.49 to 2.31)	1.80 (0.97 to 3.37)	1.04 (0.38 to 2.80)	1.07 (0.91 to 1.26)	1.29 (0.42 to 3.96)
Diluting or mixing cleaning products							
Yes versus no	251 (36)	1.08 (0.80 to 1.46)	0.98 (0.61 to 1.58)	1.39 (0.89 to 2.17)	1.02 (0.54 to 1.93)	1.01 (0.92 to 1.12)	1.26 (0.63 to 2.52)
0 min/week	446 (64)	1	1	1	1	1	1
1–99 min/week	213 (31)	1.10 (0.80 to 1.50)	1.02 (0.62 to 1.67)	1.37 (0.86 to 2.18)	1.06 (0.54 to 2.05)	0.99 (0.89 to 1.10)	1.23 (0.59 to 2.53)
≥100 min/week	38 (5)	1.00 (0.54 to 1.86)	0.82 (0.30 to 2.26)	1.53 (0.63 to 3.75)	0.80 (0.18 to 3.60)	1.16 (0.94 to 1.44)	1.49 (0.39 to 5.69)
Changing sterilisation solutions							
Yes versus no	157 (23)	1.38 (1.00 to 1.92)	1.32 (0.78 to 2.23)	1.53 (0.95 to 2.45)	0.78 (0.36 to 1.66)	1.04 (0.93 to 1.16)	1.28 (0.59 to 2.74)
0 min/week	540 (78)	1	1	1	1	1	1
1–99 min/week	135 (19)	**1.48 (1.05 to 2.08)***	1.53 (0.89 to 2.63)	1.23 (0.73 to 2.08)	0.77 (0.35 to 1.72)	1.03 (0.91 to 1.16)	1.41 (0.63 to 3.13)
≥100 min/week	22 (3)	0.80 (0.34 to 1.93)	0.33 (0.04 to 2.52)	**4.44 (1.70 to 11.62)****	0.80 (0.10 to 6.34)	1.13 (0.86 to 1.48)	0.66 (0.08 to 5.75)
Manually sterilise/disinfection of medical instruments							
Yes versus no	143 (21)	1.30 (0.92 to 1.84)	1.25 (0.72 to 2.16)	1.35 (0.79 to 2.28)	1.05 (0.47 to 2.31)	1.09 (0.97 to 1.23)	1.42 (0.64 to 3.17)
0 min/week	554 (80)	1	1	1	1	1	1
1–99 min/week	106 (15)	1.36 (0.93 to 2.00)	1.33 (0.73 to 2.41)	0.94 (0.49 to 1.79)	0.92 (0.37 to 2.33)	1.08 (0.95 to 1.24)	1.75 (0.76 to 4.06)
≥100 min/week	37 (5)	1.11 (0.59 to 2.06)	1.03 (0.38 to 2.84)	**2.92 (1.33 to 6.41)****	1.42 (0.40 to 5.03)	1.11 (0.89 to 1.39)	0.52 (0.07 to 4.20)
Sterilise medical instruments using automated systems							
Yes versus no	15 (2)	1.56 (0.65 to 3.70)	2.30 (0.68 to 7.77)	1.70 (0.45 to 6.37)	3.62 (0.72 to 18.26)	1.19 (0.87 to 1.63)	1.79 (0.33 to 9.62)
0 min/week	682 (98)	1	1	1	1	1	1
1–99 min/week	8 (1)	NC	NC	NC	NC	NC	NC
≥100 min/week	7 (1)	NC	NC	NC	NC	NC	NC

Data are presented as OR (95% CI), unless otherwise indicated.
Adjusted for atopy, gender, smoking, age, study site and allergic sensitisation to natural rubber latex.
Bold values denote statistical significance at p<0.05 level.
*p<0.05, **p<0.01.
†Mean ratio (95% CI).
‡Geometric mean ratio (95% CI).
§A combined variable consisting of 5 tasks involved in medical instruments cleaning and disinfection, that is, precleaning of instruments by removing/flushing gross contaminants, diluting/mixing cleaning products, changing sterilisation solutions, manually sterilise/disinfection of medical instruments and sterilise medical instruments using automated systems.
FeNO, fractional exhaled nitric oxide; NC, not calculable; WRAS, work-related asthma symptoms; WRONS, work-related ocular-nasal symptoms.

Table 4 Respiratory symptoms and airway inflammation associated with specific chemical agents and tasks used in fixed surface cleaning and disinfection and in specimen preparation in tertiary hospital health workers

	n (%)	Asthma symptom score†	Asthma symptom score (≥2vs 0–1)	Wrons	WRAS	FeNO, ppb‡ (n=654)	FeNO≥50 ppb (n=654)
Prevalence (%) (n=697)			91 (13)	109 (16)	48 (7)		41 (6)
Fixed surfaces cleaning and disinfection	572 (82)	1.23 (0.80 to 1.90)	1.41 (0.68 to 2.91)	0.92 (0.53 to 1.60)	1.01 (0.44 to 2.32)	1.04 (0.92 to 1.19)	0.88 (0.35 to 2.20)
Agents							
Ammonia							
Yes versus no	73 (11)	0.77 (0.48 to 1.24)	0.90 (0.44 to 1.84)	1.07 (0.51 to 2.24)	0.17 (0.02 to 1.33)	0.89 (0.76 to 1.04)	1.02 (0.35 to 2.95)
0 min/week	624 (95)	1	1	1	1	1	1
1–99 min/week	24 (4)	1.27 (0.64 to 2.51)	2.27 (0.89 to 5.84)	1.63 (0.56 to 4.71)	NC	1.00 (0.78 to 1.29)	0.52 (0.06 to 4.18)
≥100 min/week	9 (1)	NC	NC	NC	NC	NC	NC
Bleach							
Yes versus no	474 (68)	1.09 (0.79 to 1.50)	0.99 (0.59 to 1.64)	0.97 (0.62 to 1.53)	1.11 (0.57 to 2.18)	1.03 (0.93 to 1.14)	1.12 (0.53 to 2.36)
0 min/week	223 (40)	1	1	1	1	1	1
1–99 min/week	154 (27)	**1.46 (1.00 to 2.13)***	1.43 (0.78 to 2.61)	0.79 (0.43 to 1.45)	0.67 (0.26 to 1.77)	1.08 (0.95 to 1.24)	1.42 (0.58 to 3.45)
≥100 min/week	189 (33)	1.03 (0.70 to 1.51)	0.92 (0.49 to 1.72)	1.28 (0.76 to 2.16)	1.46 (0.69 to 3.10)	1.07 (0.94 to 1.21)	1.46 (0.63 to 3.40)
Tasks							
Use more sprays versus more wipes	18 (3)	**2.81 (1.41 to 5.59)****	**5.01 (1.80 to 13.91)****	0.63 (0.14 to 2.89)	1.87 (0.39 to 9.11)	0.88 (0.66 to 1.18)	0.54 (0.07 to 4.47)
Specimen preparation products	157 (23)	1.27 (0.91 to 1.78)	1.13 (0.66 to 1.92)	1.55 (0.96 to 2.51)	1.38 (0.70 to 2.75)	**1.15 (1.03 to 1.29)***	1.19 (0.55 to 2.58)
Formalin 10% in normal saline							
Yes versus no	148 (21)	1.27 (0.91 to 1.78)	1.09 (0.64 to 1.88)	1.47 (0.90 to 2.41)	1.29 (0.64 to 2.60)	**1.16 (1.03 to 1.30)***	1.09 (0.49 to 2.43)
0 min/week	549 (82)	1	1	1	1	1	1
1–99 min/week	110 (17)	**1.49 (1.03 to 2.16)***	1.19 (0.65 to 2.16)	1.65 (0.98 to 2.81)	1.29 (0.59 to 2.81)	**1.17 (1.03 to 1.34)***	1.27 (0.55 to 2.94)
≥100 min/week	5 (1)	NC	NC	NC	NC	NC	NC
Alcohol-based cytological fixative spray							
Yes versus no	25 (4)	1.09 (0.54 to 2.20)	1.45 (0.54 to 3.89)	**2.72 (1.05 to 7.07)***	2.25 (0.60 to 8.46)	1.20 (0.94 to 1.53)	2.05 (0.53 to 7.84)
0 min/week	672 (98)	1	1	1	1	1	1
1–99 min/week	17 (2)	1.24 (0.53 to 2.90)	1.42 (0.43 to 4.66)	**3.06 (1.00 to 9.33)***	2.22 (0.45 to 10.94)	**1.36 (1.01 to 1.83)***	3.27 (0.80 to 13.36)
≥100 min/week	0 (0)	NC	NC	NC	NC	NC	NC

Data are presented as OR (95% CI), unless otherwise indicated.
Adjusted for atopy, gender, smoking, age, study site and allergic sensitisation to natural rubber latex.
Bold values denote statistical significance at p<0.05 level.
*p<0.05, **p<0.01.
†Mean ratio (95% CI).
‡Geometric mean ratio (95% CI).
FeNO, fractional exhaled nitric oxide; NC, not calculable; WRAS, work-related asthma symptoms; WRONS, work-related ocular-nasal symptoms.

Table 5 Respiratory symptoms and airway inflammation associated with specific chemical agents and tasks used for patients' skin/wound cleaning and disinfection in tertiary hospital health workers

	n (%)	Asthma symptom score†	Asthma symptom score (≥2 vs 0–1)	WRONS	WRAS	FeNO, ppb‡ (n=654)	FeNO≥50 ppb (n=654)
Prevalence (%) (n=697)			91 (13)	109 (16)	48 (7)		41 (6)
Patients' skin/wound cleaning and disinfection	327 (47)	1.06 (0.76 to 1.46)	1.06 (0.64 to 1.77)	1.20 (0.76 to 1.91)	0.81 (0.41 to 1.61)	1.10 (0.99 to 1.22)	1.42 (0.68 to 2.96)
Disinfect skin areas on patients prior to procedure							
Yes versus no	253 (36)	1.24 (0.91 to 1.69)	1.37 (0.84 to 2.24)	**1.79 (1.14 to 2.81)***	0.90 (0.45 to 1.77)	1.03 (0.93 to 1.14)	0.84 (0.41 to 1.71)
0 min/week	444 (74)	1	1	1	1	1	1
1–99 min/week	96 (16)	1.11 (0.72 to 1.73)	1.14 (0.57 to 2.28)	1.73 (0.92 to 3.28)	1.25 (0.50 to 3.14)	1.01 (0.88 to 1.16)	0.40 (0.12 to 1.40)
≥100 min/week	58 (10)	1.62 (0.98 to 2.68)	**2.46 (1.19 to 5.09)***	**2.23 (1.15 to 4.31)***	0.45 (0.11 to 1.97)	**1.28 (1.08 to 1.52)***	2.20 (0.83 to 5.85)
Clean and disinfect wounds							
Yes versus no	162 (23)	0.97 (0.67 to 1.39)	1.07 (0.62 to 1.86)	1.23 (0.72 to 2.10)	1.34 (0.62 to 2.91)	1.05 (0.94 to 1.19)	**2.28 (1.06 to 4.91)***
0 min/week	535 (90)	1	1	1	1	1	1
1–99 min/week	39 (6)	0.85 (0.44 to 1.65)	0.85 (0.30 to 2.40)	0.32 (0.08 to 1.38)	0.41 (0.05 to 3.14)	1.10 (0.90 to 1.34)	0.60 (0.08 to 4.74)
≥100 min/week	22 (4)	1.52 (0.71 to 3.23)	**3.14 (1.17 to 8.41)***	**2.69 (1.03 to 7.01)***	3.15 (0.95 to 10.41)	**1.32 (1.02 to 1.70)***	**6.95 (2.31 to 20.91)****
Apply wound dressing							
Yes versus no	143 (21)	0.97 (0.66 to 1.41)	0.95 (0.54 to 1.69)	1.68 (0.97 to 2.91)	1.42 (0.64 to 3.15)	0.93 (0.82 to 1.06)	0.75 (0.31 to 1.81)
0 min/week	554 (90)	1	1	1	1	1	1
1–99 min/week	44 (7)	0.93 (0.51 to 1.71)	0.81 (0.30 to 2.20)	0.91 (0.34 to 2.42)	0.74 (0.17 to 3.26)	1.12 (0.92 to 1.36)	1.60 (0.51 to 5.01)
≥100 min/week	18 (3)	1.03 (0.44 to 2.42)	2.06 (0.70 to 6.06)	2.92 (0.96 to 8.92)	**4.17 (1.19 to 14.64)***	0.88 (0.66 to 1.18)	NC
Use adhesives							
Yes versus no	279 (40)	1.19 (0.86 to 1.65)	1.30 (0.78 to 2.18)	1.42 (0.88 to 2.30)	1.09 (0.54 to 2.21)	1.02 (0.92 to 1.14)	1.38 (0.65 to 2.93)
0 min/week	418 (69)	1	1	1	1	1	1
1–99 min/week	154 (26)	1.35 (0.93 to 1.96)	1.32 (0.72 to 2.42)	1.43 (0.82 to 2.50)	0.62 (0.23 to 1.64)	1.07 (0.95 to 1.21)	1.53 (0.67 to 3.49)
≥100 min/week	30 (5)	0.97 (0.49 to 1.93)	1.64 (0.60 to 4.44)	**2.41 (1.00 to 5.82)***	2.74 (0.93 to 8.10)	1.04 (0.83 to 1.32)	0.59 (0.07 to 4.77)
Use adhesive removing solvents							
Yes versus no	197 (28)	1.26 (0.85 to 1.87)	1.23 (0.68 to 2.22)	1.30 (0.69 to 2.45)	0.73 (0.29 to 1.82)	1.02 (0.89 to 1.16)	1.15 (0.47 to 2.80)
0 mins/week	500 (81)	1	1	1	1	1	1
1–99 min/week	105 (17)	1.46 (0.92 to 2.30)	1.10 (0.55 to 2.21)	1.24 (0.59 to 2.62)	0.24 (0.05 to 1.15)	1.09 (0.93 to 1.27)	1.64 (0.62 to 4.37)
≥100 min/week	14 (2)	1.42 (0.57 to 3.56)	3.20 (0.93 to 10.99)	2.52 (0.72 to 8.79)	2.25 (0.43 to 11.85)	0.98 (0.70 to 1.36)	NC

Data are presented as OR (95% CI), unless otherwise indicated.
Adjusted for atopy, gender, smoking, age, study site and allergic sensitisation to natural rubber latex.
Bold values denote statistical significance at p<0.05 level.
*p<0.05, **p<0.01.
†Mean ratio (95% CI).
‡Geometric mean ratio (95% CI).
FeNO, fractional exhaled nitric oxide; NC, not calculable; WRAS, work-related asthma symptoms; WRONS, work-related ocular-nasal symptoms.

DISCUSSION

This study has identified a number of cleaning agents and tasks that are positively associated with airway disease. Furthermore, there was also specificity in some of these relationships in that consistent associations were observed for certain patient care activities (disinfecting patient's skin prior to a procedure and cleaning and disinfection of wounds). A particularly pronounced dose–response relationship was observed between WRONS and both medical instrument cleaning agents and tasks. Furthermore, a strong association was observed between higher ASS and predominant use of sprays rather than wipes for cleaning fixed surfaces.

In this study, positive dose–response relationships were observed between WRONS and specific agents (OPA, glutaraldehyde, enzymatic cleaners, alcohols and bleach) and tasks (changing sterilisation solutions and manual disinfection) in medical instrument cleaning and disinfection. Furthermore, cleaning and disinfecting tasks for medical instruments were also positively associated ASS and airway inflammation (FeNO). This finding is consistent with previous studies that have demonstrated an association between agents used in medical instrument cleaning and disinfection and asthma or rhinitis.[4–7 28 29] The lack of consistent associations between WRAS and cleaning-related exposures could be due to a healthy worker survival bias as has been reported in other similar studies.[3 4 13 30] HWs that developed symptoms due to cleaning agents may have self-selected themselves out of their jobs, redeployed to other jobs/areas with less exposure or left the workforce completely. In this study, 2% of study participants reported that they had changed their jobs due to WRAS.

The association between OPA use and asthma-related outcomes in the current study is consistent with similar studies that have implicated OPA in the causation of occupational asthma, contact dermatitis and anaphylaxis in HWs as well as in patients undergoing instrument procedures.[31 32] The results of the current study are also consistent with previous studies that have demonstrated an association between exposure to QACs and asthma or rhinitis, not only in HWs but also in domestic cleaners.[6 7 33] In the current study, a more than threefold increased odds of WRAS was observed in HWs that used hydrogen peroxide for medical instrument disinfection, as has been reported in previous studies.[11 12] Furthermore, use of enzymatic cleaners was also positively associated with WRONS and airway inflammation consistent with other studies that have reported cases of occupational asthma and rhinitis.[9 10] A review of safety data sheets of the products that were used revealed a mixture of enzymes including protease, amylase, cellulase, lipase and urease. Exposure to proteolytic enzymes is also a recognised cause of allergic respiratory and skin symptoms in other occupational groups, particularly among detergent manufacturing workers.[8 9]

The positive association between use of chlorine-based bleach and ASS in the current study is consistent with findings of previous studies that have demonstrated an association between exposure to bleach and asthma-related outcomes.[2–4 7 34 35] In a cross-sectional analysis of a population-based European cohort, domestic use of hypochlorite bleach was associated with lower rates of atopy, hay fever and allergic symptoms but higher rates of lower respiratory symptoms and non-specific bronchial hyperresponsiveness (NSBH).[36] A recent meta-analysis also reported that the risk of asthma increased when workers were exposed to bleach compared with nonexposed workers (metaRR 1.51, 95% CI 0.54 to 4.18), but this was not found to be statistically significant.[1] The lack of consistent association between bleach and eosinophilic airway inflammation (FeNO) could be due to the irritant nature of bleach-related pathophysiological changes. Similarly with bleach, more symptomatic HWs (≥2 asthma-related symptoms) in the current study had a twofold increased odds (95% CI 0.89 to 5.84) of using ammonia-based products for fixed surfaces cleaning and disinfection. Previous studies have also reported an association between exposure to cleaning products containing ammonia and asthma-related outcomes.[2 3 13] As is the case in the healthcare setting, both chlorine and ammonia are known to be associated with irritant induced asthma in other occupational settings.[3 13]

In this study, the predominant use of sprays rather than wipes for fixed surface cleaning/disinfection was associated with almost threefold higher odds of having a higher ASS. This relationship was more pronounced in more symptomatic HWs as evidenced by the fivefold increased odds of having an ASS (≥2). It is well known that the use of sprays generates higher aerosol levels of chemical agents and thereby promoting inhalation. The results of the current study are, therefore, consistent with other studies that have demonstrated a positive association between use of cleaning sprays and asthma (as well as other respiratory symptoms).[4 16 26] The study findings underscore the need to replace the use of sprays with wipes whenever possible. Previous studies have also demonstrated similar associations between fixed surface cleaning and asthma.[5 8 13]

Increased odds of having high FeNO levels were consistently observed among HWs that performed patient care activities in this study. In addition, consistent positive dose–response relationships were observed between specific asthma-related outcomes (FeNO and ASS≥2) and either disinfection of patients' skin before procedures or cleaning/disinfection of wounds. These results are consistent with a previous study by Delclos *et al*, which also demonstrated an association between bronchial hyperresponsiveness-related symptoms and the use of adhesives on patients.[8] The products used for patient care activities are mostly irritants (such as alcohols, ethers and acetone), but some such as chlorhexidine are also known sensitisers.[8 17 18]

This study also demonstrated a positive association between use of formalin solution and increasing FeNO and ASS in keeping with the findings of previous studies.[3 4] Formaldehyde is a known asthmagen with both irritant and sensitising properties.[4] Formalin (10%) solution was commonly used in both hospitals for specimen preparation (tissue fixation).[23] This was also evident in the exposure assessment study conducted in the SAH, which identified detectable levels of formaldehyde (GM=0.0025 ppm) in a considerable number (38%) of collected samples.[23]

One of the major findings of this study was that FeNO was positively associated with the use of OPA, QACs, enzymatic cleaners, chlorhexidine and formalin solution. All these agents are known sensitisers capable of causing allergic respiratory and skin symptoms in exposed individuals.[13 16] Increased FeNO was also commonly observed among HWs who performed patient care activities. This may be due to exposure to sensitising agents such as chlorhexidine commonly used in patient care activities. Alternatively, this could also be due to exposure to irritants such as alcohols and ethers used in these tasks. There have been few studies that have reported high FeNO levels in individuals exposed to irritants,[37 38] although this is not a common finding. Since irritant exposures are known to enhance allergic inflammation,[39] increased FeNO levels could also be explained by coexposure of HWs to irritants and sensitisers during the course of their work. This is suggested by the findings of a Spanish study,[40] which demonstrated an association between FeNO and usage of

multiuse cleaning products, glass cleaners and polishes among professional cleaners.[40]

In a study of this nature, the impact of potential biases needs to be considered. There is a possibility of recall bias since self-reported information of chemical usage by HWs in relation to asthma symptoms was used in the study. However, this is unlikely to have had a major influence on the results since consistent associations were also observed with more objective tests such as FeNO. In addition, due to the small number of study participants in the last category (≥100 min per week) for some cleaning agents and tasks and some missing information for the duration and frequency data, the results of this study need to be replicated in other studies with a greater focus on the specific cleaning agents. For the exposure–response analyses, it is also important to mention the possible drawbacks associated with dichotomisation of continuous variables (≥100 vs <100 min per week), since those HWs close to but on opposite sides of the cut point may be categorised as being very different despite minor differences in exposure duration. Furthermore, due to the exposure misclassification, there is the possibility of under-estimation of the association between respiratory outcomes and the specific cleaning agents due to the fact that some HWs were exposed to multiple cleaning agents. Since multiple statistical tests were used to investigate the associations between a number of chemicals, spurious associations could be a possibility, hence the results should be interpreted in conjunction with the relevant contextual information. Finally, the lack of objective exposure data also hampered the ability of the study to move beyond utilisation of duration and frequency of use of chemicals to more specific exposure metrics such as exposure concentrations of respective chemical agents to further quantify the dose–response relationships.

In conclusion, a number of medical instrument cleaning agents (including OPA and enzymatic cleaners) and tasks (precleaning of medical instruments and changing sterilisation solutions) as well as patient care activities were associated with an increased risk of airway disease in HWs of two tertiary hospitals located in sub-Saharan Africa. Furthermore, a positive dose–response relationship was also found between WRONS and medical instrument cleaning agents and tasks. ASS was also positively associated with the use of sprays for fixed surface cleaning, confirming the findings of studies in other professional cleaning contexts. There is a need for larger prospective studies that use a repertoire of clinical, physiological and inflammatory markers to further characterise asthma phenotypes in HWs exposed to diverse cleaning agents. Furthermore, use of exposure metrics such as the actual exposure concentrations of respective agents will contribute to greater specificity in quantifying dose–response relationships, with a view to establishing acceptable exposure thresholds to protect respiratory health of HWs. Finally, a more upstream preventive measure that requires health facilities to establish chemical oversight committees, which comprise occupational health, infection prevention and control personnel, as well procurement staff to better anticipate and mitigate the risks associated with regular use of cleaning agents in tertiary hospital settings is vital.

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