# THE ASSOCIATION OF CLEANING PRODUCTS AND PRACTICES WITH ASTHMA AMONG TEXAS HEALTHCARE PROFESSIONALS

by

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DEDICATION

To my grandfather Late Shri Bhailalbhai K. Patel and my entire family

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THE ASSOCIATION OF CLEANING PRODUCTS AND PRACTICES WITH ASTHMA AMONG TEXAS HEALTHCARE PROFESSIONALS

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Healthcare professionals (HCPs) are at risk for work-related asthma (WRA). The 2003 Texas Asthma Study (TAS) found higher odds of new-onset asthma (NOA) associated with medical instrument and building surface cleaning, and powdered latex glove use in 1992-2000. Subsequent changes in cleaning practices may have affected asthma risk. We assessed changes in WRA prevalence and its risk factors, and examined asthma burden in Texas HCPs.

This was a statewide representative survey of 9,914 Texas physicians, nurses, respiratory therapists, occupational therapists, and certified nurse aides. Exposures to cleaning/disinfection products and tasks were measured using an updated asthma-specific job-exposure matrix (JEM). We examined two asthma outcomes: NOA, i.e. asthma with onset after entering healthcare, and bronchial hyperresponsiveness symptoms (BHR), using a validated 8-item predictor. We used logistic regression, taking into account survey weights, to estimate associations between exposures and outcomes. Asthma burden was measured by missed workdays and the Work Role Function Questionnaire (WRFQ), a surrogate for presenteeism (working while ill).

Overall response rate was 34.8%; the final analytical sample was 2,427 participants. The weighted prevalence of NOA was 7.1%, highest among nurses; for BHR, it was

31.0%, highest for occupational therapists. NOA was associated with building surface cleaning (OR 2.03, 95%CI 1.26-3.28), orthophthalaldehyde (OR 1.93, 95%CI 1.29-2.88), bleach/quaternary ammonium compounds (OR 1.83, 95%CI 1.14-2.93) and sprays (OR 2.03, 95%CI 1.26-3.28), but not with other exposures. For BHR, there were no significant adverse associations.

Mean missed work days due to health problems among asthmatics and non-asthmatics in past 12 months were 9.9 and 13.5, respectively ($p>0.05$); however, 76% of these missed work days among asthmatics were due to asthma or breathing problems. Mean WRFQ scores were significantly lower for asthmatics, indicating greater presenteeism.

HCPs remain at risk for WRA, although there are encouraging trends. Compared to the TAS, NOA and BHR prevalence were unchanged; medical instrument cleaning/disinfection, powdered latex glove use and exposure to a workplace spill were no longer significant risk factors. Cleaning of building surfaces, orthophthalaldehyde, bleach, quaternary ammonium compounds, and using sprays to apply cleaners remain a problem. Exposure controls, together with optimum clinical management of asthma, would likely result in a decrease in asthma burden in healthcare occupations.

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LIST OF ABBREVIATIONS

| | |
|---|---|
| ATS | American Thoracic Society |
| BLS | Bureau of Labor Statistics |
| CNA | Certified Nurse Aide |
| DFP | Discriminant Function Predictor |
| FDA | Food and Drug Administration |
| HCP | Healthcare Professionals |
| JCAHO | Joint Commission on Accreditation of Healthcare Organizations |
| JEM | Job Exposure Matrix |
| LVN | Licensed Vocational Nurse |
| NIOSH | National Institute for Occupational Safety and Health |
| NOA | New-onset Asthma |
| NOES | National Occupational Exposure Survey |
| OA | Occupational Asthma |
| OSHA | Occupational Safety and Health Administration |
| RN | Registered Nurse |
| SHIELD | Midland Thoracic Society's Surveillance Scheme of Occupational Asthma |
| TAS | Texas Asthma in Healthcare Professionals Study 2003 |
| WEA | Work-Exacerbated Asthma |
| WRA | Work-related Asthma |
| WRFQ | Work Role Function Questionnaire |

## SPECIFIC AIMS

### Background & Significance

One out of 12 adults in the United States has asthma (1). Among these, approximately 15% to 25% of cases are attributable to work-related factors. Work-related asthma (WRA) is defined as asthma that is exacerbated or induced *de novo* by inhalation exposures in the workplace (2). WRA is a preventable disease associated with adverse health effects and socioeconomic consequences (2). It is estimated that around 2.25 million people in the U.S. age 15-65 years are at risk for WRA (3). In addition, studies have shown that inadequately controlled asthma can lead to work productivity loss, work limitations, and lower quality of life (4, 5).

Healthcare professionals (HCPs), especially nurses, are known to be at risk of WRA (6). Among the various causal factors and triggers of asthma in these professionals are cleaning products, disinfectants, sterilants, pharmaceuticals, sensitizing metals and medications. In particular, exposures to specific highly volatile cleaning agents, both sensitizers and irritants, can adversely affect respiratory health (7). Over the past decade, infection control and general housekeeping practices in healthcare settings have been changing in response to new environmental policies, regulations and trends (8, 9). Whether or not the changes in cleaning products and practices in these settings have modified the risk and impact of WRA among HCPs is, as yet, undetermined (10).

In 2003, researchers at The University of Texas Health Science Center at Houston (UTHealth) School of Public Health conducted the Texas Asthma in Healthcare Professionals Study (TAS), the first large study of WRA in HCPs, in a statewide representative sample of 5600 Texas HCPs (nurses, physicians, respiratory therapists and occupational therapists). Asthma-related outcomes were measured with a validated survey questionnaire and occupational exposures were determined using a newly developed asthma risk factor job-exposure matrix (JEM), designed for use in healthcare settings. The study found significant associations between occupational exposures and asthma in healthcare workers (6, 11). Specifically, risk of asthma and symptoms of asthma or bronchial hyperresponsiveness (BHR) increased for those whose tasks involved medical instrument cleaning and disinfection, exposure to general cleaning products, use of powdered latex gloves before the year 2000, and administration of aerosolized medications (6). Whereas previous studies had largely consisted of case reports, case series and a few case-control studies, this more rigorously designed, population-based study contributed to confirming HCPs as an at-risk group for asthma. Findings from the TAS also underscored the need for more detailed study of both infection control and prevention practices and HCP groups, in particular nurses as they had the highest asthma risk.

In the more than 10 years since the TAS was published (6), there have been several changes in cleaning and disinfection practices in healthcare (10, 12). There is a greater emphasis on controlling hospital-acquired infections, leading to detailed, strict cleaning and disinfection guidelines (8). However, these guidelines may have had unintended consequences for workers who perform these duties or others who are close bystanders. The use of cleaners and disinfectants related to "green" chemistry and engineering has increased, yet (13, 14) it is not known whether this has affected the magnitude of WRA in healthcare settings (10). But changes are not due only to use of new products. In addition, there have been changes in the nature of the tasks, the frequency of exposures, the general work environment, greater automation of some cleaning practices, and the degree to which personal protective equipment (PPE) is available and used appropriately (13-15). Further research is thus warranted to investigate changes in magnitude of associations between workplace exposures and asthma and asthma-like symptoms in a contemporary population (10). Moreover, our understanding of the impact of asthma on functioning at work and overall quality of life is sparse, justifying more research in this area.

In 2014, the same research team that conducted the 2003 TAS (Grant number: CDC/NIOSH5R01OH03945-01A1 PI: Delclos G) was awarded a new four-year R01 grant (Grant number: 1R01OH010648-01; PIs: Delclos G, Gimeno D) by the CDC/National Institute for Occupational Safety and Health (NIOSH) to conduct a new statewide survey. The goal was to assess whether recent changes in various healthcare practices and exposures have affected the prevalence and impact of WRA among HCPs in Texas, and to compare findings to the 2003 study. Important differences between the 2003 and 2014 TAS are: a) a larger initial sample size (9914 HCPs), with oversampling of nurses and physicians, and addition of nurse aides; b) more detailed examination of exposures and a broader spectrum of healthcare practice settings; and c) consideration of the impact of WRA on quality of life and functioning at work.

## Goals, Hypotheses and Specific Aims

This dissertation is a part of the 2014 parent grant, but with its own aims and hypotheses. It focuses primarily on associations between asthma and newer workplace exposures to cleaning products and practices while comparing the associations with older identified exposures, expanding the study population to include certified nurse aides, and examining the impact of asthma on worker performance and quality of life. Where applicable, results were compared to findings from the 2003 TAS**.**

The long-term goal of this dissertation was to contribute to reducing the incidence and prevalence of asthma in HCPs by identifying the most significant current occupational risk factors for WRA. The overall aim was to measure associations between cleaning products and practices, assess the relationship between these exposures and WRA and asthma symptoms in HCPs, and examine the impact of asthma on work capacity and quality of life. The central hypothesis was that current cleaning products and practices remain important determinants of WRA in HCPs. We also further hypothesized that WRA in HCPs is an important contributor of work-related absenteeism, presenteeism and/or lower quality of life indicated by presenteeism and missed work days. These hypotheses were addressed through three specific aims.

The **first aim** focused on ascertaining exposures in healthcare settings by revising, updating, testing and validating the original 2003 JEM to reflect recent changes in practices, products and tasks**.** In the **second aim** we revised the 2003 survey questionnaire to reflect changes in asthma epidemiological research, including the incorporation of more explicit definitions of WRA and work-relatedness of symptoms, and incorporation of measures of quality of life, lost work-time and health indicators in relation to work capacity**.** This questionnaire formed the basis for a statewide survey of 9,914 Texas HCPs that began in fall 2016. The new JEM and data obtained from the questionnaire responses were then merged, in preparation for analysis. In the **third aim**, we measured associations between cleaning/disinfection exposures and asthma/asthma symptoms, and between asthma and indicators of work capacity and quality of life, the latter focused mainly on missed work days and presenteeism.

**Specific Aim 1: To construct a job exposure matrix (JEM) for use with a statewide survey of asthma in Texas HCPs: updating, testing and validation.**

The initial source of information for the 2003 JEM was a subset of the NIOSH National Institute for Occupational Safety and Health (NIOSH) 1981-1983 National Occupational Exposure Survey (16), limited to the healthcare industry and a list of 367 asthmagens. This initial table was then updated through a series of walkthroughs at three hospitals approved by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), leading to a final set of 139 job x practice setting combinations, and 5 exposure categories (For example, Operating Room Nurse x Urban Hospital → Exposure to Glutaraldehyde). Each job-practice x exposure cell was coded to indicate the probability of exposure for workers in that cell by a team of experts in occupational medicine, industrial hygiene, hospital health and safety, and toxicology, resulting in a final JEM.

In the new 2014 study, the JEM was updated by reviewing the 2003 job x practice settings, and incorporating new exposure categories that reflect changes in tasks, products and practices, and an additional HCP group, nursing aides. We also included information derived from directly observed workplace practices through several walk-throughs and focus group sessions. The JEM was structured to preserve comparability with the original 2003 JEM, while adding new elements. After establishing the structure of the new JEM, it was coded by a new team of experts. Simultaneously with Specific Aim 3 (below), we also performed some limited content validation and construct validity testing of the JEM by measuring its ability to detect *a priori* expected associations with selected asthma outcomes.

**Specific Aim 2: To update the 2003 TAS asthma questionnaire and administer it through a survey of a representative sample of Texas HCPs.**

The questionnaire used in the 2003 TAS was tested and validated prior to its administration (17), and served as the starting point for the revised version in the survey that began in 2016. The main changes consisted of addition of new items for ascertaining work-related asthma, based on more recent literature and directly observed workplace practices, and measures of work capacity and quality of life. In addition, items found not to be useful or particularly informative in 2003 were deleted to streamline the instrument. The new version underwent preliminary testing for comprehensibility, ease of use and timing. It was then administered via a mail/internet survey to a random sample of nearly 10,000 Texas licensed HCPs (physicians, nurses, respiratory and occupational therapists, and nurse aides).

The datasets generated by Aims 1 and 2 were merged in preparation for Specific Aim 3.

**Specific Aim 3: To measure associations between cleaning products and practices and WRA in Texas HCPs, and measure the burden of asthma on work capacity and quality of life.**

After merging the datasets, associations between exposure to cleaning and disinfection products and tasks and asthma were analyzed through descriptive statistics, univariate analyses, and multivariable logistic regression modeling. A similar approach was used to measure associations between asthma, WRA and indicators of work capacity, sickness absence, and quality of life. In this aim, we also tested the ability of the JEM-coded exposures to detect expected associations between selected exposures and asthma, as an approximation to construct validation of the JEM.

# BACKGROUND

## Work-Related Asthma in Healthcare Professionals

Asthma is both a health and economic concern in the United States, with a lifetime prevalence of 8% among adults (18). Nationally, asthma has led to annual costs of more than $56 billion and around 25 million days of restricted activity (19). Work-related factors are implicated in one out of every six cases of asthma in working-aged adults (20-23). Currently, WRA is the most frequently reported work-related occupational respiratory disease in developed nations (24). In 2003, the American Thoracic Society (ATS) projected work-related obstructive airways diseases to be responsible for approximately $7 billion in annual costs (22). Occupation is one of the causative risk factors for new asthma (occupational asthma or OA). Workplace exposures can also worsen pre-existing asthma (work-exacerbated asthma, or WEA). Collectively, OA and WEA are referred to as work-related asthma (WRA). Healthcare workers are an occupational group at a high risk for WRA compared to other professions (6, 23, 25-27). Current asthma prevalence was highest among workers employed in healthcare (8.8%) (23). It is important to understand the exposures specific to occupations that are responsible for causing or triggering WRA.

OA is defined as new-onset asthma characterized by variable airflow limitation and bronchial hyperresponsiveness due to causes and conditions encountered in an occupational environment (28). OA can be caused by either exposure to an allergic sensitizing agent or to high concentrations of respiratory irritant. The prognosis of OA is poor, with only one-third of workers becoming asymptomatic following complete cessation of exposure (29). In addition to OA, exposure to agents common to many workplaces such as chemical irritants, dust, gases, fumes and second hand smoke may also worsen asthma in workers whose disease was pre-existing; this is referred to as work-exacerbated asthma (WEA) (9, 30, 31).

Collectively, both new-onset and work-exacerbated asthma make up the spectrum of WRA, but traditionally WEA has received less attention than either OA or WRA as a whole (32), with few studies examining its frequency or impact. The definitions of WEA have varied based on their use in epidemiological, clinical or medico-legal settings (30, 31). Among all cases of WRA, WEA conservatively represents around 45% to 50% of cases (30). Distinguishing between OA and WEA is important because of differences in at-risk worker populations, clinical management and impact (33).

In 2011, the ATS published an official statement on WEA (31) that established a case definition useful in both research and clinical contexts. In this definition, WEA requires fulfillment of four criteria: (1) asthma that predates or is concurrent with entering the work environment of interest; (2) the exacerbation, measured as either asthma symptoms and/or increased need for medication, is temporally related to the occupational exposure; (3) there are conditions at work capable of exacerbating asthma; and (4) OA is unlikely. These definitions emphasize the importance of occupational exposures that are responsible for causing WRA (31).

In this dissertation, the focus is on HCPs as an at-risk group for WRA. HCPs comprise up to 8% of the U.S. workforce (34). From 2006 to 2010, despite coinciding with the economic recession, healthcare added more jobs than any other sector, approximately 600,000 (35). Projections for 2010-2020 indicate an addition of another 2 million jobs, or a growth rate of 26% for healthcare professionals and healthcare support

(34, 35). Within the HCP group, job growth is greatest among nurses (especially registered nurses), physicians, respiratory therapists, occupational therapists/physical therapists, and home health aides.

In the 1990s, attention began focusing on respiratory hazards among HCPs. This was driven, in part, by increasing concern over reports of allergic reactions, including asthma, to latex, after passage of the 1992 Occupational Safety & Health Administration (OSHA) Bloodborne Pathogens Standard (6, 36), which resulted in a significant increase in use of latex-containing personal protective equipment, especially powdered latex gloves (6). As the reports of latex allergic reactions began to appear, both NIOSH and the FDA issued alerts to hospitals recommending a review of their use of latex-containing products, and adoption of hospital-wide latex control policies. In the 2003 TAS, use of latex gloves between 1992 and 2000 was found to be a risk factor for both NOA and symptoms, but this risk disappeared after the year 2000 (6). This suggested that the implementation of control policies was having a beneficial effect.

Work in healthcare settings is associated with a potential for exposures that comprise a full spectrum of workplace hazards, including biological, physical, chemical, and radiation agents, as well as psychosocial factors. Both OA and WEA have been described in the context of these exposures, and mechanisms include both sensitization threshold and irritant exposures. Furthermore, the likelihood of mixed exposures to these agents is high, and may affect allergic sensitization thresholds and irritation potential (22, 29, 31, 37). However, risk of WRA in HCPs is influenced by a number of factors, many of which have been incompletely characterized. This risk can vary by type of professional, their job tasks, the products they use, how they use them, the frequency and intensity of exposure opportunities, and/or the effectiveness of controls to mitigate those exposures.

Nurses are one of the HCP groups at greatest risk of exposure with at least twice the odds of reporting asthma compared to physicians, as was shown in the TAS (6, 11). But there are many subgroups of nurses, and risk is likely to vary according to subgroup (11). In the longitudinal Nurses' Health Study, significant associations were found between working as an operating room nurse and severe, persistent asthma, as compared to administrative nurses (adjusted odds ratio 2.48) (38). In a recent study (39) based on the UK's voluntary reporting Midland Thoracic Society's Surveillance Scheme of Occupational Asthma (SHIELD) program (1991-2011), over 75% of OA cases occurred in nursing, operating theatre, endoscopy and radiology staff. There has been a significant growth in nursing professions and also more diverse classification of nursing occupations, including nursing assistants and home health aides (17).

Not all nursing professions have been studied separately to assess risk factors for WRA in each sub-profession, considering the diversity in tasks and work roles ranging from a nurse aide to an advanced nurse practitioner. In a separate but concurrent pilot study, this dissertation examined WRA in nurse aides, a growing nursing profession that has been much less studied compared to registered nurses in terms of prevalence and risk factors for WRA. By definition, nurse aides assist other higher nursing professions and physicians by performing other unspecialized services (40). These include providing hands-on care to patients in various settings, cleaning and disinfecting tasks, feeding patients, performing light housekeeping duties in patient rooms, providing skin care, changing linens, and many other duties (41). This raises a reasonable question that, since nurse aides perform more cleaning and disinfecting tasks than LVNs or RNs, might they be at a higher risk of WRA compared to other nursing professions? In 2014, there were 1.5 million jobs related to nursing assistants and orderlies in the US (42). According to the BLS (Bureau of Labor Statistics), this number is projected to increase by 17% by 2024 (42). In Texas alone, there were 124,616 certified nurse aides (CNAs) providing care in 2014(43). This represents a 2.5% increase since 2009 and a 12% increase since 2004(43). In addition, nurse aides have an unequal geographic distribution, with non-metropolitan areas having 61.4% more CNAs than metropolitan areas even after controlling for population differences (43). These numbers anticipate consistent growth and geographic variability in this job profession in coming years, and thus a need to specifically study the risk of WRA in nursing sub-occupations.

With respect to tasks and products, several studies of nursing personnel and female hospital workers have found that exposure to cleaning/disinfection is as a risk factor for WRA. The previous literature as well as newer studies have indicated that nurses are at a consistently increased risk of occupational asthma compared to other healthcare professionals. Among healthcare workers, nurses, nurse aids and cleaning workers have been marked as high-risk occupations for WRA (44-46). Among the identified products are bleach, glutaraldehyde, formaldehyde, and quaternary ammonium compounds (7, 11, 47, 48). However, most of these studies were unable to characterize these various risks in detail, due to small sample size, not gathering sufficiently detailed exposure information, or both (7, 11).

Known factors responsible for WRA are types of task (e.g., cleaning of general building surfaces or medical instrument cold sterilization) (6), product use (e.g., decalcifying agents, toilet cleaners) (7, 49), method of application (e.g., sprays, which can volatilize chemicals that are usually fairly non-volatile) (37, 47, 50), or work environment (e.g., operating rooms, where exposures are among the highest in healthcare settings) (48), along with use of respiratory protection. High level disinfectants (HLDs), such as glutaraldehyde, paracetic acid, or orthophthalaldehyde are used on a daily basis in healthcare environments (39, 51). Other disinfectants are alcohol, bleach and sprays (52). Newer studies have indicated the need for determining the role of individual vs. complex agents in the workplace responsible for causing WRA (52, 53). Factors such as frequency of use of certain products also play a role in modifying risk, as was shown in relation to number of days per week on which powdered latex gloves were used by nursing personnel (47). Most important, yet one of the least studied effects, are temporal changes in the prevalence of risk factors related to healthcare practices that may have changed the risk factor profiles of HCP.

Since the 2003 TAS study, new practices have emerged for reasons unrelated to controlling asthma risk. Cleaning and disinfection practices and products in hospitals have changed, including greater use of “green” chemistry and engineering (13, 14). The effects of green products, which contain fewer synthetic chemicals but more nature-derived substances and were designed to minimize environmental impact on WRA is unknown. Studies have also shown there may have been ways to achieve novel assessment decisions such as newer JEMs, to protect against non-allergic sensitization and asthma (54).

To decrease hospital-acquired infections, the emphasis on cleaning and disinfection has increased. In addition to the introduction of the new “green” products, there has been a resurgence in the use of bleach in response to increases in hospital-acquired resistant infections, particularly *Clostridium difficile* (55-57). Bleach is a well-established respiratory irritant (58-61). Whether or not this has resulted in a parallel increase in bleach-related WRA is also not known, and was also explored in this dissertation.

In summary, further research is warranted on details of agents, tasks and occupations associated with asthma in HCPs (10, 54). Specifically, nurse subgroups, given their growing number and multiplicity of roles, and a focus on tasks and work environments related to cleaning and disinfection merit greater attention.

Although several studies have addressed the health and socioeconomic consequences of WRA, to our knowledge none have examined this issue in HCPs. Work disability is common among asthmatic adults, as are missed school days in children; these are collectively referred to as “days of restricted activity” (62). According to the 1983-1985 National Health Interview Survey, approximately 10% of all persons with asthma from age 18 to 44 reported limitation in work ability due to asthma (63). Asthma incidence and severity has increased in recent decades, and it is conceivable that this has translated into increases in work limitations, suggestive of an increase in work disability due to asthma as well (62). However, little is known about how asthma affects work in terms of social, physical or mental demands in HCPs. This indicates the need to study whether work demands and capacity are being affected by WRA, which we addressed by incorporating questions related to missed work days, work-role functioning (a surrogate for presenteeism), and work-related quality of life.

## Job Exposure Matrices: Uses and Applications

Prior epidemiological studies focused on WRA have shown that self-reported exposures are prone to recall or misclassification bias, influenced by the status of asthma among respondents (64, 65). One way of limiting recall bias is through the use of a JEM (66). A JEM is a two-dimensional matrix structure, with relevant occupational exposures on one axis, and detailed job/practice settings on another axis; sometimes, additional axes (e.g., time) are included as well. The individual cells of a JEM are coded, usually by one or more experts, based on their knowledge and a wide range of data sources. This results in an externally determined (rather than self-reported) exposure assessment. Computerized JEMs were introduced in the 1970s (67).

Once the matrix structure has been established, the individual cells in a JEM are coded on the basis of measurements of different exposures in workplaces (67). If quantitative measurements are not available, coding relies on different methods such as expert assessment, aided by the published literature and communication with industrial personnel (67). Coding scales can vary from simple binary ("exposed"/"not exposed") to semi-quantitative, in which probability or intensity of exposures are estimated.

JEMs provide summary estimates for groups of workers sharing similar occupations or job titles, thus allowing group-based estimates to be applied to individuals according to their job titles (68). In large occupational epidemiology studies, JEMs provide researchers with a means to analyze multiple exposure-occupation data across different sub-occupations in one or more industries. Originally, JEMs were most often used in cancer epidemiology studies. However, for the past several years they have been applied to other outcomes, including asthma (69-71). More recent JEMs have been further classified into jobs and tasks (Job-exposure or Job-Task Exposure) for a better classification of exposures (52, 72). In OA, JEMs have not only helped in reducing misclassification bias, but also provide better characterization of suspected agents for OA. Recent JEMs have identified exposure to alcohol, bleach, sprays, chlorhexidine, formaldehyde, and quaternary ammonium ("quat") compounds as still being common in healthcare environments (72-74).

Despite being useful for measuring exposures across different occupations, JEMs reflect exposures at a given point in time, and can become static or outdated if not reviewed periodically. With ongoing changes in the work environment and environmental practices and policies, it is necessary to update a JEM. Consequently, the first specific aim of this dissertation focused on revising, updating and recoding the 2003 TAS JEM, and attempting some degree of validation (as part of the third specific aim).

The 2003 TAS JEM was initially derived from the NIOSH National Occupational Exposure Survey (NOES) (6, 16), conducted in the early 1980s. The main advantages of the NOES database are its origin on direct observations of representative sample of US workplaces, consideration of exposures during that period, and also use of common industry, hazard and occupation codes (6, 16). After developing additional sources of chemical lists from the literature, a subset JEM was developed specific to the healthcare industry and asthma, with 367 asthmagens cross-referenced on NOES hazard codes, and 139 job-practice settings combinations. On the basis of three Houston area hospital walkthroughs by industrial hygienists and occupational physicians in 2002-2003, this JEM was updated and structured around two main axes: job x practice and exposures (6). Coding of the JEM was performed by a multidisciplinary panel that included hospital safety professionals, industrial hygienists, occupational physicians and toxicologists. After the codings were performed, the TAS JEM was merged with data from the statewide survey, resulting in a final dataset that allowed measurement of associations between the JEM-based exposures and survey-based asthma outcomes.

In the initial stages of the 2014 R01 grant of asthma in Texas healthcare professionals, a new series of walk-throughs were conducted. Compared to the 2003 study, these walk-throughs included not only hospitals but also outpatient clinic settings and nursing homes. They were also supplemented with focus groups involving workers and managers knowledgeable about cleaning and disinfection practices in healthcare settings. In addition, these walkthroughs examined practice changes over the past several years. The walk-throughs and focus groups confirmed the need to study subgroups of HCPs and to include a more detailed approach for assessing cleaning and disinfection exposures that includes not only the products used, but also tasks and settings. These observations were incorporated into the updating and recoding of the JEM, performed as Specific Aim 1 in this dissertation.

## Asthma Survey Questionnaire & Work Role Function

The asthma questionnaire used in the TAS study was developed and validated by a group of industrial hygienists, occupational physicians, epidemiologists and survey design experts at the UTHealth School of Public Health (17). Questionnaire items were originally derived from the International Union against Tuberculosis and Lung Diseases bronchial symptoms questionnaire, supplemented with questions on physician-diagnosed asthma and age at asthma diagnosis (75). The final instrument had 43 main questions in four sections. Completion time was 13 to 25 minutes.

A validation study was conducted in a sample of 118 Houston area healthcare workers. For criterion validity, items on asthma and asthma symptoms were compared to physician diagnosis of asthma and to the presence of bronchial hyperresponsiveness, measured using methacholine bronchial challenge testing and a previously validated 5-item discriminant function predictor (DFP) (17). Questionnaire items correctly classified physician-diagnosed asthma in 93% of cases, with a sensitivity of 71% and specificity of 98%. Test-retest reliability and internal consistency of the asthma and allergy items ranged from 75% to 94%. The final instrument was formatted in two versions: a hard-copy version and an identical web-based version (6).

As mentioned earlier, the literature on measuring work role functioning and quality of life in asthma is sparse. There is a need for studies detailing external and socio-economic factors influencing respiratory-related absence of work. One way of assessing presenteeism is by examining work capacity in relation to health status, also known as work role function. The Work Role Function Questionnaire (WRFQ) is a validated questionnaire that measures work role function of an individual in detailed demands of work capacity (76). It provides an overall work functioning score along with an estimate of work functioning in relation to each domain of work demands that include work scheduling, output, physical, mental and social demands (76).

The WRFQ allows an approximation to measuring presenteeism. This dissertation has a unique focus on assessing these indicators by incorporating previously validated measures for work role functioning in the existing questionnaire in Specific Aim 2. To our knowledge, this is the first study to assess work role functioning in HCPs with asthma.

To summarize, given the time passed since the 2003 TAS, together with changes in cleaning/disinfection practices and subsequent literature on WRA, a repeat study of asthma in Texas HCPs seemed justified. In order for this to be successful, however, the 2003 JEM and questionnaire needed to be revised and updated. Specific Aims 1 and 2 address this process.

## PUBLIC HEALTH SIGNIFICANCE

Asthma prevalence is increasing in the US, and WRA (including both OA and WEA) likely accounts for 15-25% of all asthma. HCPs are among the occupational groups at risk for WRA and comprise around 8% of the total US workforce. Jobs in the healthcare sector continue to grow. Occupations related to health care are characterized by a multiplicity of roles, tasks and work environments, with associated exposure risks that have not been completely characterized and that have changed over time creating a gap in the literature. The dissertation helped in addressing this gap and hence addressing the long term goal of reducing the overall burden of WRA among HCPs.

The main aim of this dissertation was to measure associations between occupational exposures to cleaning and disinfection products and practices, and WRA among Texas HCPs. Since 2003, cleaning and disinfecting products and practices in hospitals have evolved. In part, there has been a reported increase in use of cleaners and disinfectants related to green chemistry and engineering; some "old" products have reemerged as well (33, 77). This dissertation reexamined these associations using updated exposure and outcome measures, while also examining the impact of asthma on HCPs lives and work.

The resources developed through this dissertation should play an important role in guiding future researchers in conducting studies pertaining to occupational asthma. These are the newly developed questionnaire and a revised JEM. The questionnaire is one-of-a-kind, with inclusion of parameters related to workplace absenteeism, presenteeism and work-related quality of life. This will be helpful for future researchers studying different populations across the globe. Moreover, studies and literature on JEMs specific to occupational asthma are still relatively sparse. The JEM developed as part of this study is also one-of-a-kind, with an extensive list of occupational exposures, healthcare occupations and practice settings. This will be a useful addition in the literature, and a helpful resource for further research on occupational asthma in future.

Lastly, the results of the study yielded knowledge about current status in terms of occupational asthma, and how the exposures are related to it, whether strong or weak. With that information in hand, it could assist policymakers in designing specific interventions and policies on occupational asthma in order to reduce the prevalence and severity of the disease overall.

# METHODS

## Initial Process

As an initial step in the updating of the JEM, beginning in Fall 2015, walk-throughs and focus group sessions were conducted in three large Houston area hospitals (a general tertiary level hospital – Methodist, a pediatric hospital – Texas Children's, and a cancer center – MD Anderson), two area nursing homes and two outpatient clinics, to reflect smaller healthcare settings. The walkthroughs were conducted by a multidisciplinary team with expertise in occupational medicine, toxicology, pulmonary medicine and hospital safety, focusing on areas where potential at-risk practices may occur, including patient care, operating theaters, procedure rooms and cleaning/disinfection areas. The data gathered from walkthroughs was discussed among the experts and used to update a list of potential respiratory hazards in healthcare settings. Simultaneously, a total of six focus group sessions were also conducted with key healthcare and services personnel at each of the walk-through locations. Each focus group session was guided by same facilitators (78). The discussions centered on location-specific cleaning practices, products, medication administration, use of personal protective equipment and perceived changes in cleaning/disinfection practices over the years.

The walk-through and focus group observations were contrasted and used to complement each other. This information was summarized, in preparation for a workshop of experts held in October 2015 at UTHealth School of Public Health. The objective of the workshop was to generate initial drafts of the new JEM structure and survey questionnaire.

## Methods for Aim 1

### *JEM Development*

Attendees, consisting of a diverse group of occupational health professionals, at the October 2015 workshop discussed and incorporated current cleaning and disinfection practices and products, and administration of newer aerosolized medications to the JEM originally developed in 2003.

### *JEM Coding*

After finalizing the updated JEM structure, the cells corresponding to job-practice by exposure categories were coded. This process was conducted by a group of five to seven experts comprised of industrial hygienists, occupational physicians, toxicologists and occupational health professionals who work in healthcare settings (hospitals and outpatient clinics). The panel members used their professional experience, the literature and any available quantitative measures to help guide them. The same coding scale used in 2003 was used again. “Exposed” was defined as the probability that a worker in a given cell is exposed to the product or task at least once per week. A code of ‘0’ was assigned if there was a high probability of no exposure. Within the “Exposed” categories, there were two levels. A ‘1’ was assigned when the probability of exposure existed, but was low. A ‘2’ was assigned when the coder felt there was a high probability of exposure. Each coder was asked to independently assign codes to the entire JEM. Then the JEM was reviewed by the research team to identify areas of agreement and discrepancy. Meetings were then scheduled with the panel to resolve the discrepancies by consensus.

In Aim 3, the coded matrix was applied to each respondent’s current and longest held job as a HCP, based on the job title and practice setting reported by respondents in the questionnaire.

In summary, we sought to: a) preserve the original JEM categories, so as to allow comparison of results to the 2003 findings; b) include more specific exposure categories that reflect certain tasks, application methods and work environments; c) broaden nursing professions to capture differences between nurse practitioners, registered nurses, licensed vocational nurses and nurse aides; and d) expand practice settings to specific areas within and outside hospitals, such as surgical suites and outpatient clinics.

***JEM Construct Validation***

A limited validation of the JEM was conducted as part of Aim 3, after data collection. There is limited literature on how a JEM should be validated. In fact, this is one of its limitations. The different types of validation used in survey research are criterion validity, content validity and construct validity. Of these, **criterion validity** (which measures the performance of a new procedure or test against a benchmark or 'gold standard'), is not feasible for JEMs because of the absence of a gold standard. Instead, we focused on content validity and construct validation for our JEM. **Content validity** is based on expert knowledge, obtained from various information sources, including the literature and content experts. To optimize content validity, our JEM was coded by a group of experienced industrial hygienists, occupational epidemiologists and occupational medicine physicians. **Construct validity** is considered present when a new procedure or test is able to predict *a priori*-determined associations. In this study, the construct validation was conducted after the JEM was merged with the survey data. For this, exposure to an established respiratory irritant (bleach) and two sensitizers (glutaraldehyde and powdered latex), as defined by the JEM, were tested for associations with NOA and an asthma symptom (wheezing). The expectation was that these exposures should be positively associated (OR>1) with one or both of these outcomes. This was performed concurrently with Specific Aim 3.

## Methods for Aim 2

### *2016 Questionnaire Development*

The previously validated 2003 survey questionnaire was revised and updated to include new exposures, components related to occupational history, and to better characterize WRA in terms of exacerbated or occupational asthma. Along with these components, one new aspect was added as a surrogate for socioeconomic impact of asthma, by measuring work-related presenteeism in addition to missed work days.

To assess the socioeconomic impact of asthma, in addition to already existing questions regarding days absent from work due to asthma, the validated Work Role Function Questionnaire (WRFQ) was added to the questionnaire. This allowed us to measure self-perceived health in relation to work capacity, as a surrogate of presenteeism (i.e., working despite not being well) in this collective. The WRFQ measures self-perceived difficulties in performing a job due to health problems (76). All the versions used until now (American English, Canadian French, Brazilian Portuguese, Dutch and Spanish spoken in Spain) have shown good psychometric properties (76).

The WRFQ consists of 27 questions on performing work tasks over the previous two weeks (76, 79). As used in literature previously, these 27 items were collapsed into

5 scales: Work Scheduling Demands, Physical Demands, Mental Demands, Social Demands, and Output Demands (76). Responses are scored on a 6-point Likert scale (All of the time, most of the time, half of the time, some of the time, none of the time, and does not apply to my job) that measures how often the respondent is limited in his/her ability to perform tasks. Points were then summed and converted to a 100-point scale, where ‘0’ represents being limited “all the time” and ‘100’ represents not ever being limited (79, 80).

***Initial Testing of Questionnaire***

The new questionnaire was pilot tested by administering it to a small convenience sample of 14 local Houston healthcare professionals, both with and without asthma. This pilot assessed ease of use, timing and comprehensibility of the questionnaire. Based on the respondent’s feedback, further refinements were made, leading to the final questionnaire for use in the statewide survey.  Time to completion ranged from eight to twenty minutes. The final questionnaire was formatted in two versions: a) on paper and b) an Internet-based version. These formats were compatible for direct data entry into the HP Teleform™ (Version 11, Sunnyvale, CA).

In summary, the questionnaire was updated based on more recent literature regarding asthma definitions, together with the knowledge gained through healthcare setting walkthroughs and expert consultations. The new version of the questionnaire includes: 1) updated asthma and asthma symptom items, based on more specific and newer updated definitions of asthma, WRA, new onset asthma and WEA; 2) indicators to measure asthma burden through the incorporation of the WRFQ; and 3) an updated list of self-reported jobs and practice settings that can be linked to the new JEM.

***Survey of Texas HCPs***

Five groups of Texas health professionals with active professional licenses or certification in 2016 were targeted for a cross-sectional confidential mail survey of asthma: physicians (n=61,661), nurses (n=361,719), respiratory therapists (n=13,223), occupational therapists (n=12,556) and nurse aides (n=108,718).

For physicians, nurses, respiratory and occupational therapists, a stratified random sample was generated from the most current state professional licensing boards. These are the Texas Medical Board for physicians, Texas Board of Nursing for nurses, Executive Council of Physical Therapy and Occupational Therapy Examiners for occupational therapists and Texas Department of Health for respiratory therapists. Lists of licensees and mailing addresses are in the public domain and easily obtainable, in computerized format. The licensing board registries included: name, age, license number, telephone number, address, status of license, and county of residence. The registries are updated continuously and the licenses are renewed yearly. The sampling frame was defined as all members listed on the most current list of active licensees. The sampling unit was defined as individual members on the mailing lists eligible to participate in the study. For the nurse aides, who are not required to have a state license but who may be certified, we used the most recent registry of certified nurse aides (CNAs) from the Texas Department of Aging and Disability Services (81-84)

For the first four groups, based on sample size calculations to assure $\alpha$=0.05 and $\beta$=0.20, adjusted for an expected response rate of at least 50% and an expected proportion of eligible respondents of 90%, the required sample size for each group was calculated as 1,400 each (total = 5,600) (85). For the CNAs, sample size based on $\alpha$=0.05

and margin of error of 3% was 1,057. The sample size calculations for the first four groups were conducted similar to the original TAS study, while for CNAs, the sample size calculations were done separately based on another method available in literature for a single-group cross-sectional study (86), as the latter was conducted as a separate pilot study later. With 50% expected response rate, a total of 2,114 surveys were to be sent to CNAs. Since nurses may practice in a variety of settings, they have consistently been identified as being at risk for asthma and prior studies have been limited in the extent to which their work habits and environments have been characterized. As a result we oversampled this group, by increasing the number of surveys mailed to them in each subgroups (RNs=1,600, LVNs=800 and APRN=800) (total n=3,200). In addition, given historically low response rates of physicians to mail surveys (87), we also did some limited oversampling of this group to assure a sufficient number of physicians for final analysis (n=400 additional surveys for a total of 1,800). Thus, a total of 9,914 surveys were sent to the target population.

Inclusion criteria for participants were (a) age 18 years and older and (b) working as a nurse, nurse aide, occupational therapist, physician or respiratory therapist with an active license or certification.

### ***Survey Conduct***

Participants received a general description of the nature of session and measures to protect confidentiality. Based on the approach of Dillman (88), five contact waves with potential study participants were initially planned. However, due to lower response rates than expected, we later modified the approach to include an additional round of postcard mailing, in part because the mailing period overlapped with the end-of-year holiday season. We also added a token $1 incentive to two of the survey contact waves. This approach was conducted as follows. An initial “warm contact” letter was followed by a hard copy questionnaire, an explanatory cover letter, a $1 token financial incentive, and a business reply envelope. Participants were given the option of returning the hard copy questionnaire by mail or completing it online.  Information on how to complete the survey online rather than by hard copy was also included. Follow-up post card reminders were sent in two rounds (one of which included a holiday seasons greeting), a replacement questionnaire with another $1 incentive and a final reminder letter was mailed subsequently over the next three months.

Data entry and cleaning: The returned surveys (by mail or directly over the Internet) were scanned into the HP Teleform™ system for direct data entry; each questionnaire was visually scanned for errors, underwent routine range and logic checks and the final dataset was prepared for merging with the JEM dataset.

## Methods for Aim 3

***Study Variables***

The main outcome asthma (presence vs. absence) was examined in different ways: (a) physician-diagnosed asthma, (b) new onset physician-diagnosed asthma after entry into the health profession (as a surrogate for occupational asthma), (c) work-exacerbated asthma (WEA) and (d) bronchial hyperresponsiveness symptoms. Of these, (a), (b) and (d) allowed comparison to the 2003 results and (c) allowed us to distinguish between new onset and preexisting asthma worsened by the workplace. Physician-diagnosed asthma was defined as a 'Yes' response to the question '*If yes, has your asthma been confirmed by a doctor?*'. New onset asthma among persons with a history of physician-diagnosed asthma was calculated by comparing the age at which this diagnosis was made to the number of years employed as a healthcare professional; this served as a surrogate for OA. WEA was defined as a 'Yes' response to both the questions '*Have you had an attack/ episode while you were at work in the last 12 months?*' and '*If Yes, do you know what triggered the last attack/ episode of asthma while you were at work?'*. Presence or absence of bronchial hyperresponsiveness symptoms was determined based on a previously validated 8-item symptom predictor of $PC_{20}$ (provocative concentration of methacholine causing a 20% fall in $FEV_1$), published in 2006 (17). The eight items addressed were trouble breathing, wheezing and/or attacks of shortness of breath in the previous 12 months, nocturnal cough and/or chest tightness in the previous 12 months, and current allergic symptoms when in the presence of animals, feathers, dust, trees, grasses, flowers, or pollen.

The main independent variables were occupational exposures, as defined by the

JEM. Exposure to an accidental spill or chemical release was a separate exposure variable, obtained from the questionnaire. All exposure variables were categorical. Covariates in the analysis included from the survey were age, sex, race/ethnicity, type of profession, years as a healthcare professional, smoking status, and obesity (body mass index [kg/m$^2$] $\geqslant$ 30). Atopy was calculated using variables related to exposure to dust and animals.

***Data Analysis***

For the Aim 3, we obtained estimates of both counts and prevalence of physician-diagnosed asthma, NOA, WEA and BHR symptoms as initial descriptive statistics. The mean, median, and frequency distribution of each independent variable were calculated for all variables including exposures and different occupations, *viz.,* nurses, physicians, occupational therapists, respiratory therapists, and nurse aides.

Being a complex survey dataset with samples from various units across the state, weighting adjustments with proportions based on licensing data for healthcare professionals were applied to the data to overcome the problem of under or over-representativeness of the sample. Stata/SE v. 14.0 was used for the statistical analyses (89). Further, Stata's survey data commands were used to appropriately take into account the sample weights (90).

Some participants (n=394) had not answered all the 8-items for the BHR scale. Rather than restricting the analysis to only participants who completed all eight items, we applied the following strategy to be able to use as much of the information provided as possible. BHR scores were calculated if at least 80% of the scale items were complete, and were coded missing otherwise. For all the one or more missing 8-item responses, we created two scenarios. One was the best case scenario where all missing items were coded to zero except wheezing, and other being the worst case scenario where all missing items were coded to one except wheezing. If the BHR score for first (best) scenario was equal to one, we kept those values since the score could not be less than or equal to 0.5 despite the number of missing items. For the second (worst) case scenario score was equal to ten, we kept those values since the score could not be greater than 0.5 despite the number of missing items. This helped in imputing 184 further responses. Similarly, for observations with incorrect or missing age, we imputed the age based on the number of years in the healthcare profession and the average number of years at which the profession started (e.g., 26 years for physicians, 22 years for nurses, RTs and OTs, and 16 years for CNAs).

As had been the case in the 2003 TAS, we anticipated a high degree of collinearity between some of the exposure variables (e.g., endoscopy and glutaraldehyde), so collinearity among independent variables was assessed by a correlation matrix, with significant correlations defined as a Pearson coefficient ≥0.70). We knew this would later result in the need to construct individual models for each exposure class. To assure continuity and comparability of the study population across these different models, we reduced the sample to a set consisting only of persons for whom there were no missing data for either independent or outcome variables; this was termed the ‘analytical sample’. The sample of participants who had some missing data was termed the ‘excluded sample’. Differences in the distribution of variables in the analytical and excluded samples were then tested for significance using chi-square analysis.

After the descriptive statistics, univariate analysis was performed to examine associations between each independent variable and two main outcomes, new onset asthma and bronchial hyperresponsiveness, for this dissertation. For the univariate analysis, unadjusted associations were estimated using logistic regression models for each independent covariate with each outcome. Associations were expressed as the crude odds ratios (OR) and corresponding 95% confidence intervals (CI). Variables with $p \leq 0.25$ with outcomes and/or those identified as important confounders based on the literature were included in the final models. Multivariable regression models were developed for each of the two asthma outcomes using a separate model for each cleaning agent to avoid collinearity due to correlated exposures and accounting for potential confounders.

Results for the final models were expressed as the adjusted ORs with corresponding 95% CIs, with a 95% CI not including the null considered as statistically significant. Goodness-of-fit was assessed using simulated Wald and Hosmer-Lemeshow test, as these are the recommended approaches for survey sample data, with $p<0.05$ considered as indicative of a poor fit (91).

Separate analyses were conducted for assessing presenteeism and burden of asthma in healthcare workers using the WRFQ questionnaire and questions related to missed days at work. The response options for the 27-item WRFQ questionnaire ranged on a five point scale as 0=difficult all the time (100%), 1=difficult most of the time, 2=difficult half of the time (50%), 3=difficult some of the time, and 4=difficult none of the time (0%). Work role functioning for the analytical sample was assessed by deriving weighted percentage score means and standard errors for all the five domains and overall scale by adding the answers in the subscale, dividing by the number of items and then multiplying by 25 to obtain percentage scores between 0 (difficult all the time) and 100 (difficult none of the time). The responses on ‘Does not apply to my job’ were transformed to missing values. The WRFQ analysis was only conducted for the analytical dataset with no missing values. Weighted 25$^{th}$, 50$^{th}$, (median) and 75$^{th}$ percentiles were calculated for each subscale and overall scale. Reliability for all the scales was assessed using Cronbach’s alpha. All the mentioned statistics were also calculated by stratifying participants into those with and without a physician diagnosis of asthma (i.e., response ‘Yes’ or ‘No’ to the question ‘*If yes, was your asthma confirmed by a physician?*’).

Missed work days were assessed based on a ‘Yes’ response to the question “*In the last 12 months, have you had to miss any days of work due to ANY health-related issue (whether asthma or other)?*” and then number of days entered for days missed due to health-related issues and days missed due to asthma or breathing problems. Weighted mean number of days in the last 12 months for both physician-diagnosed asthmatics and non-asthmatics were calculated. P-values of the differences in the means were calculated by weighted t-test. Weighted 25$^{th}$, 50$^{th}$ (median) and 75$^{th}$ percentiles were obtained for both these groups separately for missed work days due to overall health issues and missed work days due to asthma or breathing problems.

# RESULTS

## Aim 1

The final version of the revised JEM is presented in Appendix A. Table 1 shows the changes in components of the previous JEM in detail. The complete JEM structure was finalized in early summer 2016. Instrument cleaning was subcategorized into four further categories: endoscopy, glutaraldehyde, orthophthalaldehyde, and enzymatic cleaners. Building surface cleaners were also subcategorized into four categories: bleach, quaternary compounds, sprays and floor waxing/stripping/buffing for building surface cleaners. The types of procedures were also further subcategorized as patient care cleaning, instrument cleaning, endoscopy, and building surface cleaning that included spraying and floor stripping/waxing and buffing.

To allow comparisons to the 2003 TAS, each major category was also subclassified as pre-2003 and post-2003. The exception was for powdered latex glove use, since this exposure was already broken down into time periods (pre-1992, 1992-2000 and post-2000). Instead, an additional time period was added to reflect changes since the TAS (2001-2006 and 2007 onwards).

To ensure that exposures were specifically captured for each different nursing occupation, the nursing category was subcategorized into four further categories: general/specialized, operating room, administrative and others. Job categories not adequately captured such as dental hygienists and other allied healthcare professionals were removed. Hospitals and health departments were classified into rural (<50,000 population) and urban (≥50,000) to acknowledge possible geographic differences in exposures. Other changes are further detailed in Table 1.

For the JEM construct validation, we evaluated previously established associations between exposure to two sensitizers (glutaraldehyde and powdered latex gloves) and one irritant (bleach) with NOA and one of the symptoms of asthma (wheezing) using exposure data generated from our updated JEM. Table 2 shows the associations for the two sensitizers and bleach with NOA and wheezing. Glutaraldehyde (OR 1.23, 95% CI 0.80-1.88), powdered latex glove use from 1992-2000 (OR 1.49, 95% CI 0.85-2.63) and bleach (OR 1.60, 95% CI 1.02-2.52) were all positively associated with NOA as would be expected based on the literature. Powdered latex glove use from 1992-2000 was also positively associated with wheezing (OR 1.09, 95% CI 0.82 – 1.43) in the expected direction. However, bleach use and glutaraldehyde were inversely associated with wheezing (OR<1), and not in the initially expected direction.

**Aim 2**

The components that were added to the questionnaire were WEA questions, effects on daily activities, unplanned care for asthma, assessment of work-hours and shifts and the WRFQ. The components that were updated were asthma symptoms (awakening at night), missed days of work related to WEA, occupational history with an updated list of self-reported exposures to match with the updated JEM, an updated comprehensive list of jobs and practice settings for professions, and time periods (i.e., previous 12 months) for wheezing and shortness of breath. All the changes and new components are mentioned in detail in Table 3. Not all of these additions were analyzed in Specific Aim 3 of the dissertation.

Of the original 9,914 intended participants, the questionnaire was mailed to 9,893 HCPs in Texas, after removing incorrect addresses identified by the postal service. Table

4 shows the response rates by type of response and healthcare professions. The overall response rate across all professions was 34.8% (n=3,444). This number also accounted for returned refusals considered as response. After the first round of mailing, a total of 577 bad addresses/relocated addresses were identified based on returns. New replacements from the respective randomized lists were sent out to the identified bad addresses. Of these, 135 participants responded. The final number of responses, after accounting for bad addresses and refusals, was 3,318. Response rates were highest among occupational therapists (41%, n=573), followed by registered nurses (40.2%, n=1,285), respiratory therapists (37.9%, n=529), physicians (34.1%, n=613) and lowest among certified nurse aides (21.1%, n=444). Of these, the highest percent of complete responses was among occupational therapists (97.4%) and lowest was among physicians (94.8%). However, 126 participants indicated their refusal to participate by returning a blank questionnaire. In comparison to the 2003 response rate (66%), after excluding CNAs (which were not included in 2003), the overall response rate was 38.5%.

Survey weights were applied to the entire dataset by using the total number of professionals obtained from the original license or certification registries for each group. Adjustment factors based on population weights were calculated by dividing the percent population of each group in the original registry by the percent population in the study sample. Weights were then assigned based on the adjustment factor for each occupational group for all five professional groups.

## Aim 3

Table 5 summarizes the descriptive statistics for the final analytic sample with complete responses (n=2,427), and the excluded missing data sample with at least one or more missing values for exposure or outcome (n=899). The missing data sample (i.e., excluded in the main analyses) was considered when one or more covariates for further analysis were missing due to missed responses from the survey. Only the analytical dataset (i.e. complete responses) was considered for main univariate and multivariate analyses.

The analytical and excluded samples differed significantly in terms of age, race and profession. Mean age among participants in the analytical sample (49.5 years) compared to the excluded sample (51.8 years). For race/ethnicity, there was a significantly higher prevalence of non-Hispanic whites, and lower prevalence of Hispanics in the analytical sample. Among professions, the percentage of physicians, nurses, RTs and OTs, was significantly higher in the analytical sample ($p<0.001$). There were no significant differences with respect to gender, atopy, obesity, smoking, and years as healthcare professional.

For occupational exposures, the analytical and excluded groups differed significantly with respect to orthophthalaldehyde use and powdered latex gloves use in the period 1992 to 2000.The prevalence of BHR was significantly lower in the analytical sample, but the prevalence of new onset asthma was significantly higher in the analytical sample.

The overall weighted prevalence estimates for the analytic sample for physician-diagnosed asthma, work-exacerbated asthma among physician-diagnosed asthma cases, new onset asthma and BHR-related symptoms were 16.4%, 4.0%, 7.1% and 31%, respectively (Table 5). By profession, new onset asthma was 7.7% for nurses, 7.6% for occupational therapists, 5.9% for respiratory therapists, 5.0% for physicians, and 2.6% for CNAs. For BHR symptoms, the corresponding numbers by profession were 34.7% for nurses, 38.3% for occupational therapists, 36.3% for respiratory therapists, 27.6% for physicians, and 30.5% for CNAs.

In the analytical sample, 84% (n=1,861) of respondents were female. The greatest number of women were nurses (39%), followed by OTs (18.5%), physicians (17.4%), RTs (16.5%), and CNAs (8.5%). The weighted prevalence of obesity was 29.2% (n=659). The majority of respondents, i.e. 58.2% (n=414), were Non-Hispanic whites, and 74.5% (n=1,824) respondents were never-smokers. The prevalence of atopy was 15.5% (n=394).

As expected, strong collinearity (>70%) was found among occupational exposures, mainly within instrument cleaning (glutaraldehyde, endoscopy, orthophthalaldehyde), building surface cleaning (sprays with quaternary compounds and bleach), and latex glove use (among all time axes).

Table 6 presents the univariate analyses for NOA and BHR symptoms. There were some significant associations between NOA and some of the covariates. For race, a significant inverse association was observed for NOA among non-Hispanic blacks (OR 0.36, 95% CI 0.15-0.86) as compared to non-Hispanic whites. Atopy was associated with NOA (OR 2.50, 95% CI 1.62 – 3.86). For years as healthcare professional, the odds of NOA increased with advancing age across all professional groups, with ORs ranging from 4.47 to 9.37.

For the covariates, there were significant associations between BHR symptoms and male gender (OR 0.62, 95% CI 0.48-0.82) and atopy (OR 6.88, 95% CI 5.10-9.30). Males were less likely to report BHR symptoms compared to females (OR 0.62, 95% CI 0.43 – 0.54). Associations with other covariates with BHR such as race, obesity, smoking and seniority were not significant.

Table 7 shows the crude and adjusted ORs for both NOA and BHR symptoms. For NOA, positive and statistically significant crude associations were found for orthophthalaldehyde use (OR 2.04, 95% CI 1.38-3.02), bleach and quaternary compounds (OR 1.60, 95% CI 1.02-2.25 for each), and use of sprays (OR 1.74, 95% CI 1.10-2.76). Negative associations were found for latex glove use from 2001 to 2006 (OR 0.37, 95% CI 0.16-0.84), and after 2007 (OR 0.37, 95% CI 0.16-0.86).

Multivariate models with NOA as the outcome were adjusted for race, atopy, obesity, smoking status and years on the job. There were seven significant associations for tasks and compounds with NOA. For tasks, the adjusted odds for NOA were increased for sprays used in building surface cleaning (OR 2.03, 95% CI 1.26 – 3.27). For compounds, the adjusted odds for new onset asthma were significantly increased for orthophthalaldehyde used in instrument cleaning (OR 1.93, 95% CI 1.29-2.88), bleach and quaternary ammonium compounds used to clean building surfaces (OR 1.83, 95% CI 1.14-2.93 for both), and sprays applied to cleaning surfaces (OR 2.03, 95% CI 1.26-3.27). Inverse (i.e., protective) odds were observed for use of latex gloves from years 2001-2006 (OR 0.30, 95% CI 0.13-0.72), and 2007 onwards (OR 0.31, 95% CI 0.13-0.73). Positive, yet non-significant associations with NOA were observed for patient care cleaning and disinfection (OR1.82, 95% CI 0.85-3.92), instrument cleaning (OR 1.19 95%

CI 0.77-1.85), enzymatic cleaners used in instrument cleaning (OR 1.26, 95% CI 0.71-2.23), latex glove use before 1992 (OR 1.30, 95% CI 0.73-2.32) and latex glove use from 1992-2000 (OR 1.09, 95% CI 0.70-1.69). A history of exposure to a spill at the workplace was positively associated with NOA (OR 1.06, 95% CI 0.48-2.37).

For BHR symptoms, statistically significant inverse crude associations were found for patient care cleaners and disinfection (OR=0.60, 95% CI 0.44-0.83). Similar associations, although not statistically significant, were found for instrument cleaning including endoscopy (OR 0.92, 95% CI 0.72-1.17) and orthophthalaldehyde (OR 0.88, 95% CI 0.71-1.09), building surface cleaning including bleach (OR 0.81, 95% CI 0.64-1.02) and sprays (OR 0.82, 95% CI 0.65-1.04). Non-significant associations were found for glutaraldehyde (OR 1.01 95% CI 0.79-1.28) and enzymatic cleaners (OR 1.16, 95% CI 0.83-1.60). In the adjusted analysis with BHR symptoms as the outcome, only an inverse association with a self-reported exposure to a chemical spill at work was statistically significant (OR 0.53, 95% CI 0.32 – 0.88). No other significant associations were found, and most of the point estimates were protective (OR <1.0).

For NOA, model fit was good for all associations except glutaraldehyde and latex use before 1992. Model fit was good for all models that had BHR symptoms as the outcome.

Table 8 shows the mean, standard error and percentile (25$^{th}$, median and 75$^{th}$) for each WRFQ subscale (work scheduling, output, physical, mental, social demands) and the overall scale for the weighted sample of 2,427 individuals. Work scheduling and social demand subscales scored the highest mean (85.2 and 84.6, respectively), and the mental demands subscale scored the lowest (82.9). For reliability assessment, Cronbach alpha coefficients were 0.99 for the overall scale and above 0.94 for all the subscales.

Table 9 shows work-role functioning scores and missed work days due to health issues and asthma or breathing problems in the last 12 months by physician-diagnosed asthma status. For physician-diagnosed asthma cases, the average number of days missed in the last 12 months due to overall health issues and asthma or breathing problems were 9.9 (1.85) and 7.5 (2.12), respectively. For non-asthmatics, the average number of days for health issues and asthma or breathing problems were 13.5 (2.70) and 4.0 (0.79) respectively. The differences among physician-diagnosed asthmatics and non-asthmatics were not significant. Seventy-six percent (7.5 out of 9.9) of the missed days due to health-related issues among asthmatics were due to days missed due to asthma or breathing problems. For non-asthmatics, that proportion was 30% (4.0 out of 13.5).

Table 9 also shows separate WRFQ subscale and overall scores by physician-diagnosed asthma status. For physician-diagnosed asthma, three subscales (work scheduling, output, social) and overall scores were significantly different ($p<0.05$), and those with asthma scored lower on all the WRFQ subscales and overall scales compared to those without asthma. The overall mean score for physician-diagnosed asthma cases was lower (meaning more difficulty at work due to physical health or emotional problems) compared to non-asthmatics (82.6 *vs.* 84.3). The 25$^{th}$ percentile scale for overall scores showed a significantly lower mean score (74.1) for physician-diagnosed asthmatics compared to non-asthmatics (84.3).

To examine changes since the 2003 TAS, we also compared the main results from this study to those from the earlier study. Since CNAs were not included in 2003, the comparison was based only on nurses, physicians, respiratory therapists and occupational therapists. In contrast to the larger sample, there was no significant difference between the analytical and excluded samples in terms of the prevalence of new onset asthma (7.6% *vs.* 5.9%, respectively), although the difference with respect to BHR symptoms persisted (Table 10). In the multivariable analysis, there was little change in the direction and magnitude of the previously described associations, except that the previously significant inverse association between exposure to a spill at work and BHR symptoms became nonsignificant (Table 11).

Table 12 summarizes the comparison between the 2003 TAS and the current study. For NOA, the odds for patient care cleaners were essentially unchanged (1.82 *vs.* 1.60) and neither was statistically significant. The odds for instrument cleaning was reduced by nearly half compared to the previous study (2.22 *vs.* 1.19). There was no change observed in odds for building surface cleaners (2.03 *vs.* 2.02), both statistically significant. The odds for exposure to spills at workplace also decreased compared to previous study (ORs 1.06 *vs.* 1.23), and both were not significant. The odds for powdered latex glove use for all time periods after the year 2000 remained low and the magnitude was unchanged since the previous study (0.31 *vs.* 0.30). For BHR symptoms, the previously significantly increased odds following an exposure to a spill in the workplace (OR 2.02) had become “protective” (OR 0.53). Likewise, the odds for instrument cleaning reduced went from increased to no-risk (ORs 1.00 *vs.* 1.26), and was unchanged for building surface cleaners (ORs 0.84 *vs.* 0.63). The odds for powdered latex glove use remained low and had not changed since the previous study (ORs 0.78 *vs.* 0.77).

# DISCUSSION

This dissertation examined the associations between asthma and asthma symptom and cleaning and disinfection products and tasks, and the burden of asthma (i.e. missed work days and presenteeism) in HCW in 2018. We also compared the main results from this study to results from a similar study conducted in 2003.

The overall prevalence of NOA (7.1%) and BHR symptoms (31.0%) among healthcare professionals remains high and similar to 2003, but the associations with some of the risk factors has changed in important ways (6). Mainly, risk of NOA associated with cleaning and disinfection of medical instruments, such as endoscopes, and exposure to chemical spills at work has decreased. Glutaraldehyde, as a cold disinfectant, appears to be less of an issue than in prior years, probably due to a significant decrease in its use over the past 15 years. However, its replacement, orthophthalaldehyde, is associated with a two-fold increase in risk of NOA. Risks related to use of powdered latex gloves remain controlled, and there were no statistically significant associations with symptoms of BHR. In contrast, exposure to cleaning of building surfaces remains an important risk factor for NOA, particularly in association with use of sprays, bleach and quaternary ammonium compounds.

HCPs who are asthmatics do not miss more days of work than those who are non-asthmatics, and in fact the former may take fewer days off due to illness than the latter. However, a large proportion of the missed work days in HCPs with asthma are due to asthma or other breathing problems. Further, our results suggest that HCP asthmatics are more likely to work while being ill (i.e., presenteeism) than non-asthmatics, reflecting asthma's effect on work capacity and quality of life in these workers.

The decrease in what was previously a greater than two-fold risk for NOA associated with medical instrument cleaning is encouraging. Most likely, this reflects the greater use of enclosed and automated disinfection procedures for endoscopes in recent years, known as Automated Endoscope Reprocessors (AERs) (92). This technique has evolved over the past 10-15 years, incorporating several functions including leak testing, cleaning, post-cleaning rinse, followed by high-level disinfection (HLD), a second rinse and drying, all of which were previously done manually. Use of these AERs is now widespread (93).

Over this period, glutaraldehyde, the main cold sterilant used to disinfect medical instruments, and which had been repeatedly identified as a sensitizer capable of inducing asthma (94-97), has been steadily replaced by orthophthalaldehyde. Orthophthalaldehyde, being less volatile than glutaraldehyde, was expected to affect the respiratory system less (98). However, we also observed a two-fold significant increase in odds of NOA associated with orthophthalaldehyde. This is consistent with recent reports of acute respiratory symptoms and skin sensitization associated with use of orthophthalaldehyde (99, 100). Although it is used primarily for medical instrument disinfection, using the same enclosed system described above, orthophthalaldehyde is also used in other situations, some of which may entail a greater risk of direct exposure These include disinfection of other heat-sensitive devices such as electrocardiographic probes or cryosurgical equipment (98). Orthophthalaldehyde is also used in tasks related to cleaning the container systems, removing and rinsing soaked instruments, its disposal and while performing other maintenance procedures for AERs (98). More research is needed on the situations in which orthophthalaldehyde is used, as a precursor to limiting the opportunities it presents for direct exposure of workers.

The persistent risk of new onset asthma associated with the cleaning of general building surfaces is concerning. The magnitude of the association is similar to that found in the TAS, but the current study also examined risk associated with common tasks and cleaning products, which was not done in the 2003 TAS). Specifically, use of both bleach and quaternary ammonium compounds have been increasingly identified as risk factors for asthma, as has application of cleaners by spraying, in studies of nurses and housekeeping personnel (12, 39). The risk associated with bleach may be due to a resurgence in the use of bleach in the U.S. as part of intensified attempts to control hospital-acquired infections, particularly those associated with *Clostridium difficile* (58-61). In Europe, use of bleach remains widespread, in both healthcare and domestic environments, and has long been recognized as a risk factor for asthma (61). Quaternary ammonium compounds are used on a daily basis in hospitals for cleaning of floors, countertops and patient rooms as disinfectant sprays and wipes (101). Reports of asthma associated with exposure to quaternary ammonium compounds surfaced over 18 years ago (102), and have continued to appear (39, 73, 103, 104). Spraying a cleaning product increases the chance of aerosolization and subsequent inhalation of the chemical. Previous studies have described frequent use of cleaning sprays as a relevant and important risk factor for causing asthma (50, 105). In our walk-throughs (data not shown) we observed less use of sprays than cleaning wipes for general surface cleaning, but there were some instances, such as when cleaning wheelchairs and physical therapy equipment where a cleaner was first sprayed onto the equipment and then wiped down with a cloth. It is obvious that hospital-acquired infections must be controlled, but consideration of methods that simultaneously reduce opportunities for direct or bystander worker exposure are imperative (100).

The disappearance of risk of NOA associated with powdered latex glove use observed in the TAS was further confirmed by our results. This suggests that current latex control policies, from limiting the availability of these types of gloves, mainly to improvements in the manufacturing of less allergenic lightly powdered or non-powdered latex gloves, to their substitution with non-latex gloves remains an effective approach. Similar findings have been found by other authors (106-110).

Another encouraging finding was the absence of significant risk of BHR symptoms with any of the occupational exposures. In the 2003 TAS, both exposure to surface cleaners and to a chemical spill at the workplace were significantly associated with BHR symptoms; these no longer appear to be as prominent. In the case of chemical spills, this may be due to more standardized procedures for detecting, alerting and controlling a chemical spill, together with better training of personnel and use of appropriate personal protective equipment, in accordance with newer OSHA guidelines (111).

For building surface cleaning, there was no increased risk associated with BHR symptoms, despite an increased risk of NOA. The apparent discrepancy between risks associated with NOA but not with BHR symptoms deserves further examination and explanation, some of which is speculative. Asthma is a chronic disease; hence, once present, it is lifelong, as reflected by the accumulating prevalence of NOA with increasing age groups that we observed. In contrast, BHR symptoms may be more a reflection of acute or recent symptoms that can come and go. As an example, asthma may be present, but well controlled and asymptomatic. If this hypothesis is true, then the absence of associations with BHR symptoms is encouraging, suggesting that current controls are doing a better job of preventing acute symptoms than in the past. This should not be taken as reason for not continuing to chip away at the risk factors we identified in this study. The past successes in controlling asthma risk factors should serve to continue along the same path of finding safer ways to control healthcare-associated infections.

Finally, an important finding in this study is that asthma takes its toll on affected workers, in terms of missed work days and presenteeism. To our knowledge, this study is the first to assess the impact of asthma on work capacity, sickness absence and presenteeism, all of which are important aspects of quality of life. The large proportion of days missed due to asthma identifies an area for intervention, with better clinical management of asthma in combination with continued improvement in exposure control. Yet, even while they do not miss work, asthmatics appear to be more likely to continue working despite not being completely well. Our results showed consistently lower WRFQ scores, both overall as well as by domain, for asthmatics compared to non-asthmatics. Healthcare workers, as a whole, are reluctant to miss work. Whereas this certainly reflects great commitment to their job, it is not necessarily healthy. Supervisors and managers have an important role to play in encouraging employees to report when they are not well, and to develop contingency measures for covering patient needs while protecting their employees.

This dissertation has several strengths. The sampling and weighting strategy produced a statewide representative sample of five groups of HCPs, making results generalizable to similar workers in the U.S. Results may also be generalizable to other countries, particularly industrialized nations, but should be done cautiously. Cleaning and disinfection products may vary by country, or even in healthcare environments within a same country. In the U.S., accreditation of hospitals and other healthcare settings by the Joint Commission is common, and criteria and standards are uniform. The same may not be true in other countries. Likewise, the job duties ascribed to certain groups of HCPs, for example nurses or therapists, may be different than in the U.S. These considerations can limit the generalizability of our findings.

Another strength is that exposure classifications were based on a detailed and updated JEM that contained more exposure categories, subclasses, and some content and construct validation. JEM validation is not straightforward (and rarely performed); as such, it should be considered incomplete in our study. Nevertheless, the fact that for NOA all associations, and one for BHR symptoms, were in the expected direction provides some level of assurance of reasonably good functioning of the JEM. Using externally derived exposures decreases the chance of recall bias. The use of an updated questionnaire that incorporates more definitions of asthma, more symptoms in relation to work, and measures of asthma burden allowed for more detailed examination of asthma-exposure relationships and for additional analyses that go beyond the scope of this dissertation. The addition of CNAs, a previously unstudied group, is also a strength, allowing comparison to other nursing professionals. In addition, we prepared a stand-alone manuscript that describes asthma and BHR risks associated with working as a CNA, which has been added to this dissertation (see Journal Article in Appendix B). Finally, by preserving the same study design, sampling strategy and execution as the 2003 TAS, we were able to comment on changes in associations that have transpired since the original study, with findings of improvement in the control of some risks and persistence of others.

The dissertation also has several limitations; among these are a lower response rate than in 2003 and the presence of missing data for some of the variables. The overall response rate for this study was 34.8% (~39% for the four main occupational groups), compared to a response of 66% in the TAS, 10 years ago. In part, this reflects a general trend towards declining response rates in epidemiological surveys that has been widely described (112-114). Many reasons are suggested, including internal company policies limiting participation in research, an increase in security measures in new housing communities, and more rigorous filtering of mail to avoid spam and phishing, or ability to delete or ignore the emails or surveys due to high volumes. However, we did undertake measures to limit the effect of this lower response rate as the final number of responses in the analytical sample (n=2,427) was comparable to the TAS (n=2,738). This would likely be addressed by obtaining knowledge about representativeness of the sample to the census population. The weighting technique used in the dissertation assumes the sample to be a simple random sample from the population, however questionable to a certain extent due to low response rate.

There was missing data for some key variables for our analysis. The BHR symptom variable was constructed based on responses to eight questions. Missing data in more than two variables out of eight, or missing any of the key covariates would lead to a missing count and a smaller analytical sample; this was a similar issue in the TAS. If missing, and restricting the level of acceptable uncertainty, we only imputed up to two of the eight items if at least 80% of the items (i.e., six) were nonmissing. Additional analyses could be done with the use of advanced statistical techniques (e.g., regression-based multiple imputations) (115) before the final results are published, and are beyond the scope of this dissertation.

## CONCLUSIONS AND NEXT STEPS

Based on the results in this dissertation, the prevalence of new onset asthma and BHR symptoms is similar to that observed in 2003. For those categories that are comparable between the two studies, the risks for new onset asthma remain unchanged for building surface cleaning, have decreased for instrument cleaning, and remain well controlled for powdered latex glove use. Within instrument cleaning, endoscopic procedures and exposure to glutaraldehyde are not significantly associated with either new onset asthma or BHR, possibly reflecting the greater use of enclosed and automated disinfection procedures for endoscopes, and the decline in use of glutaraldehyde in general. Instead, there is an increased risk of NOA in association with exposure to orthophthalaldehyde, which has largely replaced glutaraldehyde and merits further study.

The continued risk of NOA associated with cleaning of building surfaces is supported in this study by elevated risks associated with general cleaning compounds (bleach and quaternary ammonium compounds) and with spraying as a method of applying cleaning products. Alternatives to bleach and less use of aerosolizing procedures may help reduce this risk. Overall, the risk of BHR symptoms from workplace exposures appears to have decreased across the board, possibly reflecting a lower likelihood of acute symptoms in the presence of putative exposures to workplace risk factors. Having asthma as a healthcare professional creates an impact on work capacity and quality of life. Although asthmatics missed similar or even fewer workdays than non-asthmatics, a large proportion of missed days were due to asthma or breathing problems. Results also point to asthmatics being more likely to work while “ill” than non-asthmatics, an indication of presenteeism.

Beyond this dissertation, the next steps for the project include conducting multiple imputations to increase the size of the analytic sample, and performing more detailed analyses. In particular, examination of asthma risk by professions, especially within nursing categories is needed. Also, we will estimate associations for other asthma outcomes, in particular work-exacerbated asthma as well as analysis of other quality of life indicators.

# DISSERTATION TABLES

**Table 1.** Job-Exposure Matrix update (2014): summary of changes made to the original 2003 job-exposure matrix, and rationale.

| Axis | Old Component | New Component | Comments |
|---|---|---|---|
| **Exposure** | | | |
| Cleaning Agents/ Disinfectants | Instrument cleaning and disinfection | Subcategorized into<br>1. Endoscopy<br>2. Glutaraldehyde<br>3. Orthophthalaldehyde<br>4. Enzymatic cleaners | Subcategorized to better capture the procedure type and chemical products used, and identified in the literature as risk factors. |
| | Building surfaces cleaning and disinfection | Subcategorized into<br>1. Bleach<br>2. Quaternary ammonium compounds<br>3. Sprays<br>4. Floor stripping/ waxing/ buffing | Subcategorized to better capture exposure to specific compounds, and methods of application known to be risk factors |
| Powdered latex gloves | Powdered latex gloves | Added a newer time axis (Current), and changed previous axis from 2000-current to 2000-TAS | This is to capture changes in use of latex gloves over the period of time, and update to the present. |
| Adhesives/ Solvents/ Gases | Patient care, surface cleaning and miscellaneous | Removed Miscellaneous categories | This category did not capture useful information in the 2003 study and was removed. |
| **Time Axis** | All categories | A Pre-2003 and Post-2003 time axes were added to each category excluding powdered latex, which has pre-existing time axes as mentioned in powdered latex gloves category. | This allowed comparability between the original and newer versions of the JEM |
| **Job** | | | |
| Nurses (RN, LVN, and CNA) | All nursing categories | Subcategorized into 4 maim categories:<br>a. Generalized Medicine/ Surgery/ Specialized<br>b. Operating room nurses<br>c. Administrative nurses<br>d. Others | This was included to recognize the various levels of nursing roles . |
| Other Dental, Dental Hygienists and Other Allied Health Professionals | Miscellaneous job categories | These categories were deleted. | These categories were deleted, either because they were not adequately captured, or separate detailed studies were conducted on these populations. |
| **Practice Setting** | | | |
| Hospitals and Health Departments | Hospitals and health departments | Added Rural and Urban subcategories to all hospitals and health departments | To capture possible differences in exposures in rural and urban settings |

**Table 2.** Job-exposure matrix construct validation: Association[a] of sensitizers and irritant with NOA and wheezing for JEM Validation (n=2427 from analytical dataset).

| Outcome | Exposure Type | Exposure | Odds Ratio (95% CI) |
|---|---|---|---|
| NOA | Sensitizer | Glutaraldehyde | 1.23 (0.80 – 1.88) |
| | | Powdered Latex(1992-2000) | 1.27 (0.82 – 1.96) |
| | Irritant | Bleach | 1.60 (1.02 – 2.52) |
| Wheezing | Sensitizer | Glutaraldehyde | 0.77 (0.57 – 1.03) |
| | | Powdered Latex1992-2000) | 1.09 (0.82 – 1.43) |
| | Irritant | Bleach | 0.86 (0.65 – 1.12) |

[a] From weighted logistic regression models.

**Table 3.** Questionnaire update (2004): summary of changes made to the original 2003 survey instrument, and rationale.

| Questionnaire Section | Type of change | New Indicators/ Change in old Indicators |
|---|---|---|
| Asthma Symptoms | As is, along with new addition | Added item on awakening at night, based on Sunyer et al (116) |
| Work-exacerbated asthma (WEA) | New addition | Added question assessing episode of asthma at work in past 12 months, and trigger associated with it if known. |
| Wheezing/ whistling/ shortness of breath | As is, with changes | Changed time axis for symptoms from 'all the time' to 'past 12 months', for consistency with other studies. |
| Effects on daily activities | New addition | This new section is derived from mini-AQLQ questionnaire to measure the quality of daily life affected due to work-related asthma.(117) |
| Unplanned care for asthma | New addition | The unplanned care of asthma is a new section added to better capture work exacerbated asthma, based on newer published indicators |
| Occupational history | Changes | Updated list of exposures, jobs and practice settings based on new update of the JEM (As described in Table 1), to allow comparison of self-reported exposures to JEM-derived exposures.<br>Added a question to assess the number of work-hours and days (type of shift at workplace)<br>Added a new question to know the history of past 4 jobs and the most recent and longest held job of those |
| Work Role Functioning Questionnaire (WRFQ) | New addition | Added a new 27-item WRFQ questionnaire to measure the impact of WRA on work-related quality of life and functioning |
| Updated comprehensive list of jobs and practice settings | Changes | Jobs were further classified for each occupation such as general/special, operating room, administrative and other categories for all nursing professionals including registered nurse, licensed vocational nurses and nurse aides.<br>Practice settings were also further classified to incorporate both urban and rural facilities for hospitals and health departments |

**Table 4.** Summary of responses by occupation among Texas healthcare workers (n=9,914)

| Occupation | Initial Sample | Population Sent to (Final) | Total Responses by type: Paper | Online | Refusal | Total Responses | Non-blank Responses | % Non-blank Responses | % Response Rate |
|---|---|---|---|---|---|---|---|---|---|
| MD | 1800 | 1799 | 470 | 111 | 32 | 613 | 581 | 94.8 | 34.1 |
| OT | 1400 | 1397 | 444 | 114 | 15 | 573 | 558 | 97.4 | 41.0 |
| RN | 3200 | 3197 | 1017 | 228 | 40 | 1285 | 1245 | 96.9 | 40.2 |
| RT | 1400 | 1396 | 419 | 96 | 14 | 529 | 515 | 97.4 | 37.9 |
| Total HCWs | 7800 | 7789 | 2350 | 549 | 101 | 3000 | 2899 | 96.6 | 38.5 |
| CNAs | 2114 | 2104 | 366 | 53 | 25 | 444 | 419 | 94.4 | 21.1 |
| All Combined | 9914 | 9893 | 2716 | 602 | 126 | 3444 | 3318 | 96.3 | 34.8 |

*MD= Physicians, OT=Occupational Therapists, RN=Registered Nurses, RT=Respiratory Therapists, HCW=Healthcare Workers, CNAs=Certified Nurse Aides*

**Table 5.** Descriptive characteristics[a] of the analytical sample (n=2,427) and the excluded sample (n=899) of Texas healthcare workers.

| **Characteristics** | **Analytical sample (n = 2427)** | **Excluded sample (n=899)** | **p-value**[b] |
|---|---|---|---|
| **Age** (years) (mean ± SE) | 49.5 ± 0.35 | 51.8 ± 0.65 | 0.002 |
| **Gender** [n (%)] | | | 0.07 |
| Women | 1861 (83.7) | 648 (6.6) | |
| Men | 563 (16.3) | 153 (13.4) | |
| **Race** [n (%)] | | | <0.001 |
| Non-Hispanic white | 1414 (58.2) | 398 (44.0) | |
| Hispanic | 448 (18.0) | 154 (21.6) | |
| Non-Hispanic black | 246 (11.8) | 119 (17.3) | |
| Others | 316 (12.0) | 146 (17.1) | |
| **Atopy** [n (%)] | 394 (15.5) | 140 (18.0) | 0.17 |
| **Obesity** | | | 0.66 |
| (BMI ≥ 30 $kg/m^2$) [n (%)] | 659 (29.2) | 204 (30.2) | |
| **Smoking** [n (%)] | | | 0.17 |
| Never smokers | 1824 (74.5) | 619 (75.3) | |
| Current smokers | 114 (5.7) | 51 (7.5) | |
| Former smokers | 486 (19.8) | 142 (17.2) | |
| **Job seniority** [n (%)] | | | 0.28 |
| 0-10 years | 621 (25.7) | 220 (29.8) | |
| 11-20 years | 674 (26.9) | 203 (25.3) | |
| 21-30 years | 531 (20.8) | 183 (20.2) | |
| ≥31 years | 598 (26.6) | 196 (24.7) | |
| **Profession** [n (%)] | | | <0.001 |
| Physicians | 423 (11.6) | 146 (9.7) | |
| Nurses | 945 (69.6) | 300 (53.4) | |
| Respiratory Therapists | 401 (2.5) | 131 (2.0) | |
| Occupational Therapists | 449 (2.5) | 112 (1.5) | |
| Certified Nurse Aides | 206 (13.7) | 208 (33.4) | |
| **Physician-Diagnosed Asthma** (PDA) | 416 (16.4) | 113 (13.0) | 0.04 |
| **Work-Exacerbated Asthma** (among PDA) | 19 (4.0) | 5 (3.1) | 0.45 |
| **NOA** [n (%)] | 167 (7.1) | 32 (4.2) | 0.02 |
| **BHR Symptoms** [n (%)][c] | 778 (31.0) | 276 (40.2) | <0.001 |
| **Cleaning agents** (>2003 for all) | | | |
| Patient cleaning & disinfection | 2095 (88.2) | 525 (87.1) | 0.55 |
| Instrument cleaning | | | |
| Endoscopy | 724 (29.4) | 174 (26.7) | 0.28 |
| Glutaraldehyde | 713 (28.6) | 172 (26.4) | 0.38 |
| Orthophthalaldehyde | 960 (46.4) | 222 (39.3) | 0.01 |
| Enzymatic cleaners | 483 (10.6) | 110 (10.1) | 0.75 |
| Building surface cleaning | | | |
| Bleach | 1775 (75.8) | 449 (76.5) | 0.73 |
| Quaternary ammonium compounds | 1775 (75.8) | 449 (76.5) | 0.73 |
| Sprays | 1791 (77.1) | 451 (77.2) | 0.93 |
| Stripping/waxing/buffing | 0 | 0 | -- |
| **Powdered latex gloves** | | | |
| Pre 1992 | 1761 (84.2) | 464 (84.7) | 0.79 |
| 1992 – 2000 | 1509 (72.0) | 367 (64.9) | 0.00 |
| 2001 – 2006 | 211 (5.8) | 57 (5.6) | 0.82 |
| 2007 onwards | 210 (5.8) | 57 (5.6) | 0.89 |
| **Aerosolized medications** (>2003) | 1134 (58.3) | 257 (48.7) | 0.05 |
| **Adhesives/Removers/Glues/Solvents/Gases/ Vapors** (< & >2003) | | | |
| Patient Care | 1850 (71.6) | 413 (59.2) | <0.001 |
| Surface | 362 (2.1) | 73 (1.5) | 0.02 |
| **Spill at work** [n (%)] | 114 (5.1) | 28 (4.3) | 0.47 |

[a] From weighted sample; [b] P-values of chi-squared test for differences in proportions and of *t* test for mean differences; [c] Bronchial-hyperresponsiveness.

**Table 6.** Unadjusted associations[a] (n=2,427) of sample demographic and job-related characteristics with asthma-related outcomes among Texas healthcare workers.

| | New onset asthma | BHR Symptoms[b] |
|---|---|---|
| **Characteristics**[c] | **OR (95% CI)** | **OR (95% CI)** |
| **Age** (continuous) | **1.03 (1.02 – 1.04)*** | 1.00 (0.99 – 1.01) |
| **Sex** | | |
| Female | 1.00 | 1.00 |
| Male | 0.62 (0.36 – 1.06)* | **0.62 (0.48 – 0.82)*** |
| **Race** (Non-Hispanic White) | 1.00 | 1.00 |
| Hispanic | 0.61 (0.35 – 1.07)* | 0.83 (0.62 – 1.11)* |
| Non-Hispanic Black | **0.36 (0.15 – 0.86)*** | 0.71 (0.49 – 1.02)* |
| Others | 0.74 (0.40 – 1.38) | 1.05 (0.76 – 1.46) |
| **Atopy** | **2.50 (1.62 – 3.86)*** | **6.88 (5.10 – 9.30)*** |
| **Obesity** | 1.39 (0.92 – 2.09)* | 1.36 (1.07 – 1.71)* |
| **Smoking** (Non-Smokers) | 1.00 | 1.00 |
| Current Smokers | 0.91 (0.36 – 2.32) | 1.33 (0.83 – 2.11)* |
| Former Smokers | 1.19 (0.74 – 1.92) | 1.29 (0.99 – 1.69)* |
| **Job seniority** (0-9 years) | 1.00 | 1.00 |
| 10-16 years | **4.47 (1.84 – 10.87)*** | 1.18 (0.88 – 1.60) |
| 17-26 years | **6.80 (2.82 – 16.36)*** | 1.22 (0.88 – 1.67)* |
| >= 27 years | **9.36 (4.02 – 21.80)*** | 1.04 (0.77 – 1.41) |
| **Spill at Work** | 0.71 (0.33 – 1.52) | 0.44 (0.28 – 0.70)* |

[a] From weighted logistic regression models; [b] Bronchial-hyperresponsiveness; [c] All from self-reported questionnaire, except cleaning agents and latex use, which were assessed with the job-exposure matrix; [d] Quaternary Ammonium Compounds
*Bold indicates p<0.05 and * indicates p-value≤0.25.*

**Table 7.** Adjusted associations[a] (n=2427) of cleaning tasks and compounds with asthma-related outcomes among Texas healthcare workers.

| | NOANOA | | BHR Symptoms[b] | |
|---|---|---|---|---|
| **Cleaning-related tasks** | **Unadjusted OR (95% CI)** | **Adjusted OR (95% CI)** | **Unadjusted OR (95% CI)** | **Adjusted OR (95% CI)** |
| Patient care cleaning & disinfection | 1.89 (0.91 – 3.92) | 1.82 (0.85 – 3.93) | **0.60 (0.44 – 0.83)** | **0.63 (0.45 – 0.89)** |
| Instrument cleaning | | | | |
| Endoscopy | 1.18 (0.77 – 1.80) | 1.19 (0.77 – 1.85) | 0.92 (0.72 – 1.17) | 1.00 (0.77 – 1.30) |
| Building surface cleaning | | | | |
| Sprays | **1.74 (1.10 – 2.76)** | **2.03 (1.26 – 3.28)** | 0.82 (0.6 – 1.04) | 0.84 (0.66 – 1.08) |
| **Cleaning compounds** | | | | |
| Instrument cleaning | | | | |
| Glutaraldehyde | 1.23 (0.80 – 1.88) | 1.22 (0.79 – 1.88) | 1.01 (0.79 – 1.28) | 1.03 (0.79 – 1.34) |
| Orthophthalaldehyde | **2.04 (1.38 – 3.02)** | **1.93 (1.29 – 2.88)** | 0.88 (0.71 – 1.09) | 0.87 (0.69 – 1.09) |
| Enzymatic cleaners | 1.34 (0.76 – 2.36) | 1.26 (0.71 – 2.23) | 1.16 (0.83 – 1.60) | 1.14 (0.79 – 1.64) |
| Building surface cleaning | | | | |
| Bleach | **1.60 (1.02 – 2.52)** | **1.83 (1.14 – 2.93)** | 0.81 (0.64 – 1.02) | 0.81 (0.63 – 1.03) |
| Quaternary ammonium compounds | **1.60 (1.02 – 2.52)** | **1.83 (1.14 – 2.93)** | 0.81 (0.64 – 1.02) | 0.81 (0.63 – 1.03) |
| Sprays | **1.74 (1.10 – 2.76)** | **2.03 (1.26 – 3.27)** | 0.82 (0.65 – 1.04) | 0.84 (0.66 – 1.08) |
| Powdered Latex Glove Use | | | | |
| Pre-1992 | 1.49 (0.85 – 2.63) | 1.30 (0.73 – 2.32) | 0.85 (0.64 – 1.13) | 0.85 (0.63 – 1.17) |
| 1992 – 2000 | 1.27 (0.82 – 1.96) | 1.09 (0.70 – 1.69) | 0.99 (0.78 – 1.25) | 0.94 (0.73 – 1.21) |
| 2001 – 2006 | **0.37 (0.16 – 0.84)** | **0.30 (0.13 – 0.72)** | 0.74 (0.53 – 1.03) | 0.77 (0.55 – 1.07) |
| 2007 onwards | **0.37 (0.16 – 0.86)** | **0.31 (0.13 – 0.73**) | 0.76 (0.54 – 1.05) | 0.78 (0.56 – 1.09) |
| Spill at workplace | 0.71 (0.33 – 1.52) | 1.06 (0.48 – 2.37) | 0.44 (0.28 – 0.70)* | **0.53 (0.32 – 0.88)** |

[a] From weighted logistic regression models adjusted for race, atopy, obesity, smoking and job seniority; [b] Bronchial-hyperresponsiveness.

*Bold indicates p<0.05 * indicates p-value≤0.25.*

**Table 8.** Descriptive statistics[a] of the 27-item Work-Role Functioning Questionnaire (WRFQ) among Texas healthcare workers (n=2,427).

| ***WRFQ scales*** | **Mean (SE)** | **Percentile** | | | **Cronbach's Alpha** |
|---|---|---|---|---|---|
| | | **25th** | **50th (median)** | **75th** | |
| Work Scheduling | 85.2 (0.70) | 80.0 | 100 | 100 | 0.94 |
| Output demands | 83.7 (0.79) | 82.1 | 100 | 100 | 0.98 |
| Physical demands | 84.1 (0.75) | 83.3 | 100 | 100 | 0.97 |
| Mental demands | 82.9 (0.80) | 79.2 | 100 | 100 | 0.99 |
| Social demands | 84.6 (0.80) | 92.0 | 100 | 100 | 0.97 |
| Overall scale | 84.0 (0.73) | 82.4 | 98.1 | 100 | 0.99 |

[a] All from weighted sample except Cronbach's alpha; scale scoring ranges from 0 "Difficult meeting work demands all of the time" to 100 "Difficult meeting work demands none of the time".

**Table 9.** Work-role function (WRF) scores[a] and missed work days due to health in the last 12 months[a] by physician-diagnosed asthma in Texas healthcare workers (n=2,427).

| | Physician- diagnosed asthma | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Yes | | | | No | | | | |
| | | Percentile | | | | Percentile | | | |
| ***Measures*** | **Mean (SE)** | **25th** | **50th (median)** | **75th** | **Mean (SE)** | **25th** | **50th (median)** | **75th** | **p-value[b]** |
| **WRF scales** | | | | | | | | | |
| Work Scheduling | 84.1 (1.66) | 75 | 100 | 100 | 85.4 (0.77) | 80.0 | 100 | 100 | 0.02 |
| Output demands | 82.4 (1.95) | 75 | 100 | 100 | 83.9 (0.86) | 85.7 | 100 | 100 | 0.01 |
| Physical demands | 82.5 (1.90) | 75 | 100 | 100 | 84.4 (0.82) | 83.3 | 100 | 100 | 0.41 |
| Mental demands | 81.1 (2.04) | 75 | 100 | 100 | 83.2 (0.88) | 83.3 | 100 | 100 | 0.11 |
| Social demands | 84.1 (1.92) | 83.3 | 100 | 100 | 84.7 (0.88) | 91.7 | 100 | 100 | 0.03 |
| Overall scale | 82.6 (1.78) | 74.1 | 96.3 | 100 | 84.2 (0.80) | 84.3 | 98.1 | 100 | 0.02 |
| **Missed work days in last 12 months (n=649)[c]** | | | | | | | | | |
| Due to health-related issues (n=648)[d] | 9.9 (1.85) *n=169* | 2.0 | 5.0 | 10.0 | 13.5 (2.70) *n=479* | 2.0 | 3.0 | 5.0 | 0.26 |
| Due to asthma or breathing problems (n=159)[e] | 7.5 (2.12) *n=86* | 2.0 | 5.0 | 8.0 | 4.0 (0.79) *n=73* | 1.0 | 3.0 | 4.0 | 0.12 |

[a] From weighted sample; [b] P-values of *t* test for mean differences. [c] Among participants reporting at least one missed day; [d] One reported "zero" missed days; [e] Missed days due to asthma or breathing problems out of missed days due to health-related issues.

**Table 10.** Comparison of prevalence estimates for NOA and BHR symptoms among healthcare professionals based on inclusion and exclusion of CNAs.

| | **Analytical Sample**[a] | **Excluded Sample**[b] | |
|---|---|---|---|
| | **n (%)** | **n (%)** | p-value[c] |
| **NOA [n(%)]** | | | |
| Among all professionals | 167 (7.1) | 32 (4.2) | 0.02 |
| All professionals without CNAs | 159(7.6) | 30 (5.9) | 0.29 |
| **BHR Symptoms [n(%)]** | | | |
| Among all professionals | 778 (31.0) | 276 (40.2) | <0.001 |
| All professionals without CNAs | 718(31.4) | 225(44.1) | <0.001 |

[a] *n=2427 with CNA, n=2221 without CNA*
[b] *n=899 with CNA, n=691 without CNA*
[c] p-values of chi-squared test for differences in proportions

**Table 11.** Comparison of adjusted multivariate odds ratios for NOA and BHR symptoms among healthcare professionals based on inclusion and exclusion of CNAs.

| | **Adjusted NOA** | | **Adjusted BHR Symptoms[a]** | |
|---|---|---|---|---|
| | **Among all healthcare professionals** | **All professionals without CNAs** | **Among all healthcare professionals** | **All professionals without CNAs** |
| **Cleaning-related tasks** | **OR (95%CI)** | **OR (95%CI)** | **OR (95%CI)** | **OR (95%CI)** |
| Patient care cleaning & disinfection | 1.82 (0.85 – 3.93) | 1.89 (0.87-4.09) | **0.63 (0.45 – 0.89)** | **0.56(0.39-0.81)** |
| Instrument cleaning Endoscopy | 1.19 (0.77 – 1.85) | 1.13 (0.71-1.79) | 1.00 (0.77 – 1.30) | **0.97(0.73-1.29)** |
| Building surface cleaning Sprays | **2.03 (1.26 – 3.28)** | **1.99(1.23-3.21)** | 0.84 (0.66 – 1.08) | **0.77 (0.59-0.99)** |
| **Cleaning compounds** | | | | |
| Instrument cleaning | | | | |
| Glutaraldehyde | 1.22 (0.79 – 1.88) | 1.15 (0.73-1.80) | 1.03 (0.79 – 1.34) | 0.01(0.76-1.34) |
| Orthophthalaldehyde | **1.93 (1.29 – 2.88)** | **1.93 (1.27-2.93)** | 0.87 (0.69 – 1.09) | 0.83(0.65-1.07) |
| Enzymatic cleaners | 1.26 (0.71 – 2.23) | 1.27 (0.72-2.27) | 1.14 (0.79 – 1.64) | 1.24 (0.84-1.83) |
| Building surface cleaning | | | | |
| Bleach | **1.83 (1.14 – 2.93)** | **1.99(1.23-3.21)** | 0.81 (0.63 – 1.03) | **0.77 (0.59-0.99)** |
| Quaternary ammonium compounds | **1.83 (1.14 – 2.93)** | **1.99(1.23-3.21)** | 0.81 (0.63 – 1.03) | **0.77 (0.59-0.99)** |
| Sprays | **2.03 (1.26 – 3.27)** | **2.07 (1.27-3.36)** | 0.84 (0.66 – 1.08) | 0.79 (0.61-1.03) |
| Powdered Latex Glove Use | | | | |
| Pre-1992 | 1.30 (0.73 – 2.32) | 1.39 (0.77-2.52) | 0.85 (0.63 – 1.17) | 0.79 (0.57-1.11) |
| 1992 – 2000 | 1.09 (0.70 – 1.69) | 1.10 (0.69-1.74) | 0.94 (0.73 – 1.21) | 0.88 (0.66-1.17) |
| 2001 – 2006 | **0.30 (0.13 – 0.72)** | **0.31 (0.13-0.73)** | 0.77 (0.55 – 1.07) | 0.77 (0.55-1.08) |
| 2007 onwards | **0.31 (0.13 – 0.73**) | **0.32 (0.14-0.75)** | 0.78 (0.56 – 1.09) | 0.78 (0.56-1.10) |
| Spill at workplace | 1.06 .48 – 2.37) | 0.96 (0.44-2.12) | **0.53 (0.32 – 0.88)** | 0.60 (0.35-1.01) |

; [a] Bronchial hyperresponsiveness

**Table 12.** Comparison of prevalence estimates and adjusted multivariate odds ratios for current study with Texas Asthma Study conducted in 2003 for NOA and BHR symptoms.

| | NOA | | BHR[a] Symptoms | |
|---|---|---|---|---|
| | **2003 Study[b]** | **2018 Study[c]** | **2003 Study** | **2018 Study** |
| **Prevalence (%)** | 6.6% | 7.1% | 27.4% | 31.0% |
| **Cleaning Agents** | **OR 95%CI** | **OR 95%CI** | **OR 95%CI** | **OR 95%CI** |
| Patient Care Cleaners | 1.60 (0.18-14.16) | 1.82 (0.85-3.93) | 0.79 (0.35-1.78) | 0.63 (0.45-0.89) |
| Instrument Cleaning | 2.22 (1.34-3.67) | 1.19 (0.77-1.85) | 1.26 (0.95-1.67) | 1.00 (0.77-1.30) |
| Surface Cleaners | 2.02 (1.20-3.40) | 2.03 (1.26-3.28) | 1.63 (1.21-2.19) | 0.84 (0.66-1.08) |
| Latex 2000-2006 | 0.42 (0.13-1.29) | 0.30 (0.13-0.72) | 0.61 (0.34-1.11) | 0.77 (0.55-1.07) |
| Latex 2007 and later | -- | 0.31 (0.13-0.73) | -- | 0.78 (0.56-1.09) |
| Spill at Workplace | 1.23 (0.53-2.87) | 1.06 (0.48-2.37) | 2.02 (1.28-3.21) | 0.53 (0.32-0.88) |

[a] *Bronchial hyperresponsiveness*
[b] *n=2738 in analytical sample*
[c] *n=2427 in analytical sample*

# APPENDIX A

# JOB EXPOSURE MATRIX

JEM (Rows (Exposures) – Top, Columns (Job x Practice Settings)

Exposures

| Code | LEVEL Description (Major chemical class) | Cleaning agents/disinfectants | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | LEVEL Description (Chemical subclass) (Original 2003 Exposure Categories) | Patient-care cleaning and disinfection-PT | | Instrument cleaning and disinfection-IN | | | | | | | | |
| | Original 2003 Exposure Categories C | As 2003 CLPT | | As 2003 CLIN | | | | | | | | |
| | | CLPT | | CLIN | Endoscopy | | Glutaraldehyde | | Orthophtaldehyde | | Enzymatic cleaners | |
| | | CLPCPE | CLPCPO | CLIN | CLINEPE | CLINEPO | CLINGPE | CLINGPO | CLINOPE | CLINOPO | CLINEZPE | CLINEZPO |
| | Time-dependent consideration | <=2003 | Post 2003 | | <=2003 | Post 2003 | <=2003 | Post 2003 | <=2003 | Post 2003 | <=2003 | Post 2003 |

| Code | LEVEL Description (Major chemical class) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | LEVEL Description (Chemical subclass) (Original 2003 Exposure Categories) | Building surfaces cleaning & disinfection-BD | | | | | | | | |
| | Original 2003 Exposure Categories C | As 2003 CLBD | | | | | | | | |
| | | CLBD | Bleach | | Quaternary Ammonium Compounds | | Sprays | | Stripping/ Waxing/ Buffing | |
| | | CLBD | CLBDBPE | CLBDBPO | CLBDQPE | CLBDQPO | CLBDSPE | CLBDSPO | CLBDXPE | CLBDXPO |
| | Time-dependent consideration | | <=2003 | Post 2003 | <=2003 | Post 2003 | <=2003 | Post 2003 | <=2003 | Post 2003 |

| Code | LEVEL Description (Major chemical class) | Powdered latex gloves | | | | Aerosolized medications | | Adhesives/removers/glues | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | LEVEL Description (Chemical subclass) (Original 2003 Exposure Categories) | Powdered latex gloves-LX | | | | Aerosolized medications-AM | | Adhesives/removers/glues-AD | | | |
| | Original 2003 Exposure Categories C | As 2003 | As 2003 | As 2003 | | As 2003 | | 2003 ADPT | | 2003ADBD | |
| | | As 2003 | As 2003 | As 2003 | | AM | | Patient Care | | Surface | |
| | | LX1992 | LX2000 | LX2001 | LXC | AMPE | AMPO | ADPTPE | ADPTPO | ADBDPE | ADBDPO |
| | Time-dependent consideration | Pre 1992 | 1992-2000 | 2000-NAG1 | Current | <=2003 | Post 2003 | <=2003 | Post 2003 | <=2003 | Post 2003 |

## Job-Practice Settings

| OCCUPATION X PRACTICE SETTING |
|---|
| **MD-ALL (Physicians)** |
| MD-Urban Hospital - Surgical Specialty |
| MD-Urban Hospital - Other Specialties |
| MD-Rural Hospital - Surgical Specialty |
| MD-Rural Hospital - Other Specialties |
| MD-Private practice |
| MD-Outpatient clinic - Surgical Specialty |
| MD-Outpatient clinic - Other Specialties |
| MD-Nursing home |
| MD-Health department (Urban) |
| MD-Health department (Rural) |
| MD-Health insurance agency |
| MD-Research |
| MD-Academia |
| |
| **RN-ALL (Registered Nurses)** |
| **- General Medicine/Surgery/Specializ** |
| RN-Hospital (Urban-Floor-Intensive Care) |
| RN-Hospital (Urban-Floor-Nonsurgical) |
| RN-Hospital (Urban-Floor-Surgical) |
| RN-Hospital (Urban-Special Endoscopy/ B |
| RN-Hospital (Urban-Special Infusion/Injecti |
| RN-Hospital (Rural-Floor-Intensive Care) |
| RN-Hospital (Rural-Floor-Nonsurgical) |
| RN-Hospital (Rural-Floor-Surgical) |
| RN-Hospital (Rural-General Floor) |
| RN-Hospital (Rural-Special Endoscopy) |
| RN-Hospital (Rural-Special Bronchoscopy |
| RN-Hospital (Rural-Special Infusion/Injectio |
| RN-Private practice |
| RN-Outpatient clinic |
| RN-Nursing home |

| RN-Operating Room Nurses |
|---|
| RN-Hospital (Urban) |
| RN-Hospital (Rural) |
| RN-Private practice |
| RN-Outpatient clinic |
| **RN-Administrative Nurses** |
| RN-Hospital (Urban) |
| RN-Hospital (Rural) |
| RN-Private practice |
| RN-Outpatient clinic |
| RN-Nursing home |
| RN-Health department |
| **RN-Others** |
| RN-Public school |
| RN-Health insurance agency |
| RN-Research |
| RN-Medical sales |
| RN-Academia |
| RN-Home health |
| RN-Dental office |
| |
| **LVN-ALL (Licensed Vocational Nurses)** |
| **LVN- General Medicine/Surgery/Specialized)** |
| LVN-Hospital (Urban-Floor-Intensive Care) |
| LVN-Hospital (Urban-Floor-Nonsurgical) |
| LVN-Hospital (Urban-Floor-Surgical) |
| LVN-Hospital (Urban-Special Endoscopy/ Broncho |
| LVN-Hospital (Urban-Special Infusion/Injection/Oth |
| LVN-Hospital (Rural-Floor-Intensive Care) |
| LVN-Hospital (Rural-Floor-Nonsurgical) |
| LVN-Hospital (Rural-Floor-Surgical) |
| LVN-Hospital (Rural-General Floor) |
| LVN-Hospital (Rural-Special Endoscopy) |
| LVN-Hospital (Rural-Special Bronchoscopy) |
| LVN-Hospital (Rural-Special Infusion/Injection/Othe |
| LVN-Private practice |
| LVN-Outpatient clinic |
| LVN-Nursing home |

| LVN-Operating Room Nurses |
|---|
| LVN-Hospital (Urban) |
| LVN-Hospital (Rural) |
| LVN-Private practice |
| LVN-Outpatient clinic |
| **LVN-Administrative Nurses** |
| LVN-Hospital (Urban) |
| LVN-Hospital (Rural) |
| LVN-Private practice |
| LVN-Outpatient clinic |
| LVN-Nursing home |
| LVN-Health department |
| **LVN-Others** |
| LVN-Public school |
| LVN-Health insurance agency |
| LVN-Research |
| LVN-Medical sales |
| LVN-Academia |
| LVN-Home health |
| LVN-Dental office |
| |
| **NP-ALL (Nurse Practitioners)** |
| NP-Hospital (Urban) |
| NP-Hospital (Rural) |
| NP-Private practice |
| NP-Outpatient clinic |
| NP-Nursing home |
| NP-Health department (Urban) |
| NP-Health department (Rural) |
| NP-Public school |
| NP-Health insurance agency |
| NP-Research |
| NP-Medical sales |
| NP-Academia |
| NP-Home health |
| NP-Dental office |

| RT-ALL (Respiratory therapists) |
|---|
| RT-Hospital (Urban) |
| RT-Hospital (Rural) |
| RT-Private practice |
| RT-Outpatient clinic |
| RT-Nursing home |
| RT-Public school |
| RT-Health insurance agency |
| RT-Research |
| RT-Medical sales |
| RT-Academia |
| RT-Home health |
| |
| **OT-ALL (Occupational therapists)** |
| OT-Hospital (Urban) |
| OT-Hospital (Rural) |
| OT-Private practice |
| OT-Outpatient clinic |
| OT-Nursing home |
| OT-Health department (Urban) |
| OT-Health department (Rural) |
| OT-Public school |
| OT-Health insurance agency |
| OT-Research |
| OT-Medical sales |
| OT-Academia |
| OT-Home health |
| OT-Dental office |

| PA-ALL (Physician Assistant) |
|---|
| PA-Hospital (Urban) |
| PA-Hospital (Rural) |
| PA-Private practice |
| PA-Outpatient clinic |
| PA-Nursing home |
| PA-Health department (Urban) |
| PA-Health department (Rural) |
| PA-Public school |
| PA-Health insurance agency |
| PA-Research |
| PA-Academia |
| PA-Home Health |
| |
| **PT-ALL (Physical therapists)** |
| PT-Hospital (Urban) |
| PT-Hospital (Rural) |
| PT-Private practice |
| PT-Outpatient clinic |
| PT-Nursing home |
| PT-Health department (Urban) |
| PT-Health department (Rural) |
| PT-Public School |
| PT-Health insurance agency |
| PT-Research |
| PT-Medical sales |
| PT-Academia |
| PT-Home health |
| PT-Dental office |

■ END

# APPENDIX B

# JOURNAL ARTICLE

**Work-Related Asthma among Certified Nurse Aides in Texas**

**Journal of Occupational and Environmental Medicine**

***Authors: Jenil Patel MBBS, MPH, George Delclos MD MPH PhD, David Gimeno, PhD, Laura E Mitchell, PhD***

## Introduction

Asthma poses a serious health and economic concern to the United States, with a prevalence of 8% among all adults. Over the past decade, the proportion of individuals with asthma grew by 15% in the United States (1). Around 14.2 million working days were missed among all adults who were employed and had one or two attacks of asthma in the previous month, with a reported annual cost of 56 billion dollars to the nation (2). It is also reported that asthma is responsible for causing 9 deaths each day in the United States(1). Non-hereditary asthma risk factors should be the target of prevention efforts, particularly since it is estimated that one in six cases among adult asthmatics of working age are related to work factors (3-5).

Work-related asthma (WRA) encompasses both pre-existing asthma worsened by workplace factors (i.e., work-exacerbated asthma) and new onset adult asthma caused by a workplace sensitizer or irritant (i.e., occupational asthma, OA). Workers at risk of OA according to established literature include bakers, isocyanate workers, and Western red cedar workers, spray painters and, more recently, health care workers (HCWs) (6-9).

The U.S. healthcare sector added approximately 600,000 jobs from 2006 to 2010, more than any other sector (10, 11). Projections through 2020 forecast an additional two million new healthcare jobs (10, 11), greatest among home health aides, medical assistants, and nurses (6). Previous studies have described an increased occurrence of OA among specific HCW groups, notably nursing, in association with exposures involving cleaning, disinfecting, use of powdered latex gloves and administration of certain aerosolized medications (6, 12, 13). Nurses reported a significantly higher risk of new onset physician-diagnosed asthma and nasal symptoms at work than administrative staff working in healthcare. This risk was particularly marked during disinfection tasks and with exposure to quaternary ammonium compounds, a commonly used disinfectant and known sensitizer (14). Latex gloves were widely used before 1992, owing to the increase in risk of hospital-acquired infections as a result of OSHA Bloodborne Pathogen Standard (6). The use of latex gloves between 1992 and 2000 was found to be a risk factor for both NOA and symptoms, but this risk disappeared after the year 2000 due to reports from NIOSH and FDA indicating the hospitals on control of use of latex due to reported allergies and respiratory hazards in healthcare environments. This suggested that the implementation of control policies had a beneficial effect. Whether or not the trend of latex use continues and is impactful on nurse aides, or has been replaced by the emergence of new asthma risks related to the use of protective equipment, has not been determined (6, 12, 13).

Although not widely studied, the risk among nurses, however, may vary by the different nursing career tracks (e.g., nurse practitioners, registered nurses, licensed vocational nurses, nursing aides and other personal care attendants), healthcare environments (e.g., hospitals and nursing homes), units (e.g., operating rooms and general wards) and a wide range of tasks (e.g., direct patient care, cleaning and disinfection, assisting in medical procedures, general administrative duties). Of all those nursing groups, the nursing aides group is of particular interest because of their active involvement in cleaning and disinfection tasks in the healthcare workplace.

In 2014, there were 1.5 million jobs related to nursing assistants and orderlies in the US, projected to increase by 17% by 2024 (15). Nurse aides assist other higher nursing professions and physicians by performing certain unspecialized services (16). These include providing hands-on care to patients in various settings, cleaning and disinfecting tasks, performing light housekeeping duties in patient rooms, providing skin care, and/or changing bed linen (17). Since nurse aides may perform more cleaning and disinfecting than licensed vocational or registered nurses, they may be at a higher risk of WRA.

Previous research has reported that among nursing professionals, registered nurses had the highest prevalence of new onset adult asthma (10.2%), followed by vocational nurses (8.0%) and nurse practitioners/nurse aides (6.9%; $p<0.001$) (18).

In the current study we determined the prevalence of asthma risk factors and WRA among certified nursing aides (CNAs) in Texas, and then examined the association of asthma and asthma symptoms with exposures to selected products, tasks and practices. Along with using standard NOA outcomes from questionnaire, we also used another outcome variable, presence of bronchial hyperresponsiveness symptoms (BHR Symptoms), which was based on a combination of different questions on asthma and allergy symptoms in the questionnaire, and has been used in previous studies (6, 18).

## Methods

Nurse aides in Texas are not required to be licensed, although to have an active status, they can voluntarily become certified by completing a certain number of hours of coursework and passing a state-administered exam (19). After certification, they can get to a licensed status in case they opt to work as a Licensed Nursing Assistant (LNA) which has similar roles to CNA, along with payment of licensure fee. This study focuses on only certified nurse aides obtained from a primary registry from Texas Department of Aging and Disability Services.

This cross-sectional study combined a statewide survey with an asthma risk factor job-exposure matrix (JEM), specifically designed for use in healthcare settings. The survey instrument was adapted from a previously validated questionnaire developed to study asthma in Texas HCWs. The questionnaire included questions on asthma and asthma-related symptoms, occupational exposures and non-occupational exposures (e.g., pre-existing allergies) (20).

The target population and sampling frame for our survey consisted of 108,718 CNAs registered in 2016 through the Texas Department of Aging and Disability Services. The minimum estimated sample size for the study was 383 CNAs. Calculations were based on a 95% confidence level and a 3% margin of error (21, 22), an eligibility proportion of 90% to allow for incorrect addresses and deceased individuals, and a conservative expected response rate to the mail survey of 50%, based on a substantially higher response rate (70%) among nurses achieved in a prior 2003 study (6).

The survey was mailed to 2114 randomly selected CNAs, using six contact waves:

(1) initial introduction or ‘warm-contact’ letter’; (2) a hard-copy questionnaire with a $1 token incentive, and an explanatory cover letter with a business reply envelope, sent one week later; (3) a follow-up reminder postcard, sent one week after the second contact; (4) a second postcard reminder sent after another three weeks; (5) a second hard-copy questionnaire with another $1 token incentive, four weeks later; and (6) a final reminder sent two weeks after the second questionnaire mailing. This method of mailing was modified from an existing 5-step mailing method described by Dillman *et al.* to increase our response rate (23). After removal of 10 incorrect addresses, surveys were mailed to 2104 CNAs. Of these, 311 were returned as “undeliverable addresses” and were replaced with new randomized list from the registry to obtain 90 further responses.

Occupational exposures were coded using an updated version of a previously developed asthma-specific risk factor JEM for use in HCW populations (6). This JEM was updated for newer exposures using walkthroughs and focus groups led by a multidisciplinary team of occupational health professionals, conducted in three hospitals, three nursing homes and two outpatient clinics in Houston, Texas(6). The JEM-derived exposures were classified into two broad categories: (a) tasks, and (b) compounds. Tasks consisted of patient care cleaning and disinfection, instrument cleaning (including endoscopy), and building surface cleaning (including use of sprays). Compounds were classified into cleaning agents that included glutaraldehyde, orthophthalaldehyde, enzymatic cleaners, bleach, quaternary ammonium compounds, sprays, and powdered latex glove use from 1992-2000.

Six experts (one occupational physician, one environmental safety specialist, two industrial hygienists, and two research health scientists) assigned codes to each cell of the JEM, based on the probability that the majority of workers in that cell were occupationally exposed at least once per week to this class of agents. A code of “0” was assigned if there was a high probability of no exposure; a “1” or a “2” was assigned when the probability of exposure at least once a week was low or high, respectively. Disagreements were resolved by consensus among the expert panel. The coded matrix was then applied to each respondent’s current and longest held jobs as a CNA, based on the job title and practice setting reported for that job.

Two dichotomous outcome variables were defined: (1) physician-diagnosed asthma with onset after entry into the health care profession (“new onset asthma”) and (2) bronchial-hyperresponsiveness (BHR)–related symptoms. New onset asthma was calculated among persons with a history of physician-diagnosed asthma by comparing the age at which this diagnosis was made to the number of years employed as a healthcare professional. The presence of BHR-related symptoms was determined based on 8-items that have shown to predict fall of PC20 (provocative concentration of methacholine causing a 20% fall in FEV1) of 4 mg/ml for methacholine. The eight items related to trouble breathing, wheezing and/or attacks of shortness of breath in the previous 12 months, nocturnal cough and/or chest tightness in the previous 12 months, and current allergic symptoms when in the presence of animals, feathers, dust, trees, grasses, flowers, or pollen (20).

After examining the coded JEM, it became apparent that the number of occupation–practice setting combinations assigned a code “1” (low probability) for exposure was very small for almost all considered exposures. As a result, this intermediate exposure group was too small for meaningful analyses. Therefore, occupational exposure variables were dichotomized by collapsing codes 1 and 2 from the JEM into a single “exposed” category, with code “0” reflecting the non-exposed groups. JEM codes for longest held HCW/CNA job were used because the majority (59%) of respondents indicated their current job was also their longest held job. For those whose longest held job was outside the health care sector, JEM codes from the current CNA job were used. Covariates from the questionnaire were age, sex, race/ethnicity, years as a health professional (i.e., years at job), smoking, and obesity (i.e., body mass index ≥30 $kg/m^2$). Atopy was defined based on a previously validated combination of history of allergies to dust and animals (20).

Post-stratification weighting was performed to obtain estimates of both counts and prevalences that were representative of the actual population size (i.e., the state list of 108,718 CNAs), based on four age groups: ≤25, 26-40, 41-60, and ≥61 years. Regression analyses were performed on a subsample (analytic sample) that excluded anyone with missing values for variables related to outcomes and exposures (n=174). The data were examined for high collinearity (correlation coefficient ≥ 0.70) to decide whether exposure covariates from JEM needed to be separately entered into multivariable logistic regression models with the adjustment variables. Associations were expressed as the adjusted logistic odds ratio (OR) and corresponding 95% confidence interval (95% CI). Goodness-of-fit was assessed using simulated Wald and Hosmer-Lemeshow test, as these are the recommended approaches for survey sample data, with $p<0.05$ considered model not a good fit criterion (24). Stata/SE v. 14.0 was used for the statistical analyses (25).

## Results

Of the total 455 respondents (21%), 25 refused to participate, 17 no longer worked as CNAs or their longest held job was not as a CNA. Thus, the final sample for analysis consisted of 413 participants.

Table 1 summarizes the descriptive statistics for the final analytic sample (n=239), and the missing data sample (n=174). The overall weighted prevalence estimates for physician-diagnosed asthma, new onset asthma and BHR-related symptoms were 16.1%, 3.6% and 26.9%, respectively. Ninety percent of respondents (n=216) were female. The weighted prevalence of obesity (BMI≥30 $kg/m^2$) was 41.2% (n=101); 36.7% (n=85) of respondents were Hispanic, and 75.3% (n=178) were non-smokers.

Since there were very few cases of new onset asthma (n=11) only BHR-symptoms were considered as the main outcome in the multivariate analysis. Of these 11 cases, five were current or former smokers, and three had atopy. Two reported a simultaneous diagnosis of COPD/emphysema; both had a history of smoking. Over 50% of new onset asthma cases reported exposures to bleach, abrasive cleaners, detergents, disinfectants, and nebulized drugs.

Compared to the analytic sample, the excluded sample had significantly higher atopy ($p<0.001$) and lower weighted prevalence of BHR symptoms ($p=0.03$). There were no significant differences between samples with respect to age, gender, race, obesity, smoking status, years at job or prevalence of new onset asthma.

Moderate to strong collinearity (>50%) was found among occupational exposures, mainly among building surface cleaners (bleach and quaternary ammonium compounds), patient care cleaners, and latex use (before 1992). For this reason, separate multivariable regression models were built for different subclasses of exposures in the JEM.

Table 2 presents the univariate analysis for BHR symptoms. Positive associations were found for obesity, years at job and latex glove use in the 1992-2000 time period. For race, an inverse association was observed for BHR-related symptoms among non-Hispanic blacks (OR 0.39, 95% CI 0.16-0.94) as compared to non-Hispanic whites.

The final multivariate models with BHR symptoms as the outcome were adjusted for race, atopy, obesity, smoking status and years at job (Table 3). There were no statistically significant associations, but some showed elevated point estimates. For tasks, elevated odds for BHR-related symptoms were observed for patient care cleaning and disinfection (OR 1.71, 95% CI 0.45-6.51), instrument cleaning that included endoscopy (OR 1.33, 95% CI 0.66-2.68), and building surface cleaning that included sprays (OR 1.39, 95% CI 0.35-5.60). For compounds, elevated odds were observed for instrument cleaning compounds including glutaraldehyde (OR 1.33, 95% CI 0.66-2.68), orthophthalaldehyde (OR 1.33, 95% CI 0.66-2.68), enzymatic cleaners (OR 1.23, 95% CI 0.39-3.86), and use of latex gloves from years 1992-2000 (OR 1.62, 95% CI 0.84-3.12).

Model fit was good for models with BHR-related symptoms for instrument cleaning classes and latex glove use from 1992-2000 (Archer-Lemeshow goodness of fit, $p > 0.05$), but not for the other exposure models, i.e., patient care cleaners, building surface cleaners and sprays.

## Discussion

We report several elevated odds of BHR-related symptoms for tasks performed by CNAs: patient care cleaning and disinfection, instrument cleaning (endoscopy), building surface cleaning, use of sprays, exposure to glutaraldehyde, orthophthalaldehyde, enzymatic cleaners, as well as use of latex gloves in the period 1992 to 2000. Although not statistically significant, these results are consistent with previous studies that focused primarily on nurses and other major healthcare occupations (18). To our knowledge, this is the first study to specifically examine nurse aides, an understudied group.

These results underscore the relevance of nurse aides as an at-risk worker population. The associations with cleaning tasks and products were similar or slightly less than those reported for other nursing professions. Specifically, Arif *et al.* found a 2.7 higher odds for new onset asthma as compared to the 1.7 times higher odds in this study. Also, for instrument cleaning, Arif *et al.* found a 1.7 times higher odds compared to 1.3 times in this study (6, 18, 26). We found a lower odds for building surface cleaners, such as bleach and quaternary compounds (OR 1.08), compared to Arif *et al.* (OR 1.72). This could be due in part to differences in workplaces among nurse aides and nurses. Nurse aides are more often employed in nursing homes, hospice and home facilities compared to registered nurses. These workplaces tend to use less bleach and quaternary ammonium compounds than in hospitals (27). Another explanation could be that cleaning practices and instruments have changed over the past decade, resulting in a lower opportunity for exposure to the same compounds. Although the need to control *Clostridium difficile* has led to a resurgence of bleach in recent years, we did not find this to be associated with an increased risk of BHR symptoms.

Our findings for use of latex gloves was similar to previous studies, reflecting a trend of marked increase in use of latex-containing protective equipment in years 1992-2000, in comparison to prior years, followed by an important decrease in its use after the turn of the century (6).

Some demographic differences between nurses and nurse aides in Texas may also have influenced some of our results. Among these, a higher proportion of Hispanics among nurse aides (37%) could explain the low prevalence of new onset asthma in this collective. In general, Hispanics, notably Mexican-Americans, have a lower prevalence of asthma as compared to whites and African-Americans (28). In the CDC report of 'Most Recent Asthma Data' as of 2016 (updated May 2018), the prevalence of 5.7% of current asthma in Mexican-Americans was much lower than in whites (8.3%) and African-Americans (11.6%) (28).

Another difference is in the age distribution, with 23.3% of our participants being under age 30 years, whereas in the study by Arif *et al.*, only 4.1% of all nurses were in this younger age group (18). It is possible that this shift towards a younger workforce represents a shorter 'at risk' time for developing asthma than in other nursing professionals. In addition, there is a tendency of nurse aides to change jobs sooner than other nursing professions, which would also lessen potential exposure time to workplace asthmagens. The prevalence of BHR symptoms among nurse aides (27%) was similar to that observed in other nursing professionals (31%) by Arif *et al*. (18).

The study had several strengths. To our knowledge, it is the first to address the burden of work-related asthma in the population of nurse aides. The results should be generalizable to nurse aides in Texas and possibly the U.S., given its population-based design. The use of a statewide registry to identify the target population and representative sampling approach affords it external validity. Using previously validated methods for ascertainment of exposures (i.e., an updated JEM, specific to nurse aide job and practice categories) and respiratory outcomes also add solidity to the findings. Similar methods are being used in a larger, ongoing study of Texas healthcare workers where the data collection period overlapped with the present study. When complete, this will allow us to compare our findings in nurse aides to those of other healthcare professionals, and to earlier findings in the 2007 study by Delclos *et al.*(6).

The study also had some limitations. The final size of the analytical sample (n=239) was 38% smaller than the minimum estimated sample size (n=383). Consequently, our study had less power than originally estimated to detect differences and, thus, our results were less precise (i.e., confidence intervals were often wide) than intended. We considered multiple imputation techniques but given the main source of missingness in our sample was related to the main outcome, BHR symptoms, imputing was decided against. It is known that the outcome carries information about the missing values of the potential predictors, thus, with a large proportion of the outcome missing, the imputation procedures may have not performed adequately (29). Nonetheless, our results were coherent with prior literature, both regarding the direction and magnitude of the association estimates (i.e., odds ratios).

Another potential limitation was the overall response rate (20.1%) as compared to a previous study on OA in healthcare professionals in Texas by Delclos *et al.* (6), which approximated 66%. Even though both these studies focused on OA in healthcare professionals, the respondent groups are not comparable as the current study focuses only on CNAs that were not a part of the previous study. Since the previous study focused on physicians, nurses, respiratory and occupational therapists, there is a possibility of differences in the characteristics of these groups that might be leading to a lower response rate such as frequent change in jobs and younger population in CNAs. It must also be noted that declining response rates to surveys in recent years have been widely described in literature (30-32). Many reasons are suggested, including internal company policies limiting participation in research, and more rigorous filtering of mail to avoid spam and phishing. Some of these reasons may underlie the low response rate in our study, along with factors more specific to nurse aides, such as their tendency to switch jobs frequently. Oftentimes the change is due to “moving up” the professional ladder, to nursing or other healthcare professions. At other times, nurse aides move entirely out of healthcare. Finally, although the prevalence of BHR-related symptoms was high, the small number of new onset asthma cases, likely influenced by reasons previously stated, precluded more detailed statistical analysis.

In summary, this study observed elevated odds of asthma symptoms among nurse aides, associated with specific tasks, products and practices, suggesting this is an at-risk group for work-related respiratory disease, as occurs with other healthcare occupations. Despite being limited by statistical significance, the results should serve as a starting point for further research in this worker collective. Among these, more detailed comparison of nurse aides to other at-risk healthcare professionals, and more detailed analysis of exposures to current cleaning products and practices, setting the stage for preventive interventions.

**Table 1.** Descriptive statistics for analytical sample (n=239, all missing values excluded) vs. excluded sample (n=174, only those with any missing value) out of a total 413 CNA respondents, 2016-17.

| Factors | Analytical sample no missing values (n = 239) | Excluded sample missing values (n=174) | p-value (weighted) |
|---|---|---|---|
| Age (years) (mean ± SD) | 38.0 ± 0.89 | 39.5 ± 1.17 | 0.32 |
| Gender [n (%)] | | | |
| Women | 216 (89.8) | 134(91.9) | 0.52 |
| Men | 23 (10.2) | 11(8.1) | |
| Race [n (%)] | | | |
| Non Hispanic white | 56(24.2) | 37(26.5) | 0.73 |
| Hispanic | 85(36.7) | 49(34.3) | |
| Non Hispanic black | 68(28.0) | 34(24.8) | |
| Others | 30(11.1) | 25(14.3) | |
| Atopy [n (%)] | 23 (10.2) | 28 (20.7) | 0.01 |
| Obesity (BMI ≥ 30 $kg/m^2$)[n (%)] | 101(41.2) | 54(38.8) | 0.67 |
| Smoking [n (%)] | | | |
| Never smokers | 178(75.3) | 98(69.3) | 0.36 |
| Current smokers | 29(11.2) | 25(16.2) | |
| Former smokers | 32(13.5) | 22(14.5) | |
| Years at job [n (%)] | | | |
| 0-4 years | 69(35.7) | 33(30.6) | 0.48 |
| 5-10 years | 53(24.0) | 36(31.3) | |
| 11-20 years | 70(26.9) | 39(25.2) | |
| ≥21 years | 47(13.3) | 27(12.8) | |
| Physician-Diagnosed Asthma [n(%)] | 33(13.8) | 26(14.9) | 0.75 |
| **New onset asthma** [n (%)] | 11(3.6) | 2(1.5) | 0.25 |
| **BHR Symptoms** [n (%)] | 65(26.9) | 42(39.2) | 0.03 |
| **Cleaning agents (>2003 for all)** | | | |
| Patient cleaning & disinfection | 223(92.2) | 59(89.9) | 0.59 |
| Instrument cleaning | | | |
| Endoscopy | 68(29.1) | 11(16.8) | 0.07 |
| Glutaraldehyde | 68(29.1) | 11(16.8) | 0.07 |
| Orthophthalaldehyde | 68(29.1) | 11(16.8) | 0.07 |
| Enzymatic cleaners | 26(11.4) | 3(5.0) | 0.18 |
| Building surface cleaning | | | |
| Bleach | 216(89.6) | 58(88.5) | 0.82 |
| Quaternary ammonium compounds | 216(89.6) | 58(88.5) | 0.82 |
| Sprays | 225(93.2) | 59(89.9) | 0.41 |
| Stripping/waxing/buffing | 0 | 0 | -- |
| **Powdered latex gloves** | | | |
| Pre 1992 | 200(83.2) | 56(85.9) | 0.63 |
| 1992 – 2000 | 86(36.6) | 19(27.1) | 0.18 |
| 2000 – 2003 | 0 | 0 | -- |
| 2003 – Current | 0 | 0 | -- |
| **Aerosolized Medications (>2003)** | 0 | 0 | -- |
| **Adhesives/Removers/Glues/Solvents/Gases/ Vapors (< & >2003)** | | | |
| Patient Care | 0 | 0 | -- |
| Surface | 0 | 0 | -- |
| **Spill at work** [n (%)] | 6(2.2) | 2(1.3) | 0.57 |

**Table 2.** Univariate analysis for analytical sample (n=231 – excludes missing values) between independent variables assessed by JEM among Texas CNAs and the two asthma outcomes, weighted by age groups.

| Factors | New onset asthma OR(95% CI) & p-value | BHR Symptoms OR(95% CI) & p-value |
|---|---|---|
| Age, in years (continuous) | 1.04 (1.01 – 1.08) | 1.01 (0.99 – 1.03) |
| Sex (Female) | 1.00 | 1.00 |
| Male | 0.96 (0.11 – 8.07) | 0.52 (0.17 – 1.66) |
| Race (Non-Hispanic White) | 1.00 | 1.00 |
| Hispanic | 1.56 (0.31 – 7.95) | 0.55 (0.25 – 1.20) |
| Non-Hispanic Black | 0.45 (0.04 – 4.73) | 0.39 (0.16 – 0.94) |
| Others | 3.53 (0.58 – 21.53) | 1.28 (0.49 – 3.33) |
| Atopy | 3.74(0.82 – 17.04) | 2.29 (0.90 – 5.81) |
| Obesity | 4.78 (1.14 – 20.05) | 2.32 (1.26 – 4.25) |
| Smoking (Non-Smokers) | 1.00 | 1.00 |
| Current Smokers | 2.03 (0.33 – 12.54) | 2.34 (0.99 – 5.51) |
| Former Smokers | 1.69 (0.37 – 7.82) | 1.86 (0.79 – 4.36) |
| Years at job (0-9 years) | 1.00 | 1.00 |
| 10-16 years | -- | 1.97 (0.81 – 4.84) |
| 17-26 years | -- | 2.83 (1.24 – 6.48) |
| >= 27 years | -- | 2.19 (0.86 – 5.55) |
| **Spill at Work** | 0.47 (0.05 – 4.59) | 0.10 (0.01 – 0.96) |
| **Cleaning agents (>2003 for all)** | | |
| Patient Care Cleaning & Disinfection | 1.00 (--) | 1.44 (0.39 – 5.35) |
| Instrument Cleaning | | |
| Endo/Glut/Orth | 2.90 (0.79 – 10.60) | 1.36 (0.71 – 2.60) |
| Enzymatic Cleaners | 0.84 (0.10 – 7.02) | 1.05 (0.39 – 2.82) |
| Building Surface Cleaning | | |
| Bleach / Quats | 0.70 (0.08 – 5.90) | 0.98 (0.36 – 2.68) |
| Sprays | 1.00 (--) | 1.19 (0.31 – 4.50) |
| Latex (Pre-1992) | 1.24 (0.15 – 10.30) | 1.08 (0.47 – 2.49) |
| Latex (1992 – 2000) | 2.43 (0.66 – 8.99) | 1.89 (1.03 – 3.49) |

**Table 3.** Crude and Adjusted odds (Multivariable) for tasks and compounds and their association with bronchial-hyperresponsiveness (BHR) symptoms. Adjusted for race, atopy, obesity, smoking and years at job.

| | BHR Symptoms | |
|---|---|---|
| | **Crude** | **Adjusted** |
| **TASKS** | **OR(95% CI)** | **OR(95% CI)** |
| Patient care cleaning & disinfection | 1.44 (0.39 – 5.35) | 1.71 (0.45 – 6.51) |
| Instrument cleaning | | |
| Endoscopy | 1.36 (0.71 – 2.60) | 1.33 (0.66 – 2.68)* |
| Building surface cleaning | | |
| Sprays | 1.19 (0.31 – 4.50) | 1.39 (0.35 – 5.60) |
| **COMPOUNDS** | | |
| **Cleaning agents** | | |
| Instrument cleaning | | |
| Glutaraldehyde | 1.36 (0.71 – 2.60) | 1.33 (0.66 – 2.68)* |
| Orthophthalaldehyde | 1.36 (0.71 – 2.60) | 1.33 (0.66 – 2.68)* |
| Enzymatic cleaners | 1.05 (0.39 – 2.82) | 1.23 (0.39 – 3.86)* |
| Building surface cleaning | | |
| Bleach | 0.98 (0.36 – 2.68) | 1.08 (0.36 – 3.26) |
| Quaternary ammonium compounds | 0.98 (0.36 – 2.68) | 1.08 (0.36 – 3.26) |
| Sprays | 1.19 (0.31 – 4.50) | 1.39 (0.35 – 5.60) |
| Latex (Pre-1992) | 1.08 (0.47 – 2.49) | 1.03 (0.41 – 2.62) |
| Latex (1992 – 2000) | 1.89 (1.03 – 3.49) | 1.62 (0.84 – 3.12)* |

*Indicates good fit model

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