

Occupational Exposure Prevention and the Co-occurrence of Work-Related Skin
and Respiratory Symptoms and Disease

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EXECUTIVE SUMMARY

In workplaces, workers are exposed to chemicals through their skin and respiratory system sometimes resulting in disease in one system or both. There is evidence that the same chemicals may cause disease in these two systems and also that sensitization may occur through the other system. However, there is little clinical information available regarding co-occurrence of disease in both systems and scant evidence on the prevention strategies employed in the workplace to minimize dermal and inhalation exposures. We do not know whether both the skin and lungs are protected by current exposure control strategies.

The knowledge gaps that this study sought to examine were:

1. Do workers with skin or respiratory symptoms experience symptoms in the other system?
2. Do workers with skin or respiratory symptoms receive training and use prevention practices for both dermal and inhalation exposure prevention?
3. Are workers with both skin and respiratory symptoms different from those with only skin or respiratory symptoms?

We completed a cross-sectional study of workers who were seeking treatment for occupational skin or lung disease in occupational health clinics in Toronto and Winnipeg. Information was obtained on clinical history, symptoms, prevention practices and workplace characteristics for all subjects.

In total, 225 subjects completed the study; 218 of these subjects were recruited from Toronto, Ontario and 7 were recruited from Winnipeg, Manitoba. In total, 211 subjects from both sites were included in the final analysis; 46% of the subjects were female and the mean age was 45.5 years (sd 10.5). Most subjects (n=172, 82%) were being seen in the clinic for possible work-related skin disease, compared to 39 (18%) subjects for possible work-related respiratory disease. Eighty-five (40%) of subjects reported concurrent skin and respiratory symptoms; 19% (n=41) reported concurrent skin and respiratory symptoms that were both work-related. Compared with previous studies, a relatively large portion of subjects reported symptoms in both systems; this fact may be under-recognized both in the workplace and the clinic. Very few subjects (13%) reported receiving any education on work-related disease. Only 53% reported receiving any education on personal protective equipment use. Both of these areas can, and should, be improved.

There were no observed associations between specific occupational exposures and concurrent skin and respiratory symptom outcomes. However, subjects who wore a respirator at work, those who worked in larger workplaces, were current smokers and who had a history of eczema were at increased odds of reporting concurrent symptoms. The association between history of eczema and concurrent skin and respiratory symptoms suggests a role for impaired barrier function but requires investigation.

PROJECT OVERVIEW

OVERVIEW

Occupational lung disease and occupational skin disease are common problems. 2004 data from the United States Bureau of Labor Statistics suggests that skin and respiratory conditions represent 22.7% of all occupational disease (15.6% skin and 7.1% respiratory) [US Department of Labor, 2004].

A recent study from the US suggests that the prevalence of dermatitis among employed adults is approximately 10% [Luckhaupt et al., 2012]. Over a six year period (1996-2001), McDonald et al estimated that there were approximately 27,500 new cases of work-related skin disease in the United Kingdom, of which contact dermatitis was the predominant diagnosis [MacDonald et al., 2006]. Cherry et al focused only on contact dermatitis, and estimated the annual incidence of occupational contact dermatitis in the United Kingdom to be 12.9 per 100,000 workers between 1993 and 1999 [Cherry et al., 2000].

A 1999 study by Kogevinas et al reported that 9.9% of adult onset asthma in the European Community Respiratory Health Study was attributable to occupation [Kogevinas et. al., 1999]. Using the results of Kogevinas and others, Blanc and Toren reviewed twenty-three studies and determined that the mean risk of asthma attributable to occupation was 12% (median 9%) [Blanc and Toren, 1999]. Another review endorsed by the American Thoracic Society estimates that 15% of all asthma is likely to be work-related [Blames et. al., 2003].

In workplaces, workers are exposed to chemicals through their skin and respiratory systems sometimes resulting in disease in one system (or both) [Fent et. al., 2008; Liljelind et. al., 2010]. Recent animal evidence shows that dermal exposure can lead to both skin and respiratory disease [Vanoirbeek et. al., 2004; Zhang et. al., 2004]. Evidence from case reports and workplace studies shows that some workers are diagnosed with both occupational contact dermatitis and occupational asthma [Lockman, 2002; De Raeve et. al., 1998], and workplace based studies have found that workers report symptoms in both the skin and respiratory systems [Lynde et. al., 2009].

There is scant evidence on the prevention strategies employed in the workplace to minimize dermal and inhalation exposures. We do not know whether both the skin and lungs are protected by current exposure control strategies. It is possible that a route of exposure, leading to sensitization is being ignored in some workplaces due to lack of either training or compliance.

In light of these recent developments, we must further explore the inter-relationships between routes of exposure (inhalation and dermal) and disease outcomes in both the respiratory and skin systems. Only once we have a greater understanding of these

associations can we begin to develop suitably protective exposure limits and appropriate prevention strategies.

This study summarized here is the first step toward understanding concurrent skin and lung disease. The paucity of human research leaves many research questions unanswered. The aim of this study was to describe a group of workers who have either skin or lung symptoms, or both, with respect to their personal and workplace characteristics, including the agents and routes of exposure and any prevention practices employed in the workplace. The overall goal is to identify factors that may be associated with having either skin or lung symptoms or both, so that these factors may be targeted for future hypothesis testing research.

RESEARCH QUESTIONS AND STUDY OBJECTIVES

The main research questions that this study proposed to answer were:

1. Do workers with skin or respiratory symptoms experience symptoms in the other system?
2. Do workers with skin or respiratory symptoms receive training and use prevention practices for both dermal and inhalation exposure prevention?
3. Are workers with both skin and respiratory symptoms different from those with only skin or respiratory symptoms?

The research questions were translated into more detailed Research Objectives as described:

Objective 1

To characterize the clinical state of patients presenting for investigation of possible work-related skin or respiratory symptoms with respect to:

- Skin and respiratory symptoms
- Past and family history of skin and respiratory disease
- Clinical test results
- Diagnoses

Objective 2

To characterize the workplace exposure characteristics and prevention activities (training and practices) of patients presenting for investigation of possible work-related skin and respiratory symptoms with respect to:

- Agent and route of workplace exposures
- Training received in the prevention of dermal and inhalation exposure
- Workplace prevention practices aimed at dermal and inhalation exposures used in their daily work activities.

Objective 3

To determine how patients with both skin and respiratory symptoms differ from those with only skin or respiratory symptoms with respect to:

- Clinical history and diagnoses
- Past and family history of skin and respiratory disease
- Clinical test results
- Diagnoses
- Agent and route of workplace exposures
- Training received in the prevention of dermal and inhalation exposure
- Workplace prevention practices aimed at dermal and inhalation exposures used in their daily work activities.

METHODS

Ethics

The study was approved by the Research Ethics Board of St Michael's Hospital, the University of Manitoba Health Research Ethics Board, and the Toronto Academic Health Science Network Research Ethics Board at the University of Toronto.

Data Collection

Subjects were recruited concurrently from the Toronto, ON site and the Winnipeg, MB site. Subject recruitment, the consent process and the questionnaire completion differed slightly between sites.

Toronto, ON

In Toronto, subjects were recruited consecutively from a hospital-based out-patient occupational health clinic between July 2009 and June 2010. Patients with possible work-related respiratory disease were seen through the Allergy/Asthma (AA) clinical stream and those with possible work-related skin disease were seen through the Dermatology (Derm) clinical stream; both were eligible to participate. In both streams, patients were either referred through the public health care insurance system or through the workers' compensation insurance system.

Patients were approached in person in the clinic and provided written informed consent. An interviewer-administered questionnaire was completed during the clinic visit by one of two trained interviewers. If there was insufficient time to complete the questionnaire, subjects were given the option of completing the questionnaire via telephone.

Winnipeg, MB

In Winnipeg, subjects were recruited from two out-patient occupational health clinics between July 2009 and December 2011. Patients may have been seen for possible work-related respiratory disease, possible work-related skin disease or both. In both streams, patients were either referred through the public health care insurance system or through the workers' compensation insurance system.

Patients were approached in person in the clinic and provided with a written informed consent form. In addition to the consent form, subjects were asked to provide their home telephone number and a convenient time to be contacted. Once completed and signed, this consent form was faxed to the Research Assistant in Toronto, ON. The Toronto-based Research Assistant then contacted the subject by telephone to complete the questionnaire.

Questionnaire

An identical questionnaire was completed for both the Toronto, ON subjects and the Winnipeg, MB subjects. The questionnaire contained questions on respiratory symptoms (modified ATS questionnaire [Ferris, 1978]), skin symptoms, health history, smoking history, workplace characteristics and workplace exposures. Following the clinic visit(s), the final physician diagnosis was abstracted from the subjects' medical chart.

Data Analysis

For all analyses, smoking included any reported tobacco smoking. Atopy was defined based on the subjects' positive responses to having allergies to dust, dust mites or other animals, or having had doctor-diagnosed hay fever [Lakwijk et. al., 1998]. A history of asthma and eczema were recorded as a positive response to both "have you ever had asthma/eczema?" and, "was it confirmed by a doctor?"

Workplace size was categorized into four groups based on the number of employees (<20, 20-99, 100-499 and >500) [Industry Canada, 2011]. Self-reported job title and industry information was coded using the National Occupational Classification System (NOCS) [Statistics Canada, 2006]. Occupations were further condensed into 6 groups (trades, sales/service, office, manufacturing, health, other).

Differences between participants and patients who refused to participate were tested using chi square for categorical variables and Student's t-test continuous variables.

All analyses were completed in triplicate:

1. Toronto, ON subjects,
2. Winnipeg, MB subjects
3. Combined population (Toronto, ON and Winnipeg, MB)

For the ease of reporting we have presented only the results for the combined population in the main report text. The corresponding tables for the Toronto, ON and Winnipeg, MB subjects separately are presented in Appendix I

Knowledge Gap 1: Do workers with skin or respiratory symptoms experience symptoms in the other system?

Objective 1

To characterize the clinical state of patients presenting for investigation of possible work-related skin or respiratory symptoms with respect to:

- Skin and respiratory symptoms
- Past and family history of skin and respiratory disease
- Clinical test results
- Diagnoses

Basic descriptive statistics for each variable of interest were calculated using means (standard deviations) for continuous variables, and frequencies (percentages) for categorical variables.

Workers who reported both skin and respiratory symptoms were identified based on their questionnaire responses. This was conceptualized as subjects who reported any respiratory symptom (any of cough, phlegm, wheeze, shortness of breath, or chest tightness) as well as current skin rash. Symptoms were considered work-related if they were reported to be worse at work, or better when away from work (days off or holidays).

Knowledge Gap 2: Do workers with skin or respiratory symptoms receive training and use prevention practices for both dermal and inhalation exposure prevention?

Objective 2

To characterize the workplace exposure characteristics and prevention activities (training and practices) of patients presenting for investigation of possible work-related skin and respiratory symptoms with respect to:

- Agent and route of workplace exposures
- Training received in the prevention of dermal and inhalation exposure
- Workplace prevention practices aimed at dermal and inhalation exposures used in their daily work activities.

Basic descriptive statistics for each variable of interest were calculated using means (standard deviations) for continuous variables, and frequencies (percentages) for categorical variables. Workers who reported both skin and respiratory education on personal protective equipment were identified based on their questionnaire responses. Association between education on personal protective equipment and education on occupational disease were investigated using chi square tests.

Knowledge Gap 3: Are workers with both skin and respiratory symptoms different from those with only skin or respiratory symptoms?

Objective 3

To determine how patients with both skin and respiratory symptoms differ from those with only skin or respiratory symptoms with respect to:

- Clinical history and diagnoses
- Past and family history of skin and respiratory disease
- Clinical test results
- Diagnoses
- Agent and route of workplace exposures
- Training received in the prevention of dermal and inhalation exposure
- Workplace prevention practices aimed at dermal and inhalation exposures used in their daily work activities.

The main outcome of interest for Objective 3 was concurrent skin and respiratory symptoms; the same outcome as in Objective 1. Differences between subjects with both skin and respiratory symptoms and only skin or respiratory symptoms were investigated using a multiple logistic regression model. The outcome variable was a yes/no variable where:

Yes = both skin and respiratory symptoms were reported, and

No = either skin or respiratory symptoms were reported, but not both.

Variables considered as possible predictors of concurrent symptoms included: history of asthma, history of eczema, workplace size, use of gloves at work, use of a respirator at work, occupation, insurance scheme (workers' compensation vs. public system), clinical stream (asthma/allergy vs. dermatology), presence of a union in the workplace, workplace education on personal protective equipment, workplace education on occupational disease(s) and a series of possible workplace exposures (cement, dander, dust, fumes, isocyanates, paints, pesticides, wet work and others). For this analysis, workplace education variables were condensed into two variables: education on skin and/or respiratory personal protective equipment and education on skin and/or respiratory occupational disease. This decision was made because the individual system variables for each of PPE and occupational disease were highly correlated.

Possible predictors of concurrent symptoms were first investigated using simple logistic regression. The outcome in these models was concurrent skin and respiratory symptoms; the comparison group was subjects who reported either skin or respiratory symptoms but not both. Predictors where the parameter estimate in simple logistic regression results had a $p < 0.20$ were offered into multiple logistic models. Multiple

logistic regression models were adjusted for age, sex, smoking, atopy and interviewer. All analyses were completed in SAS v.9 software (SAS Institute Inc., Cary, NC, USA).

Reliability Testing of Questionnaire

In addition to the three main research objectives, we also completed reliability testing of the workplace characteristics and exposure questionnaire, as this specific questionnaire had not previously been used in a research setting.

Reliability testing was completed among Toronto, ON subjects only. Subjects who consented to being contacted for further research were randomly selected and contacted by telephone at an interval following their clinic appointment. Subjects were required to have no significant changes at their job since first completing the initial questionnaire (in-clinic) in order to participate in the reliability study. The goal was to complete the questionnaire a second time with 10% of the larger study population, or approximately 20 subjects.

Differences between subjects who participated in the reliability testing and those who did not were tested using chi square (categorical variables) and Student's t-test (continuous variables).

The frequency of responses to each of the workplace characteristics and exposure question was calculated individually. Cohen's Kappa, percent observed agreement, percent positive agreement and percent negative agreements were calculated to assess reliability of the workplace and exposure questionnaire.

% Positive Agreement: positive answers at both test and re-test, out of positives at either test or re-test

% Negative Agreement: negative answers at both test and re-test, out of negatives at either test or re-test

Percent (%) Total Agreement: unadjusted test/re-test agreement

Additionally, the frequency and direction of change in the responses was investigated. The cut points described by Landis and Koch [Landis and Koch, 1977] were used to interpret calculated Cohen's Kappa values. Correlation between the calculated Kappa values and the prevalence of workplace characteristics or exposures was investigated using Pearson correlation.

REVIEW OF WORK COMPLETED

ORIGINAL WORK PLAN

Milestone	Date	Activity/Deliverable
1	Pre Dec 09	Ethics Application – Ethics Approval
2	Pre Dec 09	Development of Questionnaire (including Pilot Testing)
3	Dec 09 – Dec 11	Data Collection (extended for Winnipeg, MB site)
4	Feb 10 – Jan 12	Data Entry & Data Cleaning
5	Jan 11 – May 12	Data Analysis
6	July 11-June 12	Report Writing

WORK COMPLETED

Milestone 1 – Pre start

Ethics approval obtained

Dr Charanjit Sandhu hired as research coordinator

Milestone 2 – Pre start

Questionnaire finalized, pilot tested and revised – completed

Milestone 3 - Month 1-24

Data Collection - Completed

Toronto site – Completed

Subject recruitment - Completed

Collection of clinical test results and diagnoses - Completed

Milestone 4 – Month 3-25

Database created

Data entry - Completed

Andrij Wynnyckyj hired for data entry

Data Cleaning – Completed

Milestone 5 – Month 16-32

Data Analysis – Completed

RESULTS AND EVALUATION

STUDY POPULATION

The recruitment, enrollment and data collection process differed slightly between the Toronto, ON and Winnipeg, MB sites and the reliability testing was completed only for Toronto, ON subjects. Figure 1 and Figure 2 display the study progression for the two sites separately.

In total, 232 patients consented to participate in the study. Of these, 225 had complete data (questionnaire and diagnostic information) and 211 had at least one skin or respiratory symptom. The participation rate for subjects at the Toronto, ON site was 74% (299 invited, 222 consented).

The final analyses were based on 211 subjects, 204 from Toronto, ON and 7 from Winnipeg, MB.

Patients in Toronto, ON who refused study participation did not differ from the participants in terms of age or sex (Table 13) but were more likely to be from the AA clinical stream (41% vs. 18%, $p < 0.001$). Winnipeg, MB subjects who completed the questionnaire did not tend to differ from those who did not complete the questionnaire (Table 22) though significance testing was not completed due to small sample sizes.

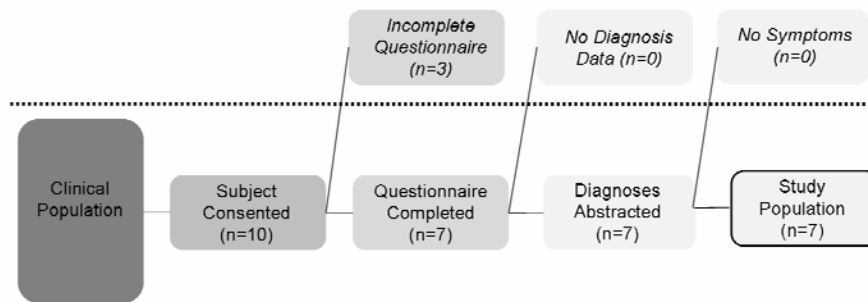


Figure 1 Flow Chart Describing Study Progression for Winnipeg Site

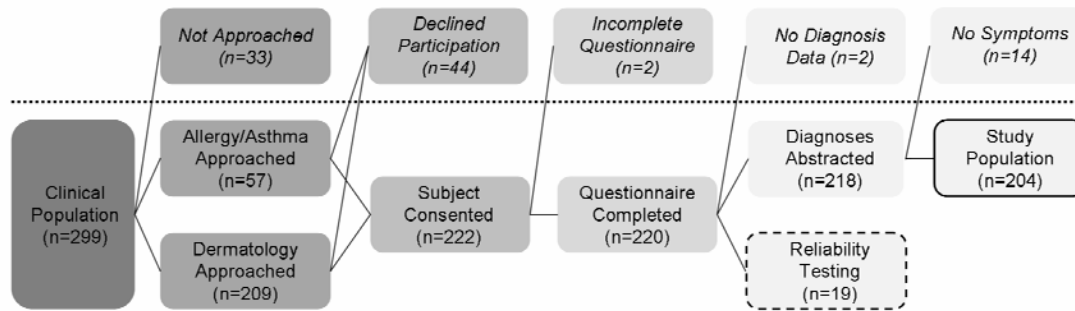


Figure 2 Flow Chart Describing Study Progression for Toronto Site

KNOWLEDGE GAP 1: Do workers with skin or respiratory symptoms experience symptoms in the other system?

Of the total 211 subjects, 46% (n=98) were female and the mean age was 45.5 years (sd 10.5 years) (Table 2). Over half of the population had a smoking history, either current (n=56, 27%) or former (n= 55, 26%). Just under a third (n=70, 30%) of the population were classified as atopic, based on questionnaire responses. Approximately one-quarter of the population reported a history of eczema (n=59, 28%) and one-quarter (n=53, 25%), a history as asthma.

Most of the participants (n = 172, 82%) were being seen for possible work-related skin disease; only 39 (18%) subjects were seen for possible work-related respiratory disease. This distribution of participants between the Derm and AA streams is reflective of the overall patient breakdown in the Toronto clinic.

One hundred and forty two (n=142, 67%) subjects were diagnosed with work-related disorders after their assessment (Table 3). An additional 37 (18%) subjects were diagnosed with a possible work-related disorder.

Among all study subjects, symptom prevalence was high, as expected in a clinical population (Table 1). General concurrent skin and respiratory symptoms were reported by 40% (n=85) of the subjects. Work-related concurrent symptoms were reported by 19% (n=41) of subjects.

Among the subjects being assessed for possible work-related skin disease (Derm stream), 31% reported at least one work-related respiratory symptoms and 7% reported work-related asthma-like symptoms. Work-related skin symptoms were less common in the AA stream, but were still reported (10% work-related rash, 8% work-related hand/arm rash) (Table 1).

Table 1: Skin and Respiratory Symptom Prevalence, Stratified by Clinical Stream. Frequencies Reported as n (%).

	Overall	Clinical Stream	
		Dermatology	Asthma/Allergy
n	211	172	39
General Symptoms:			
Current Skin Rash	149 (71%)	142 (82%)	7 (18%)
Hand/Arm Rash	143 (64%)	130 (76%)	4 (10%)
Any Respiratory Symptom	147 (70%)	108 (63%)	39 (100%)
Asthma-like Symptoms	49 (23%)	25 (14%)	24 (62%)
Work-Related Symptoms:			
Current Skin Rash	131 (62%)	127 (74%)	4 (10%)
Hand/Arm Rash	120 (57%)	117 (68%)	3 (8%)
Any Respiratory Symptom	89 (42%)	54 (31%)	35 (90%)
Asthma-like Symptoms	34 (16%)	12 (7%)	22 (56%)
Concurrent Skin and Respiratory Symptoms	85 (40%)	78 (45%)	7 (18%)
Concurrent Work-Related Skin and Respiratory Symptoms	41 (19%)	37 (22%)	4 (10%)

Table 2: Demographic Description of Study Population, Stratified by Subjects Who Reported Both Skin and Respiratory Symptoms. All Frequencies Reported as n (%) Unless Otherwise Noted.

	Overall	Either Symptoms or Symptoms Only	Skin Only Respiratory Symptoms	Both Skin and Respiratory Symptoms	p-value
n	211	126		85	
Female	98 (46%)	62 (49%)		36 (42%)	0.3276
Male	113 (54%)	64 (51%)		49 (58%)	
Age in years, mean (sd)	45.5 (10.5)	45.8 (10.1)		45.1 (11.1)	0.6253
Age <35 years	43 (20%)	23 (18%)		20 (24%)	0.6128
Age 35-49 years	88 (42%)	55 (44%)		33 (39%)	
Age ≥50 years	80 (38%)	48 (38%)		32 (38%)	
Never Smoker	100 (47%)	65 (52%)		35 (41%)	0.0601
Former Smoker	55 (26%)	35 (28%)		20 (24%)	
Current Smoker	56 (27%)	26 (21%)		30 (35%)	
Interviewer 2	117 (55%)	70 (56%)		47 (55%)	0.9701
Interviewer 1	94 (45%)	56 (44%)		38 (45%)	
Telephone Questionnaire	12 (6%)	7 (6%)		5 (6%)	0.9310
Asthma Clinical Stream	39 (18%)	32 (25%)		7 (8%)	0.0016
Derm Clinical Stream	172 (82%)	94 (75%)		78 (92%)	
Atopy	70 (30%)	43 (34%)		27 (32%)	0.7208
Doctor-diagnosed Asthma	53 (25%)	30 (24%)		23 (27%)	0.5935
Doctor-diagnosed Eczema	59 (28%)	23 (18%)		36 (42%)	0.0001

Table 3: Physician Diagnoses Stratified by Symptom Groups. All Frequencies Reported as n (%).

		Overall	Either Symptoms Only Respiratory Symptoms Only	Skin or Both Skin and Respiratory Symptoms	p-value
n		211	126	85	
Possible Diagnosis	Work-Related	179 (85%)	105 (83%)	64 (87%)	0.4593
Definite Diagnosis	Work-Related	142 (67%)	82 (65%)	60 (70%)	0.4028
Asthma		24 (11%)	19 (15%)	5 (6%)	0.0390
Work-Related Asthma		22 (10%)	18 (14%)	4 (5%)	0.0255
Occupational Asthma		20 (9%)	17 (13%)	3 (4%)	0.0154
Allergic Occupational Asthma		13 (6%)	11 (9%)	2 (2%)	0.0588
All Contact Dermatitis		156 (74%)	86 (68%)	70 (82%)	0.0221
Work-Related Dermatitis	Contact	120 (57%)	63 (50%)	57 (67%)	0.0141
Work-Related Allergic Contact Dermatitis	Contact	56 (26%)	28 (22%)	28 (33%)	0.0837

Evaluation

Work-related symptoms (either skin or respiratory) were common, as would be expected in a clinical population being assessed for possible work-related disease. A large proportion of workers also reported work-related symptoms in the system other than the one they were being assessed for; 31% of Derm stream subjects reported work-related respiratory symptoms and 10% of AA subjects reported work-related skin rash.

Concurrent skin and respiratory symptoms were observed in the study population. The concurrent symptom outcomes were more common among the Derm stream subjects (22%) compared with the AA stream subjects (10%), but both groups had a higher prevalence of concurrent skin and respiratory symptoms than previous studies [Lynde et al., 2008; Moulin et al., 2009]. In a clinical study, Moulin et al. reported on 234 patients with diagnosed contact dermatitis, of whom 10 (4%) had both work-related contact dermatitis and respiratory symptoms [Moulin et al., 2009]. This is one-fourth the prevalence observed here in the Derm patients, 88% of whom were diagnosed with contact dermatitis. Lynde et al. studied working professional cleaners and still found that 7.2% reported both a current skin rash and two or more respiratory symptoms; 5.9%

reported current skin rash as well as two or more work-related respiratory symptoms [Lynde et. al., 2009]. The lower prevalence in the Lynde et al study may be due to the more stringent requirement of having to report two or more respiratory symptoms, instead of reporting any respiratory symptoms as in the current study.

KNOWLEDGE GAP 2: Do workers with skin or respiratory symptoms receive training and use prevention practices for both dermal and inhalation exposure prevention?

Approximately half of the study population was unionized and the subjects worked in a wide variety of workplace sizes (Table 4). Forty-four percent (44%) of subjects reported having received education on skin PPE though almost double (89%) reported using gloves at work. For respiratory PPE, 43% reported receiving education and 39% reported wearing a respirator at work. Almost half (47%) of workers received no education on either skin or respiratory PPE; 35% had education on both. Most subjects (87%) had no education on work-related disease, either skin or respiratory. Only 7% of subjects reported receiving education on work-related skin disease, while 9% reported receiving education on work-related respiratory disease.

Workers who reported having education on skin PPE were significantly more likely to report having education on respiratory PPE ($p < 0.0001$). The same relationship was observed for workers reporting having education on work-related skin and respiratory disease ($p < 0.0001$). Use of PPE, both respirators and gloves, was more common among workers who reported both skin and respiratory symptoms though this only reached significance for respirator use.

Dust was the most commonly reported occupational exposure (68%); exposure to wet work (65%), fumes (55%) and paint (41%) were also commonly reported (Table 6). None of the self-reported exposures were associated with reporting concurrent skin and respiratory symptoms.

Table 4: Self-Reported Workplace Characteristics, Stratified by Subjects Who Reported Both Skin and Respiratory Symptoms. All Frequencies Reported as n (%).

	Overall	Either Symptoms Only Respiratory Symptoms Only	Skin Only or and Respiratory Symptoms	Both Skin and Respiratory Symptoms	p-value
n	211	126		85	
Union in the Workplace	103 (49%)	66 (52%)		37 (44%)	0.2071
< 20 Employees in the Workplace	53 (25%)	31 (25%)		22 (26%)	0.1237
20-99 Employees	58 (27%)	39 (31%)		19 (22%)	
100-499 Employees	54 (26%)	35 (28%)		19 (22%)	
>499 Employees	46 (22%)	21 (17%)		25 (29%)	
Gloves Worn at Work	188 (89%)	10 (8%)		79 (93%)	0.1414
Respirator Worn at Work	83 (39%)	41 (33%)		42 (49%)	0.0139
Trades Occupations	51 (24%)	29 (23%)		22 (26%)	0.1692
Sales and Service Occupations	43 (20%)	26 (21%)		17 (20%)	
Manufacturing Occupations	39 (19%)	26 (21%)		13 (15%)	
Health Related Occupations	32 (15%)	13 (10%)		19 (22%)	
Office Occupations	28 (13%)	20 (16%)		8 (9%)	
Other Occupations	19 (9%)	12 (10%)		6 (7%)	
Education: Skin PPE	93 (44%)	53 (42%)		40 (47%)	0.4735
Education: Respiratory PPE	91 (43%)	51 (40%)		40 (47%)	0.3437
Education: Work-Related Skin Disease	15 (7%)	7 (6%)		8 (9%)	0.2850
Education: Work-Related Respiratory Disease	20 (9%)	11 (9%)		9 (11%)	0.6513
Education: PPE (either skin or resp)	111 (53%)	62 (49%)		49 (58%)	0.2285
Education: Work-Related Disease (either skin or resp)	28 (13%)	14 (11%)		14 (16%)	0.2604

Table 5: Summary of Education Received on Personal Protective Equipment. (χ^2 results, $p < 0.0001$)

		Education on Skin PPE	
		No	Yes
Education on Respiratory PPE	No	100 (47%)	20 (9%)
	Yes	19 (8%)	73 (35%)

Table : Summary of Education Received on Work-Related Disease. (χ^2 results, $p < 0.0001$)

		Education on Work-Related Skin Disease	
		No	Yes
Education on Work-Related Respiratory Disease	No	183 (87%)	8 (4%)
	Yes	13 (6%)	7 (3%)

Table 6: Self-Reported Workplace Exposures. All Frequencies Reported as n (%). No Significant Differences.

	Overall	Either Respiratory Symptoms Only	Skin Only or Both Skin and Respiratory Symptoms	p-value
n	211	126	85	
Cement Exposure at Work	41 (19%)	21 (17%)	20 (24%)	0.2166
Animal Dander Exposure at Work	26 (12%)	15 (12%)	11 (13%)	0.8223
Dust Exposure at Work	143 (68%)	89 (71%)	54 (64%)	0.2787
Fume Exposure at Work	117 (55%)	73 (58%)	44 (52%)	0.3763
Isocyanate Exposure at Work	33 (16%)	18 (14%)	15 (18%)	0.5097
Paint Exposure at Work	85 (40%)	53 (42%)	32 (38%)	0.5212
Pesticide Exposure at Work	23 (11%)	14 (11%)	9 (11%)	0.9049
Wet Work Exposure at Work	136 (44%)	80 (63%)	56 (66%)	0.7220

Evaluation

The use of gloves was more common than the use of respirators among the study participants. Education on the use of PPE was much more common than education on work-related disease. In the case of PPE the majority of subjects either had education on both skin and respiratory PPE or they had neither; only 17% of subjects reported having only education on only one of skin or respiratory PPE. This suggests that the workplaces that are completing workplace education on PPE are including both skin and respiratory PPE. Very few subjects reported having education on work-related diseases, either skin or respiratory. This is an area of workplace education that could be targeted for future improvements.

Though a large number of occupational exposures were investigated as part of this study, none were associated with reporting both skin and respiratory symptoms. This lack of an association could be due the fact that the questionnaire only addressed the type of exposure and not the route of exposure. In future, it would be desirable to consider the reported exposure as well as the reported route of contact to try and tease these two factors apart.

KNOWLEDGE GAP 3: Are workers with both skin and respiratory symptoms different from those with only skin or respiratory symptoms?

A multiple logistic regression model was constructed to compare subjects with concurrent skin and respiratory symptoms to those with symptoms in only one system. The results of the multiple logistic regression models are shown in Table 7.

The variables age, sex, atopy, smoking and interviewer were kept in the model as covariates of interest. The model results (Table 7) indicated that subjects with a history of eczema (OR 3.40, 95% CI 1.64-7.04) had significantly greater odds of reporting both work-related skin and respiratory symptoms. Additionally, subjects from larger (>499 employees) workplaces (OR 2.73, 95% CI 1.04-7.17), those who reported wearing a respirator while at work (OR 2.68, 95% CI 1.36-5.25) and those reported as current smokers (OR 2.32, 95% CI 1.05-5.15) were more likely to report concurrent skin and respiratory symptoms..

Table 7: Multiple Logistic Regression Model Results for Predictors of Reporting Concurrent Skin and Respiratory Symptoms. Significant results are those where the 95% confidence intervals do not include 1.0. These are noted with an asterisk (*).

Predictor↓	Model Description
	Both Skin and Respiratory Symptoms OR (95% Confidence Intervals)
Age <35 years	1.28 (0.55-2.97)
Age 35-49 years	1.00
Age ≥50 years	1.47 (0.70-3.08)
Female Sex	0.74 (0.38-1.46)
Never Smoker	1.00
Former Smoker	1.00 (0.44-2.27)
Current Smoker	2.32 (1.05-5.15)*
Atopy	0.84 (0.40-1.72)
Interviewer 2 (vs. 1)	1.35 (0.69-2.66)
History of Asthma	1.92 (0.85-4.36)
History of Eczema	3.40 (1.64-7.04)*
< 20 Employees	0.97 (0.40-2.36)
20-99 Employees	1.00
100-499 Employees	1.16 (0.46-2.90)
>499 Employees	2.73 (1.04-7.17)*
Respirator Worn at Work	2.68 (1.36-5.25)*
Union in the Workplace	0.49 (0.24-0.99)*
AA Clinical Stream (vs. Derm)	0.22 (0.08-0.65)*
# Outcomes	85
Model n	211

Evaluation

In this model, as in the univariate analysis (Knowledge Gap 2), none of the specific exposures investigated were significant risk factors for concurrent symptoms.

A history of eczema was a risk factor for reporting concurrent skin and respiratory symptoms but a history of asthma was not. Childhood eczema has been reported as a risk-factor for developing adult onset asthma [Martin et. al., 2011] but the relationship between general eczema and concurrent symptoms is less clear.

It is possible that the eczema is associated with impaired barrier function and thus increased exposure absorption through the skin. Previous studies have found the skin abnormalities are associated with elevated internal exposure levels [Hino et. al., 2008; Vermeulen et. al., 2003]. However, this study did not assess the extent (if any) of skin barrier function impairment in the study subjects, the location of the eczema or its relevance to occupational exposures.

Subjects reporting respirator use at work were observed to have significantly greater odds of reporting concurrent skin and respiratory symptoms. In this case, respirator use may serve as proxy for general exposure at work. The observed association may suggest an association between higher exposure, or perhaps higher risk exposure, and concurrent symptoms. It is also possible that workers, once they develop symptoms may start to use protective equipment. We do not know if the reported use of PPE was prior to the development of symptoms or after. It is also possible that, regardless of the other workplace exposures, the respirator itself is a source of exposure (e.g., rubber components of a respirator). In cases of contact dermatitis and patch testing, gloves and the chemical components of gloves are sometimes implicated as causal occupational exposures. This is less common in the case of respirators but it is still plausible [Warshaw et. al., 2008].

Atopy was considered a possible confounder in the relationship between eczema and symptoms and was included in all models. The observed association between a history of eczema and concurrent skin and respiratory symptoms persists after adjusting for atopy (defined by questionnaire), suggests that the association between atopy and concurrent symptoms is not a result of confounding.

We are unable to adequately explain the association between large workplaces and reporting concurrent skin and respiratory symptoms. There may be social factors (i.e., a lack of a personal relationship with their employer or greater communication between employees) that make workers from larger workplaces more likely to report symptoms as associated with their work but these underlying factors cannot be determined from this study. Neither having a union in the workplace nor receiving occupational health and safety education (PPE or work-related disease) was associated with reporting concurrent skin and respiratory symptoms, though both tended to be more likely in larger workplaces.

Additionally, current smokers had increased odds of concurrent skin and respiratory symptoms. Smoking was included in the models due to the known association between smoking and respiratory symptoms [Higgins, 1959], however when investigated further in a nested model (results not shown), comparing subjects with respiratory symptoms only to subjects with skin symptoms only smoking was not associated with reporting respiratory symptoms.

This is the first study to report on the predictors of reporting concurrent symptoms, thus there is no literature with which to compare our results. The model results indicate that the two symptom groups are different with respect to smoking, respirator use, history of eczema and workplace size. In addition to further exploration of the exposures, and route of exposure, these factors should be more thoroughly considered in future research.

RELIABILITY TESTING OF QUESTIONNAIRE

In total, 19 (9%) subjects completed the workplace characteristics and workplace exposure questionnaire at two time points as part of the reliability portion of the study. The questionnaire is included in Appendix 2; the reliability portion of the study tested only Part 4 of the questionnaire.

The mean interval between questionnaire completion and re-test was 172 days (sd 64 days, range 78-284). Compared with subjects who did not participate in the test/re-test study, the reliability participants were older (50.1 yrs vs. 44.6 yrs, $p=0.005$). There were no differences between reliability subjects and the larger study population observed in any of the other demographic variables (Table 11, Appendix 1).

The prevalence of the workplace characteristics and exposures are shown in Table 4 and Table 6. Kappa values, as well as percent of observed agreement (total, positive and negative) are shown for both workplace characteristics (Table 8) and self-reported workplace exposures (Table 9). Calculated Kappa values were not correlated with the prevalence of the questionnaire item either at baseline (Pearson $r = 0.12$, $p=0.42$) or follow-up (Pearson $r = 0.15$, $p=0.30$).

Results are shown in order from most agreement to least, based on Kappa values. Using the benchmarks of Landis et al, 71% of workplace characteristic questions and 59% of workplace exposure questions demonstrated at least a moderate level of reliability (Kappa > 0.40) [Landis and Koch, 1977].

Table 8: Test/Re-test Reliability Statistics for Workplace Characteristics Questionnaire

	Kappa	% Observed Agreement	% Positive Agreement	% Negative Agreement
Union	1.00	100%	100%	100%
Respiratory Protection Program	0.79	89%	91%	88%
Education on Skin PPE	0.69	84%	84%	84%
Education on Respiratory PPE	0.67	84%	87%	80%
Gloves Worn at Work	0.64	95%	97%	67%
Skin Protection Program	0.58	79%	78%	80%
Education on Respiratory Disease	0.48	84%	57%	90%
Respirator Worn at Work	0.48	74%	74%	74%
Skin Problems in the Workplace	0.46	74%	78%	67%
MSDS available at work	0.46	89%	94%	50%
Joint Health and Safety Committee	0.44	89%	94%	50%
Education on Skin Disease	0.44	89%	50%	94%
Lung Allergens in the Workplace	0.37	68%	70%	67%
Skin Allergens in the Workplace	0.36	68%	73%	63%
Breathing Problems in the Workplace	0.36	68%	63%	73%
Lung Irritants in the Workplace	0.27	74%	83%	44%
Skin Irritants in the Workplace	0.11	63%	74%	36%

Table 9: Test/Re-test Reliability Statistics for Workplace Exposure Questionnaire Items.

Variable	Kappa	% Observed Agreement	% Positive Agreement	% Negative Agreement
Dusts	0.88	95%	96%	92%
Body Care Products	0.78	89%	88%	91%
Silica	0.78	89%	88%	91%
Pesticides	0.77	95%	80%	97%
Solvents	0.69	84%	82%	86%
Printing Inks	0.68	89%	75%	93%
Corrosives	0.68	84%	82%	86%
Paints	0.68	84%	82%	86%
Food, Flavors or Spices	0.62	84%	73%	89%
Glues, Adhesives, Sealants	0.62	84%	89%	73%
Oils, Greases, Lubricants	0.58	79%	80%	78%
Wet Work	0.52	79%	85%	67%
Disinfectants	0.51	79%	85%	67%
Fumes	0.49	74%	78%	67%
Oils and Coolants	0.47	74%	71%	76%
Textiles	0.46	79%	60%	86%
Bodily Fluids	0.44	89%	50%	94%
Mechanical Irritation	0.41	79%	87%	50%
Pharmaceuticals	0.41	79%	50%	87%
Plastics	0.37	68%	70%	67%
Cement	0.36	74%	55%	81%
Photographic Chemicals	0.31	84%	40%	91%
Asbestos	0.31	84%	40%	91%
Preservatives	0.28	68%	50%	77%
Bleaching Agents	0.18	63%	46%	72%
Dyes/Pigments	0.16	58%	56%	60%
Environmental Tobacco Smoke	0.14	58%	64%	50%
Dander	0.13	74%	29%	84%
Metals	0.10	53%	47%	57%
Detergents	0.05	68%	80%	25%
Rubber Compounds	0.03	53%	40%	61%
Isocyanates	-0.06	89%	0%	94%

Evaluation

The majority of items on the workplace questionnaire had moderate or greater reliability. The interval between the test and re-test portion of the reliability study was longer than initially planned but similar to other reliability testing of occupational exposure questionnaires in the literature [Blanc et. al., 2005; Quinlan et. al. 2009]. Subjects were required to report no changes in their job since the original questionnaire was completed but we were unable to confirm this independently. Subjects may also have changed some of their preventive practices after their clinical assessment and also may have become more aware of some workplace factors as a result of discussions with clinic staff.

The most unreliable questions (lowest Kappa) in the workplace characteristics section involved questions that asked subjects about the presence of allergens and irritants in the workplace. It would seem that the subjects struggled to classify their workplace exposures as allergens or irritants because the reliability of the questions assessing specific exposures (both allergens and irritants) was moderate or better in most cases.

In the case of some specific occupational exposures, i.e. isocyanates, the calculation of the Kappa values was hindered by lack of variability in the responses; 17 of 19 reliability testing subjects reported no isocyanate exposure at both test and re-test. In the case of isocyanates a better measure of the repeatability of the question is the percent of observed agreement (89%) rather than the reported Kappa value (-0.06, less than chance). This particular limitation could have been avoided with a larger sample size.

Among workplace exposures, dusts had the highest reliability as measured by Kappa. The questionnaire tested did not ask specifically about vapour or gases but did ask about fumes, which had a lower Kappa value, 0.49. Previously, Quinlan et al reported test/re-test reliability Kappa of 0.35 for a questionnaire item that asked about exposure to vapours, gases, dusts and fumes (VGDF), the reported interval between the two interviews was longer (2 years) than the current study which may have affected reliability [Quinlan et. al. 2009]. In another study, Blanc et al reported a Kappa of 0.58 for the agreement between the VGDF item versus 16 specific occupational inhalant questions, similar to the exposure questions asked in this study [Blanc et. al., 2005].

The majority of the questionnaire items had acceptable reliability, though there was variability in the reliability of the items. The reliability of previously untested questionnaire items should be considered before selecting variables for analysis. If possible, the validity of questionnaire items should also be investigated. This was not undertaken as part of this study.

LIMITATIONS

The main limitation of this study is that it was cross-sectional and only able to describe association rather than causation. Secondly, this study was completed in a selective clinical population of patients with suspected work-related disease and may not be applicable to all workers.

We also encountered challenges in recruiting subjects from the Winnipeg, MB site and were unable to reach our target sample size for this site. After consultation with the Manitoba Workers' Compensation Board representative, we decided to stop recruitment short of our target, despite a recruitment time period more than twice that of the Toronto, ON site. We believe that these challenges were related to the lack of a dedicated research assistant at the Winnipeg, MB site.

Additionally, it proved challenging to contact participants who had given written consent in the Winnipeg, MB clinic by telephone. The study protocol called for the clinic staff in Winnipeg, MB to complete the consent process with the subjects, then the Toronto Research Assistant to complete the questionnaire via telephone with the Winnipeg MB subjects. Unfortunately, several subjects who gave consent in the Winnipeg, MB clinic were unable to be reached by telephone to complete the questionnaire. In contrast, the Toronto subjects gave informed consent and completed the questionnaire during the same clinic visit such that there was no need for a follow-up telephone.

When analyzing the responses around use of PPE, it is also important to remember that these responses are self-reported accounts of whether PPE is used or not. They do not provide any information on whether PPE should be worn or not. It is possible that subjects reported using PPE and were wearing it in situations where PPE was not required, and also that subjects who reported not wearing PPE were working in situations where PPE should have been used.

A limitation of the reliability portion of the study is its inability to address validity of the questionnaire responses. The reported results only provide a measure of the repeatability of responses to the questionnaire items; they do not measure the responses against what is actually happening in the workplace.

The mechanism(s) underlying the reported symptoms cannot be ascertained from this study. The reported symptoms could be due to either allergic or irritant mechanisms; in the case of concurrent symptoms it is possible that one symptom is allergic in nature, while the other is irritant. Additionally, these results cannot say whether workers who report either skin or respiratory symptoms are likely to develop the other symptom or the mechanism by which this may occur.

CONTRIBUTIONS TO THE SCIENTIFIC LITERATURE

1. Among workers with suspected work-related disease, very few have received education or training about the potential for work-related disease, either skin or respiratory. Just over half had received education on personal protective equipment. (Knowledge Gap 2)
2. Among workers with suspected work-related disease, the observed trend suggested that workers either had education about both skin and respiratory PPE or they had neither; very few workers reported having only skin or respiratory PPE education. (Knowledge Gap 2)
3. Workers with suspected occupational disease do not have symptoms in isolation. Many (40%) of these workers reported concurrent skin and respiratory symptoms. Almost half of these concurrently symptomatic subjects had work-related symptoms in both systems. (Knowledge Gap 1)
4. Subjects who report a history of eczema, are current smokers, wear a respirator at work and work in large workplaces are more likely to report concurrent skin and respiratory symptoms (both work-related and non-work-related). The relationship between eczema and concurrent symptoms may suggest a role of increased skin absorption in the development of symptoms. (Knowledge Gap 3)

PUBLICATIONS RESULTING FROM THIS STUDY

PEER-REVIEWED POSTER CONFERENCE PRESENTATIONS

1. V.H. Arrandale, I. Kudla, A.G. Kraut, S.D. Betschel, J.A. Scott, P. Corey, F. Silverman, S.M. Tarlo, C. Redlich, D.L. Holness. Predictors Of Personal Protective Equipment Use Among Workers With Suspected Occupational Disease. (2012 Canadian Association of Research on Work and Health, Vancouver BC)
2. V.H. Arrandale, I. Kudla, A.G. Kraut, S.D. Betschel, J.A. Scott, P. Corey, F. Silverman, S.M. Tarlo, C. Redlich, D.L. Holness. Predictors Of Concurrent Work-Related Skin And Respiratory Symptoms Among Workers With Suspected Occupational Disease. (2012 American Thoracic Society Conference, San Francisco, CA & 2012 Canadian Association of Research on Work and Health, Vancouver BC)
3. V.H. Arrandale, I. Kudla, A.G. Kraut, S.D. Betschel, J.A. Scott, P. Corey, F. Silverman, S.M. Tarlo, C. Redlich, D.L. Holness. Test-Retest Reliability Of A Workplace Characteristics & Occupational Exposure Questionnaire. (2012 American Thoracic Society Conference, San Francisco, CA)
4. V.H. Arrandale, I. Kudla, A.G. Kraut, S.D. Betschel, J.A. Scott, P. Corey, F. Silverman, S.M. Tarlo, C. Redlich, D.L. Holness. Concurrent skin and respiratory symptoms among workers with suspected occupational disease. (American Contact Dermatitis Society Annual Meeting 2012, San Diego CA)
5. V.H. Arrandale, I. Kudla, A.G. Kraut, S.D. Betschel, J.A. Scott, P. Corey, F. Silverman, S.M. Tarlo, C. Redlich, D.L. Holness. Skin and Respiratory Symptoms in a Clinical Population with Suspected Work-Related Disease. (2011 American Thoracic Society Conference, Denver CO)

PEER-REVIEWED ORAL CONFERENCE PRESENTATIONS

6. V.H. Arrandale, I. Kudla, A. Kraut, S. Betschel, J.A. Scott, P. Corey, F. Silverman, S.M. Tarlo, C.A. Redlich, D.L. Holness. Skin and respiratory exposure prevention in a clinical population with suspected work-related disease. *Dermatitis* 2011;22:303.

PEER-REVIEWED JOURNAL ARTICLES

7. V.H. Arrandale, I. Kudla, A. Kraut, J.A. Scott, S.M. Tarlo, C.A. Redlich, D.L. Holness. Predictors of Concurrent Skin and Respiratory Symptoms among Workers with Suspected Work-Related Skin or Respiratory Disease. *Occupational Medicine (London)*. *In Press*.

IMPLICATIONS & RECOMMENDATIONS

1. There is a need for better education and improved awareness of work-related disease as well as personal protective equipment among workers. This education should include information on the hazardous exposures, prevention strategies, the types of diseases that may result from exposure, personal risk factors and the disease burden on individuals and populations.
2. There is a need to ensure that occupational health and safety professionals as well as health professionals are aware that occupational exposures do not occur in isolation, and that health outcomes may not always occur in isolation either.
3. The design of prevention activities, workplace recommendation and return-to-work strategies should consider all potential routes of exposure to hazardous agents, including both airborne and skin contact.

FINANCIAL REPORT

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APPENDIX A – ADDITIONAL TABLES FOR THE TOTAL STUDY POPULATION

Table 10: Physician Diagnoses Stratified by Clinical Stream (all frequencies reported as n (%))

		Overall	Dermatology	Asthma/Allergy	p-value
n		211	172	39	
Possible Diagnosis	Work-Related	179 (85%)	152 (88%)	27 (69%)	0.0026
Definite Diagnosis	Work-Related	142 (67%)	119 (69%)	23 (59%)	0.2197
Asthma		24 (11%)	0 (0%)	24 (62%)	N.C.
Work-Related Asthma		22 (10%)	0 (0%)	22 (56%)	N.C.
Occupational Asthma		20 (9%)	0 (0%)	20 (51%)	N.C.
Allergic Asthma	Occupational	13 (6%)	0 (0%)	13 (33%)	N.C.
All Contact Dermatitis		156 (74%)	152 (88%)	4 (10%)	<0.0001
Work-Related Dermatitis	Contact	120 (57%)	119 (69%)	1 (2%)	N.C.
Work-Related Contact Dermatitis	Allergic	56 (26%)	55 (32%)	1 (2%)	N.C.

Table 11: Comparison Between Participants and Non-Participants in the Reliability Testing Stud (all frequencies reported as n (%))

	Total	No Reliability	Reliability	p-value
Overall	218	199	19	
Interviewer 1	96 (44%)	94 (47%)	2 (11%)	0.0033
Interviewer 2	122 (56%)	106 (53%)	16 (84%)	
In Clinic	212 (98%)	194 (97%)	18 (95%)	0.4963
Telephone	5 (2%)	5 (3%)	0 (0%)	
Male	117 (54%)	108 (54%)	9 (47%)	0.7444
Female	101 (46%)	92 (46%)	9 (47%)	
Age <35 years	43 (20%)	42 (21%)	1 (5%)	0.1447
Age 35-49 years	94 (43%)	87 (44%)	7 (37%)	
Age ≥50 years	81 (37%)	71 (36%)	10 (53%)	
Doctor A	38 (17%)	35 (18%)	3 (16%)	0.8311
Doctor B	58 (27%)	51 (26%)	7 (37%)	
Doctor C	17 (8%)	16 (8%)	1 (5%)	
Doctor D	22 (11%)	21 (11%)	1 (5%)	
Doctor E	78 (36%)	72 (36%)	6 (32%)	
Doctor F	5 (2%)	5 (3%)	0 (0%)	
Never Smoker	106 (49%)	100 (50%)	6 (32%)	0.3451
Former Smoker	54 (25%)	49 (25%)	5 (26%)	
Current Smoker	58 (27%)	51 (26%)	7 (37%)	
Dermatology	179 (82%)	163 (82%)	16 (84%)	0.4334
Asthma/Allergy	39 (18%)	37 (19%)	2 (11%)	
OHIP	122 (56%)	113 (57%)	9 (47%)	0.5947
ODSP	96 (44%)	87 (44%)	9 (47%)	
No Cross Referral	207 (95%)	190 (95%)	17 (89%)	0.9179
Cross Referral Made	11 (5%)	10 (5%)	1 (5%)	

APPENDIX B – RESULTS FOR TORONTO SUBJECTS

Table 12: Demographic Description of Study Population, Stratified by Subjects Who Reported Both Skin and Respiratory Symptoms (all frequencies reported as n (%) unless otherwise noted)

	Overall	Either Skin Symptoms Only or Respiratory Symptoms Only	Both Skin and Respiratory Symptoms
n	204	121	83
Female	94 (46%)	59 (49%)	35 (42%)
Male	110 (54%)	62 (51%)	48 (58%)
Age in years, mean (sd)	45.4 (10.5)	45.7 (10.0)	45.1 (11.2)
Age <35 years	38 (19%)	20 (17%)	18 (22%)
Age 35-49 years	88 (43%)	55 (45%)	33 (40%)
Age ≥50 years	78 (38%)	46 (38%)	32 (39%)
Never Smoker	98 (48%)	64 (53%)	34 (41%)
Former Smoker	50 (24%)	31 (26%)	19 (23%)
Current Smoker	56 (27%)	26 (21%)	30 (36%)
Interviewer 2	115 (56%)	69 (57%)	46 (55%)
Interviewer 1	89 (44%)	52 (43%)	37 (45%)
Telephone Questionnaire	5 (2%)	2 (2%)	3 (4%)
In Clinic Questionnaire	198 (98%)	118 (98%)	80 (96%)
AA Clinical Stream	37 (18%)	31 (26%)	6 (7%)
Derm Clinical Stream	167 (82%)	90 (74%)	77 (93%)
Workplace Insurance	91 (45%)	59 (49%)	32 (39%)
Public Insurance	113 (55%)	62 (51%)	51 (61%)
Atopy	68 (33%)	42 (35%)	26 (31%)
Doctor-diagnosed Asthma	50 (24%)	29 (24%)	21 (25%)
Doctor-diagnosed Eczema	54 (26%)	20 (17%)	34 (41%)

Table 13: Comparison Between Participants and Patients Who Refused Study Participation (all frequencies reported as n (%))

	Total	Refused	Participant	p-value
Overall	262	44	218	
Female	117 (45%)	16 (36%)	101 (46%)	0.2251
Age <35 years	49 (19%)	6 (14%)	43 (20%)	0.3544
Age 35-49 years	118 (45%)	24 (54%)	94 (43%)	
Age ≥50 years	95 (36%)	14 (32%)	81 (37%)	
Doctor A	44 (17%)	6 (14%)	38 (17%)	0.0132
Doctor B	67 (26%)	9 (20%)	58 (27%)	
Doctor C	26 (10%)	9 (20%)	17 (8%)	
Doctor D	32 (12%)	10 (23%)	22 (20%)	
Doctor E	88 (34%)	10 (23%)	78 (36%)	
Doctor F	5 (2%)	0 (0%)	5 (2%)	
Dermatology	205 (78%)	26 (59%)	179 (82%)	0.0007
Asthma/Allergy	57 (22%)	18 (41%)	39 (18%)	
OHIP	140 (53%)	18 (41%)	122 (56%)	0.0678
ODSP	122 (47%)	26 (59%)	96 (44%)	

Table 14: Comparison Between Dermatology (Derm) Stream and Asthma/Allergy (AA) Stream Subjects (all frequencies reported as n (%))

	Total	Derm	AA	p-value
OVERALL	204	167	37	
Interviewer 1	89 (44%)	75 (45%)	14 (38%)	0.4325
Interviewer 2	115 (56%)	92 (55%)	23 (62%)	
In Clinic	199 (98%)	163 (98%)	36 (97%)	0.9128
Telephone	5 (2%)	4 (2%)	1 (3%)	
Male	110 (54%)	90 (54%)	20 (54%)	0.9857
Female	94 (46%)	77 (46%)	17 (46%)	
Age <35 years	38 (19%)	34 (20%)	4 (11%)	0.3942
Age 35-49 years	88 (43%)	71 (43%)	17 (46%)	
Age ≥50 years	78 (38%)	62 (37%)	16 (43%)	
Doctor A	35 (17%)	35 (21%)	0 (0%)	<0.0001
Doctor B	55 (27%)	55 (33%)	0 (0%)	
Doctor C	17 (8%)	0 (0%)	17 (46%)	
Doctor D	20 (10%)	0 (0%)	20 (54%)	
Doctor E	72 (35%)	72 (43%)	0 (0%)	
Doctor F	5 (2%)	5 (3%)	0 (0%)	
Never Smoker	98 (48%)	82 (49%)	16 (43%)	0.2396
Former Smoker	50 (25%)	37 (22%)	13 (35%)	
Current Smoker	56 (27%)	48 (29%)	8 (22%)	
OHIP	113 (55%)	108 (65%)	5 (14%)	<0.0001
ODSP	91 (45%)	59 (35%)	32 (86%)	
No Cross Referral	195 (96%)	164 (98%)	31 (84%)	0.0001
Cross Referral Made	9 (4%)	3 (2%)	6 (16%)	

Table 15: Comparison Between Public Insurance Subjects (OHIP) and Workplace Insurance Subjects (ODSP) (all frequencies reported as n (%))

	Total	OHIP	ODSP	p-value
Overall	204	113	91	
Interviewer 1	89 (44%)	45 (40%)	44 (48%)	0.2221
Interviewer 2	115 (56%)	68 (60%)	47 (52%)	
In Clinic	199 (98%)	109 (96%)	90 (99%)	0.2624
Telephone	5 (2%)	4 (4%)	1 (1%)	
Male	110 (54%)	57 (50%)	53 (58%)	0.2666
Female	94 (46%)	56 (50%)	38 (42%)	
Age <35 years	38 (19%)	25 (22%)	13 (14%)	0.2748
Age 35-49 years	88 (43%)	49 (43%)	39 (43%)	
Age ≥50 years	78 (38%)	39 (35%)	39 (43%)	
Doctor A	35 (17%)	10 (9%)	25 (27%)	<0.0001
Doctor B	55 (27%)	23 (20%)	32 (35%)	
Doctor C	17 (8%)	0 (0%)	17 (19%)	
Doctor D	20 (10%)	5 (4%)	15 (16%)	
Doctor E	72 (35%)	70 (62%)	2 (2%)	
Doctor F	5 (2%)	5 (4%)	0 (0%)	
Never Smoker	98 (48%)	59 (52%)	39 (43%)	0.4063
Former Smoker	50 (25%)	25 (22%)	25 (27%)	
Current Smoker	56 (27%)	29 (26%)	27 (30%)	
Dermatology	167 (82%)	108 (96%)	59 (65%)	<0.0001
Asthma/Allergy	37 (18%)	5 (4%)	32 (35%)	
No Cross Referral	195 (96%)	111 (98%)	84 (92%)	0.0406
Cross Referral Made	9 (4%)	2 (2%)	7 (8%)	

Table 16: Skin and Respiratory Symptom Prevalence, Stratified by Clinical Stream (frequencies reported as n (%))

	Overall	Clinical Stream	
		Dermatology	Asthma/Allergy
n	204	167	37
General Symptoms:			
Current Skin Rash	146 (72%)	140 (84%)	6 (16%)
Hand/Arm Rash	134 (66%)	130 (78%)	4 (11%)
Any Respiratory Symptom	141 (69%)	104 (62%)	37 (100%)
Asthma-like Symptoms	48 (24%)	24 (14%)	24 (65%)
Work-Related Symptoms:			
Current Skin Rash	129 (63%)	125 (75%)	4 (11%)
Hand/Arm Rash	120 (59%)	117 (70%)	3 (8%)
Any Respiratory Symptom	83 (41%)	50 (30%)	33 (89%)
Asthma-like Symptoms	33 (16%)	11 (6%)	22 (59%)
Concurrent Skin and Respiratory Symptoms	83 (41%)	77 (46%)	6 (16%)
Concurrent Work-Related Skin and Respiratory Symptoms	40 (20%)	36 (22%)	4 (11%)

Table 17: Self-Reported Workplace Characteristics, Stratified by Subjects Who Reported Both Skin and Respiratory Symptoms (all frequencies reported as n (%))

	Overall	Either Skin Symptoms Only or Respiratory Symptoms Only	Both Skin and Respiratory Symptoms
n	204	121	83
Union in the Workplace	98 (48%)	62 (51%)	36 (43%)
< 20 Employees in the Workplace	52 (25%)	31 (26%)	21 (25%)
20-99 Employees	57 (28%)	38 (31%)	19 (23%)
100-499 Employees	52 (25%)	34 (28%)	18 (22%)
>499 Employees	43 (21%)	18 (15%)	25 (30%)
Gloves Worn at Work	183 (90%)	10 (8%)	78 (94%)
Respirator Worn at Work	80 (39%)	39 (32%)	41 (49%)
Trades Occupations	49 (24%)	28 (23%)	21 (25%)
Sales and Service Occupations	42 (20%)	25 (21%)	17 (20%)
Manufacturing Occupations	38 (19%)	25 (21%)	13 (16%)
Health Related Occupations	30 (15%)	12 (10%)	18 (22%)
Office Occupations	27 (13%)	19 (16%)	8 (10%)
Other Occupations	18 (9%)	12 (10%)	6 (7%)
Education: Skin PPE	90 (44%)	50 (41%)	40 (48%)
Education: Respiratory PPE	88 (43%)	48 (40%)	40 (48%)
Education: Work-Related Skin Disease	15 (7%)	7 (6%)	8 (10%)
Education: Work-Related Respiratory Disease	20 (10%)	11 (9%)	9 (11%)
Education: PPE (either skin or resp)	108 (53%)	59 (49%)	49 (59%)
Education: Work-Related Disease (either skin or resp)	28 (14%)	14 (12%)	14 (17%)

Table 18: Self-Reported Workplace Exposures (all frequencies reported as n (%))

	Overall	Either Skin Symptoms Only or Respiratory Symptoms Only	Both Skin and Respiratory Symptoms
n	204	121	83
Cement Exposure at Work	41 (20%)	21 (17%)	20 (24%)
Animal Dander Exposure at Work	25 (12%)	14 (12%)	11 (13%)
Dust Exposure at Work	139 (68%)	85 (70%)	54 (65%)
Fume Exposure at Work	113 (55%)	69 (57%)	44 (53%)
Isocyanate Exposure at Work	32 (16%)	17 (14%)	15 (18%)
Paint Exposure at Work	84 (41%)	52 (43%)	32 (39%)
Pesticide Exposure at Work	22 (11%)	13 (11%)	9 (11%)
Wet Work Exposure at Work	133 (65%)	78 (64%)	55 (66%)

Table 19: Physician Diagnoses Stratified by Symptom Groups (all frequencies reported as n (%))

	Overall	Either Skin Symptoms Only or Respiratory Symptoms Only	Both Skin and Respiratory Symptoms	p-value
n	204	121	83	
Possible Work-Related Diagnosis	174 (85%)	102 (84%)	72 (87%)	0.6275
Definite Work-Related Diagnosis	139 (68%)	81 (67%)	58 (70%)	0.6583
Asthma	23 (11%)	19 (16%)	4 (5%)	0.0158
Work-Related Asthma	21 (10%)	18 (15%)	3 (4%)	0.0093
Occupational Asthma	19 (9%)	17 (14%)	2 (2%)	0.0050
Allergic Occupational Asthma	12 (6%)	11 (9%)	1 (1%)	0.0187
All Contact Dermatitis	152 (75%)	83 (69%)	69 (83%)	0.0193

		Overall	Either Symptoms Only Respiratory Symptoms Only	Skin Only or Both Skin and Respiratory Symptoms	p-value
Work-Related Dermatitis	Contact	118 (58%)	62 (51%)	56 (67%)	0.0211
Work-Related Dermatitis	Allergic Contact	56 (27%)	28 (23%)	28 (34%)	0.0958

Table 20: Physician Diagnoses Stratified by Clinical Stream (all frequencies reported as n (%))

		Overall	Dermatology	Asthma/Allergy	p-value
n		204	167	37	
Possible Diagnosis	Work-Related	174 (85%)	148 (89%)	26 (70%)	0.0043
Definite Diagnosis	Work-Related	139 (68%)	117 (70%)	22 (59%)	0.2105
Asthma		23 (11%)	0 (0%)	23 (62%)	<0.0001
Work-Related Asthma		21 (10%)	0 (0%)	21 (57%)	<0.0001
Occupational Asthma		19 (9%)	0 (0%)	19 (51%)	<0.0001
Allergic Occupational Asthma		12 (6%)	0 (0%)	12 (32%)	<0.0001
All Contact Dermatitis		152 (75%)	148 (89%)	4 (11%)	<0.0001
Work-Related Dermatitis	Contact	118 (58%)	117 (70%)	1 (3%)	<0.0001
Work-Related Allergic Contact Dermatitis		56 (27%)	55 (33%)	1 (3%)	0.0002

APPENDIX C – RESULTS FOR WINNIPEG SUBJECTS

Table 21: Demographic Description of Study Population, Stratified by Subjects Who Reported Both Skin and Respiratory Symptoms (all frequencies reported as n (%)) unless otherwise noted; P-values not calculated due to small cell sizes)

	Overall	Either Skin Symptoms Only or Respiratory Symptoms Only	Both Skin and Respiratory Symptoms
n	7	5 (71%)	2 (29%)
Female	4 (57%)	2 (67%)	1 (33%)
Male	3 (43%)	3 (75%)	1 (25%)
Age in years, mean (sd)	49.2 (11.1)	50.0 (12.5)	47.3 (9.8)
Age <35 years	5 (71%)	3 (60%)	2 (40%)
Age 35-49 years	0 (0%)	-	-
Age ≥50 years	2 (29%)	2 (100%)	0 (0%)
Never Smoker	2 (29%)	1 (50%)	1 (50%)
Former Smoker	5 (71%)	4 (80%)	1 (20%)
Current Smoker	0 (0%)	-	-
Interviewer 2	2 (29%)	1 (50%)	1 (50%)
Interviewer 1	5 (71%)	4 (80%)	1 (20%)
Telephone Questionnaire	7 (100%)	5 (71%)	2 (29%)
Asthma Clinical Stream	2 (29%)	1 (50%)	1 (50%)
Derm Clinical Stream	5 (71%)	4 (80%)	1 (20%)
Atopy	2 (29%)	1 (50%)	1 (50%)
Doctor-diagnosed Asthma	3 (43%)	1 (33%)	2 (67%)
Doctor-diagnosed Eczema	5 (71%)	3 (60%)	2 (40%)

Table 22: Comparison Between Participants (Consented) Who Completed the Questionnaire, and Patients (Consented) Who Did Not Complete the Questionnaire (all frequencies reported as n (%); P-values not calculated due to small cell sizes)

	Total	Incomplete	Complete
Overall	10	3	7
Female	4 (40%)	0 (0%)	4 (57%)
Age <35 years	8 (80%)	3 (100%)	5 (71%)
Age 35-49 years	0 (0%)	0 (0%)	0 (0%)
Age ≥50 years	2 (20%)	0 (0%)	2 (28%)
Dermatology	7 (70%)	2 (67%)	5 (71%)
Asthma/Allergy	2 (20%)	0 (0%)	2 (28%)
Both Complaints	1 (10%)	1 (33%)	0 (0%)

Table 23: Comparison Between Dermatology (Derm) Stream and Asthma/Allergy (AA) Stream Subjects (all frequencies reported as n (%); P-values not calculated due to small cell sizes)

	Total	Derm	AA
OVERALL	7	5	2
Interviewer 1	5 (71%)	3 (60%)	2 (100%)
Interviewer 2	2 (28%)	2 (40%)	0 (0%)
Male	3 (43%)	1 (20%)	2 (100%)
Female	4 (57%)	4 (80%)	0 (0%)
Age <35 years	5 (71%)	4 (80%)	1 (50%)
Age 35-49 years	0 (0%)	0 (0%)	0 (0%)
Age ≥50 years	2 (28%)	1 (20%)	1 (50%)
Never Smoker	2 (28%)	2 (40%)	0 (0%)
Former Smoker	5 (71%)	3 (60%)	2 (100%)
Current Smoker	0 (0%)	0 (0%)	0 (0%)
Cross Referral Made	0 (0%)	0 (0%)	0 (0%)

Table 24: Skin and Respiratory Symptom Prevalence, Stratified by Clinical Stream (frequencies reported as n (%))

	Overall	Clinical Stream	
		Dermatology	Asthma/Allergy
n	7	5	2
General Symptoms:			
Current Skin Rash	3 (43%)	2 (40%)	1 (50%)
Hand/Arm Rash	0 (0%)	0 (0%)	0 (0%)
Any Respiratory Symptom	6 (86%)	4 (80%)	2 (100%)
Asthma-like Symptoms	1 (14%)	1 (20%)	0 (0%)
Work-Related Symptoms:			
Current Skin Rash	2 (28%)	2 (40%)	0 (0%)
Hand/Arm Rash	0 (0%)	0 (0%)	0 (0%)
Any Respiratory Symptom	6 (86%)	4 (80%)	2 (100%)
Asthma-like Symptoms	1 (14%)	1 (20%)	0 (0%)
Concurrent Skin and Respiratory Symptoms	2 (28%)	1 (20%)	1 (50%)
Concurrent Work-Related Skin and Respiratory Symptoms	1 (14%)	1 (20%)	0 (0%)

Table 25: Self-Reported Workplace Characteristics, Stratified by Subjects Who Reported Both Skin and Respiratory Symptoms (all frequencies reported as n (%); P-values not calculated due to small cell sizes)

	Overall	Either Skin Symptoms Only or Respiratory Symptoms Only	Both Skin and Respiratory Symptoms
Overall	7	5	2
Union in the Workplace	5 (71%)	4 (80%)	1 (50%)
< 20 Employees in the Workplace	1 (14%)	0 (0%)	1 (50%)
20-99 Employees	1 (14%)	1 (20%)	0 (0%)
100-499 Employees	2 (28%)	1 (20%)	1 (50%)
>499 Employees	3 (43%)	3 (60%)	0 (0%)
Gloves Worn at Work	5 (71%)	4 (80%)	1 (50%)
Respirator Worn at Work	3 (43%)	2 (40%)	1 (50%)
Trades Occupations	2 (28%)	1 (20%)	1 (50%)
Sales and Service Occupations	1 (14%)	1 (20%)	0 (0%)
Manufacturing Occupations	1 (14%)	1 (20%)	0 (0%)
Health Related Occupations	2 (28%)	1 (20%)	1 (50%)
Office Occupations	1 (14%)	1 (20%)	0 (0%)
Other Occupations	0 (0%)	0 (0%)	0 (0%)
Education: Skin PPE	3 (43%)	3 (60%)	0 (0%)
Education: Respiratory PPE	3 (43%)	3 (60%)	0 (0%)
Education: Work-Related Skin Disease	0 (0%)	0 (0%)	0 (0%)
Education: Work-Related Respiratory Disease	0 (0%)	0 (0%)	0 (0%)
Education: PPE (either skin or resp)	3 (43%)	3 (60%)	0 (0%)
Education: Work-Related Disease (either skin or resp)	0 (0%)	0 (0%)	0 (0%)

Table 26: Self-Reported Workplace Exposures (all frequencies reported as n (%); P-values not calculated due to small cell sizes)

	Overall	Either Skin Symptoms Only or Respiratory Symptoms Only	Both Skin and Respiratory Symptoms
Overall	7	5	2
Cement Exposure at Work	0 (0%)	0 (0%)	0 (0%)
Animal Dander Exposure at Work	1 (14%)	1 (20%)	0 (0%)
Dust Exposure at Work	4 (57%)	4 (80%)	0 (0%)
Fume Exposure at Work	4 (57%)	4 (80%)	0 (0%)
Isocyanate Exposure at Work	1 (14%)	1 (20%)	0 (0%)
Paint Exposure at Work	1 (14%)	1 (20%)	0 (0%)
Pesticide Exposure at Work	1 (14%)	1 (20%)	0 (0%)
Wet Work Exposure at Work	3 (43%)	2 (40%)	1 (50%)

Table 27: Physician Diagnoses Stratified by Symptom Groups (all frequencies reported as n (%); P-values not calculated due to small cell sizes)

	Overall	Either Skin Symptoms Only or Respiratory Symptoms Only	Both Skin and Respiratory Symptoms
n	7	5	2
Possible Diagnosis	Work-Related 5 (71%)	3 (60%)	2 (100%)
Definite Diagnosis	Work-Related 3 (43%)	1 (20%)	2 (100%)
Asthma	1 (14%)	0 (0%)	1 (50%)
Work-Related Asthma	1 (14%)	0 (0%)	1 (50%)
Occupational Asthma	1 (14%)	0 (0%)	1 (50%)
Allergic Occupational Asthma	1 (14%)	0 (0%)	1 (50%)

	Overall	Either Symptoms Only Respiratory Symptoms Only	Skin Only or Both Skin and Respiratory Symptoms
All Contact Dermatitis	4 (57%)	3 (60%)	1 (50%)
Work-Related Dermatitis	Contact 2 (28%)	1 (20%)	1 (50%)
Work-Related Allergic Dermatitis	Contact 0 (0%)	0 (0%)	0 (0%)

Table 28: Physician Diagnoses Stratified by Clinical Stream (all frequencies reported as n (%); P-values not calculated due to small cell sizes)

		Overall	Dermatology	Asthma/Allergy
n		7	5	2
Possible Diagnosis	Work-Related	5 (71%)	4 (80%)	1 (50%)
Definite Diagnosis	Work-Related	3 (43%)	2 (40%)	1 (50%)
Asthma		1 (14%)	0 (0%)	1 (50%)
Work-Related Asthma		1 (14%)	0 (0%)	1 (50%)
Occupational Asthma		1 (14%)	0 (0%)	1 (50%)
Allergic Occupational Asthma		1 (14%)	0 (0%)	1 (50%)
All Contact Dermatitis		4 (57%)	4 (80%)	0 (0%)
Work-Related Dermatitis	Contact	2 (28%)	2 (40%)	0 (0%)
Work-Related Allergic Contact Dermatitis		0 (0%)	0 (0%)	0 (0%)

APPENDIX D - INTERVIEWER-ADMINISTERED QUESTIONNAIRE