

Estimating the Extent and Distribution of New-Onset Adult Asthma in British Columbia Using Frequentist and Bayesian Approaches

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Introduction: We previously described a method to identify the incidence of new-onset adult asthma (NOAA) in Alberta by industry and occupation, utilizing Workers' Compensation Board (WCB) and physician billing data. The aim of this study was to extend this method to data from British Columbia (BC) so as to compare the two provinces and to incorporate Bayesian methodology into estimates of risk.

Methods: WCB claims for any reason 1995–2004 were linked to physician billing data. NOAA was defined as a billing for asthma (ICD-9 493) in the 12 months before a WCB claim without asthma in the previous 3 years. Incidence was calculated by occupation and industry. In a matched case-referent analysis, associations with exposures were examined using an asthma-specific job exposure matrix (JEM). Posterior distributions from the Alberta analysis and estimated misclassification parameters were used as priors in the Bayesian analysis of the BC data.

Results: Among 1 118 239 eligible WCB claims the incidence of NOAA was 1.4%. Sixteen occupations and 44 industries had a significantly increased risk; six industries had a decreased risk. The JEM identified wood dust [odds ratio (OR) 1.55, 95% confidence interval (CI) 1.08–2.24] and animal antigens (OR 1.66, 95% CI 1.17–2.36) as related to an increased risk of NOAA. Exposure to isocyanates was associated with decreased risk (OR 0.57, 95% CI 0.39–0.85). Bayesian analyses taking account of exposure misclassification and informative priors resulted in posterior distributions of ORs with lower boundary of 95% credible intervals >1.00 for almost all exposures.

Conclusions: The distribution of NOAA in BC appeared somewhat similar to that in Alberta, except for isocyanates. Bayesian analyses allowed incorporation of prior evidence into risk estimates, permitting reconsideration of the apparently protective effect of isocyanate exposure.

Keywords: animal antigens; asthma; Bayesian analysis; isocyanates; wood dust

INTRODUCTION

Determining the true incidence of occupational asthma is difficult. In Canada, studies have been carried out of self-reported physician-diagnosed asthma (Johnson *et al.*, 2000) and of voluntary reporting by physicians (Contreras *et al.*, 1994; Provencher *et al.*, 1997).

However, in practice, the profile of occupational injury and disease in Canada is usually estimated from Workers' Compensation claims data (Association of Workers' Compensation Boards of Canada, 2007). Such figures are limited, in that, they only reflect disease or injury for which claims are made [perhaps some 60% of injuries (Shannon and Lowe, 2002) or occupational disease (Biddle *et al.*, 1998)]: they do not include, or seriously under-represent, some important sectors of the population, particularly agriculture.

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We previously described a method to identify the incidence of new-onset adult asthma (NOAA), by industry and occupation, using a data linkage approach (Cherry *et al.*, 2009). This allowed an estimate of differences in incidence of NOAA between occupations and industries by linking information on occupation and industry from Workers' Compensation Board (WCB) databases with information on use of physician services from the single governmental provider of universal healthcare in Alberta. In addition, by utilizing an asthma-specific job exposure matrix (JEM) (Kennedy *et al.*, 2000), we were able to identify workplace exposures conferring significant excess risk of NOAA. While NOAA is not the same as occupational asthma, it is thought that work is important in a significant proportion of NOAA among individuals of working age and is estimated to account for ~10 to 25% of risk (Karjalainen *et al.*, 2001; Kogevinas *et al.*, 2007; Torén and Blanc, 2009). Based on estimates from our earlier paper, it appeared that the true level of occupational asthma in Alberta was significantly under-represented by WCB claims for this condition.

The aim of the present study was to extend the data linkage approach developed in Alberta to another Canadian province, British Columbia (BC), and to apply information from the Alberta analysis to estimates from BC, using a Bayesian approach developed for our previous study in Alberta, to correct for exposure misclassification (Liu *et al.*, 2009).

METHODS

Data were provided from linked tables within the BC Linked Health Database. These included: (i) a main Registry file showing periods of residence and eligibility for public healthcare in BC, (ii) a Medical Services Plan File showing diagnostic and billing information for treatment provided under the provincial healthcare plan, and (iii) a WorkSafe BC file containing data on WCB claims. Files were linked by a unique study ID number created by the BC Linked Health Database.

The study included information on occupation and industry for all WCB claims made from 1 January 1995 to 31 December 2004, the same time frame as used in the previous report using Alberta data (Cherry *et al.*, 2009). Information on asthma was included for the period 1 January 1991 to 31 December 2004.

Occupational data

WCB claims data were screened for inclusion (Fig. 1). Records were restricted to the relevant time

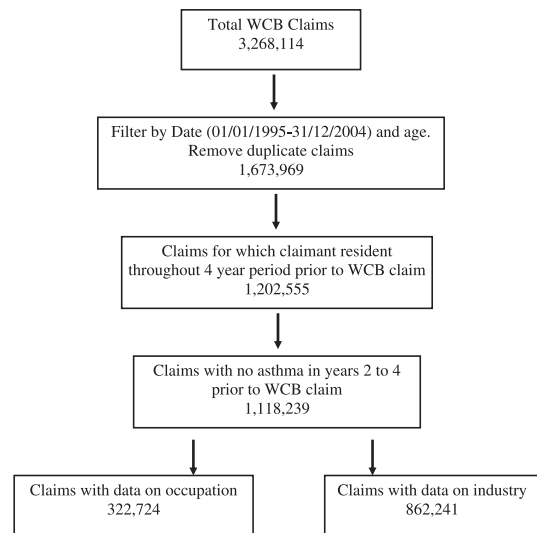


Fig. 1. Flow chart to illustrate data selection from within WCB claims data.

period and age range 18–65 years. Duplicate claims for the same individual on the same day were removed using the algorithm that had been used for the Alberta data (Cherry *et al.*, 2009). WCB files contained a four-digit occupational code based on Standard Occupational Classification 1991 (SOC91) for the work done at the time of the injury (or the onset of symptoms for a chronic condition) that triggered the claim. A six-digit industry code [classification unit (CU) number] developed internally by WorkSafe BC was also provided.

Health data

The Medical Services Plan file was restricted to individuals aged 15–65 years at some point during this period. A diagnosis of asthma was indicated by a code of 493, 493.0, 493.1, or 493.9 in the diagnostic code fields.

Linkage

Linkage between the WCB data and administrative records for provision of medical services was through the unique study ID. For each WCB claim, the algorithm first established whether the individual involved had been 'resident' in the province for health insurance purposes (and so able to consult a provincial physician) for 4 years prior to the WCB claim. It was then determined whether they had received medical services for asthma in these 4 years. If there had been at least one physician billing for asthma in the 12 months prior to the WCB claim, Flag 1 was set to 'yes'; for billings for asthma in the

3 years prior to this (i.e. Years 2–4 prior to the WCB claim), Flag 2 was set to 'yes'. A claim was an incident one (a case of NOAA) if Flag 1 was 'yes' and Flag 2 was 'no'.

Job exposure matrix

SOC-91 codes were matched to those occupational codes included in an asthma-specific JEM (Kennedy *et al.*, 2000) to identify likely exposures to known workplace asthmagens [either a single substance of high-molecular weight (HMW) or low-molecular weight (LMW) or to mixed environments], which accounted for the majority of cases of reported occupational asthma in the study used to develop the matrix. The information on exposure was used for an individually matched case-referent analysis analogous to that performed in Alberta (Cherry *et al.*, 2009). When the value assigned to an occupation by the JEM (i.e. exposed or not) was dependent on the industry setting (for example, the workplace of healthcare workers in assessing their likely exposure to latex), three occupational health professionals reviewed that occurrence and classified it as exposed or unexposed based on a majority decision utilizing rules suggested by the JEM developers (Kennedy *et al.*, 2000).

Statistical methods

Incidence rates were calculated by age, gender, and year of WCB claim. Relative risks (RRs) for incidence of NOAA adjusted for age and gender were calculated for each occupation or industry, collapsing categories where required to ensure a minimum of 250 WCB claims for any cause over the 10-year period within each group so that relatively stable estimates were obtained. The largest occupational or industry group with the same incidence as the overall mean incidence was used as the reference category ('grocery clerk and store shelf stackers' for occupation and 'supermarket' for industry). RRs were calculated using log-binomial regression in SPSS/PASW Statistics release 18 (SPSS Inc.). For the case-referent analysis, cases of NOAA with occupational data were matched 1:1 to referents with known occupation and without asthma to the date of the case claim, on gender, age (within 1 year), date of claim (referent claims being within 2 months after the case), and prior number of claims. The odds ratios (ORs) for exposure to each of the JEM asthmagens were calculated first for both genders combined and then separately for men and women using the conditional logistic regression models fitted by the CLOGIT procedure in Stata 10.1 (StataCorp).

Bayesian correction for exposure misclassification

The methods used for correction for attenuation bias due to exposure misclassification were previously described by Liu *et al.* (2009). We applied this correction only to exposures likely associated with allergic asthma because the informative priors required for the methods could not be estimated for other exposures. Exposure to enzymes was almost perfectly correlated with exposure to flour and was not considered separately. The method required investigators to posit informative priors on the ORs, as well as the estimated extent of misclassification contained in the JEM (sensitivity and specificity). For 12 of the 16 exposures, posterior distributions from the prior Alberta analysis were available for use as priors (Table 1) (Liu *et al.*, 2009). Priors were elucidated before examining the data. Analyses were performed for both genders combined and did not include any covariates. Additional details of the methods and details of the R-code that was used to determine hyper-parameters of the prior distribution

Table 1. Priors on ORs of 'allergic asthma' for different exposures used for Bayesian analyses.

Exposure	Percentiles		
	50th	2.5th	97.5th
HMW animal antigens ^a	1.99	1.10	3.81
HMW fish/shell fish ^{b,c}	—	1.30	3.67
HMW flour ^a	1.79	1.34	2.43
HMW other plant ^b	—	1.07	2.13
HMW mite & insect ^{b,c}	—	1.17	2.13
HMW latex ^a	1.91	1.38	2.66
HMW bioaerosol ^a	1.64	1.05	2.58
HMW pharmaceutical ^a	1.86	1.25	2.82
LMW reactive ^a	1.82	1.11	3.24
LMW isocyanates ^a	2.43	1.67	3.67
LMW cleaning products ^a	1.62	1.04	2.86
LMW wood dusts ^{b,c}	—	1.23	3.27
LMW metal & metal fume ^a	2.06	1.39	3.05
Mixed: metal working fluids ^a	2.17	1.63	2.95
Mixed: textiles ^a	1.72	1.14	2.69
Mixed: agriculture ^a	1.71	1.22	2.45

^aDerived from posterior distributions from Liu *et al.* (2009), when both informative prior on OR and misclassification of exposure were considered.

^bDerived from mean of three independent estimates of 2.5th and 97.5th percentiles only.

^cPriors from analysis of data available to Liu *et al.* (2009) and Cherry *et al.* (2009) were not available due to small number of exposed cases (0–3) and expected difference in nature of exposure between Canadian provinces of Alberta and BC (see Appendix 1, available at *Annals of Occupational Hygiene* online, for detailed rationale).

are given in Appendices 1 and 2, available at *Annals of Occupational Hygiene* online, which are part of a supplementary file in the online edition only. WinBUGS(5) was used to obtain samples from posterior distributions of ORs as well as sensitivity and specificity. An overview of this process is given in Appendix 1, available at *Annals of Occupational Hygiene* online, with additional details in Appendices 3 and 4, available at *Annals of Occupational Hygiene* online, in the supplementary file in the online edition.

The project was considered and approved by the University of Alberta Health Research Ethics Board and the Behavioural Research Ethics Board of the University of British Columbia.

RESULTS

The overall incidence of NOAA was 1.4% (15 520/1 118 239), with women having almost twice the rate (2.0%: 7057/351 896) as men (1.1%: 8463/766 308). Incidence decreased slightly with age, being 1.5% in the lowest age group (<30years) compared with 1.4% in the highest age group (≥30years). This change with age was more apparent in women than men, incidence decreasing from 2.3 to 1.9% among women and 1.2 to 1.1% among

men. There was little consistent change in incidence over time, but the lowest incidence, 1.2%, was in the earliest year studied (in 1995) and the highest (1.5%) in the later years, giving a statistically significant trend ($P < 0.001$, Chi squared for trend = 49.1, $df = 1$).

After recategorizing to ensure all occupations and industries contained at least 250 claims, there were 211 categories for occupation and 356 for industry. Among occupations, there were 16 with increased risk ($P \leq 0.05$) and none at decreased risk (Table 2). Among industries, there were 44 at increased risk ($P \leq 0.05$) and 6 at decreased risk ($P \leq 0.05$) (Tables 3 and 4).

In the case-referent analysis, 5154 of the 6332 cases (83%) of NOAA with an occupation recorded were matched successfully with a referent. Within the 5154 pairs, the number exposed to any specific exposure was low, ranging from 1051 (20%) cases assigned exposure to 'other exposure: irritants' to 25 cases (0.5%) assigned exposure to 'mixed agricultural antigens' (Table 5). Only two exposures were associated with a statistically significant ($P \leq 0.05$) increased risk of NOAA overall, animal antigens [OR = 1.66, 95% confidence interval (CI) 1.17–2.36] and wood dusts (OR = 1.55, 95% CI 1.08–2.24). The OR for animal antigens was raised

Table 2. Log-binomial regression of linked WCB and Medical Services Plan data identifying occupations in BC with increased risk of NOAA ($P \leq 0.05$). Reference group = grocery clerk and store shelf stackers.

Occupation code	Occupation description	Number of claims	Number with NOAA	RR unadjusted	RR adjusted*	95% CI
G62	Other occupations in protective services	387	14	2.43	2.62***	1.47–4.69
D313	Other aides and assistants in support of health services	297	14	3.17	2.58**	1.44–4.63
H3	Machinists, metal forming, shaping, and erecting	288	8	1.87	2.35**	1.12–4.94
J141	Sawmill machine operators	1757	48	1.84	2.29***	1.58–3.31
H113	Gas fitters	375	10	1.79	2.25**	1.15–4.40
H713	Taxi and Limousine Drivers and Chauffeurs	994	26	1.76	2.23***	1.41–3.51
B51	Clerical occupations and general office skills	312	12	2.58	2.06**	1.11–3.85
D212	Medical laboratory technicians	454	16	2.37	1.94**	1.12–3.37
H	Trades, transport equipment op and related	923	21	1.53	1.92**	1.17–3.14
J222	Furniture and fixture assemblers and inspectors	536	13	1.63	1.84**	1.01–3.34
J172	Industrial butchers and meat cutters and poultry preparers and related workers	1527	39	1.72	1.72**	1.16–2.56
G812	Elementary and secondary school teacher assistants	1600	52	2.18	1.76**	1.22–2.53
G512	Bartenders	610	18	1.98	1.69**	1.00–2.85
G813	Early childhood educators and assistants	784	25	2.14	1.64**	1.03–2.60
E131	Secondary school teachers	1187	30	1.70	1.60**	1.04–2.47
H712	Bus drivers, transit, and other transit operators	2859	54	1.27	1.47**	1.03–2.10

*Adjusted for age and gender. *** $P \leq 0.001$, ** $P \leq 0.05$ to >0.001 .

Table 3. Log-binomial regression of linked WCB and Medical Services Plan data identifying industry sectors in BC with increased risk of NOAA ($P \leq 0.05$). Reference group = supermarket.

CU number	Industry description	Number of claims	Number with NOAA	RR unadjusted	RR adjusted*	95% CI
714023	Shake or shingle mill	2398	67	1.95	2.61***	2.01–3.39
711022	Sugar refining and packaging	267	7	1.83	2.52**	1.18–5.38
723009	Traffic control—road construction or maintenance	443	18	2.83	2.45***	1.51–3.96
714012	Oriented strand board manufacture	367	10	1.90	2.39**	1.26–4.52
764012	Cemetery or crematorium	285	7	1.71	2.29**	1.08–4.89
714030	Wood preserving	286	7	1.71	2.27**	1.07–4.84
841104	Workers' Compensation Board of British Columbia	753	26	2.41	2.27***	1.52–3.40
732022	Limousine, chauffeur, and Handydart services	308	9	2.04	2.22**	1.14–4.34
712026	Metal pipe or fitting manufacture	307	7	1.59	2.14**	1.00–4.55
761040	Sport facility	411	12	2.04	2.12**	1.19–3.80
762005	Broker news or wholesale	431	12	1.94	2.12**	1.18–3.79
766016	Religious organization	432	12	1.94	2.04**	1.14–3.66
732037	Taxi service	1726	36	1.45	2.00***	1.42–2.83
764013	Day care, preschool, and playschool	1272	44	2.41	1.96***	1.43–2.69
7140	Wood and paper products	875	20	1.59	1.92**	1.22–3.02
767004	Gas utilities	820	17	1.45	1.87**	1.15–3.06
764046	Security or patrol services	1685	38	1.57	1.82***	1.30–2.55
766010	Life and job skills training	1136	31	1.90	1.71**	1.18–2.48
761033	Property management, building rental, and mobile home park	3689	78	1.47	1.67***	1.31–2.13
7130	Petroleum, coal, rubber, plastic, and chemical manufacturing	1859	36	1.35	1.62**	1.15–2.29
711019	Poultry processing	2753	59	1.49	1.60***	1.21–2.11
711012	Food product manufacturing	1380	29	1.47	1.56**	1.07–2.29
7620	Business services	2154	49	1.59	1.55**	1.15–2.09
731002	Grain elevator operation	1687	28	1.16	1.52**	1.03–2.24
7010	Agriculture	1912	36	1.31	1.51**	1.07–2.13
732020	General wharf operations	1827	28	1.07	1.49**	1.01–2.20
764014	Commercial cleaning or janitorial service	3093	65	1.47	1.46**	1.12–1.91
712040	Truck body or trailer manufacturing	2339	36	1.07	1.46**	1.03–2.06
714032	Wooden component manufacture news	6306	104	1.15	1.42**	1.14–1.76
732008	Barge, tug, and other water transport of goods news	3178	46	1.01	1.41**	1.03–1.91
714042	Woodworking or carpentry shop	5618	87	1.08	1.38**	1.09–1.74
732009	Bus line or chartered bus tours	6526	98	1.05	1.36**	1.08–1.70
7640	Other services news	3511	56	1.11	1.35**	1.02–1.78
766017	Residential social service facility	3281	71	1.51	1.34**	1.04–1.73
742015	Wholesale trade news	4190	67	1.11	1.31**	1.01–1.70
841102	Government of BC	10610	191	1.26	1.31**	1.10–1.56
766007	Counseling or social services news	4045	83	1.43	1.30**	1.03–1.65
714010	Paper recycling or cellulose insulation manufacturing	6243	85	0.95	1.29**	1.02–1.63
732011	Courier services	5134	77	1.05	1.29**	1.01–1.65
765008	Public school district	26260	463	1.23	1.28***	1.11–1.46

Table 3. *Continued*

CU number	Industry description	Number of claims	Number with NOAA	RR unadjusted	RR adjusted*	95% CI
741008	Department store	8784	167	1.33	1.23**	1.03–1.48
714022	Chemical pulp and paper mill	37175	461	0.86	1.17**	1.02–1.34
753004	Local government and related operations	32895	440	0.93	1.16**	1.01–1.33
766001	Acute care—health care and social assistance	52638	974	1.29	1.13**	1.01–1.27

*Adjusted for age and gender. *** $P \leq 0.001$, ** $P \leq 0.05$ to >0.001 .

Table 4. Log-binomial regression of linked WCB and Medical Services Plan data identifying industry sectors in BC with decreased risk of NOAA ($P \leq 0.05$). Reference group = supermarket.

CU number	Industry description	Number of claims	Number with NOAA	RR unadjusted	RR adjusted*	95% CI
704013	Underground metal or mineral mining	1352	6	0.31	0.43	0.19–0.97
831001	Specific employer—transport	1752	9	0.36	0.49	0.25–0.95
711015	Liquid dairy product manufacture	2641	15	0.40	0.53	0.31–0.89
732012	Distribution centre—transport and related services	1876	11	0.41	0.54	0.29–0.98
810804	Specific employer—mining	3160	19	0.42	0.59	0.37–0.93
703008	Integrated logging	16 328	136	0.58	0.80	0.65–0.97

*Adjusted for age and gender, all $P \leq 0.05$ to >0.001 .

Table 5. Case-referent analysis of known HMW, LMW, and mixed exposures from JEM using BC data; 5154 individually matched pairs.

Exposure	All				Men				Women			
	<i>N</i> exposed				<i>N</i> exposed				<i>N</i> exposed			
	Cases referents	OR	95% CI		Cases referents	OR	95% CI		Cases referents	OR	95% CI	
HMW animal antigens	84	51	1.66	1.17–2.36	38	20	1.9	1.11–3.27	46	31	1.50	0.95–2.38
HMW fish/shell fish	59	57	1.04	0.72–1.49	27	29	0.93	0.55–1.57	32	28	1.14	0.69–1.90
HMW flour	30	28	1.07	0.64–1.79	13	15	0.87	0.41–1.82	17	13	1.31	0.64–2.69
HMW other plant	52	47	1.11	0.75–1.64	33	29	1.14	0.69–1.87	19	18	1.06	0.55–2.01
HMW mite and insect	77	92	0.83	0.61–1.13	0	4	-	-	77	88	0.87	0.64–1.19
HMW antigenic enzymes	30	27	1.11	0.66–1.87	13	14	0.93	0.44–1.98	17	13	1.31	0.64–2.69
HMW latex	480	487	0.98	0.84–1.14	26	22	1.18	0.67–2.09	454	465	0.97	0.83–1.13
HMW bioaerosol	38	39	0.97	0.62–1.52	37	37	1.23	0.63–1.58	1	2	0.50	0.05–5.51
HMW pharmaceutical	188	168	1.13	0.91–1.41	9	11	0.82	0.34–1.97	179	157	1.16	0.92–1.45
LMW reactive	205	220	0.93	0.76–1.13	142	152	0.93	0.73–1.18	63	68	0.93	0.66–1.31
LMW isocyanates	40	69	0.57	0.39–0.85	36	63	0.56	0.37–0.85	4	6	0.67	0.19–2.36
LMW cleaning products	385	385	1.00	0.86–1.16	119	93	1.28	0.98–1.68	266	292	0.90	0.75–1.07
LMW wood dusts	74	48	1.55	1.08–2.24	71	43	1.67	1.14–2.44	3	5	0.60	0.14–2.51
LMW metal and metal fume	147	122	1.22	0.95–1.56	142	117	1.23	0.95–1.58	5	5	1.00	0.29–3.45
Mixed: metal working fluids	34	28	1.21	0.74–2.00	34	27	1.26	0.76–2.09	0	1	—	—
Mixed: textiles	27	19	1.42	0.79–2.56	5	5	1.00	0.29–3.45	22	14	1.57	0.80–3.07
Mixed: agriculture	25	22	1.14	0.64–2.02	13	6	2.16	0.82–5.70	12	16	0.75	0.35–1.59
Other exposure: irritants	1051	1055	1.00	0.90–1.10	700	715	0.97	0.86–1.10	351	340	1.03	0.88–1.22
Combustion particles	516	530	0.97	0.85–1.11	461	477	0.96	0.83–1.11	55	53	1.04	0.71–1.51
Environmental tobacco smoke	79	76	1.04	0.75–1.44	18	9	2.00	0.90–4.45	61	67	0.90	0.63–1.30

Odds ratios for which 95% confidence interval excludes 1.00 are shown in bold.

for both men and women, but significantly so only for men, whereas that for wood dusts was raised only for men, few women reporting exposure. Conversely, exposure to isocyanates was associated with a decreased likelihood of being a case, with men and women having similar ORs, albeit only being statistically significant for men.

Bayesian correction for imperfections in the JEM in combination with prior beliefs about the effects of the studied exposures on risk of asthma resulted in ORs that were all elevated above the null effect (Table 6).

DISCUSSION

One of the aims of the present study was to show that the approach used in Alberta (Cherry *et al.*, 2009; Liu *et al.*, 2009) could be applied elsewhere, and we believe we have demonstrated it can. This implies that it might be a feasible and useful approach to surveillance in any jurisdiction where similar data were available.

There were a number of reassuring consistencies in results between the two provinces and with previous studies of asthma. For example, both Alberta and BC showed a higher risk of NOAA for women than

men, consistent with previous studies (Karjalainen *et al.*, 2001; Thomsen *et al.*, 2005; Kogevinas *et al.*, 2007). Similarly, in both provinces, and as previously described, there was a decreased risk of NOAA with increasing age (Senthilselvan 1998; Janson *et al.*, 2001; Thomsen *et al.*, 2005). In both Alberta and BC, there was a trend towards increased incidence of NOAA in more recent years, although it appeared more pronounced in BC.

A number of occupations and industries were identified as being at a higher risk of NOAA in BC. Those that might have been expected to have an increased risk included those with wood dust exposure, recognized as a cause of asthma in BC for some years (Contreras *et al.*, 1994). Examples included 'Sawmill machine operator' among occupations and 'Wood and paper products', 'Oriented strand board manufacture', and 'Woodworking or carpentry shop' among industries. There were some occupations and industries where an excess risk might not have been anticipated, such as workers in some road transport linked activities, although other studies have suggested an increased risk (Karjalainen *et al.*, 2001), and it is possible that this represents a risk related to vehicle exhaust. A high risk of asthma among teachers and protective service workers has also previously been reported (Kraut *et al.*,

Table 6. Bayesian correction for exposure misclassification after taking into account informative prior in the OR of allergic asthma in case-referent analysis of the risk of NOAA in relation to occupational exposures; posterior distributions summarized by medians and 2.5th and 97.5th percentiles.

Exposure	π^a	Sensitivity			Specificity			OR		
		Median	2.5 Percentile	97.5 Percentile	Median	2.5 Percentile	97.5 Percentile	Median	2.5 Percentile	97.5 Percentile
HMW animal antigens	0.93	0.420	0.137	0.762	0.992	0.990	0.994	2.42	1.45	4.30
HMW fish/shell fish	0.96	0.389	0.112	0.748	0.991	0.989	0.994	2.06	1.26	3.49
HMW flour	1.00	0.438	0.146	0.768	0.994	0.993	0.995	1.80	1.34	2.42
HMW other plant	0.97	0.402	0.118	0.754	0.992	0.990	0.994	1.51	1.08	2.12
HMW mite and insect	0.96	0.334	0.080	0.721	0.991	0.987	0.994	1.48	0.98	2.37
HMW latex	1.00	0.342	0.284	0.467	0.991	0.988	0.994	1.79	1.27	2.53
HMW bioaerosol	0.99	0.420	0.138	0.763	0.993	0.991	0.995	1.61	1.05	2.55
HMW pharmaceutical	1.00	0.300	0.127	0.689	0.991	0.988	0.994	1.60	1.16	2.43
LMW reactive	0.87	0.320	0.065	0.725	0.991	0.988	0.994	1.10	0.84	2.15
LMW isocyanates	1.00	0.384	0.117	0.741	0.991	0.989	0.993	2.35	1.60	3.54
LMW cleaning products	1.00	0.258	0.106	0.702	0.991	0.988	0.994	1.16	0.91	2.21
LMW wood dusts	0.95	0.419	0.138	0.762	0.992	0.990	0.994	2.17	1.39	3.46
LMW metal and metal fume	1.00	0.340	0.112	0.719	0.991	0.988	0.994	1.82	1.34	2.66
Mixed: metal working fluids	0.99	0.432	0.144	0.769	0.994	0.992	0.995	2.29	1.71	3.12
Mixed: textiles	1.00	0.447	0.154	0.774	0.995	0.993	0.996	1.75	1.15	2.72
Mixed: agriculture	1.00	0.445	0.151	0.780	0.995	0.993	0.996	1.72	1.23	2.46

^aProbability that the constraint imposed by the disease model is satisfied [see Liu *et al.* (2009) for details].

1997; Arif *et al.*, 2003; Mazurek *et al.*, 2008). Poultry processing involves exposure to known respiratory hazards (Senthilselvan *et al.*, 2011).

Some employment including Federal Government, Armed Forces, banks, and some transportation was not covered by the provincial WCB and risks for these workers could not be assessed in this analysis. Other sectors, particularly agriculture, where WCB coverage was optional, were likely to have been both under-represented and unrepresentative.

Results of the frequentist analysis of the case-referent study using the JEM showed little overlap with results from Alberta. Mixed agricultural antigens and isocyanates were the exposures with highest risk in Alberta compared with wood dust and animal antigens in BC. This may reflect differences in climate, agriculture, and forestry between provinces as well as some changes to the matrix. The apparently protective effect associated with isocyanate exposure in BC is more difficult to understand. Bayesian analysis, accounting for exposure misclassification and errors in the JEM and using posterior distributions from the Alberta analysis, provided a markedly different estimate of risk for isocyanates than that obtained from the frequentist analysis, the direction of effect being reversed. The biggest contribution to this was likely the incorporation of the posterior distributions from the Alberta analysis: indeed an analysis including priors without accounting for misclassification and errors produced very similar results to those shown in Table 6. Furthermore, our previous work with the Alberta data showed that if we omitted the prior, correcting for misclassification in the JEM alone, we ended up with estimates that were so uncertain that they could not be interpreted (Liu *et al.*, 2009). How to best interpret the resulting risk estimates from this study is a difficult question but for the traditional conditional logistic regression analyses, it was assumed exposure estimates were perfect and that we had no a priori expectations about associations. By using a Bayesian approach, we believe more plausible results were obtained. Overall, it seems sensible to conclude that, while there are grounds for optimism, the asthma risk due to isocyanates has not necessarily been eliminated in BC.

There are, of course, considerable limitations with these data, as already discussed in the previous paper reporting this approach (Cherry *et al.*, 2009). There are likely errors in recorded occupation and industry in WCB claims, as well as individuals who changed job between getting asthma and making their WCB claim. It is difficult to estimate the magnitude and impact of these on our results, but it is on average expected that they will serve to bias estimates

towards the null, even after Bayesian correction. The information on asthma was extracted from physician billing records and so is dependent upon the accuracy of those forms. The case definition used for asthma, although identical to that used for the Alberta data, is less stringent than used in some other studies (Arif *et al.*, 2003; Kogevinas *et al.*, 2007; Mazurek *et al.*, 2008). In addition, some individuals could have been flagged as NOAA more than once if they had had several WCB claims in this period, although they would need to be >4 years apart so as not to count as prevalent. In fact, the numbers where this occurred were small (237 individuals with NOAA twice and 2 with NOAA three times) and had a negligible effect on the estimate of incidence. This definition of incidence was also used for the Alberta analyses, and we wished to keep the data as comparable as possible. Finally, because of the large number of comparisons undertaken in the analyses, some of the positive findings may be simply due to chance. Results should therefore be interpreted with caution, but given that the underlying purpose is surveillance, a high level of sensitivity is likely desirable.

Taking these data, and using a recent estimate of the fraction of NOAA attributable to work, we can come up with an approximate estimate of the expected cases of occupational asthma in BC. In 2004, WorkSafe BC insured ~1.9 million workers (WorkSafe BC, 2004) of which perhaps 10% would have prevalent asthma, leaving 1.71 million at risk of NOAA. If 1.4% of these developed NOAA during that year (~24 000), and if 15% of these were attributable to work (Karjalainen *et al.*, 2001; Kogevinas *et al.*, 2007; Torén and Blanc, 2009) that would give ~3600 cases of occupational asthma. This compares with an average of 59 cases compensated by WorkSafe BC per year between 1995 and 2004 (WorkSafe BC, 2010). This suggests considerable under recognition and under reporting. This may stem partly from uncertainty about causality and a lack of awareness about populations at risk. The data linkage approach used here provides an alternative to reporting schemes as a population surveillance tool. Analysis by occupation and industry allows the identification of previously unrecognized groups at risk, which could be included in workplace surveillance programs and educational initiatives designed to reduce the wholly preventable burden of occupational asthma.

CONCLUSIONS

The methods utilized in Alberta appeared to be applicable in BC and presumably could be used to estimate the incidence of NOAA in other jurisdictions

also. The distribution of NOAA in BC appeared somewhat similar to that in Alberta, with the notable exception that exposure to isocyanates appeared protective. Bayesian analyses usefully allowed incorporation of prior evidence into risk estimates, permitting reconsideration of this apparently protective effect of isocyanate exposure. Occupational asthma appears to be under recognized in BC, as in other jurisdictions.

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Estimating the extent and distribution of new onset adult asthma in British Columbia using frequentist and Bayesian approaches.

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Supplementary file: Appendices

Appendix 1. Additional details of methods used for Bayesian analyses.

The method required investigators to posit informative priors on the odds ratios, as well as the estimated extent of misclassification contained in the JEM (sensitivity and specificity). Wherever possible, posterior distributions from the prior Alberta analysis were used as priors.[12] For sensitivity and specificity, which did not appear to depend on the exposure assessed, we used beta distributions with 2.5th and 97.5th percentiles of 0.282 and 0.845 for sensitivity, and beta distribution with 2.5th and 97.5th percentiles of 0.988 and 0.994 for specificity. Priors on each OR, also in the form of beta distributions, were derived from the posterior distributions in Liu et al,[12] but if they were not available from that source, or there was a reason to believe that exposures in Alberta were qualitatively different in BC (such as wood dust, with significantly more use of Western Red Cedar in BC), the priors for these ORs were taken as the average of three independent estimates (by the authors) of the odds ratio's 2.5th and 97.5th percentiles (as in Liu et al.[12]).

WinBUGS(5) was used to draw samples from posterior distributions and thereby obtain estimates of ORs as well as sensitivity and specificity. Additional details of implementing this analysis are given in Appendices 3 and 4. In each analysis, we drew 45,000 posterior samples after 5,000 burn-in iterations in order to estimate medians and symmetrical 95% credible intervals of the posterior distributions. All Monte Carlo Markov Chains converged after the initial 5,000 samples.

Appendix 2: R code for setting hyper-parameters, with specific examples from the article

```
### provided with two percentiles
beta2<-function(para) {# para[1] is the 1st percentile
# para[2] is the 2nd percentile
# para[3] is the percentage associated with para[1]
# para[4] is the percentage associated with para[2]
sum.sqr<-function(x){
sum1<-(pbeta(para[1],shape1=x[1],shape2=x[2])-para[3])^2
sum2<-(pbeta(para[2],shape1=x[1],shape2=x[2])-para[4])^2
ans<-sum1+sum2}
opt<-optim(c(1,1),sum.sqr,lower=c(0.01,0.01),method="L-BFGS-B")
out<-list(a=opt$par[1],b=opt$par[2])
print(out)}
```

```
###OR
#percentiles are from posteriors in Jiu et al SEI 2009, case D
#incorporate informative priors in Sn, Sp, and OR
```

```
g<-function(x){1/(1+1/x)}
```

```
#1 ANIMAL
### 2.5% and 97.5% prior percentile of OR is 1.10 and 3.81
beta2(c(g(1.10),g(3.81),0.025,0.975))
```

```
#2 LATEX
### 2.5% and 97.5% prior percentile of OR is 1.38 and 2.66
beta2(c(g(1.38),g(2.66),0.025,0.975))
```

```
#3 FLOUR
### 2.5% and 97.5% prior percentile of OR is 1.34 and 2.43
beta2(c(g(1.34),g(2.43),0.025,0.975))
```

```
#4 ISOCYANATES
### 2.5% and 97.5% prior percentile of OR is 1.67 and 3.67
beta2(c(g(1.67),g(3.67),0.025,0.975))
```

```
#5 CLEANING
### 2.5% and 97.5% prior percentile of OR is 1.04 and 2.86
beta2(c(g(1.04),g(2.86),0.025,0.975))
```

```
#6 HMW bioaerosol antigens
### 2.5% and 97.5% prior percentile of OR is 1.05 and 2.58
```

beta2(c(g(1.05),g(2.58),0.025,0.975))

#7 HMW pharmaceutical product

2.5% and 97.5% prior percentile of OR is 1.25 and 2.82

beta2(c(g(1.25),g(2.82),0.025,0.975))

#8 LMW highly reactive chemicals

2.5% and 97.5% prior percentile of OR is 1.11 and 3.24

beta2(c(g(1.11),g(3.24),0.025,0.975))

#9 LMW metal & metal fume

2.5% and 97.5% prior percentile of OR is 1.39 and 3.05

beta2(c(g(1.39),g(3.05),0.025,0.975))

#10 Mixed environments-metal working

2.5% and 97.5% prior percentile of OR is 1.63 and 2.95

beta2(c(g(1.63),g(2.95),0.025,0.975))

#11 Mixed environments-textiles

2.5% and 97.5% prior percentile of OR is 1.14 and 2.69

beta2(c(g(1.14),g(2.69),0.025,0.975))

#12 Mixed environments-agricultural antigens

2.5% and 97.5% prior percentile of OR is 1.22 and 2.45

beta2(c(g(1.22),g(2.45),0.025,0.975))

#expert priors for BC data

#13 HMW fish/shell fish

2.5% and 97.5% prior percentile of OR is 1.3 and 3.67

beta2(c(g(1.3),g(3.67),0.025,0.975))

#14 HMW other plant

2.5% and 97.5% prior percentile of OR is 1.07 and 2.13

beta2(c(g(1.07),g(2.13),0.025,0.975))

#15 HMW mite & insect

2.5% and 97.5% prior percentile of OR is 1.17 and 2.83

beta2(c(g(1.17),g(2.83),0.025,0.975))

#16 Wood dust

2.5% and 97.5% prior percentile of OR is 1.23 and 3.27

beta2(c(g(1.23),g(3.27),0.025,0.975))

###SeNsitivity and SPecificity

#percentiles are from
#medians of 12 percentiles of posteriors in Jiu et al. SIM 2009
#FROM analysis in with informative priors on all parameters
#negligible variance in percentiles across 12 exposures

2.5% and 97.5% prior percentile of SN is 0.282 and 0.845
beta2(c(0.282,0.845,0.025,0.975))

2.5% and 97.5% prior percentile of SP is 0.988 and 0.994
beta2(c(0.988,0.994,0.025,0.975))

Appendix 3: WinBUGS code for sampling from posterior distributions: models, initial values and the data

```
#N is the number of matched pairs
#beta(a, b) is the prior on OR (odds ratio)
#p is SN ~ beta(alpha0, alpha1), sensitivity of job-exposure matrix
#q is SP ~ beta(beta0, beta1), specificity of job-exposure matrix
#note T -- data -- in order of (1,1) (1,0) (0,1), (0,0): count of matched pairs (case
exposure, referent exposure)
#theta[1,1]=theta00, theta[1,2]=theta01, theta[2,1]=theta10, theta[2,2]=theta11

model {
  T[1:4]~dmulti(pp[1:4], N);

  #constraints on theta (theta10+theta01, theta11, theta00)
  X~dbeta(a,b)
  OR<-X/(1-X)
  delta[1]~dgamma(gamma[1],1)
  #no constraint
  delta[2]~dgamma(gamma[2],1)
  delta[3]~dgamma(gamma[3],1)

  for (k in 1:3){
    theta[k] <- delta[k] / sum(delta[])
  }

  theta[1,1]<-theta[3]
  theta[1,2]<-theta[1]/(OR+1)
  theta[2,1]<-theta[1]-theta[1]/(OR+1)
  theta[2,2]<-theta[2]

  pp[4]<-theta[1,1]*q*q+theta[2,1]*(1-p)*q+
  theta[1,2]*q*(1-p)+theta[2,2]*(1-p)*(1-p)

  pp[2]<-theta[1,1]*(1-q)*q+theta[2,1]*p*q+
  theta[1,2]*(1-q)*(1-p)+theta[2,2]*p*(1-p)

  pp[3]<-theta[1,1]*q*(1-q)+theta[2,1]*(1-p)*(1-q)+
  theta[1,2]*q*p+theta[2,2]*(1-p)*p

  pp[1]<-theta[1,1]*(1-q)*(1-q)+theta[2,1]*p*(1-q)+
  theta[1,2]*(1-q)*p+theta[2,2]*p*p

  p~dbeta(alpha0,alpha1)I(con1,)
  q~dbeta(beta0,beta1)I(con2,)
```

```

con1<-1-q
con2<-1-p
const<-theta[1,1]*theta[2,2]-theta[1,2]*theta[2,1]
ind<-step(const)
}

#initial values: the same for all models
list(delta=c(1,1,1),p=0.5,q=0.9,X=0.6)

##exposures
#animal
list(N=5154,
T=c(1,83,50,5020),gamma=c(1,1,1),a=30.6,b=15.4,alpha0=5.91,alpha1=4.32,beta0=3648
,beta1=32)

#flour
list(N=5154,T=c(0,30,28,5096),gamma=c(1,1,1),a=122,b=68,alpha0=19.6,alpha0=5.91,al
pha1=4.32,beta0=3648,beta1=32)

#latex
list(N=5154, T=
c(138,349,342,4325),gamma=c(1,1,1),a=104.3,b=54.9,alpha0=5.91,alpha1=4.32,beta0=3
648,beta1=32)

#Bioaerosol
list(N=5154, T=
c(0,38,39,5077),gamma=c(1,1,1),a=50.7,b=31.2,alpha0=5.91,alpha1=4.32,beta0=3648,be
ta1=32)

#pharmaceutical product
list(N=5154, T=
c(17,171,151,4815),gamma=c(1,1,1),a=67.1,b=36.2,alpha0=5.91,alpha1=4.32,beta0=364
8,beta1=32)

#LMW reactive chemicals
list(N=5154, T=
c(11,194,209,4740),gamma=c(1,1,1),a=39.1,b=21.1,alpha0=5.91,alpha1=4.32,beta0=364
8,beta1=32)

#isocyanates
list(N=5154, T=
c(1,39,68,5046),gamma=c(1,1,1),a=86.3,b=35.4,alpha0=5.91,alpha1=4.32,beta0=3648,be
ta1=32)

#cleaning product

```

```
list(N=5154, T=
c(41,344,344,4425),gamma=c(1,1,1),a=41.3,b=24.3,alpha0=5.91,alpha1=4.32,beta0=364
8,beta1=32)
```

#Metal and metal fume

```
list(N=5154, T=
c(8,139,114,4893),gamma=c(1,1,1),a=76.4,b=37.6,alpha0=5.91,alpha1=4.32,beta0=3648,
beta1=32)
```

#Mixed environments: metal WF

```
list(N=5154, T=
c(0,34,28,5092),gamma=c(1,1,1),a=139.6,b=61.2,alpha0=5.91,alpha1=4.32,beta0=3648,b
eta1=32)
```

#Mixed environment: textile

```
list(N=5154, T=
c(0,27,19,5108),gamma=c(1,1,1),a=57.7,b=33.4,alpha0=5.91,alpha1=4.32,beta0=3648,be
ta1=32)
```

#Mixed environment: agricultural

```
list(N=5154, T=
c(0,25,22,5107),gamma=c(1,1,1),a=86.6,b=50.5,alpha0=5.91,alpha1=4.32,beta0=3648,be
ta1=32)
```

#expert priors

#fish

```
list(N=5154, T= c(0,59,57,5038),gamma=c(1,1,1),a=
45.64055,b=21.41425,alpha0=5.91,alpha1=4.32,beta0=3648,beta1=32)
```

#plant

```
list(N=5154, T= c(0,52,47, 5055),gamma=c(1,1,1),a=81.79765,b=54.50875
,alpha0=5.91,alpha1=4.32,beta0=3648,beta1=32)
```

#dust mites & insects

```
list(N=5154, T= c(2 ,75 ,90 ,4987 ),gamma=c(1,1,1),a= 55.86772,b=
31.13573,alpha0=5.91,alpha1=4.32,beta0=3648,beta1=32)
```

#wood dust

```
list(N=5154, T= c(1 ,73 ,47 ,5033 ),gamma=c(1,1,1),a=48.5819,b=24.70502
,alpha0=5.91,alpha1=4.32,beta0=3648,beta1=32)
```

Appendix 4: R code for processing WinBUGS CODA to apply the constraint imposed by the model and to discard burn-in iterations

```
## f.or should be the file name together with the directory where you save the CODA for
OR
## f.ind should be the file name together with the directory where you save the CODA for
ind
####indicating whether the constraint is satisfied=1 or not=0
## f.p should be the file name together with directory where you save the CODA for p
i.e., sensitivity
## f.q should be the file name together with directory where you save the CODA for q
i.e., specificity

f.or<-"c:/or.txt"
f.p<-"c:/p.txt"
f.q<-"c:/q.txt"
f.ind<-"c:/ind.txt"

OR<-read.table(f.or)[,2]
ind<-read.table(f.ind)[,2]
p<-read.table(f.p)[,2]
q<-read.table(f.q)[,2]
OR.tr<-OR[ind==1]
p.tr<-p[ind==1]
q.tr<-q[ind==1]

output<-list(
OR=quantile(OR.tr[5001:50000],prob=c(0.5, 0.025,0.975), na.rm = TRUE , type=3),
SN=quantile(p.tr[5001:50000],prob=c(0.5, 0.025,0.975), na.rm = TRUE , type=3),
SP=quantile(q.tr[5001:50000],prob=c(0.5, 0.025,0.975), na.rm = TRUE , type=3),
prob=mean(ind))
print(output)
```