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Characteristics of asthma and COPD overlap syndrome (ACOS) in the Canadian population

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ABSTRACT

Objective: Asthma is a chronic disease affecting both children and adults, whereas chronic obstructive pulmonary disease (COPD) is a respiratory disease most commonly related to smoking and is usually seen in adults. When the airway disease shares features of both asthma and COPD, the phenotype is referred to as asthma and COPD overlap syndrome (ACOS). The objective of this cross-sectional study is to characterize ACOS in the Canadian population. **Methods:** Data from the first three cycles of the Canadian Health Measures Survey (CHMS) were used in this study. The study included 9059 subjects aged 30 years and above. The CHMS included a detailed interviewer-administered questionnaire and spirometry measurements. Based on the self-report, subjects were categorized into control, ACOS, COPD only and asthma only groups. **Results:** The prevalence of ACOS, COPD and asthma groups was 1.59%, 2.21% and 6.65%, respectively. The proportion of females was significantly greater than males in the ACOS group. The proportion of wheeze was highest in the ACOS group (64.93%) whereas the prevalence of shortness of breath was the highest in the COPD group (46.25%). Heart disease, cancer, arthritis and liver disease were more prevalent in the ACOS group than in COPD, asthma and control groups. Severity of airway obstruction was the highest in the ACOS group and was followed by COPD, asthma and control groups, respectively. **Conclusions:** Characteristics of ACOS in the Canadian population were similar to those observed in the developed countries and longitudinal studies are required to determine the incidence and risk factors of ACOS.

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sex; smoking

Introduction

Asthma is a chronic disease affecting both children and adults whereas chronic obstructive pulmonary disease (COPD) is primarily considered a respiratory disease related to smoking and is characteristically seen in subjects older than 40 years of age. Asthma is characterized by a history of varying respiratory symptoms, and reversible airway obstruction [1]. COPD, in contrast, is characterized by persistent respiratory symptoms, and irreversible airway obstruction [2]. A joint committee of the Global Initiative for Asthma (GINA) and the Global Initiative of Chronic Obstructive Lung disease (GOLD) defined “asthma-COPD overlap syndrome” (ACOS) as a syndrome “characterized by persistent airflow limitation with several features usually associated with asthma and several features usually associated with COPD” [3]. In comparison to subjects with asthma or COPD, subjects with ACOS are reported to have frequent

exacerbations, poor quality of life, greater prevalent of comorbidities, accelerated lung function decline and increased health care utilization and mortality [4–7].

The prevalence of ACOS varies in epidemiological studies depending on the criteria used to define asthma and COPD [8]. In a population-based study from the USA, the prevalence of ACOS based on self-reported health professional diagnosed current asthma and COPD was 3.2% which was almost similar to that reported in a Swedish study (3.4%) and was greater than that reported in studies from Central and South America (1.8%) and Denmark (1.2%) [9–12]. In a study from Italy, the prevalence of ACOS increased from 1.6% in younger adults to 4.5% in older adults [13]. Age, sex, obesity, smoking status, quality of life, healthcare utilization and lung function parameters have been considered as potential risk factors for ACOS [14].

This study examined the prevalence of ACOS and factors associated with ACOS in the Canadian adult

population and determined the association of respiratory symptoms, comorbidities and severity of airway obstruction with ACOS, COPD and asthma groups.

Methods

Canadian health measures survey

Data from the Canadian Health Measures Survey (CHMS) were used in this study. The CHMS is a biennial survey conducted by Statistics Canada to collect health information of Canadians through a household interview and direct physical measures taken at a mobile examination center (MEC) [15]. The initial survey (CHMS-Cycle 1) was conducted from March 2007 to February 2009 and approximately 5604 subjects aged 6 to 79 years participated in the survey. CHMS-Cycle 2 conducted from August 2009 to November 2011, and CHMS-Cycle 3 conducted from January 2012 to December 2013 included approximately 6395 subjects aged 3 to 79 years and 5785 subjects aged 3 to 79 years, respectively. The sample in each cycle was chosen to be representative of the Canadian population. Details of the sampling design, data collection and data description are available in the Statistics Canada publications [15]. In the three cycles of the CHMS, similar household and MEC interview questionnaires were used and the same protocol and equipment were used to obtain physical measures. Data from the three CHMS cycles were appended and design weights and bootstrap weights for the three cycles provided by the Statistics Canada were merged with the appended data. Information on demographic and lifestyle factors including sex, cultural/racial background, location of residence and smoking habit were collected during the household interview. Height, weight and spirometry measurements were taken at the MEC. As the information on COPD was collected only for subjects aged 30 years and above, subjects below 30 years were excluded from these analyses, resulting in a sample of 9059 subjects for the study.

Chronic conditions

Information on chronic conditions was obtained using the response to the interviewer-administered question “Now I’d like to ask about certain chronic health conditions which you may have. We are interested in “long-term conditions” which are expected to last or have already lasted 6 months or more and that have been diagnosed by a health professional.” The questions on chronic conditions included asthma, COPD,

chronic bronchitis, emphysema, heart disease, diabetes, cancer, arthritis or rheumatism, depression, liver disease, cancer, kidney dysfunction or disease and stroke. The responses to the questions on asthma and COPD were later confirmed during the visit to the MEC by including the following questions in the clinic questionnaire: “During the interview in your home, it was reported that you had asthma. Is this correct?” and “During the interview in your home, it was reported that you had chronic obstructive pulmonary disease (COPD). Is this correct?”

Obstructive airway disease categories

Subjects who reported a healthcare professional had diagnosed them with COPD, emphysema or chronic bronchitis were assigned to a broader COPD group. The subjects who reported a healthcare professional had diagnosed them with asthma and COPD were assigned to the asthma-COPD syndrome group (ACOS). The subjects were categorized into four mutually exclusive obstructive airway disease categories: control group (neither asthma nor COPD), ACOS, COPD only (COPD, no asthma) and asthma only (asthma, no COPD) [16]. These mutually exclusive groups are referred in the remainder of the manuscript as: as control group; ACOS group; COPD group; and, asthma group. A categorical variable with four categories was defined to represent the four groups.

Respiratory symptoms and general health

The responses to the following questions in the clinic questionnaire administered at the MEC were used to determine chronic cough, chronic cough up phlegm, shortness of breath and wheeze: “Do you cough regularly?” “Do you cough up phlegm regularly?” “Do even simple chores make you short of breath?” and “Do you wheeze when you exert yourself, or at night?”, respectively. The general health of the participant was determined from the question “In general, would you say that your health is: excellent? very good?, good? fair or poor?.”

Spirometry measurements

The details of the methods used for the spirometry measurements are reported in detail elsewhere [17]. Briefly, 337 subjects who were not eligible to participate in spirometry measurements were excluded and trained technicians performed the spirometry using

the American Thoracic Society/European Respiratory Society guidelines [18]. A Koko Pneumotach spirometer (Koko; nSpire Health, Longmont, CO) was used for the spirometry. An expert reviewed the spirograms to determine the quality of the measurements and only those measurements with at least one acceptable spirometer test (quality A or B or C) were considered in this study. The spirometric measures of lung function included forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), forced expiratory flow between 25% and 75% of FVC ($FEF_{25-75\%}$) and FEV_1/FVC ratio. Median percent-predicted lung function values and lower limit of normal (LLN) values were obtained using the reference equations for the Canadian population [17]. These equations were derived using the data from the three cycles of CHMS which were also used in this study. As post-bronchodilator spirometry measurements were not obtained in CHMS, a modification of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) for COPD, based on pre-bronchodilator spirometry, was used to classify subjects into varying COPD severity categories: severe COPD (GOLD Stage III or IV; $FEV_1/FVC < 0.70$ and $FEV_1 < 50\%$ predicted), moderate COPD (GOLD Stage II; $FEV_1/FVC < 0.70$ and $50\% \leq FEV_1 < 80\%$ predicted), mild COPD (GOLD Stage I; $FEV_1/FVC < 0.70$ and $FEV_1 \geq 80\%$ predicted) and no airflow limitation ($FEV_1/FVC \geq 0.70$) [19]. This modification has been used previously in population-based studies [16,20,21]. The severity of airflow obstruction was also classified using the two criteria: (i) $FEV_1/FVC < LLN$ and (ii) $FEV_1/FVC < LLN$ and $FEV_1 < LLN$, hereafter referred to as non-GOLD criteria [22,23].

Variable definitions

Age was calculated by the difference between the date of visit to the MEC and the date of birth and was categorized into 30 to 40 years, 41 to 64 years and 65 to 79 years. After excluding pregnant women, body mass index (BMI) was determined by dividing weight (kg) by height (cm) squared and obesity was classified, based on BMI, into underweight ($BMI < 18.5 \text{ kg/m}^2$), normal weight ($18.5\text{--}24.9 \text{ kg/m}^2$), overweight ($25.9\text{--}29.9 \text{ kg/m}^2$), obese ($\geq 30.0 \text{ kg/m}^2$). Because of the small number of participants in the underweight category in the outcome groups, the data were -grouped with the underweight and normal weight categories combined. Based on a variable derived by Statistics Canada to describe smoking habits, a categorical variable was defined to indicate never smoker,

former smoker and current smoker. A binary variable was defined to indicate any comorbidity if subjects reported a health professional diagnosis of heart disease, diabetes, cancer, arthritis or rheumatism, depression, liver disease, cancer, kidney dysfunction or disease or stroke. This study was approved by the University of Alberta Health Research Ethics Board.

Statistical methods

Design weights provided by Statistics Canada were incorporated in all the statistical analyses. Standard error, level of significance and 95% confidence interval of the regression coefficients were obtained using the 500 bootstrap weights provided by the Statistics Canada. The prevalence of ACOS, COPD and asthma for the age groups were obtained using weighted proportions. Chi-squared statistics were used to test overall significant differences in general characteristics between control, ACOS, COPD and asthma groups. For pairwise comparisons, p values from chi-squared tests were adjusted for multiple comparisons using Bonferroni's correction. Multinomial logistic regression was used to determine the personal, demographic and lifestyle factors that were associated with ACOS, COPD and asthma. In the model building, initially, each factor was considered one at a time in the multinomial logistic regression, secondly the factors that were significant at $p < 0.20$ were considered in a multivariable multinomial logistic regression and finally the variables that were significant at $p < 0.05$ were retained in the final model. Logistics regression analyses were used to determine the overall association between respiratory symptoms and ACOS, COPD and asthma groups after controlling for age, sex and smoking and for pairwise comparison, p values were adjusted for multiple comparisons. Chi-squared tests were used to determine the overall association between nominal outcomes (general health, comorbidities and severity of airway obstruction based on GOLD and non-GOLD criteria) and ACOS, COPD and asthma groups and for pairwise comparison, p values were adjusted for multiple comparisons. Stratified analyses were conducted in the control, ACOS, COPD and asthma groups to examine the effect severity of airway obstruction determined using non-GOLD criteria ($FEV_1/FVC < LLN$ and $FEV_1 < LLN$) on wheeze and shortness of breath. Non-GOLD criteria were considered instead of the GOLD criteria to obtain adequate cell frequencies for statistical analyses in the ACOS, COPD and asthma groups. Chi-squared tests were used to test the

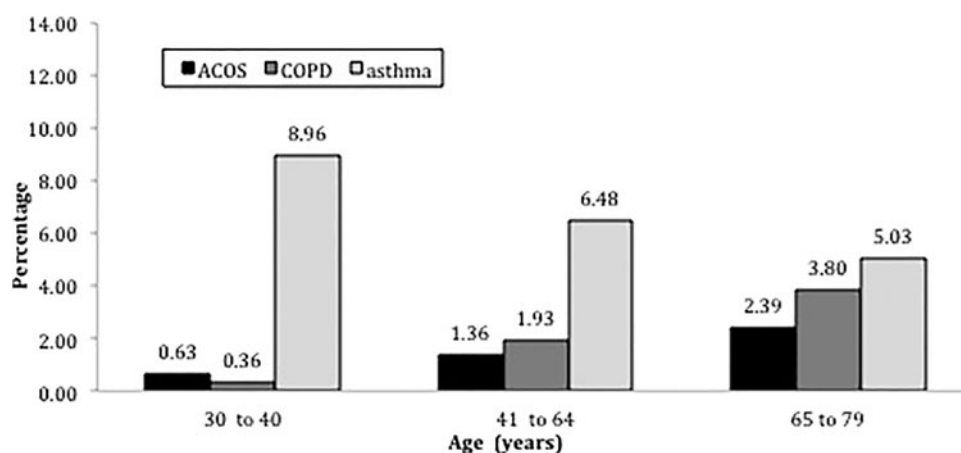


Figure 1. Prevalence of ACOS, COPD only and asthma only groups across age categories.

association between severe airway obstruction and wheeze and shortness of breath. All statistical analyses were performed using the procedures for the analysis of complex survey data in STATA (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP).

Results

The prevalence of ACOS, COPD and asthma was 1.59%, 2.21% and 6.65%, respectively. The mean age ($\pm$ SE) of the COPD group (60.58 ± 0.97 years) was greater than that of the ACOS (57.09 ± 1.64 years), asthma (48.67 ± 0.82 years) or control (50.84 ± 0.19 years) groups with the overall differences in the mean age being statistically significant ($p < 0.001$). As shown in Figure 1, the prevalence of ACOS and COPD increased with age whereas the prevalence of asthma decreased with age.

The distribution of characteristics of the control, ACOS, COPD and asthma groups are shown in Table 1. The highest proportion of subjects in the age category 30 to 40 years was in the asthma group. The distribution of age categories in the ACOS and COPD groups was significantly different from the control group. There were more females than males in ACOS, COPD and asthma groups with only the proportion of females in the ACOS group being significantly different from that in the control group. There was a significant difference in the distribution of educational level completed between the control group, and the ACOS and COPD groups, with a greater proportion of subjects with less than secondary education in the latter groups. There was no significant difference in the educational level completed between the asthma and controls groups. The proportion of current and former smokers was significantly greater in the ACOS

and COPD groups than in the control group. The proportion of obese subjects was highest in the ACOS group, with the overall difference in BMI categories between ACOS and control groups being statistically significant (Table 1).

Adjusted odds ratios from the final multinomial logistic regression for the factors associated with being included in the ACOS, COPD and asthma groups are shown in Table 2 with the control group as the reference category. Subjects in the age category 65 to 79 years were more likely to be in the ACOS and COPD groups than those in the age category 30 to 40 years whereas subjects in the older age categories were less likely to be in asthma group. Subjects who had completed secondary and post-secondary education groups were less likely to be in the ACOS and COPD groups than those who had completed less than secondary education. Similar results were seen in the asthma group, but the association was not statistically significant. Current and former smokers were more likely to be in the ACOS and COPD groups than nonsmokers. In contrast, there was no significant association between smoking and asthma. Obese subjects were significantly more likely to be in the ACOS group in comparison to those in the underweight or normal weight category. No significant association with BMI categories was seen for the COPD or asthma groups.

The distribution of respiratory symptoms and self-reported general health for control, ACOS, COPD and asthma groups are shown in Table 3. The proportions of regular cough, regular cough with phlegm and wheeze were significantly greater in the ACOS group than in other three groups. In addition, the proportion of subjects reporting wheeze was highest in the ACOS group (64.93%) with the differences between the ACOS group, and the COPD, asthma and control

Table 1. Distribution of characteristics of control, ACOS, COPD only and asthma only groups.

Characteristic	Control group (n = 8113) (%)	ACOS group (n = 144) (%)	COPD group (n = 200) (%)	Asthma group (n = 602) (%)	p Value*
Age group (years)					<0.001
30 to 40	25.15	11.75 ^a	04.90 ^c	32.79	
41 to 64	58.34	58.63	60.76	54.95	
65 to 79	16.51	29.62	34.35	12.26	
Sex					0.04
Female	50.12	66.62 ^a	56.42	57.21	
Male	49.88	33.38	43.58	42.79	
Ethnicity					0.16
Caucasians	73.68	91.36	78.87	81.28	
Others	21.32	8.64	21.13	18.72	
Education					0.009
Less than secondary	13.14	31.00 ^b	30.25 ^b	15.96	
Secondary	18.60	17.02	13.34	16.16	
Post-secondary	68.25	51.98	56.40	67.88	
Marital status					<0.001
Married	74.99	51.79 ^b	64.45 ^c	69.87	
Single	11.07	15.50	06.06	17.11	
Widowed	13.94	32.71	29.48	13.02	
Province					0.51
Atlantic	06.99	06.52	09.96	07.39	
Ontario	23.53	30.87	19.88	26.96	
Quebec	39.04	40.25	45.27	33.28	
Prairies	16.81	14.39	16.30	15.85	
British Columbia	13.63	07.98	08.58	16.52	
Smoking status					<0.001
Never smoker	48.43	20.18 ^c	16.19 ^c	40.51	
Current smoker	19.62	44.83	40.96	23.05	
Former smoker	31.95	34.99	42.85	36.44	
Obesity					0.04
Underweight or Normal weight	34.23	23.55 ^a	28.88	32.19	
Overweight	38.67	31.71	32.86	35.75	
Obese	27.10	44.74	38.26	32.06	

*p values from chi-squared statistics for overall comparison between control, ACOS, COPD and asthma groups.

^ap < 0.05, ^bp < 0.01, ^cp < 0.001 from chi-squared statistics for comparison with controls after adjusting for multiple comparison using Bonferroni's correction.

Table 2. Adjusted odds ratios for the factors associated with ACOS, COPD and asthma in the final model: results from the multinomial logistic regression analysis.*

Characteristic	ACOS group OR (95% CI)	COPD group OR (95% CI)	Asthma group OR (95% CI)
Age group (years)			
30 to 40	1.00	1.00	1.00
41 to 64	1.99 (0.68, 5.60)	4.78 ^b (2.03, 11.27)	0.66 (0.43, 1.02)
65 to 79	3.32 ^a (1.25, 8.80)	9.00 ^c (3.31, 24.51)	0.49 ^a (0.29, 0.83)
Sex			
Female	1.00	1.00	1.00
Male	0.43 ^b (0.25, 0.73)	0.65 (0.40, 1.03)	0.67 ^a (0.46, 0.98)
Education			
Less than secondary	1.00	1.00	1.00
Secondary	0.45 ^a (0.21, 0.97)	0.40 ^a (0.17, 0.93)	0.63 (0.31, 1.29)
Post-secondary	0.52 ^a (0.29, 0.92)	0.61 (0.30, 1.23)	0.77 (0.41, 1.43)
Smoking status			
Never smoker	1.00	1.00	1.00
Current smoker	6.21 ^c (3.25, 11.86)	6.98 ^c (3.37, 14.50)	1.40 (0.86, 2.28)
Former smoker	2.32 ^b (1.30, 4.14)	3.35 ^b (1.49, 7.52)	1.49 ^a (1.04, 2.14)
BMI (kg/m ²)			
Underweight (< 18.5) or Normal weight (18.5–24.9)	1.00	1.00	1.00
Overweight (25.9–29.9)	1.28 (0.59, 2.78)	0.95 (0.52, 1.71)	1.17 (0.77, 1.79)
Obese (≥ 30.0)	2.52 ^b (1.27, 4.99)	1.61 (0.98, 2.64)	1.42 (0.94, 2.13)

*In the multinomial logistic regression, ACOS, COPD and asthma groups were compared with the control group.

^ap < 0.05, ^bp < 0.01, ^cp < 0.001 from multinomial logistic regression.

groups being statistically significant after adjusting for age, sex and smoking. The proportion of subjects reporting shortness of breath was highest in the COPD group (46.25%) with the difference between the COPD group, and the asthma and control groups

being statistically significant. However, there was no significant difference in the proportion of subjects reporting shortness of breath between the ACOS and COPD groups. The proportion of subjects reporting respiratory symptoms was significantly lower in the

Table 3. Distribution of respiratory symptoms and general health among control, ACOS, COPD only and asthma only groups.*

Characteristic	Control group (%)	ACOS group (%)	COPD group (%)	Asthma group (%)	<i>p</i> Value**
Regular cough	12.80	64.86 ^{b,d}	45.86 ^b	22.88 ^b	<0.001
Regular cough with phlegm	09.53	49.21 ^{b,d}	37.29 ^{b,c}	13.43	<0.001
Shortness of breath	08.75	33.15 ^b	46.25 ^{b,c}	19.79 ^a	<0.001
Wheeze	06.28	64.93 ^{b,d}	39.81 ^{b,e}	26.14 ^a	<0.001
General health					<0.001
Poor	02.44	21.30 ^b	11.41 ^b	05.37 ^a	
Fair	08.44	29.76	21.85	13.72	
Good	36.11	37.18	39.76	36.41	
Very good/Excellent	53.01	11.76	26.98	51.38	

**p* values reported in the table were obtained after adjusting for age group, sex and smoking using multinomial or multiple logistic regression analysis. The distribution of general health was compared only between controls and other three disease groups.

***p* values for overall comparison between ACOS, COPD and Asthma group and control subjects.

^a*p* < 0.05, ^b*p* < 0.001 for comparison with controls after adjusting for multiple comparisons using Bonferroni's correction.

^c*p* < 0.01, ^d*p* < 0.001 for comparison with asthma after adjusting for multiple comparisons using Bonferroni's correction.

^e*p* < 0.05 for comparison with ACOS after adjusting for multiple comparisons using Bonferroni's correction.

control group than in the other three groups. The proportion of subjects reporting poor health was highest in the ACOS group, followed by the COPD, asthma and control groups, with the overall difference in general health between the control group and the other three groups being significantly different after controlling for age, sex and smoking.

As shown in Table 4, the proportion reporting comorbidities was highest in the ACOS group and was followed by the COPD, asthma and control groups. Except for heart disease, the proportion of comorbidities in the control group was significantly lower than the proportion in the ACOS, COPD and asthma. Significant differences were observed between the ACOS and asthma groups in the proportion reporting liver disease and arthritis, and between the COPD and asthma groups in the proportion reporting arthritis. The proportion of any reported comorbidity was the highest in the ACOS group and was followed by the COPD, asthma and control groups.

The distribution of severity of airway obstruction defined by GOLD and non-GOLD criteria for control, ACOS, COPD and asthma groups are shown in Table 5. The severity of airway obstruction was highest in the ACOS group, was followed by the COPD, asthma and control groups, respectively. However, only the differences between the control group and the other three groups were statistically significant. Not all those who self-reported COPD had COPD confirmed by spirometry at the time of this assessment, including approximately 49.91% of the ACOS group and 54.40% of the COPD group.

The difference in the proportion of severe airway obstruction between subjects with and without wheeze was significant in the control group (19.75% vs. 4.52%; *p* < 0.001) and non-significant in the ACOS (40.95% vs. 23.77%; *p* = 0.10), COPD (40.16% vs.

20.30%; *p* = 0.08) and asthma (28.87% vs. 17.99%; *p* = 0.08) groups. Similar results was observed for shortness of breath with the difference in the proportion of severe airway obstruction between subjects with and without shortness of breath being statistically significant in the control group (9.89% vs. 5.05%; *p* = 0.002) but non-significant in the ACOS (37.61% vs. 33.85%; *p* = 0.76), COPD (34.43% vs. 22.74%; *p* = 0.30) and asthma (22.63% vs. 20.36%; *p* = 0.76) groups.

Discussion

In this study, the prevalence of ACOS was 1.59% which was very similar to that reported in a prior cross-sectional study conducted in Central and South America (1.8%) and in a cohort study conducted in Denmark (1.2%) [11,12]. However, it was lower than that reported in the cross-sectional studies conducted in the USA (3.2%) and Sweden (3.4%) and greater than that reported in a cross-sectional study from Spain (0.56%) [7,9,10]. Similar to this study, self-reported health professional diagnosed asthma and COPD were used to define ACOS in studies conducted in Spain, USA and Italy whereas post-bronchodilator FVC and FEV₁ measurements were used to define asthma and COPD in the studies conducted in Sweden and from Central and South America [7,9–11,13]. The study from Denmark included both prevalent and incident ACOS cases [12]. Similar to the finding in this study, the prevalence ACOS and COPD increased with age and the prevalence of asthma decreased with age in studies conducted in the USA, Spain and Italy [7,9,13].

The proportion of females in the ACOS group was significantly greater than the proportion in the control group in these data. Although there was also a greater

Table 4. Distribution of comorbidity characteristics among control, ACOS, COPD only and asthma only groups.

Comorbidity	Control group (%)	ACOS group (%)	COPD group (%)	Asthma group (%)	p Value*
Heart disease	04.86	20.1 ^c	14.48 ^{a,f}	03.61 ^f	<0.001
Diabetes	06.77	14.2 ^a	15.74 ^a	08.69	0.002
Cancer	07.50	19.45 ^a	15.64 ^a	09.28	<0.001
Arthritis	18.56	53.48 ^c	49.36 ^{c,g}	23.57 ^e	<0.001
Depression	09.74	35.44 ^c	21.79 ^b	21.90 ^c	<0.001
Liver disease	02.98	08.32 ^a	06.95	02.71 ^d	0.005
Any comorbidity	36.01	84.43 ^c	73.48 ^{c,f}	52.06 ^{c,e}	<0.001

*p values from chi-squared test for overall comparison between ACOS, COPD and asthma group and control.

^ap < 0.05, ^bp < 0.01, ^cp < 0.001 from chi-squared test for comparison with controls after adjusting for multiple comparisons using Bonferroni's correction.

^dp < 0.05, ^ep < 0.001 from chi-squared test for comparison with ACOS after adjusting for multiple comparisons using Bonferroni's correction.

^fp < 0.05, ^gp < 0.001 from chi-squared test for comparison with asthma after adjusting for multiple comparisons using Bonferroni's correction.

Table 5. Distribution of airway obstruction using modified GOLD and non-GOLD criteria among control, ACOS, COPD only and asthma only groups.

Characteristic	Controls (%)	ACOS (%)	COPD group (%)	Asthma group (%)	p Value**
Modified GOLD criteria*					<0.001
No airflow limitation	88.65	49.91 ^a	54.40 ^a	67.04 ^a	
Stage I	06.99	12.56	14.28	11.77	
Stage II	04.12	26.33	19.88	18.88	
Stages III and IV	00.24	11.20	11.44	02.31	
Non-GOLD staging criteria					
FEV ₁ /FVC < LLN	7.40	36.87 ^a	31.73 ^a	26.00 ^a	<0.001
FEV ₁ /FVC < LLN and FEV ₁ < LLN	5.45	35.04 ^a	28.07 ^a	20.81 ^a	<0.001

*Because of the small sample sizes in Stage III and IV, the p values were obtained after collapsing Stages II and III and IV in to a single category.

**p values for overall comparison between ACOS, COPD and asthma group and control subjects.

^ap < 0.001 for comparison with controls after adjusting for multiple comparison using Bonferroni's correction.

proportion of females in the COPD and asthma groups, the sex distribution of these groups was not significantly different from the control group. The highest proportion of females was in the ACOS group that was similar to studies conducted in Finland, the USA, Spain and Italy [6,7,9,13,16]. The protective effect for participants of having completed secondary or post-secondary education in terms of their risk for ACOS that was observed in this study was also reported in other studies [9,10,12]. This may be related to a healthier lifestyle, or possibly a less hazardous workplace, among subjects who completed secondary or higher education in comparison to those who completed less than secondary education [24].

In this study, the proportion of current and former smokers was greater in the ACOS and COPD groups than in asthma and control groups. These findings are similar to reports from other studies including those from Spain and USA [7,9]. However, the proportion of never smokers was greater in the ACOS group than in the COPD group in this study (20.18% vs. 16.19%), and this, coupled with the findings on the proportion with obesity in the different groups, provides some support to the observation that ACOS is more prevalent in individuals whose main risk factor for airways obstruction is body weight rather than exposure to

tobacco smoke [25]. In this study, the likelihood of being obese for those in the ACOS group was more than twice that for the control group. Similar trends were observed in the COPD and asthma groups, but these were not statistically significant. This finding was also observed in the study from USA and according to the authors, the association between obesity and ACOS was the most important finding of their study [9].

The clinical feature which best distinguished between the ACOS and COPD groups was the differences in the proportion reporting wheeze or shortness of breath. The proportion of subjects reporting wheeze was the highest in the ACOS group (64.93%) whereas the proportion of subjects reporting shortness of breaths was the highest in the COPD group (46.25%). The proportion of both these symptoms was lower in the asthma group. The proportion reporting "regular cough" and "regular cough with phlegm" was greater in the ACOS group than in the COPD group. In the stratified analyses, the severity of airway obstruction based on non-GOLD criteria (FEV₁/FVC < LLN and FEV₁ < LLN) was not associated with wheezing or shortness breath in the ACOS, COPD and asthma groups. The reasons for the increased proportion of shortness of breath in the COPD group and increased

proportion of wheeze in the ACOS group cannot be explained from these data but may be related to clinical factors that were not considered in this study. Similar to the findings in this study, the proportion reporting wheeze, cough and cough with phlegm was greater in the ACOS group than in the COPD and asthma groups in the studies from Sweden and Italy [10,13]. However, the proportion reporting dyspnea determined by dyspnea scale of the Medical Research Council scale (grade ≥ 3) was the highest in the ACOS group in the Italian study [13].

The association between comorbidities and ACOS has been investigated in several studies [5–7,9–11]. Although several comorbidities were more prevalent in the ACOS group in comparison to the COPD and asthma groups, no single comorbidity was consistently more prevalent across the studies. In this study, the proportion of subjects with heart disease, cancer, arthritis and liver disease was the highest in the ACOS group than those in the control, COPD and asthma groups with the differences in these proportions between ACOS and control groups being statistically significant.

In this study, modified GOLD criteria and LLN were used to determine the severity of airway obstruction in the ACOS, COPD, asthma and control groups. Although the severity of airway obstruction in the ACOS group was significantly different from the control group and greater than other three groups, there was no significant difference between ACOS, COPD and asthma groups. Pre-bronchodilator lung function measurements in this study may not be adequate to differentiate the airway obstruction between three disease groups. This finding is not surprising given that diagnosis of ACOS remains a challenge for the clinicians [3,8]. What was somewhat surprising was the proportion in the COPD and ACOS groups who did not have evidence of airway obstruction at the time of testing. Airway obstruction in these groups is usually considered largely irreversible, but less than 50% of the COPD group had COPD as defined by modified GOLD criteria, similar to the results reported in a study using the data from the CHMS-Cycle 1 [21]. This suggests possibly a reporting error by the participants, diagnostic error by the healthcare professionals or perhaps greater potential for reversibility in these conditions than is often anticipated.

Although patients of ages 40 years and above are considered in the definition of COPD by the GOLD Science Committee [19], this study included younger adults in the age group 30 to 40 years so that the results from this study are comparable to those from other

population-based studies. Adolescents and younger adults were included in the majority of the population-based studies examining ACOS [5–7,9,10,13,16].

This study has strengths and limitations. This study used the data from the two CHMS cycles, which allowed the results from the study to be generalized to the Canadian population. Lung function parameters were measured in this large population-based study according to the American Thoracic Society/European Respiratory Society guidelines. One of the limitations in the study was that the history of asthma and COPD was determined from the self-report of a diagnosis by health professional. The self-report of asthma has been shown to have acceptable validity [26,27], whereas self-report of COPD has been shown to have low sensitivity and high specificity [28]. In addition, a number of biomarkers which might have helped in distinguishing ACOS from pure asthma and pure COPD, including serum eosinophilia and serum IgE, were not collected in this study.

In conclusion, characteristics of ACOS in the Canadian population were similar to those reported in the studies conducted in the developed countries. There is no suggestion that ACOS is a less severe variant of COPD in terms of either symptoms or spirometry. An important finding in the study was an association between body weight and being in the ACOS group, which was not observed so clearly, or possibly at all, in the COPD or asthma groups. Wheeze was more prevalent in the ACOS group whereas shortness of breath was more prevalent in the COPD group. Longitudinal studies would provide additional information about the incidence and risk factors of ACOS.

Disclosure statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper. The research and analysis are based on the data from Statistics Canada and opinions expressed herein do not represent the views of Statistics Canada.

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References

1. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention; 2016. Available from: www.ginasthma.org [last accessed 06 Oct 2018].

2. Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management, and Prevention of COPD (2018 Report); 2018. Available from: http://goldcopd.org/wp-content/uploads/2017/11/GOLD-2018-v6.0-FINAL-revised-20-Nov_WMS.pdf [last accessed 26 Mar 2018].
3. Asthma, COPD, Asthma-COPD Overlap Syndrome (ACOS) Global Initiative for Asthma (GINA); 2015. Available from: www.ginasthma.org [last accessed 06 Oct 2018].
4. Gibson PG, Simpson JL. The overlap syndrome of asthma and COPD: what are its features and how important is it? *Thorax* 2009;64:728–735.
5. Kauppi P, Kupiainen H, Lindqvist A, Tammilehto L, Kilpeläinen M, Kinnula VL, Haahtela T, et al. Overlap syndrome of asthma and COPD predicts low quality of life. *J Asthma* 2011;48:279–285.
6. Andersén H, Lampela P, Nevanlinna A, Säynäjäkangas O, Keistinen T. High hospital burden in overlap syndrome of asthma and COPD. *Clin Respir J* 2013;7:342–346.
7. van Boven JF, Román-Rodríguez M, Palmer JF, Toledo-Pons N, Cosío BG, Soriano JB. Comorbidome, pattern, and impact of asthma-COPD overlap syndrome in real life. *Chest* 2016;149:1011–1020.
8. Tho NV, Park HY, Nakano Y. Asthma-COPD overlap syndrome (ACOS): a diagnostic challenge. *Respirology* 2016;21:410–418.
9. Kumbhare S, Pleasants R, Ohar JA, Strange C. Characteristics and prevalence of asthma/chronic obstructive pulmonary disease overlap in the United States. *Ann Am Thorac Soc* 2016;13:803–810.
10. Ekerljung L, Mincheva R, Hagstad S, Bjerg A, Telg G, Stratelis G, et al. Prevalence, clinical characteristics and morbidity of the Asthma-COPD overlap in a general population sample. *J Asthma* 2018;55:461–469.
11. Menezes AMB, Montes de Oca M, Pérez-Padilla R, Nadeau G, Wehrmeister FC, Lopez-Varela MV, Muiño A, et al. PLATINO Team. Increased risk of exacerbation and hospitalization in subjects with an overlap phenotype: COPD-asthma. *Chest* 2014;145:297–304.
12. Barnes CB, Andersen ZJ, Overvad K, Tjønneland A, Ulrik CS. Prevalence and mortality of the asthma-COPD overlap syndrome (ACOS) in Denmark: a long-term follow-up study of a large random population sample. *Am J Respir Crit Care Med* 2016;193:A6161.
13. de Marco R, Pesce G, Marcon A, Accordini S, Antonicelli L, Bugiani M, Casali L, et al. The coexistence of asthma and chronic obstructive pulmonary disease (COPD): prevalence and risk factors in young, middle-aged and elderly people from the general population. *PLoS One* 2013;8:e62985.
14. Alshabanat A, Zafari Z, Albanyan O, Dairi M, FitzGerald JM. Asthma and COPD Overlap Syndrome (ACOS): a systematic review and meta analysis. *PLoS One* 2015;10:e0136065.
15. Statistics Canada. Accessing CHMS Information online; 2016. Available from: http://www23.statcan.gc.ca/imdb-bmdi/document/5071_D5_T9_V1-eng.htm [last accessed 06 Oct 2018].
16. Wheaton AG, Pleasants RA, Croft JB, Ohar JA, Heidari K, Mannino DM, Liu Y, et al. Gender and asthma-chronic obstructive pulmonary disease overlap syndrome. *J Asthma* 2016;53:720–731.
17. Coates AL, Wong SL, Tremblay C, Hankinson JL. Reference equations for spirometry in the canadian population. *Ann Am Thorac Soc* 2016;13:833–841.
18. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. *Eur Respir J* 2005;26:319–338.
19. From the Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD); 2017. Available from: <http://goldcopd.org> [last accessed 06 Oct 2018].
20. Mannino DM, Buist AS, Petty TL, Enright PL, Redd SC. Lung function and mortality in the United States: data from the First National Health and Nutrition Examination Survey follow up study. *Thorax* 2003;58:388–393.
21. Evans J, Chen Y, Camp PG, Bowie DM, McRae L. Estimating the prevalence of COPD in Canada: reported diagnosis versus measured airflow obstruction. *Health Rep* 2014;25:3–11.
22. Swanney MP, Ruppel G, Enright PL, Pedersen OF, Crapo RO, Miller MR, Jensen RL, et al. Using the lower limit of normal for the FEV1/FVC ratio reduces the misclassification of airway obstruction. *Thorax* 2008;63:1046–1051.
23. Ferguson GT, Enright PL, Buist AS, Higgins MW. Office spirometry for lung health assessment in adults: a consensus statement from the National Lung Health Education Program. *Chest* 2000;117:1146–1161.
24. National Center for Health Statistics. Health, United States, 2011: with Special Feature on Socioeconomic Status and Health. Available from: <https://www.cdc.gov/nchs/data/abus/abus11.pdf> [last accessed 06 Oct 2018].
25. Golpe R, Sanjuán López P, Cano Jiménez E, Castro Añón O, Pérez de Llano LA. Distribution of clinical phenotypes in patients with chronic obstructive pulmonary disease caused by biomass and tobacco smoke. *Arch Bronconeumol* 2014;50:318–324.
26. Senthilselvan A, Dosman JA, Chen Y. Relationship between pulmonary test variables and asthma and wheezing: a validation of self-report of asthma. *J Asthma* 1993;30:185–193.
27. Kilpeläinen M, Terho EO, Helenius H, Koskenvuo M. Validation of a new questionnaire on asthma, allergic rhinitis, and conjunctivitis in young adults. *Allergy* 2001;56:377–384.
28. Murgia N, Brisman J, Claesson A, Muzi G, Olin AC, Torén K. Validity of a questionnaire-based diagnosis of chronic obstructive pulmonary disease in a general population-based study. *BMC Pulm Med* 2014;14:49.