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Prevalence and burden of COPD misclassification in the Canadian Longitudinal Study on Aging (CLSA)

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ABSTRACT

Introduction To examine the prevalence of chronic obstructive pulmonary disease (COPD) misclassification and the associated burden of symptoms, healthcare utilisation and physical performance status in the Canadian general population. This information is presently lacking from large population-based studies with high-quality spirometry data that can be generalised to the general population.

Methods The prevalence of self-reported physician-diagnosed COPD and the concordance with spirometry airflow obstruction (AO) were assessed in a cross-sectional cohort of Canadian older adults. The associations between confirmed COPD, under-diagnosis and over-diagnosis with self-reported respiratory symptoms, healthcare utilisation and physical performance (timed up and go, handgrip strength and 4 metres walk test) were assessed, adjusting for baseline characteristics using multivariable linear and logistic models.

Results A total of 21 242 participants (mean age 64 (SD 10) years; 42% men) with high quality spirometry were included. Physician-diagnosed COPD was reported in (n=973) 5% of the participants. Only (n=217) 1% of the entire cohort had confirmed COPD supported by spirometry AO. Discordance between self-reported COPD and spirometry findings was observed in (n=1565) 8%: with 4% representing under-diagnosis cases (no self-reported COPD but AO) and 4% representing over-diagnosis cases (self-reported COPD but no AO). Compared with normals (no self-reported COPD and normal spirometry), those with confirmed, under-diagnosed or over-diagnosed COPD showed higher risks for respiratory symptoms (adjusted OR (aOR) 2.1 (95% CI: 1.6 to 2.7); aOR 1.8 (95% CI: 1.6 to 2.1]; aOR 1.6 (95% CI: 1.4 to 1.9)); healthcare utilisation in the prior 12 months (β coefficient 0.8 (95% CI: 0.2 to 2.6); β 0.9 (95% CI: 0.5 to 1.5); β 1.6 (95% CI: 0.7 to 4.0)). Mood disorders were higher in confirmed and over-diagnosed COPD (aOR 1.7 (95% CI: 1.3 to 2.4); 1.7 (95% CI: 1.4 to 2.0), respectively). Physical performance was lower for COPD groups.

Conclusions The prevalence of COPD misclassification is high in the general population of older adults. These were associated with significantly high burden of respiratory symptoms, healthcare utilisation and low physical performance compared with the general population with normal spirometry and no self-reported COPD. These findings highlight the high burden of COPD misclassification, which may be substantially reduced with

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Key messages

What is already known on this topic
► Misclassification of patients with chronic obstructive pulmonary disease (COPD) is common. The health burden of this misclassification remains unclear.

What this study adds
► Misclassified patients with COPD have a high burden of respiratory symptoms, healthcare utilisation and lower physical performance compared with those with normal spirometry.

How this study might affect research, practice or policy
► We highlight the high burden of COPD misclassification, which may be substantially reduced with greater accessibility to spirometry measurements in the community. We also highlight the individual-level factors that could help to identify those vulnerable to misclassification.

greater accessibility to spirometry measurements in the community.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is the third leading cause of death in North America and claimed an estimated 3 million lives worldwide in 2016.[1] In Canada, the reported prevalence of COPD has increased by 82% between 2001 and 2013 and affecting 17% of all Canadians aged 35–79.[2] This rising trend in diagnosed COPD is expected to continue to rise, as the population ages.[3] Furthermore, misclassification of COPD is believed to be common, with more than 50% of COPD cases currently under recognised (undiagnosed). Similarly, high rates of self-reported physician-diagnosed COPD have been shown to be unsupported by spirometry-based airflow obstruction (AO).[4 5] Therefore, the true population prevalence of

confirmed COPD and its burden remains uncertain. To date, there are no Canadian studies that have examined COPD misclassification using large, population-based data that is generalisable to the population. Most prevalence studies have used small sample size cohorts (<2000 participants),[2 6] self-reported or administrative data, and have relied on self-reported COPD diagnosis without supportive spirometry findings. In the present study, we used data from the Canadian Longitudinal Study on Aging (CLSA), to inform the prevalence of physician-diagnosed COPD with and without AO on spirometry and the extent of misclassification. Furthermore, the comprehensive data collected on self-reported respiratory symptoms, healthcare utilisation and direct physical performance measurements were used to estimate the burden associated with confirmed and misclassified COPD. Therefore, the objectives were to examine (1) the prevalence of physician diagnosed COPD, supported (diagnosed COPD) or not supported (over-diagnosed COPD) by AO on spirometry; (2) patient-related factors associated with misclassification (under-diagnosis and over-diagnosis), which may provide insight into the vulnerable population for misclassification; and (3) the burden of respiratory symptoms, healthcare utilisation and physical performance assessments with COPD misclassification.

METHODS

Participants

The study design and methodology of CLSA have been previously published.[7 8] In brief, a random stratified sample of 51 338 Canadians aged 45–85 years old were enrolled from 2011 to 2015. Recruitment was limited to participants who speak and read English or French. Residents from the Canadian three territories; First Nations reserves; remote geographical regions; long-term care facilities and members of the Armed Forces were excluded. Between 2012 and 2015, a subset of participants (comprehensive cohort n=30 097) were randomly selected within 25–50 km radius of the 11 participating centres (Victoria, Vancouver, Surrey, Calgary, Winnipeg, Hamilton, Ottawa, Montreal, Sherbrooke, Halifax and St John's) to participant in home interviews and in-person visits for physical and clinical assessments. Only participants from the comprehensive cohort with acceptable quality and reproducible spirometry were included in the present study.

Spirometry

Forced expiratory volume in the first second (FEV_1) and forced vital capacity (FVC) were collected using the TruFlow Easy-On Spirometer (Ndd Medical Technologies, Zurich, Switzerland) following the American Thoracic Society guidelines.[9] Only participants with three acceptable manoeuvres and a variability of less than 150 cc between two highest FEV_1 and FVC values were selected. All measurements were conducted without
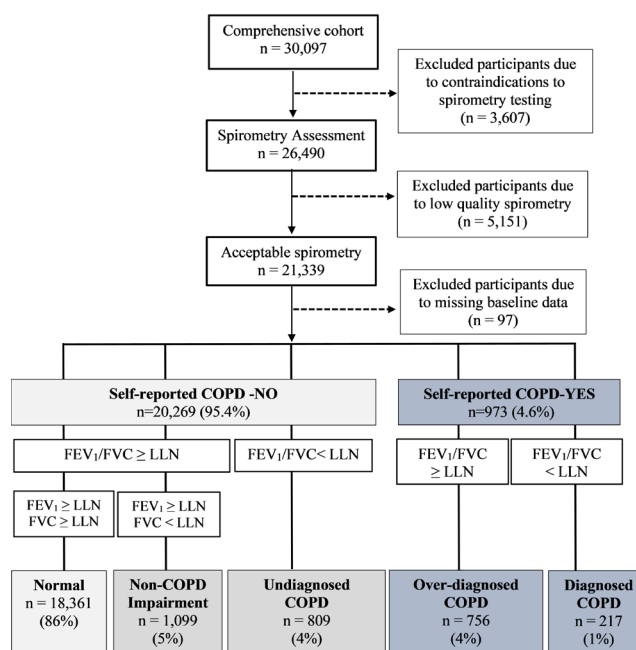

Figure 1 Flow diagram of included and excluded participants in the analysis. Self-reported chronic obstructive pulmonary disease (COPD) included self-reported emphysema, COPD and chronic bronchitis. FEV1 (forced expiratory volume in 1 s); FVC (forced vital capacity); LLN (lower limit of normal or −1.645 SD below the mean of Global Lung Initiative normative population matched for age, sex, height and ethnicity). The percentages in parenthesis represent the number of individuals within each category divided by the total sample size included the analysis (n=21 242).

bronchodilation and in a sitting position with a nose-clip. The Global Lung Initiative (GLI) reference values appropriate for age, sex, height and self-reported ethnicity were used to interpret observed FEV_1, FVC and FEV_1/FVC ratio. Values below the GLI lower limit of normal (LLN) or −1.64 SD were considered abnormal. AO was defined as FEV_1/FVC ratio <LLN; non-obstructive impairment as FEV_1/FVC ≥LLN and FVC <LLN; and normal as FEV_1/FVC, FEV_1 and FVC, all ≥LLN. Spirometry and self-reported physician-diagnosed COPD (including emphysema, COPD or chronic bronchitis) data were used to classify participants into four groups: (1) confirmed COPD (AO and self-reported physician-diagnosed COPD); (2) under-diagnosed COPD (AO and no self-reported COPD); (3) over-diagnosed COPD (self-reported COPD and no AO); (4) non-obstructive impairment (no self-reported COPD and non-obstructive impairment on spirometry) and (5) normals (no self-reported COPD and normal spirometry) (figure 1).

Questionnaire

Baseline covariates from interview-based questionnaires included: age; sex; education; total household income (from all sources before taxes and deductions in prior 12 months); smoking status; chronic diseases (eg,

asthma, coronary artery disease, congestive heart failure and diabetes); short-acting and long-acting inhaler use; self-reported mood disorders; and falls in the past year. A multimorbidity index was created by summing the number of chronic medical conditions reported. Self-reported respiratory symptoms were obtained from questionnaires asking for the presence of daily dyspnoea, wheeze, cough and frequency of colds. Self-reported healthcare utilisation over the prior year was asked (family physicians; medical specialists; psychologists; dentists; ophthalmologists, optometrists; physiotherapists; social workers; emergency department; in-hospital stay and nursing home placement). The sum of the positive responses to these healthcare services provided an index of healthcare utilisation.

Physical assessments
Weight and height were measured using validated standardised procedures.[10] Body mass index (BMI) was calculated as weight (kg) divided by height (metres, m) squared. Physical performance included the Timed-Up-and-Go (TUG), which recorded the time (seconds, s) to rise from a chair, walk 3 m at usual pace (with or without walking aids), turn around, walk back and sit down.[11] Handgrip strength was measured with a dynamometer (Tracker Freedom Wireless) and the highest value (kg) from three consecutive efforts in the dominant hand was recorded.[12] The 4 m walk recorded the time (s) to walk at usual pace.

Statistical analysis
Data were summarised using means (SD) or frequencies (n, %) as appropriate. Differences in baseline characteristics between categories were compared with χ^2 and analysis of variance tests. Associations between categories with outcomes (respiratory symptoms, healthcare utilisation, mood disorders, frequency of falls and physical performance) were assessed using multivariable logistic or linear regression with analytical sampling weight accounted for in the analysis. The goodness-of-fit tests (likelihood ratio test, deviance, Akaike's Information Criteria (AIC), Bayesian Information Criteria (BIC)), multicollinearity (tolerance and variance inflation factor) and visual inspection of residuals were performed to assess model stability and robustness. The strength of associations were reported as adjusted ORs (aOR (95% CI)) relative to normal (normal spirometry and no self-reported COPD). All regression analyses were adjusted for covariates (age, sex, education, smoking status, BMI, coronary heart disease, heart failure, cerebrovascular disease and diabetes mellitus). The analyses were conducted using SAS V.9.4 (SAS Institute).

RESULTS
There were 30 097 participants enrolled in the comprehensive cohort (figure 1). Of these, 3607 were excluded due to medical contraindications to spirometry testing; 5151 had low quality spirometry efforts and 97 with missing data. The final analysis included 21 242 participants (mean age 64 (SD 10) years; 42% men) with baseline characteristics according to the spirometry categories provided in table 1.

Demographics
Of the 21 242 included participants, 1% were confirmed COPD (n=207, self-reported COPD and spirometer-based AO); 3.8% were undiagnosed cases (n=809, AO without self-reported COPD); 3.6% were over-diagnosed cases (n=753, self-reported COPD without spirometer based AO); and 5.2% had non-obstructive impairment (n=1099, no self-reported COPD). The remaining 18 361 were classified as normals with normal spirometry and no self-reported COPD.

Self-reported COPD (confirmed and over-diagnosed cases) were more likely to be older, current or former smokers, with higher smoking intensity and lower socioeconomic status (lower education and income level), (table 1). Mean FEV_1 as a per cent of predicted were lowest for confirmed COPD (mean 61.5% (SD 16.6)), followed by non-obstructive impairment (68.9% (8.9)), and undiagnosed COPD (70.4% (15.1)); while over-diagnosed cases had the highest average $FEV_1\%$ predicted (88.3% (16.6)). Compared with confirmed COPD, the over-diagnosed cases were more likely to be women with higher mean BMI. Confirmed COPD were common in the oldest participants, in current smokers with the highest intensity of cigarette smoking. Undiagnosed cases were more common in the younger age groups, higher socioeconomic status and reported lower smoking intensity. Non-obstructive impairment was common in the youngest participants, men and had the highest average BMI. This group reported similar smoking rates and smoking intensity as the undiagnosed group.

Burden of disease for spirometry categories
Self-reported inhaler use was highest among confirmed COPD (44%), followed by over-diagnosed (16%), and undiagnosed individuals (11%). The lowest rate of inhaler use was in the non-obstructive cases (5%). Only approximately half of confirmed COPD cases, reported inhaler use (table 2). The burden of comorbidities was highest in self-reported COPD, particularly with concurrent asthma and mood disorders. Self-reported diabetes was more common among the over-diagnosed cases, while there were no differences in self-reported coronary artery disease and heart failure between confirmed and over-diagnosed COPD.

In multivariable analyses, aORs for respiratory symptoms were significantly higher for all categories compared with normal participants (figure 2). Specifically, the aORs (95% CI) for frequent colds were similar between confirmed COPD (4.1 (95% CI: 2.7 to 6.1))

Table 1 Baseline characteristics by spirometry classification

	Normal	Non-obstructive	Undiagnosed COPD	Over-diagnosed COPD	Diagnosed COPD
N (%)	18 361 (86)	1099 (5)	809 (4)	756 (4)	217 (1)
FEV$_1$ %predicted					
Mean (SD)	97.9±13.0	68.9±8.9*†	70.4±15.1*†	88.3±16.6*†	61.5±16.6*
>80%	17 008 (93)	78 (7)*††	232 (29)*†	534 (71)*†	28 (13)*
50%–80%	1353 (7)	992 (90)	500 (62)	212 (28)	142 (65)
30%–50%	0 (0)	29 (3)	73 (9)	10 (1)	38 (18)
Age					
Mean±SD	62.0±10.0	60.8±9.8*†	61.9±10.5	64.6±10.0*†	67.0±9.9*
45–54	5111 (28)†	365 (33)*†	243 (30)†	140 (18)*†	25 (11)*
55–64	6310 (34)	245 (33)	257 (32)	245 (32)	65 (30)
65–74	4233 (23)	243 (22)	172 (21)	215 (28)	64 (29)
75+	2707 (14)	131 (12)	137 (17)	156 (20)	63 (29)
Males	8660 (47)	656 (60)*†	373 (45)	283 (37)*	97 (45)
Cigarette smoking					
Mean±SD	17.6±16.9	27.2±24.3*†	27.3±22.2*†	29.3±22.6*†	42.7±25.7*
Current	1183 (6)	135 (12)*†	162 (20)*†	133 (18)*†	79 (36)*
Former	6139 (34)	583 (53)	442 (55)	495 (66)	126 (58)
Never	10 936 (60)	376 (35)	203 (25)	124 (16)	12 (6)
Level of education/schooling					
<Secondary	767 (4)	74 (7)*	47 (5)*†	70 (9)*	24 (11)*
Secondary	1657 (9)	104 (10)	78 (9)	79 (10)	23 (10)
>Secondary	15 913 (87)	917 (83)	917 (84)	606 (70)	170 (77)
Yearly income					
<20 k	678 (4)	77 (8)*†	44 (5)*†	77 (10)*	27 (13)*
20–50	3402 (20)	220 (31)	208 (27)	220 (31)	67 (32)
50–100	6144 (36)	237 (34)	252 (33)	237 (33)	77 (37)
>100	7042 (40)	172 (27)	248 (33)	172 (24)	36 (17)
BMI					
Mean±SD	27.8±8.8	31.2±7.0*†	26.3±4.9*†	29.7±6.7*†	27.8±5.6
<20	444 (2)	19 (2)*†	46 (6)*†	23 (3)*†	8 (4)
20–25	5345 (29)	185 (17)	304 (38)	152 (20)	73 (34)
25–30	7579 (41)	344 (31)	304 (38)	267 (35)	73 (34)
>30	4979 (27)	551 (50)	155 (19)	313 (42)	63 (29)
Bronchodilator use, n (%)					
No inhaler	17 906 (98)	1036 (94)*†	700 (87)*†	614 (81)*†	115 (53)*
Short acting	92 (0.5)	7 (0.5)	21 (3)	20 (3)	7 (3)
Long acting	361 (2)	55 (5)	88 (11)	122 (16)	95 (44)

Data are presented as frequency (% of total column) or as mean±SD. The mean±SD for cigarette smoking were calculated for smokers only.
**P<0.05 compared with normal category.
†P<0.05 compared with diagnosed COPD using univariate analysis (analysis of variance or Mann-Whitney tests).
BMI, body mass index; COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in the first second.

and over-diagnosed COPD (4.0 (95% CI: 3.2 to 5.0)), and less frequent in undiagnosed COPD (1.8 (95% CI: 1.3 to 2.4)). Wheeze was most common in confirmed COPD (3.9 (95% CI: 3.0 to 5.1)), followed by over-diagnosed COPD (2.6 (95% CI: 2.2 to 3.0)) and lowest in undiagnosed COPD (2.1 (95% CI: 1.7 to 2.4)). Rates of cough and dyspnoea were similar across the three groups of confirmed, over-diagnosed and undiagnosed COPD.

Both confirmed and over-diagnosed COPD groups were more likely to report mood disorder with aORs of

Table 2 Clinical and physical performance data

	Normal	Non-obstructive	Undiagnosed COPD	Over-diagnosed COPD	Diagnosed COPD
N (%)	18 361 (86)	1099 (5.2)	809 (3.8)	756 (3.6)	217 (1.02)
Comorbidities					
Asthma	1965 (11)	202 (18)*†	246 (31)*†	253 (34)*†	89 (42)*
CAD	1015 (6)	131 (12)*	57 (7.1)†	103 (14)*	32 (15)*
CHF	1618 (9)	198 (18)*	69 (9)†	138 (18)*	34 (16)*
Diabetes	2787 (15)	339 (31)*†	107 (13)†	204 (27)*†	42 (19)
Mood disorders	2951 (16.1)	174 (15.8)	116 (14.3)	212 (28.1)*	61 (28.2)*
Comorbid index					
0	2015 (11)	84 (7.6)*†	66 (8.2)†	23 (3)*	8 (3.7)*
1	7519 (41)	420 (38.2)	353 (43.6)	165 (21.8)	45 (20.7)
2	6238 (34)	382 (34.8)	275 (34)	307 (40.6)	100 (46.1)
3 and more	2589 (14)	213 (19.4)	115 (14.2)	261 (34.6)	64 (29.5)
Fall in 12 month	1779 (10.1)†	107 (10.4)†	72 (9.2)†	98 (13.6)*	33 (16.3)*
Symptoms, n (%)					
SOB	5593 (30.6)	552 (50.6)†*	388 (48.2)*†	455 (60.4)*†	164 (77)*
Wheeze	2863 (15.6)	326 (29.9)*†	307 (38)*†	381 (50.5)*†	150 (69.8)*
Cough	4719 (25.8)	351 (32.1)*	293 (36.3)*	386 (51.2)*	134 (61.8)*
Cold	664 (3.6)	80 (7.3)*	55 (6.8)*	122 (16.2)*	39 (18.1)*
Any symptom	9150 (50.1)	739 (67.8)*	567 (70.4)*	624 (82.5)*	201 (93.1)*
Healthcare utilisation					
Mean±SD	3.5±1.4	3.5±1.5	3.4±1.4*	3.7±1.5*	3.8±1.6*
TUG (s)					
Mean (SD)	9.3±2.1	10.4±3.5*	9.4±1.8	10.2±2.8*	10.6±3.1*
HGS (kg)					
Mean (SD)	35.6±11.9	35.1±11.7	34.4±11.8*	32.3±11.3*	32±10.9*
4 metres walk (s)					
Median (IQR)	4.0 (3.6, 4.6)	4.4. (3.8, 5.1)	4.1 (3.6, 4.6)	4.3 (3.8, 5.0)	4.4 (3.9, 5.1)

Comorbidity index was calculated as the sum of self-reported comorbidities. Healthcare utilisation was calculated as the sum of 10 types of healthcare used in the past 6 months, including visits to family physician, medical specialty, psychologist, dentist, ophthalmologist or optometrist, physiotherapist, social worker, emergency department, hospital overnight and nursing home.
*P<0.05 compared with normal category.
†P<0.05 compared with diagnosed COPD using unadjusted analysis (analysis of variance or Mann-Whitney test).
CAD, coronary artery disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; HGS, handgrip strength; SOB, shortness of breath; TUG, Timed-Up-and-Go.

1.7 (95% CI: 1.3 to 2.4) and 1.7 (95% CI: 1.4 to 2.0), respectively. In contrast, undiagnosed COPD and non-obstructive cases were less likely compared with normals to report mood disorders (0.8, (95% CI: 0.7 to 1.0) and 0.9 (95% CI: 0.7 to 1.0)), although this was not statistically different. The highest rate of falls was seen in confirmed COPD (1.5, (95% CI: 1.0 to 2.2)), while the other groups had similar or non-statistically elevated aOR compared with normal participants.

Lastly, healthcare utilisation was significantly higher for all spirometry groups compared with normal participants, showing similar magnitude across all groups (figure 3). The functional outcomes measured on physical performance were significantly and consistently worse on TUG, handgrip strength and 4 metres walk time in the non-obstructive group (table 3). For the remaining spirometry groups, there was a trend for a graded worsening in physical function ranging from undiagnosed and over-diagnosed groups to the worse performance observed in confirmed COPD.

DISCUSSION

In this generalisable sample of the Canadian population aged 45–85 years, the prevalence of self-reported COPD was 5%. Only 1% of the cohort with self-reported physician-diagnosed COPD were supported by airflow obstruction on spirometry (confirmed COPD). For every case of confirmed COPD, there were four cases
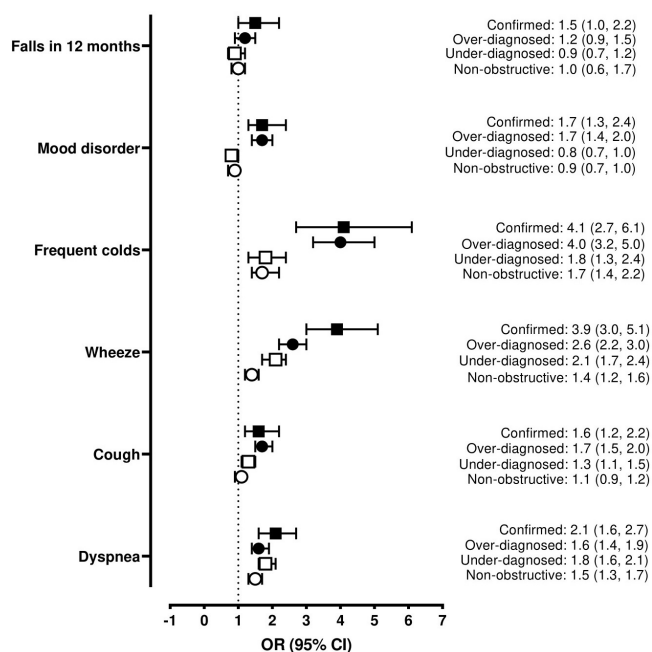
Figure 2 Adjusted ORs (95% CI)) for self-reported symptoms, mood disorder, frequent colds and falls in the past 12 months. Reference group: Normal category. All multivariable models were adjusted for age, sex, education, smoke, body mass index, inhaler use, stroke, coronary artery disease, myocardial infarction, congestive heart failure and diabetes.

of self-reported COPD without AO (over-diagnosis) and equally prevalent cases of AO without self-reported COPD (under-diagnosis). This data highlights the high rate of misclassification in the general population. Over-diagnosis was more likely in women, former smokers,
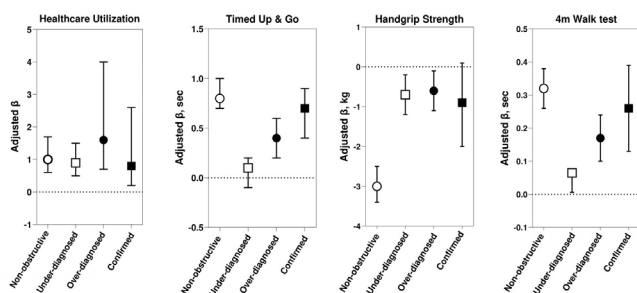
Figure 3 Adjusted differences (β coefficient) in healthcare utilisation, and physical performance relative to normal category. Adjusted β (95% CI) represents coefficient of change/difference relative to normal category adjusted for age, sex, education, smoke, body mass index, inhaler use, stroke, coronary artery disease, myocardial infarction, congestive heart failure and diabetes. Comorbidity index was calculated as the sum of self-reported comorbidities. Healthcare utilisation was calculated as the sum of 10 types of healthcare used in the past 6 months, including visits to family physician, medical specialty, psychologist, dentist, ophthalmologist or optometrist, social worker physiotherapist, emergency department, hospital overnight and nursing home.

morbid obesity and high comorbidity burden. Under-diagnosis was more common with younger age and higher socioeconomic status. In both cases, spirometry testing demonstrated only mild ventilatory impairment, but high rates of self-reported respiratory symptoms, healthcare utilisation and lower physical performance were observed compared with normal participants. These findings emphasise the high burden of disease associated with misclassified COPD.

COPD is a major cause of mortality and morbidity worldwide,[1] and yet accurate estimates on the prevalence rates have been difficult to ascertain due to limited access and under-utilisation of spirometry measurements.[13] Current international and national guidelines are consistent in their recommendation for the need of spirometry to detect airflow obstruction in order to confirm the diagnosis of COPD.[14] This is critical, since the symptomatology, disability and risk factors for COPD are similar and often overlap with other chronic diseases. Furthermore, current available therapies with proven benefits have only been studied in patients with COPD with airflow obstruction.[15] Therefore, misclassification should be viewed as missed opportunities to provide disease specific therapy that could substantially lead to a reduction in disease burden and improve the long-term health trajectory.

Similar to other national and international studies,[5 16] we had found that the rate of self-reported physician-diagnosed COPD was low at 5% in this general population. Only 1% had airflow obstruction on spirometry to support the diagnosis of COPD. The prevalence could be four times or more higher if undiagnosed cases were included. Similar to other studies,[5 6] we found undiagnosed COPD was more likely in healthier and younger individuals with higher socioeconomic status, lower smoking rates and smoking intensity. Undiagnosed COPD also tended to have overall lower burden of comorbidity and milder airflow obstruction. Other studies have also reported on the association between under-utilisation of spirometry and higher rates of COPD under-diagnosis.[17] Our findings add to the emerging evidence supporting the high healthcare utilisation and burden of respiratory symptoms associated with undiagnosed COPD.[18 19] Furthermore, we have included novel data on lower physical performance measurements, which are validated markers for poor long-term outcomes.[20 21] These findings, together with the substantially higher number of undiagnosed cases, suggest that this group may be contributing to a large and under-appreciated burden of disease. We speculate that case-finding of undiagnosed COPD could lead to early implementation of symptomatic therapies. This may in turn could lead to substantial improvement in functional and physical performance and better longer-term outcome.[22]

Our finding on the high prevalence of self-reported COPD without spirometric evidence of airflow obstruction, is in keeping with previous studies. Prevalence of over-diagnosis have been reported to be as high as five

Table 3 Results from multivariable analysis for physical performance and healthcare utilisation by spirometry categories

Adjusted β (95% CI)	Non-obstructive	Undiagnosed COPD	Over-diagnosed COPD	Diagnosed COPD
Healthcare utilisation	1.0 (0.6 to 1.7)	0.9 (0.5 to 1.5)	1.6 (0.7 to 4.0)	0.8 (0.2 to 2.6)
TUG, s	0.8 (0.7 to 1.0)	0.1 (−0.1 to 0.2)	0.4 (0.2 to 0.6)	0.7 (0.4 to 0.9)
HGS, kg	−3.0 (−3.4 to −2.5)	−0.7 (−1.2 to −0.2)	−0.6 (−1.2 to −0.1)	−0.9 (−2.0 to 0.1)
4 metres walk, s	0.32 (0.26 to 0.38)	0.01 (0.006 to 0.07)	0.17 (0.10 to 0.24)	0.26 (0.13 to 0.39)

Adjusted β (95% CI) represents coefficient of change/difference relative to normal category adjusted for age, sex, education, smoke, body mass index, inhaler use, TIA, CVA, CAD, MI, CHF, and diabetes. Comorbidity index was calculated as the sum of self-reported comorbidities. Healthcare utilisation was calculated as the sum of 10 types of healthcare used in the past 6 months, including visits to family physician, medical specialty, psychologist, dentist, ophthalmologist or optometrist, social worker physiotherapist, emergency department, hospital overnight and nursing home.
CAD, coronary artery disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CVA, stroke; HGS, handgrip strength; MI, myocardial infarction; TIA, transient ischemic attack; TUG, Timed-Up-and-Go.

times higher than confirmed cases.[4] Similar to prior studies, we found that despite the higher lung function levels, over-diagnosed cases have a high burden of comorbidity, respiratory symptoms and healthcare utilisation comparable to confirmed cases.[18] Moreover, over-diagnosis was more likely in women and those with elevated BMI, while the rate of current tobacco use and self-reported smoking intensity tended to be lower in this group. Unlike other studies,[18 19] we did not find higher rates of asthma, coronary artery disease or congestive heart failure which are conditions that may obscure the finding of AO on spirometry. Despite the label of COPD and high rates of respiratory symptoms, this group reported lower rates of bronchodilator inhaler use. Therefore, our data do not support prior concerns regarding inappropriately higher use of inhaler therapies in over-diagnosed COPD.[23] Furthermore, recent evidence has highlighted the heterogeneity in COPD phenotypes, some of which (ie, emphysema, early COPD and smaller airways disease) may not exhibit spirometry AO as defined by the FEV_1/FVC ratio <LLN or 0.7.[24] Lastly, the mechanical restriction imposed by obesity that is prevalent in this group, may obscure the finding of reduced FEV_1/FVC ratio.[25]

In the present study, we also examined individuals without a label of COPD but showed moderate non-obstructive impairment on spirometry. This group was equally prevalent as undiagnosed COPD and have been increasingly reported in the literature.[26] We found this group had similar smoking rates and smoking intensity as undiagnosed COPD. However, there was a higher proportion of men with markedly elevated BMI. Except for self-reported wheeze, the burden of symptoms, healthcare utilisation and mood disorders were similar to undiagnosed COPD. Importantly, these individuals showed overall lower physical performance particularly in handgrip strength, suggesting a more systemic pathophysiological process, which may contribute to the non-obstructive findings on spirometry. This aligns with emerging data, which report on the high mortality and disease burden associated with non-obstructive spirometric impairment in the general population.[27]

Our study has several strengths. This is the largest representative study of the Canadian general population, which systematically collected clinical and physical data including spirometry using high quality standardised methodology. Second, the large sample size and scope of variables allowed for robust adjustments of potential confounders to provide unbiased estimates. Third, we included high quality, well validated physical performance data to corroborate the self-reported outcomes, which further strengthens our findings. The limitations include the use of pre-bronchodilator spirometry values, which may overestimate the prevalence of COPD by 25%–30% .[28] It is possible that a subset of these patients may have asthma since we did not collect post-bronchodilator measurements. However, post-bronchodilator measurements were not feasible given the scale of the study and concerns over adverse effects in older adults.[29] Furthermore, the over-estimation of COPD prevalence would have the effect of diluting and reducing the strength of any associations observed between spirometry groups with outcome. Another limitation is the cross-sectional nature of the data, which is commonly used in this field of study. Future follow-up of this cohort will provide prospective data on healthcare utilisation and outcomes that will provide robust estimates on the burden of disease.

In conclusion, our findings confirm the high rate COPD misclassification in a large representative study of the Canadian general population. Compared with confirmed COPD, misclassified cases exhibited similarly high rates of respiratory symptoms, mood disorders and healthcare utilisation. We also provide novel data on reduced physical performance, which corroborated the high burden of disease with misclassification. We also reported on individual-level characteristics that may help identify subgroups prone to misclassification. Greater availability and access to spirometry testing in the community may help to reduce the rates of misclassification. Early implementation of disease-specific therapy will likely alleviate the burden of disease and improve patient health outcomes.

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