

Outcomes of patients with chronic obstructive pulmonary disease diagnosed with or without pulmonary function testing

Andrea Gershon MD MSc, Graham McCreedy MSc, Ruth Croxford MSc, Teresa To PhD, Matthew B. Stanbrook MD PhD, Shawn D. Aaron MD; for the Canadian Respiratory Research Network

ABSTRACT

Background: A small number of people with chronic obstructive pulmonary disease (COPD) receive pulmonary function testing around the time of diagnosis. Because omitting testing increases misdiagnosis, we sought to determine whether health outcomes differed between patients whose COPD was diagnosed with or without pulmonary function testing.

Methods: We conducted a longitudinal population study of patients with physician-diagnosed COPD from 2005 to 2012 using health administrative data from Ontario, Canada. We assessed whether having pulmonary function testing around the time of diagnosis was associated with the composite outcome of admission to hospital for COPD or all-cause death, using adjusted survival analysis.

Results: Chronic obstructive pulmonary disease was diagnosed in 68 898 patients during the study period; 41.2% of patients received peridiagnostic pulmonary function testing. In

adjusted analysis, patients who underwent testing were less likely to die or be admitted to hospital for COPD (adjusted hazard ratio [HR] 0.91, 95% confidence interval [CI] 0.89–0.94) and were more likely to be prescribed an inhaled long-acting bronchodilator than patients who did not undergo testing. Subgroup analysis suggested that the association of testing and outcomes was confined to patients with COPD diagnosed in the ambulatory care setting (adjusted HR 0.80, 95% CI 0.76–0.84).

Interpretation: Confirmation of a COPD diagnosis using pulmonary function testing is associated with a decreased risk of death and admission to hospital for COPD. In ambulatory patients, this effect may be from increased use of appropriate COPD medications. The findings of this study validate current guideline recommendations that encourage pulmonary function testing for diagnosis in all patients with suspected COPD.

Competing interests: None declared.

This article has been peer reviewed.

Disclaimer: Matthew Stanbrook is a deputy editor for CMAJ and was not involved in the editorial decision-making process for this article.

Accepted: Sep. 14, 2016

Online: Nov. 14, 2016

Correspondence to: Andrea Gershon, andrea.gershon@ices.on.ca

CMAJ 2016. DOI:10.1503/cmaj.151420

Chronic obstructive pulmonary disease (COPD) is the third leading cause of death, a leading cause of hospital admission and affects more than 10% of adults.^{1–3} Pulmonary function testing plays a fundamental role in COPD diagnosis by confirming persistent air-flow obstruction and ruling out other diseases. However, despite recommendations that all patients with suspected COPD undergo pulmonary function testing, only 30% to 50% of patients with physician-diagnosed COPD do.^{3–9} Thus, the diagnosis and subsequent management of COPD appears to be largely based on clinical assessment — despite the frequency of misdiagnosis that occurs.¹⁰ Although a lack of pulmonary function testing has been associated with suboptimal prescribing, smoking cessation and specialist

referral,^{11–15} studies showing better patient outcomes are lacking. This gap has been used by some physicians to justify not ordering testing.^{5,16}

We conducted the current study to determine if obtaining pulmonary function testing for suspected COPD was associated with improved health outcomes.

Methods

We conducted a longitudinal population study from 2005 to 2012 using health administrative data from Ontario, Canada.

Data sources

Residents of Ontario have universal public health insurance for all medically necessary

services. Details are captured in large health administrative databases: the Registered Persons Database provides demographic information and date of death; the Canadian Institute of Health Information Discharge Abstract Database and National Ambulatory Care Reporting System Databases contain hospital admission and emergency department visit information, respectively; the Ontario Health Insurance Plan Physician Claims database provides information about physician services; the Ontario Drug Benefit Program database contains prescription claim records for all residents aged 65 years or older that are subject to a small copayment, which does not affect the rate they are obtained;¹⁷ the Institute for Clinical Evaluative Sciences (ICES) Physician Database contains information on all physicians. These data sets were individually linked using unique encoded identifiers and analyzed at ICES.

The 2001, 2003, 2005 and 2007/8 national, population-based Canadian Community Health Surveys provided additional information, including smoking history, for the patients who participated in the survey.

Study population

Physician-diagnosed COPD is an imperfect measure of COPD — likely, at least in part, because not all patients receive pulmonary function testing.^{8,18} All patients aged 43 and older with physician-diagnosed COPD between 2005 and 2012 were identified using a previously validated case-definition of physician-diagnosed COPD: age 35 years and older, and 1 or more COPD-related hospital admission or 3 or more physician COPD ambulatory care visits within 2 years.^{19,20} This case definition has a specificity of 95% and a positive predictive value of 81% compared with a clinical reference standard (which may or may not have considered pulmonary function testing).¹⁹ Although the exact COPD diagnoses dates are not available from the data, because COPD is a disease with insidious onset, it was presumed that patients likely had COPD as per the earliest of these health service encounters. The start of follow-up (the study index date) was the latest health service encounter that was used to identify patients with COPD to avoid immortal time. A minimal 5-year look-back period ensured that COPD was newly diagnosed (Figure 1). Ages 43 years and older were studied to allow a sufficient look-back period to measure guideline-based care (Table 1). Patients were excluded if they were ineligible for health insurance, if they died during their stay in hospital, if they had previous lung volume reduc-

tion surgery or lung transplant or if their primary care physician demographic data were missing.

Exposure

The primary exposure was empiric use of pulmonary function testing around the time of diagnosis, which was defined as a period extending from 1 year before the earliest health service encounter to the latest encounter (the index date) that identified a patient's disease (Figure 1).⁸ Pulmonary function testing was generously defined as spirometry before or after bronchodilation and could have been performed in any location.

Baseline characteristics

We obtained demographic, COPD-related and general care-related characteristics from health administrative data. Patient socioeconomic status was derived ecologically using the patient's residential postal code.²³ Rural or urban residence was determined according to Statistics Canada definitions.²⁴ Comorbidities were grouped using the Johns Hopkins Adjusted Clinical Group Case-Mix System.²¹ Characteristics of patients' primary care physicians were considered because they were most responsible for arranging pulmonary function testing. Physician propensity for quality care was determined using the proportion of eligible patients who received glucose or cholesterol testing in the last 3 years — a continuous variable with a higher proportion suggesting better quality care.^{25,26} Pulmonary function testing after the peridiagnostic period was also considered — if it occurred more than once, only the first instance was counted.

Outcome measures

The primary outcome was a composite of COPD-related hospital admission or all-cause death. All-cause death was used because COPD is underestimated by about 50% as a cause of death in vital statistics records.^{27,28}

Statistical analysis

Outcomes were analyzed using Cox proportional hazards regression analysis. To compare patients with similar observed characteristics, the propensity for each patient to receive pulmonary function testing was calculated using logistic regression and all covariables (see Table 1). This propensity score was then used as a covariate in the survival analyses to estimate the effect of testing on the outcomes of interest. Full details on the calculation and use of propensity scores to address bias in observa-

tional studies is provided elsewhere.²⁹ Pulmonary function testing after the peridiagnostic period was the only time-varying covariable. To account for the possibility that physicians more likely to order testing were also more likely to provide better quality care all round, we clustered patients by their primary care physicians and adjusted for other markers of good quality care. To see if results differed by age, sex, a codiagnosis of asthma or diagnosis with COPD in the ambulatory or hospital setting, we tested the significance of interaction terms between each of these and pulmonary function testing. Analyses were performed using SAS version 9.3 (SAS Institute Inc., Cary, North Carolina).

Sensitivity analyses

Propensity score matching was performed.²⁹ However, this was not used as the primary analysis because it could not accommodate the time-varying covariate. To account for variables not available in the data, such as smoking, propensity score calibration was used. In brief, gold-standard propensity scores, one for each of the representative subcohort of people who had additional data from the Canadian Community Health Survey, were compared with original propensity scores. The relative difference was used to calibrate the propensity scores of the rest of the participants. Analysis for patients aged 67 years and older (for whom we had 2 years of look back for medication) was conducted to exclude patients who might

have had earlier unrecorded COPD — as evident by them receiving a COPD medication — and to adjust for previous medication use. Finally, we determined whether it was plausible that an unmeasured confounder or misclassification could account for the results using methods described elsewhere.³⁰ Details of all sensitivity analyses are available in Appendix 1 (available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.151420/-/DC1).

Process of care

The association of pulmonary function testing and medication use was examined in patients aged 67 years and older. Medications received were compared before and after testing or an equivalent date between patients receiving and not receiving testing (see Appendix 1). This analysis was done in the propensity score-matched group.

Ethics approval

Ethics committee approval was obtained from Sunnybrook Health Sciences Centre, Toronto, Ontario.

Results

A total of 68 898 patients had a diagnosis of COPD, of whom 41.2% received pulmonary function testing (Table 1 and Appendix 1). Patients who received testing were younger, more likely to have seen a specialist, less likely to have comorbidities and more likely to be

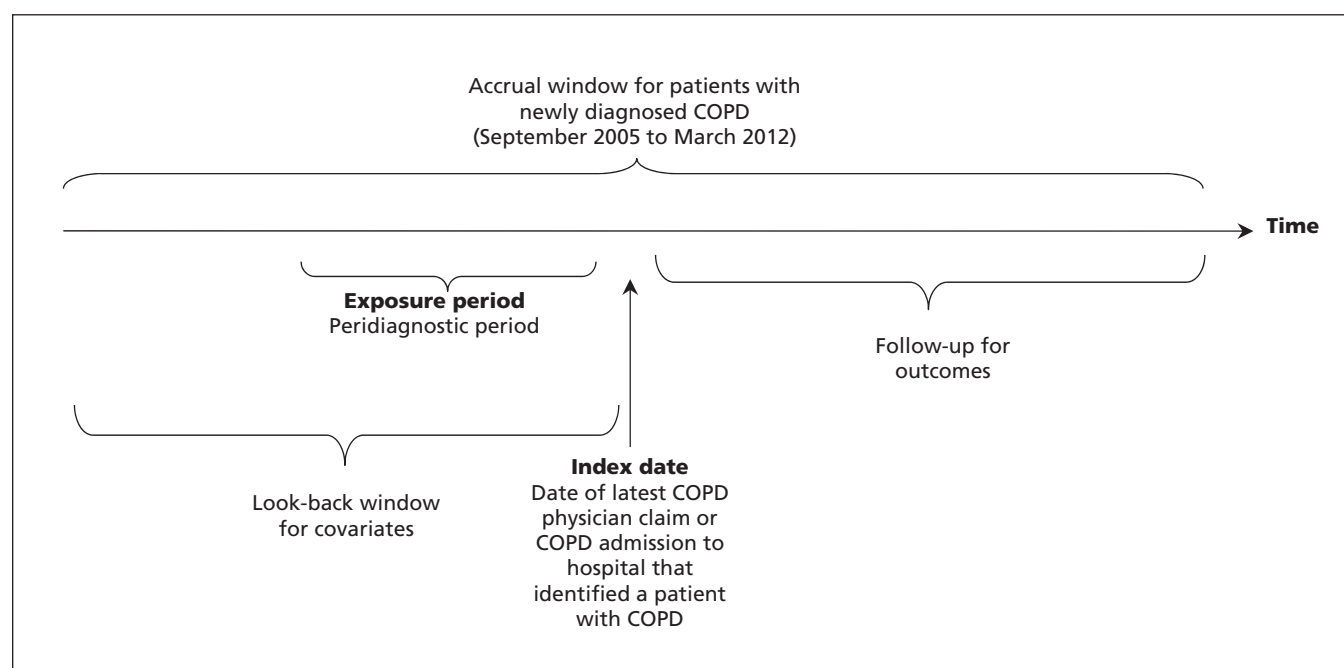


Figure 1: Study design.

Table 1 (part 1 of 2): Selected baseline characteristics, before and after propensity score matching, of patients with physician-diagnosed COPD who did and did not receive pulmonary function testing in the peridiagnostic period*

Characteristic	Before propensity score matching				After propensity score matching			
	Testing in peridiagnostic period		Standardized difference, %	p value†	Testing in peridiagnostic period		Standardized difference, %	p value†
	Yes	No			Yes	No		
Patients, <i>n</i>	28 386	40 512			17 783	17 783		
Demographic characteristics								
Mean age, years (SD)	66.86 (11.53)	70.27 (13.31)	0.27	< 0.001	67.20 (11.87)	67.20 (11.88)	0.00	1.0
Women, %	47.4	49.4	0.04	< 0.001	47.4	47.4	0.00	1.0
Income quintile, %								
1 (lowest)	22.6	25.7	0.07	< 0.001	24.1	24.2	0.00	0.9
2	21.5	22.3	0.02		22.2	22.4	0.01	
3	19.8	19.3	0.01		19.8	19.5	0.01	
4	18.7	17.4	0.03		18.0	17.8	0.00	
5 (highest)	17.4	15.4	0.05		16.0	16.1	0.00	
Rural (v. urban) residence, %	13.1	17.9	0.13	< 0.001	15.3	15.9	0.01	0.2
Immigrant, %	7.3	6.5	0.03	< 0.001	7.2	7.2	0.00	0.9
Living in long-term care, %	0.9	7.9	0.32	< 0.001	1.3	1.2	0.01	0.3
COPD-related characteristics, %								
Ambulatory during the peridiagnostic period	70.5	43.7	0.56	< 0.001	62.6	62.6	0.00	1.0
Spirometry before peridiagnostic period								
Up to 1 yr before	13.4	5.2	0.30	< 0.001	8.4	8.3	0.00	1.0
More than 1–2 yr before	5.6	3.8	0.09		4.9	5.0	0.00	
More than 2–5 yr before	10.3	7.9	0.08		9.6	9.7	0.00	
More than 5 yr before or never	70.7	83.1	0.30		77.1	77.0	0.00	
Pulmonologist visit in previous year‡	26.8	2.9	0.76	< 0.001	6.5	5.7	0.03	0.004
Internal medicine or geriatrics specialist visit in previous year‡	51.0	35.2	0.32	< 0.001	44.9	43.6	0.03	0.01
Long-term oxygen therapy	2.9	1.5	0.10	< 0.001	1.6	1.5	0.01	0.6
General health characteristics								
Median primary care physician visits in previous year (IQR)‡	7 (4–11)	7 (4–11)	0.05	< 0.001	7 (4–11)	6 (4–11)	0.03	< 0.001
Influenza vaccination, %	48.6	42.9	0.11	< 0.001	45.9	46.4	0.01	0.3
Previous or coexisting medical conditions, %								
Asthma	29.4	19.7	0.23	< 0.001	23.5	23.5	0.00	1
Other chronic respiratory disease	17.5	8.2	0.29	< 0.001	6.4	5.7	0.03	0.008
Lung cancer	8.9	4.0	0.21	< 0.001	11.3	10.6	0.02	0.04
Pulmonary embolism	2.7	2.9	0.01	0.3	2.6	2.4	0.01	0.4
Cor pulmonale	0.1	0.0	0.02	0.007	0.1	0.0	0.01	0.3
Acute myocardial infarction	30.2	34.1	0.08	< 0.001	30.3	30.3	0.00	0.9
Other ischemic heart disease	24.7	26.8	0.05	< 0.001	24.5	24.3	0.00	0.8
Congestive heart failure	19.6	26.4	0.16	< 0.001	20.6	20.1	0.01	0.2
Dementia	5.4	15.3	0.31	< 0.001	6.2	7.2	0.04	< 0.001
Arrhythmias	21.5	25.2	0.09	< 0.001	21.7	21.1	0.02	0.2
Cerebrovascular disease	11.0	17.6	0.18	< 0.001	12.4	12.2	0.00	0.7
Osteoporosis	2.2	4.2	0.11	< 0.001	2.4	2.4	0.01	0.6
Psychiatric disease								
Requiring hospital admission	0.7	1.7	0.09	< 0.001	0.9	0.9	0.00	0.8
Requiring ambulatory care visits	9.3	9.5	0.01		8.9	8.9	0.00	

Table 1 (part 2 of 2): Selected baseline characteristics, before and after propensity score matching, of patients with physician-diagnosed COPD who did and did not receive pulmonary function testing in the peridiagnostic period*

Characteristic	Before propensity score matching				After propensity score matching			
	Testing in peridiagnostic period		Standardized difference, %	p value†	Testing in peridiagnostic period		Standardized difference, %	p value†
	Yes	No			Yes	No		
Previous or coexisting medical conditions, %								
None	90.0	88.8	0.04		90.2	90.3	0.01	
Palliative	1.2	2.1	0.06	< 0.001	1.3	1.3	0.00	0.7
Overall level of comorbidity§								
High	30.4	28.4	0.04	< 0.001	27.2	26.5	0.02	0.2
Medium	43.3	40.4	0.06		42.2	42.2	0.02	
Low	26.3	31.2	0.11		30.6	31.3	0.02	
Recent acute events, %								
Most recent admission for acute bronchitis, pneumonia or influenza								
In the past 6 mo	2.4	3.2	0.05	< 0.001	2.3	2.1	0.01	0.09
> 6 mo before index date	4.6	6.2	0.07		4.6	4.2	0.02	
Never	93.0	90.6	0.09		93.2	93.7	0.02	
Most recent admission for asthma								
In the past 6 mo	0.5	0.2	0.05	< 0.001	0.3	0.3	0.00	0.2
> 6 mo before index date	1.0	0.7	0.03		0.8	0.7	0.02	
Never	98.5	99.1	0.06		98.9	99.1	0.02	
Most recent admission for other respiratory disease								
In the past 6 mo	1.6	1.2	0.03	< 0.001	0.7	0.7	0.00	0.7
> 6 mo before index date	2.3	1.5	0.06		1.6	1.5	0.01	
Never	96.1	97.2	0.06		97.8	97.9	0.01	
Most recent emergency department visit for acute bronchitis, pneumonia or influenza								
In the past 6 mo	3.6	3.9	0.02	< 0.001	3.8	3.7	0.01	0.5
> 6 mo before index date	8.2	7.6	0.02		8.1	7.8	0.01	
Never	88.2	88.4	0.01		88.1	88.5	0.01	
Most recent emergency department visit for asthma								
In the past 6 mo	1.4	0.9	0.05	< 0.001	1.3	1.2	0.01	0.9
> 6 mo before index date	2.8	1.9	0.06		2.4	2.4	0.00	
Never	95.7	97.2	0.08		96.3	96.4	0.01	
Most recent emergency department visit for other respiratory disease								
In the past 6 mo	0.6	0.4	0.02	< 0.001	0.4	0.4	0.00	0.7
> 6 mo before index date	0.7	0.4	0.04		0.4	0.4	0.01	
Primary care physician characteristics								
Mean age, years (SD)	52.87 (10.33)	53.61 (10.23)	0.07	< 0.001	52.99 (10.40)	53.10 (10.19)	0.01	0.3
Women, %	23.4	18.8	0.11	< 0.001	21.3	21.4	0.00	0.8
Graduated from a Canadian medical school, %	75.6	76.0	0.01	0.266	75.5	75.5	0.00	1.0
Median continuity of care index¶ (IQR)	1 (1–1)	1 (1–1)	0.03	0.018	1 (1–1)	1 (1–1)	0.01	0.7
Quality of care measures, %								
Glucose testing in previous 3 yr	88.8	83.4	0.15	< 0.001	86.5	86.6	0.00	0.8
Cholesterol testing in previous 3 yr	79.4	68.6	0.24	< 0.001	76.1	76.7	0.01	0.3

Note: COPD = chronic obstructive pulmonary disease, IQR = interquartile range, SD = standard deviation.

*Region of province and index year were also considered in propensity score.

†Testing the hypothesis of no difference between the groups with and without pulmonary function testing.

‡In Ontario, primary care is provided by family and general practitioner physicians, and specialist COPD care is usually provided by pulmonologists, general internists or geriatricians.

§As indicated by Johns Hopkins Collapsed Ambulatory Diagnostic Groups.²¹

¶A measure of patients' access to ambulatory care through the same care provider over time, calculated using the Bice method.²²

cared for by a primary physician who practised guideline-based care (Table 1).

In unadjusted analyses, fewer patients who received pulmonary function testing had a COPD-related hospital admission or died of any cause compared with patients who did not.

In adjusted analyses, patients with COPD who received pulmonary function testing were 9% less likely be admitted to hospital for COPD or to die of any cause than those who did not (hazard ratio [HR] 0.91, 95% confidence interval [CI] 0.89–0.94) (Table 2).

Table 2: Adjusted hazard ratios for death and COPD-related admissions to hospitals and other outcomes associated with peridiagnostic pulmonary function testing in individuals with physician diagnosed COPD in all patient and those diagnosed with COPD in the ambulatory care and hospital settings

Outcome	With peridiagnostic testing (n = 28 386)		Without peridiagnostic testing (n = 40 512)		Unadjusted risk difference in outcome at 3 yr, % (95% CI)†	Adjusted regression	
	Had outcome, %	Median time to outcome, d (IQR)*	Had outcome, %	Median time to outcome, d (IQR)*		Adjusted HR (95% CI)‡	p value§
All patients							
Hospital admission for COPD or death from any cause	30.9	1001 (562–1504)	43.5	936 (398–1468)	10.4 (9.7–11.2)	0.91 (0.89–0.94)	< 0.001
Hospital admission for COPD or a related respiratory disease¶ or death from any cause	33.1	974 (527–1483)	45.9	895 (354–1440)	10.5 (9.8–11.3)	0.92 (0.89–0.94)	< 0.001
Hospital admission for any reason or death from any cause	53.3	705 (224–1223)	65.9	524 (104–1091)	11.7 (10.9–12.5)	0.91 (0.89–0.93)	< 0.001
Death from any cause	22.6	1098 (684–1576)	35.9	1043 (560–1553)	11.0 (10.3–11.7)	0.87 (0.84–0.90)	< 0.001
COPD diagnosed in the ambulatory care setting							
Hospital admission for COPD or death from any cause	23.0	1061 (651–1546)	30.7	994 (547–1498)	7.01 (7.01–7.02)	0.80 (0.76–0.84)	< 0.001
Hospital admission for COPD or a related respiratory disease or death from any cause¶	24.9	1037 (629–1533)	32.8	969 (511–1476)	7.08 (7.07–7.09)	0.80 (0.76–0.83)	< 0.001
Hospital admission for any reason or death from any cause	44.6	810 (361–1320)	51.4	717 (244–1218)	7.11 (7.10–7.12)	0.82 (0.79–0.85)	< 0.001
Death from any cause	16.1	1131 (715–1595)	25.1	1058 (638–1544)	8.16 (8.16–8.17)	0.72 (0.69–0.76)	< 0.001
COPD diagnosed in the hospital setting							
Admission to hospital for COPD or death from any cause	49.8	839 (304–1402)	53.5	882 (283–1442)	1.06 (1.04–1.07)	1.05 (1.01–1.09)	0.02
Admission to hospital for COPD or a related respiratory disease or death from any cause¶	52.7	804 (268–1366)	56.1	841 (242–1413)	0.79 (0.78–0.80)	1.06 (1.02–1.10)	0.005
Admission to hospital for any reason or death from any cause	74.3	365 (69–936)	77.3	344 (61–967)	1.22 (1.21–1.23)	1.02 (0.99–1.05)	0.3
Death from any cause	38.3	1016 (534–1520)	44.3	1031 (472–1564)	3.73 (3.71–3.74)	1.03 (0.99–1.08)	0.1

Note: COPD = chronic obstructive pulmonary disease, CI = confidence interval, HR = hazard ratio, IQR = interquartile range.

*Time until 50% of patients experienced the event derived from Kaplan–Meier survival curves.

†For each group (testing and nontesting), the unadjusted estimated survival at 3 years, along with the standard error of the estimate, was obtained using a Kaplan–Meier analysis. The risk difference for the outcome is the difference between the unadjusted estimated survivals at 3 years. The variance of this difference is the sum of the variances of the individual measures.

‡Reflects the risk in the group with pulmonary function testing compared with the group without pulmonary function testing. Hazard ratios are adjusted for propensity score, pulmonary function testing before and after the peridiagnostic period, age, sex, whether patients were ambulatory or in hospital for COPD in the peridiagnostic period, asthma, and hospital admission within the previous 6 months for a COPD-related disease.

§Testing the hypothesis that the hazard ratio is equal to 1.00.

¶Pneumonia, influenza or acute bronchitis.

There was no evidence that the association between peridiagnostic pulmonary function testing and COPD hospital admission or death from any cause differed by sex ($p = 0.87$) or asthma status ($p = 0.22$); however, it differed by whether patients received their diagnosis in the ambulatory care or hospital setting ($p < 0.001$) and by age ($p = 0.003$). Among patients who received their diagnosis while ambulatory, pulmonary function testing was associated with a significantly reduced risk of COPD-related hospital admission or death from any cause across all age groups, whereas among those who received their diagnosis while in hospital, testing was associated with a modest but significantly increased risk of these events (Table 2, Figure 2). Because it seemed apparent that the former was an important distinction, further analyses were done taking this division into account (Appendix 1).

Sensitivity analysis

Propensity score matching (which achieved no clinically meaningful differences in baseline variables between those receiving and not receiving testing) and calibrated propensity score analysis (which accounted for smoking and other variables not available in the health administrative data) produced results similar to the main results. Only under very unlikely assumptions would an unmeasured confounder or misclassification account for the results observed among patients who received their diagnosis in the ambulatory care setting (Appendix 1). As expected, in the analysis of data from patients aged 67 years and older, which adjusted for medication use — a process of care on the causal pathway to all the outcomes — the association between testing and death or hospital admission for COPD no longer reached statistical significance.

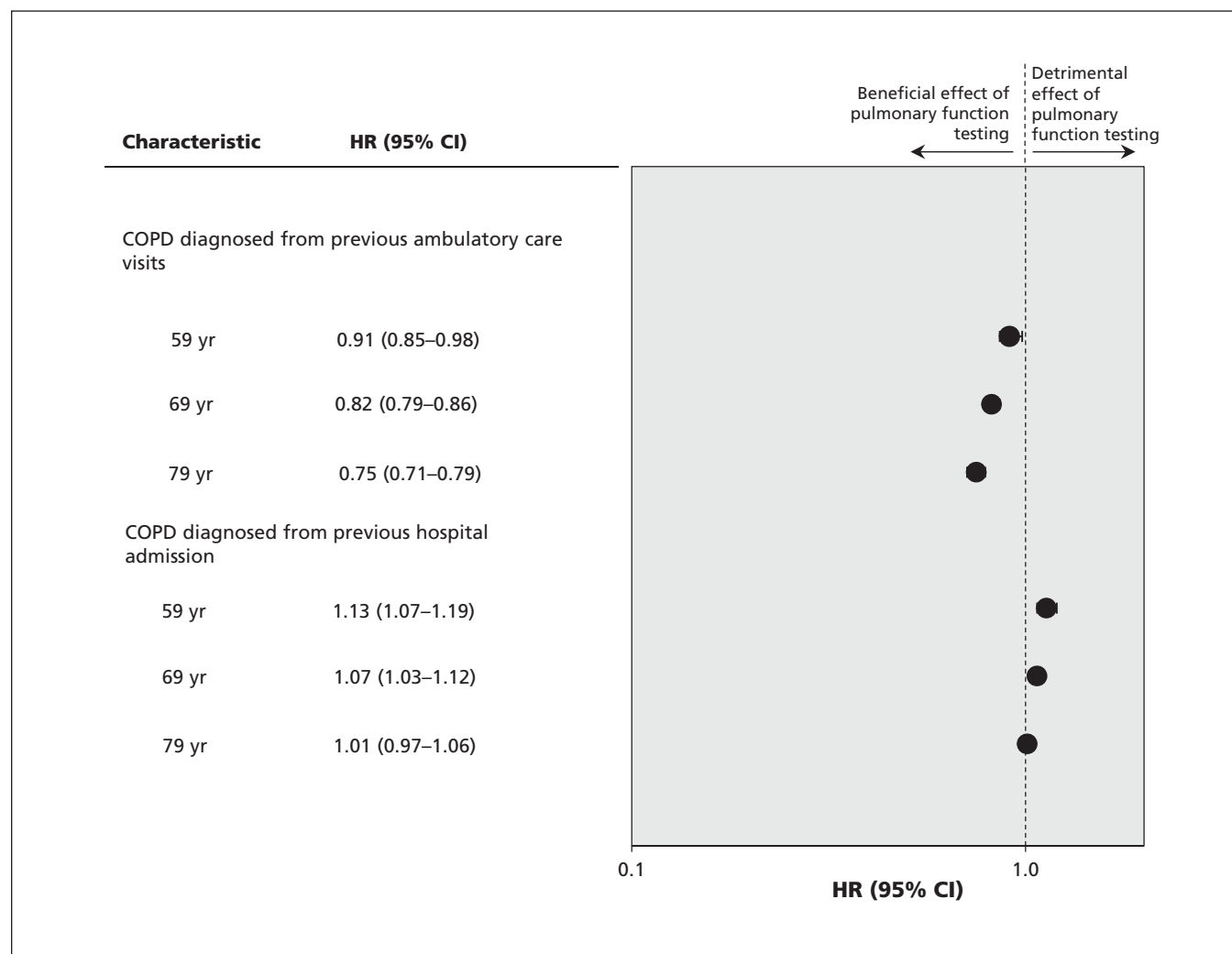


Figure 2: Adjusted effect of peridiagnostic pulmonary function testing on risk of death or admission to hospital for COPD, by whether patients were ambulatory or admitted to hospital for COPD in the peridiagnostic period and by age. Error bars indicate 95% confidence intervals. CI = confidence interval, COPD = chronic obstructive pulmonary disease, HR = hazard ratio.

Processes of care

There were 16 798 patients aged 67 years and older with newly diagnosed COPD. Patients who were not already taking an inhaled long-acting bronchodilator or long-acting β -agonist–inhaled corticosteroid combination were significantly more likely to have those medications added to their treatment regimen if they were in the testing as opposed to the non-testing group ($p < 0.001$). The same increase in medication use was not observed with inhaled corticosteroids ($p = 0.040$) (Table 3).

Interpretation

We examined the association between pulmonary function testing and important patient outcomes in a large, complete, real-world population of patients with newly diagnosed COPD. We found that patients who underwent testing around the time of diagnosis were 9% less likely to be admitted to hospital for COPD or die of any cause than were those who did not. The association between pulmonary function

testing and better outcomes was significantly influenced by where the condition was diagnosed, with cases diagnosed in the ambulatory care setting 20% less likely to have an outcome of interest. Although the overall risk reduction was modest, the larger benefit observed in this group, who likely had milder disease, is comparable with that observed with the regular use of some COPD medications.^{31,32} We also found pulmonary function testing to be associated with increased addition of long-acting bronchodilators and long-acting β -agonist–inhaled corticosteroid medications, which offers a plausible mechanism by which testing might have led to better health outcomes.

Patients who received their diagnosis in the ambulatory care setting may have derived greater benefits from pulmonary function testing because they had more lung function to preserve through good COPD management and were less likely to die or be admitted to hospital overall. Alternatively, unmeasured confounding might explain this finding (although we believe

Table 3: Percentage of COPD patients aged 67 years and older who had a medication added* to their treatment in the year following their pulmonary function test date or equivalent†, in the propensity score matched sample overall, and in patients who received their diagnosis in the ambulatory care or hospital settings

Medication	Medication added to treatment		p value
	Patients with peridiagnostic pulmonary function testing who had a medication added, %	Patients without peridiagnostic pulmonary function testing who had a medication added, %	
Overall			
Long-acting anticholinergic	44.5	25.4	< 0.0001
Long-acting β agonist	3.0	1.8	< 0.0001
Long-acting β agonist and inhaled corticosteroid combination	30.1	18.7	< 0.0001
Inhaled corticosteroid	13.6	12.5	0.04
COPD diagnosed in the ambulatory care setting			
Long-acting anticholinergic	44.1	21.0	< 0.0001
Long-acting β agonist	2.7	1.1	< 0.0001
Long-acting β agonist and inhaled corticosteroid combination	28.6	16.9	< 0.0001
Inhaled corticosteroid	12.5	10.7	0.01
COPD diagnosed in the hospital setting			
Long-acting anticholinergic	44.9	30.5	< 0.0001
Long-acting β agonist	3.3	2.8	0.2
Long-acting β agonist and inhaled corticosteroid combination	31.8	20.9	< 0.0001
Inhaled corticosteroid	14.9	14.7	0.8

*A medication was considered to be newly added to a patient's treatment if there were no prescriptions for the medication in the year before the pulmonary function test date or its equivalent, and at least 1 prescription for it in the year after the pulmonary function test date.

†For patients with pulmonary function testing (cases), the pulmonary function test date was the date on which they received their pulmonary function test. For patients without pulmonary function testing (controls), the pulmonary function test equivalent date was determined by calculating the number of days between the pulmonary function test and the index date of their matched case and then counting back that number of days from their index date.

this unlikely for the reasons outlined below), as well as the worse outcomes found in the admitted group who received testing.

Our results support the commonly held understanding that pulmonary function testing is key to the accurate diagnosis and quality care of COPD.^{3,4,9} Our findings are consistent with literature showing an association between pulmonary function testing and increased use of COPD medication and other interventions.^{11,12,14,15} Our study extends these findings by showing an association between pulmonary function testing and morbidity and mortality.

Limitations

Our validated case-definition of physician-diagnosed COPD has a specificity of 95% and positive predictive value of 81% compared with a clinical reference standard,¹⁹ so misclassification may have occurred and biased our results. However, the disease most often misclassified as COPD is asthma, which is associated with better health outcomes.^{33,34} Because misclassification was more likely in the group of patients who did not undergo testing, this would have biased our results toward better outcomes in this group, yet we observed the opposite. Furthermore, our sensitivity analyses showed that only under unlikely conditions would misclassification render our findings null in patients who were ambulatory in the peridiagnostic period.

Variables not available in health administrative data, such as lung function or smoking, create potential for unmeasured confounding. However, we used propensity score adjustment and matching to control for a large number of prognostically important variables, many of which are highly correlated with these 2 variables. We also performed a sensitivity analysis taking into account smoking and other variables from a population health survey and found little difference. Finally, our sensitivity analyses showed that the significant results seen in those who were ambulatory in the peridiagnostic period were not easily explained by an unmeasured confounder.

An association between pulmonary function testing and patient outcomes does not prove causation. It is possible that testing was a marker of overall quality of care rather than a direct source of improved outcomes. Trying to tease apart the effects of testing and other good-quality COPD care is challenging because they are likely to be highly correlated. Nonetheless, a positive association was found even after clustering by primary care physician; adjusting for many markers of good quality COPD care (that were highly correlated with pulmonary function testing) such as influenza vaccination, specialist visits and pri-

mary ambulatory care visits; and adjusting for markers of quality overall care such as glucose and cholesterol testing.

Finally, we examined the empiric impact of having pulmonary function testing, but could not discern if physicians acted on good-quality tests in an appropriate manner because the results were not known. However, failure of them to do so would have biased our results toward finding no association between testing and outcomes, yet an association was found. In addition, we only examined pulmonary function testing used for diagnosis. Future studies should examine the value of ongoing testing as monitoring for people with COPD.

Conclusion

The use of pulmonary function testing in the diagnostic workup of people with physician-diagnosed COPD is associated with a decreased risk of admission to hospital for COPD or death in the ambulatory care setting. Given low rates of testing, these findings point to an opportunity to improve patient outcomes, reduce health services use and decrease health care costs by increasing rates of testing for suspected COPD.

References

- Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;380:2095-128.
- Buist AS, McBurnie MA, Vollmer WM, et al.; BOLD Collaborative Research Group. International variation in the prevalence of COPD (the BOLD Study): a population-based prevalence study. *Lancet* 2007;370:741-50.
- Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease (updated 2015). Global Initiative for Chronic Obstructive Lung Disease (GOLD); 2015.
- O'Donnell DE, Hernandez P, Kaplan A, et al. Canadian Thoracic Society recommendations for management of chronic obstructive pulmonary disease — 2008 update — highlights for primary care. *Can Respir J* 2008;15(Suppl A):1A-8A.
- Lee TA, Bartle B, Weiss KB. Spirometry use in clinical practice following diagnosis of COPD. *Chest* 2006;129:1509-15.
- Arne M, Lisspers K, Stållberg B, et al. How often is diagnosis of COPD confirmed with spirometry? *Respir Med* 2010;104:550-6.
- Han MK, Kim MG, Mardon R, et al. Spirometry utilization for COPD: how do we measure up? *Chest* 2007;132:403-9.
- Gershon AS, Hwee J, Croxford R, et al. Patient and physician factors associated with pulmonary function testing for COPD: a population study. *Chest* 2014;145:272-81.
- Qaseem A, Wilt TJ, Weinberger SE, et al. Diagnosis and management of stable chronic obstructive pulmonary disease: a clinical practice guideline update from the American College of Physicians, American College of Chest Physicians, American Thoracic Society, and European Respiratory Society. *Ann Intern Med* 2011;155:179-91.
- Lusuardi M, De Benedetto F, Paggiaro P, et al. A randomized controlled trial on office spirometry in asthma and COPD in standard general practice: data from spirometry in Asthma and COPD: a comparative evaluation Italian study. *Chest* 2006;129:844-52.
- Yawn BP, Enright PL, Lemanske RF Jr, et al. Spirometry can be done in family physicians' offices and alters clinical decisions in management of asthma and COPD. *Chest* 2007;132:1162-8.
- Joo MJ, Au DH, Lee TA. Use of spirometry in the diagnosis of chronic obstructive pulmonary disease and efforts to improve quality of care. *Transl Res* 2009;154:103-10.

13. Abramson MJ, Schattner RL, Sulaiman ND, et al. Do spirometry and regular follow-up improve health outcomes in general practice patients with asthma or COPD? A cluster randomised controlled trial. *Med J Aust* 2010;193:104-9.
14. Walker PP, Mitchell P, Diamantea F, et al. Effect of primary-care spirometry on the diagnosis and management of COPD. *Eur Respir J* 2006;28:945-52.
15. Joo MJ, Lee TA, Au DH, et al. Medication use patterns associated with spirometry in diagnosing COPD. *COPD* 2008;5:360-8.
16. O'Dowd LC, Fife D, Tenhave T, et al. Attitudes of physicians toward objective measures of airway function in asthma. *Am J Med* 2003;114:391-6.
17. Hux JE, Naylor CD, Fielding DA. The Ontario Drug Benefit Program copayment: its impact on access for Ontario seniors and charges to the program. Toronto: Institute for Clinical Evaluative Sciences in Ontario; 1997.
18. Collins BF, Feemster LC, Rinne ST, et al. Factors predictive of airflow obstruction among veterans with presumed empirical diagnosis and treatment of COPD. *Chest* 2015;147:369-76.
19. Gershon AS, Wang C, Guan J, et al. Identifying individuals with physician diagnosed COPD in health administrative databases. *COPD* 2009;6:388-94.
20. Gershon AS, Warner L, Cascagnette P, et al. Lifetime risk of developing chronic obstructive pulmonary disease: a longitudinal population study. *Lancet* 2011;378:991-6.
21. Reid RJ, MacWilliam L, Verhulst L, et al. Performance of the ACG case-mix system in two Canadian provinces. *Med Care* 2001;39:86-99.
22. Bice TW, Boxerman SB. A quantitative measure of continuity of care. *Med Care* 1977;15:347-9.
23. PCCF+ Version 4D user's guide. Automated geographic coding based on the Statistics Canada Postal Code Conversion files, including postal codes to December 2003 [computer program]. Catalogue 82-F0086-XDB. Ottawa: Statistics Canada; 2004.
24. du Plessis V, Beshiri R, Bollman RD, et al. Definitions of "rural". *Rural and Small Town Canada Analysis Bulletin*. Cat. no. 21-006-XIE. Ottawa: Statistics Canada; 2001.
25. Genest J, McPherson R, Frohlich J, et al. 2009 Canadian Cardiovascular Society/Canadian guidelines for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease in the adult — 2009 recommendations. *Can J Cardiol* 2009;25:567-79.
26. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2013 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2013;37(Suppl 1):S1-212.
27. Hansell AL, Walk JA, Soriano JB. What do chronic obstructive pulmonary disease patients die from? A multiple cause coding analysis. *Eur Respir J* 2003;22:809-14.
28. Camilli AE, Robbins DR, Lebowitz MD. Death certificate reporting of confirmed airways obstructive disease. *Am J Epidemiol* 1991;133:795-800.
29. D'Agostino RB Jr. Propensity score methods for bias reduction in the comparison of a treatment to a non-randomized control group. *Stat Med* 1998;17:2265-81.
30. Gershon A, Croxford R, To T, et al. Comparison of inhaled long-acting beta-agonist and anticholinergic effectiveness in older patients with chronic obstructive pulmonary disease: a cohort study. *Ann Intern Med* 2011;154:583-92.
31. Calverley P, Pauwels R, Vestbo J, et al. Trial of Inhaled STeroids ANd long-acting beta2 agonists study group. Combined salmeterol and fluticasone in the treatment of chronic obstructive pulmonary disease: a randomised controlled trial. *Lancet* 2003;361:449-56.
32. Tashkin D, Celli B, Kesten S, et al. Effect of tiotropium in men and women with COPD: results of the 4-year UPLIFT trial. *Respir Med* 2010;104:1495-504.
33. Gershon AS, Guan J, Wang C, et al. Trends in asthma prevalence from 1996 to 2004: a population-based study. *Am J Respir Crit Care Med* 2009;179:A4754.
34. Gershon AS, To T, Guan J, et al. Trends in chronic obstructive pulmonary disease (COPD) prevalence, incidence and mortality in Ontario, overall and by LHIN, 1996/97–2009/10. Toronto: Institute for Clinical Evaluative Sciences; 2011.

Affiliations: Institute for Clinical Evaluative Sciences (Gershon, Mecredy, Croxford, To, Stanbrook); Sunnybrook Health Sciences Centre (Gershon); Institute of Health Policy, Management and Evaluation (Gershon, Stanbrook) and Dalla Lana School of Public Health (To), University of Toronto; The Hospital for Sick Children (To); University Health Network (Stanbrook), Toronto, Ont.; Ottawa Hospital Research Institute (Aaron), University of Ottawa, Ottawa, Ont.

Contributors: All authors participated in the design, analysis and interpretation of the data and critical revision of the manuscript, all approved the final version, and all agreed to be accountable for all aspects of the work. Andrea Gershon, the corresponding author, had full access to all the data in the study and had final responsibility for the decision to submit for publication. Andrea Gershon, Teresa To, Matthew Stanbrook and Shawn Aaron conceived of the study and Andrea Gershon obtained funding. Andrea Gershon and Graham Mecredy drafted the manuscript. The statistical analyses were performed by Ruth Croxford.

Disclaimer: This study was supported by a grant from the Ontario Lung Association and Pfizer Canada. It also received support from the Institute for Clinical Evaluative Sciences (ICES), which is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care (MOHLTC). The study sponsors had no role in study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication. Andrea Gershon is supported by a Fellowship in Translational Research from The Physicians' Services Incorporated Foundation, Toronto, Ontario, Canada and was supported by New Investigator Award funded by team grant (9 OTG-88591) from the Canadian Institutes of Health Research Institute of Nutrition, Metabolism and Diabetes while working on this study.