

NB-IRDT Chronic Obstructive Pulmonary Disease Research Program – Report Two:

Investigation of the Canadian Chronic Disease
Surveillance System (CCDSS) and the
New Brunswick COPD Health Information Platform
(NB-CHIP)



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Project Title

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Table of Contents

Introduction	1
Background	1
Impacts of COPD on Daily Living	1
Approaches to Estimating the Prevalence of COPD	2
NB-CHIP (New Brunswick COPD Health Information Platform)	5
Research Objectives	5
Methods.....	6
Results	8
Concordance Categories and Select Individual Characteristics	12
Age	12
Sex	14
Health Zone of Individual Residence	16
Area-Level Income Quintiles.....	19
Body Mass Index (BMI)	22
Frailty Risk	25
Severity of Airflow Limitation	27
Discussion.....	28
CCDSS and PFT Coincidence and Concordance.....	28
Coincidence, Concordance, and Select Individual Characteristics	29
Age	29
Sex	30
Health Zone	30
Area-Level Income	31
BMI (Body Mass Index)	32
Frailty	33
Severity of Airflow Limitation	34
Limitations.....	35
Time Effects.....	35
Use of Administrative Data for Research Purposes.....	36
Variable Operationalizations	37
Conclusion	38
References	39

List of Tables

Table 1: Proportion of Individuals in Coincidence Groups Describing CCDSS COPD Diagnosis and Presence of PFT	8
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List of Figures

Figure 1: Proportion of PFT Usage Among CCDSS Cases (n=46,700)	9
Figure 2: Proportion of CCDSS Cases Among Individuals Who Received a PFT (n=57,905)	9
Figure 3: Completeness of PFTs Within NB-CHIP (n=57,905)	9
Figure 4: Classification of All CCDSS Cases According to PFT Presence and Results	10
Figure 5: Proportion of Overdiagnosed CCDSS Cases Among CCDSS Cases With Complete PFT Results (n=12,390)	10
Figure 6: Proportion of Non-PFT Diagnosed CCDSS Cases (i.e., Those Completely Lacking a PFT Value or Having Only a Pre-Bronchodilator Value), Excluding Records Missing Airflow Measurement Data Due to Data Quality Issue (n=44,465)	11
Figure 7: Classification of All Non-CCDSS Cases According to PFT Results	11
Figure 8: Proportion of Underdiagnosed Cases Among All Records With Complete Positive PFT Results (n=4,170)	12
Figure 9: CCDSS and PFT Coincidence by Age Group	12
Figure 10: CCDSS and PFT Concordance Among CCDSS Cases With Complete PFT Results, by Age Group	13
Figure 11: Proportion of Underdiagnosed Cases Among All Records With Complete Positive PFT Results, by Age Group	13
Figure 12: Proportion of Non-PFT Diagnosed CCDSS Cases (i.e., Those Completely Lacking a PFT Value or Having Only a Pre-Bronchodilator Value), Excluding Records Missing Airflow Measurement Data Due to Data Quality Issue, by Age Group	14
Figure 13: CCDSS and PFT Coincidence by Sex	14
Figure 14: CCDSS and PFT Concordance Among CCDSS Cases With Complete PFT Results, by Sex	15
Figure 15: Proportion of Underdiagnosed Cases Among All Records With Complete Positive PFT Results, by Sex	15
Figure 16: Proportion of Non-PFT Diagnosed CCDSS Cases (i.e., Those Completely Lacking a PFT Value or Having Only a Pre-Bronchodilator Value), Excluding Records Missing Airflow Measurement Data Due to Data Quality Issue, by Sex	15
Figure 17: CCDSS and PFT Coincidence by Health Zone of Residence	16
Figure 18: CCDSS and PFT Concordance Among CCDSS Cases With Complete PFT Results, by Health Zone of Residence	17
Figure 19: Proportion of Underdiagnosed Cases Among All Records With Complete Positive PFT Results, by Health Zone of Residence	18

Figure 20: Proportion of Non-PFT Diagnosed CCDSS Cases (i.e., Those Completely Lacking a PFT Value or Having Only a Pre-Bronchodilator Value), Excluding Records Missing Airflow Measurement Data Due to Data Quality Issue, by Health Zone of Residence.....	19
Figure 21: CCDSS and PFT Coincidence by Area Income Quintile	20
Figure 22: CCDSS and PFT Concordance Among CCDSS Cases With Complete PFT Results, by Area Income Quintile	21
Figure 23: Proportion of Underdiagnosed Cases Among All Records With Complete Positive PFT Results, by Area Income Quintile	21
Figure 24: Proportion of Non-PFT Diagnosed CCDSS Cases (i.e., Those Completely Lacking a PFT Value or Having Only a Pre-Bronchodilator Value), Excluding Records Missing Airflow Measurement Data Due to Data Quality Issue, by Area Income Quintile	22
Figure 25: CCDSS and PFT Coincidence by BMI Classification	23
Figure 26: CCDSS and PFT Concordance Among CCDSS Cases With Complete PFT Results, by BMI Classification	23
Figure 27: Proportion of Underdiagnosed Cases Among All Records With Complete Positive PFT Results, by BMI Classification	24
Figure 28: Proportion of Non-PFT Diagnosed CCDSS Cases (i.e., Those Having Only a Pre-Bronchodilator Value), Excluding Records Missing Airflow Measurement Data Due to Data Quality Issue, by BMI Classification	24
Figure 29: CCDSS and PFT Coincidence by Frailty Risk	25
Figure 30: CCDSS and PFT Concordance Among CCDSS Cases With Complete PFT Results, by Frailty Risk	26
Figure 31: Proportion of Underdiagnosed Cases Among All Records With Complete Positive PFT Results, by Frailty Risk	26
Figure 32: Proportion of Non-PFT Diagnosed CCDSS Cases (i.e., Those Completely Lacking a PFT Value or Having Only a Pre-Bronchodilator Value), Excluding Records Missing Airflow Measurement Data Due to Data Quality Issue, by Frailty Risk	27
Figure 33: Proportion of Underdiagnosed Cases Among All Records With Complete Positive PFT Results, by Severity of Airflow Limitation	27

Introduction

Background

Impacts of COPD on Daily Living

Chronic Obstructive Pulmonary Disease (COPD) is a preventable and treatable chronic lung condition that causes airflow limitation and is characterized by persistent symptoms such as shortness of breath and excessive coughing with or without the production of phlegm. A common inflammatory disease, COPD is primarily caused by exposure to gases and particulates, with tobacco smoke being the most common source of exposure.^(1, 2) COPD has significant effects on the quality of life, morbidity, and mortality of individuals living with it. For example, regarding quality of life, Canadians living with COPD have reported limitations to their daily activities, their ability to work outside the home, and even socialization.^(3, 4)

Between 2015 and 2019, COPD was the 4th/5th leading cause of death in Canada⁽⁵⁾ and the 2nd leading cause (after childbirth) of hospitalizations.⁽⁶⁻¹⁰⁾ During the same period, the province of New Brunswick (NB) had very similar mortality and morbidity effects to those seen across Canada: COPD was the 3rd/4th leading cause of death in the province⁽⁵⁾ and the 3rd leading cause of hospitalizations.⁽⁶⁻¹⁰⁾

A previous report⁽¹¹⁾ from the New Brunswick Institute for Research, Data and Training (NB-IRDT) utilizing Statistics Canada Public Use Microdata Files of the Canadian Community Health Survey (CCHS) data demonstrated the effect COPD can have on quality of life. New Brunswickers who reported a diagnosis of COPD had increased rates of indicators associated with reduced quality of life when compared against the general population in NB. Those quality of life indicators included self-perceived poor health, life stress, having difficulties with activities, needing help doing housework/moving about the house, and being unable to work:

Quality of Life Indicator	NBers with COPD	General Population
Self-perceived poor health	53%	20%
Life stress	29%	21%
Having difficulties with activities	38%	16%
Needing help doing housework / moving about the house	41%	17%
Being unable to work	16%	5%

Approaches to Estimating the Prevalence of COPD

While the downstream effects of COPD are well documented, obtaining accurate estimations of the population burden can be difficult. For example, estimates of the prevalence of COPD among New Brunswickers aged 35 and older ranged from 24,800⁽¹²⁾ to 57,000⁽¹³⁾ in two reports using data describing the prevalence of COPD as of 2016.

The discrepancy between these estimates can be attributed to differences in the methodology used to obtain them. The former estimate (24,800) uses self-reported COPD diagnosis as recorded in Statistics Canada's Canadian Community Health Survey.⁽¹²⁾ The latter estimate (57,000)⁽¹³⁾ relies on the Canadian Chronic Disease Surveillance System (CCDSS) methodology developed by the Public Health Agency of Canada (PHAC), which uses case identification algorithms applied to provincial administrative health databases to obtain estimates of the incidence and prevalence of COPD in the reporting jurisdiction. The CCDSS case definition for COPD requires one visit to a physician or one hospital separation reflecting a COPD diagnosis among individuals aged 35 and older.⁽¹⁴⁾

A systematic review by Diab et al.⁽¹⁵⁾ that examined COPD case identification between 2008 and 2018 identifies the two approaches described above (population surveying and health administrative data) as the two most common approaches to estimating COPD prevalence and incidence. However, Diab et al.⁽¹⁵⁾ note that "a major limitation of these methodologies is that confirmatory spirometry demonstrating persistent airflow obstruction is rarely available to validate the diagnosis" (p. 1130).

Spirometry is a pulmonary function test (PFT) used to obtain objective measurements of airflow limitation. It is a critical component in the diagnosis of COPD and is also used in the diagnosis and assessment of other respiratory conditions (e.g., asthma) and for other applications such as pre-operative risk assessment. Diab et al.⁽¹⁵⁾ note that much of the difficulty in defining COPD's population burden comes from its complex diagnostic criteria, which require the presence of respiratory symptoms (shortness of breath, dyspnea), objective airflow measurements, and a personal history of exposure to inhaled substances.

While these diagnostic criteria are available at the clinical level, population-level data collection tools rarely capture all components required for a diagnosis in a single system. For example, administrative health database approaches (CCDSS) describe the diagnosis of COPD but do not capture how a physician arrived at that diagnosis (which could include consideration of PFT results, presence of symptoms, and history of exposure).

Similarly, patient self-report of COPD (Statistics Canada) indicates that a diagnosis was made but also lacks the details underlying the diagnosis. Finally, population health surveys that include PFTs as a component of the survey methodology are challenging (training is required to administer PFTs), cost-prohibitive, and can fail to include physician diagnosis of COPD, symptoms, and exposure history.

Many of the studies reviewed by Diab et al.⁽¹⁵⁾ did not systematically compare PFTs performed during regular care practice with either diagnosis-defining approach (i.e., health administrative

data or self-report surveys) on a large scale. Instead, in many cases, the researchers gave PFTs to survey respondents,⁽¹⁶⁻¹⁹⁾ though one study⁽¹⁸⁾ linked the survey data to health administrative data.

To our knowledge, only a single Canadian study⁽²⁰⁾ compared health administrative data algorithms methodology against administrative data describing the presence of pulmonary function testing. In this 2014 study,⁽²⁰⁾ Gershon et al. found that among 491,754 individuals identified as COPD cases between 2000-2010, almost 65 percent of cases did not have confirmatory PFTs performed. The PFT data used by Gershon et al.⁽²⁰⁾ indicated the presence of a PFT but did not include PFT results.

Overdiagnosis and Underdiagnosis of COPD

In addition to the presence of a PFT, the actual results of the PFT can be used to characterize COPD case identification methods such as the CCDSS in increased detail. In previous research,^(15, 17, 18, 20-23) when a physician diagnosis of COPD (or proxies such as the CCDSS) was compared against the results of a PFT, two common discordant categories were observed: 'overdiagnosed' and 'underdiagnosed.'

A recent systematic review⁽²³⁾ demonstrated that the operational definition of overdiagnosis varies across the literature, and includes the following instances:

- A physician diagnoses COPD despite normal PFT results. This includes instances where:
 - A PFT is not used in the diagnostic process, but follow-up testing demonstrates normal values.
 - A PFT is used in the diagnostic process with normal results, but the results are not considered in making the diagnosis.
- Disparities exist in the criteria for interpreting the PFT as indicative of COPD.
- The COPD diagnosis is based on pre-bronchodilator PFT values rather than post-bronchodilator values (guidelines recommend diagnosis based on post-bronchodilator values.⁽¹⁾)
- Health conditions such as heart failure are incorrectly identified as COPD by having similar presentation in terms of symptoms and PFT results.
- Results from an initial PFT indicate COPD and result in a diagnosis, but future PFT results are normal, and the COPD diagnosis is not rescinded.

For the purpose of this report, we are focusing primarily on the operational definition 1B from the 2019 review by Thomas et al.:

Overdiagnosed patients are individuals who have been flagged as COPD cases by tools such as the CCDSS or CCHS but have PFT data indicating normal airway functioning.

Underdiagnosed patients are individuals who have airflow limitation on PFT results which are consistent with COPD diagnostic criteria but are not COPD cases according to health data algorithms or surveys.

Correctly identifying who has COPD is crucial. At the individual level, confirmatory spirometry has been associated with a decrease in risk of mortality and hospitalization,⁽²⁴⁾ while another study⁽²⁵⁾ demonstrated that 35 percent of individuals with a COPD diagnosis but lacking PFT data were likely to have been treated with inhaled drugs unnecessarily – suggesting both medical and financial considerations for individuals and the health system.

Further, accurately understanding the population burden of COPD, how future levels can be reduced, and how current levels can be mitigated is crucial in health system planning.

As summarized in two systematic reviews,^(15, 21) the reported prevalence of COPD over- and underdiagnosis, while exhibiting a great deal of heterogeneity, is generally quite high. Based on a review of 17 studies published between 2008 and 2018, Diab et al.⁽¹⁵⁾ estimate that 65 to 80 percent of individuals with PFT results indicating persistent airflow limitation consistent with COPD diagnostic criteria do not have a physician diagnosis of COPD (i.e., underdiagnosed).

Further, using an operationalization of overdiagnosis akin to the definition above, the review found that 33 to 50 percent of individuals with a previous physician diagnosis of COPD had PFT results which did not demonstrate persistent airflow limitation consistent with COPD diagnostic criteria (i.e., overdiagnosed).

A second systematic review from 2019,⁽²¹⁾ which examined 47 studies spanning 1998 to 2016, estimated that 10 to 95 percent of individuals with PFT results indicative of COPD lack a corresponding physician diagnosis and are therefore underdiagnosed, while 5 to 60 percent of individuals with a COPD diagnosis lack PFT results indicative of COPD and are therefore overdiagnosed. However, it appears the second systematic review⁽²¹⁾ used a more expansive definition of overdiagnosis, including studies that incorporated both definitions (1A and 1B) from the list found in the review by Thomas et al.⁽²³⁾

Among Canadian studies, and focusing exclusively on definition 1B from the list by Thomas et al.,⁽²³⁾ reported prevalence was 79 to 82 percent for underdiagnosis^(15, 16, 21) and 58 percent for overdiagnosis.⁽¹⁸⁾

NB-CHIP (New Brunswick COPD Health Information Platform)

In New Brunswick, a dataset describing large-scale PFT results exists: the New Brunswick COPD Health Information Platform (NB-CHIP). NB-CHIP contains nearly all pulmonary function testing (PFT) lab data from the province of New Brunswick since 2007, linkable with other provincial administrative databases at the individual level.

This current report uses NB-CHIP to examine the extent to which COPD diagnosis as recorded in the CCDSS aligns with PFT testing, allowing for estimation of the occurrence of overdiagnosis, underdiagnosis, and lack of PFT testing for COPD-diagnosed individuals.

Research Objectives

The primary goal of this research was to examine the prevalence of COPD based on the CCDSS case identification algorithm and compare it to clinical measurements from the PFT testing derived from NB-CHIP.

By exploring how the data sources relate to and are consistent with one another, we can improve our understanding of the presentation and, by extension, treatment of COPD in the province.

Specifically, this research aimed to:

1. Describe the extent of PFT presence and absence among CCDSS-defined COPD cases.
2. Describe the results of PFTs in relation to CCDSS case designation:
 - a. Estimate the prevalence of a COPD diagnosis in accordance with a positive PFT result ('PFT diagnosed').
 - b. Estimate the prevalence of a COPD diagnosis in the absence of a PFT result or the absence of a post-bronchodilator PFT result ('non-PFT diagnosed').
 - c. Estimate the prevalence of overdiagnosed COPD.
 - d. Estimate the prevalence of underdiagnosed COPD.
3. Describe how individual and health system characteristics relate to the relationship between CCDSS case status, PFT presence, and PFT results.

Methods

Pseudonymous data from four datasets – NB-CHIP, CCDSS COPD, Discharge Abstract Data (DAD), and Citizen Data (see the [Technical Appendix](#) for data set details) – were linked via a scrambled unique individual identifier based on an individual's Medicare number to create a retrospective cohort of New Brunswickers with respiratory complaints.

All New Brunswickers identified as incident cases in the CCDSS, and individuals over the age of 35 who received a PFT (recorded in NB-CHIP), between January 1, 2007, and December 31, 2017 were included in the analyses. Combining the CCDSS and NB-CHIP for the accrual period from 2007 to 2017 allowed us to create a 10-year pooled 'respiratory complaint' cohort that identified individuals who had a physician visit or hospitalization associated with COPD (CCDSS) or had a PFT (NB-CHIP). CCDSS COPD case status was then compared against both the presence and results of PFTs.¹ Note that NB-CHIP contains data on all PFTs without specifying indication, so the respiratory complaint cohort will include individuals who received a PFT for any reason, including reasons other than the diagnosis of COPD (e.g., the diagnosis of other respiratory conditions, or pre-operative assessments).

The pooled 10-year respiratory cohort combined COPD case identification and PFT information, allowing us to identify three coincidence groups which describe how CCDSS cases and non-cases ('No CCDSS') co-occur with pulmonary function testing:

Coincidence groups:

- CCDSS, PFT
- CCDSS, no PFT
- No CCDSS, PFT

Further, using the clinical results from the PFTs, we established four concordance groups describing the relationship between CCDSS case status and pulmonary function testing results:

Concordance groups:

- PFT diagnosed
(CCDSS case, positive PFT)
- Overdiagnosed
(CCDSS case, negative PFT)
- Non-PFT diagnosed
(CCDSS case, PFT absent or no
post-bronchodilator value)
- Underdiagnosed
(non-CCDSS case, positive PFT
indicative of COPD)

Individuals were assigned to these groups based on their presence in the CCDSS COPD ("CCDSS/No CCDSS"), NB-CHIP ("PFT/no PFT"), and PFT results (PFT+, PFT-) at any point during the 10-year period. Detailed specifications on how these groups were created can be viewed in this report's [Technical Appendix](#).

¹ Censoring may result in incomplete observations at the beginning and end of the 10-year period. See the [Limitations](#) section for more details.

These groups were then used in analyses examining the following characteristics.

Demographic Characteristics:

Age groups (defined using Citizen Data):

- Three age groups: 35-64, 65-84, 85+

Sex (defined using Citizen Data):

- Two categories: Male/Female

Geographic Characteristics:

Health zone of residence (defined using Citizen Data):

- Seven administrative geographic regions established by GNB (Zones 1-7)

Area level income of residence (Defined by place of residence in Citizen Data and using Statistics Canada information):

- 5 area income quintiles (Q1-Q5)

Health Status:

Body Mass Index (defined using NB-CHIP and Health Canada BMI Health Risk Nomogram⁽²⁶⁾):

- Four categories: Underweight, Normal Weight, Overweight, Obese

Frailty Risk (defined with the DAD using Hospital Frailty Risk Score algorithm⁽²⁷⁾):

- Three categories: No Risk, Low Risk, Intermediate-to-High risk

Airflow limitation (Defined with NB-CHIP positive PFT results using GOLD criteria⁽¹⁾):

- Four categories: Mild, Moderate, Severe, Very Severe

Further information about these constructs can be viewed in this report's [Technical Appendix](#).

Results

In pooled data ranging from 2007 to 2017, 46,700 CCDSS COPD cases and 57,905 PFTs were identified. When duplication within and across datasets was accounted for, the number of individuals in the respiratory complaint cohort was 87,895.

Table 1 describes the distribution of included individuals between the three PFT coincidence groups. Approximately 19 percent of the records had coincidence between CCDSS and NB-CHIP, while the remaining 81 percent did not. Notably, 34 percent of all individuals in our respiratory complaint cohort were CCDSS COPD cases but had no PFT.

Table 1: Proportion of Individuals in Coincidence Groups Describing CCDSS COPD Diagnosis and Presence of PFT

CCDSS and NB-CHIP Coincidence	Number of individuals	Percentage
CCDSS, PFT	16,710	19%
CCDSS, no PFT	29,990	34%
No CCDSS, PFT	41,195	47%

Among CCDSS cases, 64 percent had no history of PFT (Figure 1). Further, 29 percent of individuals evaluated by PFT between 2007 and 2017 were CCDSS cases (Figure 2).

Among all PFT records in NB-CHIP, 35 percent had incomplete information, preventing classification of these records as either meeting or not meeting the clinical criteria for COPD (Figure 3).

Among the NB-CHIP records with an incomplete PFT, we observed two ways in which a PFT result could be defined as incomplete:

1. A data quality issue that led to PFT records missing all airflow measurement information (44% of incomplete PFTs; these issues originated from two facilities).
2. PFTs wherein the pre-bronchodilator test was not followed with a post-bronchodilator test, resulting in a record missing post-bronchodilator information (56% of incomplete PFTs).

Figure 1: Proportion of PFT Usage Among CCDSS Cases (n=46,700)

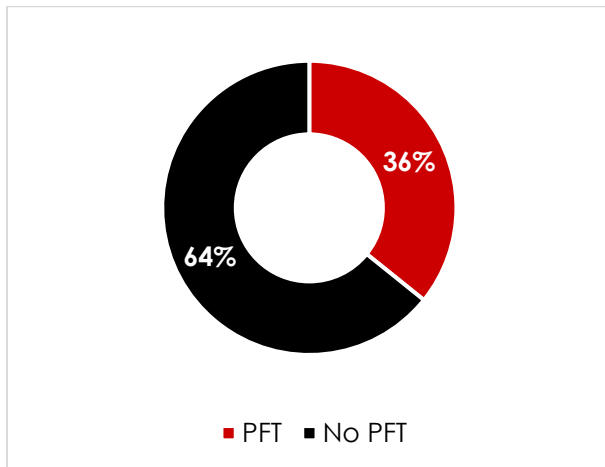


Figure 2: Proportion of CCDSS Cases Among Individuals Who Received a PFT (n=57,905)

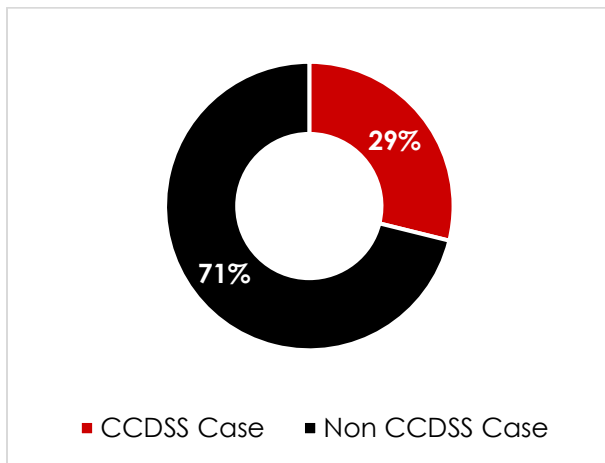


Figure 3: Completeness of PFTs Within NB-CHIP (n=57,905)

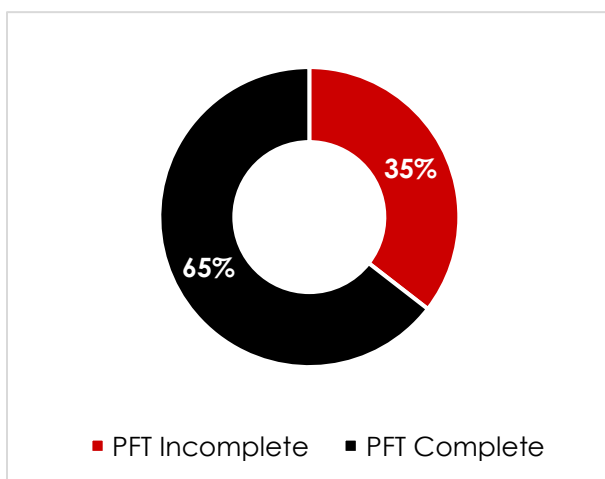


Figure 4 presents PFT presence and results among individuals who were flagged as CCDSS cases. Sixty-nine percent of CCDSS cases had either no PFT or a PFT that did not include a post-bronchodilator test and can therefore be classified as non-PFT diagnosed. Meanwhile, 23 percent had discordant negative PFT results and can therefore be classified as overdiagnosed.

Five percent of records were missing airflow information and could not be classified. Finally, 4 percent of all CCDSS records had a concordant positive PFT result and can therefore be classified as PFT diagnosed.

Figure 4: Classification of All CCDSS Cases According to PFT Presence and Results

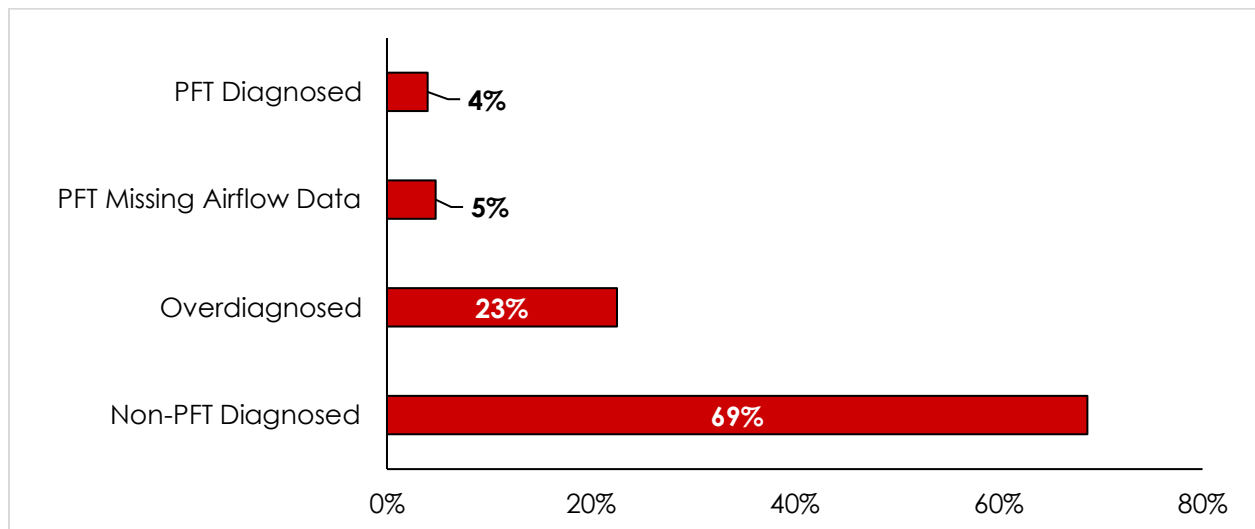


Figure 5 describes the proportion of overdiagnosed cases when only CCDSS cases with a complete PFT (n=12,390) were considered. Specifically, 85 percent of these can be labelled as overdiagnosed, with only 15 percent of the CCDSS cases being PFT diagnosed.

Figure 5: Proportion of Overdiagnosed CCDSS Cases Among CCDSS Cases With Complete PFT Results (n=12,390)

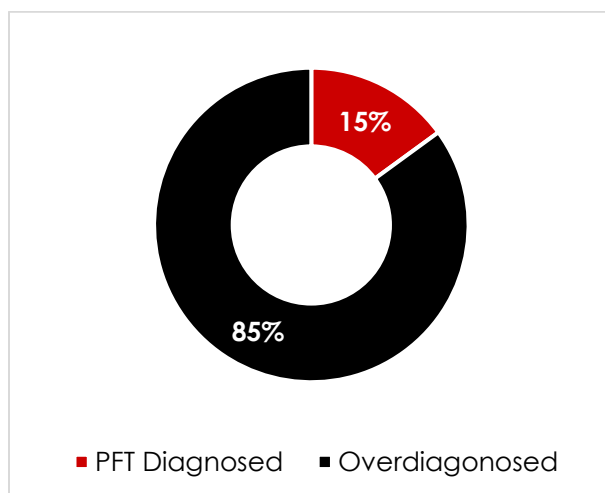


Figure 6: Proportion of Non-PFT Diagnosed CCDSS Cases (i.e., Those Completely Lacking a PFT Value or Having Only a Pre-Bronchodilator Value), Excluding Records Missing Airflow Measurement Data Due to Data Quality Issue (n=44,465)

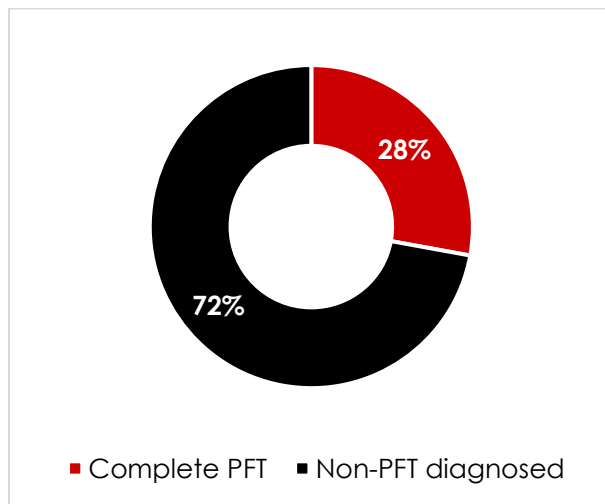


Figure 6 shows the proportion of CCDSS cases that have a confirmatory PFT (28%) versus those with that were non-PFT diagnosed (i.e., PFT absent or incomplete, 72%), among all CCDSS cases that were not affected by the missing airflow data issue.

Figure 7: Classification of All Non-CCDSS Cases According to PFT Results

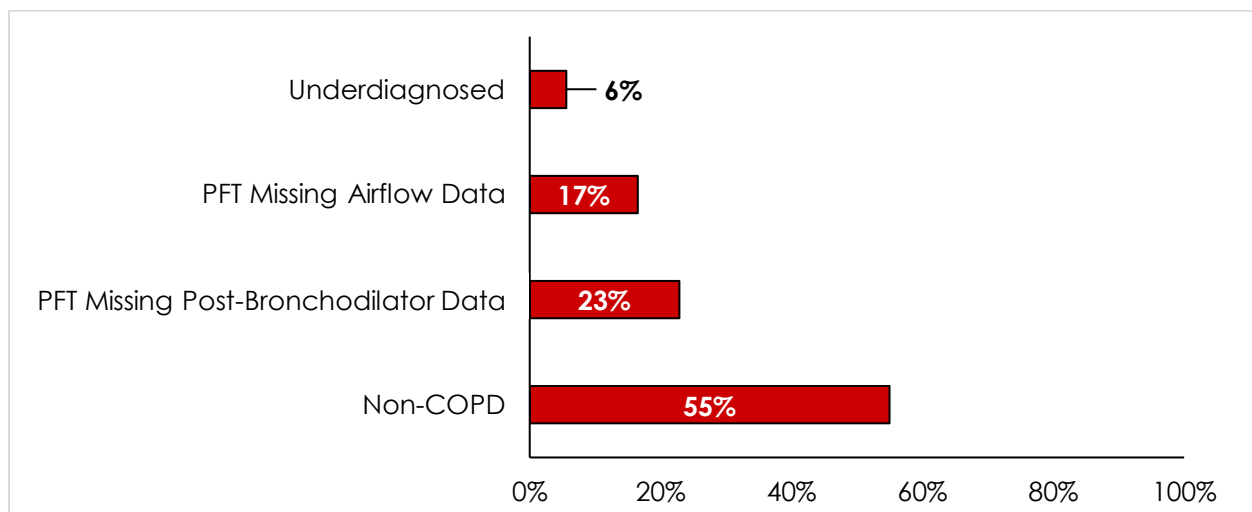
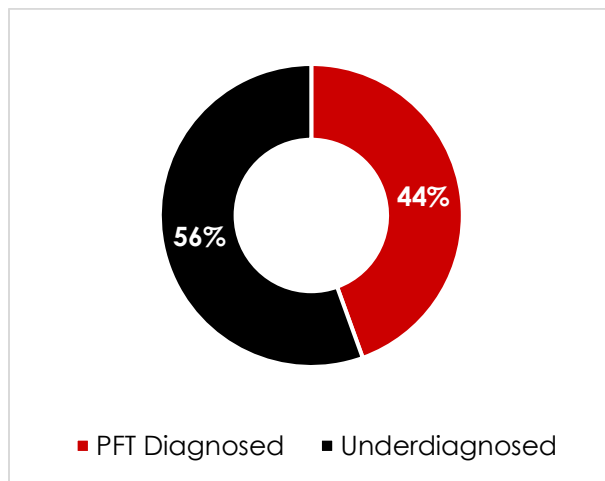


Figure 7 presents the classification of non-CCDSS records according to PFT results. The majority (55%) of individuals in NB-CHIP that were not CCDSS cases had negative PFT results, suggesting their airway complaint was non-COPD. Forty percent of individuals in NB-CHIP that were not CCDSS cases lacked sufficient information to classify the record with respect to COPD diagnosis (17% missing airflow data; 23% missing post-bronchodilator data). Finally, 6 percent of non-CCDSS cases had a positive PFT, meeting the criteria to be classified as underdiagnosed. Figure 8 shows that 56 percent of all records with a complete PFT are underdiagnosed.

Figure 8: Proportion of Underdiagnosed Cases Among All Records With Complete Positive PFT Results (n=4,170)

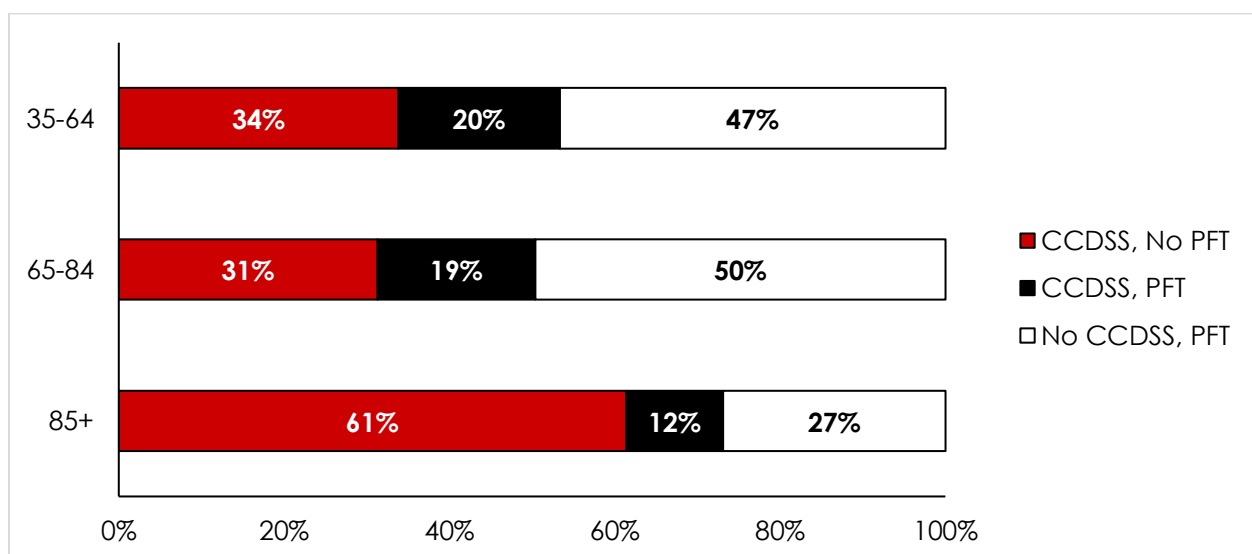


Concordance Categories and Select Individual Characteristics

Age

Figures 9 to 12 describe how age relates to CCDSS COPD status and PFTs. Figure 9 describes the coincidence of CCDSS and PFT in the overall respiratory complaint cohort by age group. Prevalence of COPD diagnosis without a PFT was relatively consistent across the younger age groups (34% and 31% among ages 35-64 and 65-84, respectively), and markedly higher among those aged 85 and over (61%).

Figure 9: CCDSS and PFT Coincidence by Age Group



Figures 10 and 11 describe CCDSS and PFT concordance among records with complete PFT information. Figure 10 shows that the prevalence of overdiagnosis was the same (85%) in both younger age groups and slightly higher (91%) among individuals aged 85 and older, while Figure 11 shows that the prevalence of underdiagnosis increases with age, i.e. 45%, 65%, and 77% among ages 35-64, 65-84, and 85+, respectively.

Figure 12 shows the proportion of non-PFT diagnosed CCDSS cases by age, combining all CCDSS cases that did not get a PFT with the cases that had no post-bronchodilator information available. The proportion of non-PFT diagnosed cases was the same (71%) in both younger age groups and higher (91%) among CCDSS cases aged 85 years and older.

Figure 10: CCDSS and PFT Concordance Among CCDSS Cases With Complete PFT Results, by Age Group

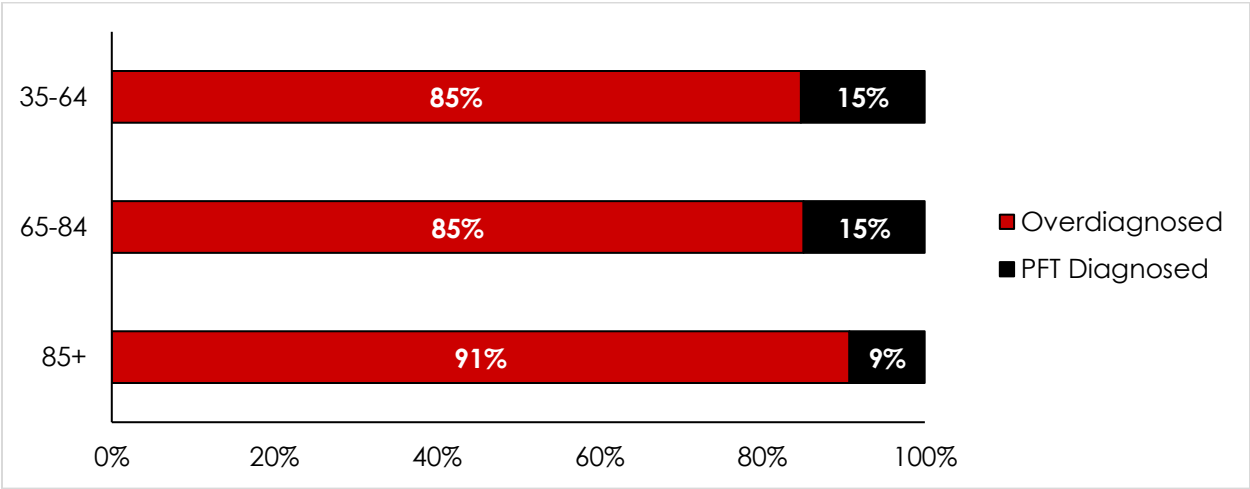


Figure 11: Proportion of Underdiagnosed Cases Among All Records With Complete Positive PFT Results, by Age Group

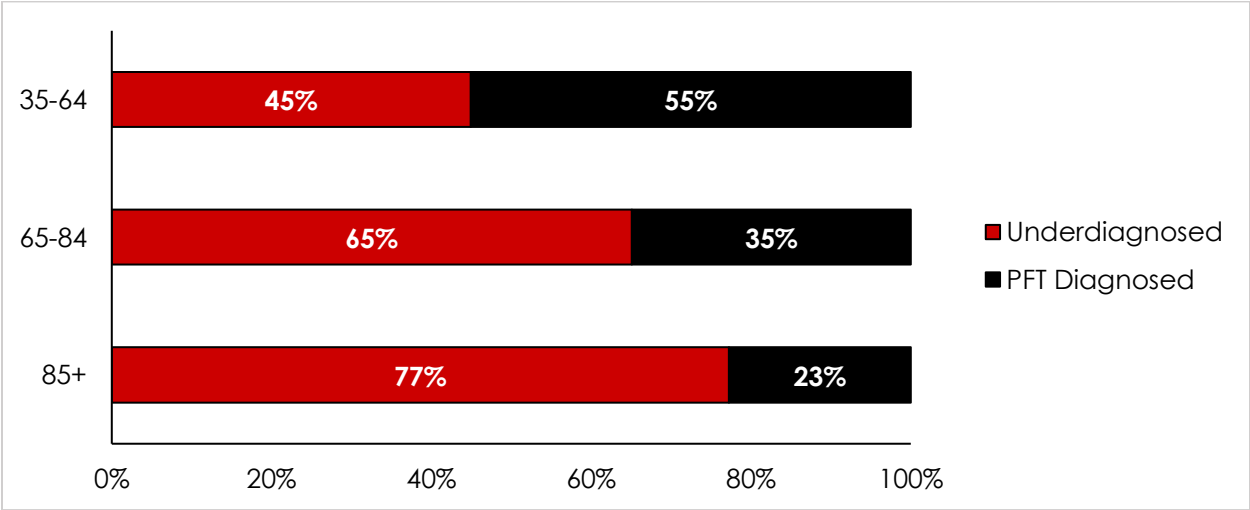
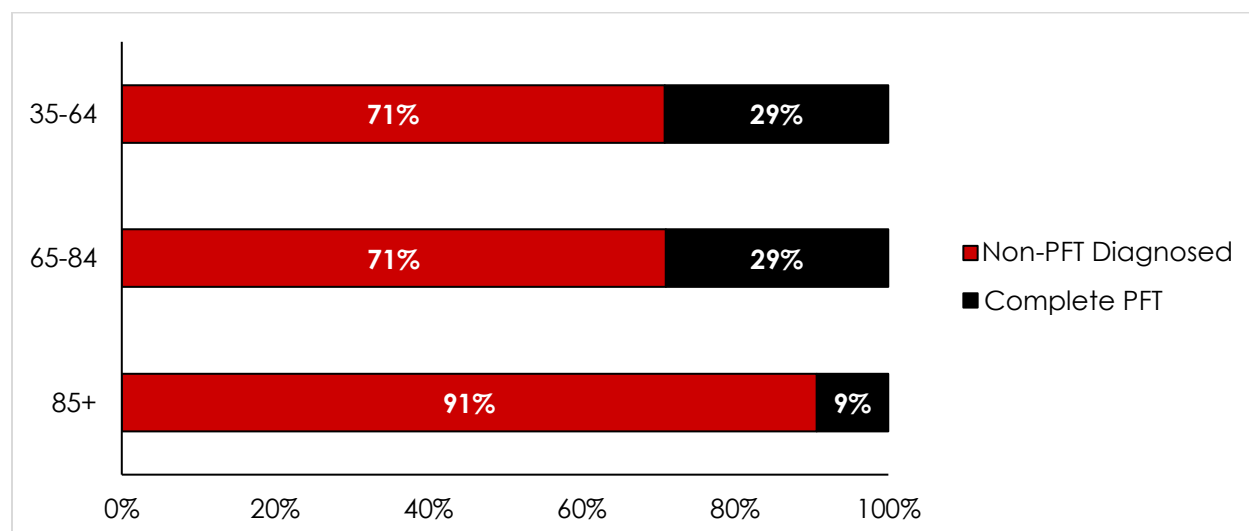


Figure 12: Proportion of Non-PFT Diagnosed CCDSS Cases (i.e., Those Completely Lacking a PFT Value or Having Only a Pre-Bronchodilator Value), Excluding Records Missing Airflow Measurement Data Due to Data Quality Issue, by Age Group

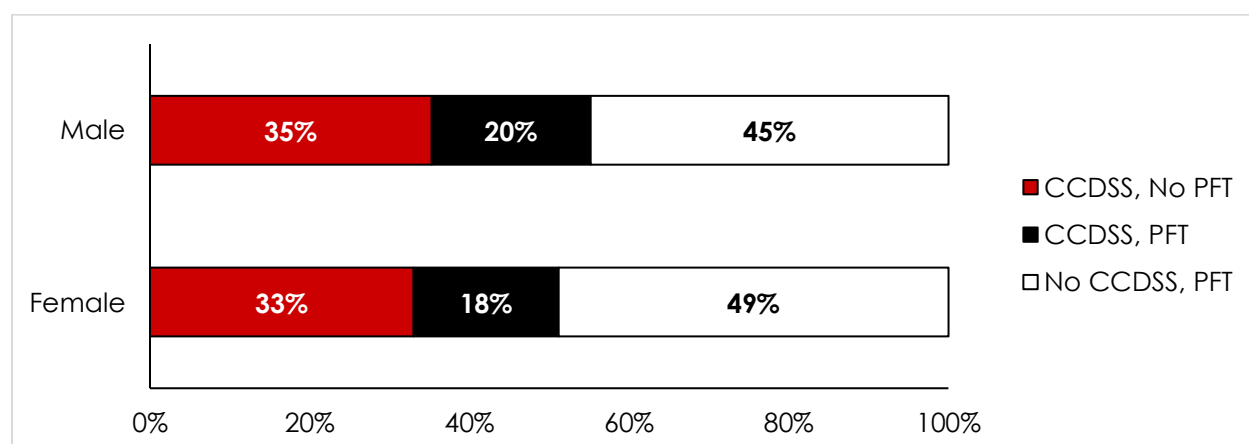


Sex

Figures 13 to 16 describe how sex relates to CCDSS COPD status and PFTs.

In Figure 13, which describes the coincidence of CCDSS and PFT by sex, males have a slightly higher proportion of coincidence (20%) than females (18%). Further, the proportion of males identified as a CCDSS case without a PFT was slightly greater than the proportion of females (35% for males versus 33% for females).

Figure 13: CCDSS and PFT Coincidence by Sex



Figures 14 and 15 describe CCDSS and PFT concordance among records with complete PFT information. Figure 14 shows a greater proportion of overdiagnosed cases among females in comparison to males (88% versus 82%), while Figure 15 shows that underdiagnosis is also more common among females (59% versus 53%).

Figure 14: CCDSS and PFT Concordance Among CCDSS Cases With Complete PFT Results, by Sex

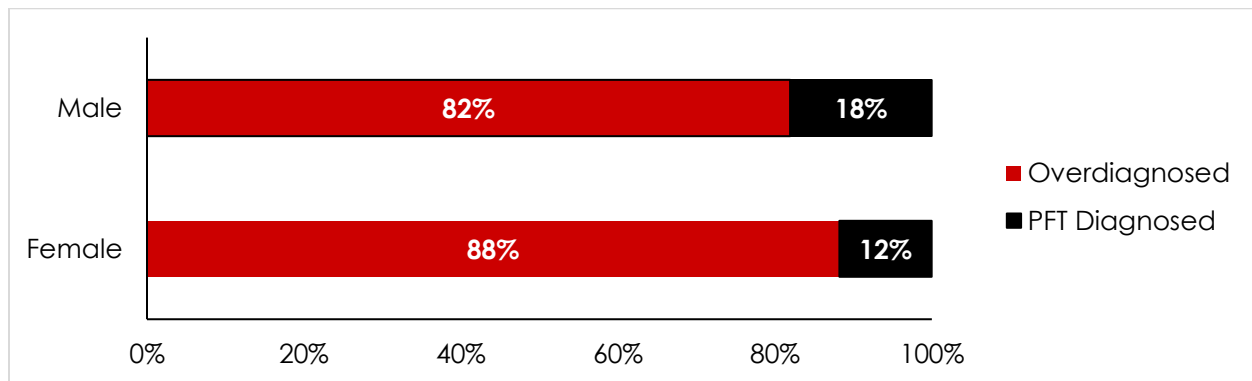


Figure 15: Proportion of Underdiagnosed Cases Among All Records With Complete Positive PFT Results, by Sex

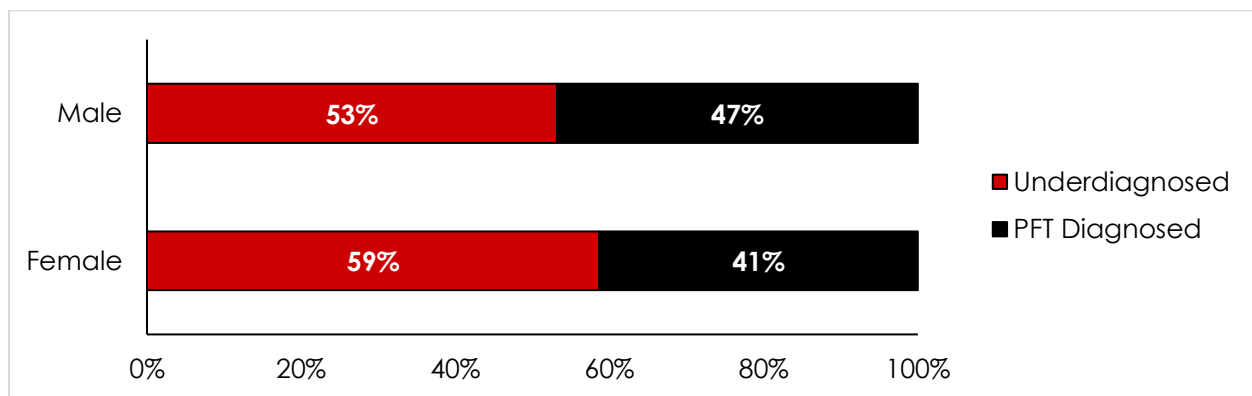


Figure 16: Proportion of Non-PFT Diagnosed CCDSS Cases (i.e., Those Completely Lacking a PFT Value or Having Only a Pre-Bronchodilator Value), Excluding Records Missing Airflow Measurement Data Due to Data Quality Issue, by Sex

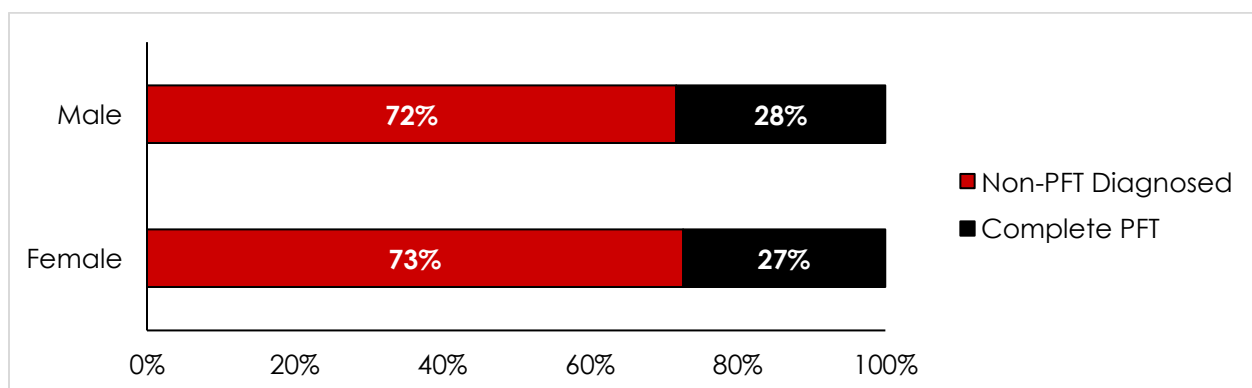


Figure 16 shows that, among all CCDSS cases, 73 percent of women were non-PFT diagnosed compared to 72 percent of men.

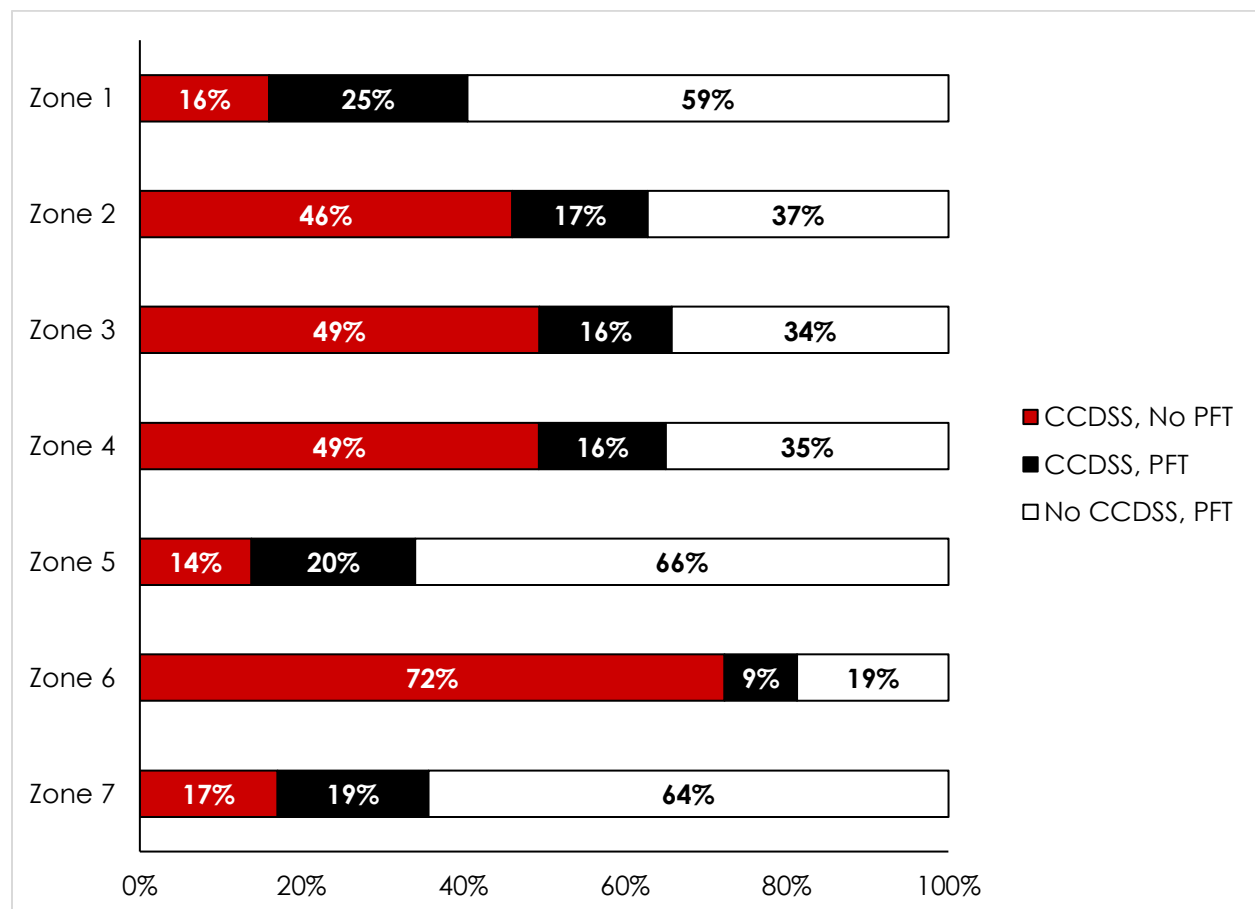
Health Zone of Individual Residence

Figures 17 to 20 describe how the health zone of an individual's residence relates to CCDSS case status and PFTs.

Figure 17 describes CCDSS and PFT coincidence by health zone of residence and demonstrates a great deal of variation in relative proportion of coincidence groups across the seven health zones.

Zone 6 had the largest proportion (72%) of individuals identified as a CCDSS case who did not receive a PFT, compared to a range of 14 to 49 percent among the other health zones. Zones 1 (59%), 5 (66%) and 7 (64%) had the greatest proportion of individuals not flagged as CCDSS cases who did receive a PFT, with the proportions among other health zones ranging from 19 to 37 percent. Finally, Zone 1 had the greatest proportion (25%) of individuals flagged as a CCDSS case that received a PFT, with the other zones ranging from 9 to 20 percent.

Figure 17: CCDSS and PFT Coincidence by Health Zone of Residence



Figures 18 and 19 describe how CCDSS and PFT concordance varies by health zone of residence among records with complete PFT information. Among CCDSS cases, the proportion of

overdiagnosed individuals varied from 82 to 92 percent across health zones, with the greatest proportion in Zone 4 (92%) and the lowest proportion in Zone 3 (82%) (Figure 18).

Figure 18: CCDSS and PFT Concordance Among CCDSS Cases With Complete PFT Results, by Health Zone of Residence

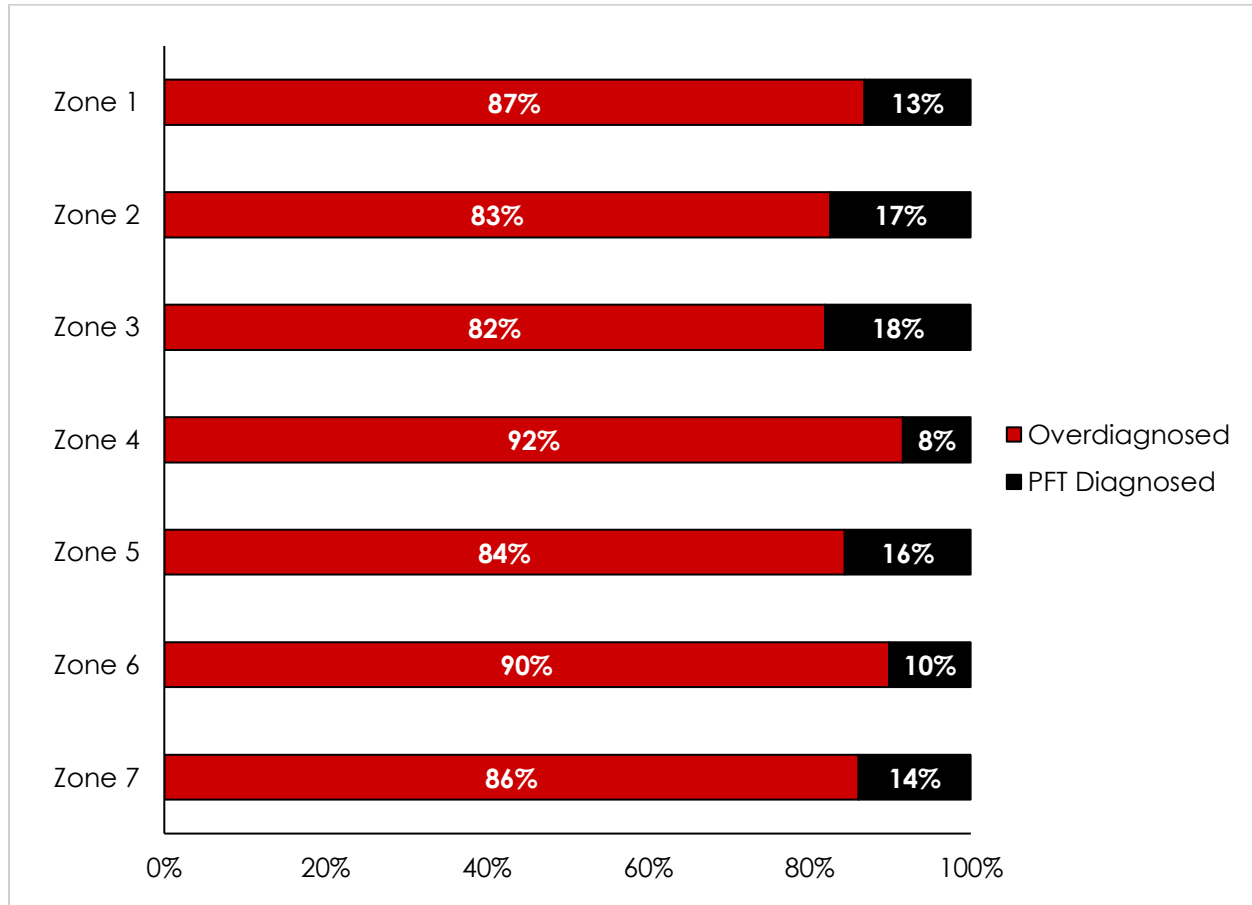


Figure 19 shows that the proportions of underdiagnosis ranged from 48 percent (Zone 1) to 67 percent (Zone 4).

Figure 19: Proportion of Underdiagnosed Cases Among All Records With Complete Positive PFT Results, by Health Zone of Residence

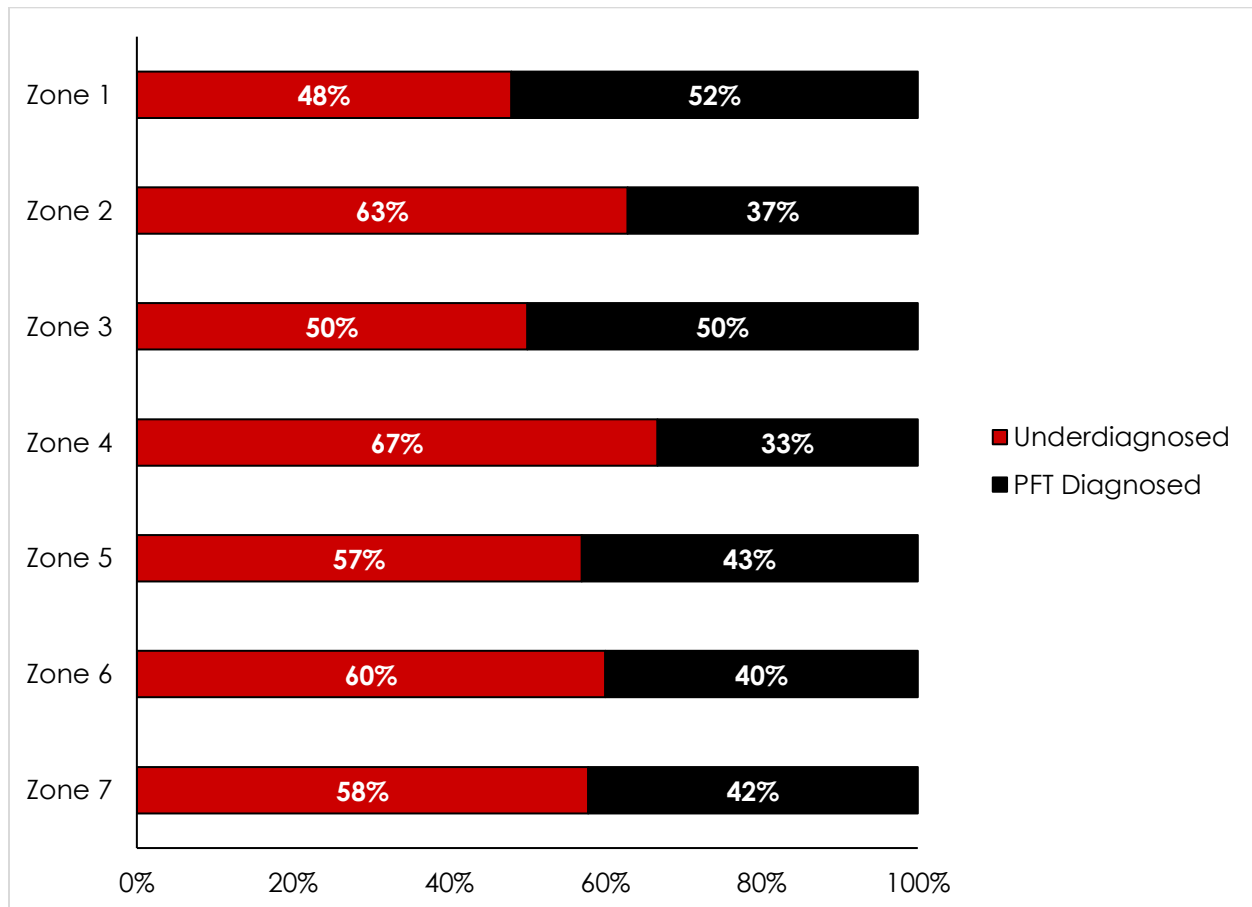
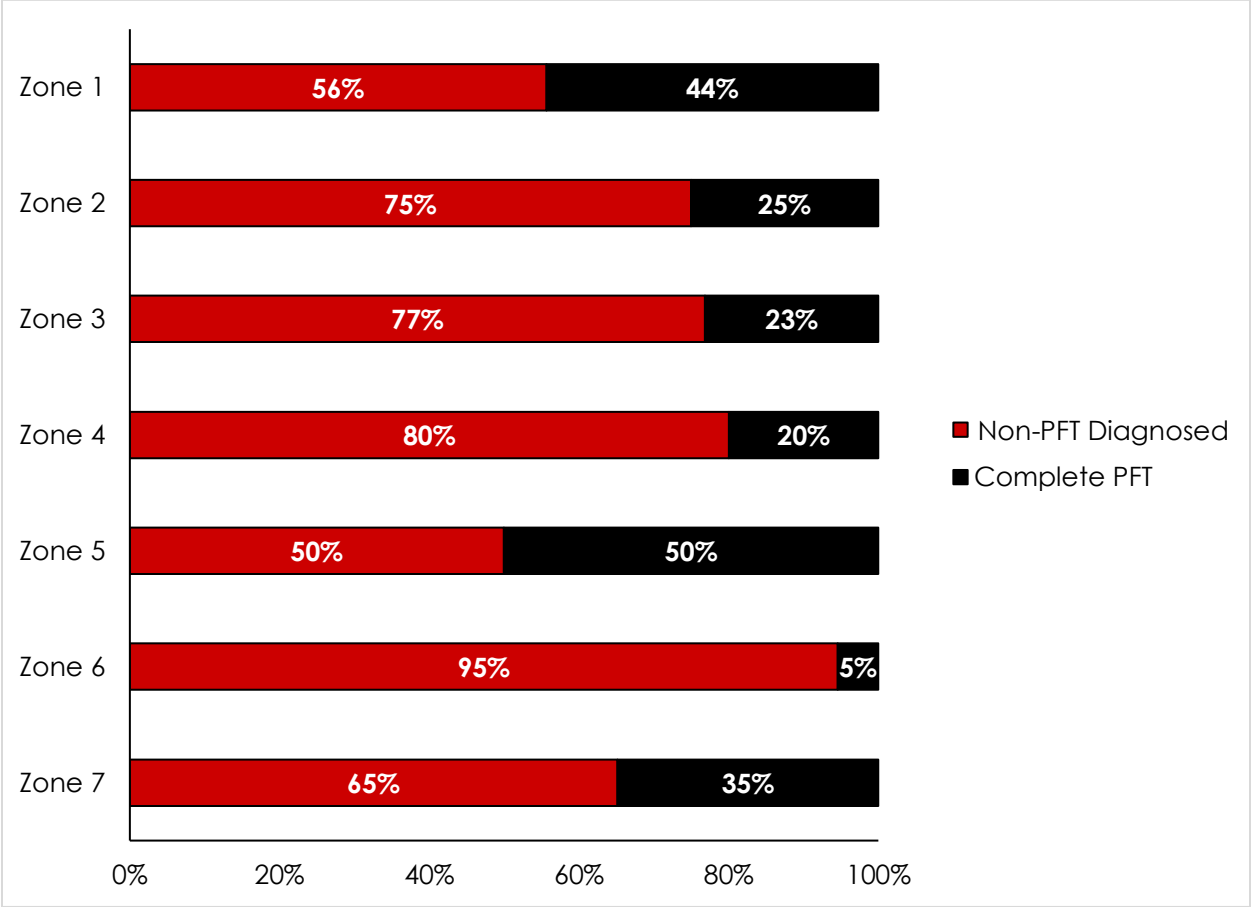


Figure 20 shows that the proportion of non-PFT diagnosed CCDSS cases among all CCDSS cases ranged from 50 percent (Zone 5) to 95 percent (Zone 6) according to the health zone in which an individual lived.

Figure 20: Proportion of Non-PFT Diagnosed CCDSS Cases (i.e., Those Completely Lacking a PFT Value or Having Only a Pre-Bronchodilator Value), Excluding Records Missing Airflow Measurement Data Due to Data Quality Issue, by Health Zone of Residence

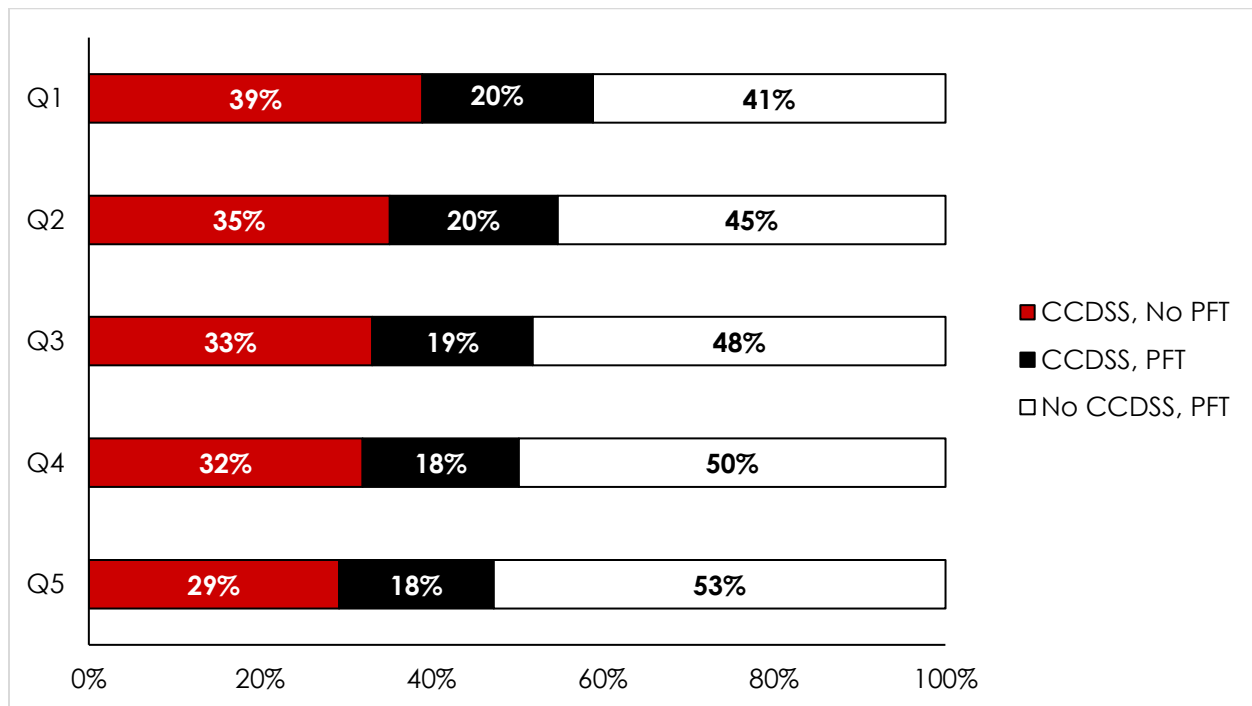


Area-Level Income Quintiles

Figures 21 to 33 describe how neighbourhood income relates to CCDSS COPD case status and PFTs. Presented as area-level income quintiles, areas classified as Quintile 1 (Q1) have the lowest area-level income, while areas classified as Quintile 5 (Q5) have the highest area-level income.

Figure 21 describes CCDSS and PFT coincidence by neighbourhood income. The proportion of individuals who were CCDSS COPD cases without a PFT decreased as neighbourhood income increased. Conversely, the proportion of individuals who were not CCDSS cases but were PFT-tested increased with increasing income, while there was little variation with income in the proportion of individuals who were CCDSS cases with a PFT.

Figure 21: CCDSS and PFT Coincidence by Area Income Quintile



Figures 22 and 23 describe the relationship between neighbourhood income and CCDSS and PFT concordance among records with complete PFT information.

Among CCDSS cases (Figure 22), there was no variation according to neighbourhood income; all quintiles show 85 percent of records were overdiagnosed.

Figure 23, however, does demonstrate variation, with the proportion of underdiagnosed individuals decreasing from 58 percent to 52 percent as area level income increased.

Figure 22: CCDSS and PFT Concordance Among CCDSS Cases With Complete PFT Results, by Area Income Quintile

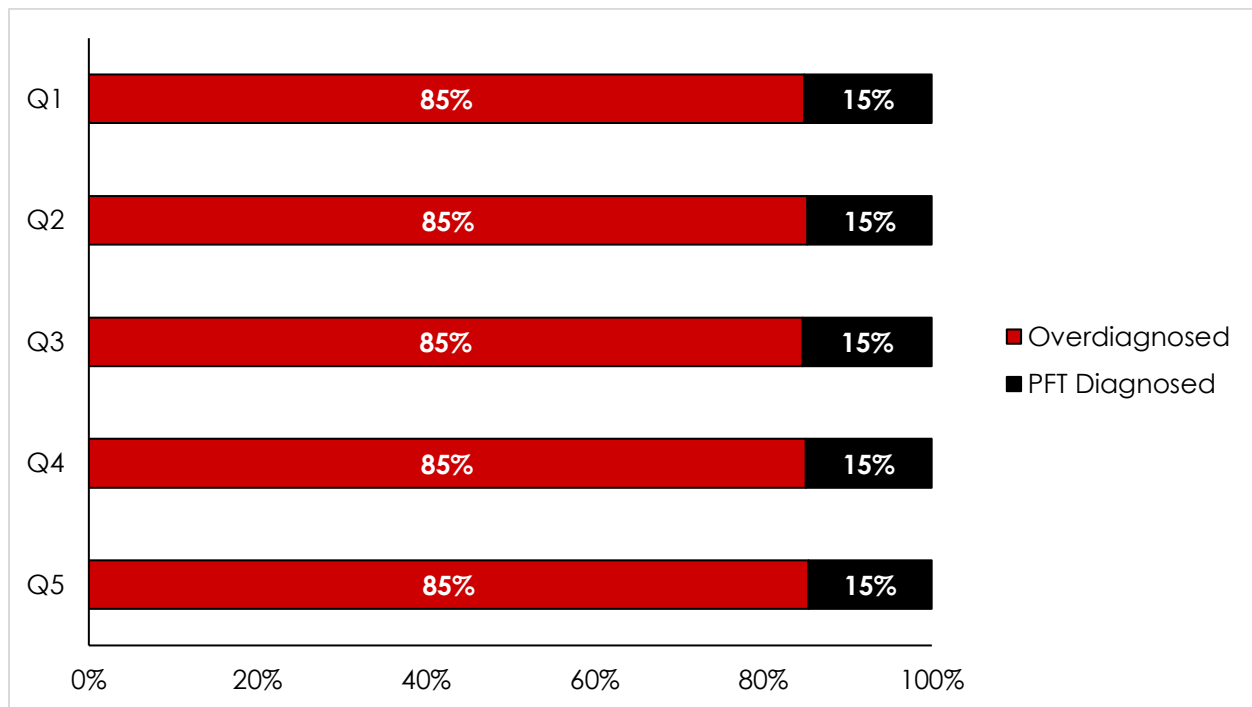


Figure 23: Proportion of Underdiagnosed Cases Among All Records With Complete Positive PFT Results, by Area Income Quintile

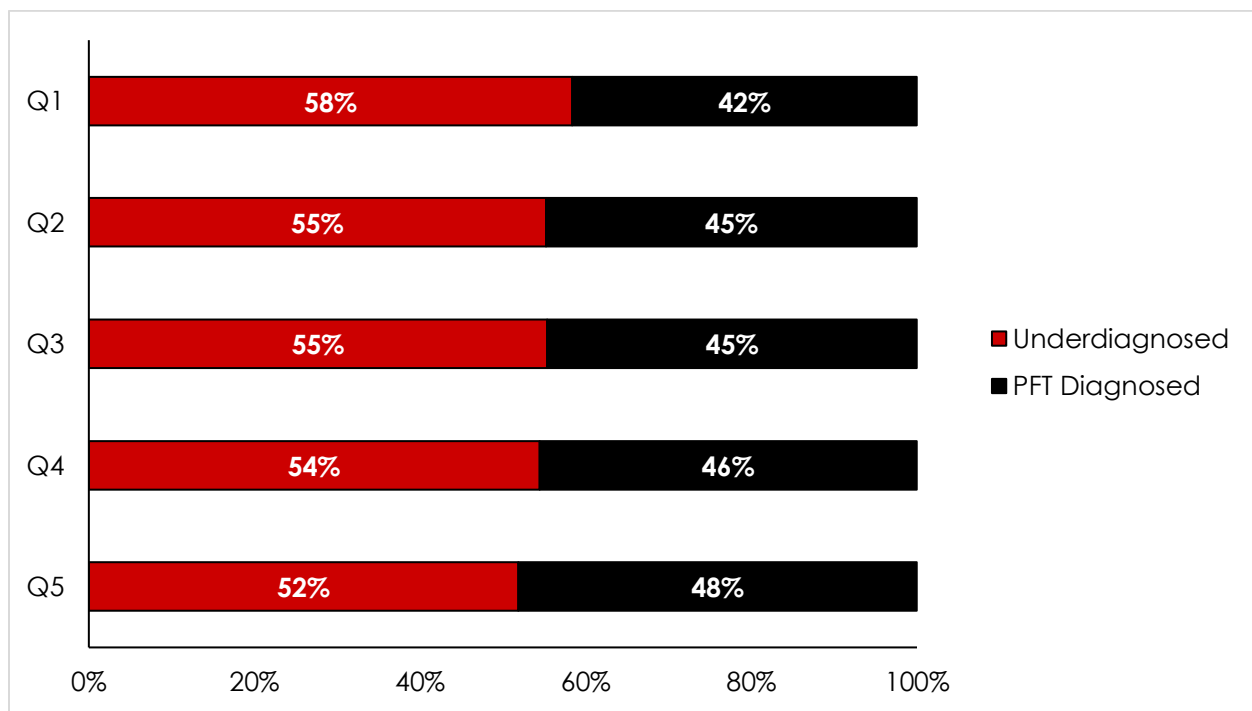
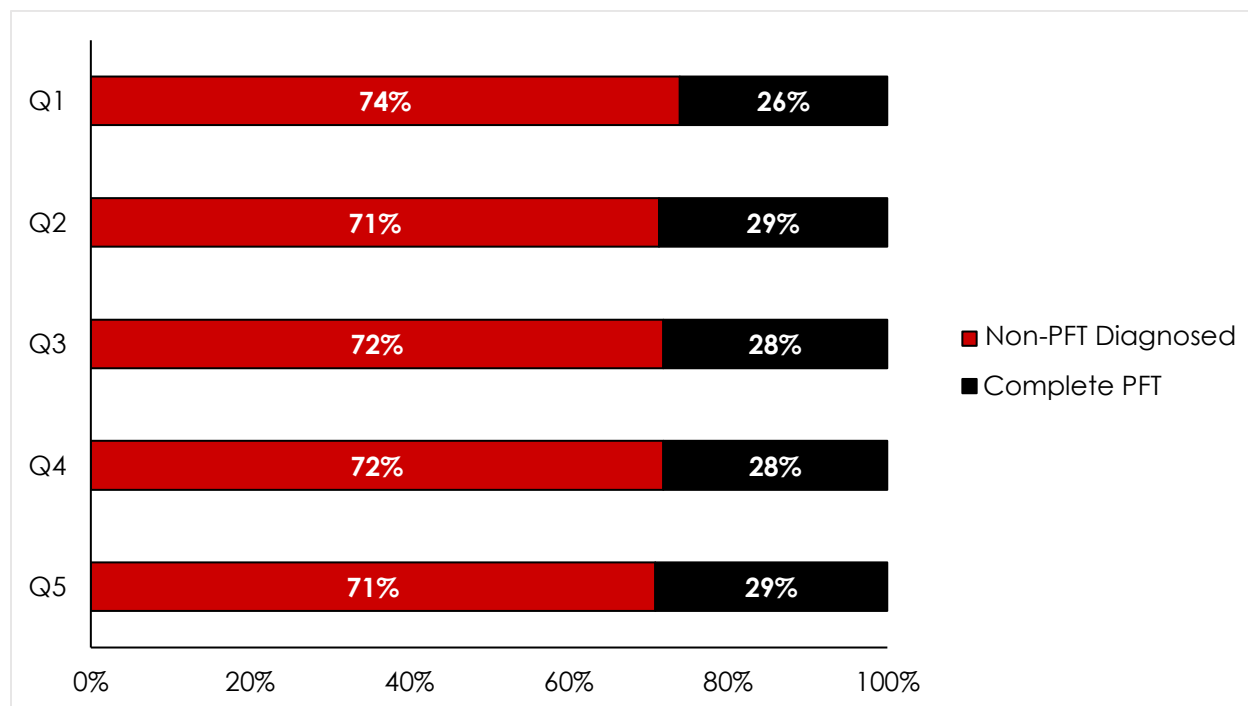


Figure 24 demonstrates that the proportion of non-PFT diagnosed CCDSS cases among all CCDSS cases ranges from 71 to 74 percent when examining area-level income quintiles.

Figure 24: Proportion of Non-PFT Diagnosed CCDSS Cases (i.e., Those Completely Lacking a PFT Value or Having Only a Pre-Bronchodilator Value), Excluding Records Missing Airflow Measurement Data Due to Data Quality Issue, by Area Income Quintile

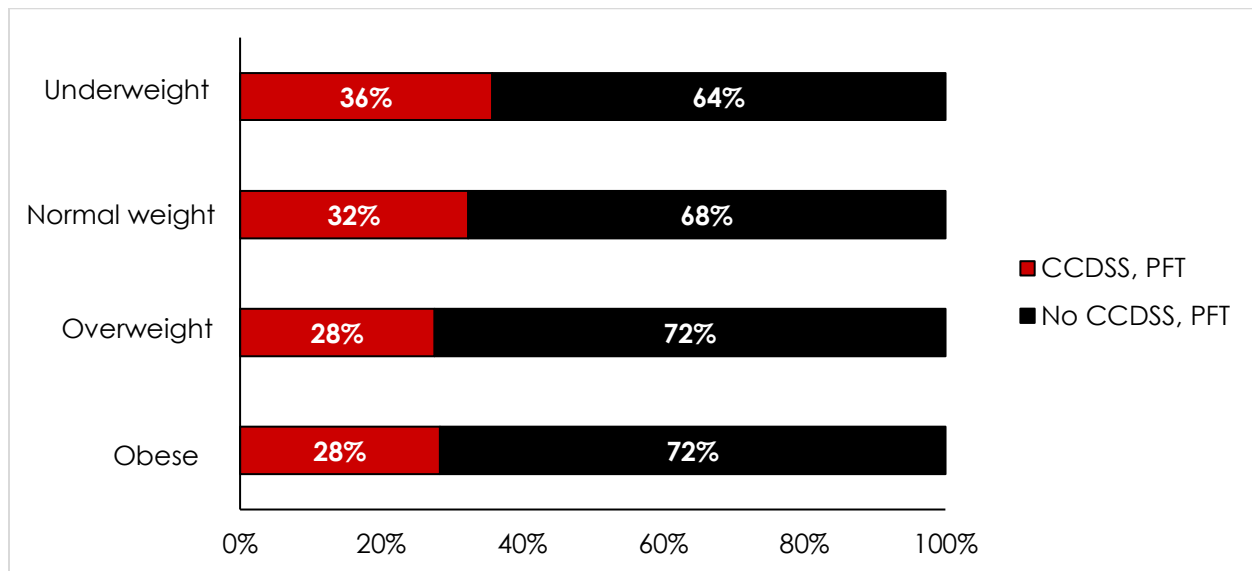


Body Mass Index (BMI)

Figures 25 to 28 describe how BMI relates to CCDSS COPD status and PFTs. Note that BMI is derived from PFT clinic records; therefore, only records captured in NB-CHIP were included in the following analyses (n=57,915).

In Figure 25, which describes the coincidence of CCDSS case status and PFT by BMI classification, CCDSS and PFT coincidence was greater among individuals classified as underweight (36%) and normal weight (32%). Individuals classified as overweight or obese had a smaller proportion (28% for both BMI classifications) of CCDSS and PFT coincidence.

Figure 25: CCDSS and PFT Coincidence by BMI Classification



Figures 26 and 27 present CCDSS and PFT concordance among records with complete PFT information. Among individuals identified as CCDSS cases (Figure 26), the prevalence of overdiagnosis varied according to BMI classification, ranging from 65 percent among underweight individuals to 91 percent among overweight individuals.

Figure 26: CCDSS and PFT Concordance Among CCDSS Cases With Complete PFT Results, by BMI Classification

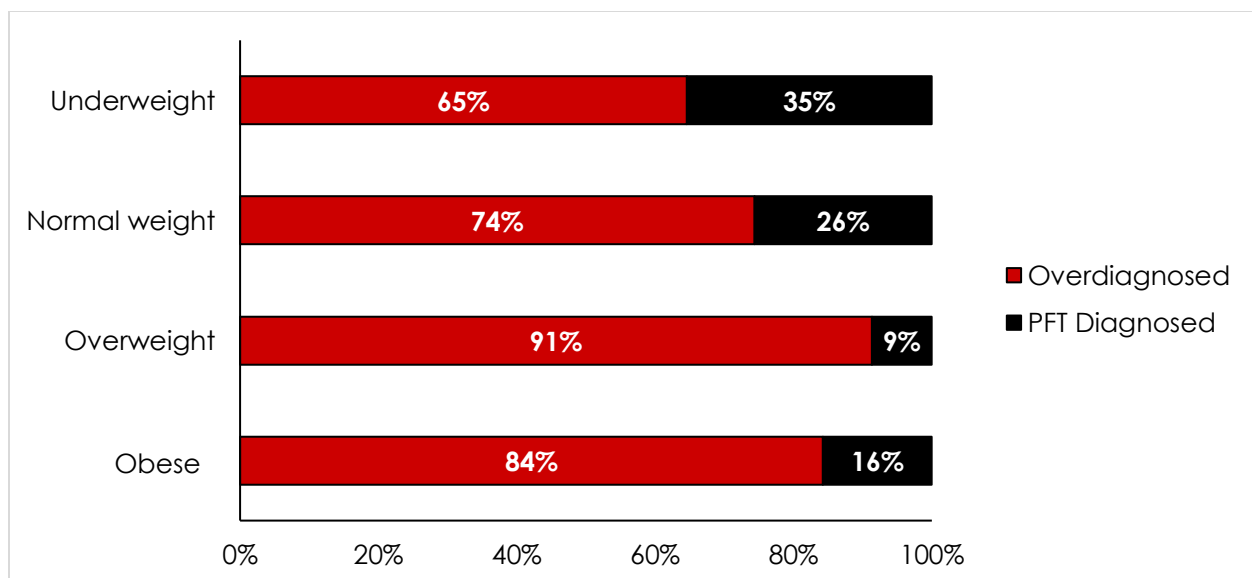


Figure 27 shows that the proportion of underdiagnosis decreased as BMI increased, ranging from 60 percent of underweight individuals being identified as underdiagnosed to 55 percent of obese individuals identified as underdiagnosed.

Figure 27: Proportion of Underdiagnosed Cases Among All Records With Complete Positive PFT Results, by BMI Classification

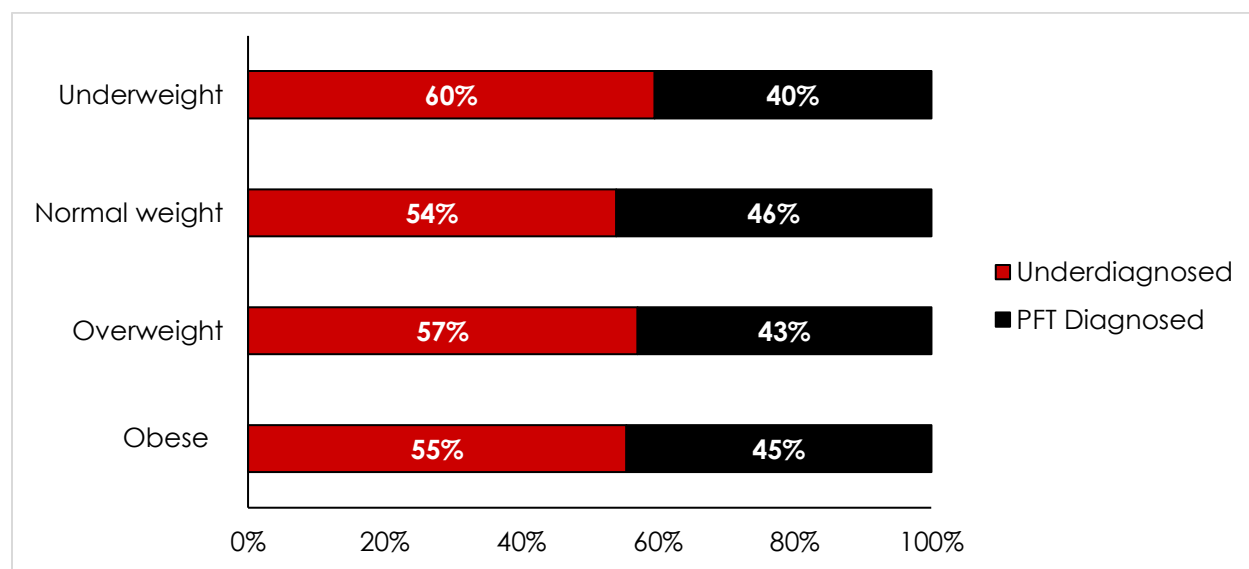
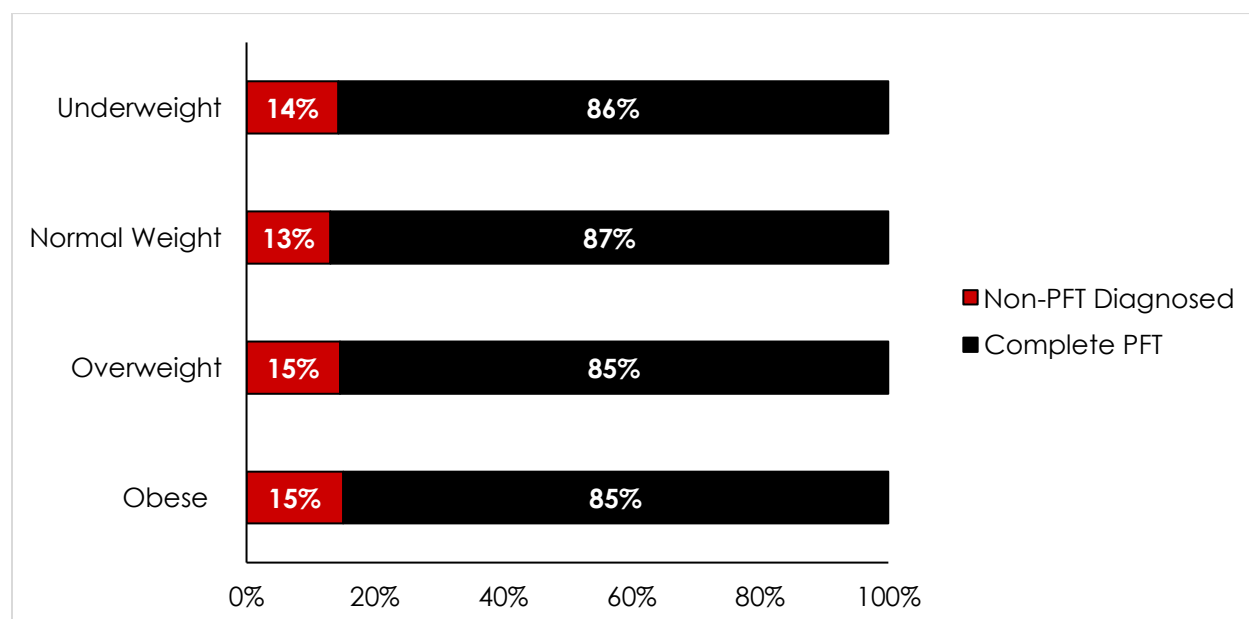


Figure 28 demonstrates that, among all CCDSS cases, the proportion of non-PFT diagnosed CCDSS cases ranged from 13 to 15 percent across the various BMI classifications. Note that for the BMI analysis, non-PFT diagnosed CCDSS cases included only those records that were missing a post-bronchodilator value (as BMI information was not available when PFT records were completely absent).

Figure 28: Proportion of Non-PFT Diagnosed CCDSS Cases (i.e., Those Having Only a Pre-Bronchodilator Value), Excluding Records Missing Airflow Measurement Data Due to Data Quality Issue, by BMI Classification

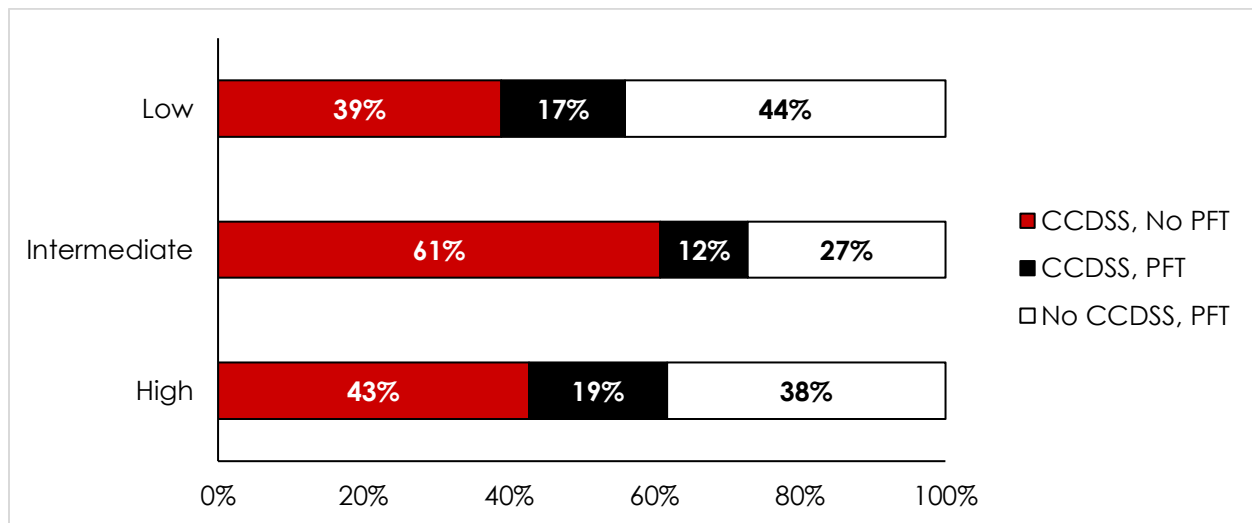


Frailty Risk

Figures 29 to 32 describe how frailty risk relates to CCDSS COPD status and PFTs. Note that frailty risk was drawn from a subsample of individuals aged 75 and over and hospitalized during the study period (n=15,930.)

Figure 29, which describes the coincidence of CCDSS and PFT by frailty risk, shows that both the low- and the high-frailty risk groups had smaller proportions (39% to 43%) of individuals flagged as CCDSS cases with no PFT, while the intermediate-frailty risk group had a much larger proportion (61%).

Figure 29: CCDSS and PFT Coincidence by Frailty Risk



Figures 30 and 31 describe CCDSS case status and PFT result concordance among records with complete PFT information. Among CCDSS cases (Figure 30), 87 to 93 percent of records were overdiagnosed, with the intermediate-frailty risk group having the greatest proportion of overdiagnosed individuals (93%).

Figure 31 shows that 81 percent of individuals classified as having intermediate-frailty risk were underdiagnosed, while 67 percent of those with high-frailty risk were underdiagnosed.

Figure 30: CCDSS and PFT Concordance Among CCDSS Cases With Complete PFT Results, by Frailty Risk

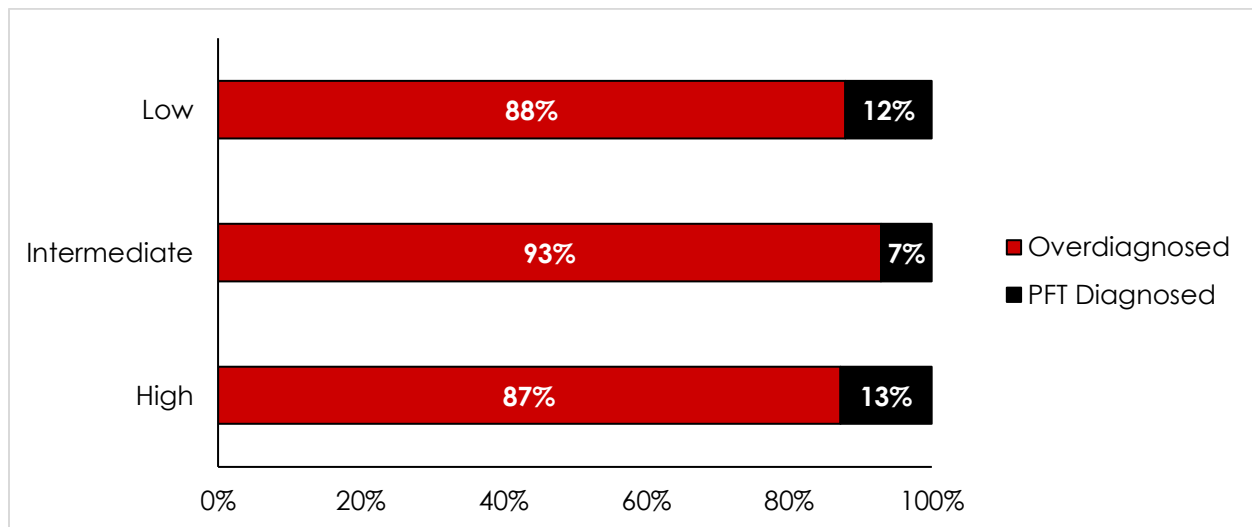


Figure 31: Proportion of Underdiagnosed Cases Among All Records With Complete Positive PFT Results, by Frailty Risk

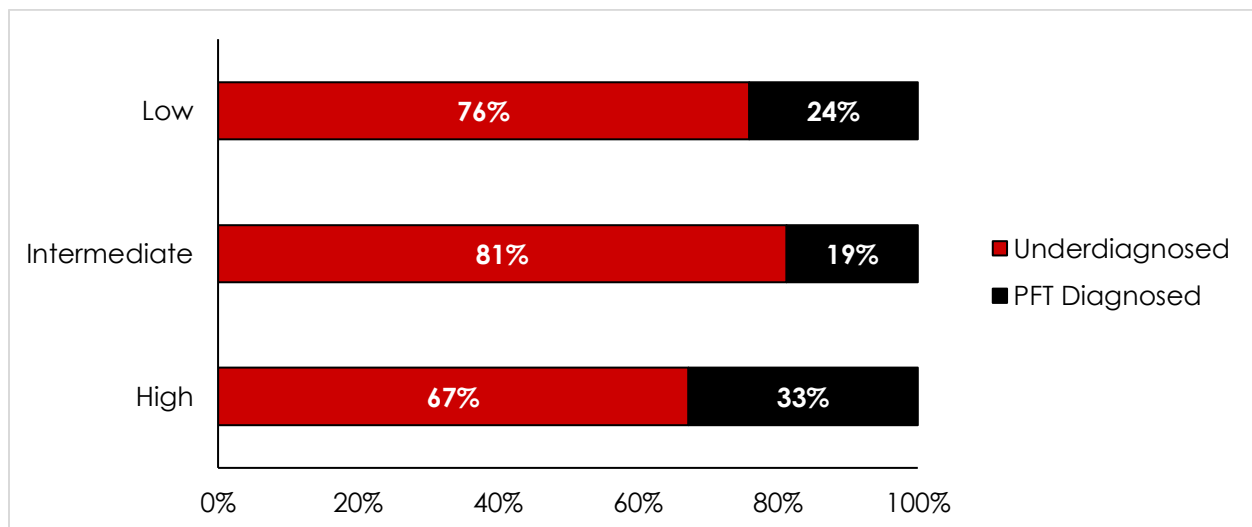
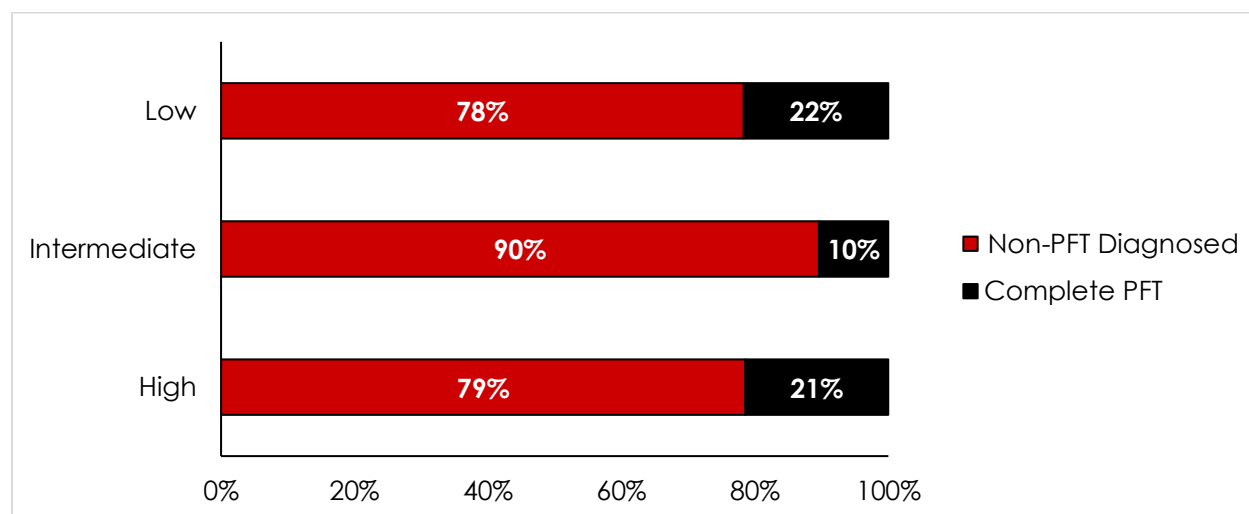


Figure 32 demonstrates that the proportion of non-PFT diagnosed CCDSS among all CCDSS cases ranged from 78 to 90 percent across frailty risk groups, with intermediate-frailty risk having the greatest proportion of non-PFT diagnosed CCDSS cases.

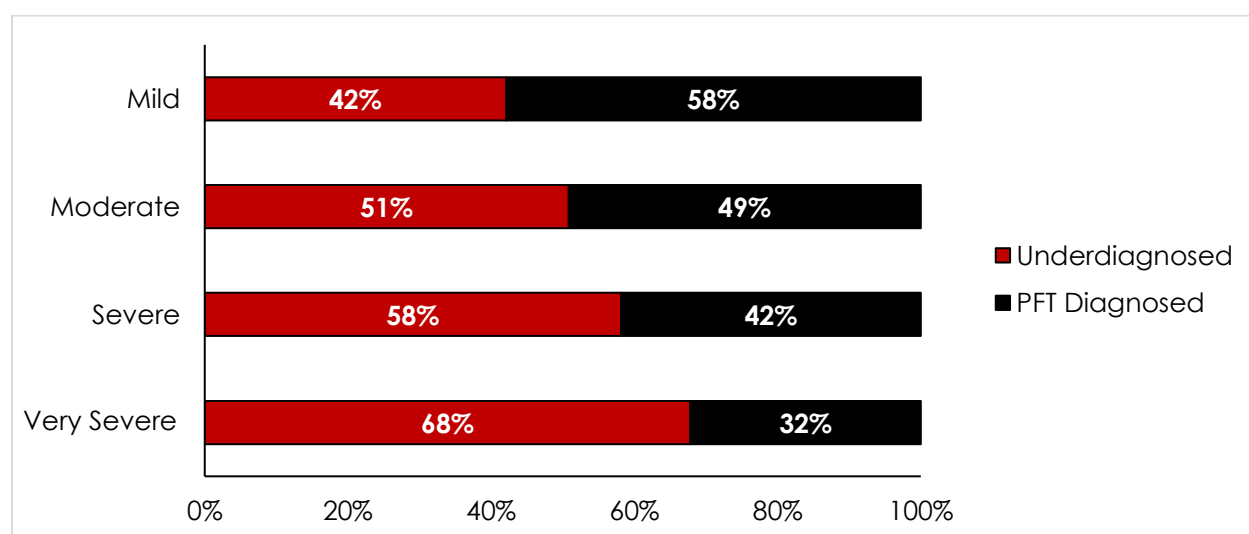
Figure 32: Proportion of Non-PFT Diagnosed CCDSS Cases (i.e., Those Completely Lacking a PFT Value or Having Only a Pre-Bronchodilator Value), Excluding Records Missing Airflow Measurement Data Due to Data Quality Issue, by Frailty Risk



Severity of Airflow Limitation

Figure 33 describes concordance of CCDSS case status and PFT result by severity of airflow limitation determined by PFT. We categorized severity of airflow limitation according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria.⁽¹⁾ The definition of severity of airflow limitation according to GOLD criteria requires a positive PFT result (i.e., a PFT result that is indicative of COPD); therefore, this analysis is limited to a subsample of individuals with positive PFT results (n=4,180). In [Figure 25](#), the proportion of individuals flagged as underdiagnosed increased as the severity of airflow limitation increased (42% to 68%).

Figure 33: Proportion of Underdiagnosed Cases Among All Records With Complete Positive PFT Results, by Severity of Airflow Limitation



Discussion

CCDSS and PFT Coincidence and Concordance

Between January 1, 2007, and December 31, 2017, 23 percent (10,535) of all CCDSS COPD cases were overdiagnosed, and 69 percent (32,075) were non-PFT diagnosed.

Taken together, 92 percent (51,060) of CCDSS-defined incident COPD diagnoses in New Brunswick either lack complete confirmatory PFT results supporting the physician diagnosis or have PFT results inconsistent with the diagnosis. Only 4 percent of CCDSS COPD cases had a positive PFT that met the clinical criteria used to identify COPD.

When focusing exclusively on CCDSS cases with a complete PFT (12,390), the proportion of overdiagnosed cases rises to 85 percent, notably higher than the range of estimates reported in the literature (29% to 65%) from other Canadian and international sources.^(15, 18)

During the observation period, 2,315 individuals (3% of all individuals in the entire sample and 6% of all individuals with a PFT) met the criteria for underdiagnosed COPD (no formal diagnosis, presence of positive PFT results indicative of COPD).⁽¹⁵⁾ The proportion of individuals with underdiagnosed COPD increases to 56 percent when focusing exclusively on the individuals with complete positive PFT results, falling within the international range of estimates (52.6% to 86.8%) reported in Diab et al.,⁽¹⁵⁾ but lower than the Ontario estimate of 79 percent underdiagnosed reported by Gershon et al.⁽¹⁸⁾

The overdiagnosis and underdiagnosis of COPD can have implications for individual morbidity, health service use, and quality of life, as well as health system planning for future burden. Gershon et al.⁽¹⁸⁾ demonstrate that overdiagnosed patients have more ambulatory care visits, emergency department visits, and hospitalizations than individuals without COPD, while also showing that, overall, underdiagnosed individuals have more ambulatory care visits than individuals without COPD.

As Gershon et al.⁽¹⁸⁾ note, both instances likely demonstrate higher rates of health service use because the individual's actual health complaint is going untreated. That is, underdiagnosed patients are not receiving care for COPD, while overdiagnosed patients are getting care for COPD instead of other lung diseases or circulatory system issues that are actually causing their health complaints.

Coincidence, Concordance, and Select Individual Characteristics

Age

Examining the respiratory cohort by age demonstrated considerable variation in three of the four analyses implemented.

When examining CCDSS and PFT coincidence by age, the proportion of the respiratory complaint cohort with CCDSS records having no corresponding PFT was relatively consistent across the younger age groups (31-34%), but substantially higher among individuals aged 85 years and older. A similar pattern was evident for non-PFT diagnosis and overdiagnosis: the prevalence of both was consistent across ages 35-84 and increased at age 85 and older, though the disparity between younger and older age groups was more substantial for non-PFT diagnosis. Underdiagnosis, by contrast, increased with each age category.

One possible explanation for the outsized proportion of records among the 85 years and older category in the coincidence and non-PFT diagnosed analyses is that the analyses may reflect the difficulty in obtaining quality PFT results in elderly patients. Pulmonary function testing is effort-dependent, and some older patients may be unable to complete the test due to physical or cognitive limitations.⁽²⁸⁾ Additionally, for these same reasons, some care providers may opt not to utilize PFTs in some of their older patients.

The effort-dependent nature of PFTs may also contribute to the increased prevalence of overdiagnosis in the oldest age group, and the increased prevalence of underdiagnosis as age increases. For example, physicians may be more likely to doubt the validity of PFT results among these patients due to a perception that older patients may be less likely to complete the test correctly. Consequently, physicians may be more inclined to make diagnostic decisions in these patients that are contrary to PFT results (i.e., overdiagnosis or underdiagnosis).

Interestingly, assuming the effort-dependent nature of PFTs has a role in our observations with respect to age, our findings may suggest that its impact on the coincidence/concordance of COPD diagnosis manifests differently according to age. For example, the effort-dependent nature of PFTs may create circumstances that increase the likelihood of overdiagnosis or diagnosis without a PFT only among the oldest individuals (i.e., around age 85 or older), whereas its effect on the increased likelihood of underdiagnosis may be apparent at younger ages. Future studies would be required to investigate this hypothesis.

Increased prevalence of other (non-COPD) airflow-limiting conditions among older patients may also contribute to the increasing observed prevalence of underdiagnosis with increasing age. For example, conditions such as heart failure may produce a PFT result that is consistent with COPD, but if COPD is otherwise ruled out in a heart failure patient, a COPD diagnosis would not be applied, and the patient would be labelled as underdiagnosed in our analysis.

Sex

All four of the analyses demonstrated slight degrees of variation when they were disaggregated by sex.

When examining CCDSS and PFT coincidence by sex ([Figure 13](#)), men had a slightly greater proportion (35%) of CCDSS cases missing a PFT than women (33%). A slight degree of variation was also observed in the non-PFT diagnosed analysis ([Figure 16](#)), with women having a greater proportion of CCDSS cases with either no PFT or no post-bronchodilator result (73%) than men (72%). The analyses examining over- and underdiagnosis demonstrated more variation between men and women, with women having a greater proportion of both overdiagnosis (88%) and underdiagnosis (59%) compared to men (82% and 53%, respectively).

Gendered care-seeking tendencies could explain the differences observed in the overdiagnosis analysis. It is well established that women are more likely to say they would seek care than men, and they are more likely to receive care.^(29, 30) Increased frequency of encounters with care providers among women may increase the likelihood of being flagged as a COPD case in CCDSS records, even when PFT results are not indicative of COPD, thereby increasing the prevalence of overdiagnosis.

The increased prevalence of underdiagnosis we observed among women compared to men contrasts with findings from previous studies, which found that underdiagnosis was more common among men.⁽¹⁵⁾ The reasons for this discrepancy are not clear, though differences in methodology and/or differences in how underdiagnosis was defined are likely contributing factors. Using our definition of underdiagnosis, it is not unexpected that underdiagnosis is more prevalent among women, as women are likely to survive longer than men, and we observed that underdiagnosis is more prevalent among older individuals.

Health Zone

Considerable variation was observed in both the CCDSS and PFT coincidence and non-PFT diagnosed analyses.

Zones 1, 5, and 7 all had fewer than 20 percent of records reflecting a CCDSS diagnosis in the absence of a PFT. This scenario was substantially more common in the other zones, comprising nearly 50 percent of records in Zones 2, 3, and 4 and 72 percent of records in Zone 6 ([Figure 17](#)).

It is noteworthy that, compared to other zones, a substantial proportion of records in Zones 1, 5, and 7 (59% to 66%) reflect a PFT with no CCDSS case status. The proportion of non-PFT diagnosed CCDSS cases across zones mirrored the pattern observed in the coincidence analysis, being lowest in Zones 1, 5, and 7; higher in Zones 2, 3, and 4; and highest in Zone 6. Less variation is observed in the underdiagnosis and overdiagnosis analyses, with the proportion of underdiagnosed records ranging from 48 to 67 percent, and the proportion of overdiagnosed records ranging from 82 to 92 percent across zones.

The differences between the various coincidence groups observed across health zones may reflect the role of both health system organization and physician behaviour, and how they likely interact. For example, the 72 percent of individuals residing in Health Zone 6 with a COPD diagnosis but no PFT, in comparison to the 14 percent in Zone 5, could be the result of physician tendencies, lack of PFT resources, or some combination of the two. As the CCDSS and NB-CHIP data sets do not provide clinical patient information (i.e., chart notes), confirmation of the actual reasons behind these variations is not within the scope of the current analysis.

A similar explanation could account for the variability in the proportion of non-PFT diagnosed CCDSS cases across health zones, and differing physician tendencies across zones may contribute to variability in the prevalence of over- and underdiagnosis. The increased prevalence of PFT usage in the absence of CCDSS case status observed in Zones 1, 5, and 7 ([Figure 17](#)) could reflect differences in physician tendencies (e.g., decreased stringency in selecting candidates for PFT evaluation, or increased preference for PFT usage for reasons unrelated to COPD), differences in disease burden (e.g., increased prevalence of asthma or other non-COPD conditions requiring PFT evaluation), or both.

The potential for differences in physician behaviour affecting PFT usage is supported by the literature. For example, research indicates that physician characteristics such as age⁽¹⁸⁾ and beliefs regarding the necessity of PFTs⁽³¹⁾ may influence the rate at which physicians refer patients to PFT labs for testing.

The impact of differing PFT resources between health zones may be evident when considering our results for Health Zone 1. Zone 1 has two hospital-based lab facilities (compared to only one in other zones) and has among the lowest (though not the absolute lowest) rates of diagnosis without PFT (56% in Zone 1 versus 50% in Zone 5). However, it is acknowledged that the notion of 'PFT resources' is more complex than just the number of facilities available, that consideration must be given to testing capacity per capita, and that other factors beyond resource availability also likely impact inter-zone differences.

Area-Level Income

Three outcomes of interest – CCDSS case status without a PFT (29% to 39%), underdiagnosis (52% to 58%), and non-PFT diagnosed CCDSS cases (71% to 74%) – increase in prevalence as area level income decreases. Conversely, overdiagnosis does not vary by area-level income, remaining consistent at 85 percent across all income quintiles.

PFT-diagnosed CCDSS cases are likely to be associated with multiple health care encounters (i.e., at least one encounter to meet CCDSS diagnosis criteria, and likely a separate encounter for administration of PFT), while diagnosis without a PFT or underdiagnosis are in theory possible with a single encounter (i.e., a diagnostic encounter only, or a PFT encounter without an accompanying diagnostic encounter). Previous research in Canada^(32, 33) has demonstrated that lower-income individuals are less likely to have contact with general practitioners. Therefore, our observation that diagnosis without a PFT and underdiagnosis are more common among lower-income individuals may reflect the decreased likelihood of health care encounters with primary care physicians among this population. Of note, reduced access to

primary care providers may result in increased frequency of emergency department (ED) visits among lower-income individuals. Our observations may nevertheless be consistent with this scenario as well, as reliance on the ED may be associated with reduced continuity of care, decreasing the likelihood of alignment between testing and follow-up that is required for a PFT-supported COPD diagnosis.

Previous research has also found that underdiagnosis of COPD is more likely among individuals with lower education,⁽³⁴⁾ suggesting an association between underdiagnosis and lower socioeconomic status. This association may be reflected in our observation of increased prevalence of underdiagnosis among lower-income individuals.

The lack of variability in the prevalence of overdiagnosis we observed across income quintiles is consistent with previous research which found that overdiagnosis was not associated with socioeconomic status.⁽¹⁷⁾ Validation of our findings (regarding overdiagnosis and other dimensions of coincidence/concordance) using other measures of socioeconomic status besides income quintile is a topic of interest for future study.

BMI (Body Mass Index)

All four of the analyses demonstrate differing degrees of variation when disaggregating by BMI categories.

CCDSS and PFT coincidence decreased as BMI increased (underweight: 36%; obese: 28%). A strong trend of increased overdiagnosis with increased BMI was observed, with the underweight category having the lowest proportion (65%) and the overweight category the greatest proportion (91%) of overdiagnosed records. Underdiagnosis represents another instance of an observable trend in the variation, with the proportion of underdiagnosed records generally decreasing as BMI increased. Finally, the proportion of non-PFT diagnosed CCDSS cases showed little variation, ranging from 13 percent among individuals of normal weight to 15 percent among overweight or obese individuals.

The relationship between BMI and the CCDSS and PFT coincidence and concordance groups may be explained by the relationship between COPD and higher BMI. Overweight and obese BMI classifications are commonly comorbid with COPD^(35, 36) and often interplay with COPD in ways that are difficult to untangle at the clinical level. For example, shortness of breath – one of the primary respiratory complaints associated with COPD – is also strongly associated with obesity, and increasing levels of BMI can lead to decreases in respiratory capacity like those observed in COPD.⁽³⁷⁾

Given that certain signs and symptoms^(37, 38) are common across both COPD and high levels of BMI, misdiagnosis has been suggested to occur among select subpopulations.⁽³⁸⁾ The competing and comorbid presentation of COPD and obesity diagnoses may help explain the trends observed in the analyses presented here.

The decrease in CCDSS and PFT coincidence as BMI increases could be explained by the diagnostic process ruling out differential diagnoses. As noted above, increases in BMI can lead

to symptoms that are also indicative of COPD. These symptoms could prompt PFT testing in higher BMI individuals that ultimately do not end up with a COPD diagnosis, potentially resulting in an elevated proportion of high BMI individuals classified as "No CCDSS, PFT." Conversely, at lower BMI levels, the symptoms that prompt PFT testing may be more likely to result from COPD, resulting in higher coincidence ("CCDSS, PFT") among lower BMI individuals.

The observed trends in the underdiagnosis and overdiagnosis analyses when disaggregating by BMI may be explained similarly to those seen in the age disaggregation. Specifically, for underdiagnosis, these records could represent instances in which the care provider was exploring various explanations for respiratory complaints but ultimately decided that high BMI itself was the best explanation for the patient's respiratory complaints despite a positive PFT result. This type of scenario would result in a record in our data with a positive PFT result but no physician diagnosis of COPD.

This scenario could account for the higher observed prevalence of underdiagnosis among overweight and obese individuals compared to normal weight individuals, although it does not explain why underdiagnosis is also more common among underweight compared to normal weight individuals.

The higher proportion of overdiagnosed cases among higher BMIs may be similarly attributable to the complex relationship between COPD and high BMI described above, in which a physician may be more likely to label someone with high BMI as having COPD in spite of a negative PFT because of the symptoms and signs shared between the two health conditions. In these instances, a negative PFT value not indicative of COPD is not incorporated into the diagnostic process of care providers who are exploring COPD as the cause of patient respiratory complaints.

Further, the relationship between BMI and relevant PFT values is complicated. Previous research⁽³⁹⁾ has demonstrated that obesity can affect pre-bronchodilator PFT values in a way that masks the presence of PFT results indicative of COPD, so it is possible that our observations reflect this obesity-masking effect (although this study did not explore how post-bronchodilator PFT values are affected by obesity). Again, the validity of these clinical decisions cannot be explored with these analyses.

Frailty

All four analyses demonstrated variation when disaggregated by hospital frailty risk scores.

CCDSS cases with no confirmatory PFT were highest in the intermediate-frailty risk category (61%), followed by the high-frailty (43%) and low-frailty (39%) risk categories. The proportion of overdiagnosed records was also highest in the intermediate-frailty risk group (93%), followed by similar proportions in the low-frailty (88%) and high-frailty (87%) risk groups.

The intermediate-frailty risk group also had the highest proportion of underdiagnosed records (81%), followed by the low-frailty (76%) and high-frailty (67%) risk groups. Finally, the proportion of

non-PFT diagnosed CCDSS cases was also highest among the intermediate-frailty risk group (90%), with the high-frailty (79%) and low-frailty (78%) risk groups having similar proportions.

As discussed above, the effort-dependent nature of spirometry may explain in part the variation observed when results were disaggregated by age, and the complex and comorbid relationship between COPD and high BMI may help to explain the observed results when disaggregating by BMI. These two explanations may also be applicable to the observed results when disaggregating the analyses by frailty.

As in the age analyses described above, frail patients may be physically unable to meet the effort-dependent requirements of a PFT. Increased levels of physical or cognitive impairment and decreased executive function in frail patients may lead to poor quality PFT measurements or inability to perform PFTs altogether.⁽²⁸⁾ Moreover, care providers may elect not to attempt PFT measurements in patients expected to be unable to complete the test. These factors may lead to increased proportions of non-PFT diagnosed CCDSS cases among frail patients.

In addition to the effects of the effort-dependent nature of PFTs, the comorbidity and similar presentation of COPD and frailty could help explain some of the observed results. Similar to higher levels of BMI, frailty has been associated with both self-reported respiratory symptoms⁽⁴⁰⁾ and PFT-measured respiratory impairments.⁽⁴¹⁾ As such, the potential for diagnosing COPD in lieu of frailty (or vice versa) exists, and depending on care provider decision making, this could help explain results observed in the overdiagnosis and underdiagnosis analyses.

These explanations would suggest a correlative increase in the prevalence of non-PFT diagnosis and over/underdiagnosis with increasing frailty; however, we observed that these situations were actually most prevalent in the intermediate-frailty risk group. This finding suggests that other factors may be influencing the relationship between frailty and PFT completion and results.

For example, individuals in the high-frailty risk group may have a higher frequency of interactions with the health system than intermediate-risk individuals, which may ultimately increase their likelihood of receiving a PFT (thereby contributing to the elevated prevalence of non-PFT diagnosis in the intermediate-frailty risk group compared to the high-frailty risk group).

Another possibility is that care provider behaviour may be modified by the degree of patient frailty. For example, providers may be more likely to adhere to guideline recommendations when ordering and interpreting PFTs for their highly frail patients, which could decrease the prevalence of non-PFT diagnosis and over/underdiagnosis in the high-frailty risk group compared to the intermediate-frailty risk group.

Severity of Airflow Limitation

Since severity of airflow limitation is derived from positive PFTs, the only analysis available is underdiagnosis. The proportion of underdiagnosed records increases as severity of airflow limitation increases, ranging from 42 percent of mild cases to 68 percent of very severe cases.

The differences observed in the severity of airflow limitation are counterintuitive. We would expect individuals with the highest degree of airflow limitation to be more likely to have a physician diagnosis and be flagged as such by the CCDSS algorithm. Indeed, Lamprecht et al.⁽³⁴⁾ found that underdiagnosis is most strongly associated with mild airflow limitation, in contrast to our findings. It should be noted, however, that this study differed from ours in potentially significant ways. For example, COPD diagnosis information was derived from survey data, and the analysis employed a multivariate model that controlled for several covariates. It is possible that such methodological differences may account, at least in part, for the disparity between our findings and those of Lamprecht et al.⁽³⁴⁾ Further work will be required to better understand the influence of severity of airflow limitation on underdiagnosis in our sample.

Limitations

This study has several limitations arising from a variety of sources including time effects, data sources, and variable operationalizations.

Time Effects

Several potential biases may result from left and right censoring of PFTs or diagnoses that occur outside of the accrual period.

PFT left censoring would occur if an individual was identified as a CCDSS case after the accrual period start date (January 1, 2007) but had PFTs only prior to the start of the study period. Similarly, PFT right censoring would occur if an individual was identified as a CCDSS case prior to the end of the study accrual period (December 31, 2017) but only had PFTs after December 31, 2017. Like above, CCDSS left censoring would occur if an individual had a PFT during the study period but was an incident CCDSS case prior to January 1, 2007.

Conversely, CCDSS right censoring would occur if an individual had a PFT during the study period but was only flagged as a CCDSS case after December 31, 2017. These censoring issues could bias the coincidence and non-PFT diagnosis analyses by inflating the number of CCDSS cases without a PFT, and they could affect the overdiagnosis and underdiagnosis analyses by decreasing the number of records available to be included in their respective subsamples (in the case of PFT censoring).

Moreover, CCDSS censoring may bias analyses towards overestimation of underdiagnosis (e.g., a positive PFT result has its corresponding CCDSS diagnosis censored and is therefore erroneously counted as underdiagnosis) and underestimation of overdiagnosis (e.g., a negative PFT result has its corresponding CCDSS diagnosis censored and therefore fails to be rightfully counted as overdiagnosis).

A second issue associated with censoring is related to the potential for variability in PFT results with repeat testing. Research has shown that relying on a single PFT result – which we do here in our definitions of coincidence and concordance groups – can be prone to error, as serial testing

often shows variability in PFT results ("diagnostic instability").⁽⁴²⁾ This instability, combined with censoring, may lead to misclassification in coincidence/concordance groups. For example, an individual identified as PFT- during the accrual period may have conflicting (i.e., positive) PFT results outside of the accrual period due to diagnostic instability. Assuming their clinical status did not actually change between test dates, this scenario could result in misclassification of coincidence/concordance due to the individual being erroneously identified as PFT-.

The possibility of diagnostic instability highlights another potential source of bias which may occur regardless of censoring. In our definitions of coincidence/concordance groups, a single positive PFT result was taken as sufficient evidence that an individual met spirometric criteria for COPD, even when the same individual may have had several negative PFT results before or after the positive result. This approach does not account for the possibility of diagnostic instability, and therefore has the potential to result in misclassification.

Accounting for diagnostic instability using administrative data is challenging, particularly since it cannot conclusively be distinguished from actual changes in clinical status. One potential approach to be explored in future studies would be to exclude PFT results which are close to the diagnostic threshold, since these are most likely to be subject to diagnostic instability.⁽⁴²⁾

Use of Administrative Data for Research Purposes

The administrative data (NB-CHIP and CCDSS COPD) used in this analysis were not generated or structured for the purpose of conducting research. Their use for this application therefore introduces limitations which must be acknowledged.

Since administrative data were not originally intended for research purposes, important elements of a patient's interaction with the clinician are missing from the administrative data record. For example, NB-CHIP contains the values of successful PFT measurements applied by care providers but does not record attempts resulting in unsuccessful PFTs. Such instances might arise, for example, where it was not practical to conduct a successful PFT. Such instances would be classified as "no PFT administered" in our analyses.

A further limitation of NB-CHIP is that it only captures PFTs conducted in one of NB's designated clinics and does not include PFTs administered in a physician's office or other setting. As such, any PFT conducted in a setting outside of the clinics included in NB-CHIP could inform a physician diagnosis that may be identified as a COPD case in CCDSS data but would be absent from NB-CHIP. Our analyses would incorrectly classify any such record as non-PFT diagnosed, even though the diagnosis was in fact supported by a PFT.

There are also limitations associated with the use of CCDSS data. While health administrative database COPD algorithms, including the CCDSS, have been validated in other Canadian jurisdictions,^(14, 43) their validity has not been tested in New Brunswick. This is significant because New Brunswick's CCDSS algorithm is fundamentally different from the one used in other provinces. While other provinces employ International Classification of Diseases (ICD) codes in physician billing records to define diagnoses, NB cannot do so because NB physician billing

records do not use ICD codes to record diagnoses. Rather, the NB CCDSS algorithm relies on free text analysis of physician billing records. This approach may be at risk of inconsistency and inaccuracy as it infers diagnosis based on COPD-related keywords found in physician notes, without the context to confirm that these keywords necessarily represent an actual clinical diagnosis. It should be noted, however, that the NB COPD prevalence and incidence estimates presented on PHAC's CCDSS data tool do not differ drastically from ICD-based estimates from other provinces⁽²⁹⁾ - so it is possible that any accuracy issues unique to the NB CCDSS algorithm do not significantly impact estimates of disease burden.⁽⁴³⁾

Another potential limitation associated with CCDSS, not unique to NB, relates to CCDSS case definition criteria. The current CCDSS case definition for COPD requires only a single physician encounter or acute care separation reflecting a COPD diagnosis. This definition may be prone to misclassification due to, for example, uncertain or changing diagnoses, or errors in data entry. Inadvertent application of a COPD diagnosis to individuals who do not actually have the disease would increase the apparent prevalence of overdiagnosis and diagnosis without a PFT. A more stringent definition requiring, for example, two encounters may reduce the likelihood of such misclassification. This alternate approach may be explored in future work.

Variable Operationalizations

The instability of PFT results⁽²¹⁾ can also add bias via how we defined PFT+ cases. Our analysis defined anyone who ever had a single positive PFT as COPD positive. However, it is possible that subsequent PFTs over the course of the study period were PFT- and that the individual did not meet the clinical criteria for COPD. Depending on the presence of a corresponding CCDSS COPD case identification record, this limitation could bias estimates of either over- or underdiagnosis.⁽²¹⁾

Another limitation relates to our use of GOLD⁽¹⁾ criteria for the classification of PFT results (where a post-bronchodilator FEV1/FVC ratio of $< .7$ is indicative of COPD). Although this fixed ratio (FR) cut-off is a recommended and widely used approach, it is thought to be less accurate among certain populations (for example, it may result in increased frequency of COPD diagnosis among older patients and decreased frequency among younger patients) when compared to a different approach defining a cut-off based on the lower limit of normal (LLN) FEV1/FVC values. Both the FR and LLN methods have merits and limitations, and one method has not been clearly recognized as superior.

As noted in two systematic reviews,^(21, 44) the choice of cut-off for defining COPD can affect estimates of overdiagnosis and underdiagnosis. Therefore, it must be acknowledged that our exclusive use of the FR approach carries with it the limitations inherent to this approach and neglects to explore the variability of results that may be obtained using different criteria such as the LLN approach.

Conclusion

COPD is a highly treatable and preventable chronic condition that significantly impacts the quality of life, morbidity, and mortality of New Brunswickers. Understanding the population burden of COPD is crucial in ensuring New Brunswick's healthcare system meets the needs of New Brunswickers living with COPD. Estimating the true population burden of COPD is difficult, and it is limited by the complex nature of COPD diagnosis and existing epidemiological tools.

Utilizing a combination of several data sources available in New Brunswick, we have identified that a large proportion of individuals diagnosed with COPD have not had a PFT, and among individuals who have had a PFT there are pronounced instances of both overdiagnosis and underdiagnosis. Future work should rely on multiple linked sources of data for more reliable COPD case identification and prevalence estimates in New Brunswick.

References

1. Global Initiative for Chronic Obstructive Lung Disease, Inc. Global strategy for the diagnosis, management, and prevention of Chronic Obstructive Pulmonary Disease. 2020 [cited 2022 Dec 14]. Available from: https://goldcopd.org/wp-content/uploads/2019/12/GOLD-2020-FINAL-ver1.2-03Dec19_WMV.pdf
2. Mayo Clinic. COPD. [cited 2022 Dec 14]. Available from: <https://www.mayoclinic.org/diseases-conditions/copd/symptoms-causes/syc-20353679>
3. Benady S. The human and economic burden of COPD: a leading cause of hospital admission in Canada. Ottawa: Canadian Thoracic Society; 2010.
4. Chapman KR, Kaplan A, COPD Canada, Family Physician Airways Group of Canada. Breaking the surface - breaking the silence: how the under-reporting of "Lung Attacks" in Canada impacts patient outcomes in COPD. COPD Canada; 2012 [cited 2022 Dec 14]. Available from: <http://copdcanada.info/resources/Breaking+the+Surface+-+Breaking+the+Silence+2012.pdf>
5. Statistics Canada. Table 13-10-0394-01 leading causes of death, total population, by age group [Data table]. 2022 [cited 2022 Dec 14]. Available from: <https://doi.org/10.25318/1310039401-eng>
6. Canadian Institute for Health Information. Inpatient hospitalizations, surgeries, newborns and childbirth indicators, 2015-2016. 2017 [cited 2022 Dec 14]. Available from: <https://secure.cihi.ca/estore/productFamily.htm?pf=PFC3424&lang=en&media=0>
7. Canadian Institute for Health Information. Inpatient hospitalizations, surgeries, newborns and childbirth indicators, 2016-2017. 2018 [cited 2022 Dec 14]. Available from: <https://secure.cihi.ca/estore/productFamily.htm?pf=PFC3714&lang=en&media=0>
8. Canadian Institute for Health Information. Inpatient hospitalizations, surgery, newborn, alternate level of care and childbirth statistics, 2017-2018. 2019 [cited 2022 Dec 14]. Available from: <https://secure.cihi.ca/estore/productFamily.htm?pf=PFC3954&lang=en&media=0>
9. Canadian Institute for Health Information. Inpatient hospitalization, surgery and newborn statistics, 2018-2019 [XLS file]. 2020 [cited 2022 Dec 14]. Available from: <https://secure.cihi.ca/estore/productFamily.htm?pf=PFC4179&lang=en&media=0>
10. Canadian Institute for Health Information. Inpatient hospitalization, surgery and newborn statistics, 2019-2020. 2021 [cited 2022 Dec 14]. Available from: <https://secure.cihi.ca/estore/productFamily.htm?pf=PFC4562&lang=en&media=0>
11. McDonald T, Rogers K, Daigle B, Ziv A. NB-IRDT Chronic Obstructive Pulmonary Disease research program – report one: investigation of Statistics Canada Public Use Microdata Files. Fredericton, NB: New Brunswick Institute for Research, Data and Training; 2020 [cited 2022 Dec 14]. Available from: <https://www.unb.ca/nbirdt/research/publications/nb-irdt-chronic-obstructive-pulmonary-disease-research-program-report-one.html>
12. Statistics Canada. Table 13-10-0096-01 health characteristics, annual estimates [Data table]. 2022 [cited 2022 Dec 14]. Available from: <https://doi.org/10.25318/1310009601-eng>

13. New Brunswick Department of Health. Profiles on health: chronic obstructive pulmonary disease (COPD) in New Brunswick. Government of New Brunswick; 2016 [cited 2022 Dec 14]. Available from: <https://www2.gnb.ca/content/dam/gnb/Departments/h-s/pdf/en/Publications/Profiles/ProfilesHealthCOPD.pdf>
14. Public Health Agency of Canada. Report from the Canadian Chronic Disease Surveillance System: asthma and chronic obstructive pulmonary disease (COPD) in Canada, 2018. 2018 [cited 2022 Dec 14]. Available from: <https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/diseases-conditions/asthma-chronic-obstructive-pulmonary-disease-canada-2018/pub-eng.pdf>
15. Diab N, Gershon AS, Sin DD, Tan WC, Bourbeau J, Boulet L-P, et al. Underdiagnosis and overdiagnosis of Chronic Obstructive Pulmonary Disease. *Am J Respir Crit Care Med*. 2018 [cited 2022 Dec 14];198(9):1130-9. Available from: <https://doi.org/10.1164/rccm.201804-0621CI>
16. 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 [cited 2022 Dec 14];25(3):3-11. Available from: <https://www150.statcan.gc.ca/n1/en/pub/82-003-x/2014003/article/11908-eng.pdf?st=sknYYvE5>
17. Gershon AS, Hwee J, Chapman KR, Aaron SD, O'Donnell DE, Stanbrook MB, et al. Factors associated with undiagnosed and overdiagnosed COPD. *Eur Respir J*. 2016 [cited 2022 Dec 14];48(2):561-4. Available from: <https://doi.org/10.1183/13993003.00458-2016>
18. Gershon AS, Thiruchelvam D, Chapman KR, Aaron SD, Stanbrook MB, Bourbeau J, et al. Health services burden of undiagnosed and overdiagnosed COPD. *Chest*. 2018 [cited 2022 Dec 14];153(6):1336-46. Available from: <https://doi.org/10.1016/j.chest.2018.01.038>
19. Labonté LE, Tan WC, Li PZ, Mancino P, Aaron SD, Benedetti A, et al. Undiagnosed Chronic Obstructive Pulmonary Disease contributes to the burden of health care use: data from the CanCOLD Study. *Am J Respir Crit Care Med*. 2016 [cited 2022 Dec 14];194(3):285-98. Available from: <https://doi.org/10.1164/rccm.201509-1795OC>
20. Gershon AS, Hwee J, Croxford R, Aaron SD, To T. Patient and physician factors associated with pulmonary function testing for COPD: a population study. *Chest*. 2014 [cited 2022 Dec 14];145(2):272-81. Available from: <https://doi.org/10.1378/chest.13-0790>
21. Ho T, Cusack RP, Satia I, Kurmi OP. Under- and over-diagnosis of COPD: a global perspective. *Breathe*. 2019 [cited 2022 Dec 14];15(1):24-35. Available from: <https://doi.org/10.1183/20734735.0346-2018>
22. Lamprecht B, Mahringer A, Soriano JB, Kaiser B, Buist AS, Studnicka M. Is spirometry properly used to diagnose COPD? Results from the BOLD study in Salzburg, Austria: a population-based analytical study. *Prim Care Respir J*. 2013 [cited 2022 Dec 14];22(2):195-200. Available from: <https://doi.org/10.4104/pcrj.2013.00032>
23. Thomas ET, Glasziou P, Dobler CC. Use of the terms "overdiagnosis" and "misdiagnosis" in the COPD literature: a rapid review. *Breathe*. 2019 [cited 2022 Dec 14];15(1):e3-9. Available from: <https://doi.org/10.1183/20734735.0354-2018>

24. Gershon A, Mecredy G, Croxford R, To T, Stanbrook MB, Aaron SD. Outcomes of patients with chronic obstructive pulmonary disease diagnosed with or without pulmonary function testing. *CMAJ*. 2017 [cited 2022 Dec 14];189(14):e530-8. Available from: <https://doi.org/10.1503/cmaj.151420>
25. Spyrtos D, Chloros D, Michalopoulou D, Sichletidis L. Estimating the extent and economic impact of under and overdiagnosis of chronic obstructive pulmonary disease in primary care. *Chron Respir Dis*. 2016 [cited 2022 Dec 14];13(3):240-6. Available from: <https://doi.org/10.1177/1479972316636989>
26. Health Canada. Body Mass Index (BMI) Nomogram. 2003. Available from: <https://www.canada.ca/en/health-canada/services/food-nutrition/healthy-eating/healthy-weights/canadian-guidelines-body-weight-classification-adults/body-mass-index-nomogram.html>
27. Gilbert T, Neuburger J, Kraindler J, Keeble E, Smith P, Ariti C, et al. Development and validation of a Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: an observational study. *Lancet*. 2018 [cited 2022 Dec 14];391(10132):1775-82. Available from: [https://doi.org/10.1016/S0140-6736\(18\)30668-8](https://doi.org/10.1016/S0140-6736(18)30668-8)
28. Allen SC, Yeung P. Inability to draw intersecting pentagons as a predictor of unsatisfactory spirometry technique in elderly hospital inpatients. *Age Ageing*. 2006 [cited 2022 Dec 14];35(3):304-6. Available from: <https://doi.org/10.1093/ageing/afj090>
29. Statistics Canada. Care receivers in Canada, 2018. 2020 [cited 2022 Dec 14]. Available from: <https://www150.statcan.gc.ca/n1/daily-quotidien/200122/dq200122e-eng.htm>
30. Thompson AE, Anisimowicz Y, Miedema B, Hogg W, Wodchis WP, Aubrey-Bassler K. The influence of gender and other patient characteristics on health care-seeking behaviour: a QUALICOPC study. *BMC Fam Pract*. 2016 [cited 2022 Dec 14];17:38. Available from: <https://doi.org/10.1186/s12875-016-0440-0>
31. Joo MN, Sharp LK, Au DH, Lee TA, Fitzgibbon ML. Use of spirometry in the diagnosis of COPD: a qualitative study in primary care. *COPD: J Chron Obstruct Pulmon Dis*. 2013 [cited 2022 Dec 14];10(4):444-9. Available from: <https://doi.org/10.3109/15412555.2013.766683>
32. Allin S. Does equity in healthcare use vary across Canadian provinces? *Healthc Policy*. 2008 [cited 2022 Dec 14];3(4):83-99. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2645154/pdf/policy-03-083.pdf>
33. Asada Y, Kephart G. Equity in health services use and intensity of use in Canada. *BMC Health Serv Res*. 2007 [cited 2022 Dec 14];7(41):1-12. Available from: <https://doi.org/10.1186/1472-6963-7-41>
34. Lamprecht B, Soriano JB, Studnicka M, Kaiser B, Vanfleteren LE, Gnatiuc L, et al. Determinants of underdiagnosis of COPD in national and international surveys. *Chest*. 2015 [cited 2022 Dec 14];148(4):971-85. Available from: <https://doi.org/10.1378/chest.14-2535>
35. Franssen FME, O'Donnell DE, Goossens GH, Blaak EE, Schols AMWJ. Obesity and the lung: 5. obesity and COPD. *Thorax*. 2008 [cited 2022 Dec 14];63(12):1110-7. Available from: <https://doi.org/10.1136/thx.2007.086827>

36. Liu Y, Pleasants RA, Croft JB, Lugogo N, Ohar J, Heidari K, et al. Body mass index, respiratory conditions, asthma, and chronic obstructive pulmonary disease. *Respir Med*. 2015 [cited 2022 Dec 14];109(7):851-9. Available from: <https://doi.org/10.1016/j.rmed.2015.05.006>
37. Poulain M, Doucet M, Major GC, Drapeau V, Sériès F, Boulet L-P, et al. The effect of obesity on chronic respiratory diseases: pathophysiology and therapeutic strategies. *CMAJ*. 2006 [cited 2022 Dec 14];174(9):1293-9. Available from: <https://doi.org/10.1503/cmaj.051299>.
38. Petrie K, Toelle BG, Wood-Baker R, Maguire GP, James AL, Hunter M, et al. Undiagnosed and misdiagnosed chronic obstructive pulmonary disease: data from the BOLD Australia Study. *Int J Chron Obstruct Pulmon Dis*. 2021 [cited 2022 Dec 14];16:467-75. Available from: <https://doi.org/10.2147/COPD.S287172>
39. Çolak Y, Marott JL, Vestbo J, Lange P. Overweight and obesity may lead to under-diagnosis of airflow limitation: findings from the Copenhagen City Heart Study. *COPD: J Chron Obstruct Pulmon Dis*. 2015 [cited 2022 Dec 14];12(1):5-13. Available from: <https://doi.org/10.3109/15412555.2014.933955>
40. Verschoor CP, Dales RE, Duong M, Bourque C, Mian O, Ma J, et al. Respiratory symptoms are associated with frailty in older adults with normal spirometry, independent of smoking, in the Canadian Longitudinal Study of Aging. *Respir Care*. 2021 [cited 2022 Dec 14];66(12):1848-57. Available from: <https://doi.org/10.4187/respcare.09225>
41. Vaz Fragoso CA, Enright PL, Van Ness PH, Gill TM. Frailty and respiratory impairment in older persons. *Am J Med*. 2012 [cited 2022 Dec 14];125(1):79-86. Available from: <https://doi.org/10.1016/j.amjmed.2011.06.024>
42. Aaron SD, Tan WC, Bourbeau J, Sin DD, Loves RH, MacNeil J, et al. Diagnostic instability and reversals of Chronic Obstructive Pulmonary Disease diagnosis in individuals with mild to moderate airflow obstruction. *Am J Respir Crit Care Med*. 2017 [cited 2023 Apr 4];196(3):306-14. Available from: <https://doi.org/10.1164/rccm.201612-2531OC>
43. Gershon AS, Wang C, Guan J, Vasilevska-Ristovska J, Cicutto L, To T. Identifying individuals with physician diagnosed COPD in health administrative databases. *COPD*. 2009 [cited 2022 Dec 14];6(5):388-94. Available from: <https://doi.org/10.1080/15412550903140865>
44. Hangaard S, Helle T, Nielsen C, Hejlesen OK. Causes of misdiagnosis of chronic obstructive pulmonary disease: a systematic scoping review. *Respir Med*. 2017 [cited 2022 Dec 14];129:63-84. Available from: <https://doi.org/10.1016/j.rmed.2017.05.015>