Title: Identifying Heart Failure in patients with Chronic Obstructive Lung Disease through the Canadian Primary Care Sentinel Surveillance Network in British Columbia: A Case Validation Study

Study Type: Case Validation Study (Diagnostic Accuracy)

Rohit Vijh BSc MD[1,2], Sabrina T. Wong, RN, PhD[4,5] , Matthew Grandy BSc, MD[6,7], Sandra Peterson MSc[4], Allison M. Ezzat PT, PhD[4,5], Andrew Gibb PhD[4], Nathaniel M Hawkins MD MPH[3]

1. School of Population and Public Health, University of British Columbia
2. Public Health and Preventative Medicine Residency, Postgraduate Medical Education, University of British Columbia
3. Division of Cardiology, University of British Columbia, Vancouver, Canada
4. Centre for Health Services and Policy Research, University of British Columbia
5. School of Nursing, University of British Columbia
6. Primary Care Research Unit, Dalhousie Department of Family Medicine, Halifax, Nova Scotia
7. Family Medicine, Dalhousie University, Halifax, Nova Scotia

Correspondence to:
Sabrina T. Wong, RN, PhD. Professor and Co-Chair
University of British Columbia Centre for Health Services and Policy Research and School of Nursing; Canadian Primary Care Sentinel Surveillance Network
2211 Wesbrook Mall, Vancouver, BC V6T-2B5
Sabrina.wong@ubc.ca

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Abstract

Background: Heart failure (HF) poses a significant global health burden. Appropriate surveillance is critical to ensure health promotion and healthcare programming is effectively targeting populations. Case definitions for HF have predominantly centered around hospitalizations and physician billings data. The Canadian Primary Care Surveillance Sentinel Network (CPCSSN) offers the ability to identify HF from primary care electronic medical records. We validated a case definition for HF among a retrospective cohort of patients with Chronic Obstructive Pulmonary Disease (COPD) in British Columbia.

Methods: HF case definitions were developed by combining diagnostic codes, medication and laboratory values from primary care electronic medical records. These were compared to HF diagnoses identified through detailed chart review as the gold standard. Sensitivity, specificity, negative (NPV) and positive predictive values (PPV) were calculated for each definition.

Results: Charts of 311 patients with COPD were reviewed, of whom 72 (23.2%) had HF. Five categories of definitions were constructed, all of which had excellent sensitivity, specificity and NPV. PPV performed moderately well. The optimal case definition consisted of 1 HF billing code or a specific combination of medications for HF. This definition had an excellent specificity (93.3% [95% CI: 89.4-96.1]), sensitivity (90.2% [95% CI: 80.9-96.0), PPV (80.3% [95% CI: 69.9-88.3]) and NPV (96.9% [95% CI: 93.8-98.8]).

Interpretation: A case definition for HF was validated and can be utilized in CPCSSN to accurately identify HF in patients with COPD in primary care.

Background

Heart Failure (HF) is a global public health problem affecting 40 million individuals worldwide (1) with healthcare costs exceeding $100 billion (2). Chronic Obstructive Pulmonary Disease (COPD) is highly prevalent in individuals with HF (20-30% of HF patients have COPD)(3). To facilitate high quality management of HF in COPD, an accurate case definition is necessary. Despite many patients with HF being largely managed in primary care without specialist contact,(4) studies examining the accuracy of HF diagnosis and coding have been predominantly hospital based(5)(6)(7). A systematic review of validated case definitions for HF found that hospital discharge data were used in 25 out of 35 studies, with all studies utilizing exclusively ICD9/10 codes(8). Additionally, physician billing services provides only limited data resulting in variable accuracy parameters (sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV).)(8)(9). In Canada, HF failure is often identified through discharge abstract databases or physician billing data(10)(11). A significant gap exists in accurately understanding the prevalence and burden of HF across the entire health care system.

Identifying HF cases from primary care would be beneficial for several reasons. First, electronic medical records (EMR) provide prospective and systematic collection of clinically verified data regarding individual patient management. Second, the availability of additional clinical variables such as medication history and lab data have the potential to improve case validity. Lastly, EMRs will characterize community patients with HF that would not otherwise be captured from hospital sources. Only a handful of studies have evaluated a HF case definition utilizing primary care databases and comparing against a gold standard (ie. chart review) in an unselected generalizable population(11)(12)(13). Of these studies, two originated in the United States, while the remaining study compared administrative and billing data to primary care records in Ontario(12). No studies have examined a case definition of HF in a COPD population.

The objective of this study was to validate an EMR-based definition of HF in primary care in British Columbia (BC), Canada. Establishing a rigorous definition for HF will allow future epidemiological studies to examine HF across Canada. An accurate case definition will define the overall population burden of disease, characterize the contemporary medical management

in primary care, and create opportunities for quality improvement. The study was nested within a broader program of research examining HF in patients with COPD. These two conditions are common partners, each being associated with undertreatment and worse prognosis in the alternate condition(14).

Methods

Study Design. The study was a cross-sectional retrospective chart review of a cohort of patients from primary care practices in BC recruited through the BC Canadian Primary Care Sentinel Surveillance Network (CPCSSN).

CPCSSN data. Case definitions for multiple chronic diseases, including COPD, have been validated using the CPCSSN database (15). CPCSSN is a pan-Canadian 'network of networks' with over 1500 primary care providers, covering all provinces except Saskatchewan using 17 different EMR systems(16). Point-of-care de-identified data are extracted semi-annually and transformed to a standard CPCSSN schema. The architecture and approach has been previously described, including data flow, quality, mapping, cleaning and de-identification (Appendix 1)(16). As of December 2019, CPCSSN includes over 200 million records from almost 2 million patients. This project used BC CPCSSN data extracted on December 31, 2018 (2018-Q4). The data includes socio-demographics, providers, encounters, health conditions, risk factors, biometrics, laboratory results, procedures, medications and referral information(15).

Study Population. Fourteen BC-CPCSSN physicians working in three general practices were invited to contribute patients with COPD for chart review to identify HF. Assuming a prevalence for HF of 20% in patients with COPD, a sample size of 311 patients with COPD was estimated to achieve a precision of 10% around accuracy parameters. Nine of the fourteen physicians consented to participate in the study. We used the EMR data extracted for CPCSSN for each consenting physician. For each physician patient panel, a random sample of their COPD patients was generated by AG. Individuals were excluded if they did not meet the CPCSSN COPD case

definition (which excludes individuals <35 years), if they did not have a valid BC Personal Health Number or if their provider did not consent to participate in the study.

Sampling. AG generated the initial sample of all BC patients in CPCSSN (n=102,867 patients) from the 2018-Q4 period. From this cohort, we selected individuals with COPD (>35 years, based on validated CPCSSN definition) from the participating 3 clinics and 9 physicians (n=625). From this cohort, random selection and review of 311 patient charts from each clinic was carried out (by RV) from September-November 2019(17)(Figure 1).

Insert Figure 1 here

Chart Review and 'Gold standard'.

In British Columbia, "Gold" standard validation was conducted by a medical resident (RV) who verified presence or absence of HF for each patient by manually reviewing their entire EMR. A data abstraction tool was developed in Qualtrics (Qualtrics, Provo, UT) with input from a cardiologist and family physician, focused on variables required to establish a diagnosis of HF (Appendix 2). The chart review included clinic site visits to confirm further evidence of HF by reviewing unstructured data (e.g. echocardiogram reports, free text notes). The abstracted data was then reviewed by both the abstractor (RV) and cardiologist (NH), to determine classification of HF status. The presence of HF was defined by symptoms and/or signs of reduced cardiac output and/or pulmonary or systemic congestion, supported by objective evidence of structural and/or functional cardiac abnormality, including left ventricular systolic (defined by reduced left ventricular ejection fraction using any imaging modality), diastolic dysfunction (typically by echocardiography), elevated natriuretic peptides, or structural disease (such as severe valve disease)(18)(19).

Case Definition

An initial case definition was developed by the Maritime Family Practice Research Network (MaRNet-FP), based on ICD9/10 codes or prescribed combinations of medical therapies for HF (see Table 1 and Appendix 3). BC-CPCSSN examined this original definition, then proposed and tested amendments (Table 1). These modifications were developed for several reasons: based on additional data element locations within different EMR systems (e.g. billing versus encounter diagnoses), expanded ICD-9 codes (based on review of HF coding literature), addition of HF specific medications (e.g. sacubitril-valsartan, ivabradine), and laboratory data (BNP and pro-NT BNP)(Table 1). Two thresholds for natriuretic peptides were applied 1) the recommended low 'rule out' threshold (BNP > 50 or NT-proBNP > 125) and higher 'probable diagnosis' threshold (BNP (>400) or NT-proBNP (age<50 > 450; age 50-75 >900; age>75 >1800)) (18). We compared each of these case definitions in BC CPCSSN data against the HF cases identified by the gold standard chart review. Case definitions were plotted by their sensitivity and PPV.

Insert Table 1 here

Statistical Analysis

Sensitivity, specificity, PPV, and NPV were calculated. The data were organized into 2x2 tables comparing each case definition (case/no case) with the chart review diagnosis (case/no case). 95% confidence intervals were constructed for each validity parameter using the Clopper-Pearson approach for proportions. Measures above 80% were considered acceptable for epidemiological research(15). All data were analyzed in SAS version 9.4 (SAS Institute Inc., Cary, NC).

Sensitivity Analysis

A sensitivity test was performed due to an unanticipated consequence of the timing of chart reviews (September-November 2019) and dates of data available for developing and testing the HF definition (up until December 31, 2018). We hypothesized that some of the cases

categorized as false negatives may have been incident in 2019, and so the algorithms would be unable to detect a HF diagnosis using data to end-2018. As a sensitivity test we were able to examine BC CPCSSN data to June 30, 2019 (2019-Q2) for a subset of the false negatives, to determine if they would meet the HF definition criteria with the addition of more up-to-date information.

Ethics Approval

The scope of this project fell under CPCSSN ongoing quality improvement to improve the operationalization of the primary care network. Each clinician gave consent to access and use EMR data. BC-CPCSSN received ethics approval from UBC Research Ethics Board and this project is part of its ongoing quality improvement initiatives.

Results

Case Validation Results

Among 649 patients with COPD from the 3 primary care practices in BC, 311 (47.9%; 113 (36.3%) male and 198 (63.7%) female) were randomly selected for full chart abstraction. Seventy two (23.2%) were identified in file review as having HF. The mean (SD) age of cases was 83.6 (10.9) and non-cases was 70.0 (12.8) years. Thirty (41.7%) cases were male and 42 (58.3%) were female (Table 2).

Insert Table 2 here

Table 3 and Appendix 5 details accuracy parameters and counts for all tested case definitions in BC-CPCSSN, respectively. Overall there was high sensitivity (range 75%-93%; this excludes definition 2.4), specificity (range 87%-99.6%) and NPV (range 80.1%-98.1%). PPV had a greater variability, ranging from 68.4% to 92.9%. Addition of billing data (Definition 1.1 to 1.2) improved the sensitivity and NPV, but diminished the specificity and PPV. Modification of diagnoses codes and drugs included from Appendix 3 to Appendix 4, resulted in a mild decrease in performance (Definition 1.1 vs. 2.5), with a small reduction in specificity, sensitivity, PPV and

NPV. Further adjustment in Definition 3.2 built upon Definition 2.5 with the inclusion of furosemide and billings data, which resulted in comparable performance to Definition 1.1, with a much poorer PPV. Our preferred case definition with the optimal accuracy parameters was definition 1.1.

Insert Table 3 here

Definition 4 and 5 included BNP and pro-BNP lab data in the various definitions. Of the 311 patients, 20.9% (n=65) of patients had BNP or pro-BNP data, of which 50.8% were cases and 49.2% were non-cases from chart review. Including either low and high thresholds for BNP did not significantly alter or improve the accuracy of the case definition.

Definition 2.4 had excellent PPV but extremely low sensitivity. Most case-definitions had high sensitivity with varying PPV (Figure 2). Definition 1.1 and 5.1 represented case definitions with an excellent combination of sensitivity (90.3%, 91.7%) and PPV (80.2%, 79.5%).

Insert Figure 2 here

For the sensitivity test, data from January 1, 2019 – June 30, 2019 was examined for 10 patients who were false negatives for one or more of the case definitions. These 10 patients accounted for 94/110 (85%) of all the false negatives across all case definitions excluding Definition 2.4. With the additional data, two of these patients met the criteria for case definitions that they did not otherwise meet using data to December 31, 2018. This marginally increased the sensitivity, PPV and NPV marginally for all of the case definitions except Definitions 2.3 and 2.4 (Appendix 6).

Interpretation

Overall, the case definitions each performed well in the BC-CPCSSN database. There are several different options with excellent PPV as well as specificity that could be used to meet

surveillance objectives by various stakeholders. The majority of the case definitions met our criteria for acceptable validity parameters. However, definition 1.1 is our recommended case definition for HF within the CPCSSN database. Definition 5.1 performed well, but the abstraction of and reliance on a BNP may vary between provincial networks. BNPs may also not be collected from all patients with HF within the jurisdiction, creating a biased sample. Moreover, definition 1.1 is simpler and more consistent with other CPCSSN case definitions. Lastly, the change in parameters was minimal when adding natriuretic peptides.

Our findings are comparable to other studies looking at HF case definitions in EMR database/networks. In a US primary care EMR database, reported sensitivities for a HF case definition ranged from 41.3-78.7% and PPV from 68.5%- 86.5%(12). In comparison, our case definitions performed slightly better. In Ontario, the Electronic Medical Record Administrative data Linked Database (EMRALD) was utilized to validate HF case definitions. The optimal case definition included 1 hospital visit or physician billing visit and second physician billing visit within one year. This yielded a sensitivity 84.8%, specificity 97%, and PPV 55.7%. Our preferred case definition improves in terms of sensitivity and PPV, yet is slightly lower, but acceptable in terms of specificity. This highlights the utility of medication codes in CPCSSN compared to EMRALD(10). Lastly, the accuracy parameters of our HF definition are similar to other validated case definitions in CPCSSN(14).

There are several implications for future research. Our case definition provides a relatively accurate sample of patients with COPD and HF in the BC-CPCSSN. Subsequent analyses will provide insights into the contemporary management of these patients in primary care, and explore HF classification in terms of reduced versus preserved ejection fraction. This case definition will permit epidemiological estimates (i.e. prevalence) of HF in COPD across Canada. Our findings will support screening and treatment of cardiovascular risk and disease in patients with COPD in primary care. Lastly, this work will instigate the development of a Primary Care Clinician Advisory Group to guide further projects within BC-CPCSSN. This will enable a collaborative integrated knowledge translation strategy and help inform design of future epidemiological and intervention studies, as well as quality improvement initiatives.

There are several strengths to our study. First, we used an excellent gold standard reference in the form of chart review by two medical professionals utilizing a standardized chart abstraction form that minimized misclassification and instrument bias. Second, a variety of case definitions were tested with very minimal alterations to the accuracy parameters, providing evidence that a simple definition is most robust to accurately identify HF in COPD patients. Third, our case definitions utilized a variety of parameters beyond billing codes to include medication codes and lab data.

However, this work is not without limitations. The chart validation occurred in one province where clinicians may record data more similarly than those in another province. The case definition may perform differently in other provinces, given the heterogeneity of the primary care clinicians and EMR systems. Chart data abstraction was done across different EMR systems and there are differences in how EMRs record data (i.e. ICD9 codes recorded in the health condition and encounter tables vs. billing table). These data capture COPD patients from 3 clinics and may not be representative of all individuals with COPD and HF in BC. In addition, the 3 clinics (n=9 clinicians) may have different practices compared to other clinicians. Lastly, chart reviews were performed late 2019; data available for developing and testing the HF definition was to December 31, 2018. Thus, people with newly diagnosed HF in 2019 might be undetectable in the data available for algorithm development (i.e. the algorithms would not be able to see the relevant data from 2019). A sensitivity test was performed that found marginal improvement in validity parameters with the addition of a subset of 2019 data; however in future it would be preferential to have better correspondence between the dates of data available for analysis and the dates of the chart review.

Conclusion

Our study provides valid case definitions for HF in the pan-Canadian CPCSSN database. Several different case definitions were constructed and tested with excellent performance in the BC-CPCSSN database. The findings of this study will support ongoing research activities, chronic disease surveillance, and quality improvement initiatives in primary care for HF amongst people with COPD across Canada.

Data-Sharing Statement:

The data used in this study are available through the BC-CPCSSN. A data access request would need to be completed, along with an application. University-based researchers are eligible to apply for access to these data.

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Contributory Statement:

Authors contributed substantially to conception and design (SW, NH, MG), acquisition of data (AG, SP, RV), analysis (SP, RV) and interpretation of data (all authors). RV initially drafted the manuscript and all authors subsequently revised it critically for important intellectual content. All authors gave final approval of version to be published.

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Table 1. Case Definitions of Heart Failure used in BC CPCSSN

Definition	Classify as have Heart Failure if the following conditions are met:
1.1. Nova Scotia MAR-net definition)	• >= 1 ICD9 diagnostic codes in **Health Condition** table or **Encounter Diagnosis (Appendix 1) OR** • Combination of ATC Codes in Medication table (Appendix 1): (ACE Inhibitor or ARB) and Beta blocker and Diuretic
1.2 Identical to 1.1 but also searching billings	• >= 1 ICD9 diagnostic codes in **Health Condition** table or **Encounter Diagnosis** or **Billings (Appendix 1) OR** • Combination of ATC codes in Medication table (Appendix 1): (ACE Inhibitor or ARBs) and Beta blocker and Diuretic
2.1 ICD-9 AND ATC codes Also revised ICD-9 and ATC codes	• >=1 ICD-9 codes in Health Condition or Encounter Diagnosis or Billings (Appendix 2) **AND** • >=1 ATC code for *any* ACE Inhibitor or *any* ARB or Beta blocker or MRA or Hydralazine (Appendix 2 Medication table)
Definition 2.2 Subset of 2.1, diagnoses only	• >=1 ICD-9 codes in Health Condition or Encounter Diagnosis or Billings (Appendix 2)
Definition 2.3 Require two codes separated in time	• >=2 ICD-9 codes (Appendix 2) in Health Condition, Encounter Diagnosis and Billings combined, separated >=30 days
Definition 2.4 Specific HF therapies	• >=1 ATC code for Sacubitril-valsartan **OR** • Combination of ATC codes for (ACE Inhibitor or ARB) and Beta blocker and MRA (Appendix 2 Medication table)
Definition 2.5	Definition 2.1 OR Definition 2.3 OR Definition 2.4
Definition 3.1	Definition 2.1 with furosemide and without Billing file, as follows: ○ >=1 ICD-9 Codes in Health Condition or Encounter Diagnosis (Appendix 2) AND ○ >=1 ATC code for any ACE Inhibitor or any ARB or Beta blocker or MRA or Hydralazine **or furosemide**; as listed in Appendix 2 Medication table ○ OR • Definition 2.3 without Billing file: >=2 ICD-9 Codes(Appendix 2) in Health Condition or Encounter Diagnosis, separated >=30 days OR • Definition 2.4
Definition 3.2	• Definition 2.1 with furosemide, as follows: ○ >=1 ICD-9 Codes in Health Condition or Encounter Diagnosis **or Billings** AND

	○ >=1 ATC code for any ACE Inhibitor or any ARB or Beta blocker or MRA or Hydralazine **or furosemide**; as listed in Appendix 2 Medication table OR • Definition 2.3 OR • Definition 2.4
Definition 4.1 Low threshold BNP	• Definition 1.1 OR • BNP > 50 or NT-proBNP > 125
Definition 4.2	• Definition 1.2 OR • BNP > 50 or NT-proBNP > 125
Definition 4.3	• Definition 3.2 OR • BNP > 50 or NT-proBNP > 125
Definition 5.1 High threshold BNP	• Definition 1.1 OR • BNP (>400) or NT-proBNP(age<50 > 450; age 50-75 >900; age>75 >1800)
Definition 5.2	• Definition 1.2 OR • BNP (>400) or NT-proBNP(age<50 > 450; age 50-75 >900; age>75 >1800)
Definition 5.3	• Definition 3.2 OR • BNP (>400) or NT-proBNP(age<50 > 450; age 50-75 >900; age>75 >1800)

Table 2. Participant Characteristics

	Overall	Heart failure	No heart failure
N (%)	311	72 (23.2)	239 (76.8)
Female, n (%)	198 (63.7)	42 (58.3)	156 (65.3)
Age, mean (sd)	73.2 (13.6)	83.6 (10.9)	70.0 (12.8)
Age, n (%)			
35- <50	19 (6.1)	0 (0.0)	19 (7.9)
50 – 75	162 (52.1)	17 (23.6)	145 (60.7)
> 75	130 (41.8)	55 (76.4)	75 (31.4)
Clinic, n (%)			
A (Urban)	130 (41.8)	40 (30.8)	90 (69.2)
B (Rural)	117 (37.6)	24 (20.5)	93 (79.5)
C (Urban)	64 (20.6)	8 (12.5)	56 (87.5)
Other chronic conditions, n (%)			
Chronic Kidney Disease	28 (9.0)	12 (16.7)	16 (6.7)
Dementia	30 (9.6)	16 (22.2)	14 (5.9)
Depression	125 (40.2)	26 (36.1)	99 (41.4)
Diabetes	69 (22.2)	26 (36.1)	43 (18.0)
Herpes Zoster	32 (10.3)	6 (8.3)	26 (10.9)
Hypertension	178 (57.2)	52 (72.2)	126 (52.7)
Osteoarthritis	116 (37.3)	33 (45.8)	83 (34.7)
No. of comorbid conditions*			
1	45 (14.5)	7 (9.7)	38 (15.9)
2	84 (27.0)	11 (15.3)	73 (30.5)
3	94 (30.2)	20 (27.8)	74 (31.0)
4+	88 (28.3)	34 (47.2)	54 (22.6)

n: total count; sd: standard deviation; No.:number

* all have COPD so starts at 1; Limited to other conditions for which the Canadian Primary Care Sentinel Surveillance Network has validated algorithms: Chronic Kidney Disease, Dementia, Depression, Diabetes, Herpes Zoster, Hypertension, Osteoarthritis, Epilepsy, Parkinson. Epilepsy and Parkinson were not included because n<5 for both conditions.

Table 3. Accuracy Parameters of Case Definitions in BC CPCSSN

Definition	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
1.1 MaRNet-FP 1 ICD9 code OR ACEI/ARB+BB+diuretic	90.3 (81.0, 96.0)	93.3 (89.4, 96.1)	80.2 (69.9, 88.3)	97.0 (93.8, 98.8)
1.2 MaRNet-FP Including billings	93.1 (84.5, 97.7)	90.8 (86.4, 94.1)	75.3 (65.0, 83.8)	97.7 (94.8, 99.3)
Expanding codes and testing iterations and specific combinations (British Columbia group 1)				
2.1 One expanded code AND specific medication	75.0 (63.4, 84.5)	92.9 (88.9, 95.8)	76.1 (64.5, 85.4)	92.5 (88.4, 95.5)
2.2 One expanded code only	91.7 (82.7, 96.9)	91.2 (86.9, 94.5)	75.9 (65.5, 84.4)	97.3 (94.4, 99.0)
2.3 Two expanded codes	83.3 (72.7, 91.1)	94.6 (90.9, 97.1)	82.2 (71.5, 90.2)	95.0 (91.4, 97.4)
2.4 Specific medication only	18.1 (10.0, 91.1)	99.6 (97.7,100.0)	92.9 (66.1, 99.8)	80.1 (75.1, 84.5)
2.5 (2.1 or 2.3 or 2.4)	87.5 (77.6, 94.1)	92.1 (87.9, 95.1)	76.8 (66.2, 85.4)	96.1 (92.7, 98.2)
Addition of furosemide (British Columbia group 2)				
3.1 (2.1 OR Furosemide)	80.6 (69.5, 88.9)	94.1 (90.4, 96.8)	80.6 (69.5, 88.9)	94.1 (90.4, 96.8)
3.2 (3.1 including billing)	90.3 (81.0, 96.0)	91.6 (87.4, 94.8)	76.5 (66.0, 85.0)	96.9 (93.7, 98.7)
Including low threshold natriuretic peptide (Low NP)				
4.1 (1.1 or low NP)	93.1 (84.5, 97.7)	88.7 (84.0, 92.4)	71.3 (61.0, 80.1)	97.7 (94.7, 99.2)
4.2 (1.2 or low NP)	94.4 (86.4, 98.5)	87.0 (82.1, 91.0)	68.7 (58.6, 77.6)	98.1 (95.2, 99.5)
4.3 (3.2 or low NP)	93.1 (84.5, 97.7)	87.0 (82.1, 91.0)	68.4 (58.2, 77.4)	97.7 (94.6, 99.2)
Including high threshold NP (High NP)				
5.1 (1.1 or high NP)	91.7 (82.7, 96.9)	92.9 (88.9, 95.8)	79.5 (69.2, 87.6)	97.4 (94.4, 99.0)
5.2 (1.2 or high NP)	93.1 (84.5, 97.7)	90.8 (86.4, 94.1)	75.3 (65.0, 83.8)	97.7 (94.8, 99.3)
5.3 (3.2 or high NP)	90.3 (81.0, 96.0)	91.6 (87.4, 94.8)	76.5 (66.0, 85.0)	96.9 (93.7, 98.7)

PPV: Positive Predictive Value; NPV: Negative Predictive Value; 95% CI: 95% Confidence Interval; NS: Nova Scotia Definition; NP: natriuretic peptide; exp: expanded ICD-9 codes (see Appendix 3); Rx: medications (see Appendix3)

Figure 1 . Flow diagram showing process of sample selection of patient charts from electronic medical record (EMR) in BC-CPCSSN database.

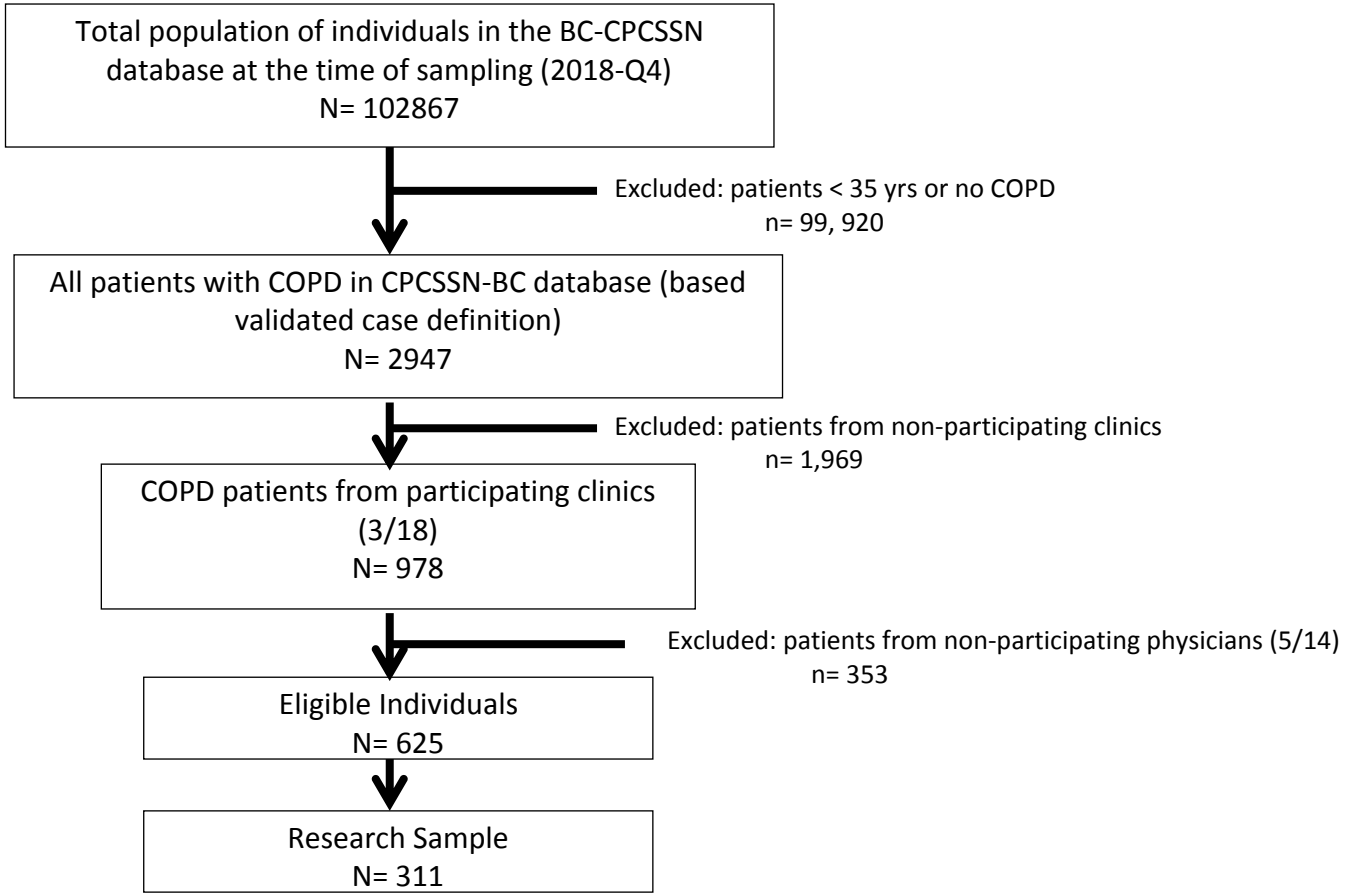


Figure 1

BC-CPCSSN: British Columbia Canadian Surveillance Sentinel Network; COPD: Chronic Obstructive Pulmonary Disorder; 2018-Q4: December 31, 2018;

***Anonymized data from these patient charts were reviewed. Case definitions for heart failure was then applied to this cohort of COPD patients for validation analysis

Figure 2A

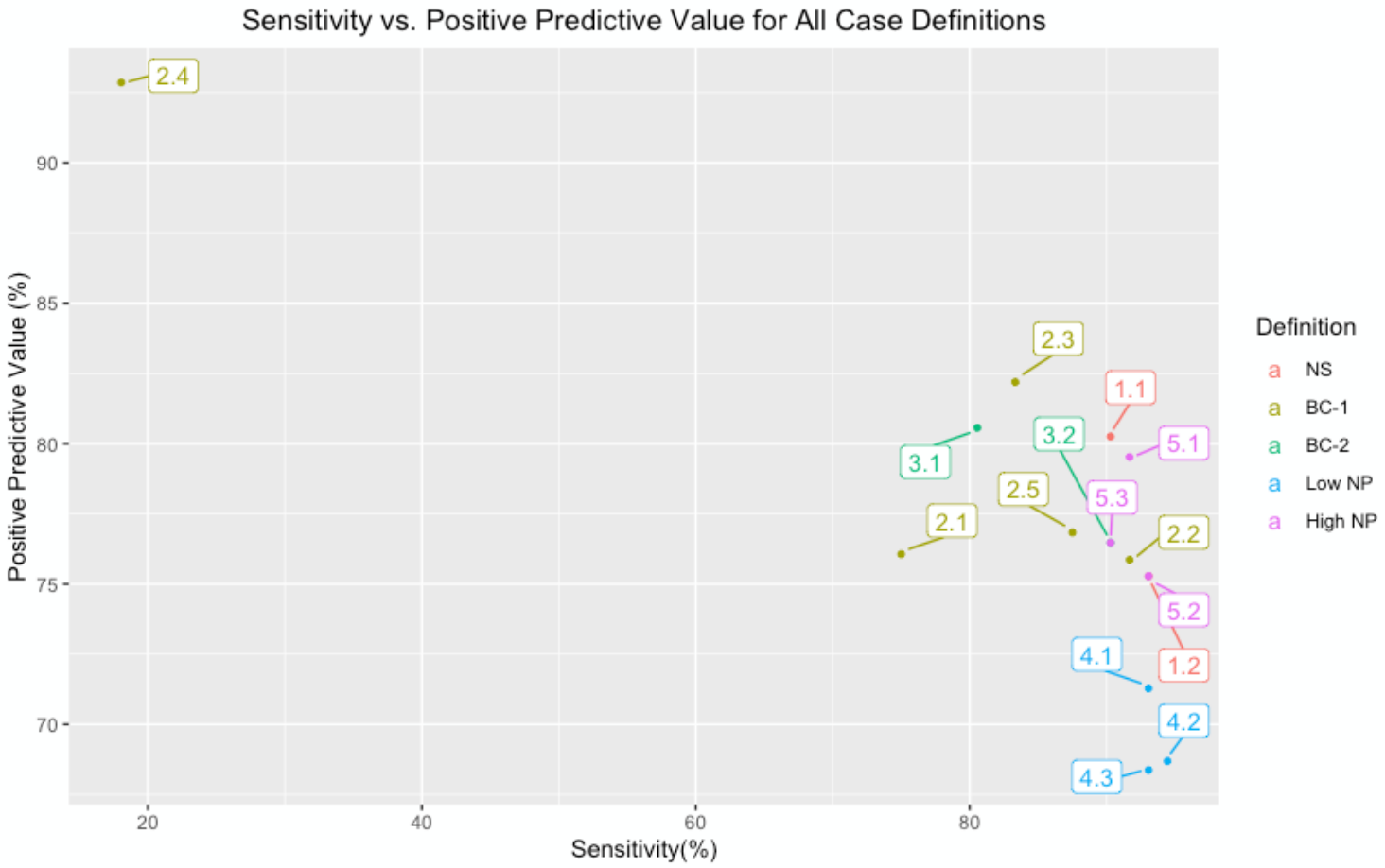


Figure 2B

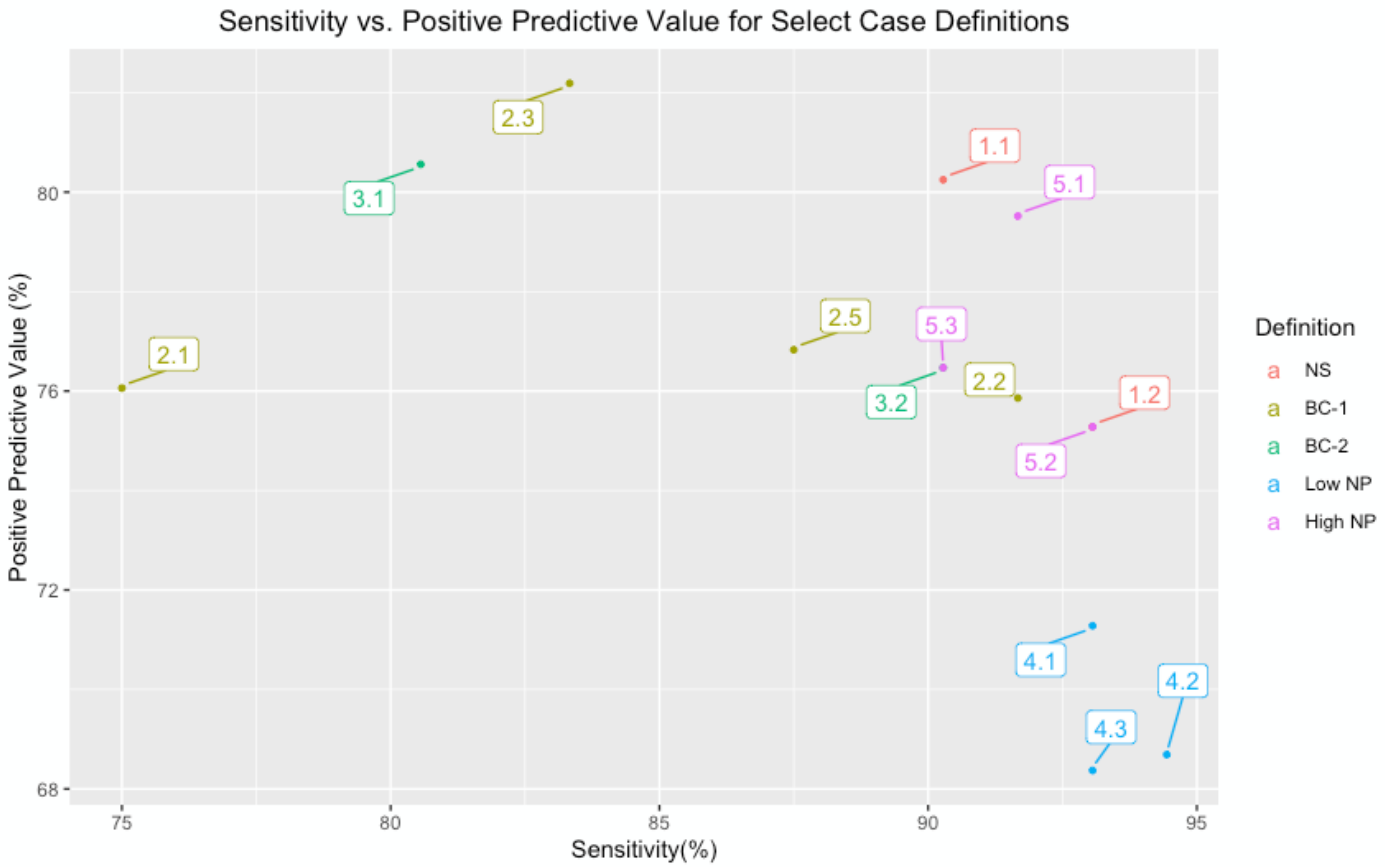


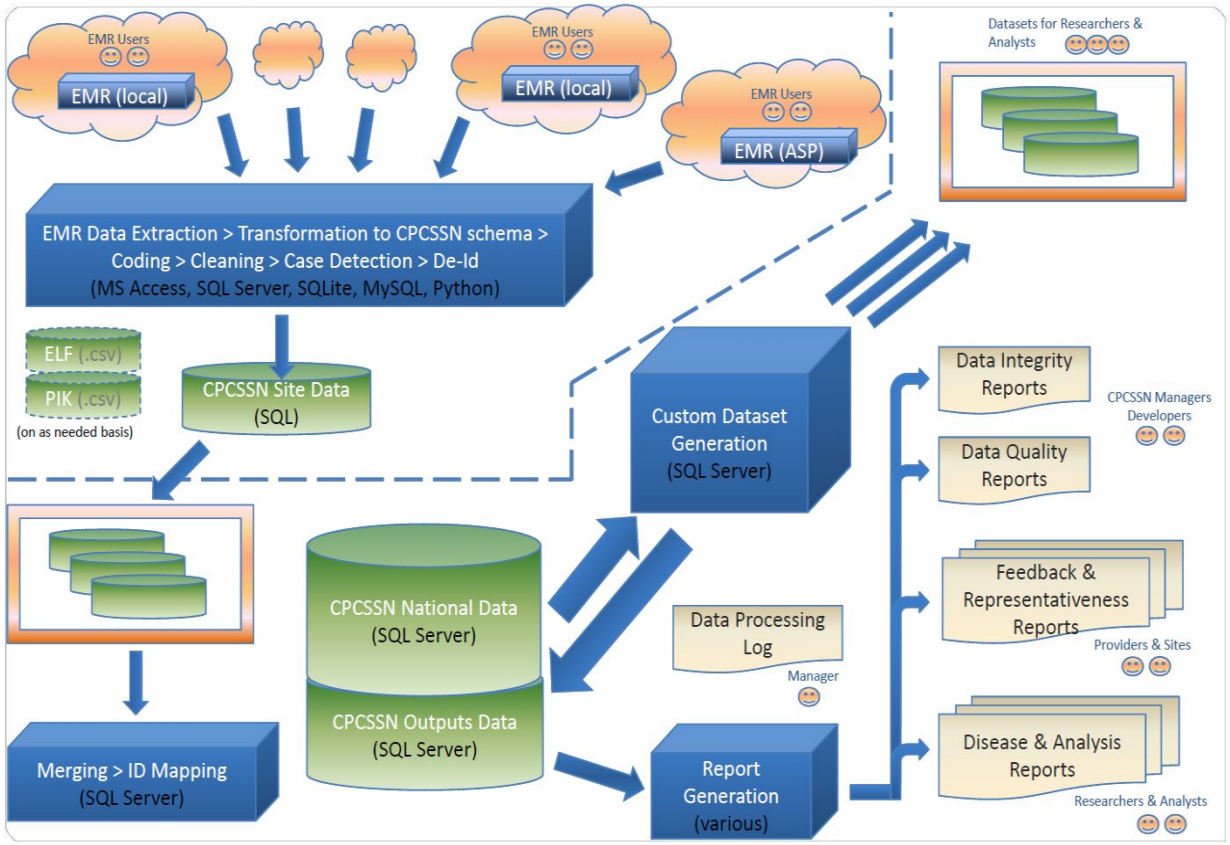
Figure 2

Figure 2A depicts all case definitions in Table 2; Figure 2B. depicts all case definitions except Definition 2.4 for better visualizations of remaining case definitions

Definitions correspond to categories in Table 2; NS: Original Nova Scotia MaRNet definition; BC-1: Expanding codes and testing iterations and specific combinations; BC-2: Addition of Furosemide; Low NP: Including low threshold natriuretic peptide; High NP: Including high threshold natriuretic peptide

Appendices

Appendix 1. CPCSSN Architecture and Flow



Appendix 2. Chart abstraction template used for the manual data extraction of heart failure among those with a diagnosis of chronic obstructive pulmonary disease

Elements collected	
Physician diagnosis in EMR of Heart Failure (HF)	Yes/No/Uncertain
Physician speciality reporting HF diagnosis in EMR	Family physician, cardiologist, other
Signs and symptoms	Dyspnea/Orthopnea/PND Peripheral Edema Elevated JVP Respiratory findings
BNP > 50	Yes/No and Value
NT-pro BNP >125	Yes/No and Value
ECHO	Moderate/Severe LV systolic dysfunction Moderate/Severe LV diastolic dysfunction Severe valve abnormality LVEF % (lowest reported)
MUGA	LVEF
Cardiac MRI	LVEF
Medication Hx	ACEi/ARB, Beta-blocker, aldosterone antagonist, Ivabradine, Diuretic (loop or thiazide), Hydralazine, Nitrate, Sacubitril-valsartan
Implantable Cardiac Defibrillator or Hx of Cardiac Resynchronization therapy	Yes/No

Appendix 3. Diagnosis codes table

ICD-9 Code	
428	Heart failure
428	Congestive heart failure, unspecified
428.1	Left heart failure convert
428.2	Systolic heart failure
428.2	Systolic heart failure, unspecified
428.21	Acute systolic heart failure
428.22	Chronic systolic heart failure
428.23	Acute on chronic systolic heart failure
428.3	Diastolic heart failure
428.3	Diastolic heart failure, unspecified
428.31	Acute diastolic heart failure
428.32	Chronic diastolic heart failure
428.33	Acute on chronic diastolic heart failure
428.4	Combined systolic and diastolic heart failure
428.4	Combined systolic and diastolic heart failure, unspecified
428.41	Acute combined systolic and diastolic heart failure
428.42	Chronic combined systolic and diastolic heart failure
428.43	Acute on chronic combined systolic and diastolic heart failure
428.9	Heart failure, unspecified
425	Cardiomyopathy
425.0	Endomyocardial fibrosis
425.1	Hypertrophic cardiomyopathy
425.11	Hypertrophic obstructive
425.18	Other hypertrophic cardiomyopathy
425.2	Obscure cardiomyopathy
425.3	Endocardial fibroelastosis
425.4	Other primary cardiomyopathies
425.5	Alcoholic cardiomyopathy
425.7	Nutritional and metabolic cardiomyopathy
425.8	Cardiomyopathy in other diseases classified elsewhere
425.9	Secondary cardiomyopathy, unspecified

Medication table (ATC codes)

ACE inhibitors	
C09AA01	Captopril
C09AA02	Enalapril
C09AA03	Lisinopril
C09AA04	Perindopril
C09AA05	Ramipril
C09AA06	Quinapril
C09AA07	Benazepril
C09AA09	Cilazapril
C09AA10	Trandolapril
Angiotensin receptor blockers (ARBs)	
C09CA01	Losartan
C09CA02	Eprosartan
C09CA03	Valsartan
C09CA04	Irbesartan
C09CA06	Candesartan
C09CA07	Telmisartan
C09CA08	Olmesartan medoxomil
C09DX04	Valsartan and sacubitril
Beta blockers	
C07AB02	Metoprolol
C07AB03	Atenolol
C07AB04	Acebutolol
C07AB07	Bisoprolol
C07AB12	Nebivolol
C07AG02	Carvedilol
Diuretic	
C03DA01	Spironolactone
C03DA04	Eplerenone
C03CA01	Furosemide
C03BA11	Indapamide

Appendix 4. Diagnosis codes table

ICD-9 Codes	
428; any or no decimals is acceptable	Heart failure
425 (no decimals)	Cardiomyopathy
425.4	Other primary cardiomyopathies
425.5	Alcoholic cardiomyopathy
425.7	Nutritional and metabolic cardiomyopathy
425.8	Cardiomyopathy in other diseases classified elsewhere
425.9	Secondary cardiomyopathy, unspecified
402.x1*	Hypertensive heart disease with cardiovascular disease with heart failure
404.x1, 404.x3*	Hypertensive heart disease with cardiorenal with heart failure

* x indicates any number in that position.
**Changes from Appendix 1 included removing 425.0-425.3 (425.0 Endomyocardial fibrosis, 425.1 Hypertrophic cardiomyopathy, 425.2 Obscure cardiomyopathy and 425.3 Endocardial fibroelastosis) and addition of 402.X1, 404.X1 and 404.X3

Medication table (ATC codes)

ACE inhibitors / ARBs	
C09A-C09D	
Beta blockers	
C07AB02	Metoprolol
C07AB03	Atenolol
C07AB04	Acebutolol
C07AB07	Bisoprolol
C07AB12	Nebivolol
C07AG02	Carvedilol
MRA	
C03DA01	Spironolactone
C03DA04	Eplerenone
Hydralazine	
C02DB02	Hydralazine
Sacubitril-valsartan	
C09DX04	Sacubitril-valsartan
Loop/Thiazide Diuretic	
C03CA01	Furosemide

Appendix 5. 2x2 tables for Case Definitions in BC CPCSSN vs Gold Standard (Chart Review)

		Gold Standard (Chart Review)	
		COPD	No COPD
Definition 1.1	COPD	65	16
	No COPD	7	223
Definition 1.2	COPD	67	22
	No COPD	5	217
Definition 2.1	COPD	54	17
	No COPD	18	222
Definition 2.2	COPD	66	21
	No COPD	6	218
Definition 2.3	COPD	60	13
	No COPD	12	226
Definition 2.4	COPD	13	1
	No COPD	59	238
Definition 2.5	COPD	63	19
	No COPD	9	220
Definition 3.1	COPD	58	14
	No COPD	14	225
Definition 3.2	COPD	65	20
	No COPD	7	219
Definition 4.1	COPD	67	27
	No COPD	5	212
Definition 4.2	COPD	68	31
	No COPD	4	208
Definition 4.3	COPD	67	31
	No COPD	5	208
Definition 5.1	COPD	66	17
	No COPD	6	222
Definition 5.2	COPD	67	22
	No COPD	5	217
Definition 5.3	COPD	65	20
	No COPD	7	219

Appendix 6. Accuracy Parameters from Sensitivity Test of Case Definitions in BC CPCSSN

Definition	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
1.1 MaRNet-FP 1 ICD9 code OR ACEI/ARB+BB+diuretic	93.1 (84.5, 97.7)	93.3 (89.4, 96.1)	80.7 (70.6, 88.6)	97.8 (95.0, 99.3)
1.2 MaRNet-FP Including billings	94.4 (86.4, 98.5)	90.8 (86.4, 94.1)	75.6 (65.4, 84.0)	98.2 (95.4, 99.5)
Expanding codes and testing iterations and specific combinations (British Columbia group 1)				
2.1 One expanded code AND specific medication	76.4 (64.9, 85.6)	92.9 (88.9, 95.8)	76.4 (64.9, 85.6)	92.9 (88.9, 95.8)
2.2 One expanded code only	93.1 (84.5, 97.7)	91.2 (86.9, 94.5)	76.1 (65.9, 84.6)	97.8 (94.8, 99.3)
2.3 Two expanded codes	83.3 (72.7, 91.1)	94.6 (90.9, 97.1)	82.2 (71.5, 90.2)	95.0 (91.4, 97.4)
2.4 Specific medication only	18.1 (10.0, 28.9)	99.6 (97.7,100.0)	92.9 (66.1, 99.8)	80.1 (75.1, 84.5)
2.5 (2.1 or 2.3 or 2.4)	88.9 (79.3, 95.1)	92.1 (87.9, 95.1)	77.1 (66.6, 85.6)	96.5 (93.2, 98.5)
Furosemide (British Columbia group 2)				
3.1 (2.1 OR Furosemide)	83.3 (72.7, 91.1)	94.1 (90.4, 96.8)	81.1 (70.3, 89.3)	94.9 (91.3, 97.4)
3.2 (3.1 including billing)	91.7 (82.7, 96.9)	91.6 (87.4, 94.8)	76.7 (66.4, 85.2)	97.3 (94.3, 99.0)
Including low threshold natriuretic peptide				
4.1 (1.1 or low NP)	94.4 (86.4, 98.5)	88.7 (84.0, 92.4)	71.6 (61.4, 80.4)	98.1 (95.3, 99.5)
4.2 (1.2 or low NP)	95.8 (88.3, 99.1)	87.0 (82.1, 91.0)	69.0 (59.0, 77.9)	98.6 (95.9, 99.7)
4.3 (3.2 or low NP)	94.4 (86.4, 98.5)	87.0 (82.1, 91.0)	68.7 (58.6, 77.6)	98.1 (95.2, 99.5)
Including high threshold NP (High NP)				
5.1 (1.1 or high NP)	93.1 (84.5, 97.7)	92.9 (88.9, 95.8)	79.8 (69.6, 87.7)	97.8 (94.9, 99.3)
5.2 (1.2 or high NP)	94.4 (86.4, 98.5)	90.8 (86.4, 94.1)	75.6 (65.4, 84.0)	98.2 (95.4, 99.5)
5.3 (3.2 or high NP)	91.7 (82.7, 96.9)	91.6 (87.4, 94.8)	76.7 (66.4, 85.2)	97.3 (94.3, 99.0)

PPV: Positive Predictive Value; NPV: Negative Predictive Value; 95% CI: 95% Confidence Interval; NS: Nova Scotia Definition; NP: natriuretic peptide; exp: expanded ICD-9 codes (see Appendix 3); Rx: medications (see Appendix 3)