

Review**Variations in COPD Health Care Access and Outcomes: A Rapid Review**

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Abstract

Background: Health inequities among individuals with chronic obstructive pulmonary disease (COPD) are often associated with differential access to healthcare and health outcomes. A greater understanding of the literature concerning such variation is necessary to determine where gaps or inequities exist along the continuum of COPD care.

Methods: A rapid review of the published and grey literature reporting variations in healthcare access and/or health outcomes for individuals with COPD was completed. Variation was defined as differential patterns in access indicators or outcome measures within socio-demographic categories, including age, ethnicity, geography, race, sex, and socio-economic status. Emergent themes were identified from the included literature and synthesized narratively.

Results: Thirty-five articles were included for final review; the majority were retrospective cohort studies. Twenty-five studies assessed variation in access to healthcare. Key indicators included: access to spirometry testing, medication adherence, participation in pulmonary rehabilitation, and contact with general practitioners and/or respiratory specialists. Twenty-one studies assessed variation in health outcomes in COPD and key metrics included: hospital-based resource utilization (length of stay and admissions/readmissions), COPD exacerbations, and mortality. Patients who live in rural environments and those of lower socio-economic status had both poorer access to care and outcomes at the system and patient level. Other sociodemographic variables, including ethnicity, race, age, and sex were associated with variation in healthcare access and outcomes, although these findings were less consistent.

Conclusions: The results of this rapid review suggest that substantial variation in access and outcomes exists for individuals with COPD, highlighting opportunities for targeted interventions and policies.

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a chronic condition characterized by progressive airflow obstruction, which has a substantial impact on both patients (1) and healthcare systems (2). Effective and integrated management of COPD, both on an individual and population-wide scale, requires an understanding of how health equity and social determinants of health can impact a person's illness experience. Health equity or inequity is also intrinsically tied to healthcare access; defined as the ability to obtain healthcare services, including the diagnosis, treatment, and management of diseases (3). Furthermore, an individual's level of access to healthcare has a profound effect on their health outcomes, including morbidity and mortality.

Health inequities are described as the unjust differential allocation of healthcare resources and/or differing health status between different population groups, arising from social factors (4). Consequently, health inequities may develop when variations in healthcare access and outcomes, between different demographic groups of patients, are unwarranted (5). Such inequities can result in poorer health outcomes for already marginalized populations (4). Health inequities have been identified among individuals with COPD worldwide (6). Individuals with COPD of lower socioeconomic status (SES), living in rural settings, and those from marginalised communities often have decreased access to healthcare that is necessary to manage and treat their condition (6). Furthermore, this correlation between the aforementioned demographic variables and decreased access to COPD care has been investigated and established in grey literature reports from multiple countries (e.g. (7-9) Thus, these determinants of healthcare access are considered

important in the study of COPD care and policy, and continue to be the focus of many health authorities.

To inform solutions aimed at resolving health inequities experienced by individuals with COPD, it is imperative that we identify whether and where equity-related variations in healthcare access and health outcomes exist. As such, the objective of this research was to examine the existing literature surrounding equity-related variations in healthcare access and health outcomes for individuals with COPD.

Methods

A rapid review of the published and grey literature reporting variations in healthcare access and/or relevant health outcomes for individuals with COPD was completed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (6), where applicable. For this review, we considered variations in terms of differential patterns of healthcare access indicators or health outcome metrics within any of the socio-demographic categories examined by an included article, which included but were not limited to sex, gender, age, geographic location (or rurality), race, ethnicity, SES, level of education, and income.

Search Strategy

A comprehensive electronic database search strategy for published literature was developed by an information specialist. Specifically, MEDLINE and EMBASE were searched from January 1 2012 to August 2, 2022; the complete search strategies for both databases are outlined in the **Appendix 1**. Terms such as “variation* in care”, “health inequity”, and “healthcare access” were

combined using the Boolean operator “and” with terms such as “length of stay”, “quality of life”, and “hospital discharge”, as well as terms such as “COPD” or “chronic obstructive pulmonary disease”. Results were limited to studies in English, published within the past 10 years, and conducted in North America, Europe, Australia, and New Zealand only. Limiting results to these countries was necessary due to the rapid nature of this review. As we approached this work from the lens of a provincial Canadian healthcare system context, studies from these limited jurisdictions were also selected due to the comparable aspects of their healthcare systems and their routine comparison in terms of healthcare system performance (10). Only original research and review articles were included. A scan of the grey literature using the first 5 results pages of a google search was also performed to supplement the information collected from the published peer-reviewed literature. The search terms used in this grey literature scan were “COPD”, “atlas of variation”, “health outcomes”, and “healthcare access”. Eligibility of grey literature reports were assessed in accordance with the same inclusion and exclusion criteria listed in Appendix 2.

Selection of Literature

Studies were included if: they were primary observational studies or review articles in which the population studied were adult patients with COPD; the study objective was to evaluate and/or define healthcare access and/or related health outcomes for individuals with COPD; the outcome assessed potential variation or disparities in healthcare access and/or outcomes; and if such outcomes were assessed within sociodemographic subgroups of COPD patients (e.g., females, older age, lower SES, etc.). Studies were excluded if they did not meet the criteria above and were also excluded if the primary study objective was to assess the effectiveness of an intervention and/or quality improvement initiative/programme. A complete list of inclusion and

exclusion criteria is available in **Appendix 2**. An initial sample of 20 citations was screened by two independent reviewers to assess reliability, with any disagreement between reviewers resolved through discussion and consensus. All remaining screening was performed by one reviewer, with final inclusions discussed and reviewed by the entire research team.

Data Extraction and Analysis

Data from the included studies was extracted using standardized data extraction forms. For all studies, author, study design, publication year, country, number of participants, population characteristics including age, study duration, quantitative and qualitative data assessing variations in healthcare access indicators, as well as quantitative and qualitative data assessing variation in healthcare outcomes were extracted. When reported, the breakdown of study participants by relevant sociodemographic variables was also extracted. Major themes among included studies were identified inductively and synthesized narratively. Specifically, studies which assessed variation in healthcare access indicators were grouped according to which aspect of the continuum of care (prevention, diagnosis, and treatment or management) was most relevant to the indicators assessed. Studies which assessed variation in healthcare outcomes were grouped according to whether their outcome metrics reflected the patient and/or systems level. The Newcastle Ottawa Scale (NOS) was used to assess the risk of bias among included cohort studies (11). As this scale was originally designed for cohort and case-control studies, a previously adapted NOS was also utilized to assess risk bias among the included cross-sectional studies (12). The risk of bias assessment was completed by one reviewer.

Results

Search results

Two hundred and fifty-three citations were identified through the electronic database search. Of those, 187 were excluded after abstract review, leaving 66 studies for full-text review. Thirty-six studies were excluded after full-text review and 30 articles were included for the final analysis (**Figure 1**). Five reports were included from the grey literature scan, all of which assessed and identified geographical variation in COPD access to care and/or outcomes (7-9, 13, 14).

Characteristics of included studies

The characteristics of the 35 included studies are summarized in **Table 1**. Included articles were published between 2012 and 2022. The majority of studies were conducted in Europe (n = 17) and the United States (n = 12); 3 in Canada; 2 in Australia; and 1 in New Zealand. Most studies were retrospective cohort studies (n = 24) (7-9, 13-33) and the majority reviewed administrative health data or patient charts with a physician diagnosis of COPD (e.g. COPD case definition based on ICD-10 codes). The remaining studies were prospective observational cohort studies (n = 2) (34, 35) and cross-sectional studies (n = 9) (36-44), which included, for example, health surveys that rely upon the self-reporting of a COPD diagnosis by patients. In terms of study setting, 21 studies were country-wide (7, 13, 14, 16, 23, 24, 27-30, 32, 36-44), 9 were specific to a smaller region of a country (e.g. the province of Alberta, Canada) (9, 18, 19, 21, 22, 25, 26, 31, 35), and 5 were set in either a single centre/hospital or multiple hospitals (15, 17, 20, 33, 34). All patients in the included articles were adults (age 18+) diagnosed with COPD. **Appendices 3 and 4** detail the NOS risk of bias scores for all included cohort studies, including those from the grey literature, and cross-sectional studies, respectively. Broadly, the 26 included cohort studies from the published and grey literature scored between 4 and 9 on the NOS suggesting minimal risk of

bias; the median score among studies was 7, with the majority of studies (n=20) scoring 7 and above (e.g., low risk of bias). Similarly, the NOS risk of bias scores for the 9 included cross-sectional studies ranged from 5-9, with a median score of 7 (e.g., low risk of bias). Importantly, no included studies had unsatisfactory scores (e.g., 0-3).

Study Outcomes

The major findings from the included studies are reported in **Tables 2** and **3**. Statistically significant findings from included studies are also summarized in **Figure 2**.

Variation in Healthcare Access

Table 2 presents a summary of main findings from the 25 studies that assessed *variations in access to healthcare* for COPD patients. Studies were identified across the following stages within the continuum of care: prevention (n = 1) (24, 45); diagnosis (n = 4) (37, 39-41); treatment or management (n = 12) (15, 17, 18, 20, 21, 27-30, 34-35, 44). Additionally, there were 8 studies that reported indicators across the continuum and were grouped into a “pan-continuum” category (8, 9, 13, 19, 23, 25, 38, 42). No studies investigated variation in access to palliative care or primary prevention interventions.

Prevention

Four studies examined variation in the secondary prevention stage (19, 23, 24, 38). In a cohort of 1511 individuals with COPD, the authors identified that individuals who were black or of older age had significantly reduced odds of receiving smoking cessation medication within 48 hours of hospital discharge (24).

Diagnosis

The most common access indicator around diagnosis was access to spirometry testing (n = 5 studies) (13, 25, 39, 41). Mowls et al. identified that patients who were Hispanic and younger were less likely to be diagnosed with COPD using spirometry. Access to spirometry testing does not appear to vary according to educational level (39). In a retrospective medical record audit of 234 COPD admissions at 8 acute care hospitals in the Hunter New England Region of Australia, Pretto et al. (2012) identified wide interhospital geographical variability in access to spirometry testing upon admission (25).

Treatment or Management

Key access indicators around the treatment of COPD were primarily focused on medication adherence (n = 7 studies) (18, 21, 23, 29, 38, 42, 44) and referral to or completion of pulmonary rehabilitation (PR) (n = 10 studies) (8, 13, 17, 19, 20, 25, 27, 28, 30, 34). Probability of adherence to COPD maintenance medications was found to be lower for patients who are female (18, 44). In a retrospective study of 13 369 incident outpatients with COPD, adherence to COPD maintenance pharmacotherapy was also found to be lower in individuals with lower SES, specifically those who are unemployed, living alone, immigrants, or of low income [26]. Interestingly, Di Martino et al. (2017) found that the geography of a patient's hospital of discharge was a stronger determinant of adherence to long-acting bronchodilators, and therefore a stronger source of potential unwarranted variation compared to other patient-level factors, including age, educational level, and sex.

Across studies, PR access at the patient-level was examined by frequency of PR program attendance, adherence (e.g. > 63% attendance rate), and/or completion. Included studies report conflicting results regarding the influence of age, sex, and SES on an individual's PR access. For example, Hayton et al. found that women were less likely than men to attend PR at a community hospital in the United Kingdom (20). However, a prospective observational study in two inner London (UK) boroughs suggested that there was no significant difference in PR attendance between males and females (34). Access to PR was also examined at a healthcare system level in terms of regional programme density and was found to vary considerably by geographic region within the United States (27, 28). Similar findings were observed in the UK, with metropolitan hospitals reporting more frequent referrals of discharged patients to pulmonary specialists or PR in comparison to rural hospitals (25). Also with respect to outpatient COPD treatment, three studies compared GP/PCP visits among patient populations and found that patients with a significantly decreased likelihood of visiting a GP/PCP were male (40); while patients with a significantly increased likelihood of visiting a GP/PCP were women belonging to a lower social class (37), older (age 70+) men (37), African Americans (40), and middle-aged COPD patients with lower education (39).

Six studies also assessed variation in access to long-term COPD care or management, including outpatient specialist visits and follow-up with GPs following an initial hospitalization (8, 9, 13, 15, 35, 42). One large 4-year retrospective cohort study of COPD patients following hospital discharge in Ontario, Canada found that patients were significantly less likely to receive follow-up with a family doctor, respirologist, or internal medicine specialist within 7 days of discharge if they were female, did not have a family doctor, or lived in a rural location (15). Patients from

higher income regions and those younger than 85 years old were more likely to receive follow up (15). In a report of adult patients diagnosed with COPD in Alberta, Canada, geographical location in terms of patient residence prior to hospitalization was concomitantly associated with variation in GP access, specialist care, as well as acute discharge destination (9). No studies focused on patient access to respiratory therapists.

Variation in Health Outcomes

A total of 21 included studies examined *variation in health outcomes* in COPD (**Table 3**) in terms of healthcare utilization (n = 10) (7-9, 19, 25, 26, 31, 32, 37, 40), patient-level outcomes (n = 4) (14, 21, 35, 43), or both (n = 7) (13, 16, 17, 29, 33, 36, 42).

Healthcare Utilization

The healthcare utilization outcomes focused primarily on hospital-based resource use, including COPD exacerbations requiring inpatient hospitalization (26), emergency department (ED) visits (37), hospital length of stay (LOS) (19), and hospital readmissions (32).

The impact of age, geography, sex, and SES on variations in hospitalizations and ED visits is mixed (**Table 3**). For example, a retrospective medical record audit from Australia found that despite increased readmission rates in rural hospitals, the median LOS did not significantly differ between rural and metropolitan settings (25). In contrast, a similar study from New Zealand found that the geometric mean LOS was 1.0 days longer for rural hospital admissions compared to urban (19). In addition, the impact of an individual's SES—which may include related determinants such as education, and insurance coverage, and living status—on health resource

utilization was examined in n=6 studies (7, 19, 26, 31, 37, 40). Various indices were used to quantify aspects of SES, including the English Index of Multiple Deprivation (IMD). For instance, in a retrospective cohort study of COPD patients attending outpatient respiratory clinics, higher IMD scores (more deprived areas) were independently associated with increased emergency hospitalisations, longer LOS, and patient mortality at 1-year post initial-assessment (17).

COPD Patient Outcomes

The most common patient-level outcome evaluated was mortality (n=3) (14, 22, 35); one study also investigating patient quality of life (QoL), dyspnea grade, and COPD assessment test (CAT) score (43). Increased mortality in COPD patients may be associated with male sex (35), increased age (35), and lower SES (17, 29). Associations between mortality and ethnicity/race were less conclusive (16, 22, 33). A cross-sectional analysis investigating the impact of COPD on QoL found no significant difference in CAT scores between males and females (43).

Acute COPD exacerbations, which affect health outcomes at the patient-level but also commonly result in the need for inpatient hospitalization, are more likely in younger patients (36) and those with lower education (29). Two cross-sectional studies in Europe found no significant difference in COPD exacerbations with sex (42, 43).

Four studies evaluated mortality among COPD patients concomitant to health system-level outcomes, such as acute care LOS and readmissions and found that SES (17, 29), age (36), and race (33) led to statistically significant variations in these outcomes.

Discussion

Through this rapid review we identified several studies from the published and grey literature that report differential patterns of healthcare access and health outcomes for individuals with COPD. As summarized in **Figure 2**, substantial variation was detected in healthcare access in terms of primary care provider or GP visits, pharmacotherapy adherence, and pulmonary rehabilitation. Considerable variation in health outcomes was also observed with respect to inpatient hospitalizations, emergency department visits, as well as mortality. Most studies included in the present review characterized observed variation by differential access to care and/or health outcomes due to specific socio-demographic variables or determinants, such as a patient's age, SES, sex, geography and/or ethnicity or race. Geography was the most widely evaluated determinant of variation among included studies, with nearly half of the studies reporting statistically significant geographical variation in access to care (10 of 25 studies) and health outcomes (10 of 21 studies) for those with COPD.

The present rapid review expands on the current evidence base (6) regarding health inequities for patients with COPD by examining how access and health outcomes can vary across the continuum of COPD care for a greater variety of patient subgroups (i.e., age, sex, SES, geography). It is important to note that the objective of most of the included studies was not necessarily to identify variation in COPD care, but rather to assess the differential impact of one or more socio-demographic variables on specific quality indicators relevant to individuals with COPD. However, in doing so, the findings from these studies suggest that variation in access and

outcomes does exist in different subgroups, across a variety of clinical settings, and in varying healthcare systems.

A particular strength of this review is that we were able to understand how, where, and the extent to which variation has currently been studied and identified, as well as visualize where current gaps in the literature exist. For example, the current literature was primarily centered on the following indicators: inpatient hospitalizations (71%), mortality (38%), access to pulmonary rehabilitation (36%), access to primary care providers (32%), pharmacotherapy adherence (28%), and emergency department visits (24%). We found that, among included studies, healthcare access (**Table 2**) was studied more extensively—with more statistically significant findings—compared to health outcomes in different patient groups (**Table 3**), with much of the literature on variation in access focused on the treatment or management for COPD. In contrast, few studies examined variation in access to preventative care and no studies examined key prevention-related measures such as influenza vaccination rates; this represents a clear gap in the current literature (**Figure 2**). Given the importance of both primary and secondary preventative approaches in chronic disease progression, further study of variation in access to preventive care is warranted. Importantly, only two studies evaluated access to pulmonary subspecialty care (9, 15). Referral and access to pulmonary physicians and/or respiratory therapists is critical to the overall understanding of variation in healthcare access for individuals with COPD, especially when considering geographic variation.

Of the different socio-demographic determinants studied, as noted, geography was most commonly associated with variation in both health access and outcomes. Three of the grey

literature reports were described as “atlases of variation”, which are series of reports summarizing how healthcare access and use varies depending on a person’s location within a country or region (7). All three atlases of variation identified significant variation in both access indicators across the care continuum, as well as healthcare utilization with geographical location (7, 8, 13). Specifically, patients living in rural and more deprived areas were frequently identified as being more likely to experience poorer healthcare access and health outcomes, even across different countries of study and COPD patient populations. However, geography alone is unlikely to be a sufficient surrogate for the effects of other determinants of variation. Thus, future “atlas of variation” projects would benefit from considering how additional socio-demographic factors, such race, education, income stability, and gender, may intersect with geography and influence metrics of interest. Atlases of variation are important from both population surveillance and quality improvement stances, as they provide a context specific visualization of where and for who health policy changes and/or healthcare system intervention would be most impactful on reducing health inequities within a given region.

Race and ethnicity were also frequently identified determinants of variation in healthcare access and health outcomes for individuals with COPD. A focus on race is especially prevalent within studies from the United States (40). Mixed results were identified in terms of variation by ethnicity, and such variation is likely closely knit with other social determinants of health, including SES. When interpreting these studies, it is important to remember that race is a social construct and social context must be considered (46). Moreover, other factors or determinants of variation, such as SES and experiences of interpersonal and/or systemic racism, are likely more relevant determinants of health disparities and inequities as compared to race alone and should

be integrated into future studies. The latter was not considered among the included literature which likely reflects the difficulty in capturing and stratifying results by ethnicity in studies of secondary data (47).

Variation in access and outcomes due to differences in SES and sex were also mixed. For instance, variation due to SES was observed in hospitalization rates, hospital length of stay, and ED visits for those with COPD; however, hospital readmission rates did not appear to differ by patient SES. The included studies also represented a bias towards reporting sex rather than gender. As such, there is a lack of literature concerning gender-based variation in COPD care and outcomes. Certainly, there appears to be a link between lower SES and worsened healthcare access, along with poorer health outcomes as a result, indicating an opportunity for intervention to improve the care of individuals with COPD of lower SES. However, such an intervention would be complex, as other upstream social determinants of health, including housing, financial security, and social support, should ideally be addressed first (48).

Implications for Future Research

Given the number of determinants of variation identified through this rapid review, future research assessing the impact of intersectionality on variation in COPD healthcare access and outcomes is warranted. Intersectionality involves assessing how multi-level interacting social locations, determinants of health, and power structures can shape and influence human life and health (49). Within the context of this research, such an approach may involve evaluating the differential effects of intersectional strata on COPD-related outcomes. Our research results highlight a dearth of research assessing the extent to which intersectional variables, or the

cumulative effect of multiple determinants of variation, impact access to care and health outcomes for individuals with COPD. This is gap in the current knowledge surrounding health equity and access to care in COPD. Further, studies incorporating theories of intersectional theory are lacking in COPD research; these would provide critical insights for the improvement of patient-centred care in this field.

To better inform healthcare professionals and policymakers on the differential allocation of resources and outcomes of individuals with COPD, future work should consider broadening assessments of variation to *all* stages of the care continuum, from prevention and screening to palliative care. This is particularly important for indicators of access to preventative and palliative care, where current research is highly limited or nonexistent. Improved understanding of variation within specific contexts (e.g., geographical locations and patients with similar demographics) may additionally help tailor future interventions by providing indications of where such an intervention should be applied (e.g., acute versus community care, rural versus urban) and which specific target population the intervention should focus upon. An example of such a tailored, evidence-informed intervention approach might include an initiative to improve rural primary care provider's compliance to COPD guidelines in terms of ensuring diagnosis is confirmed with spirometry.

Finally, we suggest that further consensus on standard indicators and/or benchmarks to assess access to care for those with COPD is required. Such an initiative would not only improve generalizability of individual study findings to other jurisdictions, but also permit better comparability of interventions to address access across studies. For example, one health outcome

recognized internationally to evaluate healthcare utilization and efficiency among hospitalized patient groups—including those with COPD—is hospital “length of stay” in days (50). Without such standardized benchmarks of access to care for those with COPD, we were limited in our ability to interpret the extent of variation in access across studies and jurisdictions included in our present review. Specifically, we saw multiple indicators for access to PR in the included literature, such as referral to PR and PR program attendance or adherence; however, a metric or approach of measuring “PR density” would more adequately account for availability of PR, hence access to PR, and if adopted would aid in generalizability when assessing geographic variation in access.

Study Limitations

The literature included in this rapid review does not or insufficiently addressed longitudinal or temporal evaluation of variation in care, as well as potential variation in care and access for individuals with COPD within the unique context of the COVID-19 pandemic. Most included studies were also conducted in the United States and Europe. Therefore, observed heterogeneity in findings may be attributable, in part, to differences in healthcare systems and/or patient populations between countries of study and the generalizability of findings across jurisdictions with may be limited. Due to the rapid nature of this review, limitations in the breadth of literature included (i.e., language, date, country restrictions) may have introduced bias into our present findings. Pooled analysis of included articles was also not completed; thus, we were unable to quantify the relative impact of different sociodemographic factors on variation in access and outcomes.

Conclusions

Through this rapid review, we identified multiple patterns of potential equity-related variations in healthcare access and health outcomes for individuals with COPD. Although the present findings may not be generalizable to all patient populations and/or healthcare settings, it is apparent that variations in both access to care and healthcare utilization likely exist for patients with COPD, on the basis on multiple determinants, including geography, sex, ethnicity, and SES. To mitigate unwarranted variation and resulting health disparities, these determinants of variation in COPD care and outcomes should be the focus of future research and policy work. Further, this understanding of sociodemographic variation should provide a starting point to evaluate the potential systemic underpinnings of the various health inequities experienced by individuals with COPD, as well as inform more equitable health policies and clinical practices in the care of those with COPD.

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Table 1. Characteristics of Included Studies

Author (Year) Country	Study Design	Study Setting	Population	Participants/records, <i>N</i> ^a	Patient Age	Study Duration	Objective	
							Assesses variation in health outcomes	Assesses variation in healthcare access
Alexopoulos (2015) Greece	Cross-Sectional Study	Multi-centre, Country-wide (199 respiratory physicians interviewed)	COPD patients seen by respiratory physicians in the outpatient setting	<i>N</i> = 6125 (28.7% female)	40+	October 2010 - March 2011	Yes	No
Appleton (2021) Canada	Retrospective Cohort Study	Single hospital in the province of Ontario	Patients discharged from the hospital with a diagnosis of COPD	<i>N</i> = 24438	35+	April 2012 - March 2016	No	Yes
Bhopal (2015) Scotland	Retrospective Cohort Study	Country-wide	COPD cases from the Scottish Health and Ethnicity Linkage Study (SHELS)	<i>N</i> = 114000 COPD cases (17.4% of total respiratory cases)	40+	April 2001 - 2010	Yes	No
Collins (2018) United Kingdom	Retrospective Cohort Study	Two hospitals in Hampshire, England (one large teaching, one rural)	Individuals with a confirmed COPD diagnosis attending outpatient respiratory clinics	<i>N</i> = 424	Mean age = 73 (SD = 10)	1 year from initial assessment	Yes	Yes
deMiguelDiez (2015) Spain	Repeated Cross- Sectional Study	Country-wide	Individuals who self-identified as having COPD from the 2006 and 2012 National Health Surveys conducted in Spain	<i>N</i> = 2321 (<i>N</i> = 1320 in 2006, <i>N</i> = 1001 in 2012)	40+	2006 and 2012 (2 cross- sectional timepoints)	Yes	Yes
DiMartino (2017) Italy	Retrospective Cohort Study	Lazio Region of Italy	Patients discharged from hospital with main diagnosis of COPD or main diagnosis of COPD-related causes with a secondary diagnosis of COPD	<i>N</i> = 13178	45+	January 2007 - June 2011	Yes	No
Dummer (2020) New Zealand	Retrospective Case Note Review	Single Region (hospitals within the Southern District Health Board)	Patients with a spirometry-confirmed diagnosis of COPD and an ED visit and/or IP stay at a hospital within the Southern District Health Board	<i>N</i> = 340	Mean age = 71.8 (SD = 10.3)	January 2015 - December 2015	Yes	Yes
Hayton (2013) United Kingdom	Retrospective Cohort Study	1 community hospital in Norwich, United Kingdom	Individuals with COPD invited to attend a PR program at the community hospital	<i>N</i> = 711 (<i>n</i> = 417 male)	Mean age = 69.0 (SD = 9.0)	January 2005 - December 2010	No	Yes
Henoch (2016) Sweden	Cross-Sectional Study	Country-wide	Patients with COPD from the Swedish National Airway Registry	<i>N</i> = 7810 (<i>n</i> = 4362 female)	Mean age = 69 (SD = 9.1)	2009 (cross- sectional)	No	Yes

							Objective	
Author (Year) Country	Study Design	Study Setting	Population	Participants/records, N*	Patient Age	Study Duration	Assesses variation in health outcomes	Assesses variation in healthcare access
Hetlevik (2016) Norway	Cross-Sectional Study	Country-wide	Adults with a GP diagnosis of COPD and/or asthma	n = 67832 COPD only, N = 160306 COPD total (including patients with both COPD and asthma). 44% had basic education, 47% intermediate education, and 7% had higher education.	40+	2009-2011	No	Yes
Hogg (2012) United Kingdom	Prospective Observational Study	Two inner London boroughs	Patients with diagnosis of COPD referred for PR	N = 1266 (n = 382 female)	0+	April 2008 - March 2010	No	Yes
Hu (2017) Denmark	Retrospective Cohort Study	Restricted to patients who received a COPD diagnosis within the municipality of Copenhagen	Patients diagnosed with COPD (ICD-10) between 2003-2007 (incident patients) during a hospital contact and who were receiving COPD maintenance pharmacotherapy	N = 1129 (6.7% had ethnic background other than Danish)	>35	2003 - 2007	No	Yes
Hu (2017) Denmark	Retrospective Cohort Study	Restricted to patients who received a COPD diagnosis within the municipality of Copenhagen	Patients who received an ICD-10 diagnosis of COPD in hospital setting between 2003-2007	N = 2845 (4.6% non- Western ethnic minority)	>35	2003 - 2010	Yes	No
Kim (2016) United States	Cross-Sectional Study	Country-wide	Adults with COPD who completed the 2011- 2012 Behavioral Risk Factor Surveillance System, linked with 2014 Area Health Resource Files	N = 9332	18+	2014 (cross- sectional)	Yes	Yes
Make (2012) United States	Retrospective Analysis of Claims Data	Country-wide	Medical and pharmaceutical claims data of COPD patients enrolled in a health plan, with at least one inpatient claim or two outpatient claims coded for COPD.	n = 43565 commercial insurance, n = 8507 Medicare	40+	July 2004 - June 2005	No	Yes
Melzer (2016) United States	Retrospective Cohort Study	Country-wide	Patients hospitalized within the Veterans Integrated Service Network (VISN)-20 with a primary diagnosis of COPD or admission note indicating COPD exacerbation, and is a current smoker	N = 1511	40+	2005-2012	No	Yes

Mowls (2015) United States	Cross-Sectional Study	Country-wide	Individuals who self-indicated a clinician diagnosis of COPD on the Behavioral Risk Factor Surveillance System (BRFSS)	N = 16615 (n = 13484 with spirometry diagnosis)	18+	2011 (cross-sectional)	No	Yes
							Objective	
Author (Year) Country	Study Design	Study Setting	Population	Participants/records, N*	Patient Age	Study Duration	Assesses variation in health outcomes	Assesses variation in healthcare access
Papaioannou (2014) Greece	Cross-Sectional Survey of respiratory medicine physicians	Multi-centre, Country-wide (199 respiratory physicians interviewed)	COPD patients seen by respiratory physicians in the outpatient setting	N = 6125 (28.7% female)	40+	October 2011 - March 2011	Yes	Yes
Pretto (2012) Australia	Retrospective Medical Record Audit	Hunter New England Region	All admissions for COPD with non-catastrophic or severe comorbidities or complications at 8 acute care hospitals	N = 234 admissions (203 individual patients), 53% of admissions were to the 5 rural hospitals	Mean age = 72 (SD = 10)	July 2008 - September 2008	Yes	Yes
Sansgiry (2019) United States	Retrospective Cohort Study	South-eastern texas region	Medicare beneficiaries with continuous eligibility for 24 months with at least one medical claim for COPD in the baseline year	N = 3142 (79% no coverage gap)	65+	January 2011 - December 2014 (patients followed for 1 year after baseline)	Yes	No
Spitzer (2020) United States	Retrospective Chart Review	Country-wide	Medicaid fee-for-service beneficiaries hospitalized for COPD in 2012	N = 223832 (8% black, 85% NHW)	66+	January 2012 - December 2012	No	Yes
Spitzer (2019) United States	Retrospective Cohort Study	Country-wide	Medicare beneficiaries hospitalized for COPD during 2012	N = 223832	66+	January 2012 - December 2012	No	Yes
Tottenborg (2016) Denmark	Retrospective Cohort Study	Country-wide	Incident hospital clinic outpatients with COPD from the nationwide healthcare registry data	N = 13369	30+	2008 - 2012	Yes	Yes
Trigueros (2019) Spain	Cross-Sectional Study	Multi-centre, Country-wide	All patients consecutively diagnosed with COPD (according to the 2014 GOLD criteria) in primary care centers and pneumology services	N = 1610 (17.9% female)	35+	March 2015 - May 2015 (90 days)	Yes	No
Unni (2021) United States	Cross-Sectional Study	Country-wide	Respondents of the 2018 National Health and Wellness Study (NHWS) who self-reported a physician diagnosis of COPD and who self-reported taking daily prescription medications for COPD	N = 1632 with self-reported COPD	18+	2018 (cross-sectional)	No	Yes
Vanasse (2020) Canada	Observational Cohort Study	Province of Quebec	Patients with an "urgent" COPD (ICD-10) hospitalization for the first time over a 3-year period prior to the 2013 index date and who survived over the follow-up period	N = 2581 survivors (study cohort), n= 616 deceased	40-84	First hospitalization between January 1 and December 31, 2013	Yes	Yes
Vercammen-Grandjean	Retrospective Cohort Study	Country-wide	Eligible patients who participated in PR after hospitalization for an acute exacerbation of COPD	n = 32856 VHA beneficiaries and n =		January 2007- December 2011	No	Yes

(2018) United States				158137 Medicare beneficiaries				
Walker (2016) United Kingdom	Retrospective Cohort Study	150 UK primary care trusts (PCTs)	Adult emergency admissions to medical specialties with a COPD diagnosis (ICD-10) at the time of discharge	N = 245540	16+	2006 - 2008	Yes	No
							Objective	
Author (Year) Country	Study Design	Study Setting	Population	Participants/records, N*	Patient Age	Study Duration	Assesses variation in health outcomes	Assesses variation in healthcare access
Wong (2016) United States	Retrospective Cohort Study	Country-wide (130 VA hospitals)	Patients hospitalized with a principal diagnosis of COPD in one of 130 VA hospitals and dually enrolled in Veterans Affairs (VA) and Medicare	N = 21273	Mean age = 71.4 (SD = 9.6)	October 2008 - September 2011	Yes	No
Wu (2022) United States	Retrospective Chart Review	Single centre (University of Oklahoma Medical Centre)	American Indian (AI) and non-Hispanic White (NHW) adult patients hospitalized for COPD exacerbations	N = 380 (76 AI, 304 NHW)	18+	July 2001 - June 2020	Yes	No
Australian Commission on Safety and Quality in Healthcare (2021) Australia	Retrospective Cohort	Country-wide (data from the National Hospital Morbidity Database)	Adult patients hospitalized for COPD	77 754 hospitalizations for COPD	NR	2017-2018	Yes	No
Northern Norway Regional Health Authority (2022) Norway	Retrospective Cohort	Country-wide	Adult patients with COPD	N = 10,500 for emergency admissions, 49 000 for GP/emergency primary care consultations, 20 500 for outpatient contacts, 2500 for PR	40+	2013-2015	Yes	Yes
Public Health England (2019) England	Retrospective Cohort	Country-wide	Individuals with COPD	NR	NR	2015-2017	Yes	Yes
Canadian Institute for Health Information (2017) Canada	Retrospective Cohort	Province-wide (Alberta)	Adult patients diagnosed with COPD in Alberta, Canada defined as "high-healthcare users"	NR	NR	2012-2014	Yes	Yes
Centers for Disease Control and Prevention (2019) USA	Retrospective Cohort	Country-wide	Adult patients with COPD	NR	45+	2019	Yes	No

NR: not reported; ED: emergency department; IP: inpatient; PR: Pulmonary rehabilitation; GP: general practitioner.

*when reported, the breakdown of study participants by relevant sociodemographic variables are included in this column.

Table 2. Variation in Healthcare Access

Author, year	Study Population	Indicator	Determinants	Major Findings
<i>Prevention: smoking cessation, vaccines</i>				
Melzer 2016	Patients hospitalized within the Veterans Integrated Service Network (VISN)-20 with a primary diagnosis of COPD (ICD-9 codes) or admission note indicating COPD exacerbation, and who is a current smoker	Pharmacy dispensation of any approved smoking cessation medication within 48 hours of hospital discharge (including nicotine patch, short-acting nicotine replacement therapy, varenicline, and bupropion)	Age, Race	Patients with decreased odds of receiving smoking cessation medications were: black (OR 0.34 95% CI 0.12-0.97 and of older age (OR 0.96 95% CI 0.95-0.98).
<i>Diagnosis: spirometry, gp visits</i>				
deMiguelDiez 2015	Individuals who self-identified as having COPD from the 2006 and 2012 National Health Surveys conducted in Spain	GP visit in last 4 weeks	Age, Sex, SES	There was a significant decrease in the number of GP visits from 2006 to 2012 in both women ($p < 0.05$) and men ($p < 0.05$). Women who were living with a partner (OR 1.48, CI 95% (1.04-2.10)) or belonging to a lower social class (OR 1.51, 95% CI (1.07-2.14)) had a higher probability of visiting a GP in the past 4 weeks. Men of higher age (70+) had a higher probability of GP visits (OR 1.92, CI 95% (1.17-3.14)).
Kim 2016	Adults who self-identify with COPD who completed the 2011-2012 Behavioral Risk Factor Surveillance System	Primary Care Provider (PCP) visits	Race, sex	African Americans had a 8.5 pp increased likelihood of PCP visits compared to Caucasians ($p < 0.01$). Males had a 10.4 pp decreased likelihood of PCP office visits compared to females ($p < 0.01$).
Hetlevik 2016	Adults with a GP diagnosis of COPD or asthma	(1) GP consultation rates, (2) spirometry test	Education level	(1) COPD patients in the 40-59 years age group with lower education had a 12% higher GP consultation rate compared to COPD patients with higher education in the same age group ($p < 0.001$). (2) In unadjusted analyses, there was an increase in spirometry rate with higher education. However, no significant association with education differences remained in adjusted models.
Mowls 2015	Individuals who indicated a clinician diagnosis of COPD on the BRFSS	Access to spirometry testing for COPD diagnosis	Age, ethnicity, sex, SES	Patients who were Hispanic ($p < 0.0001$) and younger ($p < 0.0001$) were less likely to be diagnosed with COPD using spirometry. No significant difference in access to spirometry was found for income level, gender, education level, or marital status.
<i>Treatment or Management: medications, pulmonary rehab, outpatient specialist visits, follow-up with general practitioner</i>				
Appleton 2021	Patients diagnosed with COPD, discharged from hospital.	Follow-up with family doctor, respirologist or internal medicine specialist within 7 days of discharge	Age, geography, income, sex	Patients less likely to receive follow-up after COPD discharge were: women (OR 0.89, 95% CI 0.86-0.91), patients without a family doctor (OR 0.38, 95% CI, 0.78-0.85), and rural dwellers (OR 0.86, 95% CI, 0.82-0.90). Patients more likely to receive follow up were younger than 85 and those located in higher income regions.
DiMartino 2017	Patients discharged from hospital with main diagnosis of COPD (ICD-9-CM) or main diagnosis of COPD-related causes and secondary diagnosis of COPD.	Adherence to long-acting bronchodilators (LBs), defined as medication possession ratio $> 80\%$.	Geography (Local Health Districts - LHD), sex, educational level, age	There was significant variation in LB adherence between LHDs (MOR = 1.21, $p = 0.001$) and between GPs working in the same LHD (MOR = 1.28, $p = 0.035$). Lower probability of LB adherence was associated with female sex (OR = 0.56, $p < 0.001$). Compared to 45-54 year olds, 55-64 year olds, 65-74 year olds, and 75-84 year olds had a higher probability of LB adherence (OR = 1.63, OR = 2.11, OR = 1.87, respectively, all $p < 0.001$). Educational level was not associated with LB adherence. Variation in LB adherence by hospital of discharge was considerably greater than other sources of variation (MOR = 1.38, $p < 0.001$).
Hu 2017	Patients diagnosed with COPD (ICD-10) between 2003-2007 (incident patients) during a hospital contact and	Persistence of long-acting bronchodilator (LB) treatment. Defined as the time period from	Ethnicity	In stratified multivariate analysis, patients with ethnic background other than Danish (immigrants or both parents are immigrants) had an increased likelihood of LB combination therapy treatment discontinuation (HR = 1.40, 95% CI (1.03 -

	who were receiving COPD maintenance pharmacotherapy	first prescription date to date of discontinuation. Discontinuation is defined as the time when the interval between two prescriptions was longer than the number of days of cumulative medication supply.		1.90), $p = 0.03$). There was no significant association between LB therapy discontinuation and ethnicity for monotherapy or multiple therapy groups.
Tottenborg 2016	Incident hospital clinic outpatients with COPD from nationwide healthcare registry data	Medication adherence as measured using proportion of days covered (PDC) one year from first contact with the patient	SES	There was a higher risk of poor adherence (defined as $PDC < 0.8$) to inhaled maintenance medications among patients with the following characteristics: unemployed ($aRR=1.36$, 95% CI 1.20-1.54), immigrant status ($aRR=1.29$, 95% CI 1.17-1.44), low income ($aRR=1.07$, 95% CI 1.00-1.16), and living alone ($aRR=1.17$, 95% CI 1.11-1.24). Non-use ($PDC=0$) was associated with immigrant status ($aRR=1.56$, 95% CI 1.17-2.08), living alone ($aRR=1.53$, 95% CI 1.30-1.81), unemployment ($aRR=2.75$, 95% CI 2.09-3.62), and low income ($aRR=1.37$, 95% CI 1.10-1.70).
Unni 2021	Respondents of the 2018 National Health and Wellness Study (NHWS) who self-reported a physician diagnosis of COPD and who self-reported taking daily prescription medications for COPD	Medication adherence according to the Medication Adherence Reasons Scale (MAR-Scale).	Education level, ethnicity/race, gender	Females had a higher rate of non-adherence to daily COPD medications compared to men (F: 60.48% vs. M: 39.52%). For ethnicity/race, non-adherence was 80.13% for white, 4.32% for Hispanic, 10.37% for African American, 1.30% for Asian, and 3.89% for other. For education level, non-adherence to daily COPD medications was 5.83% for less than high school/some high school, 24.41% for high school graduate or equivalent, 45.79% for completed some college/associate degree, 18.36% for college graduate/completed some grad school, and 5.40% for completed graduate school. The rate of non-adherence to daily COPD meds was 92.66% for individuals with health insurance and 95.10% for those who have prescription coverage through insurance. There was no significant difference in top reasons for medication non-adherence and number of days missed by gender or race.
Collins 2018	COPD patients attending outpatient respiratory clinics	(1) Participation in exercise rehabilitation, (2) secondary care outpatient appointments	Deprivation/SES as quantified using the English Index of Multiple Deprivation (IMD).	IMD was inversely related to participation in exercise rehab ($p=0.002$) and access to secondary care outpatient appointments ($p<0.001$).
Hayton 2013	COPD patients invited to attend PR at a community hospital	PR attendance (0 vs >0 attendance) and PR adherence (< or > 63% attendance)	Age, living status, sex	Patients were less likely to attend if they were female (62.8 vs 72.1%) or lived alone (61.4% vs 73.7%). Co-habituating was an independent predictor of attendance (OR 1.82, 1.02-3.24, $p=0.042$). Patients in the youngest and oldest age quartiles were the least likely to complete PR.
Hogg 2012	Patients with a diagnosis of COPD referred to an integrated PR service	(1) Attendance at PR program, (2) completion of PR program	Age, deprivation, sex	(1) There was no significant difference in PR attendance by IMD deprivation quintile. Ages 55-64 (OR 2.17, 95% CI 1.38-3.44) and 65-74 (OR 2.24, 95% CI 1.43-3.5) were associated with increased PR attendance compared to ages 0-54. No significant difference between sexes or for ages 75+. (2) Patients were less likely to complete PR if they were in the 4th deprivation quintile (OR 0.56, 0.33-0.94) or 5th deprivation quintile (OR 0.39, 0.16-0.93). No significant differences in completion when comparing sex or age.
Spitzer 2020	Medicaid FFS beneficiaries hospitalized for COPD in 2012	(1) Pulmonary rehab program density (programs per 1000 FFS beneficiaries), (2) Hospital Referral Region (HRR)-specific risk-standardized rate of PR participation within 6 months of hospitalization	Geography, race	(1) The PR density per 1000 geographically range was 0-0.28. (2) HRR-specific risk-standardized rate of PR within 6 months of hospitalization for COPD ranged from 0.53% to 6.66%. HRR-specific risk-standardized PR rates for NHW= 2.08%, for NHB=1.19%. PR density was associated with higher rates of PR for NHW beneficiaries, but not black beneficiaries.
Spitzer 2019	Medicare beneficiaries hospitalized for COPD during 2012	Participation in PR programs	Age, ethnicity, geography, SES	Individuals less likely to receive PR were: aged 75-84 years (OR 0.7, 95% CI, 0.66-0.75), aged 85+ (OR 0.25, 95% CI, 0.22-0.28), individuals living over 10 miles from a PR facility (OR 0.42, 95% CI, 0.39-0.46), Black or African-American

				patients (OR 0.69 95% CI, 0.6-0.79), Hispanic patients (OR 0.59, 95% CI, 0.47-0.75) and those of lower SES (OR 0.42, 95% CI, 0.38-0.46).
Vanasse 2020	Patients with an "urgent" COPD (ICD-10) hospitalization for the first time over a 3-year period prior to the 2013 index date	Healthcare utilization as described using 5 distinct care trajectory (CT) types	Geography (rurality), sex,	Patients in CT Type 4 (high healthcare use - cardiovascular disease group) were more likely to be older and living in rural communities. Patients in CT Type 5 (high healthcare use - other condition group) were less likely to be rural. Patients in CT Type 3 (high healthcare use - respiratory group) were also older than those in lower utilization groups (CT Types 1 and 2).
Vercammen-Grandjean 2018	Eligible patients who participated in PR after hospitalization for an acute exacerbation of COPD	Participation in PR programs	Age, insurance type, race, sex	Veterans who participated in PR were more likely to be younger ($p<0.001$), white ($p<0.001$), and female ($p=0.004$). Medicare beneficiaries who participated were more likely to be younger ($p<0.001$), male ($p<0.001$), and white ($p<0.001$).
<i>Across the Continuum: multiple indicators</i>				
Dummer 2020	COPD patients seen in the emergency department, or an inpatient hospital stay	(1) Smoking cessation advice provided, (2) offer for referral to PR, (3) contacts with medical/respiratory specialists/nurses	Age, ethnicity geography, race Sex, social deprivation	(1) Rates of smoking and cessation advice were similar across regions. (2) Patients less likely to be offered PR if $>20\text{km}$ away (OR = 0.12, $p=0.04$). No association was observed between age, sex, Māori ethnicity, distance between home and hospital, or deprivation decile with a patient declining PR. (3) In terms of contact with healthcare professionals, no significant difference was observed between Māori and NZ Europeans.
Henoch 2016	COPD patients from the Swedish National Airway Register	(1) Participation in smoking cessation program, (2) participation in patient education program, (3) medications, and (4) contact with physiotherapist, dietician, occupational therapist, or social worker.	Age, living status, sex	(1) In multivariable analysis, there were no factors (sex, age, social status) associated with smoking cessation program participation. (2) Women were more likely to participate in patient education programs ($p<0.001$). Older patients were more likely to be prescribed long-acting anticholinergics (OR 1.25 95% CI 1.19-1.32) and/or a steroid/long-acting beta-adrenoceptor agonist combo (OR 1.19 95% CI 1.13-1.24). There were no other significant associations with sex or social status for medications. Those with an increased probability of having contact with a physiotherapist were women (OR 1.41 95% CI 1.25-1.58) and patients who lived alone (OR 0.71 95% CI 0.62-0.81). Those with an increased probability of having contact with a dietician were women (OR 1.50 95% CI 1.29-1.74), patients of increased age (OR 1.20 95% CI 1.11-1.30), and those who lived alone (OR 0.64 95% CI 0.54-0.76).
Make 2012	COPD patients enrolled in one of 19 health plans across the United States (commercial insurance and Medicare patients)	(1) Prescription of maintenance COPD pharmacotherapy, (2) claim for smoking cessation intervention, (3) claim for influenza vaccination	Insurance coverage	(1) 66.3% of commercial patients and 70.9% of Medicare patients had no prescribed maintenance pharmacotherapy. (2) For commercial insurance, 18% of smokers had a claim for smoking cessation intervention, compared to 9.8% of smokers for Medicare patients. (3) 16.6% of commercial insurance patients had a claim for an influenza vaccination, compared to 23.5% for Medicare.
Papaioannou 2014	COPD patients seen by a respiratory physician in the outpatient setting	(1) Expected number of outpatient visits per year, (2) pharmacotherapy compliance	Sex	Females had a 19% higher expected number of outpatient visits per year compared to males ($p<0.001$). There was no significant difference in therapy compliance ($p=0.854$) between sexes.
Pretto 2012	COPD inpatient admissions with non-catastrophic or severe comorbidities or complications at 8 acute care hospitals	(1) performance of spirometry upon hospital admission, (2) referral to PR	Geography	(1) Wide inter-hospital variability in performance of spirometry at admission (4-58%, $p<0.0001$). Spirometry performance was higher in metro hospitals ($p=0.001$). (2) The inter-hospital range for referral to PR was 0-50% ($p=0.002$). Metro hospitals displayed higher rates of discharge referral to respiratory consultants ($p<0.001$) or to PR programs ($p=0.001$).
Northern Norway Regional Health Authority (2022) Norway	Adults 40+ with COPD	(1) GP/emergency primary care consultation, (2) outpatient contacts (3) PR participants per 10 000 population	Geography	(1) There is significant geographical variation in the use of GP and emergency primary care consultations (approx. 2x increase in highest use referral area compared to lowest use referral area), as well as the use of spirometry at these visits (variation by referral area = 22- 44% spirometry use). (2) Individuals in the highest access rate referral area had approx. 2x higher outpatient contacts compared to the lowest access rate referral area. (3) The highest access rate referral area had approx. 3x increased participants in PR compared to the lowest access rate referral area.
Public Health England (2019) England	Adult patients with COPD	% of patients with COPD (1) on GP registers, (2) referred to PR, (3) with diagnosis confirmed through	Geography	(1) 4.7 fold difference in this metric between the CCGs with the highest and lowest % of patients with COPD, (2) 17.9 fold difference between highest and lowest referral CCG, (3) 1.3 fold difference between the CCGs with the highest and lowest

		post-bronchodilator spirometry testing, (4) with assessment of MRC dyspnoea score within the past 12 months, (5) receiving influenza immunization in the preceding 1 August to 31 March.		number of spirometry tests performed, (4) 1.3 fold difference between the CCGs with the highest and lowest number of MRC score assessments, and (5) 1.2 fold difference between the CCGs with the highest and lowest immunizations.
Canadian Institute for Health Information (2017) Canada	Adult patients diagnosed with COPD in Alberta, Canada defined as “high-healthcare users”	(1) Use of primary care physician, (2) Use of specialist care, (3) Discharge destination	Geography	(1,2) Use of both primary care physicians and specialist care were significantly lower in the North AHS zone compared to the other 4 zones. (3) The North zone also had a lower proportion of individuals with COPD discharged with continuing care compared to all other AHS zones.

SES: socioeconomic status; GP: general practitioner; PR: pulmonary rehabilitation; OR: odds ratio; HR: hazard ratio; aRR: adjusted relative risks; CI: confidence interval; CCG: Clinical Commissioning Group.

Table 3. Variation in Health Outcomes

Author, year	Study Population	Indicator	Determinants	Major Findings
Healthcare Utilization				
deMiguelDiez 2015	Individuals who self-identified as having COPD from the 2006 and 2012 National Health Surveys conducted in Spain	(1) hospital admission, (2) ER visit	SES (marriage status, educational level, social class)	(1,2) No significant associations were identified between either hospital admission or ER visits with marriage status, educational level, or social class.
Dummer 2020	All patients with COPD seen in ED/IP of any hospital across the Southern District Health Board	(1) Hospital LOS, (2) number of hospital admissions	Age, ethnicity geography, race, sex, social Deprivation,	(1) Geometric mean LOS for hospital admissions: urban 3.0 days, rural 4.0 days. The median length of stay for patients from more deprived areas (NZDep deciles 4-10) was 2 days shorter than that for the least deprived areas (NZDep deciles 1-3) ($p=0.04$). (2) There was no association between number of COPD admissions in past 12 months with age, sex, admission location, social deprivation, rurality, distance between home and hospital, or ethnicity.
Kim 2016	Adults with COPD who completed the 2011-2012 Behavioral Risk Factor Surveillance System, linked with 2014 Area Health Resource Files	Hospital/ED visits	Age, income, race, sex	Patients with higher income (\$70000+) had a 6.5 pp decreased likelihood of hospital/ED visits compared to the reference group (\$35000-\$49999 income) ($p=0.008$). Low income (<\$15000) patients had a 6.0 pp increased likelihood of hospital/ED visits compared to the reference group ($p=0.021$). African Americans had a 9.2 pp increased likelihood of hospital/ED visits compared to Caucasians ($p<0.01$). Males had a 3.6 pp decreased likelihood of hospital/ED visits compared to females ($p<0.01$). Older adults (55+) had a 9.9-11.4 pp decreased likelihood of hospital/ED visits compared to younger patients (18-34) ($p<0.01$).
Pretto 2012	All admissions for COPD with non-catastrophic or severe comorbidities or complications at 8 acute care hospitals	(1) Readmission within 28 days, (2) median LOS	Geography	(1) Readmissions within 28 days were higher in rural hospitals (28%) compared to metropolitan hospitals (7%), ($p<0.0001$). (2) Rural and metropolitan hospitals had the same median LOS (5 days).
Sansgiry 2019	Medicare beneficiaries with continuous eligibility for 24 months with at least one medical claim for COPD in the baseline year	(1) hospitalization, (2) ER visits, (3) time to hospitalization	Insurance type	(1) Those with a coverage gap were more likely to have 1+ hospitalizations ($p<0.05$). (2) Those with a coverage gap were more likely to have 1+ ER visits ($p<0.05$). (3) Time to hospitalization was longer in the no coverage gap group ($p=0.04$).
Walker 2016	Adult emergency admissions to medical specialties with a COPD diagnosis (ICD-10) at time of discharge	(1) bed days/1000 PCT population, (2) hospital LOS	Age, geography, SES, sex	(1) The highest quintile PCT group for bed-days/1000 PCT population had 28.9 bed days/1000 PCT population and the lowest quintile PCT group had 13.5 bed days/1000 PCT. No relationship was found between bed days/1000 PCT population and any patient-level factor (sex, rate of deprivation, age). (2) Mean case-mix-adjusted LOS ranged from 5.4 to 12.1 days. Age, gender, deprivation did not vary across quintiles of hospitals with different mean LOS.
Wong 2016	Patients hospitalized with a principal diagnosis of COPD in one of 130 VA hospitals and dually enrolled in Veterans Affairs (VA) and Medicare	30-day all-cause readmission	Distance to nearest hospital (miles between patients' residence zip code and zip code of nearest VA or non-VA hospital accepting Medicare)	In unadjusted analysis, readmission rates decreased with distance to nearest VA hospital (range: 20.9% for 0-4.9-mile category to 18.3% for 40+ mile category) and nearest non-VA hospital (range: 19.9% for 0-4.9-mile category to 17.9% for 40+ mile category). In adjusted analysis, neither distance to nearest VA or non-VA hospital were found to be associated with 30-day all-cause readmission. Greater distance (10+ miles) to VA hospital was associated with a greater conditional probability ($p<0.001$) of readmission to a non-VA hospital.
Australian Commission on Safety and	Adult patients hospitalized for COPD	Number of hospitalizations for COPD per 100,000	Aboriginal/Torres Strait Islander status, geography, SES	Geographical variation: there was an 18.1 times increase in COPD hospitalizations from the lowest to highest rate areas. Hospitalization rate for COPD was 4.8 times higher for Aboriginal and Torres Strait Islander people compared to Australians. Hospitalization rates were increased in remote

Quality in Healthcare (2021) Australia		people of all age (age and sex standardized)		compared to urban areas. Hospitalization rates were also increased in socioeconomically disadvantaged areas, regardless of remoteness category.
Northern Norway Regional Health Authority (2022) Norway	Patients admitted as emergency cases of COPD	(1) Number of emergency admissions for COPD per person per year	Geography	(1) Number of emergency admissions for COPD per person per year ranged from 1.4 to 1.9 between all hospital referral areas.
Canadian Institute for Health Information (2017) Canada	Adult patients diagnosed with COPD in Alberta, Canada defined as “high-healthcare users”	Number of inpatient hospitalizations	Geography	The North zone had significantly higher inpatient hospitalizations compared to the other 4 AHS geographical zones.
<i>Patient Level Outcomes</i>				
Hu 2017	Patients who received a ICD-10 diagnosis of COPD in the hospital setting between 2003-2007	Survival time after diagnosis with COPD	Ethnicity	Patients with non-western ethnic backgrounds had a higher survival probability compared to ethnic Danish patients (HR for death during follow up for non-western patients compared to ethnic Danish patients was 0.330 (95% CI, 0.176-0.618). The hazards of death model was adjusted for age of diagnosis, sex, and socioeconomic position, including education, income, marital status, and employment.
Trigueros 2019	All patients consecutively diagnosed with COPD (according to 2014 GOLD criteria) in primary care centres and pneumology services	(1) Exacerbations, (2) ACOS phenotype, (3) mean (SD) CAT score, (4) impact of disease on quality of life (CAT scores), (5) dyspnea grade (0-4) according to modified MRC scale.	Sex	(1) There was no significant difference ($p=0.390$) between male and female patients for the presence of 2+ moderate-severe exacerbations in the previous year. (2) Female patients had a higher prevalence of the ACOS phenotype ($p=0.002$). Male patients had a higher prevalence of non-exacerbator and exacerbator with chronic bronchitis phenotypes compared to females ($p=0.002$). (3) No significant difference in mean (SD) [95% CI] CAT score between male and female patients ($p=0.546$). (4) No significant difference in COPD impact on quality of life according to CAT score between male and female patients ($p=0.137$). (5) No significant difference in dyspnea grade between male and female patients ($p=0.132$).
Vanasse 2020	Patients with an “urgent” COPD (ICD-10) hospitalization for the first time over a 3-year period prior to the 2013 index date and who survived over the follow-up	Mortality	Age, gender, geography (rurality), material/social deprivation.	Male sex ($p<0.001$) and increased age ($p<0.001$) were associated with 1-year mortality. Rurality ($p=0.7778$), material deprivation ($p=0.1771$), and social deprivation ($p=0.5804$) were not associated with 1-year mortality.
Centers for Disease Control and Prevention (2020) USA	Adult patients 45+ with COPD	Age-adjusted COPD death rates (ICD-10 codes J40-44) per 100 000 population	Geography	Variation between states ranged from 44.5 in Hawaii to 174.6 in Kentucky.
<i>Healthcare Utilization & Patient Level Outcome Measures</i>				
Alexopoulos 2015	COPD patients seen by a respiratory physician in the outpatient setting	(1) exacerbations in preceding year, (2) hospitalizations in preceding year	Age	(1) Patients aged 61-75 and 76+ had 13.7% ($p<0.001$) and 19% ($p<0.001$) fewer exacerbations in preceding year, respectively, compared to patients younger than 60. (2) Patients 61-75 and 76+ had 16.8% ($p=0.017$) and 21.9% ($p<0.009$) higher expected number of hospitalizations, respectively, compared to patients younger than 60.
Bhopal 2015	COPD cases from the Scottish Health and	(1) Death from COPD after COPD hospitalization, (2)	Ethnicity, sex	(1) The HR for death from COPD after COPD hospitalization is lower in Other White British men (90.8), Indian men (39.8), Pakistani men (55.8), and all White minority women (78-89.5) compared to white Scottish men and women (100). (2) HRs for readmission after COPD hospitalization for

	Ethnicity Linkage Study (SHELS)	readmission after COPD hospitalization		most non-white groups were similar or lower than the reference group (Scottish men and women). Only African American women had a higher HR for readmission.
Collins 2018	Individuals with COPD attending outpatient respiratory clinics	(1) Emergency hospitalization, (2) LOS, (3) mortality	SES (English Index of Multiple Deprivation)	(1) IMD was independently associated with increased emergency hospitalizations ($p=0.001$). (2) IMD was independently associated with increased LOS ($p=0.026$). (3) Mortality at 1 year-post assessment was significantly related to IMD (p for linear trend= 0.040).
Papaioannou 2014	COPD patients seen by 1 of 199 respiratory physicians interviewed	(1) hospital admissions in preceding year, (2) ICU hospitalizations, (3) number of exacerbations	Sex	(1) Hospital admissions in the preceding year did not significantly differ between sexes ($p=0.116$). (2) ICU hospitalization was higher in males ($p=0.007$). (3) No significant difference was found between sexes for number of COPD exacerbations ($p=0.826$).
Tottenborg 2016	Incident hospital clinic outpatients with COPD from the nationwide healthcare registry data	(1) Exacerbations, (2) hospital admissions, (3) deaths	SES	(1) Exacerbations were associated with low education ($aHR=1.21$, 95% CI 1.10-1.35). (2) Hospital admissions were associated with low education ($aHR=1.22$, 95% CI 1.07-1.38) and low income ($aHR=1.20$, 95% CI 1.09-1.32). (3) Death was association with low income ($aHR=1.11$, 95% CI 0.99-1.25)
Wu 2022	American Indian (AI) and non-Hispanic White adult patients hospitalized for COPD exacerbations	(1) Hospital LOS, (2) ICU days, (3) invasive mechanical ventilator use, (4) discharge disposition, (5) death	Race	(1) AI race had longer ICU stays ($OR=1.43$, $p<0.001$). AI and NHW patients did not significantly differ in hospital LOS. (2) AI race had higher odds of requiring ICU care ($OR=2.37$, $p=0.002$). (3) AI race had higher odds of requiring invasive mechanical ventilator use ($OR=2.75$, $p=0.002$) and 137.3% increase in days on invasive mechanical ventilator ($p<0.001$). (4,5) No significant difference was found between AI and NHW patients.
Public Health England (2019) England	Adult patients with COPD	(1) primary and contributory mortality, (2) Use of non-invasive ventilation, (3) mortality rate of patients who died within 30 days of emergency hospital admission, (4) rate of emergency admissions to hospital for COPD per population, (5) median LOS of emergency admissions to hospital for COPD	Geography	(1) 4.0 fold difference between CCGs for primary mortality and 4.5 fold difference between CCGs for contributory mortality. (2) 8.0 fold difference between CCGs. (3) 15.5 fold difference between CCGs. (4) 5.6 and (5) 5.0 fold differences between CCGs, respectively.

ER: emergency department; IP: inpatient; SES: socioeconomic status; PCT: Primary Care Trust; LOS: length of stay; SD: standard deviation; OR: odds ratio; HR: hazard ratio; aHR: adjusted hazard ratio; AHS: Alberta Health Services; CCG: Clinical Commissioning Group.

Figure Legends

Figure 1. PRISMA Flow Diagram

Two hundred and fifty-three citations were identified from the electronic database search. After the abstract review, 187 citations were excluded, leaving 66 studies for full-text review. Of the 66 articles assessed in full-text, 36 articles were excluded, and 30 articles were included for data extraction and final qualitative synthesis. Five reports were also included from the grey literature.

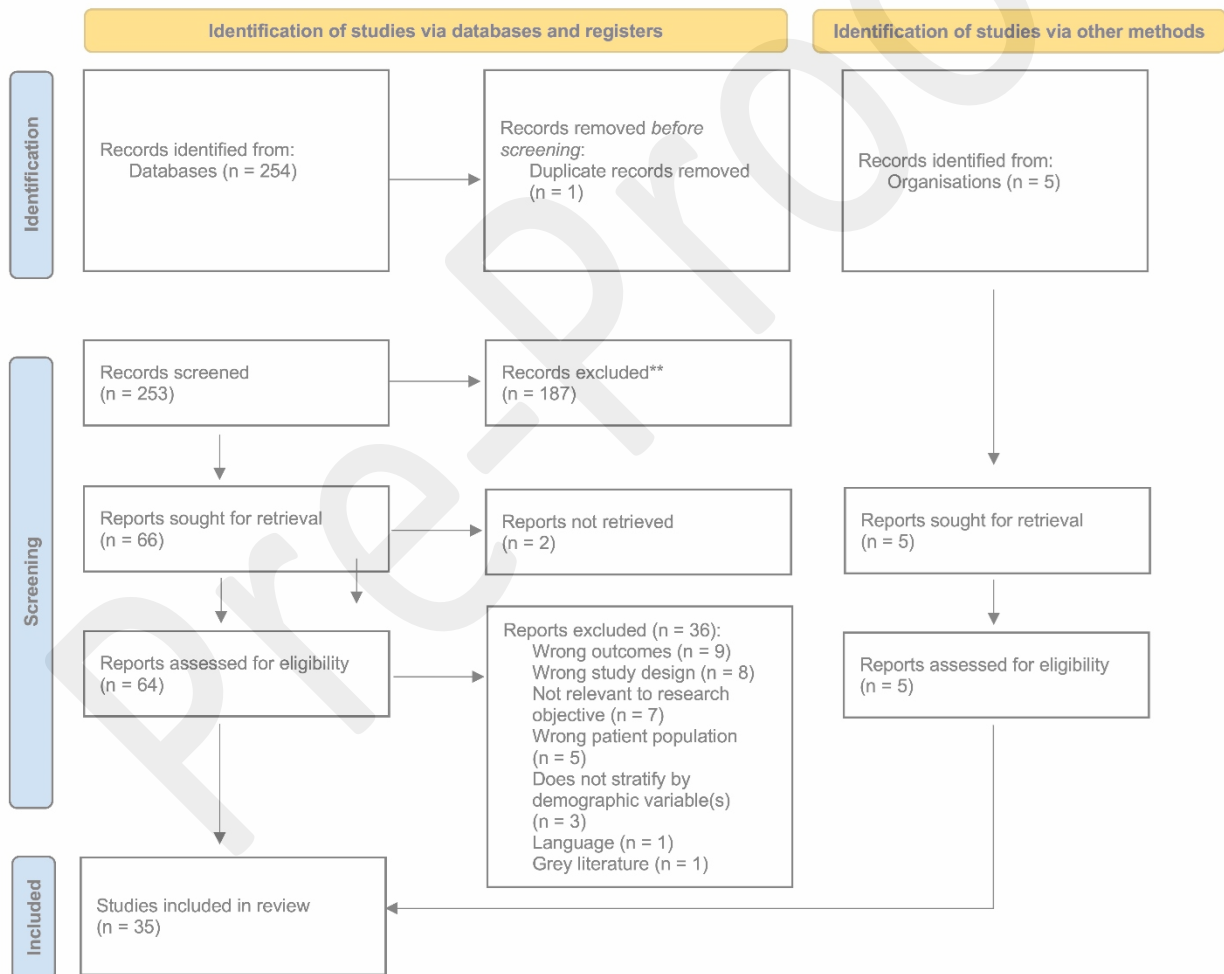


Figure 2. Summary of Identified Variation in Healthcare Access and/or Outcomes by Sociodemographic Determinants

Each coloured dot represents one study/report included in this rapid review in which statistically significant variation was identified for that determinant of variation and access or outcome indicator. Blue dots represent studies/reports with an N>1000. Orange dots represent studies/reports with an N=100-1000. Grey dots represent studies/reports in which the N value was not reported.

	Health Care Access Indicator										Health Care Outcome Indicator									
Determinant of Variation	Smoking Cessation	GP/PCP visit	Specialist Care	Follow-up after Hospital Discharge	Spirometry Testing	Pharmacotherapy Adherence	Pulmonary Rehabilitation	Influenza Vaccination	Discharge Destination	COPD exacerbations	Inpatient Hospitalizations	Hospital LOS	Emergency Department Visits	ICU hospitalization	Readmission to Hospital	Survival Time after Diagnosis	CAT	Mortality	Mechanical Ventilator Use	Discharge Disposition
Age	●	●		●		●●	●●●			●	●●		●					●		
SES	●	●●●		●	●	●●●	●●●	●		●	●●●	●	●●●●	●				●		
Sex		●●		●		●●	●				●		●		●			●●●		
Geography		●●●●		●	●●●	●	●●●●	●	●		●●	●●	●●●		●●●●			●●●●	●	
Ethnicity/Race	●	●				●●	●●●●				●●		●	●		●			●	

Online Supplement

Appendix 1

Search Summary:

Databases Used: Medline and Embase

Limits: English, published in the last 10 years, North America, Europe, Scandinavian countries, Australia and NZ, journal articles and reviews only

Search Strategies:

Embase

- 1 "variation* in care".ti. (110)
- 2 exp healthcare disparity/ (20160)
- 3 exp health disparity/ (28190)
- 4 exp healthcare access/ (87914)
- 5 "health inequit*".ti. (697)
- 6 or/1-5 (129534)
- 7 exp treatment outcome/ (2028517)
- 8 exp outcome assessment/ (725612)
- 9 exp health status/ (282830)
- 10 exp "length of stay"/ (240113)
- 11 exp hospitalization/ (467067)
- 12 exp disease exacerbation/ (159996)
- 13 exp disease severity/ (2065865)
- 14 exp hospital discharge/ (161246)
- 15 exp disease management/ (3440383)
- 16 exp convalescence/ (54983)
- 17 exp "quality of life"/ (590631)
- 18 exp morbidity/ (406580)
- 19 exp mortality/ (1265176)
- 20 or/7-19 (6503223)
- 21 exp chronic obstructive lung disease/ (158677)

- 22 COPD.ti. (40989)
 - 23 or/21-22 (164738)
 - 24 6 and 20 and 23 (872)
 - 25 limit 24 to (english language and exclude medline journals and (article or "review") and last 10 years) (68)
 - 26 exp Canada/ or (Canad* or "British Columbia" or "Colombie Britannique" or Alberta* or Saskatchewan or Manitoba* or Ontario or Quebec or "Nouveau Brunswick" or "New Brunswick" or "Nova Scotia" or "Nouvelle Ecosse" or "Prince Edward Island" or Newfoundland or Labrador or Nunavut or NWT or "Northwest Territories" or Yukon or Nunavik or Inuvialuit).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word] (355965)
 - 27 exp mexico/ or exp united states/ or chile/ or Costa Rica/ or Colombia/ or austria/ or belgium/ or exp baltic states/ or estonia/ or latvia/ or lithuania/ or czech republic/ or hungary/ or poland/ or slovakia/ or slovenia/ or exp france/ or exp germany/ or united kingdom/ or exp england/ or northern ireland/ or exp scotland/ or wales/ or greece/ or exp ireland/ or exp italy/ or luxembourg/ or netherlands/ or portugal/ or exp "scandinavian and nordic countries"/ or exp denmark/ or finland/ or iceland/ or norway/ or sweden/ or spain/ or switzerland/ or exp australia/ or exp new zealand/ or (Australia or Austria or Belgium or Canada or Chile or Colombia or "Costa Rica" or "Czech Republic" or Denmark or Estonia or Finland or France or Germany or Greece or Hungary or Iceland or Israel or Italy or Japan or Latvia or Lithuania or Luxembourg or Mexico or Netherlands or New Zealand or Norway or Poland or Portugal or "Slovak Republic" or Slovenia or Spain or Sweden or Switzerland or Turkey or "United Kingdom" or England or Ireland or Scotland or Wales or "United States").mp. (5509040)
 - 28 or/26-27 (5591041)
 - 29 25 and 28 (21)
- Medline
- 1 "variation* in care".ti. (80)
 - 2 exp Healthcare Disparities/ (21315)
 - 3 exp Health Status Disparities/ (19083)
 - 4 exp Health Services Accessibility/ (122876)
 - 5 exp Health Inequities/ (19269)
 - 6 exp "Health Services Needs and Demand"/ (62191)
 - 7 exp "Patient Acceptance of Healthcare"/ (169562)
 - 8 exp "Facilities and Services Utilization"/ (1235)
 - 9 or/1-8 (363102)
 - 10 exp Treatment Outcome/ (1204481)
 - 11 "health outcome*".ti. (7581)

- 12 exp Outcome Assessment, Healthcare/ (1295992)
- 13 exp "Length of Stay"/ (100101)
- 14 exp Hospitalization/ (281565)
- 15 exp Patient Discharge/ (37107)
- 16 exp Disease Progression/ (203431)
- 17 exp Disease Management/ (82480)
- 18 exp Convalescence/ (3926)
- 19 exp "Quality of Life"/ (247300)
- 20 exp Morbidity/ (631792)
- 21 exp Mortality/ (419229)
- 22 or/10-21 (2765915)
- 23 exp Pulmonary Disease, Chronic Obstructive/ (64135)
- 24 COPD.ti. (21551)
- 25 or/23-24 (68325)
- 26 9 and 22 and 25 (803)
- 27 limit 26 to (english language and (evaluation study or government publication or journal article or meta analysis or multicenter study or observational study or "review" or "systematic review") and last 10 years) (511)
- 28 exp Canada/ or (Canad* or "British Columbia" or "Colombie Britannique" or Alberta* or Saskatchewan or Manitoba* or Ontario or Quebec or "Nouveau Brunswick" or "New Brunswick" or "Nova Scotia" or "Nouvelle Ecosse" or "Prince Edward Island" or Newfoundland or Labrador or Nunavut or NWT or "Northwest Territories" or Yukon or Nunavik or Inuvialuit).mp. (263928)
- 29 exp mexico/ or exp united states/ or chile/ or Costa Rica/ or Colombia/ or austria/ or belgium/ or exp baltic states/ or estonia/ or latvia/ or lithuania/ or czech republic/ or hungary/ or poland/ or slovakia/ or slovenia/ or exp france/ or exp germany/ or united kingdom/ or exp england/ or northern ireland/ or exp scotland/ or wales/ or greece/ or exp ireland/ or exp italy/ or luxembourg/ or netherlands/ or portugal/ or exp "scandinavian and nordic countries"/ or exp denmark/ or finland/ or iceland/ or norway/ or sweden/ or spain/ or switzerland/ or exp australia/ or exp new zealand/ or (Australia or Austria or Belgium or Canada or Chile or Colombia or "Costa Rica" or "Czech Republic" or Denmark or Estonia or Finland or France or Germany or Greece or Hungary or Iceland or Israel or Italy or Japan or Latvia or Lithuania or Luxembourg or Mexico or Netherlands or New Zealand or Norway or Poland or Portugal or "Slovak Republic" or Slovenia or Spain or Sweden or Switzerland or Turkey or "United Kingdom" or England or Ireland or Scotland or Wales or "United States").mp. (3872985)
- 30 or/28-29 (3961575)
- 31 27 and 30 (233)
- 32 remove duplicates from 31 (232)

Appendix 2

Inclusion Criteria	Exclusion Criteria
Published in the last 10 years	Published >10 years ago
Geographic location is North America, Europe, Scandinavian countries, Australia, or New Zealand.	Geographic location other than North America, Europe, Scandinavian countries, Australia, or New Zealand.
English	Language other than English
Systematic review or observational studies	Conference proceedings, editorials, guidelines, or policies
Population: Adult Patients with COPD	Non-adult population Other conditions/respiratory diseases besides COPD
Study Objective: <ul style="list-style-type: none"> To evaluate and/or define healthcare access and/or related health outcomes for individuals with COPD To assess potential variation or disparities in healthcare access (access to pulmonary rehab, access to pulmonary function testing, access and adherence to COPD medications, access to palliative/continuing care, access to GP, access to pulmonologist/specialist) To assess potential variation/disparities in healthcare outcomes (inpatient hospitalization rate and length of stay, ED visits, readmissions, mortality rates) 	Primary study objective evaluates the effectiveness of an intervention and/or quality improvement initiative/programme
Differential patterns/variation in healthcare access/outcomes are assessed by demographic factors, including: <ul style="list-style-type: none"> Geography Ethnicity Age Sex/Gender SES Educational level 	

Appendix 3. Newcastle Ottawa Scale Risk of Bias Assessment of Cohort Studies

Author (Year)	Selection				Comparability	Outcome			Risk of Bias Score (/9)
	Representative -ness of exposed cohort	Selection of non- exposed cohort	Ascertainment of Exposure	Outcome of Interest not Present at Start of Study	Comparability of Cohorts	Assessment of Outcome	Sufficient Follow-up Length	Adequacy of Follow-up	
Published Cohort Studies									
Appleton (2021)	(a) ★	(a) ★	(a) ★	(a) ★	(a), (b) ★★	(b) ★	(a) ★	(a) ★	9
Bhopal (2015)	(b) ★	(a) ★	(a) ★	(b)	(a), (b) ★★	(b) ★	(a) ★	(d)	7
Collins (2018)	(c)	(b)	(a) ★	(b)	(a), (b) ★★	(b) ★	(a) ★	(d)	5
DiMartino (2017)	(a) ★	(a) ★	(a) ★	(a) ★	(a), (b) ★★	(b) ★	(a) ★	(a) ★	9
Dummer (2020)	(b) ★	(a) ★	(a) ★	(b)	(a), (b) ★★	(b) ★	(a) ★	(c)	7
Hayton (2013)	(c)	(a) ★	(a) ★	(a) ★	(a), (b) ★★	(b) ★	(a) ★	(b) ★	8
Hogg (2012)	(c)	(a) ★	(d)	(a) ★	(a), (b) ★★	(d)	(a) ★	(d)	5
Hu (2017a)	(b) ★	(a) ★	(a) ★	(a) ★	(a), (b) ★★	(b) ★	(a) ★	(d)	8
Hu (2017b)	(b) ★	(a) ★	(a) ★	(a) ★	(a), (b) ★★	(b) ★	(a) ★	(d)	8
Make (2012)	(a) ★	(a) ★	(a) ★	(a) ★	(a) ★	(b) ★	(a) ★	(d)	7
Melzer (2016)	(b) ★	(a) ★	(a) ★	(a) ★	(a), (b) ★★	(b) ★	(a) ★	(d)	8
Pretto (2012)	(b) ★	(a) ★	(a) ★	(b)	(a) ★	(b) ★	(b)	(d)	5
Sansgiry (2019)	(b) ★	(a) ★	(a) ★	(a) ★	(a), (b) ★★	(b) ★	(a) ★	(a) ★	9

Author (Year)	Selection				Comparability	Outcome			Risk of Bias Score (/9)
	Representative -ness of exposed cohort	Selection of non- exposed cohort	Ascertainment of Exposure	Outcome of Interest not Present at Start of Study	Comparability of Cohorts	Assessment of Outcome	Sufficient Follow-up Length	Adequacy of Follow-up	
Spitzer (2020)	(b) ★	(a) ★	(a) ★	(a) ★	(a), (b) ★★	(b) ★	(a) ★	(d)	8
Spitzer (2019)	(b) ★	(a) ★	(a) ★	(a) ★	(a), (b) ★★	(b) ★	(a) ★	(d)	8
Tottenborg (2016)	(a) ★	(a) ★	(a) ★	(a) ★	(a), (b) ★★	(b) ★	(a) ★	(d)	8
Vanasse (2020)	(a) ★	(a) ★	(a) ★	(a) ★	(a), (b) ★★	(b) ★	(a) ★	(a) ★	9
Vercammen- Grandjean (2018)	(a) ★	(a) ★	(a) ★	(a) ★	(a), (b) ★★	(b) ★	(a) ★	(d)	8
Walker (2016)	(b) ★	(a) ★	(a) ★	(b)	(a), (b) ★★	(b) ★	(a) ★	(d)	7
Wong (2016)	(b) ★	(a) ★	(a) ★	(b)	(a) ★	(b) ★	(a) ★	(a) ★	7
Wu (2022)	(c)	(a) ★	(a) ★	(b)	(a), (b) ★★	(b) ★	(a) ★	(a) ★	7
Grey Literature Cohort Studies									
Australian Commission on Safety and Quality in Healthcare (2021)	(a) ★	(a) ★	(a) ★	(b)	(a), (b) ★★	(b) ★	(a) ★	(d)	7
Northern Norway Regional Health Authority (2022)	(b) ★	(a) ★	(a) ★	(b)	(a), (b) ★★	(b) ★	(a) ★	(d)	7
Public Health England (2019)	(b) ★	(a) ★	(d)	(b)	(a) ★	(d)	(a) ★	(d)	4

Author (Year)	Selection				Comparability	Outcome			Risk of Bias Score (/9)
	Representative -ness of exposed cohort	Selection of non- exposed cohort	Ascertainment of Exposure	Outcome of Interest not Present at Start of Study	Comparability of Cohorts	Assessment of Outcome	Sufficient Follow-up Length	Adequacy of Follow-up	
Canadian Institute for Health Information (2017)	(a) ★	(a) ★	(a) ★	(b)	(a) ★	(b) ★	(a) ★	(d)	6
Centers for Disease Control and Prevention (2019)	(b) ★	(a) ★	(d)	(b)	(a) ★	(d)	(a) ★	(d)	4

Interpretation of Risk of Bias Score

Very Good Studies: 8-9 points

Good Studies: 6-7 points

Satisfactory Studies: 4-5 points

Unsatisfactory Studies: 0 to 3 points

Appendix 4. Newcastle Ottawa Scale Risk of Bias Assessment of Cross-Sectional Studies

Author (Year)	Selection				Comparability	Outcome		Risk of Bias Score (/10)
	Representativeness of the sample	Sample Size	Non-respondents	Ascertainment of Exposure	Confounding Factors Controlled	Assessment of Outcome	Statistical test	
Alexopoulos (2015)	(a) ★	(c)	(c)	(b) ★	(a) ★★	(b) ★★	(a) ★	7
deMiguelDiez (2015)	(a) ★	(c)	(a) ★	(c)	(a) ★★	(c) ★	(a) ★	6
Henoch (2016)	(b) ★	(c)	(c)	(a) ★★	(a) ★★	(b) ★★	(a) ★	8
Hetlevik (2016)	(a) ★	(c)	(c)	(a) ★★	(a) ★★	(c) ★	(a) ★	7
Kim (2016)	(b) ★	(c)	(a) ★	(b) ★	(a) ★★	(b) ★★	(a) ★	8
Mowls (2015)	(a) ★	(c)	(c)	(c)	(a) ★★	(c) ★	(a) ★	5
Papaioannou (2014)	(b) ★	(c)	(a) ★	(a) ★★	(a) ★★	(b) ★★	(a) ★	9
Trigueros (2019)	(b) ★	(a) ★	(c)	(b) ★	(a) ★★	(b) ★★	(a) ★	8
Unni (2021)	(b) ★	(c)	(c)	(b) ★	(a) ★★	(c) ★	(a) ★	6

Interpretation of Risk of Bias Scores

Very Good Studies: 9-10 points

Good Studies: 7-8 points

Satisfactory Studies: 5-6 points

Unsatisfactory Studies: 0 to 4 points