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Integrative Review

Instruments Measuring Risk Factors Predicting Hospitalization for Chronic Obstructive Pulmonary Disease: An Integrative Review

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Abstract

Introduction

The purpose of this paper is to determine which psychometric instruments have been used to identify risk factors to predict hospitalizations in patients with chronic obstructive pulmonary disease (COPD).

Methods

An integrative literature review was conducted on published studies carried out in the United States (US) and internationally, measuring risk factors related to hospital admission and readmission for COPD from 2002 to 2015. An extensive search was done using electronic databases PubMed, CINAHL, MEDLINE, and Google Scholar to find studies published in English, adults 18 years and older. Systematic manual searches produced additional empirical studies.

Results

Of the 29 studies screened from electronic data bases the literature search (n = 6) and systematic manual searches (n = 9) met the criteria. The outcome yielded (n = 15) articles that met the criteria, reflecting heterogeneity in types of measurements involving clinical data, psychosocial, and socioeconomic variables in the final data set.

Conclusions

This integrative review found a multitude of psychometric instruments for assessing risk factors for COPD admission, which highlights the need for a comprehensive and concise instrument to identify patients at risk for future hospital admissions in the acute care setting. Due to a limited number of studies examining risk factors related to COPD admission, the literature search span was conducted from 2002 to 2015.

Keywords: COPD; Admission; Risk Assessment; St. George's Respiratory Questionnaire; Quality of Life

Introduction

When a patient with COPD comes to the emergency department (ED) for treatment, a tenuous balance exists in deciding, in less critical exacerbations of COPD (ECOPD), whether or not to admit the patient? Starting 2015 new regulations stipulating what is paid from healthcare funds has increased the need for better predictors for hospitalization [1]. Medicare and Medicaid Services define a hospital readmission as an admission within 30 days for the same diagnosis [2]. Based on new regulations by the Centers for Medicare and Medicaid, (section 3025 of the Affordable Care Act, section 1886q) individuals who are readmitted to the hospital for an acute exacerbated COPD, the hospital will not be paid or not paid in full for that hospitalization [2]. Medicaid and Medicare are government-sponsored healthcare programs in the United States (US) with stipulations on payment which includes who is covered and how much will be paid for in health services [2]. Adding to this dilemma, published studies on measurements to identify risk factors related to hospitalization for individuals with COPD, reveal there is no consensus on what measurement instruments best predict hospitalization [3-6].

The Study Design

The aim of this integrative review of the literature is to present findings from studies using instruments to determine risk factors predicting hospitalization among patients with COPD. COPD is a disease with worse implications among individuals of urban, low socioeconomic status. These vulnerable individuals are more likely to have high risk factors with frequent hospitalization or readmission for the same previous diagnosis of COPD [4, 7, 8]. Risk factors can be measured and can predict the likelihood of patients with COPD being hospitalized or readmitted (either of these being the result) for treatment of their COPD. For this integrative review a *theoretical definition of risk factors for hospitalization of patients with COPD will include identified variables that are related to physical, functional, psychological, and socioeconomic status*. An *operational definition of risk factors for hospitalization for patients with COPD having dyspnea and hypoxia,* can be obtained by collecting data using scales that determine most causative risk factors related to patients with COPD hospitalizations.

Search Method

Due to a limited number of studies examining psychometric measures of risk factors related to COPD admission, the literature search span was conducted from 2002 to 2015**.** Two search strategies were conducted to identify articles describing instruments that measure risk factors for hospital admission and readmission to the hospital for COPD or exacerbated COPD treatment. Inclusion criteria: human, English, adults 18 year of age and older, risk factors for COPD admission. Exclusion criteria: studies that used an intervention and those using a machine-learning method such as Random Forest (due to lack of external cross-validation). The first search from 2002 to 2014 used MEDLINE, CINAHL, PubMed and the Cochrane Library. The search terms used for each database included MEDLINE: confounding variables (epidemiology), pulmonary disease, chronic obstructive, risk assessment, hospitalization, inpatients; patient discharge; risk factors; epidemiologic measurements; CINAHL: research instruments, pulmonary disease, chronic obstructive independent variable, risk assessment, hospitalization, inpatients, patient discharge education; PubMed: hospital predictors, chronic pulmonary disease, COPD, hospitalization, unplanned readmission, risk of admission, readmission; MeSH terms: hospitals; hospital; predictors; pulmonary disease, chronic obstructive, and the Cochrane Library: risk factors; predictors; chronic obstructive pulmonary disease; hospitalization; instruments to measure. MEDLINE: risk assessment, pulmonary disease, chronic obstructive produced 716 articles. CINAHL: risk assessment, pulmonary disease, chronic obstructive found 144 articles. PubMed: pulmonary disease, chronic obstructive MeSH and risk factors MeSH found 23 articles. From these searches, a total of 883 articles, 6 articles were obtained that met the inclusion criteria for adults 18 years and older, having COPD, male or female, and studies published in the US or other countries available in the English language.

A second search strategy was conducted using the same inclusion criteria to increase the number of studies measuring risk factors; hospital admission and readmission to the hospital for COPD treatment using MEDLINE, CINAHL, PubMed, Cochrane, and Google Scholar. Google Scholar searched with phrase: "COPD predictive instrument for hospital admission" and the phrase "St. George's Respiratory Questionnaire to measure risk factor COPD and hospitalization" between 2002 to 2015 articles. A total of 13,283 articles were obtained and screened. Articles were selected if they met the inclusion criteria for adults 18 years and older, having COPD, male or female, hospital admission for COPD, risk factors predictive of hospital admission, and studies published in the US or other countries available in the English language. Sixty-seven pages were screened and 8 articles were obtained from hand searches of the retrieved Google references. In addition, one article met criteria from MEDLINE.

Search Outcome

In total, 15 studies were included from the search strategy that met the inclusion criteria. The select sample of studies were from the following countries: Canada, India, Portugal, Scotland, Singapore, Spain, United Kingdom (UK), and the United States (US). Type of studies included: prospective (n =11), case control (n =1), observation (n =1), longitudinal (n = 1), and historical cohort (n=1). Quality appraisal used The Center for Evidence-Based Medicine Levels of Evidence to evaluate and rate the level of evidence for each study [9]. Table 1.

Instrument/references	Research subjects/Theoretical framework	Description	Method of Measure	Validity/Reliability	Findings/Level of evidence
1 A multidimensional grading system of: body mass index, airflow obstruction, dyspnea (score from the modified Medical Research Council (MRC), and exercise capacity (distance walked in 6 mins) scores (BODE index) for each as predictor of hospitalization for COPD and Global Initiative for Chronic Obstructive Lung Disease (GOLD). [10].	Patients with COPD from an outpatient clinic at a single university-affiliated hospital. N = 127 Mean age +/- SD: 70.9 years +/- 8.3 Male/Female 116/11 Exacerbation of COPD (ECOPD) defined as dyspnea, sputum production, or sputum purulence. Theoretical Framework not mentioned	Historical cohort study BODE Index 9 was calculated for all patients during the 4 week enrollment period. GOLD scale: Four stages of COPD severity compared to BODE Index scores.	Outcome measure- number of hospital admission for COPD during the follow-up.	Poisson regression model used to quantify and compare the relationship between FEV_1 and BODE scores with number of hospital admissions. BODE score significant effect on number of hospital admissions: Incidence rate ratio 1.20; 95% confidence interval 1.15 to 1.25; $p < 0.001$; FEV_1% of predicted on number of hospital admissions (incidence rate ratio, 0.08, 95% CI, 0.04 to 0.16), $p < 0.001$.	Findings from a follow-up of 16.2 months (mean): 47% of patients had one hospital admissions and 17% died (result of respiratory failure). BODE Index better predictor of COPD hospitalization than FEV_1 alone. BODE Index better predictor for hospital admission (pseudo r^2 was 0.16) than GOLD staging of COPD severity. Levels of evidence: 2b

2 Standardized data collection instrument for predictors of hospital admission for ECOPD. Tools: GOLD, Glascow Coma Scale (GCS) and Charlson Comorbidity Index (CCI). [4].	16 public health: emergency departments (ED). N = 2,487 72.8 mean age, 91% males 1,537 (61.8%) were admitted to the hospital and 950 (38.2%) were discharged. Theoretical Framework not mentioned	Prospective multicenter cohort study Standardized data collection: demographic items, assessed compliance to prescribed treatments, level of consciousness per GCS 15 and no less, paradoxical breathing and/or resting dyspnea, use of accessory muscles, lower extremity edema, respiratory rate, blood pressure, heart rate, oximetry and/or arterial blood gases. Interview 7 days post- discharge and for patients admitted to the hospital; interview before discharge to assess: level of support at home, assistance with self-care, severity of dyspnea, physical activity, baseline treatment, comorbidities using CCI, and number of hospital admissions for ECOPD the previous year.	Data from standardized data instrument predictive of hospital admission as compared to GOLD guidelines. Compare results of the standardized data collection tool to GOLD recommendations.	Multivariate analysis of factors predictive of ECOPD hospital admission. The predictive capacity for the model: Area under the curve 0.89 and 0.83. Previous hospital admission for ECOPD (OR 2.03, 95% CI 1.32 - 3.11); resting dyspnea (OR 3.05, 95% CI 2.39 – 3.88); altered $PaC0_2$ > 65mmHg (OR 6.98, 95% CI 4.03 – 12.09). Goodness of fit for the tool at ED arrival and decision time achieved p values 0.66 and 0.10 in the Hosmer Lemeshow test, respectively.	Results for factors most predictive of hospital admission: 3 or more hospitalizations for ECOPD in last year, resting dyspnea, altered dyspnea, partial arterial carbon dioxide pressure ($PaC0_2$) at time of ED arrival. Results of standardized data instrument indicated agreement in part with GOLD recommendations. Levels of evidence: 1b

3 Evaluation of COPD longitudinally to identify predictive surrogate endpoints (ECLIPSE), St. George's Respiratory Questionnaire (SGRQ-C), and GOLD. [11].	Adults: 40 - 75 years of age N = 2,138 in cohort Female % = 35% Male % = 65% Theoretical Framework not mentioned	Longitudinal evaluation: follow up at 3 months, 6 months, and every 6 months after, for a sum of 3 years, to predict surrogate endpoints. Examined time to first incidence of hospital admission.	Kaplan-Meier curves and Cox proportional hazard regression adjusted for confounders. ECLIPSE, SGRQ-C, and GOLD results.	Summary of rate per person per year (PPPY). Hazard ratio 2.71, 95% CI, 2.24 – 3.29, $p < .001$ for highest risk: previous hospitalizations for exacerbations, Hypercapnia p 0.1, CI 0.84- 5.63, poor quality of life $p < 0.05$, CI 1.03-5.41. Hosmer-Lemeshow Goodness of fit test model well calibrated p 0.85.	Total 1,452 hospitalizations for ECOPD. Highest risk for admission: previous hospitalization for exacerbation of COPD. Moderate risk: severe airflow limitation, older age, poor general health, severity of emphysema, and leukocytosis. Levels of evidence: 1b
4 Baseline clinical data, SGRQ, Hospital Anxiety and Depression Scale (HADS), CCI, Carstairs index (socioeconomic deprivation), and social support measured with self-report instrument, Enhancing Recovery in Coronary Heart Disease (ENRICHD) Social Support Inventory (ESSI). [7]	Adults COPD patients admitted for AECOPD to one of 3 acute hospitals UK referred to nurse led Early Discharge Services (EDS) N = 79 Age = 65.3 +/- 9.9 Male % = 44(56) Female % = 35 (44) Theoretical Framework not mentioned	Prospective cohort Impact of psychosocial risk factors for readmission followed by EDS after AECOPD and follow up one year after	Physiologic risk factors: baseline 3 and 12 months. Lung function (FEV_1), comorbidities, incidence of previous hospital admissions, medications, sociodemographics, SGRQ), HADS, Carstairs index (low social class, lack of car, unemployment, and overcrowding), and social support with ESSI.	Univariate logistic regression analysis of baseline psychosocial factors (SGRQ, HADS anxiety, ESSI, and Carstairs). Age, lung function, and greater proportion with readmissions (compared to those not readmitted) revealed significance $p < 0.05$. Cox regression using FEV_1 % adjusted for age and sex as predictor for AECOPD, alone was significant predictor of time to readmission or death (hazard ratio 0.97, 95% confidence interval 0.95 to 0.99, $p = 0.003$).	Age, lung function, and previous hospital admission strongest predictors of readmission for AECOPD. Researchers noted that the HADS does not measure for panic attacks which is a documented experience of many COPD patients. Levels of evidence: 3a

5 SGRQ, demographic data, socioeconomic data, and nutritional parameters. State-trait anxiety inventory (STAI-S/T). [13]	Adults with moderate to severe COPD (FEV_1/FVC </ 70, FEV_1 </ 50%) with high consumption (HC) of health care services; emergency care and hospital admission N = 32 cases, age 72 years +/- 7 N = 32 control, age 71 years +/- 9 N = 64 All males, mean 72 years of age Theoretical Framework not mentioned	Case-control Cases with COPD-HC of health care services required in one year was defined as: 1) 2 or more hospitalizations, 2) 3 or more emergency visits, or 3) one admission and 2 emergency visits	Demographic data: distance from hospital (kilometers) Clinical data: respiratory symptoms, comorbidities, and any complications related to COPD. Dyspnea assessed by Mahler's baseline dyspnea index (BDI) Socioeconomic data: 1) low socioeconomic index and limited education < 10 years, 2) intermediate socioeconomic level, 3) high socioeconomic > 14 years education, medium to high income (Prescott, et al, 1999). Anxiety, health-related quality of life scored with SGRQ, nutritional parameters Therapeutic aspects: forced spirometry, resting arterial blood gases, maximal respiratory muscle pressures, and 6-min walking test.	Logical regression Fisher t-test to compare means after conducting Kolmogorov-Smirnov test. Statistically significant difference of variables in groups, Pearson correlation (r) of quantitative data and Spearman correlation (r_s) on qualitative data. SQRQ scores: symptoms and impact, $p < 0.01$ and activity $p < 0.05$ Inhaled salmetrol multiplied risk of having COPD-HC 27.4 (95% CI 2.4 – 308.1).	Independent predictors of high incidence for hospital services (emergency care and admissions): treatment with salmeterol, presence of cardiac arrhythmias, and impaired health-related quality of life (increased SGRQ) scores. Levels of evidence: 3a

6 Data for this study partly obtained from National Emphysema Treatment Trial (NETT) a randomized controlled trial of volume reduction surgery vs continued medical treatment conducted among 17 clinics throughout the US (1998 to 2002). Tools: shortness of breath questionnaire (SOBQ), SGRQ, and 6-minute walk. (Fan, Ramsey, Make, & Martinez, 2007) United States	Adults with emphysema, severe air flow limitation (FEV_1 </ 45% predicated) and had finished 6 to 10 weeks of pulmonary rehab program prior to randomization. N = 1, 218 N = 614, randomized to medical therapy Mean age 66.5 years, 64% males. Theoretical Framework not mentioned	Prospective cohort Subjects had emphysema with severe airflow limitation (FEV_1 </ 45% predicted).	Demographics, BMI, pulmonary function, arterial blood gases, x-ray results, dyspnea SOBQ, SGRQ, 6 minute walk, exercise capacity, medication use, history of exacerbations, and comorbidity.	Multivariable logistic regression to estimate risk of ECOPD Compared predictive models used AUC and associated standard error and 95% CI were compared. AUC in original dataset: 0.70 vs 0.59. p = 0.0001 Control group had statistically higher mean $PaC0_2$ [45.1 +/- 7.7 vs 49.6 +/- 7.8 mmHg, p = 0.03].	Predictive ability in the final tool SOBQ significantly better than using FEV_1 alone. Levels of evidence: 1a

7 Measured risk factors for readmission after hospital discharge for ECOPD, which included quality of life indicators using tools: GOLD, Beck-Depression Inventory, Graffar Scale, and SGRQ. (Carneiro, Sousa, Pinto, Alemeida, Oliveira, & Rocha, 2010) Portugal	Adults 84.4% male, median age 68 years of age +/- 12.4, stage IV 51%, and median total SGRQ 50.6 Percent who resided in Domicile in the Porto district (second largest urban area in Portugual) = 70% N = 45 Questions read to illiterate subjects who were not able to read. Theoretical Framework not mentioned	Prospective study Subjects hospitalized with ECOPD (2006-2008) defined as an acute change in baseline per Anthonisen et al. (1987) criteria and GOLD criteria.	Questionnaire: Demographics, risk factors for COPD (smoking and smoking burden), asthma, workplace exposure, family history of non-malignant lung disease, and co-morbidities. 1) Clinical and functional evaluation, GOLD criteria to classify disease severity. 2) QOL per SGRQ. 3) evaluation of any depression using Beck Depression Inventory-Short form, 4)Social Status-evaluated with Graffar Scale, 5) COPD treatment before hospital admission.	Pearson correlation test (r) and nonparametric Spearman correlation test (R) to examine correlation of variables. AUC for model = 0.68. High SGRQ scores reflected worse QOL related to depression (R = 0.69; p = 0.02). FEV_1 inversely related to a worse score of depression (r = - 0.48; p = 0.054).	Findings revealed a link between depression and a high SGRQ total score, related to a poor quality of life. Small sample size noted. Levels of evidence: 1c

8 To determine if clinical risk factors and QOL risk factors as measured by questionnaire: Seattle Obstructive Lung Disease (SOLDQ) scored at baseline on patients who were followed for 12 months follow-up was predictive of hospitalization (Fan, Curtis, Tu, McDonell, & Fihn, 2002) United States	Adults assigned to one of seven primary care clinics of Veterans Affairs (VA) medical centers N = 3,282 (COPD and asthma) Male = 96.3% Race, white = 85.7% Age mean = 65.6 years (10.9) Theoretical framework not mentioned	Prospective cohort Subjects part of Ambulatory Care Quality Improvement Projects (ACQUIP) multicenter, randomized controlled trial and enrolled in the general medicine clinics at seven Department of Veterans Affairs (VA) hospitals.	Completed a health inventory, SOLDQ, and CCI. Distance of patient to hospital (per zip codes), smoking status, employment status, pulmonary function testing (PFT) results, age, marital status, and hospitalization based on International Classification of Disease, ninth revision (ICD-9) for COPD and respiratory infection.	X^2 for categoric variables. Logistic regression for QOL scores modeled as predictor variables. Hospitalization for COPD: c-index, 0.706; Hosmer-Lemeshow, 7.9; p = 0.4); lowest quartile SOLDQ for physical function 6.0 (95% CI, 3.1 to 11.5); long term steroid use (OR, 2.8; 95% CI, 1.6 to 4.9). Prior hospitalization for COPD (OR, 4.5; 95% CI, 2.2 to 9.2).	SOLDQ disease specific for COPD QOL measurement (especially physical function impacting lower QOL) found to be an independent predictor for hospitalization for COPD and mortality. Levels of evidence: 1c
9 Factors associated with hospital admission from ED for ECOPD using a standard protocol. Post hoc comparison of admissions to assess agreement with GOLD guidelines. [3]	Cohort study of patients matching (9 indications for hospital admission) Global Initiative for COPD (GOLD) guidelines. Adults, median age 69 years. 48% men 52% women White =178/76 African American = 37/16 Hispanic = 16/7 N = 233 Theoretical Framework not mentioned	Prospective multicenter cohort, observational COPD patients seen in ED for treatment of ECOPD, defined as increased shortness of breath, worsening cough, or change in sputum production, >/ 55 years of age, and able to give consent.	Hospital admission defined as a patient admitted to an inpatient unit with diagnosis of COPD, emphysema, or chronic bronchitis). Data collected: clinical findings, COPD history, symptoms described prior to admission, respiratory rate, comorbidities, new diagnosis of arrhythmia, and zip code.	Multivariate logistic regression to examine independent factors associated with hospital admission. Hosmer-Lemeshow and AUC for final model. The area under the receiver operator curve (ROC) curve was 0.80 for the multivariate model and the Hosmer-Lemeshow test demonstrated a good fit (p = 0.81). No significant two-way interactions in the final model. 61% admission rate (95% CI =56% to 66%).	Findings: age, female gender, higher pack-years of smoking, recent use of inhaled corticosteroids, self-reporting of decreased activity in past 24 hours, elevated respiratory rate in ER, and concurrent diagnosis of pneumonia increased risk of admission. Levels of evidence: 1c

10 Variables predictive of hospital admission 2 months after emergency room visit, in patients with ECOPD, GCS, CCI, and socioeconomic data. [14]	Adults: N = 2,336 (patients with index ED visit) N= 1,537 admitted to the hospital N = 950 discharged home Male = 2, 125 (91%) Female = 207 (8.8%) Mean age years = 72.5, +/- 9.64 Theoretical Framework not mentioned	Prospective cohort Subject seen in one of 16 hospitals among Spanish National Health Service. COPD defined by FEV_1 / FVC < 70%	Date collected in ED socioeconomic, respiratory status (arterial blood gases: pH, pCO_2, and 0_2, respiratory rate, and dyspnea at rest), level of consciousness (GCS), and presence of disease conditions recorded using CCI.	Univariate analyses based on patient's condition in ED (admitted to the hospital or discharged home). X^2 and Fischer exact tests used to test for statistical significance among proportions. Predictors of admission to an intermediate respiratory care unit or intensive care unit with long-term home oxygen use or noninvasive mechanical ventilation elevated pCO_2 and decreased pH at time of ED arrival. AUC 0.87 in derivation sample and 0.89 in validation sample. Previous ECOPD admission in past year (OR 1.98 & 2.33); $pC0_2$ on ED admission (OR 2.02 & 2.90); number of ED visits within one week of index ED visit (OR 5.14); dyspnea level one week after index ED visit (OR 2.66 & 1.40); and predictors for short term admission (AUC 0.82).	Collecting data at time of ED visit can be used to predict short term hospital admission. AUC could be improved. Patients admitted to the hospital during index ED visit: baseline FEV_1 % ECOPD related hospitalization in previous year, severe baseline dyspnea, and dyspnea one week after index ED visit were predictors for short term readmission (AUC 0.73). Levels of evidence: 1c.

11 Examined risk factors for hospitalization and death secondary to COPD. Medical Research Council (MRC) dyspnea scale, Airway questionnaire 20 (AQ20), (Schembri et al.,2009) Scotland	Adults N = 3,343 Females = 1657, 49.6% Males = 1686, 50.4% Patients screened from clinical network during yearly visits. Age 70 -79 years, 1,112/33% Median follow-up was 1.9 years Theoretical framework not mentioned	Prospective observational Inclusion criteria for COPD: FEV_1 < 80% of the predicted value (greatest of pre and post bronchodilator values) and FEV_1 / FVC < 70%	Demography: gender, age, deprivation score, smoking status, and history, body mass index (BMI). Severity of COPD and quality of life	Proportional hazard model (CI 95%) used to identify significant risk factors. Risk scores for predictors were described as 3 times the logarithm for the hazard ratios. Based on Hazard ratio (95% CI): Prior respiratory admission (2.68, 2.27 – 3.36); Dyspnea score (5 worse) (4.37, 2.74 – 6.95); BMI underweight (1.23 (0.94 – 1.61); Base FEV_1 < 30, (1.8, 1.39 – 2.32). Statistically significant identified risk factors for hospitalization and death ($p < 0.05$).	387 (54%) hospitalized once 160 (22%) hospitalized twice 168 (24%) hospitalized more than twice Risk factors ($p < 0.05$) low BMI, worsening MRC dyspnea score, increasing age, decreased FEV_1, previous respiratory or cardiovascular hospital admission, and use of prednisone predictive of poor outcomes. Influenza vaccine protective. Levels of evidence: 1c

12 Hospital readmission for acute exacerbation of COPD (AECOPD). SGRQ, CCI,Cognitive status Pfeiffer Questionnaire, Katz Activitiess of Daily Living Scale, Social Resources and Yesavage Scale. (Almagro et al., 2006) Spain	Adults N = 129 Age = 72 years, +/- 9.2 Men = 120/93% Women = 9/7% Admitted to acute care teaching center Theoretical Framework not mentioned	Prospective Subjects FEV_1 </ 70% Admitted for AECOPD: worsening breathlessness and change in mental status related to hypercapnia.	Questionnaire: regular treatment; number of medications. Health-related quality of life questionnaire (Spanish version of SGRQ), Dyspnea visual analog scale, CCI, Cognitive status Pfeiffer Questionnaire, Katz Activities of Daily Living Scale, Social Resources scale of Older American Research and Service Center, socioeconomic data, and presence of depression per Yesavage Scale (short version).	Multivariate model used: Qualitative variables analyzed: x^2 test or Fisher's exact test. Quantitative variables: Student's t-test or non-parametric test: Mann-Whitney. Hosmer-Lemeshow Goodness of fit test indicated model calibrated (p = 0.85): readmission significantly related to previous hospital admission, hypercapnia at discharge, and poor quality of life. 21 (16.3%) readmitted within one month. 45 (34.9%), 53 (41.1%), and 75 (58.1%) at 3, 6, and 12 months readmitted. Mean length of stay 30.1 +/- 24.2 days.	Statistically significant scores on dyspnea scale ATS p < 0.02, high number readmission in past year for ECOPD p < 0.0001, high $PaC0_2$ p < 0.005. SGRQ scores of readmitted patients significantly worse scores on: activity, impact on daily life, and distress due to respiratory symptoms. Levels of evidence: 1c

13 Predictors for hospital admission for ECOPD among ED patients. Structured ED interview with patient or family member. Canadian Triage and Acuity Scale (CTAS), respiratory rate (RR) clinical data, demographic variables, and Anthonisen criteria. (Rowe et al., 2009) Canada	N = 501 55.5% (n= 278) male Median age 71 years Race: white 94.7% Theoretical Framework not mentioned	Prospective cohort AECOPD Participants (or family) presented to one of 16 EDs with ECOPD and answered an ED structured interview and a telephone interview completed 2 weeks later.	Clinical characteristics: BMI, high school graduate, smoking history, health care use (primary care provider, ED use, and hospitalizations), admitting diagnoses, comorbidities, lung function (FEV_1), and arterial blood gas (ABG)	Bivariable analyses for dichotomous variables tested by chi-square test, bivariable analyses for continuous variables performed by Mann-Whitney U test. Multivariable logistic regression (MLR) model used. P value statistically significant at 0.05. Hospital admission significantly associated with 2 previous COPD admissions in past 2 years (OR = 2.10; 95% CI = 1.24 to 3.56), receiving oral corticosteroids for COPD (OR = 1.72; 95% CI = 1/08 to 2.74), having Canadian Triage & Acuity Scale score 1-2 (OR = 2.04; 95% CI = 1.33 to 3.12) and additional ED treatments, mostly oxygen and IV magnesium (OR = 3.95; 95% CI = 2.45 to 6.35). Hospital admission: 49.3 (95% CI = 44.9% to 53.9%). Goodness of fit assessed by deviance value, 1.23, indicating a reasonable fit. No significant difference in sex, education level, primary care support between admissions or discharge groups.	50% of patients hospitalized 62% scored Anthonisen criteria I or II. 73.4% FEV_1 < 50% Predictors for hospitalization: past COPD history, EDs being usual site for COPD care, $p < 0.001$ and treatment received adjunct to COPD treatment in ED $p < 0.001$. Levels of evidence: 1c

14 Role of anxiety, health status, and depression as risk factors for COPD rehospitalization. [15]	N = 406 Participants from university hospitals of 5 Nordic countries. Male/Female age 69.2 years mean, +/- 10.5 Female = 51.2 Male = 48.8 Theoretical framework not mentioned	Prospective study (multicenter) Patients had been admitted with AECOPD defined as change in baseline condition, so severe, acute hospital admission required. Met GOLD criteria for stage I or higher.	Data collected from pulmonary units at discharge: SGRQ, HADS, and questionnaire	Chi-squared and unpaired t-test used. Time until readmissions tested by Kaplan-Meier survival analysis and Cox regression. Linear regression used to analyze correlation between health status and psychological status. Readmission within 12 months = 60.6%, patients had lower lung function and health status. Hazard ratio (HR, 95% CI) = 0.82 (0.74 – 0.90) predicted FEV_1 and 1.06 (1.02 – 1.10) per 4 units increase in sum SGRQ score. Readmission within 12 months = 60.6%, patients had lower lung function and health status. Hazard ratio (HR, 95% CI) = 0.82 (0.74 – 0.90) predicted FEV_1 and 1.06 (1.02 – 1.10) per 4 units increase in sum SGRQ score. Previous hospitalizations (HR 95% CI: 1.98 (1.42 – 2.76) independent related to increased risk of hospitalization (2 previous hospitalizations). Significant correlation between total SGRQ score and total HAD score ($r = 0.38$; $p < 0.001$) Significant interaction between health status and psychological status related to risk of readmission ($p = 0.002$).	COPD patients having poor health status discharged after hospital admission, the risk of rehospitalization was higher in patients with anxiety. Low FEV_1 and poor health status discovered as being important risk factors for readmission. Levels of evidence 1c

15 Factors related to hospitalization of patients with acute exacerbation of COPD (AECOPD). Structured questionnaire administered by physicians to hospitalized patients for acute ECOPD, after they were clinically stable. [16]	N = 73 Participants included those with AECOPD admitted to the hospital. Male = 96% Age in years = 60 +/- 9 History of previous hospitalization = 59% Comorbidities = 46% Theoretical Framework not mentioned	Observation study AECOPD defined by World Health Organization-Government of India as ongoing deterioration of patient's condition from stable baseline to acute occurence of symptoms that require a change in medication (Jindal, Gupta & Aggarual, 2004).	Data from structured questionnaire during hospitalization, body mass index (BMI), smoking, symptoms, comorbidities, spirometry, and outcomes during hospitalization.	Univariate analysis conducted on variables. Variables found significant were put into a step-wise multivariate regression analysis. Statistically significant risk factors found were: $FEV_{1,}$ peak expiratory rate, sputum purulence, history (in past year) of previous hospitalization, and comorbidities. Risk factors identified as statistically significant for COPD hospital admission, p value significant p </ 0.05: peak expiratory flow rate p = 0.046, FEV_1 p = 0.03, sputum purulence p = 0.039, previous hospitalization in past year p = 0.048 and comorbidities p = 0.041.	Authors report this is the first study in northern India to examine COPD risk factors for hospitalization. Tuberculosis (10%), smoking 97%, Low FEV_1 is a predisposing risk factor for mortality from COPD. Levels of evidence: 1c

Note. Body mass index (BMI), air flow obstruction, dyspnea (score from the modified Medical Research Council (MRC), and exercise capacity (distance walked in 6 minutes (BODE index), Global Initiative for Chronic Obstructive Lung Disease (GOLD), Glascow Coma Scale (GCS), Charlson Comorbidity Index (CCI), evaluation of COPD longitudinally to identify predictive surrogate endpoints (ECLIPSE), St. George's Respiratory Questionnaire (SGRQ), Graffar Scale (socioeconomic score), Hospital Anxiety and Depression Scale (HADS), Carstairs index (socioeconomic deprivation), enhancing recovery in coronary heart disease (ENRICHD) social support inventory (ESSI), State-trait anxiety inventory (STAI-S/T), shortness of breath questionnaire (SOBQ), Beck-Depression Inventory, Anthoisen criteria determining severity of COPD, Seattle Obstructive Lung Disease Questionnaire (SOLDQ), Airway questionnaire 20 (AQ20), Cognitive Status Pfeiffer Questionnaire, Katz Activities of Daily Living Scale, Yesavage Scale (short version to evaluate the presence of depression), Canadian Triage and Acuity Scale (CTAS).

Levels of Evidence (Oxford Centre for Evidence-based Medicine – Levels of Evidence, March 2009) [13]

Level: Therapy/Prevention
1a Systematic reviews of random controlled trials, different populations. Prospective cohort.
1b Individual random controlled trial, single population
1c All or none case series
2a Systematic reviews of cohort studies (same type)
2b Individual retrospective cohort study
2c Outcomes research- ecological studies
3a Systematic reviews of same type of case-control studies, better studies
3b Individual case control study with limited population
4 Case-series with low quality cohort and case-control studies
5 Expert opinion with no specific critical appraisal, or based on physiology

Synthesis

Of the fifteen studies included in the integrative review, numerous instruments were identified as measuring for risk factors predictive for hospital admission or readmission of COPD, exacerbated COPD, or patients with acute exacerbated COPD. Deciphering the validity and reliability of the instruments used to measure risk factors for COPD admission was as multifaceted problem given the different types that existed across studies. Specific reports of reliability and validity are typically not reported but we assume that these attributes are subsumed within the statistical tests conducted; especially for reliability. As a result reliability and validity are reported together. Statistical analysis of measurements used in the studies were done in order to determine risk factors, which focused on the predictive capacity of variables related to hospitalization for exacerbated COPD. In other words, all of these studies examined the predictive validity of exacerbated COPD hospitalizations using multiple variables.

Reliability is necessary for validity to be established [17,18]. However, the nature of COPD progression makes it difficult for reliability to be independently established. The study conducted by Vidal et al. had the highest statistic value predictive for COPD hospitalization amid the studies included in the review [4]. The accuracy in the model to measure to predictive risk factors for hospitalization among patients with COPD was reported as being the area under the curve (AUC) 0.89. An outcome such as this, would indicate a clinical classification of the measurement tool as 'good' in predicting an admission for COPD [19]. One study in the review reported being the first to use measurements to determine risk factors in their country, consequently stability of these measures has not been established [15]. Multiple studies demonstrated the correlation between episodes of exacerbated COPD and accelerated disease progression, which in turn increase the incidence of repeated future hospital admissions, and mortality [11, 13]. As COPD patients experience exacerbations, deterioration impacts their quality of life, which is additionally challenged by those who have a low socioeconomic status, lack of social support, smoking, body mass index (BMI) being abnormally high or low, including the implications of experiencing anxiety, and depression [13].

Results

Across studies multiple complexities and diverse models were used to measure risk factors. The BODE Index: BMI, degree of airway obstruction measured by forced expiration in one sec ($FEV_{1),}$ dyspnea (modified Medical Research Council questionnaire (mMRC), and exercise capacity measured by a 6-minute walk (6MWD), is a multidimensional score of COPD disease severity. Using the BODE index and other select clinical variables included, revealed a significant effect on predicting the number of COPD hospital admissions (95% Confidence Interval, 1.15 to 1.25; < 0.001) [10]. Despite the BODE Index being valuable to clinicians because it is evaluates major indicators for hospital admission, many times the 6MWD it is not a useful instrument in the acute care setting.

In contrast, Coventry et al. from the United Kingdom measured variables with five different instruments to examine potential risk factors for COPD admission: baseline clinical data, St. George's Questionnaire (SGRQ), Hospital Anxiety and Depression Scale (HADS), Charleston Comorbidity Index (CCI), Carstairs index (socioeconomic deprivation), and Enhancing Recovery in Coronary Heart Disease (ENRICHD) that included a social support inventory [12]. Utilizing numerous tools was a common finding in all the studies. Expecting health care professionals to complete numerous scales is unrealistic, in order to determine COPD risk factors for hospitalization. The dilemma of finding a valid and reliable tool to measure risk prediction for COPD hospital admission is compounded by the regulation set by Medicare and Medicaid (2014) readmission penalty regarding reimbursement [2]. Such a regulation indiscriminately imposes a judgment, presuming a lack of quality care and services among hospitals and the health care professionals [20].

There was limited reporting in the studies about their feasibility, but all had strengths in measuring risk factors. Table 2. Some of the specific strengths of the studies relied on the combination of instruments used and the inclusion of clinical, functional status, socioeconomic, and psychosocial components. Additionally, limitations of the integrative review was the heterogeneity of the different instruments used to capture the most predictive risk factors.

Study Name	Constructs/Instruments
1 Ong, K. C., Earnest, A., & Lu, S. J. (2005). A multidimensional grading system (BODE index) as predictor of hospitalization for COPD. *Chest, 128*(6), 3810-3816. doi: 10.1378/chest.128.6.3810	A multidimensional grading system BODE Index (body mass index, airflow obstruction, dyspnea (score from the modified Medical Research Council (MRC), and exercise capacity (distance walked in 6 minutes) scores for each as predictor of hospitalization for COPD and Global Initiative for Chronic Obstructive Lung Disease scale (GOLD).
2 Vidal, S., Gonzalez, N., Barrio, I., Rivas-Ruiz, F., Bare, M., Blasco, J. A., . . . Quintana, J. M. (2013). Predictors of hospital admission in exacerbations of chronic obstructive pulmonary disease. *Int J Tuberc Lung Dis, 17*(12), 1632-1637. doi: 10.5588/ijtld.13.0177	Body mass index, airflow obstruction, dyspnea (score from the modified Medical Research Council (MRC), exercise capacity (distance walked in 6 minutes scores for each) (BODE index), GOLD, standardized data collection tool for predictors among patients with exacerbated COPD, and Glascow Coma Scale.
3 Mullerova, H., Maselli, D. J., Locantore, N., Vestbo, J., Hurst, J. R., Wedzicha, J., . . . Anzueto, A. (2014). Hospitalized Exacerbations of Chronic Obstructive Pulmonary Disease: Risk Factors and Outcomes in the ECLIPSE Cohort. *Chest*. doi: 10.1378/chest.14-0655	ECLIPSE procedure (evaluation of COPD longitudinally to identify predictive surrogate endpoints), St. George's Respiratory Questionnaire (SGRQ-C), and GOLD.
4 Coventry, P. A., Gemmell, I., & Todd, C. J. (2011). Psychosocial risk factors for hospital readmission in COPD patients on early discharge services: a cohort study. *BMC Pulm Med, 11*, 49. doi: 10.1186/1471-2466-11-49	Baseline clinical data, St. George's Questionnaire (SGRQ), Hospital Anxiety and Depression Scale (HADS), Charleston Comorbidity Index (CCI), Carstairs index (socioeconomic deprivation), and social support measured with self-report instrument, Enhancing Recovery in Coronary Heart Disease (ENRICHD) Social Support Inventory (ESSI). Authors reported the CCI for comorbidity had a predictive validity in outcomes for readmission and death. Charlson ME, Pompei P, Ales KL, MacKenzie CR: A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987, 40:373-383.
5 Soler, J. J., Sanchez, L., Roman, P., Martinez, M. A., & Perpina, M. (2004). Risk factors of emergency care and admissions in COPD patients with high consumption of health resources. *Respir Med, 98*(4), 318-329.	SGRQ, demographic data, socioeconomic data, and nutritional parameters. State-trait anxiety inventory (STAI-S/T).

6 Fan, V. S., Ramsey, S. D., Make, B. J., & Martinez, F. J. (2007). Physiologic variables and functional status independently predict COPD hospitalizations and emergency department visits in patients with severe COPD. *Copd, 4*(1), 29-39. doi: 0/15412550601169430	Data for this study partly obtained from National Emphysema Treatment Trial (NETT) a randomized controlled trial of volume reduction surgery versus continued medical treatment conducted among 17 clinics throughout the US (1998 to 2002). Tools: shortness of breath questionnaire (SOBQ), SGRQ, and 6-minute walk.
7 Carneiro, R., Sousa, C., Pinto, A., Almeida, F., Oliveira, J. R., & Rocha, N. (2010). Risk factors for readmission after hospital discharge in chronic obstructive pulmonary disease. The role of quality of life indicators. *Rev Port Pneumol, 16*(5), 759-777.	Measured risk factors for readmission after hospital discharge for ECOPD, which included quality of life indicators using tools: GOLD, Beck-Depression Inventory, Graffar Scale, and SGRQ. SGRQ was stated to be properly validated in Portuguese to assess QOL. Jones PW, Quirk FH, Baveystock CM, Littlejohns OA. Self-complete measure of health status for chronic airflow limitation. The St. George's Respiratory Questionnaire. Am Rev Respir Dis 1992; 145:1321 -1327.
8 Fan, V. S., Curtis, J. R., Tu, S. P., McDonell, M. B., & Fihn, S. D. (2002). Using quality of life to predict hospitalization and mortality in patients with obstructive lung diseases. *Chest, 122*(2), 429-436.	Clinical risk factors and QOL risk factors as measured by questionnaire: Seattle Obstructive Lung Disease (SOLDQ) scored at baseline on patients who were followed for 12 months follow-up was predictive of hospitalization. Short-form-36 questions of QOL. The SF-36 was completed by patients, reported as a reliable, valid, and responsive measure containing 36 questions that can be used to calculate a physical component summary (PCS) score and a mental component summary (MCS) score. Ware JE Jr, Gandek B. Overview of the SF-36 Health Survey and the International Quality of Life Assessment (IQOLA) Project. J Clin Epidemiol 1998; 51:903–912

9 Tsai, C. L., Clark, S., Cydulka, R. K., Rowe, B. H., & Camargo, C. A., Jr. (2007). Factors associated with hospital admission among emergency department patients with chronic obstructive pulmonary disease exacerbation. *Acad Emerg Med, 14*(1), 6-14. doi: 10.1197/j.aem.2006.07.034	Factors associated with hospital admission from ED for ECOPD using a standard protocol. Post hoc comparison of admissions to assess agreement with GOLD guidelines. Family income estimated using zip codes and insurance status categorized by private or commercial. The BODE index was reported to have been validated in predicting risk of death and hospital admission in patients with COPD who are stable. Ong KC, Earnest A, Lu SJ. A multidimensional grading system (BODE Index) as predictor of hospitalization for COPD. Chest. 2005; 128:3810–6.
10 Quintana, J. M., Esteban, C., Garcia-Gutierrez, S., Aguirre, U., Gonzalez, N., Lafuente, I., . . . Rivas-Ruiz, F. (2014). Predictors of hospital admission two months after emergency_department evaluation of COPD exacerbation. *Respiration, 88*(4), 298-306. doi: 10.1159/000365996	Variables predictive of hospital admission 2 months after emergency room visit, in patients with ECOPD, Glasgow Coma Scale, Charlson Comorbidity Index, and socioeconomic data.
11 Schembri, S., Anderson, W., Morant, S., Winter, J., Thompson, P., Pettitt, D., . . . Winter, J. H. (2009). A predictive model of hospitalisation and death from chronic obstructive pulmonary disease. *Respir Med, 103*(10), 1461-1467. doi: 10.1016/j.rmed.2009.04.02	Examined risk factors for hospitalization and death secondary to COPD. Medical Research Council (MRC) dyspnea scale, Airway questionnaire 20 (AQ20),
12 Almagro, P., Barreiro, B., Ochoa de Echaguen, A., Quintana, S., Rodriguez Carballeira, M., Heredia, J. L., & Garau, J. (2006). Risk factors for hospital readmission in patients with chronic obstructive pulmonary disease. *Respiration, 73*(3), 311-317. doi: 10.1159/000088092	Questionnaire: routine treatment at home; number of medications. Health-related quality of life questionnaire (Spanish version of SGRQ), Dyspnea visual analog scale, Comorbidity used Charlson Index, Cognitive status Pfeiffer Questionnaire, Katz Activities of Daily Living Scale, Social Resources scale of Older American Research and Service Center, socioeconomic data, and presence of depression per Yesavage Scale (short version). Airway questionnaire 20 (AQ20), structured questionnaire to assess home medications.

13 Rowe, B. H., Villa-Roel, C., Guttman, A., Ross, S., Mackey, D., Sivilotti, M. L., . . . Borgundvaag, B. (2009). Predictors of hospital admission for chronic obstructive pulmonary disease exacerbations in Canadian emergency departments. *Acad Emerg Med, 16*(4), 316-324. doi: 10.1111/j.1553-2712.2009.00366.x	Structured ED interview with patient or family member. Canadian Triage and Acuity Scale (CTAS), respiratory rate (RR). Anthoniessen et al. (1987) criteria used to define exacerbation of COPD. Clinical characteristics: BMI, high school graduate, smoking history, health care use (primary care provider, ED use, and hospitalizations), admitting diagnoses, comorbidities, lung function (FEV_1), and arterial blood gas (ABG). Visual analog scale and dyspnea Scale of American Thoracic Society, functional dependence assessed with Katz Activities of Daily Living Scale, Social Resources Scale of the Older American Research and Service Center, and Yesavage Scale (short version) to evaluate the presence of depression.
14 Gudmundsson, G., Gislason, T., Janson, C., Lindberg, E., Hallin, R., Ulrik, C. S., ... & Bakke, P. (2005). Risk factors for rehospitalisation in COPD: role of health status, anxiety and depression. *European Respiratory Journal*, *26*(3), 414-419.	Data collected from pulmonary units at discharge: SGRQ, Hospital Anxiety and Depression scale (HAD) and Questionnaire. HAD questionnaire is reported in previous studies to have fairly high validity for psychiatric morbidity. Wilkinson MJ, Barczak P. Psychiatric screening in general practice: comparison of the general health questionnaire and the hospital anxiety depression scale. J R Coll Gen Pract 1988; 38: 311–313.
15 Mohapatra, P. R., & Janmeja, A. K. (2010). Factors associated with hospital admission in patients with acute exacerbation of chronic obstructive pulmonary disease. *Indian J Chest Dis Allied Sci, 52*(4), 203-206.	Structured questionnaire administered by physicians to hospitalized patients for acute ECOPD, after they were clinically stable. Data collected from structured question during hospitalization, body mass index (BMI), smoking, symptoms, comorbidities, spirometry, and outcomes during hospitalization.

Table 2. Constructs/instruments used in each study to determine risk factors for COPD admission. Report on validity and reliability of instruments with supporting citation.

Discussion

Based on the initial literature results of 14,166 articles, 15 articles were selected that ranged in statistical rigor for determining risk factors most predictive of hospitalization for COPD or acute exacerbation of ECOPD. In addition, the studies clearly represent the global health crisis that COPD poses to patients

diagnosed with this disease and the health care system that cares for them. One of the limitations of this study was that out of the articles measuring risk factors for exacerbated COPD hospital admission, most were from studies conducted outside of the US (80%). This is a limitation since other countries differ in health care practices and resources from the US. In addition, there was no consistency in the clinical data collected and the instruments used. The strengths of the studies revealed the correlation of past hospitalizations, low $FEV_{1,}$ measuring socioeconomic, and psychological aspects of anxiety and depression impacting the QOL of COPD patients.

Among these publications no theoretical frameworks were included, which could be the result of the studies being heavily influenced by physicians, who take more of a non-theoretical physiological approach to research. Random Forest (RF) was utilized in several studies found in the search but were not included because it employs an machine learning method where fit is almost always obtained irrespective of the clinical reliability and validity of the model [5, 21]. Other researchers conducted retrospective studies that did not meet the inclusion criteria. One such study was the Medicare Provider Analysis and Review (MEDPAR) files during the years 2006 and 2010 that included: California, Illinois, Florida, New York, Ohio, Pennsylvania, and Texas to detect risk factors for COPD hospital admission. Their findings revealed increasing use of hospitalization and common prevalent risk factors being congestive heart failure (CHF), patients who were indigent, sicker, lack of support, and low education level contributing to the vulnerability of this population [6].

Conclusion

COPD is a serious global health issue with a dynamic relationship involving patients' socioeconomic status, self-rated quality of life, disease severity, comorbid factors, and geographic location. Due to the intricate problem of COPD and the fragile equilibrium of risk factors that predispose patients to being admitted to the hospital; finding one measurement instrument to identify the key potential risk factors is a daunting feat to accomplish. Access to valid and reliable instruments to measure risk factors employed by those health care professionals entrusted with the care of patients with COPD, needs to embody gestalt clinical assessment skills and follow an empirically sound predictive model [14, 18, 22].

The time is now, to create a comprehensive, efficient, and effective psychometric instrument that can measure risk factors in real-time to address this vulnerable COPD population [4, 15, 22, 23]. Use of the Socio-Ecological Model would provide a framework of four essential domains to be measured: individual (clinical, psychosocial, and socioeconomic factors); relationships (family, significant others); community setting (environment); and society (economic and social policies) [24, 25]. Research to establish statistically sound evidence of a new prediction model will bridge the gap in evidence-based practice for these patients. Therefore an instrument created with the Socio-Ecological Model and a baseline of common risk factors could be customized to meet the unique needs of populations in their geographic locations and susceptible attributes. Such an instrument could then be generalizable on a national and potentially international level. A COPD risk factor instrument, that could be used in the ED or when hospitalized patients have stabilized, would have the potential to improve outcomes, as well as conserving health care resources [10,23,24,26,27].

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