REVIEW

Predictors of Readmission, for Patients with Chronic Obstructive Pulmonary Disease (COPD) – A Systematic Review

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Introduction: Chronic obstructive pulmonary disease (COPD) is the third-leading cause of death globally and is responsible for over 3 million deaths annually. One of the factors contributing to the significant healthcare burden for these patients is readmission. The aim of this review is to describe significant predictors and prediction scores for all-cause and COPD-related readmission among patients with COPD.

Methods: A search was conducted in Ovid MEDLINE, Ovid Embase, Cochrane Database of Systematic Reviews, and Cochrane Central Register of Controlled Trials, from database inception to June 7, 2022. Studies were included if they reported on patients at least 40 years old with COPD, readmission data within 1 year, and predictors of readmission. Study quality was assessed. Significant predictors of readmission and the degree of significance, as noted by the *p*-value, were extracted for each study. This review was registered on PROSPERO (CRD42022337035).

Results: In total, 242 articles reporting on 16,471,096 patients were included. There was a low risk of bias across the literature. Of these, 153 studies were observational, reporting on predictors; 57 studies were observational studies reporting on interventions; and 32 were randomized controlled trials of interventions. Sixty-four significant predictors for all-cause readmission and 23 for COPD-related readmission were reported across the literature. Significant predictors included 1) pre-admission patient characteristics, such as male sex, prior hospitalization, poor performance status, number and type of comorbidities, and use of long-term oxygen; 2) hospitalization details, such as length of stay, use of corticosteroids, and use of ventilatory support; 3) results of investigations, including anemia, lower FEV₁, and higher eosinophil count; and 4) discharge characteristics, including use of home oxygen and discharge to long-term care or a skilled nursing facility.

Conclusion: The findings from this review may enable better predictive modeling and can be used by clinicians to better inform their clinical gestalt of readmission risk.

Keywords: predictors, readmission, chronic obstructive pulmonary disease

Introduction

Chronic obstructive pulmonary disease (COPD) is a common respiratory condition characterized by persistent airflow limitation¹ and is thought to affect over 10% of the population.² As a consequence of its chronicity, COPD is responsible for over 3 million deaths globally, making it the third most common cause of death.³

Patients with COPD commonly require hospitalized care, and COPD is one of the most common causes of hospitalization, among chronic diseases.⁴ Moreover, a notable proportion of patients with COPD will be readmitted, making readmission one of the factors contributing to the significant healthcare burden for these patients. It has been estimated that up to 50% of patients diagnosed with COPD are readmitted within 30 days of initial discharge in the USA.⁵ In addition to the utilization of healthcare resources, readmission is associated with a worse overall prognosis.⁶ Over the past decade, there has been an increased interest in identifying predictors and predictive models for readmission.⁷ Several systematic reviews have attempted

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to summarize the literature, but they only focused on all-cause or COPD-related readmission alone, and/or did not undertake a quality assessment of the included studies.^{8–10} In addition, given the rapidly developing literature, with many studies being reported in the past few years, these systematic reviews may not account for current findings.

The aim of this systematic review is to describe significant predictors and prediction scores for all-cause and COPDrelated readmission among patients with COPD.

Methods

This review was registered a priori on PROSPERO (CRD42022337035) and reported as per the PRISMA statement.

Search Strategy

A comprehensive search strategy was developed for Ovid MEDLINE, Ovid Embase, Cochrane Database of Systematic Reviews, and Cochrane Central Register of Controlled Trials from database inception to June 7, 2022, using a combination of database-specific subject headings and text words for the main concepts of COPD and hospital readmissions. An expanded search filter for clinical prediction guides was used. Results were limited to adult human studies. No other limits were applied (Appendix 1).

Eligibility Criteria

Two review authors (RC, OWS) independently screened articles for their eligibility for inclusion. A calibration exercise of 20 articles was undertaken to ensure concordance between reviewers. Discrepancies were resolved by discussion and consensus. If consensus could not be achieved, a third review author (RW) participated in the discussion to resolve discrepancies.

Articles were eligible after level 1 title and abstract screening, if they reported on primary research articles reporting on patients with COPD and readmission. Secondary research articles, such as review articles and economic analyses, as well as editorials/commentaries, were excluded at this stage. Studies included after level 2 full-text screening eligibility criteria required studies to report on patients at least 40 years old with COPD, readmission data within 1 year of a COPD hospitalization, and predictors of readmission. Studies including patients admitted for reasons unrelated to acute exacerbations of COPD (eg pneumonia, acute hypercapnic respiratory failure, obstructive sleep apnea, lung cancer, anxiety/depression) and studies reporting on home care/telemonitoring were excluded at this stage, to limit included articles to only patients with COPD.

Data Extraction

Two of the three review authors (RC, OWS, JHBI) conducted data extraction. As with screening, discrepancies were resolved by discussion and consensus, with or without the input of a third reviewer (RW). Study characteristics of country, sample size, age of participants, and percentage of females enrolled in study were noted. Studies were classified as either assessing predictors or assessing interventions. Studies assessing interventions were further subclassified as either observational cohort studies or randomized controlled trials. Significant predictors of readmission and the degree of significance, as noted by the *p*-value, were extracted for each study. For studies that did not report *p*-values, *p*-values were calculated based on the provided statistics (eg odds ratio and 95% confidence intervals) where possible.

Study Quality

Study quality was assessed for each study. For randomized controlled trials, the risk of bias version 2 tool was used.¹¹ For observational studies reporting on interventions, the ROBINS-I tool was used.¹² For observational studies reporting on predictors, the ROBINS-E tool was used.¹³

Synthesis

Significant predictors were reported by the time of readmission post-discharge and the degree of significance. Predictors were reported as significant predictors for the timepoint of 1-month readmission, the interval of 2-3-month readmission, and the interval of 6-12-month readmission. Predictors were further reported based on whether they were significant at a

type I error of 0.05, type I error of 0.01, or no degree of significance available. Significant predictors, as reported by the authors (<u>Supplementary Tables 1</u> and <u>2</u>), were grouped together into similarly reported predictors across the literature (eg all mentions of hospital length of stay were grouped together).

Because of the non-uniform reporting of non-significant predictors, where some studies explicitly reported nonsignificant predictors in the methods/results and others only mentioned significant predictors, non-significant predictors were not presented.

Results

In total, 4035 articles were identified from the database search. After 970 duplicates were removed, 3065 records were screened. Ultimately, 242 articles^{14–255} reporting on 16,471,096 patients were included in this review (Figure 1). Across the literature, there was generally a low risk of bias (Figure 2).

Overall, 153 studies were observational studies reporting on predictors; 57 studies were observational studies reporting on interventions; and 32 were randomized controlled trials of interventions. The studies were published between 1997 and 2022, with over half of the studies published since 2017. Over one-third of articles (91 studies, 37.6%) originated from the USA; 31 (12.8%) studies originated from Spain, 14 (5.8%) from Canada, 13 (5.4%) from the UK, and 13 (5.4%) from China. Sample sizes ranged from 8 to 4,587,542. The mean/median age was greater than 60

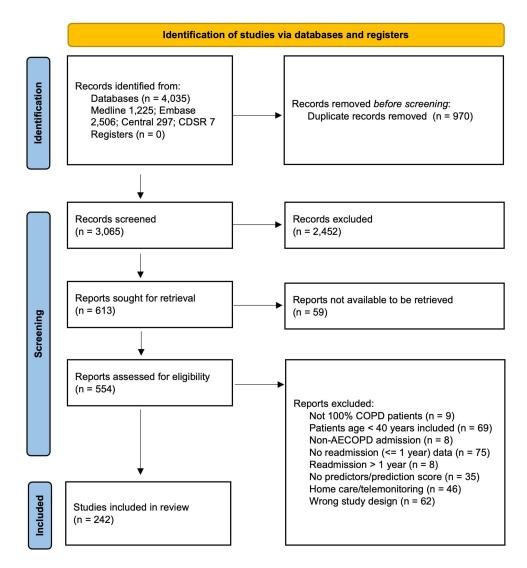


Figure I PRISMA flow diagram.

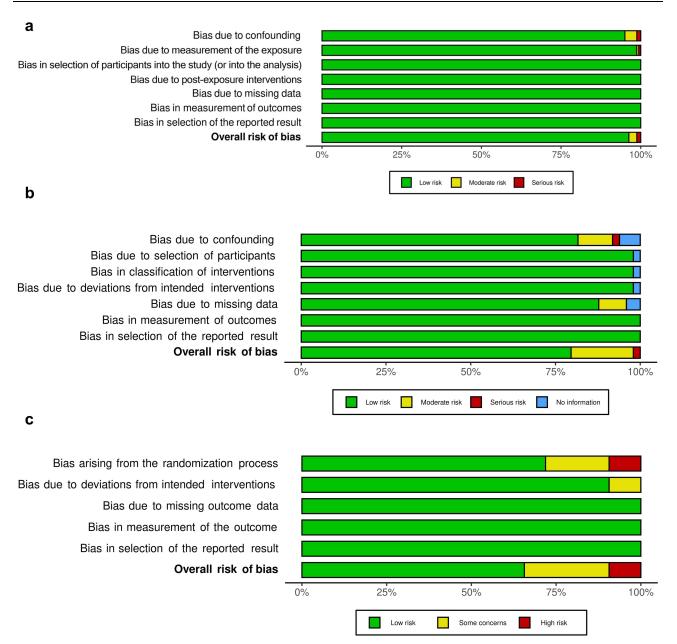


Figure 2 Quality assessment: (a) studies assessing predictors (ROBINS-E); (b) cohort studies assessing interventions (ROBINS-I); (c) randomized controlled trials assessing interventions (RoB 2).

years for nearly all studies. The percentage of females in a study ranged from 0.0% to 80.0%. Individual study characteristics are reported in Table 1 and Table 2.

A total of 64 significant predictors for all-cause readmission were reported across the literature. Summarizing across all readmission time frames, male sex, prior hospitalization, poorer performance status/activities of daily living, and older age were the most frequently reported patient characteristics that were predictors of readmission. Other significant predictors were COPD severity, alcohol/drug abuse, malnutrition, and history of community-acquired pneumonia (Figure 3a). Heart failure, mental health comorbidity, higher Charlson comorbidity index, diabetes, higher number of comorbidities, chronic kidney disease, and cancer were among the most commonly reported comorbidity predictors of readmission (Figure 3b). Among medications used prior to admission that were significant of readmission, long-term oxygen therapy was the most commonly reported predictor (Figure 3c). Hospital length of stay, non-invasive ventilation, intubation, and admission to the intensive care unit were the most common hospital care predictors of readmission

Study	Country	n	Age (years)		% Female
			Mean ± SD	Median (IQR)	
Abrams 2011 ¹⁴	USA	28,156	69.1±10.6		3.1%
Abusaada 2017 ¹⁵	USA	1419	65.1±2.3		47.7%
Agarwal 2016 ¹⁸	USA	7257		75–84	64.2%
Aksoy 2018 ¹⁹	Turkey	2727	69.8±10.2		31.5%
Al Aqqad 2017 ²⁰	Malaysia	81		72.0 (66.4–78.0)	2.5%
Almagro 2006 ²¹	Spain	129	72.0±9.2		7.0%
Almagro 2012 ²²	Spain	606	72.6±9.9		2.0%
Almagro 2014 ²³	Spain	983	72.3±9.7		8.5%
Alpaydin 2021 ²⁴	Turkey	300	73.1±10.1		28.3%
Alqahtani 2021 ²⁵	UK	82	71.0±10.4		51.2%
Bade 2019 ²⁹	USA	48,888	68.7±10.1		3.7%
Bahadori 2009 ³⁰	Canada	310	74.0±12.0		46.5%
Baker 2013 ³¹	USA	6095		55–59	58.9%
Barba 2012 ³³	Spain	275,512	72.0±15.4		30.0%
Bartels 2018 ³⁴	Canada	511	66.5±13.3		35.2%
Belanger 2018 ³⁶	Canada	479	68.9±9.4		48.0%
Bernabeu-Mora 2017 ³⁸	Spain	103	71.0±9.1		6.8%
Bishwakarma 2017 ⁴⁰	USA	6066	76.9±7.2		67.3%
Boeck 2014 ⁴¹	Switzerland	43	Not reported		53.5%
Boixeda 2017 ⁴²	Spain	120	72.9±8.6		2.5%
Bollu 2013 ⁴³	USA	2463	68.6±10.6		57.2%
Bollu 2017 ⁴⁴	USA	13,675	67.1±12.4		55.6%
Breyer-Kohansal 2019 ⁴⁵	Austria	823	68.5±10.2		40.9%
Brownridge 2017 ⁴⁶	Australia	130	72.9±10.7		51.6%
Buhr 2019 ⁴⁹	USA	1,622,983	68.0±11.9		58.9%
Buhr 2020 ⁴⁸	USA	1,622,983	68.0±11.9		57.8%
Candrilli 2015 ⁵⁰	USA	264,526	67.6±11.2		50.9%
Carneiro 2010 ⁵¹	Portugal	45	68±12.4		15.6%
Chan 2011 ⁵²	Hong Kong	65,497	76.8±9.6		23.0%
Chang 2014 ⁵³	China	135		66 (60–74)	11.9%
Chawla 2014 ⁵⁴	USA	54	70.0±12.0		70.0%
Chen 2006 ⁵⁷	Taiwan	145	72.2±10.0		26.9%

Table I Studies Assessing Predictors

Study	Country	n	Age (years)		% Female	
			Mean ± SD	Median (IQR)		
Chen 2009 ⁵⁶	Canada	108,726	72.3±10.9		45.5%	
Chen 2021 ⁵⁵	China	636	70.8±9.9		33.2%	
Chu 2004 ⁵⁸	Hong Kong	110	73.7±7.6		22.7%	
Chung 2010 ⁵⁹	Australia	100	70.6±9.5		44.0%	
Coban Agca 2017 ⁶⁰	Turkey	1490	67.7±11.1		35.0%	
Connolly 2006 ⁶²	New Zealand	7113		65–74	47.7%	
Couillard 2017 ⁶⁵	Canada	167	71.4±10.3		48.5%	
Coventry 2011 ⁶⁶	UK	79	65.3±9.9		44.3%	
Crisafulli 2014 ⁶⁸	Spain	123	69.4±9.8		6.6%	
Crisafulli 2015 ⁷⁰	Spain	125	69.2±9.8		6.4%	
Crisafulli 2016 ⁶⁹	Spain	110	70.5±9.6		6.4%	
de Miguel-Diez 2016 ⁷⁴	Spain	301,794	74.8±10.0		14.0%	
Duman 2015 ⁷⁶	Turkey	1704	Not reported		34.5%	
Ehsani 2019 ⁷⁹	USA	42	70.4±8.1		33.3%	
Emtner 2007 ⁸⁰	Sweden	21	65.0±9.3		66.7%	
Eriksen 2010 ⁸¹	Denmark	300	72.1		61.7%	
Ernst 2019 ⁸²	Canada	203,642	Not reported		Not reported	
Euceda 2018 ⁸³	USA	272	73.2±12.4		56.3%	
Fernandez-Garcia 2020 ⁸⁴	Spain	253	68.99.8		22.5%	
Fu 2015 ⁸⁵	USA	15,755	71.0±12.5		52.9%	
Ganapathy 2017 ⁸⁶	USA	11,496	70.7±10.8		52.5%	
Garcia-Aymerich 2003 ⁸⁷	Spain	340	69±9		Not reported	
Garcia-Pachon 2021 ⁸⁹	Spain	106	73±10		21.7%	
Garcia-Sanz 2020 ⁹⁰	Spain	602	73.8±10.6		14.0%	
Gavish 2015 ⁹¹	Israel	195	66±10		17.4%	
Ghanei 2007 ⁹⁷	Iran	98	58.3±11.0		37.0%	
Giron 2009 ⁹⁸	Spain	78	71±10		0.0%	
Glaser 2015 ⁹⁹	USA	617	Not reported		Not reported	
Gonzalez 2008 ¹⁰⁰	Spain	112	69.3±7.5		Not reported	
Goto 2017 ¹⁰²	USA	845,465	70		59.0%	
Goto 2018 ¹⁰¹	USA	76,697		76 (71–83)	59.6%	
Goto 2020 ¹⁰³	USA	905		76 (68–82)	54.0%	

Table I (Continued).

Study	Country	n	Age (years)		% Female
			Mean ± SD	Median (IQR)	
Gudmundsson 2005 ¹⁰⁴	Sweden	406	69.2±10.5		51.2%
Guerrero 2016 ¹⁰⁵	Spain	378	71.4±10.0		15.9%
Hajizadeh 2015 ¹⁰⁸	USA	4791	74.3±6.4		Not reported
Hakansson 2020 ¹⁰⁹	Denmark	4022		73.1 (63.7–81.1)	55.2%
Harries 2017 ¹¹⁰	UK	19,551	72.4±10.8		47.8%
Hartl 2016 ¹¹¹	European countries	16,016	70.8±10.8		32.2%
Hasegawa 2016 ¹¹²	USA	3084		70 (61–79)	50.0%
Hegewald 2020 ¹¹⁴	USA	2445	68.4±11.6		50.7%
Hemenway 2017 ¹¹⁵	USA	369	66		57.5%
Huertas 2017 ¹¹⁶	Spain	150		70 (65–76)	3.0%
Ingadottir 2018 ¹¹⁷	Iceland	121	73.7±9.0		57.0%
Islam 2015 ¹²⁰	USA	350	Not reported		54.9%
lyer 2016 ¹²¹	USA	422	64.8±11.7		49.9%
Jacobs 2018 ¹²²	USA	1,055,830		68 (59–77)	58.5%
Janson 2020 ¹²³	Sweden	51,247	74.6±10.1		54.8%
Jing 2016 ¹²⁷	China	8	Not reported		Not reported
Jo 2020 ¹²⁸	South Korea	15,101	73.4±9.7		25.4%
Johannesdottir 2013 ¹²⁹	Denmark	3176		72.1 (65.2–77.7)	55.2%
Jones 2020 ¹³⁰	UK	1029	74.4±9.9		49.0%
Kasirye 2013 ¹³²	USA	209	Not reported		Not reported
Kerkhof 2020 ¹³⁵	UK	16,661	75.1±9.9		50.3%
Keshishian 2019 ¹³⁶	USA	7892	78.1±7.6		57.7%
Kim 2010 ¹³⁹	South Korea	77	69.2±9.4		16.9%
Kim 2021 ¹⁴⁰	South Korea	4867		75–79	30.9%
Kishor 2020 ¹⁴³	India	100	64.0±8.5		16.0%
Ko 2020 ¹⁴⁴	Hong Kong	346	74.9±7.8		3.8%
Lau 2017 ¹⁵¹	USA	597,502	Not reported		55.3%
Law 2016 ¹⁵²	Australia	90	70.7±9.3		50.0%
Li 2020 ¹⁵⁶	China	108	70.6±9.3		21.3%
Lindenauer 2014 ¹⁵⁸	USA	25,628		69 (61–77)	56.6%
Lindenauer 2018 ¹⁵⁷	USA	2340	76.3±7.5		56.1%
Liu 2007 ¹⁵⁹	Taiwan	100	73.8±10.6		15.0%

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Study	Country	n	Age (years)		% Female
			Mean ± SD	Median (IQR)	
Loh 2017 ¹⁶⁰	USA	123	64.9±11.3		47.2%
Marcos 2017 ¹⁶¹	USA	143	72.3±10.0		7.0%
Martinez-Gestoso 2021 ¹⁶²	Spain	615	73.9±10.6		13.8%
Myers 2021 168	USA	7825	Not reported		55.1%
Myers 2021 167	USA	333,429		70 (61–80)	57.1%
Nantsupawat 2012 ¹⁷⁰	USA	81	73.9		53.1%
Narewski 2015 ¹⁷¹	USA	160	63.9±10.8		58.8%
Nastars 2019 ¹⁷²	USA	298,706	77.7±7.7		59.6%
Ng 2007 ¹⁷³	China	376	72.2±8.4		14.9%
Nguyen 2015 ¹⁷⁶	USA	2910	72±11		57.1%
Niu 2021 ¹⁷⁷	China	378	75.2±8.9		15.9%
Njoku 2022 ¹⁷⁸	Australia	2448		72 (64–80)	50.1%
Osman 1997 ¹⁸⁰	UK	266	68.0±9.1		47.0%
Ozyilmaz 2013 ¹⁸²	Turkey	107	66.3±8.6		15.0%
Park 2016 ¹⁸⁵	South Korea	339,379	71.5±11.6		29.8%
Peng 2021 187	China	123	71.1±9.6		26.8%
Pienaar 2015 ¹⁸⁹	South Africa	178	63±12		42.1%
Ponce Gonzalez 2017 ¹⁹¹	Spain	361	75.0±11.5		21.1%
Portoles-Callejon 2020 ¹⁹²	Spain	108	71.5±11.7		18.5%
Pouw 2000 ¹⁹⁴	Netherlands	28	70.0±7.2		42.9%
Pozo-Rodriguez 2015 ¹⁹⁵	Spain	5174	Not reported		Not reported
Price 2006 ¹⁹⁶	UK	7529	Not reported		Not reported
Quintana 2022 ¹⁹⁸	Spain	876	73.7±9.4		20.5%
Rahimi-Rad 2015 ¹⁹⁹	Iran	100	70.8±10.3		31.0%
Rinne 2015 ²⁰³	USA	25,301	68.9±10.5		3.2%
Rinne 2017 ²⁰²	USA	33,558	68.7±10.4		3.4%
Rinne 2017 ²⁰¹	USA	33,558	68.7±10.4		3.4%
Roberts 2002 ²⁰⁴	UK	1373		72 (66–78)	Not reported
Roberts 2011 ²⁰⁵	UK	9716		65–74	50.0%
Roberts 2015 ²⁰⁸	USA	306	70.3±12.3		56.2%
Roberts 2016 ²⁰⁶	USA	3612	66.6±12.1		67.2%
Roberts 2020 ²⁰⁷	USA	10,405	72.6±10.3		62.3%

Study	Country	n	Age (years)		% Female
			Mean ± SD	Median (IQR)	
Rodrigo-Troyano 2018 ²⁰⁹	Spain	106	71±8		17.9%
Ruby 2020 ²¹⁰	Egypt	190	63.1±10.1		0.0%
Shah 2015 ²¹⁴	USA	947,084	Not reported		Not reported
Shani 2022 ²¹⁵	Israel	1203	70.6±11.0		37.3%
Sharif 2014 ²¹⁶	USA	8263	56.5±5.7		58.8%
Shay 2020 ²¹⁸	USA	111	67.1±11.7		62.2%
Simmering 2016 ²²¹	USA	286,313	Not reported		Not reported
Singer 2020 ²²³	USA	28,240	72.7±8.7		51.9%
Singh 2016 ²²⁴	USA	135,498		75–84	60.2%
Snider 2015 ²²⁵	USA	378,419	76.2±6.9		56.8%
Stefan 2017 ²²⁸	USA	13,893		69	57.6%
Stuart 2010 ²³²	USA	6322	74.7±0.4		48.9%
Tran 2016 ²³⁴	USA	375	59.3±7.4		64.0%
Turner 2014 ²³⁵	England	1942	Not reported		Not reported
Ushida 2022 ²³⁶	Japan	3396	75.0±11.2		20.4%
Wang 2013 ²⁴²	Norway	481	72.8±10.5		53.4%
Wong 2008 ²⁴⁴	Canada	109	63.0±14.5		38.5%
Wu 2020 ²⁴⁵	Taiwan	625	76.3±10.6		12.0%
Wu 2021 ²⁴⁷	Taiwan	625	76.3±10.6		12.0%
Wu 2021 ²⁴⁶	USA	91	60±11		63.7%
Yilmaz 2021 ²⁴⁹	Turkey	110	67.8±9.3		18.2%
Yu 2015 ²⁵⁰	USA	18,282	56.6±5.8		62.4%
Zapatero 2013 ²⁵³	Spain	313,233	72.7±15.7		30.3%
Zhou 2021 ²⁵⁴	China	417	75±12		20.4%
Zhu 2021 ²⁵⁵	China	239		72	16.7%

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Note: Blacked out cells indicate that data are not available/applicable.

(Figure 3d). Among laboratory values, lower FEV_1 and anemia were the most common predictors (Figure 3e). Use of systemic corticosteroids during hospital admission was the most frequently reported predictor of readmission, among medications used during admission (Figure 3f). Discharge to long-term care or a skilled nursing facility was the most commonly reported predictor of readmission, of assessed predictors after admission (Figure 3f–h). Degrees of significance, and the specific studies reporting on each significant predictor, are reported in Table 3.

For COPD-related readmission, 23 significant predictors were found. The most common patient characteristics that were predictors were older age and prior hospitalization (Figure 4a). Mental health comorbidity, diabetes, high Charlson/ Elixhauser comorbidity index, and cancer were the most frequently reported comorbidity predictors of readmission

Table 2 Studies Assessing Interventions

Study	Country	n	Age (years)		% Female
			Mean ± SD	Median (IQR)	
		Cohort Studie	es		
Adamson 2016 ¹⁶	Canada	462	70.6±13.2		40.9%
Agarwal 2018 ¹⁷	USA	1248	Not reported		Not reported
Alshehri 2021 ²⁶	Saudi Arabia	80	67.0±10.3		41.3%
Ankjaergaard 2017 ²⁷	Denmark	201	71.5±10.8		56.7%
Ban 2012 ³²	Malaysia	193	68.5±8.8		13.0%
Bashir 2016 ³⁵	USA	461	71.7±13.3		32.5%
Bhatt 2017 ³⁹	USA	187	70.4±11.2		61.0%
Collinsworth 2018 ⁶¹	USA	308	70.5±12.2		58.4%
Cope 2015 ⁶⁴	UK	464	Not reported		Not reported
Dalal 2012 ⁷¹	USA	1936	63.9±9.9		55.4%
De Batlle 2012 ⁷²	Spain	274	68±8		6.9%
Gay 2020 ⁹²	USA	157	70.6±11.2		56.1%
Gentene 2021 ⁹³	USA	Not reported	Not reported		Not reported
George 2016 ⁹⁴	Singapore	340	72.6±9.1		11.8%
Gerber 2018 ⁹⁵	Australia	381	71±12		39.9%
Gerrits 2003 ⁹⁶	Netherlands	1219		65–74	40.4%
Gulati 2018 ¹⁰⁶	USA	250	69±11		42.0%
Ingadottir 2018 ¹¹⁸	Iceland	99		73.0 (71.0–77.0)	54.5%
Ingadottir 2018 ¹¹⁷	Iceland	121	73.7±9.0		57.0%
Jeffs 2005 ¹²⁴	Australia	216	67.5		63.9%
Joyner 2022 ¹³¹	USA	253	73.6±7.1		65.2%
Kawasumi 2013 ¹³³	Canada	3723	72.8		50.8%
Kim 2020 ¹³⁸	USA	65	62.5±9.0		58.5%
Kiri 2005 ¹⁴¹	UK	2557	71.1±9.0		49.6%
Kiser 2019 ¹⁴²	USA	28,700		60–69	53.9%
Ko 2014 ¹⁴⁷ Ko 2021 ¹⁴⁸	Hong Kong	185	76.9±7.37		10.3%
Lalmolda 2017 ¹⁴⁹	Spain	48	72.5±7.2		6.2%
LaRoche 2016 ¹⁵⁰	USA	3024	Not reported		Not reported
Lee 2016 ¹⁵³	USA	995	67.3±10.5		52.6%
Matsui 2017 ¹⁶³	Japan	12,572	78.4±9.5		18.7%
McGurran 2019 ¹⁶⁴	USA	2885	70.5±11.5		46.9%

Study	Country	n	Age (years)		% Female	
			Mean ± SD	Median (IQR)		
Moullec 2012 ¹⁶⁶	Canada	189	72.1±10.4		50.3%	
Myers 2020 ¹⁶⁹	USA	805,764	Not reported		56.3%	
Nguyen 2014 ¹⁷⁵	USA	4596	72.3±10.8		Not reported	
Nguyen 2021 ¹⁷⁴	USA	128	64.6±9.2		56.3%	
Ohar 2018 ¹⁷⁹	USA	1274	Not reported		56.3%	
Pant 2020 ¹⁸³	Nepal	86	70.6±11.0		47.7%	
Parikh 2016 ¹⁸⁴	USA	44	66		40.9%	
Pendharkar 2018 ¹⁸⁶	Canada	1435	70±12		48.5%	
Petite 2020 ¹⁸⁸	USA	358	67.1±11.6		60.9%	
Pitta 2006 ¹⁹⁰	Belgium	17		69 (60–78)	5.9%	
Puebla Neira 2021 ¹⁹⁷	USA	4,587,542	Not reported		42.2%	
Revitt 2013 ²⁰⁰	UK	160	70.4±8.6		45.6%	
Rueda-Camino 2017 ²¹¹	Spain	87	70.4±9.3		11.5%	
Russo 2017 ²¹²	USA	160	65.9±10.0		52.5%	
Seys 2018 ²¹³	European countries	257	69.8±10.3		33.9%	
Sharma 2010 ²¹⁷	USA	62,746		75–84	58.6%	
Shi 2018 ²¹⁹	China	6333	67.5±9.5		Not reported	
Shin 2019 ²²⁰	South Korea	308	72.3±9.5		23.7%	
Sin 2001 ²²²	Canada	22,620	75.1±6.7		43.5%	
Sonstein 2014 ²²⁶	USA	420	66.5±11.2		49.5%	
Stefan 2013 ²²⁷	USA	53,900		70 (61–78)	58.0%	
Stefan 2021 ²²⁹	USA	197,376	76.9±7.6		58.6%	
Suh 2015 ²³³	England	120	70±9		51.7%	
van Eeden 2017 ²³⁸	Netherlands	10	62.9±9.6		80.0%	
Werre 2015 ²⁴³	USA	244	Not reported		Not reported	
Zafar 2019 ²⁵²	USA	Not reported	Not reported		Not reported	
Zafar 2020 ²⁵¹	USA	133	60.0±9.8		36.1%	
	Ran	ndomized Control	ed Trials			
Atwood 2022 ²⁸	Canada	3710	71.7±12.4		49.7%	
Benzo 2016 ³⁷	USA	215	68.0±9.5		54.9%	
Bucknall 2012 ⁴⁷	UK	464	69.1±9.3		63.4%	
Conti 2002 ⁶³	Italy	49	71.8±7.8		Not reported	

Table 2 (Continued).

Study	Country	n Age (years)			% Female
			Mean ± SD	Median (IQR)	
Criner 2018 ⁶⁷	USA	64	61.7±7.9		60.9%
De Jong 2007 ⁷³	Netherlands	210	70.7±8.4		25.3%
Deutz 2021 ⁷⁵	USA	214	74.8±7.3		52.8%
Eaton 2006 ⁷⁷	New Zealand	78	77.3±7.1		53.8%
Eaton 2009 ⁷⁸	New Zealand	97	69.9±9.8		56.7%
Garcia-Aymerich 2007 ⁸⁸	Spain	113	73±8		14.2%
Gunen 2007 ¹⁰⁷	Turkey	159	64.1±8.9		12.0%
Hegelund 2020 ¹¹³	Denmark	100		73 (45–89)	58.0%
lp 2004 ¹¹⁹	Hong Kong	130	80.5±6.6		0.0%
Jennings 2015 ¹²⁵	USA	172	64.7±10.6		55.2%
Jimenez 2021 ¹²⁶	Spain	737	70.4±9.9		26.5%
Kebede 2022 ¹³⁴	Norway	40	73.8±8.2		62.5%
Khosravi 2020 ¹³⁷	Iran	60	71.0±8.9		28.3%
Ko 2011 ¹⁴⁶	Hong Kong	60	73.6±7.0		1.7%
Ko 2017 ¹⁴⁵	Hong Kong	180	74.8±8.2		4.4%
Ko 2021 ¹⁴⁸	Hong Kong	136	75.0±7.6		2.9%
Lellouche 2016 ¹⁵⁴	Canada	50	72±8		46.0%
Li 2020 ¹⁵⁵	China	378	66.3±8.1		15.9%
Monreal 2016 ¹⁶⁵	Spain	120		71 (61–78)	33.3%
Ozturk 2020 ¹⁸¹	Turkey	61	62.5±8.6		11.5%
Pourrashid 2018 ¹⁹³	Iran	62	63.4±8.5		16.1%
Stolz 2007 ²³⁰	Switzerland	226	69.5		50.4%
Struik 2014 ²³¹	Netherlands	201	63.7±8.3		58.7%
Utens 2012 ²³⁷	Netherlands	139	68.0±10.8		38.1%
Vanhaecht 2016 ²³⁹	European countries	342	69.9±10.3		32.2%
Vermeersch 2019 ²⁴⁰	Belgium	301	65.5±9.5		43.9%
Wang 2016 ²⁴¹	China	191	72.9±9.6		28.3%
Xia 2022 ²⁴⁸	China	337		70.0 (65.0–75.0)	16.9%

 Table 2 (Continued).

Note: Blacked out cells indicate that data are not available/applicable.

(Figure 4b). Longer hospital length of stay, higher eosinophil count, and home oxygen after discharge were also frequently reported predictors of readmission (Figure 4c and e). Degrees of significance, and the specific studies reporting on each significant predictor, are reported in Table 4.

Six prediction scores – the BODEX index,²³ CODEX index,²³ CORE score,²⁴⁷ DOSE index,²³ PEARL score,¹⁴³ and RACE scale¹⁵¹ – were reported to be predictive of all-cause readmission. The included components of each prediction score are reported in Table 5. CORE, PEARL, and RACE were reported to have good predictive value for readmission as a time-to-event outcome variable. The BODEX index, CODEX index, and DOSE index were reported to have good predictive ability for 2–3-month readmission. The CODEX index was reported to have good predictive ability for 6–12-month readmission (Table 3).

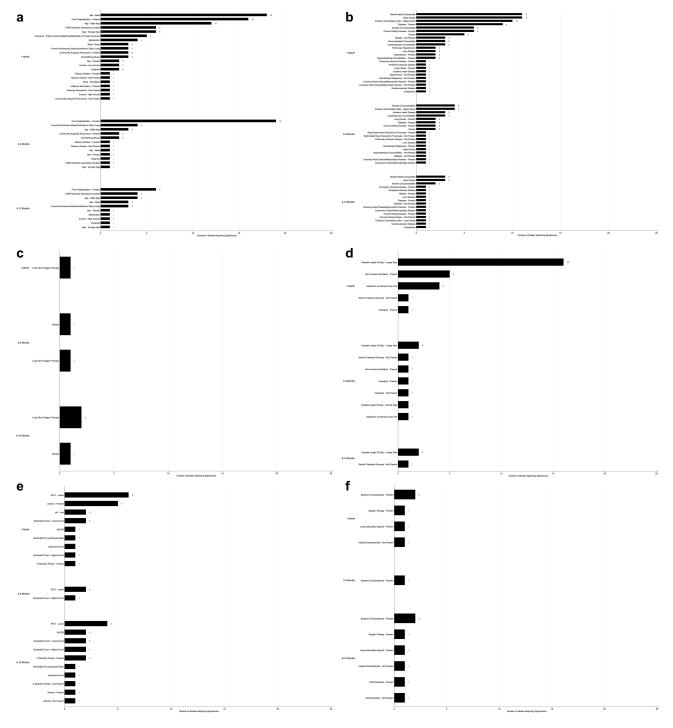


Figure 3 Continued.

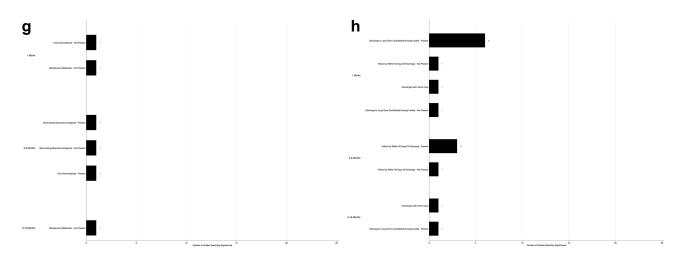


Figure 3 Significant predictors of all-cause readmission: (a) patient characteristics; (b) comorbidities; (c) medications prior to admission; (d) hospital care; (e) investigations; (f) medications during hospitalization; (g) medications on discharge; (h) disposition.

Some studies reported significant interventions that can reduce all-cause and COPD-related readmission, most notably use of a COPD-specific care package (<u>Supplementary Tables 3</u> and <u>4</u>). Most studies reporting on interventions reported that their intervention was not associated with a significant reduction in readmission rates.

Discussion

This is the largest systematic review to date, reporting on predictors for readmission of patients with COPD, with 242 articles reporting on 16,471,096 patients included in this review. We comprehensively report on predictors for both all-cause and COPD-related readmissions, for readmission at 1 month, 2–3 months, and 6–12 months. The included studies originated from around the world, and there was generally a low risk of bias. There were 64 predictors for all-cause readmission and 23 predictors for COPD-specific readmission. Significant predictors for all-cause readmissions included 1) pre-admission patient characteristics, such as male sex, prior hospitalization, poor performance status, number and type of comorbidities, and use of long-term oxygen; 2) hospitalization details, such as length of stay, use of corticosteroids, and use of ventilatory support; 3) results of investigations, including anemia, lower FEV₁, and higher eosinophil count; and 4) discharge characteristics, including the use of home oxygen and discharge to long-term care or a skilled nursing facility.

Several prior systematic reviews have also reported on predictors. Alqahtani et al reviewed 14 studies, stating that comorbidities, previous exacerbations/hospitalizations, and increased length of initial hospital stay were major risk factors for 30- and 90-day all-cause readmission.⁸ Heart failure, renal failure, depression, and alcohol use were also associated with increased 30-day all-cause readmission, with being female described as a protective factor for readmission. Bahadori and Fitzgerald examined 17 studies, and found that previous hospital admission, dyspnea, and oral corticosteroids were significant risk factors for readmission.⁹ Njoku et al reviewed 57 studies, and found that hospitalization in the year prior to index admission, comorbidities (such as asthma), living in a deprived area, and living in/or discharge to a nursing home were key predictors of COPD-related readmission.¹⁰

This review identifies some notable predictors worth highlighting that are not contained in previous studies, which were parsimonious. While prior studies reported heart failure and neuromuscular disease, we identified other significant preadmission comorbidities, including alcohol use, diabetes, and mental health. Similarly, poor performance status and malnutrition were both identified as important predictors of readmission. In-hospital use of critical care, including non-invasive ventilation, invasive ventilation, and ICU stay, was also identified as predictors. Use of steroids was also predictive of readmission; this was probably related to the severity of disease. Eosinophil count was both correlated and inversely correlated in different studies. While all studies excluded corticosteroid use prior to measurement of the

Variable Type	Type I Error	l Month	2–3 Months	6–12 Months
	-	Patient Characteristics		
Age	<0.05	Correlated ^{29,53,105,172} Inversely correlated ¹⁹¹	Correlated ³⁸ Inversely correlated ¹⁸³	Correlated ^{53,66,127}
	<0.01	Correlated ^{33,49,50,123,185,233,253} Inversely correlated ^{34,122,151,214,221}	Correlated ^{111,123}	Correlated ¹²³ Inversely correlated ⁷⁶
	Not reported	Correlated ²⁹		
Alcohol/drug abuse	<0.05	Correlated ²⁹		
	<0.01	Correlated ^{49,224}	Correlated ^{34,205}	
	Not reported			
Community-acquired pneumonia	<0.05	Correlated ^{83,210} Inversely correlated ²⁰⁸	Correlated ²⁵⁴	
	<0.01	Correlated ⁵⁰	Correlated ⁵⁰	
	Not reported			
COPD severity, assessed by scales	<0.05			
	<0.01	Correlated ^{25,49,50,105,247,250}	Correlated ⁵⁰	Correlated 53,55,127,244
	Not reported			
Dyspnea	<0.05	Correlated ⁵⁴	Correlated ³⁸	Correlated ⁸⁴
	<0.01	Correlated ¹⁰⁵		
	Not reported			
Income	<0.05	Correlated ²¹⁵		
	<0.01	Inversely correlated ^{122,224}		Correlated ⁹⁷
	Not reported			
Insurance: public insurance/Medicare/Medicaid vs private	<0.05			
insurance	<0.01	Correlated ^{49,53,122,128,151}		
	Not reported			

(Continued)

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Table 3 (Continued).

Variable Type	Type I Error	I Month	2–3 Months	6–12 Months
Male	<0.05	Correlated ^{16,35,151,172,178,215,216} Inversely correlated ¹²³	Inversely correlated ¹²³	Correlated ⁵⁹ Inversely correlated ¹²³
	<0.01	Correlated ^{49,53,74,122,128,140,185,214,224,232} Inversely correlated ²⁵³	Correlated ¹⁹⁵	Correlated ^{41,76}
	Not reported	Correlated ²⁰¹		
Malnutrition	<0.05	Correlated ⁷⁴		Correlated ¹³⁹
	<0.01	Correlated ^{33,74,253}		
	Not reported			
Poorer performance status/activities of daily living	<0.05	Correlated ^{25,84,247}	Correlated ^{25,195,198}	Correlated ^{30,84,104}
	<0.01		Correlated ⁶²	
	Not reported			
Prior hospitalization	<0.05	Correlated ^{54,84,178,212,233}	Correlated ^{20,38,178,183}	Correlated ¹⁷⁸
	<0.01	Correlated ^{25,31,49,105,125,172,175,176,208,215,216}	Correlated ^{22,25,31,45,84,89,91,111,125,195,198,209,212,215}	Correlated ^{41,55,81,87,104}
	Not reported		Correlated ⁶²	
Race: black	<0.05	Inversely correlated ¹⁷²		
	<0.01	Correlated ^{102,151,214}		
	Not reported			
Tobacco smoker	<0.05	Correlated ²⁴⁷	Correlated ⁴⁵	
	<0.01	Inversely correlated ²⁵³	Inversely correlated ³⁸	
	Not reported			
Vaccination: influenza	<0.05	Correlated ¹⁷⁰		
	<0.01	Inversely correlated ²³²		
	Not reported			

		Comorbidities		
Number of comorbidities	<0.05	Correlated ^{29,34,35,123,172}	Correlated ^{38,123}	Correlated ¹²³
	<0.01	Correlated ¹²²	Correlated ^{34,205}	Correlated ²⁴⁴
	Not reported			
Arrhythmias	<0.05	Correlated ²⁴		Correlated ⁵⁶
	<0.01			
	Not reported			
Cancer	<0.05		Correlated ³¹	
	<0.01	Correlated ^{31,33,49,50,253}	Correlated ⁵⁰	
	Not reported			
Cardiovascular comorbidities	<0.05	Correlated ^{34,103}	Correlated ^{38,198}	
	<0.01	Correlated ⁴⁹	Correlated ³⁴	
	Not reported			
Cerebrovascular disease	<0.05			
	<0.01	Correlated ⁴⁹		Correlated ³¹
	Not reported			
Charlson comorbidity index	<0.05	Correlated ^{74,215,255}	Correlated ^{195,215}	Inversely correlated ¹⁷⁸
	<0.01	Correlated ^{33,50,128,175,176,214,253}	Correlated ^{50,111}	
	Not reported			
Chronic kidney disease	<0.05	Correlated ⁵⁴	Correlated ³¹	Inversely correlated ⁷⁶
	<0.01	Correlated ^{33,49,50,122,250}	Correlated ⁵⁰	Correlated ³¹
	Not reported			
Connective tissue/rheumatologic disease	<0.05			Correlated ³¹
	<0.01		Correlated ²⁰⁸	
	Not reported			

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(Continued)

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Table 3 (Continued).

Variable Type	Type I Error	l Month	2–3 Months	6–12 Months
Coronary heart disease/myocardial infarction	<0.05		Correlated ³¹	
	<0.01	Correlated ⁴⁹ Inversely correlated ²⁵⁵		Correlated ³¹
	Not reported			
Diabetes	<0.05	Correlated ^{212,232}	Correlated ^{31,205} Inversely correlated ¹¹¹	Correlated ¹⁰⁸
	<0.01	Correlated ^{31,33,49,122,151,176,232}		Correlated ³⁰
	Not reported			
Gastrointestinal comorbidities	<0.05	Correlated ²¹²	Inversely correlated ²⁰⁸	
	<0.01	Correlated ⁴⁹		
	Not reported			
Heart failure	<0.05	Correlated ^{24,29,216,232}		Correlated ^{56,108}
	<0.01	Correlated ^{31,33,49,122,176,250,253}	Correlated ³¹	Correlated ³¹
	Not reported			
Right-sided heart failure/cor pulmonale	<0.05		Inversely correlated ²⁰⁸	
	<0.01		Correlated ²⁰⁵	
	Not reported			
Hematologic malignancy	<0.05			
	<0.01	Inversely correlated ²⁰⁸	Correlated ²⁰⁸	
	Not reported			
Hypertension	<0.05	Correlated ^{212,232}		
	<0.01	Inversely correlated ⁴⁹		
	Not reported			

Ischemic heart disease	<0.05	Correlated ²³²	Correlated ²⁰	
	<0.01		Correlated ^{50,205}	
	Not reported			
Liver disease	<0.05			Correlated ³¹
	<0.01	Correlated ^{31,49}	Correlated ³¹	
	Not reported			
Lung cancer	<0.05			
	<0.01	Correlated ^{50,216}	Correlated ^{50,205}	
	Not reported			
Mental health comorbidity	<0.05	Correlated ^{25,29,176}		Correlated ^{66,97,108}
	<0.01	Correlated ^{14,49,83,151,216,224,232,250}		
	Not reported			
Musculoskeletal comorbidity	<0.05			
	<0.01	Correlated ^{216,232,247}		
	Not reported			
Obesity	<0.05			Correlated ⁸⁴
	<0.01	Inversely correlated ^{74,122,253}		
	Not reported			
Peripheral vascular disease	<0.05			
	<0.01	Correlated ⁴⁹		Correlated ³¹
	Not reported			
Pulmonary hypertension	<0.05			
	<0.01	Correlated ^{176,250}		
	Not reported			

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(Continued)

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Table 3 (Continued).

Variable Type	Type I Error	l Month	2–3 Months	6-12 Months
Pulmonary vascular disease	<0.05		Inversely correlated ²⁰⁸	
	<0.01	Correlated ²⁵⁰		Correlated ⁵⁶
	Not reported			
		Medications Prior to Admission		
Long-term oxygen therapy	<0.05	Correlated ²⁴	Correlated ¹⁸³	Correlated ¹⁰⁰
	<0.01			Correlated ¹⁰⁴
	Not reported			
Steroid	<0.05		Correlated ²¹⁵	Correlated ²⁴⁴
	<0.01			
	Not reported			
		Hospital Care		
Admission to ICU	<0.05	Correlated ^{172,224,250}	Correlated ¹⁸³	
	<0.01	Correlated ²¹⁴		
	Not reported			
Hospital length of stay	<0.05	Correlated ^{25,33,172,216,224,250}	Correlated ³⁸ Inversely correlated ¹⁸³	Correlated ^{76,104}
	<0.01	Correlated ^{49,50,105,122,128,140,185,202,214,253}	Correlated ⁵⁰	
	Not reported			
Intubation	<0.05		Inversely correlated ²⁰⁸	
	<0.01	Correlated ⁴⁹	Correlated	
	Not reported			
Non-invasive ventilation	<0.05	Correlated ^{74,212}		
	<0.01	Correlated ^{33,49,247}	Correlated ³⁸	
	Not reported			

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Steroid treatment success	<0.05	Inversely correlated ⁶⁹		Inversely correlated ⁶⁹
	<0.01		Inversely correlated ⁶⁹	
	Not reported			
		Investigations		
Anemia	<0.05			Correlated ¹⁰⁸ Inversely correlated ⁷⁶
	<0.01	Correlated ^{33,49,175,176,250}		
	Not reported			
C-reactive protein	<0.05	Correlated ⁶⁰		
	<0.01			Correlated ^{53,127} Inversely correlated ⁷⁶
	Not reported			
Eosinophil count	<0.05	Inversely correlated ^{135,199}	Correlated ¹¹⁴	Correlated ⁶⁵ Inversely correlated ^{76,156}
	<0.01	Correlated ²⁴⁷		Correlated ¹¹⁴
	Not reported			
FEV	<0.05	Inversely correlated ^{204,235,249}	Inversely correlated ^{89,182}	Inversely correlated ⁶⁶
	<0.01	Inversely correlated ^{105,212,247}		Inversely correlated ^{53,87,104}
	Not reported			
Leukocyte count	<0.05			
	<0.01	Correlated ⁶⁰		Correlated ⁷⁶
	Not reported			
Neutrophil-to-lymphocyte ratio	<0.05			
	<0.01	Correlated ⁶⁰		Correlated ⁷⁶
	Not reported			

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Table	3 ((Continued).
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Variable Type	Type I Error	l Month	2–3 Months	6–12 Months
PaCO ₂	<0.05			Correlated ^{100,139}
	<0.01	Correlated ¹⁰⁵		
	Not reported			
pH	<0.05	Inversely correlated ^{105,255}		
	<0.01			
	Not reported			
		Medications During Hospitalization		
Anticholinergics	<0.05			Correlated ⁸⁷
	<0.01			Inversely correlated ¹⁰⁴
	Not reported			
Inhaled corticosteroids	<0.05			
	<0.01	Inversely correlated ²⁰⁸		Inversely correlated ⁵⁵
	Not reported			
Oxygen therapy	<0.05			
	<0.01	Correlated ¹⁷⁵		Correlated ³¹
	Not reported			
Long-acting beta-agonist	<0.05	Correlated ¹⁷⁶		
	<0.01			Correlated ⁵⁵
	Not reported			
Systemic corticosteroids	<0.05	Correlated ¹⁷⁵		
	<0.01	Correlated ¹⁷⁶	Correlated ³¹	Correlated ^{31,76}
	Not reported			
		Medications on Discharge		
Oral corticosteroids	<0.05	Inversely correlated ²¹⁶	Correlated ¹⁹⁵	
	<0.01			
	Not reported			

				•
Maintenance medication	<0.05	Inversely correlated ²³²		
	<0.01			Inversely correlated ²³⁴
	Not reported			
Short-acting muscarinic antagonist	<0.05			
	<0.01		Correlated ²⁰⁸	
			Inversely correlated ²⁰⁸	
	Not reported			
		Disposition		
Discharged with home care	<0.05			Correlated ⁸¹
	<0.01	Correlated ²¹⁴		
	Not reported			
Discharged to long-term care/skilled nursing facility	<0.05	Correlated ^{74,232} Inversely correlated ²²⁴		Correlated ¹⁰⁸
	<0.01	Correlated ^{35,49,122,128}		
	Not reported			
Follow-up within 30 days of discharge	<0.05		Correlated ¹²⁵ Inversely correlated ⁹¹	
	<0.01	Inversely correlated ²¹⁶	Correlated ^{182,198}	
	Not reported			
		Prediction Scores		
BODEX index ²³			p=0.008	
CODEX index ²³			p<0.0001	p<0.0001
CORE score ²⁴⁷	p<0.001			
DOSE index ²³			p<0.01	
PEARL score ¹⁴³	p<0.0001			
RACE scale ¹⁵¹	R ² =0.923			

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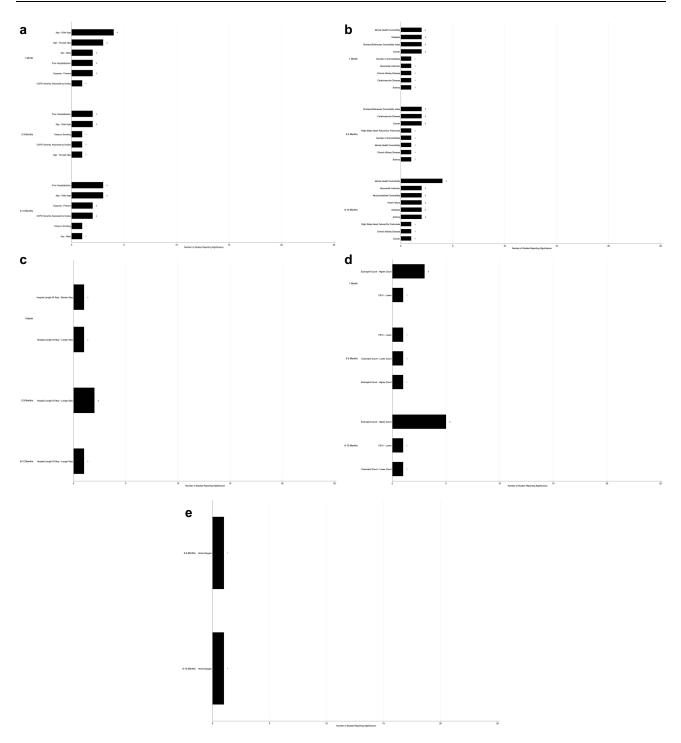


Figure 4 Significant predictors of COPD-related readmission: (a) patient characteristics; (b) comorbidities; (c) hospital care; (d) investigations; (e) medications on discharge.

eosinophil count, the studies used various cut-offs to define eosinopenia.^{114,135,199,247} Further research to determine the utility of eosinophil count is needed.

With COPD patients having a high all-cause readmission rate of 50%⁵ and being the largest single group of chronic disease patients reported in the literature, identifying those at greatest risk of readmission is a priority as more resources can be directed to this group. This comprehensive systematic review identifies many predictors across multiple domains, including prior to admission, during hospitalization, and post-hospitalization. Current prediction rules for readmissions

Table 4 Significant Predictors of COPD-Related Readmission

	Type I Error	l Month	2–3 Months	6–12 Months
	I	Patient Characteristics		
Age	<0.05	Correlated ^{219,245}		Correlated ^{31,129,234}
	<0.01	Correlated ^{50,110} Inversely correlated ^{34,48,206}	Correlated ^{50,110} Inversely correlated ³⁴	
	Not reported			
COPD severity, assessed by scales	<0.05			Correlated ^{21,187}
	<0.01	Correlated ⁵⁰	Correlated ⁵⁰	
	Not reported			
Dyspnea	<0.05	Correlated ¹¹⁶		Correlated ²¹
	<0.01	Correlated ²⁰⁶		Correlated ²⁰⁶
	Not reported			
Male	<0.05			Correlated ¹²⁹
	<0.01	Correlated ⁴⁸		
	Not reported	Correlated ²⁰¹		
Prior hospitalization	<0.05			Correlated ¹²⁹
	<0.01	Correlated ^{31,70}	Correlated ^{22,31}	Correlated ^{21,31}
	Not reported			
Tobacco smoking	<0.05			
	<0.01		Correlated ³⁴	Correlated ²⁰⁶
	Not reported			
		Comorbidities		- ·
Number of comorbidities	<0.05			
	<0.01	Correlated ²¹⁹	Correlated ³⁴	
	Not reported			
Asthma	<0.05			Correlated ¹²⁹
	<0.01	Correlated ²⁰⁶	Correlated ⁵⁰	Correlated ²⁰⁶
	Not reported			
Cancer	<0.05	Correlated ^{31,50}	Correlated ^{31,50}	
	<0.01			Correlated ³¹
	Not reported			
Cardiovascular disease	<0.05	Correlated ³⁴	Correlated ³⁴	
	<0.01		Correlated ¹³⁵	
	Not reported			

Table 4 (Continued).

	Type I Error	I Month	2–3 Months	6–12 Months
Charlson/Elixhauser comorbidity index	<0.05		Correlated ²²	
	<0.01	Correlated ^{48,50}	Correlated ⁵⁰	
	Not reported			
Chronic kidney disease	<0.05			
	<0.01	Correlated ⁵⁰	Correlated ⁵⁰	Correlated ³¹
	Not reported			
Diabetes	<0.05	Correlated ²⁰⁶		
	<0.01	Correlated ⁷⁰		Correlated ^{31,206}
	Not reported			
Heart failure	<0.05			
	<0.01			Correlated ^{31,206}
	Not reported			
Right-sided heart failure/cor pulmonale	<0.05			Correlated ²¹
	<0.01		Correlated ²²	
	Not reported			
Mental health comorbidity	<0.05			Correlated ^{21,129}
vientai neaith comorbidity	<0.01	Correlated ^{121,206}	Correlated ¹²¹	Correlated ^{121,206}
	Not reported			
Musculoskeletal comorbidity	<0.05			Correlated ¹²⁹
	<0.01			Correlated ²⁰⁶
	Not reported			
Myocardial infarction	<0.05			
	<0.01			Correlated ^{31,129}
	Not reported	Correlated ⁹⁹		
	1	Hospital Care		•
Hospital length of stay	<0.05	Inversely correlated ¹¹⁰		Correlated ¹⁸⁷
	<0.01	Correlated ⁵⁰	Correlated ^{50,110}	
	Not reported			
		Investigations		
Eosinophil count	<0.05	Correlated ¹¹⁴		Correlated ¹¹² Inversely correlated ¹⁵⁶
	<0.01	Correlated ^{114,245}	Correlated ¹¹⁴ Inversely correlated ¹³⁵	Correlated ^{36,65,114,187}
	Not reported			

Table 4 (Continued).

	Type I Error	l Month	2–3 Months	6–12 Months
FEV ₁	<0.05			
	<0.01	Inversely correlated ³⁴	Inversely correlated ^{34,135}	Inversely correlated ²⁴⁵
	Not reported			
	Medica	tions During Admission		
Oxygen therapy	<0.05			
	<0.01	Inversely correlated ¹⁸⁵		Correlated ³¹
	Not reported			
	Med	ications on Discharge		
Home oxygen	<0.05			Correlated ²¹
	<0.01		Correlated ²²	
	Not reported			

Table 5 Characteristics of Prediction Scores

	CODEX	BODEX	PEARL	CORE	RACE
Patient characteristics	Comorbidity Number of severe exacerbations (ED or admission) mMRC scale	BMI Number of severe exacerbations (ED or admission) mMRC scale	Age Previous admissions Left heart failure/ right heart failure eMRC scale Right heart failure	Lung function Neuromuscular disease exacerbations Triple inhaler management	Age Gender Income Race Payer Comorbidities
Hospitalization management	-	-	-	-	
In-hospital investigations	FEV ₁ %	FEV ₁ %		Eosinophil count	
Discharge characteristics	-	-	-	-	

have areas under the receiver operating characteristics curve in the range 0.70–0.72, and may be limited by lacking variables in all domains (Table 5). The findings from this systematic review can be used to develop other prediction scores with higher predictive power. The findings can also be used in clinical practice to help identify individual patients who may benefit from more resources to reduce their risk of readmission. While most prediction scores for COPD readmission are parsimonious, having five or fewer variables for ease of use, a more complicated model with more predictors may be more accurate. More complex models may be enabled through the increase in electronic patient records, which enable more discrete data elements as well as computer decision support.²⁵⁶

This review was not without limitations. There was heterogeneous reporting on some predictor variables; many studies used different cut-off points for predictor variables. We therefore reported on the general directionality of a predictor variable as it relates to readmission. We have reported the predictors as reported by the studies, using their original cut-off points and without any synthesis, in <u>Supplementary Tables 1</u> and <u>2</u>. In addition, we were unable to report

non-significant predictors owing to non-uniform reporting and therefore the total number of studies investigating each predictor. It is therefore unclear how many studies investigated specific predictors, and what proportion of them reported significant correlation with readmission. For certain predictors that may not be as well studied (eg malnutrition), there could be underestimation of importance.

It is also important to note that some published literature suggests that not all patients discharged with a diagnosis of "COPD" have spirometrically confirmed COPD, and therefore patients discharged with "COPD" may in fact have other comorbidities, such as congestive heart failure.²⁵⁷ Therefore, caution is needed in the interpretation of some of the included studies, given that they simply included patients with a diagnosis of COPD which may not necessarily be confirmed on spirometry. Future studies could look to assess only patients who have spirometrically confirmed COPD.

There may also be some concerns over the generalizability of individual studies to the larger population of patients with COPD admitted to hospitals. There were three studies^{127,190,238} with sample sizes of less than 20, and another three studies^{80,134,194} with sample sizes of 20–40 patients. Moreover, there were three studies^{98,119,210} with no females included in the sample, and another 52 studies^{20–23,29,32,38,42,51,53,68–70,72,74,88,90,91,94,116,139,143–149,155,159,161–163,173,177,181,182,190,192,193,201–203,209,211,245,247,249,255 where less than 20% of the sample comprised of females. Reassuringly, the significant predictors reported by these studies agree with larger and more representative studies. In addition, a large proportion of the studies originated from the USA, which may make the results of this review more generalizable to the US population and slightly less generalizable to}

other countries, especially given the lack of a universal healthcare system in the USA and therefore the potential confounding effect on readmissions. In conclusion, we found that predictors of readmissions after an admission for COPD exacerbation included patient characteristics prior to and at admission, hospitalization management, results from admission investigations, and discharge characteristics. Findings from this review may enable better model generation if predictors from all these domains are included. These findings may also be used to identify new predictors in the different domains and can be

Disclosure

The authors report no conflicts of interest in this work.

used by clinicians to help generate their gestalt of readmission.

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