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Reducing the Readmission Burden of COPD: A Focused Review of Recent Interventions

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Abstract The burden of chronic obstructive pulmonary disease (COPD) in the United States is high, especially with regard to readmission rates and annual cost of health care. However, to date, there is little consensus about which clinical interventions have the greatest impact on reducing COPD readmissions. We reviewed literature in PubMed/MEDLINE to identify interventions that have the greatest impact on COPD readmissions, stratified by four clinical domains: patient risk factors, longitudinal care, acute care, and post-discharge care. Patients with more severe disease and fewer social supports are most vulnerable to COPD readmission. Chronic treatment with combined inhaled corticosteroids-long-acting beta-agonists or tiotropium as well as early antibiotic treatment during acute hospitalization decrease readmission rates. After discharge, the greatest effect on readmission rates was seen with early pulmonary rehabilitation, outpatient follow-up within 30 days, and enrollment in an integrated care program. While the standard of care in reducing COPD readmission rates remains to be elucidated, a multi-faceted approach that targets high-risk populations is likely to be most effective.

Keywords Chronic obstructive pulmonary disease (COPD) · Acute exacerbation of COPD (AECOPD) · Bronchitis · Emphysema · Readmission · Rehospitalization

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Introduction

The impact of chronic obstructive pulmonary disease (COPD) on the American health care system and health outcomes is irrefutable, altering mortality, health-related quality of life, health care utilization, and health care spending [1]. In some regions of the United States, prevalence rates for COPD approximate 9 % and COPD mortality approaches 66 deaths per 100,000 patients [2]. Rates of all-cause Medicare readmissions in the 30 days following an index hospitalization approach 20 % [3], with similar COPD readmission rates. Acute exacerbations of COPD (AECOPD) account for greater than 600,000 hospital admissions annually, with an estimated total direct cost of at least 20 billion [4].

In thinking about a clinical system that effectively minimizes readmission rates for AECOPD, there are many different potential targets for intervention. One strategy is to accurately identify patients who are at increased risk of readmission, and those that are high utilizers of clinical resources [5]. In this population lies a significant potential benefit in reducing readmission rate, and by extension, lowering health care cost associated with frequent acute care. Another potential point of intervention is to identify the long-term treatment options and strategies that impact readmission rate, promoting these treatments to all patients (or at least the high-risk population) [6]. A third option is to modify our acute care treatment algorithms to maximize the use of therapeutics that have been shown to reduce readmission rates for COPD [7]. Finally, we are left with a reassessment of our transition of care practices, identifying and implementing post-discharge interventions that have lasting effects on readmission rate, enabling greater self-sufficiency and outpatient support for patients. Given that many admissions for AECOPD tend to cluster in time with

the greatest risk in the 2 months after a prior exacerbation [8], this post-exacerbation window seems to hold the greatest potential for benefit.

Predicting and preventing mortality have long been studied, but recent Center for Medicare and Medicaid Services (CMS) guidelines have brought thirty-day readmission rate to the forefront of the discussion [9]. As providers and health care delivery systems look toward the future of caring for patients, the need to design systems that effectively provide high-quality care and minimize overutilization of resources is pressing. The means by which we can achieve this aim have historically been unclear, as studies examining various interventions and their impact on readmission and health care utilization and/or health care cost have only recently become popular. This review is intended to succinctly summarize recent research that has examined how we can minimize readmission rates for COPD, with the longitudinal goal of decreasing the clinical and financial burden of COPD.

Methods

We searched PubMed using the following search terms: COPD, bronchitis, emphysema, rehospitalization, and readmission. Articles were narrowed by inclusion of studies published from 2010 to 2014. We then limited our search to specifically include only observational studies or clinical trials examining hospital readmission as an outcome published in the English language. All studies that addressed readmission rate or risk in patients with COPD were included. We then reviewed the reference lists of each candidate study and incorporated any relevant articles that were excluded by the parameters of the original search, including studies with significant impact on current practices (Fig 1). We classified our interventions into the following four clinical domains: patient risk factors, longitudinal care, acute care, and post-discharge care. We present overall effects of the interventions study, aggregated within each clinical domain.

Results

Patient Risk Factors

Studies have supported the strength of certain socio-demographic characteristics such as: older age [5, 10, 12], male sex [10], low monthly income [13] and being unmarried or widowed [14], in predicting readmission for AECOPD. Many clinical indicators of greater disease severity are not surprisingly also predictive of increased readmission rates, including: number of previous admissions for AECOPD [1, 10, 12, 15•, 16–21], reduced forced expiratory volume in one second (FEV_1) [5, 11, 12, 14, 15•, 17, 18, 21–23, 29, 31], duration of COPD >5 years [23], chronic prednisone use [5, 21, 24, 25], hypercapnia at discharge [19], severity of functional impairment [15•, 16, 20, 21, 26], and lower quality of life scores [19, 21, 27]. Comorbidities that increase risk for readmission notably include cardiovascular disease, asthma [5, 10, 28] and anemia [29]. A recent prospective cohort study identified depression symptoms at discharge as an independent predictor of readmission in the following 12 months, contrary to the finding of prior studies [13]. Malnutrition is correlated with increased risk of 30-day readmission rate, even when controlling for confounders. Interestingly, obesity affords a modest protective impact on readmission [30]. Poor adherence to treatment and follow-up has recently been implicated as an independent predictor of increased readmission rate [29].

BODE Index

How do we then take all of the possible factors that influence a patient's inherent risk for COPD readmission and reduce them to the most essential components? The key is to develop a clinical tool that can help stratify the risk of readmission in COPD patients. Developed by Celli et al., the BODE index is a clinical grading system developed to predict mortality in COPD patients. Components of the BODE index include body mass index (BMI), airflow obstruction (as measured by FEV_1), the Medical Research Council (MRC) dyspnea score and exercise capacity (as measured by a 6 min walk test) [32]. Prior studies have shown that the BODE index is a more accurate predictor of mortality than FEV_1 [32, 33]. Additional research has supported utility of the BODE index in predicting hospital admissions, both when used as a single data point [34, 35] or when followed serially [36]. Temporal changes in the BODE score of greater than one correlate with increased risk of earlier admissions, especially when measured at 6, 12, and 24 months after initial baseline [36].

ADO Index and DOSE Index

Newer prognostic tools include the ADO and the DOSE indices. In an attempt to simplify the BODE index for greater use in primary care settings, Puhan et al. generated and validated the ADO index in predicting COPD mortality, eliminating the 6 min walk test and substituting age for FEV_1 [37]. To achieve a similar aim, Jones and colleagues derived and validated the DOSE index as a marker of disease severity, substituting smoking status for BMI and number of prior exacerbations for 6 min walk test. The DOSE index correlates with risk of future COPD exacerbations [38] and has also been found to correlate with patient mortality in a group of primary and secondary care patients [39].

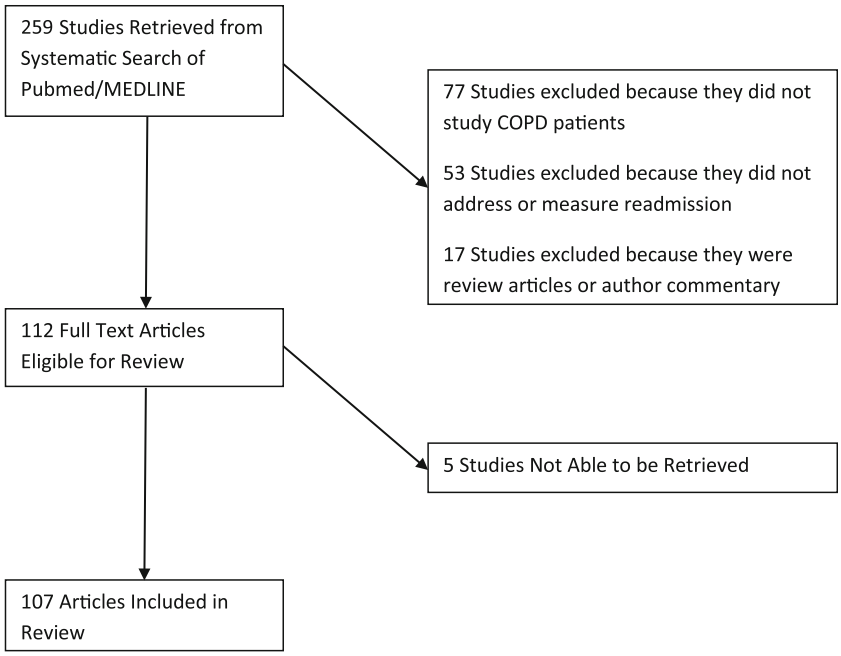

Fig. 1 Flow diagram of study selection for inclusion or exclusion

Comparing the Indices

In a comparison with the three aforementioned clinical scores, Motegi et al. demonstrated a superior ability of the DOSE index to predict future exacerbations [40•]. In the last year, Bertens and colleagues derived and validated a risk score to better predict exacerbation risk, incorporating four clinical variables: exacerbations in the previous year, smoking pack years, FEV_1 and history of vascular disease [41]. Given the multitude of prediction models now available and the variable performance of each model in different clinical settings, further study is needed to determine which model most accurately predicts readmissions for AECOPD and is the most practical to implement in daily care.

Longitudinal Care

How we treat patients in the outpatient setting may influence the stability of disease and minimize the fluctuations in disease activity that lead to hospitalization [6]. Few studies have specifically addressed this question, only recently have researchers explored how different long-term treatment regimens influence readmission rates.

Combination inhaled corticosteroid (ICS)-long-acting beta-agonist (LABA)

In two large retrospective cohorts, Dalal et al. compare treatment with anticholinergics (AC) or combined ICS–LABA therapy. Combined ICS–LABA treatment was associated with 33 % fewer admissions and 20 % lower cost of health care in the 12 months followed an index exacerbation, with a similar result in their earlier study [42, 43]. This study builds on work by Soriano et al., who showed a 41 % reduction in risk of death or rehospitalization for the 12 months after an index exacerbation in patients treated with a combination ICS–LABA compared with those given a short-acting beta-agonist only [44]. Older studies have shown reduced rates of moderate-severe COPD exacerbations with combined ICS–LABA therapy compared with LABA alone [45, 46]. Utilizing a large Medicaid database in Texas, Rascati and colleagues described a 35 % lower risk of hospitalization with ICS–LABA compared with ipratropium (IPRA) alone [41]. The use of ICS–LABA was also associated with greater prescription costs, but significant reductions in all–cause medical costs [47]. ICA–LABA combinations (in comparison with anticholinergics, short-acting beta-agonists and long-acting beta-agonists) consistently demonstrate lower rates of hospitalization and readmission.

Ipratropium/Tiotropium

Not surprisingly, tiotropium (TIO) has been shown to decrease COPD hospitalizations as compared with placebo in two randomized controlled trials [48, 49]. In contrast, a retrospective cohort study in Denmark demonstrated increased risk of COPD hospitalization with TIO [50]. A number of studies have conflicting results about AC agents, however, many also note a propensity of AC-users to have greater COPD severity, a potential confounder. As noted in the previous section, multiple retrospective studies demonstrated the inferiority of monotherapy with IPRA or TIO to combination

therapy with medium dose ICS–LABA in regard to mortality, hospitalization risk and overall cost [40•, 46, 47]. However, when comparing TIO to high-dose ICS–LABA in a large double-blinded controlled trial, Wedzicha and colleagues found no difference between the two treatments in exacerbation risk over 2 years. There was an advantage of ICS–LABA treatment in overall health status, mortality and completion of the trial [51]. A large VA cohort study by Lee et al. demonstrated a 22 % decrease in risk of hospitalization in patients taking the combination of TIO + ICS + LABA [52]. In comparing IPRA and TIO directly, researchers found no differences in rates of readmission between the two treatments, but interpretation was limited by the inability to stratify patients by disease severity [53•]. A previous double-blinded controlled trial comparing TIO and IPRA showed one-quarter decrease in exacerbations as well as greater time to first exacerbation and first hospitalization with TIO [54]. As outlined above, recent evidence supports TIO as superior to IPRA with regard to COPD readmissions, especially when paired with ICS and LABA.

Acute Care

As providers, there is a wide variability in how we treat patients who are admitted with AECOPD. Many factors contribute to the treatment plan for each patient, including provider experience and preference, patient history, local bacterial resistance patterns and subtleties of the patient's presentation. A large retrospective cohort in the US revealed that only 66 % of patients admitted for AECOPD received all recommended elements of diagnostics and therapeutics (including chest radiography, supplemental oxygen, bronchodilators, systemic steroids and antibiotics). In addition, 45 % of patients received tests or treatments that are of no proven benefit. Only one third of patients received all recommended tests and treatments without any unnecessary care [7]. A similar prospective study in Canada showed that in patients hospitalized for AECOPD, only 70 % received oral corticosteroids and only 5 % were referred to pulmonary rehabilitation [55]. These statistics clearly indicate significant room for improvement in standardizing acute care of COPD.

Emergency Medicine Care

Adherence to national standards of care for AECOPD in the Emergency Department (ED) is similarly low [56]. Leveraging the proven benefit of care bundles, McCarthy and colleagues endeavored to assess the impact an ED-based COPD care bundle might have. Their ED care bundle included 10 elements (optimized supplemental oxygen, ABG, bronchodilators, basic laboratories, chest radiography, oral corticosteroids, antibiotics, referral to COPD outreach program, referral to pulmonology and venous thromboembolism prophylaxis). After implementation of the care bundle, many markers of quality care improved, but there was no improvement of 30-day readmission rate, which may be related to small size of the study [57].

Choice of Antibiotics

Recent studies indicate a significant decrease in risk of treatment failure for inpatient treatment of AECOPD with antibiotics [58, 59]. In addition, initiation of antibiotics within the first two hospital days is associated with lower rates of 30-day readmission for COPD (but higher readmission rates for diarrhea, including *clostridium difficile*) [58]. Two large retrospective cohort studies found no difference in treatment failure or 30-day readmission rates between patients treated with macrolides (with or without cephalosporins) versus quinolones [60, 61•]. In support of prior studies, Stefan and colleagues also noted a 13 % reduction of 30-day readmission rate with early initiation of antibiotics [61•]. One study also found higher rates of antibiotic-associated diarrhea with quinolones [60].

Corticosteroid Dosing and Duration

Despite early small studies that showed mixed results on efficacy with high inter-study heterogeneity [62, 63], the impact of steroids on risks of treatment failure for AECOPD have been clearly demonstrated [64]. Oral dosing (prednisolone) was subsequently found to be non-inferior to intravenous (IV) administration with regard to treatment failure in the subsequent three months [65]. A large retrospective cohort study comparing oral and IV steroids in AECOPD found no difference in either 30-day readmission rate or treatment failure, with shorter length of stay (LOS) and lower hospital costs for the oral group [66]. Identifying the ideal duration of corticosteroid therapy has been equally difficult. A Cochrane review on this topic did not reveal any difference in risk of treatment failure between steroid courses of ≤ 7 and >7 days, but data analyzed were low quality and fraught with high heterogeneity [67]. To further this point, Leuppi et al. recently found a 5-day course of prednisone to be non-inferior to a longer 14-day course with regard to 6-month re-exacerbation rates and combined endpoint of death or exacerbation [68••].

Post-discharge Care

Discharge Medication Reconciliation

Determining the appropriate medication regimen at the time of discharge may have an impact on rate of readmission for all hospitalized patients. Admission to the

hospital has been shown to increase risk of inadvertent medication discontinuation [69]. A prospective cohort study found that the risk of 30-day readmission increased from 6 % (patients with no medication discrepancies) to 14 % in patients with at least one medication discrepancy. Not surprisingly, the risk of medication discrepancies increases with number of medications prescribed [70]. A recent study examined a pharmacist-led discharge medication reconciliation program for patients admitted with an AECOPD, finding some decrease in 30-day readmission rate from 22 % (pre-intervention) to 16 % (post-intervention). This study was significantly limited by small size ($n = 29$) and resulting inadequate power [71]. A larger prospective study targeted high-risk patients with a pharmacist phone call in the first week after discharge, noting decreased readmission rates at 7 days (0.8 vs. 4 %, $p = 0.01$) and 14 days (5 vs. 9 %, $p = 0.04$) after discharge [72]. In contrast to the studies above, a recent systematic review concluded that medication reconciliation alone did not seem to impact 30-day readmission rates, noting that studies with a positive benefit incorporated medication reconciliation into a more comprehensive post-discharge intervention, thus masking the true effect of discharge medication reconciliation [73].

Transitional Care

The recent establishment of transitional care management codes by the CMS financially incentives outpatient providers to assess their patients within one to two weeks after discharge from an acute hospitalization. However, many physicians have raised the concern that increasing access to primary care has not been definitively proven to decrease utilization of inpatient services. A Veterans Affairs (VA)-randomized controlled trial showed increased rates of readmission for patients who received intensive primary care in the 6 months after an index hospitalization. This increase in readmission remained significant even after adjusting for health care utilization in the 6 months prior to the study [74]. In contrast, a large Medicare population-based cohort study demonstrated that patients who attended an outpatient visit in the month after admission for AECOPD had 14 % fewer ED visits and 9 % fewer readmissions within 30 days [75]. While much smaller in scale, a prospective cohort by Misky and colleagues showed patients who did not attend a primary care follow-up within 4 weeks of discharge were ten times more likely to be readmitted in the 30-day window after index hospitalization [76].

Pulmonary Rehabilitation after AECOPD

Pulmonary rehabilitation has been demonstrated to safely improve symptoms, quality of life and risk of future exacerbations in patients with COPD, even in the post-exacerbation period [77]. The impact of this intervention on rates of readmission has recently been investigated. Seymour and colleagues found that patients receiving post-exacerbation pulmonary rehabilitation had 85 % fewer readmissions for AECOPD in the subsequent 90 days [78]. This benefit on readmissions was lost when measured at one year by different researchers [79]. In contrast, Revitt et al. demonstrated that 12-month admissions in patients who completed post-exacerbation pulmonary rehabilitation decreased by 38 % in comparison with the number of admissions the year prior [80•]. There does seem to be an effect of post-exacerbation pulmonary rehabilitation on readmission rates, but there is conflicting evidence about when the greatest reduction in readmissions occurs.

Nurse-led Initiatives

Building on the current outpatient care structure that includes visiting nursing services and contact with nurse educators, many studies have investigated the impact of nursing-led interventions on readmissions for COPD. Some studies investigating the impact of patient education and self-management affect readmission rates have demonstrated a positive effect of these interventions [81, 82], while others have yielded negative results [83, 84]. Cochrane reviewers found that teaching self-management skills to patients likely reduces hospital admissions, but large heterogeneity between studies precluded meta-analysis [85]. A small Spanish study compared patients randomized to nursing home visit (within 3 days after discharge) plus pulmonologist phone call to those receiving usual care and found no difference in rates of 30-day readmission [86]. Similarly, small studies in the UK and Tasmania displayed no effect on readmissions with nurse home visits or community nurse mentoring [87, 88]. A corollary study in the US found no effect on ED visit or hospitalizations in those receiving 6 months of nurse-assisted medical management or nurse-assisted collaborative management versus usual care [89]. In Scotland, investigators discovered that while supported self-management itself did not influence readmission rates, patients who were effective self-managers benefitted from a 50 % reduction in readmissions compared with patients who were ineffective self-managers [90]. A systematic review of nurse-led interventions found equivocal impact of these interventions on readmissions, limited by sparse data and methodological flaws in most trials [91].

Telephone Support

Many of the interventions described in the studies above were time and labor intensive, making them costly and marginally effective. Other researchers have investigated

the impact of less intensive interventions, such as the addition of 24-hour telephone support. Older studies looking at the impact of adding telephone support to primary care were conflicting about their impact on clinic visits and emergency care [92]. Researchers in Australia completed a two-month observational study showing 12 % of calls successfully averted emergency assistance, thus decreasing the number of presentations to the hospital [93]. In the UK, researchers provided one year of 24-hour telephone support after a COPD admission with check-in calls every 2 months and invitations to attend clinic every 6 months. Fifty-two patients completed a year of follow-up and were noted to have 45 % fewer admissions than the year prior to enrolling in the service. Importantly, there was low overall utilization of the hotline with 0.01 calls/patient/day, especially on the overnight shift, where researchers calculated the need for 2,400 patients to expect one overnight call daily [94]. The impact of telephonic follow-up in lieu of or in concert with follow-up visits has been assessed by many small studies. Unfortunately, there is wide variability in the organization and structure of the telephonic follow-up interventions as well as low methodological quality in most studies. For these reasons, a Cochrane review on the effects of post-discharge telephone follow-up was inconclusive [95].

Telemonitoring

Heralded as the future of modern medicine, incorporating advances in technology with protocol-driven care, telemedicine has unfortunately not lived up to its oversized expectations. Telemonitoring in heart failure has suffered from conflicting data on mortality and hospitalizations [96, 97]. Unfortunately, implementation of telemonitoring in COPD has been plagued by the same problems. Initial studies are small and display wide heterogeneity. A systematic review and meta-analysis by Polisena et al. included 9 studies that compared home telemonitoring or telephone support to usual care. Home telemonitoring is stated to decrease hospital admissions; however, these data are based on only one RCT and two observational studies and suffers from high methodological variability [98]. Similarly, a systematic review by Bolton and colleagues asserted that the benefit of telemonitoring remains unproven due to the high risk of bias in study design and significant heterogeneity [99]. A Cochrane review and meta-analysis on this same topic found a significant decrease in ED visits (3 studies) and hospitalization (4 studies) in patients treated with telehealthcare [100]. A recent multicenter-blinded randomized controlled trial of telemonitoring showed no difference in time to first admission or number of admissions for COPD patients [101]. Despite significant research effort, the true benefit of telemonitoring on COPD readmissions and ideal format of telemonitoring interventions remain uncertain.

Integrated Care Programs

While many of the previous interventions described above have an equivocal or uncertain effect on hospital readmission, some researchers have created integrated care programs in an effort increase the impact of each component. Many integrated care programs incorporate nursing follow-up, case management, patient education and tailored care plans. Pulmonary rehabilitation has also been included in some integrated care programs. A small European study conducted by Casas and colleagues investigated the impact of providing patient with a specialized care plan as well as access to a specialized nursing case manager at the time of discharge, finding decreased readmission rates at 12 month follow-up [102]. A subsequent study in London that evaluated the impact of pulmonary rehab, self-management education, personalized action plan, monthly telephone calls and quarterly nurse visits found no difference in rates of hospital readmission [103]. Another small randomized controlled trial in the US noted decreased 30-day readmission rate in patients who were treated with the combined intervention of medication counseling by a pharmacist, disease-specific education by a care coordinator and telephone follow-up [104]. A corollary study conducted by the VA demonstrated a 64 % fewer combined admissions and ED visits in patients who received a combination of patient education, personalized action plans and monthly telephone calls [105]. Similarly, a retrospective longitudinal cohort study in Canada found a 65 % decrease hospitalization rate in the year after patients received self-management education, written action plans, and case management with follow-up visits and access to a call center [106].

One final-integrated care program that many have studied is the concept of hospital at home care. Patients meeting criteria are discharged soon after initial assessment with continued daily close monitoring, either remotely or with daily respiratory nurse home visits, to monitor symptoms and improvement. A systemic review of 7-randomized trials found no difference in mortality or readmission rate for patients treated with the hospital at home plan. The reviewers did note that only a quarter of patients presenting to the hospital for AECOPD were suitable candidates for the hospital at home program, and this type of outpatient treatment is likely not a viable option for most patients admitted with AECOPD [107].

Conclusions

Despite the abundance of literature examining COPD outcomes, only a few interventions stand out as consistently impacting readmission rate. Patients who are older and with fewer social supports or financial resources seem to be at

highest risk for readmission, as are those with more severe COPD, more impaired function and lower quality of life. Using the DOSE index (dyspnea score, obstruction, smoking status, and number of prior exacerbations) may provide the strongest correlation with risk of readmission and seems easier to incorporate into daily care than prior risk indices. Long-term treatment with combined ICS–LABA or TIO (alone or in combination) affords the greatest readmission reduction, although the true impact of anticholinergics may be skewed by greater disease severity in patients prescribed these agents. When admitted, patients benefit most from initiation of antibiotics in the first 48 hours. After discharge, interventions with the best evidence to minimize readmission rate include early pulmonary rehabilitation, outpatient follow-up within 30 days and enrollment in an integrated care program. Most integrated care programs take advantage of the combined benefits of pulmonary rehabilitation, visiting nurses or telephonic nursing support, education in self-management techniques and individualized care plans.

There is marked heterogeneity regarding when readmission rates are assessed; studies vary in their measurement of 30-, 60-, 90-day, six-month, or one-year readmission rates, making direct comparison difficult. Many of the early studies are small in size and vary significantly in their methodology, thus blurring the conclusions that can be drawn from their cohorted data.

Looking forward, the ideal treatment for COPD with regard to minimizing readmission rates would hopefully fuse many of the interventions highlighted above. As demonstrated with integrated care programs, the impact of the care combination is greater than that of its individual parts. Perhaps a broad unified approach may be the best strategy to minimize the cost and care burden of COPD in the coming years.

Compliance with Ethics Guidelines

Conflict of Interest Andrea Poisson Irani and LeRoi S. Hicks have no conflicts of interest to disclose.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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