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Is positive airway pressure therapy underutilized in chronic obstructive pulmonary disease patients?

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Abstract

Introduction—The role of noninvasive positive pressure ventilation (NIPPV) in patients with stable chronic obstructive pulmonary disease (COPD) in the home-setting remains controversial. Despite studies suggesting potential benefits, there is an apparent under-utilization of such therapy in patients with stable COPD in a domiciliary setting.

Areas covered—The reasons for under-utilization in the home-setting are multi-factorial, and we provide our perspective on the adequacy of scientific evidence and implementation barriers that may underlie the observed under-utilization. In this article, we will discuss continuous PAP, bilevel PAP, and non-invasive positive pressure ventilation using a home ventilator (NIPPV).

Expert commentary—Many patients with stable COPD and chronic respiratory failure do not receive NIPPV therapy at home despite supportive scientific evidence. Such under-utilization suggests that there are barriers to implementation that include provider knowledge, health services and payor policies. For patients with stable COPD without chronic respiratory failure, there is inadequate scientific evidence to support domiciliary NIPPV or CPAP therapy. In patients with stable COPD without chronic respiratory failure, studies aimed at identifying patient characteristics that determine effectiveness of domiciliary NIPPV therapy needs further study. Future implementation and health-policy research with appropriate stakeholders are direly needed to help improve patient outcomes.

Keywords

Chronic Obstructive Pulmonary Disease; Noninvasive Ventilation; Artificial Respiration; Respiratory Insufficiency; Health Plan Implementation

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1. Introduction

The World Health Organization (WHO) estimates that nearly 65 million people have moderate to severe chronic obstructive pulmonary disease (COPD)[1] and that COPD accounted for 5% of all deaths globally in the year 2005[1]. In the United States (U.S.), COPD is the third leading cause of death, and there are concerns that accurate epidemiological data is difficult and expensive to collect in poor countries[2]. Globally, COPD-related mortality is expected to increase by more than 30% in the next 10 years and by the year 2030, COPD-related mortality will likely become the third leading cause of death worldwide[2]. Moreover, COPD is an important cause for hospitalization in the elderly with a discharge rate of 23.2 per 100,000 population in the U.S.[3]. It has been estimated that COPD-related hospitalizations account for nearly $50 billion in annual healthcare costs[3]. The 30-day readmission rate for re-hospitalization of patients with COPD is unacceptably high (20–39%)[4, 5, 6]. In the U.S. the recognition that repeated hospitalizations incur huge healthcare burden led the Center for Medicare and Medicaid Services (CMS) to financially penalize hospital systems with higher than expected readmission[7]. Such action has led healthcare providers and systems to develop COPD disease management programs aimed at reducing both emergency admissions to the hospital and healthcare utilization through physical rehabilitation, medication adherence promotion, and other methodologies.

Noninvasive positive pressure ventilation (NIPPV) administered by home ventilators, bilevel positive airway pressure therapy (bilevel PAP) with or without back-up rate (collectively termed Respiratory Assist Device [RAD]) in the U.S as well as continuous positive airway pressure (CPAP) therapy for coexistent obstructive sleep apnea are available therapies in the domiciliary setting. Such therapy in patients with stable COPD in the home-setting may have a significant impact on patient outcomes in COPD, but the use of such devices remains controversial. Despite recent randomized controlled trials and observational studies suggesting potential benefits, there is an apparent under-utilization of such therapy in patients with stable COPD. The reasons for such under-utilization in the home-setting are likely multi-factorial, but we provide our perspective on the adequacy of scientific evidence and implementation barriers that may underlie the observed under-utilization.

1.1 Implementation gap

NIPPV when applied to hospitalized patients with acute exacerbations of COPD and respiratory acidosis ($pH \leq 7.35$) and hypercapnia (partial pressure of CO_2 [$PaCO_2$] > 45 mmHg) has been shown to improve arterial blood gases ($PaCO_2$; oxygenation and pH), reduce in-hospital mortality, decrease the need for invasive mechanical ventilation (IMV) and intubation, and length of hospital stay[8, 9, 10, 11]. Despite such accumulating evidence in the late 1990s and early 2000s, there was an implementation gap with a disproportionately small number of hospitalized patients with acute exacerbation of COPD receiving NIPPV [12]. Such an implementation gap has begun to narrow over the years, with recent trends suggesting that the use of NIPPV has more than doubled between 2004 and 2011[13]. In this claims-based analysis of the Danish national registry, there was a 4.1 fold increase in NIPPV use alone and 3.1 fold increase in the combination of NIPPV and IMV in hospitalized

patients, whereas, the use of IMV alone reduced by 40% during the same time[13]. In general, the proportion of all COPD hospitalizations that warranted no ventilation (neither IMV or NIPPV) decreased from 95 to 88%. The trend for greater utilization of NIPPV in hospitalized patients with COPD was associated with lower mortality than that for IMV in both Danish and U.S. studies[13]. Similarly, claims-based analysis in the Agency for Health Research and Quality (AHRQ) HCUP data suggest time trends of reductions in COPD-related hospital mortality in the U.S. [14]. Following reports of adequately powered level 1 randomized controlled trials (RCTs) in premier journals in the late 1990s, the implementation of NIPPV in hospitalized patients with COPD continued to demonstrate increasing trends over the next two decades. Such a finding is not surprising considering that Balas and colleagues have previously reported that there exists a time lag of 17 years before research evidence reaches clinical practice[15, 16, 17]. Similarly, one could unfortunately anticipate that despite recent RCTs favoring the application of NIPPV or bilevel PAP therapy to patients with stable COPD and coexistent chronic respiratory failure in the home setting, we can expect a similar time lag before we appropriately implement such therapy.

1.2. Definitions

Before we embark on the issues surrounding implementation of home-based PAP therapy in patients with COPD, it would help to define some of the terminologies. The semantics need definition especially considering that varied terms and definitions are used in various countries. At first, we wish to distinguish stable patients with COPD with and without chronic respiratory failure. Patients with severe COPD, or other conditions such as morbid obesity with or without obstructive sleep apnea, neuromuscular diseases (such as Amyotrophic Lateral Sclerosis, Multiple Sclerosis), or chest wall deformities (Kyphoscoliosis) may develop chronic derangement of daytime gas exchange – daytime hypoxia and hypercapnia[18, 19, 20]. Such patients are said to have chronic respiratory failure or chronic respiratory insufficiency[18, 19, 20]. Patients with chronic respiratory failure fail to achieve adequate ventilation and gas exchange – especially during sleep – and such ineffective breathing disrupts nocturnal sleep and manifests as daytime sleepiness (hypersomnia), early morning headache (due to hypercapnia), dyspnea, and fatigue[18, 19, 20]. Correction of such ventilatory and gas exchange abnormalities using home-based noninvasive PAP therapy can improving sleep quality, heath-related quality of life, functional status, daytime gas exchange, and reduce risk for hospitalization or re-hospitalization[19, 21, 22]. Patients with stable COPD but without readily apparent chronic respiratory failure would likely need to be screened for the presence of daytime blood gas derangements (or chronic respiratory failure). Such screening is not routinely performed in non-hospitalized patients in the ambulatory setting unless they undergo arterial blood as measurements as part of pulmonary function testing. Therefore, there could potentially be an under-estimation of the proportion of patients with COPD and co-existent chronic respiratory failure.

The terminologies for home-based devices are influenced by modality and delivery device. For the purposes of this review, continuous positive airway pressure therapy delivered by a home-based device will be termed as CPAP. Bilevel PAP therapy delivered by a home-based device essentially delivers a form of non-invasive ventilation with an expiratory positive

airway pressure (EPAP) setting and pressure-assist (or pressure support) that is determined by an inspiratory positive airway pressure (IPAP) setting. In this scenario the pressure support is the difference between IPAP and EPAP. Moreover, bilevel PAP devices may have a back-up rate or be in the spontaneous mode. Most studies involve fixed settings, however there are home-based devices that can automatically adjust the EPAP and pressure support settings and are termed auto-bilevel PAP or AVAPS/iVAPS (averaged or intelligent volume assured pressure support or volume assured pressure support) [19, 22, 23, 24, 25]. When such modalities are delivered by home ventilators, we will use the term NIPPV as a way of distinguishing such therapy from smaller devices that are capable of delivering such therapy (termed “Bilevel PAP” in this review). Besides semantics and scientific data, there is a steep cost difference between home ventilators delivering pressure assistance of various modalities (bilevel PAP, AVAPS, VAPS, or auto-bilevel) versus bilevel PAP delivered by smaller devices that are not home ventilators. In the U.S., such a cost differential is further compounded by the maintenance costs for home ventilators being lifelong whereas for bilevel PAP devices the maintenance costs are capitated at 13 months with some regional variation. Domiciliary bilevel PAP devices with and without back-up rates are also called Respiratory Assistance Devices (RAD) devices by certain U.S. Payors (Medicare) in order to distinguish them from home ventilators.

Although home-based CPAP therapy may have been initiated for treatment of coexistent sleep-disordered breathing such as obstructive sleep apnea, and not COPD per se, such CPAP therapy may alleviate the work of breathing related to the underlying COPD as well. Specifically, CPAP therapy does – despite common misconception – alleviate the inspiratory work of breathing and provides inspiratory assistance in patients with COPD. This is because there is an “occult” elastic load presented by intrinsic positive end-expiratory pressure (intrinsic PEEP). In critically ill patients with COPD, CPAP set close to the intrinsic PEEP levels (~8 cm H2O) reduces the pressure time product of the diaphragm (a measure of respiratory effort) by 45% when compared with T-piece[26]. Such a “PEEP effect” may also reduce work of breathing in patients with COPD in the home setting.

1.3. Epidemiology of home-based PAP therapy in patients with stable COPD

In a recent claim-based analysis of the U.S. based Truven Health Analytics database, Vasquez and colleagues found that a vast majority of 1,881,652 patients with COPD (92.5%) were not receiving any form of domiciliary PAP therapy [21]. Prescription of such bilevel-PAP (1.5%), CPAP (5.6%), and NIPPV (<1%) in stable patients with COPD demonstrated sex, age, and geographic-related variability in prescription rates. For example, 59% of all NIPPV prescriptions in the U.S. were in the Southern U.S. which was markedly greater than that in the Northeast (10%), Midwest (17%), and Western U.S. region (12%; figure 1). Similarly, there was global variation in prescription of home-based noninvasive ventilation, with recent data suggesting that 30% of all prescription for noninvasive ventilation in European patients was for COPD with chronic respiratory failure[27]. Such data did not provide information as to whether these were home ventilators or bilevel PAP devices. In the same study, across various European countries, there was again a wide variation in the proportion of home-based noninvasive ventilation prescription for COPD indication: ranging from 65% (Germany) to 5% (Netherlands) [27]. It is unlikely that the prevalence of other

reasons for chronic respiratory failure would have been responsible for such a wide variation in prescription of domiciliary noninvasive ventilation. Such wide geographic variation in prescription practices that is not explained by comorbid conditions or differences in disease prevalence could be variably interpreted. One may consider that noninvasive ventilation is over-utilized (if the scientific evidence were lacking) or under-utilized (if there is indeed scientific evidence in favor of such therapy). The scientific evidence in support of home-based PAP therapy differs in the presence or absence of chronic respiratory failure and will be critically assessed in the section entitled, “Scientific literature in support of home-based ventilatory support in COPD” below.

It is worth reviewing the indication for home-based CPAP therapy in the COPD population briefly. In the U.S. based study by Vasquez and colleagues, COPD with co-existent sleep-disordered breathing (SDB; obstructive or central sleep apnea) was associated with a 60% prevalence rate of home-based CPAP prescription as opposed to only 3.6% of individuals with COPD without a coexistent diagnosis of SDB after matching for various confounders including a propensity score for prescription of CPAP therapy. Similar differences in home-based bilevel-PAP prescription rates – 31% with SDB versus 1.3% without coexistent SDB suggest that the presence of co-existent SDB increased the propensity for prescription of home-based respiratory devices in such patients. The influence of coexistent SDB on prescription of NIPPV home ventilators was less evident (0.3% with coexistent SDB versus 1.2% without coexistent SDB). Notably, only a minority of patients with COPD and chronic respiratory failure were prescribed various respiratory devices: bilevel PAP (22%), CPAP (21%) and NIPPV (home ventilators; 2.9%). The potential barriers for initiating such respiratory devices in patients with COPD and chronic respiratory failure will be discussed in the section entitled, “Implementation barriers” below.

2. Scientific literature in support of home-based ventilatory support in COPD

Previous studies involving respiratory assistance effected by negative pressure ventilation were not favorable [28, 29]. In 2013, a meta-analysis by Struik and colleagues found no effect of home-based NIPPV or bilevel PAP on gas exchange, 6-minute walking distance, health-related quality-of-life, lung function (forced expiratory volume in 1-second [FEV1], forced vital capacity [FVC], or maximal inspiratory pressure) and sleep efficiency[30]. Struik and colleagues at that time concluded that there was insufficient evidence to support the routine application of home-based NIPPV or bilevel PAP therapy in patients with stable COPD. Since 2013, there have been two important multi-center RCTs that suggest benefits to NIPPV therapy in patients with stable COPD and chronic respiratory failure[31, 32].

In the first multi-center study, Kohnlein and colleagues reported that 1-year mortality was lower in the intervention group (12% of 102 patients) receiving NIPPV when compared to the control group (33% of 93 patients; table 1). In this study only patients with chronic respiratory failure as evidenced by significant hypercapnia ($PaCO_2$ > 51.9 mmHg) were recruited and the pressure support level was targeted to reduce hypercapnia by at least 20%[31]. In another multi-center RCT, Murphy and colleagues reported that there was a

reduction in composite outcome of hospitalization and death in the group that was treated with home-based NIPPV therapy and oxygen as opposed to home oxygen alone group (adjusted hazard ratio [adjHR] 0.49 [95% confidence interval [CI] 0.31; 0.77; P=0.002). Although all-cause mortality alone was not reduced in this study (adjHR 0.67 95%CI 0.34; 1.30; P=0.23), home-based NIPPV significantly prolonged time to readmission or death from 1.4 months to 4.3 months (table 1). A more recent meta-analysis of NIPPV and bilevel PAP therapy in stable patients with COPD in 2017 by Liao and colleagues reported no significant difference in mortality[33]. However, in a subgroup analysis involving studies that demonstrated a significant reduction in hypercapnia, there was a reduction in mortality[33]. Moreover, studies with higher levels of pressure assist were more likely to yield favorable effects and these were more likely to be studies performed in Europe (table 1).

In prior meta-analysis, the pooled odds ratio or relative risks merely measure the number of events but do not take into consideration as to when the mortality events occur. In certain conditions such as cancer or COPD, a cure may not be possible, but there is a clear need for a new intervention that can meaningfully increase survival time. Therefore, although similar number of deaths (factored into a pooled odds ratio) may be observed, there is still need and interest in a therapeutic intervention that can decrease the rate at which the death occurs. Therefore, unlike prior meta-analysis in this area[30, 33] statistical approaches that take into consideration the time-to-event outcomes using hazard ratios (HRs) and thereby including both the number and the timing of events are needed of all the studies enumerated in Table 1 [34, 35].

With regards to hospitalization as an end-point, in a prior retrospective cohort study of a QI initiative undertaken at a single center, Coughlin and colleagues reported that a multifaceted intervention that involved initiation of home-based advanced PAP therapy modality (AVAPS) delivered by a home ventilator, RT-led respiratory care, medication reconciliation, appropriate oxygen therapy initiation, and patient education led to significant reduction in rehospitalization[42]. In another retrospective analysis of administrative claims data of hospitalizations in patients with stable COPD who received or did not receive NIPPV, bilevel PAP, or CPAP therapy, after adjusting for confounders and propensity score, home-based NIPPV (odds ratio [OR], 0.19; 95% confidence interval [CI], 0.13–0.27), bilevel-PAP (OR, 0.42; 95% CI, 0.39–0.45), and CPAP (OR, 0.70; 95% CI, 0.67–0.72) therapy were individually associated with lower hospitalization risk in the 6 months post-treatment when compared to a similar time frame pretreatment but not when compared with the baseline period between 12 and 6 months before treatment initiation[21]. Stratified analyses suggested that comorbid SDB, chronic respiratory failure, heart failure, and age < 65 years were associated with greater benefits from home-based PAP therapy[21]. In other studies, home-based NIPPV or bilevel PAP therapy achieved a reduction in hospitalization risk over variable timeframes of 3 – 36 months of follow-up[32, 36, 37].

3. Implementation Barriers

Scientific evidence of the effectiveness of home-based NIPPV or bilevel PAP therapy requires healthcare innovations in order to bring them to the homes of patients with stable

COPD. In 2008, biomedical research expenditures in the U.S. was estimated to exceed US $100 billion on health-related research [43]. However, expenditures on health services research that focused on models of care or care innovations accounted for a miniscule (1.5%) of such expenditures. Passive dissemination alone through peer-reviewed literature is unlikely to influence care delivery at the patient's bedside or home[44]. Home-based NIPPV or bilevel PAP therapy in patients with COPD – like any other medical condition – is generally determined by the 2 Rs (regulation and reimbursement)[45]. Regulatory barriers and financial incentives or dis-incentives modify behaviors of providers and healthcare systems in the absence of thoughtful quality improvement initiatives[45]. If reimbursement were tied to patient outcomes – such as the new CMS ruling for 30-day readmission – and if there is a recognition by providers that home-based PAP therapy could reduce the 30-day readmission rate, then there is greater likelihood for change in practice[7]. Despite the afore-mentioned scientific literature in favor of reducing the rate of death and hospitalizations in patients with COPD and coexistent chronic respiratory failure, and the cost-effectiveness of such interventions, health policy by payors needs to be influenced by translational (T3) research (translation to practice). Additionally, policy research that influences populations (T4; translation to populations) are traditionally lacking in funding as well. However, new efforts undertaken by the National Institutes of Health (Center for Translational Research and Implementation Science)[46], Medical Research Council in the United Kingdom and Australia, Canadian Institute of Health Research, and French National Institute of Health and Medical Research (INSERM) are all beginning to make significant inroads in this arena.

There are various barriers to implementation which are enumerated in Table 2. First, the scientific evidence that favors initiation of home-based NIPPV or bilevel PAP therapy in patients with stable COPD and chronic respiratory failure has only recently matured with the publication of two recent large multi-center studies. Despite prior older trials that indicated health benefits of NIPPV or bilevel PAP therapy in patients with COPD, the current body of scientific literature with recent publication of two large RCTs has tipped the balance in favor of implementation of home-based NIPPV or bilevel PAP therapy in patients with stable COPD and chronic respiratory failure (hypercapnia with $PaCO_2 > 45$ mmHg; Table 1). The implementation of home-based NIPPV or bilevel PAP therapy in patients with stable COPD who are not hypercapnic ($PaCO_2 \leq 45$ mmHg; i.e., without chronic respiratory failure) is unclear as the scientific evidence requires the performance of RCTs. The source of the information is vital in how quickly the message for practice change can be implemented. Messaging from professional organizations such as the American Thoracic Society (ATS) or European Respiratory Society (ERS) is more likely to be favorably received by healthcare providers than from industry or third-party payors. A recent combined ATS/ERS guideline suggested that data for home-based NIPPV or bilevel PAP therapy were conflicting with regards to outcomes in patients with COPD in the outpatient setting and they based such recommendations on data that was reviewed until that point in time [8, 31, 39, 42, 47]. However, a more current systematic review and cumulative meta-analysis of the literature in this area would have yielded additional and more current RCTs that would likely favor noninvasive ventilation in the home setting[32, 38]. The ATS/ERS guideline suggested, "more effectiveness studies should be conducted in real-life situations to confirm the findings of previous efficacy trials." [8] A clear unambiguous message of the validity of the

supportive scientific data in the context of the practice and setting (hospitalized or ambulatory patients with stable COPD with chronic respiratory failure) is needed to help the decision-maker (provider, payor, or administrator) to make the decision to initiate NIPPV or bilevel PAP therapy in the home setting. This would suggest that a more current systematic review and practice guideline is needed in this area. A systematic review is being performed by investigators with funding from the Agency of Healthcare Research and Quality but is not available as yet[48].

In many instances the perceived immediate cost of the home-based NIPPV or bilevel PAP therapy, or the cost of building a program aimed at assessing the need for such therapy, could be barriers for implementation. Strategies for qualifying a patient with stable COPD and chronic respiratory failure to receive home-based NIPPV or bilevel PAP therapy as a medical benefit need to be developed by implementation scientists. Coughlin and colleagues performed a cost-effectiveness study for home-based noninvasive ventilation using a mechanical ventilator versus a bilevel PAP device or no such therapy from a hospital and payor perspective[49]. From a hospital perspective (with assumption of 250 patients admitted annually) they projected a cumulative savings of over US$450,000 over 90 days for an advanced mode of noninvasive ventilation (AVAPS) versus bilevel PAP or no such therapy. From a payor perspective, assuming a 100,000 patient base, they projected a 3-year cumulative savings with advanced noninvasive ventilation of US$326 million versus no similar therapy and US$1.04 billion versus bilevel PAP therapy[49]. More research, however, into the health economics and cost-effectiveness of noninvasive ventilation in patients with COPD is needed.

The perceived beliefs, preferences and values of the provider or administrator plays an important role in the adoption and implementation of new practice pattern such as NIPPV or bilevel PAP therapy in patients with COPD. Their perspectives may be colored by prior negative RCTs, their willingness to accept the risk, extra work, or change their previous management approach plays an important role. The local culture of practice may play a greater role than an institutional strategy[50] (“culture beats strategy”).

3.2. Policy landscape and political will

Currently CMS approves use of home-based RADs (bilevel PAP) for patients with COPD and for symptoms (such as fatigue, dyspnea, morning headaches, etc.) and for coexistent physiologic criteria that are compatible with chronic respiratory failure ($PaCO_2 \geq 55$ mm Hg); or $PaCO_2$ 50–54 mm Hg with coexistent nocturnal oxygen desaturation (SpO2) ≤ 88% for five continuous minutes while on oxygen therapy ≥ 2 liters/minute; or $PaCO_2$ 50–54 mm Hg and ≥ 2 related hospitalizations in the prior 12-month period)[51]. Moreover, a patient with COPD needs to fail home-based bilevel PAP in the spontaneous mode before being allowed to receive bilevel PAP with a back-up rate. Regional Medicare criteria may differ from national criteria in that for the western U.S. region a $PaCO_2$, done while awake and breathing the patient’s usual FIO_2 is ≥ 52 mm Hg, and overnight pulse-oximetry demonstrates oxygen saturation ((SpO_2) ≤ 88% for at least five minutes done while breathing the patient’s usual FiO_2, and that prior to initiating therapy, obstructive sleep apnea (and treatment with continuous positive airway pressure) has been considered and

ruled out [52, 53]. In particular the regional criteria differs from national Medicare criteria with respect to clarifying that formal sleep testing is not required if there is sufficient information in the medical record to demonstrate that the beneficiary does not suffer from some form of sleep apnea (Obstructive Sleep Apnea (OSA), Central Sleep Apnea and/or Complex Sleep Apnea) as the predominant cause of awake hypercapnia or nocturnal arterial oxygen desaturation. Despite such an allowance for patients with COPD, why is it that NIPPV and bilevel PAP therapy utilization is still low? Conceivably, there are no consistent or existent strategies in the clinic (or upon discharge to home from a hospital) for a patient to be assessed and initiated on home-based NIPPV or bilevel PAP therapy.

Policy can run aground against political will when budgetary constraints occur. Alternatively, there are payor concerns that the use of home-based noninvasive ventilation in patients with stable COPD without hypercapnia is not supported by current reimbursement policies and that certain home ventilators are used to deliver more simple modes of ventilation in patients who do not meet currently accepted criteria (such as a $PaCO_2 > 52$ mmHg)[54]. Interestingly, the afore-mentioned report by the Office of Inspector General (OIG) that supervises and audits the functioning of the healthcare systems and payor (Medicare) identified that there was an 85-fold increase in prescription of home ventilators in the U.S. from 2009–2015 [54]. The corresponding cost to the payor increased from US $3.8 million to US$340 million over the same time period. They note that the indication for prescription of the home ventilators dramatically changed over this period of time in favor of a greater proportion of indication for chronic respiratory failure which increased from 29% to 85% between 2009 and 2015 [54]. One potential additional explanation for such increase in home ventilator prescriptions could be the very cumbersome requirements for bilevel PAP (spontaneous, timed, or VAPS modes) as compared to more advanced home ventilators which serves as a potential “loophole” that has been exploited which the government seeks to correct by seeking more clarity in the health policies that determine eligibility for home ventilators. Interestingly, in our cumulative meta-analysis there was a period of time in 2009 following the paper by McEvoy and colleagues that the scientific evidence favored bilevel PAP in stable patients with COPD and chronic respiratory failure[38]. The afore-mentioned OIG report identified 1% of patients received the home ventilator for an unapproved indication (i.e., obstructive sleep apnea), but the conclusion of the OIG report suggested that an 85-fold increase in prescription raises serious concerns of inappropriate billing practices and abuse.[54] Whilst, an implementation scientist would be delighted with adoption of an effective new treatment, other healthcare stakeholders may have a different point of view for legitimate reasons. Consensus across various stakeholders including patients and caregivers, payors, purchasers, policymakers, providers, and product manufacturers is direly needed in this area[55, 56]. While there have been efforts by some to engage multiple stakeholders in setting priorities for research in patients with COPD, NIPPV or bilevel PAP therapy was not identified as a promising and emerging area of study.[57]

4. Limitations

We focused on practices of NIPPV utilization in the U.S. predominantly with perhaps less emphasis on Europe and Australia/New Zealand. However, a majority of cited scientific findings are of European, Australian, and New Zealand origin. The greater emphasis on

implementation barriers in the U.S. was a major thrust of the manuscript considering that the barriers and facilitators for utilization of any therapy is always contextual in a particular setting and the authors are more familiar with the U.S. setting. Identification of similar barriers and facilitators in European and Australian settings needs to be performed.

5. Conclusion

Many patients with stable COPD and chronic respiratory failure do not receive any form of home-based NIPPV or bilevel PAP therapy despite supportive scientific evidence. Such under-utilization suggests that there are significant barriers to implementation that include provider knowledge; structure of health services; and payor policies. For patients with stable COPD without chronic respiratory failure, there is inadequate scientific evidence to support home-based NIPPV or bilevel PAP therapy. In patients with stable COPD without chronic respiratory failure, adequately powered studies aimed at identifying patient characteristics that determine effectiveness of home-based NIPPV or bilevel PAP therapy needs further study. Moreover, in such patients, studies aimed at better phenotyping the participants from the standpoint of co-existent sleep-disordered breathing, congestive heart failure, or other co-existent conditions that may modify the effect of the home-based NIPPV or bilevel PAP therapy is direly needed. Strategies for effecting the current findings in the clinic or hospital are direly needed and newer technology aimed at determining adequate device settings at a lower cost are needed. T4 research aimed at bringing all stakeholders together to determine health policy that would facilitate implementation while promoting compliance to payor regulation would go a long way to improve patient outcomes.

6. Expert commentary

The key weaknesses in clinical management of patients with chronic obstructive pulmonary disease (COPD) is the failure to implement home-based noninvasive positive pressure ventilation (NIPPV) or bilevel positive airway pressure (bilevel PAP) therapy which is a promising and cost-effective treatment in the home setting. There is a huge-potential for future implementation science research aimed at better understanding the barriers and facilitators for implementing home-based NIPPV or bilevel PAP therapy in patients with COPD. Subsequently, dissemination and implementation research aimed at improved reach, effectiveness, adoption, and maintenance of such practices needs to be performed. The ultimate goal is to reduce morbidity and mortality in patients with COPD by treating them with NIPPV or bilevel PAP therapy in the home-setting. In particular, the discordance between the scientific fund of knowledge in this area and practice begs for better understanding of the barriers and facilitators for initiating home-based NIPPV or bilevel PAP therapy in patients with COPD.

7. Five-year view

We speculate within a five-year horizon, there will be better understanding of the barriers and facilitators for implementation of home-based NIPPV or bilevel PAP therapy in patients with COPD. Systematic reviews by researchers and clinical guidelines from professional societies will better align with the scientific knowledge in bringing the best treatment

approaches to the patient bedside. Such alignment will improve the health-related quality of life and mortality in patients with COPD.

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Declaration of Interest

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*=of importance, **= of considerable importance

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Key Points

- Home-based noninvasive positive pressure ventilation (NIPPV) or bilevel positive airway pressure (bilevel PAP) therapy can reduce hospitalization and mortality in patients with stable chronic obstructive pulmonary disease (COPD).
- Despite scientific evidence of the benefits of home-based NIPPV or bilevel PAP therapy, there is under-utilization of such therapy in patients with stable COPD in a domiciliary setting.
- The reasons for under-utilization in the home-setting are multi-factorial.
- There are barriers to implementation that include provider knowledge, health services and payor policies.
- In patients with stable COPD without chronic respiratory failure, there is inadequate scientific evidence to support domiciliary NIPPV or bilevel PAP therapy.
- In patients with stable COPD without chronic respiratory failure, studies aimed at identifying patient characteristics that determine effectiveness of domiciliary NIPPV or bilevel PAP therapy needs further study.
- Future implementation and health-policy research with appropriate stakeholders are direly needed to help improve patient outcomes.

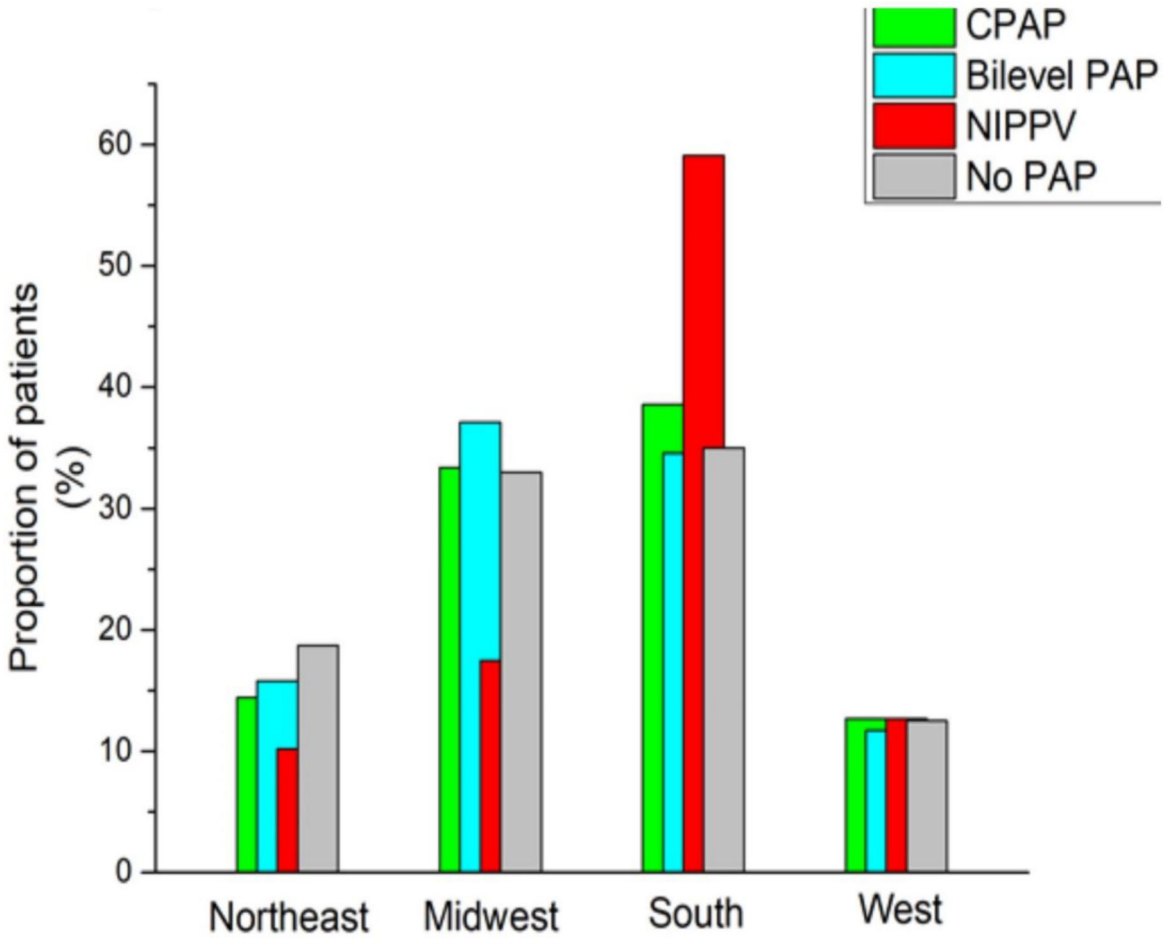

Figure 1.

Proportion of patients with chronic obstructive pulmonary disease who received various respiratory devices or did not receive such positive airway pressure (PAP) therapy are shown by regions in the United States. There was significant geographic variability in the prescription of various therapies. CPAP=continuous positive airway pressure therapy; Bilevel PAP = Bilevel positive airway pressure therapy; and NIPPV= Noninvasive positive airway pressure therapy. Reproduced with permission from American Journal of Medicine[21].

Table 1:

Randomized Controlled Trials of Positive Airway Pressure Therapy in Stable Patients with COPD at home

Study	Hypercapnia threshold *	Actual $PaCO_2$	Age	FEV_1 (% pred.)	Device	Pressures (cm H_2O)	Pressure assist	Duration (months)
Casanova 2000	None	52 ± 8.4	66 ± 5	30%	Bilevel PAP	12 / 4	8	12
Clini 2002	> 50	54.8 ± 4.5	65 ± 14	29%	Bilevel PAP	14 / 2	12	24
Xiang 2007	> 55	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	24
McEvoy 2009	> 46	53.5 ± 2.4	68 ± 1.7	24%	Bilevel PAP	12.9 / 5.1	7.8	26
Struik 2014	None	58.5 ± 9.0	63.7 ± 8.2	25.6%	Bilevel PAP (S/T mode)	19.2/14.8	4.4	12
Kohnlein 2014	> 51.9	58.1 ± 5.6	63.2 ± 8.0	26.7%	Home ventilator	21.6 / 4.8 (back-up rate 16)	16.8	12
Zhou 2017	> 50	None	67 ± 7	25.5%	Bilevel PAP	17.8 / 4.2	13.6	3
Murphy 2017	> 53	59 ± 7	67 ± 10	23.5%	Home ventilator	24 / 4 (back-up rate 14)	20	12

$PaCO_2$ = partial pressure of arterial CO_2 level (mmHg); FEV_1 = Forced expiratory volume in 1 second; % pred. = Percent predicted; cm H2O = centimeters of water; ± standard deviation; Bilevel PAP = bilevel positive airway pressure.

*mmHg of $PaCO_2$

Table 2:

Factors influencing the dissemination among healthcare administrators, policy makers, and general public

Information	
	Sound scientific basis, including knowledge of causality
	Source (e.g., professional organization, government, mass media, etc.)
Clarity of content	
	Formatting and framing
	Perceived validity
	Perceived relevance
	Cost of intervention
	Strength of message (e.g., vividness)
Perceived values, preferences, beliefs	
	Role of decision maker
	Economic background
	Previous education
	Personal experiences and involvement
	Political affiliation
	Willingness to adopt innovations and uncertainty
	Willingness to accept risk
	Ethical aspect of decision
Context	
	Culture
	Politics
	Timing
	Media attention
	Financial or political constraints

Adapted from Bero and colleagues[58] and Anderson and colleagues[59] and Colditz [60]