The long-term efficacy of domiciliary noninvasive positive pressure ventilation in COPD: A meta-analysis of randomized controlled trials

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Formal analysis: Park DA
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Writing - review and editing: Hwang YI
Approval of final manuscript: all authors.
ABSTRACT

We aimed to evaluate the long-term use or effects of domiciliary non-invasive positive pressure ventilation (NIPPV) used to treat patients with chronic obstructive pulmonary disease (COPD). Databases were searched to identify randomized controlled trials (RCTs) of COPD with NIPPV for longer than 1 year. The primary outcome as mortality rates were accessed in this meta-analysis. The eight trials included in this study comprised data from 913 patients. The mortality rates for the NIPPV and control groups were 29% (118/414) and 36% (151/419); this difference was statistically significant (risk ratio (RR): 0.79, 95% confidence interval (CI): 0.65–0.95). Mortality rates were reduced with NIPPV in four trials that included stable COPD patients. There was no difference in admission, acute exacerbation and quality of life (QOL) between the NIPPV and control groups. There was no significant difference in withdrawal rates between the two groups (RR 0.99, 95% CI 0.72-1.36, p = 0.94).

Maintaining long-term nocturnal NIPPV for more than 1 year in COPD patients, especially stable status COPD patients, leads to a decrease in the mortality rate, and the withdrawal rate is not high compared to long term oxygen treatments.

Key words: noninvasive positive-pressure ventilation, chronic obstructive pulmonary disease, mortality
Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by irreversible limitation of air inflow induced by damage to the airway and lung parenchyma due to chronic inflammation. Chronic hypoxia due to long-term airflow limitation induces pulmonary vasoconstriction, polycythemia, right heart failure, and multi-organ dysfunction. In particular, during nighttime rapid eye movement (REM) sleep, the tone of muscle is lowered, and movement of the respiratory muscles is also reduced. Thus, ventilatory dysfunction would be further exacerbated in patients with COPD in sleep state. In COPD patients, hypoxic and hypercapnic state due to ventilatory disturbance at night is not fully resolved even during the daytime, resulting in a poor prognosis.

Non-pharmacologic treatments for COPD include smoking cessation, oxygen therapy, rehabilitation, pneumococcal vaccination, and noninvasive positive-pressure ventilation (NIPPV). The use of NIPPV in patients with COPD could prevent deterioration of patient’s condition by assisting lung ventilation. Although NIPPV treatment for acute respiratory failure resulting from COPD exacerbation improves outcomes of mortality, the results of studies about mortality of domiciliary NIPPV in COPD patients vary widely. A study using nasal NIPPV to treat patients with COPD found improvements in the ventilation index such as an increase in the partial pressure of oxygen (PaO₂) and a decrease in the partial pressure of carbon dioxide in arterial blood (PaCO₂). In randomized trials of COPD treated with NIPPV, sleep quality or QOL improved, but the survival rate or pulmonary function did not improve. The results of other studies about NIPPV in COPD patients showed that the survival of patients improved. A meta-analysis of NIPPV used in COPD treatment suggested that COPD patients with high baseline PaCO₂ levels have good outcomes in terms of survival and hospital readmission.
Although meta-analyses of the effect of NIPPV in COPD patients with chronic respiratory failure have been conducted \(^{16,17}\), few studies have analyzed the long-term efficacy of NIPPV in COPD patients. In the present study, we aimed to evaluate the effects of NIPPV on the mortality rate, differences in QOL, admission rates, and withdrawal from treatment for COPD patients treated with domiciliary NIPPV for more than a year.

**Methods**

The databases were searched for identification randomized controlled trials (RCTs) about the long-term treatment of COPD with NIPPV ventilation over a period of more than 1 year. The following medical keywords and heading were employed as searching: “pulmonary disease, chronic obstructive”, or “chronic obstructive lung disease”, or “emphysema”, and “respiratory therapy”, or “non-invasive”, or “bi-level”. The detailed search strategy for retrieval method is included as a supplementary file (see Table S1). Two researchers judged a number of articles on the feasibility of this study, and in case of conflict, the two discussed and agreed. We included randomized control studies compared domiciliary NIPPV with usual therapy, including long-term oxygen therapy, for the management of adult patients (18 years of age or above) with COPD.

We requested raw data for all included studies to analyze the mortality and outcomes of patient subgroups. Two authors replied, and one sent the materials in response to our request.

Two researchers independently analyzed data from the studies, including study population, year of publication, study design, NIPPV details (including duration of the study, enrollment criteria, baseline forced expiratory volume in 1 s \([\text{FEV}_1]\), and
PaCO₂ level), mean IPAP level, actual duration of NIPPV, treatment of the control group, and clinical outcomes (including mortality, QOL, admission rate, and withdrawal rate). Disagreements regarding the interpretation of data were resolved by consensus between the two investigators. The primary outcome was the all-cause mortality rate in patients with COPD. Patients were subdivided into two groups based on status at time of enrollment: 1) stable, and 2) admitted to a hospital at the time of enrollment and subsequently discharged.

The methodological quality and risk of bias were assessed using a modified version of the Cochrane risk-of-bias instrument. If the two researchers disagreed about the quality and risk of bias of enrolled studies, they discussed those different opinions and reached an agreement. Because NIPPV equipment that is always visible for patients and medical staffs, the study cannot be completely blinded to study participants. Therefore, we analyzed that all included studies had a high degree of performance bias. However, all studies were judged to be at low risk of bias in that the outcome measurements were not influenced by a lack of blinding of the study personnel.

We studied outcome data at the trial level and performed statistical calculations using Review Manager software (RevMan version 5.3; Nordic Cochrane Centre, Cochrane Collaboration, 2011). Continuous outcomes were reported as mean differences (a measure of absolute change), and binary outcomes were reported as risk ratios (RRs) 18. All statistical results were two-sided. We considered $p < 0.05$ to be statistically significant for all analyses with 95% confidential intervals (CIs) 18, and we reported summary results for all individual trials. Furthermore, we evaluated the between-study heterogeneity of each outcome using the $I^2$ statistic. We regarded statistical heterogeneity to be low if $I^2 = 25–49\%$, moderate if $I^2 = 50–74\%$, and high if $I^2 \geq 75\%$ 18.

Results
We identified 18,408 citations for searching through electronic database. Thirteen citations were retrieved for more detailed evaluation, and eight of those studies met the criteria for inclusion in our review (Fig. 1). Two researchers had a perfectly consistent decision through discussion with each other regarding inclusion of all studies. The eight trials \(^7-14\) (Table 1) included in this study comprised data from 913 patients (median: 113 patients per trial, range: 47–201 patients). The follow-up periods in the included studies were 12–24 months.

Although there was no mortality outcome in the study of Duiverman et al.\(^{10}\), we included in our meta-analysis because it had various information including withdrawal rate and quality of life.

The baseline characteristics of the included studies are presented in Table 1. Five studies were performed on stable COPD patients, and three were performed on COPD patients who were discharged after being hospitalized. Most of the patients were over 60 years of age and had severe airflow obstruction with a mean predicted FEV\(_1\) < 50%. The treatments, outcomes, and withdrawal rates documented in the studies are presented in Table 2. Data on mortality, FEV\(_1\), QOL, admission, and withdrawal were pooled. In each study, the target of NIPPV was pressure in 6 studies and blood gas in 2 studies. Four studies after 2011 set IPAP as high as 20 or higher. The actual application time of NIPPV in each study ranged from 4.5 hours to 9 hours. FEV\(_1\) compared the two groups as a ratio or percent difference, and how much PaCO\(_2\) decrease was compared in kPa or the difference between the two groups was described at the end of the study. The methodological quality for included trials is presented in supplement figure 1.

Figure 2 presents mortality rates for the included studies, all of which provided mortality data \(^7-9,11-14\), with the exception of Duiverman et al.\(^{10}\). The mortality rates for the
NIPPV and control groups were 29% (118/414) and 36% (151/419). This difference was statistically significant (RR: 0.79, 95% CI: 0.65–0.95, \( p = 0.01 \)). There was statistical heterogeneity among the trials that provided mortality data (\( p = 0.13, I^2 = 40\% \)). The RRs for mortality in the individual RCTs are presented in Figure 2.

The results of the subgroup analyses are summarized in Figure 2. The mortality rates in the four trials that included stable COPD patients \(^{7,9,11,12}\) were reduced on application of NIPPV (RR: 0.71, 95% CI: 0.56–0.91, \( p = 0.006 \)). All-cause mortality rates in the three trials involving COPD patient post-hospital did not differ between the NIPPV and control groups (RR: 0.90, 95% CI: 0.67–1.21, \( p = 0.48 \)).

The results of admission and acute exacerbation in studies \(^{7,8,14}\) are summarized in Figure 3. There was no difference in admission (RR: 0.99, 95% CI: 0.78–1.26, \( p = 0.94 \)) and acute exacerbation (RR: 0.83, 95% CI: 0.59–1.15, \( p = 0.26 \)) between the NIPPV and control groups (Figure 3).

QOL was analyzed in studies \(^{10,14}\) that reported Chronic Respiratory Questionnaire (CRQ) scores. There was no difference in QOL between the NIPPV and control groups (standardized mean difference, SMD: -0.037, 95% CI: -0.34 to 0.29, \( p = 0.85 \)) (Figure 4).

All included RCTs reported data concerning withdrawal or dropout in the NIPPV and control groups (Table 2 and Figure 5). There was no significant difference in the dropout rate between the two groups (RR 0.99, 95% CI 0.72-1.36, \( p = 0.94 \)).

**Discussion**

The main finding of our meta-analysis was that the mortality of COPD patients could reduce if domiciliary NIPPV is used for more than a year. Furthermore, the rate of withdrawal was not high in the NIPPV group, indicating that patients adapted relatively well...
to NIPPV.

The hypoxic and hypercapnic conditions of COPD with chronic ventilatory dysfunction can lead to pulmonary vasoconstriction, polycythemia, and multiple organ dysfunctions. Therefore, long-term use or effects of home oxygen improves survival of COPD patients. However, oxygen therapy alone could not assist the ventilation of patients with COPD, and sometimes, administration of oxygen aggravates the ventilation and perfusion ratio (VQ) mismatch and increases carbon dioxide in COPD patients. Because NIPPV could improve ventilation of patients, it can improve both hypoxic and hypercapnic status and can prevent VQ mismatch from oxygen alone administration in lung of COPD patients. Especially, in REM sleep state, paralysis of muscle goes on, and the tones of respiratory muscle are reduced in healthy people. In COPD patients, this progression of ventilatory dysfunction is very serious. The exacerbation of hypoxia and hypercapnia during nighttime is not fully recovered at daytime. The deterioration of progress is accelerated in COPD patients. The improving ventilation in COPD patients with long-term use or effects of NIPPV may increase survival and QOL and reduce comorbidities or acute exacerbations. A small-population study reported that domiciliary NIPPV improved the ventilatory index, quality of sleep, and QOL in patients with COPD. However, several randomized studies have reported conflicting results, particularly in terms of the mortality rate, ventilatory index, and QOL score. Recently, Murphy et al. suggested that home NIPPV prolonged the time to readmission or death within a 12-month period among patients with persistent hypercapnia following acute exacerbation of COPD.

A systematic review by Dretzke et al. included both RCTs and retrospective studies of domiciliary NIPPV in COPD, regardless of NIPPV duration. That review suggested that domiciliary NIPPV in COPD did not reduce mortality but did reduce mortality in stable status. Our analysis of all included studies about COPD patients in stable or post-hospital status
showed decreasing mortality rates in COPD patients using NIPPV longer than 12 months. Contrary to the results of Dretzke et al.\textsuperscript{16}, the improvement in survival rate in the NIV-applied group in our study can be considered because observation studies were omitted and the latest study showing good survival rates was included. The subgroup analysis of COPD status showed that the mortality rates were not decreased among post-hospital COPD patients using NIPPV though analysis of small number of studies. A recent study\textsuperscript{13} included only COPD patients with persistent hypercapnia in post-hospital status, in which study mortality was improved in home NIPPV. In the previous studies of home NIPPV in post-hospital status, the efficacy of NIPPV would not appear to be obvious because subjects with chronic ventilation dysfunction and good lung function after acute exacerbation were mixed enrolled. Although patients in the post hospital group have elevated PaCO\textsubscript{2} due to temporary exacerbation, the effect of NIPPV ventilation assist does not appear clearly because the baseline PaCO\textsubscript{2} in a stable state of the post-hospital patient after recovery may not be high. In the other meta-analysis\textsuperscript{16}, the group with high PaCO\textsubscript{2} in the post-hospital group showed a benefit in survival rate, and the Kohnlein’s study\textsuperscript{13} showed a positive result in mortality when patients with a high baseline PaCO\textsubscript{2} were enrolled in the post-hospital group.

In the four studies that applied high IPAP after 2011, the reduction of PaCO\textsubscript{2} was greater in the NIPPV group, and the previous study showed mixed results of PaCO\textsubscript{2}. It can be inferred that high IPAP can lead to effective ventilation and reduction of PaCO\textsubscript{2}.

Analyses of additional outcomes associated with the long use of NIPPV, including QOL, lung function, and acute exacerbation, were difficult because of variation in the evaluation tools used among studies. Improvements in lung function in the included studies were assessed using the absolute FEV\textsubscript{1} value, the predicted value\textsuperscript{12}, or the mean difference\textsuperscript{10,14}. It was also very difficult to assess the readmission rate or acute exacerbation rate for COPD patients. Various studies presented data on readmissions according to the number of
readmissions per patient \(^7\), the total number of readmissions during the study period \(^{11}\), the
time to initial readmission \(^8\), and the mean difference \(^{13}\). Further analysis of the standard
assessment tools for acute exacerbation, readmission, lung function, and QOL is required in
future studies of the efficacy of long-term NIPPV in COPD. Our study showed that QOL, as
assessed by the CRQ, did not differ between the NIPPV and control groups. Future studies
that investigate the improvement of QOL in COPD patients with NIPPV are needed because
there may be conflicts between the beneficial effects of NIPPV, requirements for adaptation
to use of the equipment, and the cost of NIPPV.

Although there is a recent meta-analysis to review the effect of long-term NIPPV on
stable hypercapnic COPD \(^{20}\), it covered only stable patients with COPD with hypercapnia,
and the long-term criteria was more than 3 months \(^{20}\). However, NIPPV may be helpful in
patients with persistent hypercapnia after acute exacerbations \(^{13}\). There was no meta-analysis
of COPD survival when NIPPV persisted for more than one year.

NIPPV seems to be more difficult for patients to adjust than oxygen therapy \(^{21}\). However,
we did not find a difference in withdrawal rates between the NIPPV and control groups used
for more than a year. That result suggested that COPD patients are well adapted to NIPPV
and can be used for a long time, especially after adjustment.

There were several limitations to the present analysis. First, the included trials were
somewhat diverse, given the differences in inclusion criteria, COPD severity, NIPPV duration,
ventilation strategies, and associated treatments. We requested raw data for the included
studies to analyze subgroups of patients and assess the settings employed by each study.
Unfortunately, we received either no response or a refusal to respond to our request for these
data. Second, it is likely that we did not include all of the relevant evidence because we
limited our analysis to articles written in English. Third, the small number of available trials
may have led to an underestimation of the heterogeneity and reduced the precision of our
pooled-effect estimates.

Our systematic review demonstrated that Maintaining long-term nocturnal NIPPV for more than 1 year in COPD patients, especially stable status COPD patients, leads to a decrease in the mortality rate, and the withdrawal rate is not high compared to long term oxygen treatments. Further research in the form of large RCTs of post-hospital COPD patients with persistent hypercapnia is warranted.
REFERENCES


15. Dreher M, Storre JH, Schmoor C, Windisch W. High-intensity versus low-intensity


<table>
<thead>
<tr>
<th>Study</th>
<th>Patients (n)</th>
<th>Male (%)</th>
<th>Study period (months)</th>
<th>Enrollment criteria</th>
<th>Age (years)</th>
<th>Baseline FEV₁ (%) predicted</th>
<th>Baseline PaCO₂ (kPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Casanova et al. 2000</td>
<td>52</td>
<td>98</td>
<td>12</td>
<td>Stable patients, no exacerbations in previous 3 months, PaCO₂ &gt; 6.93 kPa</td>
<td>64 vs. 68</td>
<td>29 vs. 31</td>
<td>6.8 vs. 7.1</td>
</tr>
<tr>
<td>Clini et al. 2002</td>
<td>90</td>
<td>80</td>
<td>24</td>
<td>Stable patients, pH &gt; 7.35, no exacerbations in previous 4 weeks, PaCO₂ &gt; 6.6 kPa</td>
<td>64. vs. 66</td>
<td>27 vs. 31</td>
<td>7.2 vs. 7.4</td>
</tr>
<tr>
<td>McEvoy et al. 2009</td>
<td>144</td>
<td>65</td>
<td>12</td>
<td>Stable patients, PaCO₂ &gt; 46 mmHg</td>
<td>69 vs. 61</td>
<td>25 vs. 23</td>
<td>7.0 vs. 7.3</td>
</tr>
<tr>
<td>Cheung et al. 2010</td>
<td>47</td>
<td>91</td>
<td>12</td>
<td>Posthospital patients, PaCO₂ &gt; 6 kPa</td>
<td>70 vs. 71</td>
<td>28 vs. 31</td>
<td>10.2 vs. 10.7</td>
</tr>
<tr>
<td>Duiverman et al. 2011</td>
<td>72</td>
<td>59</td>
<td>24</td>
<td>Stable patients, no exacerbation in previous 4 weeks, PaCO₂ &gt; 6.0 kPa</td>
<td>63 vs. 61</td>
<td>NR</td>
<td>6.8 vs. 6.81</td>
</tr>
<tr>
<td>Köhnlein et al. 2014</td>
<td>195</td>
<td>62</td>
<td>12</td>
<td>Stable patients, no exacerbation in previous 4 weeks, PaCO₂ &gt; 7 kPa</td>
<td>62 vs. 64</td>
<td>26 vs. 28</td>
<td>7.8 vs. 7.7</td>
</tr>
<tr>
<td>Struik et al. 2014</td>
<td>201</td>
<td>41</td>
<td>12</td>
<td>Posthospital patients, PaCO₂ &gt; 6.0 kPa</td>
<td>63 vs. 63</td>
<td>25.6 vs. 25.7</td>
<td>7.9 vs. 7.7</td>
</tr>
<tr>
<td>Murphy et al. 2017</td>
<td>116</td>
<td>47</td>
<td>12</td>
<td>Posthospital patients, PaCO₂ &gt; 53 mmHg</td>
<td>66 vs. 67</td>
<td>24.0 vs. 22.9</td>
<td>7.9 vs. 7.9</td>
</tr>
</tbody>
</table>

Data are presented for noninvasive positive-pressure ventilation vs. usual care. All PaCO₂ measurements were converted into SI units (kPa).

FEV₁, forced expiratory volume in 1 s; PaCO₂, partial pressure of arterial carbon dioxide; NR, not reported.
### Table 2. Treatments and outcomes of the randomized controlled trials included in the meta-analysis

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>NIPPV target</th>
<th>Mean pressure (cm H₂O)</th>
<th>Actual duration of NIPPV</th>
<th>Treatment of control group</th>
<th>Outcome</th>
<th>FEV₁</th>
<th>PaCO₂</th>
<th>Quality of life</th>
<th>Admissions</th>
<th>Withdrawal rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Casanova et al. 2000</td>
<td>Pressure</td>
<td>IPAP 12</td>
<td>6.2 h/day (first 6 months)</td>
<td>LTOT</td>
<td>22 vs. 22</td>
<td>ND</td>
<td>+0.05 vs. -0.11 (kPa)</td>
<td>NR</td>
<td>20 vs. 19 (number of patients)</td>
<td>23 vs. 8</td>
<td></td>
</tr>
<tr>
<td>Clin et al. 2002</td>
<td>Pressure</td>
<td>IPAP 14</td>
<td>9 h/day</td>
<td>LTOT</td>
<td>18 vs. 17</td>
<td>-0.3 (-13.1–2.4)</td>
<td>-0.26 kPa (NIPPV-usual)</td>
<td>SGRQ -5 vs. -4 (%)</td>
<td>6.996 (-4.30–18.29)</td>
<td>19 vs. 32</td>
<td></td>
</tr>
<tr>
<td>McEvoy et al. 2009</td>
<td>Pressure</td>
<td>IPAP 12.9</td>
<td>4.5 h/day at night</td>
<td>LTOT</td>
<td>55 vs. 63</td>
<td>-1.2 vs. +2.4 (%)</td>
<td>-0.1 vs. -0.3 (kPa)</td>
<td>ND</td>
<td>NR</td>
<td>6 vs. 6</td>
<td></td>
</tr>
<tr>
<td>Cheung et al. 2010</td>
<td>Pressure</td>
<td>IPAP 14.</td>
<td>7–9 h/day at night</td>
<td>CPAP 5 cm H₂O</td>
<td>38.5 vs. 60.2</td>
<td>NR</td>
<td>-0.84 vs. -0.36 (kPa)</td>
<td>NR</td>
<td>56 vs. 71 (days at first readmission)</td>
<td>34 vs. 15</td>
<td></td>
</tr>
<tr>
<td>Duiverman et al. 2011</td>
<td>Blood gas</td>
<td>IPAP 23</td>
<td>6.9 h/day</td>
<td>LTOT plus home rehabilitation</td>
<td>NR</td>
<td>0.12 (0.02–0.21)</td>
<td>-0.4 FkPa (NIPPV-usual)</td>
<td>CRQ -1.3 (-9.7–7.4)</td>
<td>NR</td>
<td>5 vs. 42</td>
<td></td>
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<tr>
<td>Köhlnlein et al. 2014</td>
<td>Blood gas</td>
<td>IPAP 21.6</td>
<td>5.9 h/day</td>
<td>LTOT</td>
<td>12 vs. 33</td>
<td>2.8 (0.2–5.4) (%)</td>
<td>-7.4 vs. -2.4 (%)</td>
<td>SGRQ 6.2 (0.7–11.8)</td>
<td>2.2 vs. 3.1 (number of admissions)</td>
<td>2 vs. 0</td>
<td></td>
</tr>
<tr>
<td>Struijk et al. 2014</td>
<td>Pressure</td>
<td>IPAP 21.</td>
<td>6.3 h/day</td>
<td>LTOT</td>
<td>30 vs. 29</td>
<td>-0.024 (-0.12–0.07)</td>
<td>-1.3 vs. -0.8 (kPa)</td>
<td>CRQ 0.01 (-0.4–0.4)</td>
<td>NR</td>
<td>25 vs. 24</td>
<td></td>
</tr>
<tr>
<td>Murphy et al. 2017</td>
<td>Pressure</td>
<td>IPAP 24</td>
<td>7.6 h/day</td>
<td>LTOT</td>
<td>28 vs. 32</td>
<td>NR</td>
<td>-0.8 vs. -0.3 (kPa)</td>
<td>SGRQ 2.3 (-2.6–7.1)</td>
<td>0.66 (0.46–0.95)</td>
<td>9 vs. 22</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented for NIPPV vs. usual care.tlf

CPAP, continuous positive airway pressure; CRQ, Chronic Respiratory Questionnaire; FEV₁, forced expiratory volume in 1 s; IPAP, inspiratory positive airway pressure; LTOT, long-term oxygen therapy; ND, no difference; NIPPV, noninvasive positive-pressure ventilation; NR, not reported; SGRQ, St George’s Respiratory Questionnaire
Figure 1. Study flow diagram

18408 Individual abstracts identified

17387 Excluded including 1046 Duplication citations

21 Recorded retrieved for more detailed evaluation

13 Excluded
• 10 period of study less than 12 months
• 2 not English
• 1 protocol of study

8 Trials included in review
Figure 2. Forest plot describing the effect of noninvasive positive-pressure ventilation (NIPPV) on all-cause mortality, and the mortality rate according to the status of patients with chronic obstructive pulmonary disease. The vertical line depicts the equivalence point in the mortality rates between the two groups (NIPPV vs. control), and horizontal lines correspond to the 95% confidence intervals. The size of each square represents the proportion of information provided by each study.
Figure 3. Forest plot depicting the effect of noninvasive positive-pressure ventilation (NIPPV) 
A) on admission and B) acute exacerbation. The vertical line depicts the equivalence point in 
the mortality rates between the two groups (NIPPV vs. control), and the horizontal lines 
correspond to the 95% confidence intervals. The size of each square represents the 
proportion of information provided by each study.

Figure 4. Forest plot depicting the effect of noninvasive positive-pressure ventilation (NIPPV) 
on the Chronic Respiratory Questionnaire. The vertical line depicts the equivalence point in 
the mortality rates between the two groups (NIPPV vs. control), and the horizontal lines 
correspond to the 95% confidence intervals. The size of each square represents the proportion 
of information provided by each study.
Figure 5. Forest plot depicting the effect of noninvasive positive-pressure ventilation (NIPPV) on withdrawal rates according to mean level of inspiratory positive airway pressure (IPAP) ($\geq 20\ \text{cm H}_2\text{O}$). The vertical line depicts the equivalence point in the mortality rates between the two groups (NIPPV vs. control), and the horizontal lines correspond to the 95% confidence intervals. The size of each square represents the proportion of information provided by each study.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>NIPPV</th>
<th>Control</th>
<th>Weight</th>
<th>Risk Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Casanovas 2000</td>
<td>6</td>
<td>26</td>
<td>26</td>
<td>3.00 [0.67, 13.51]</td>
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<tr>
<td>Cheung 2010</td>
<td>4</td>
<td>23</td>
<td>24</td>
<td>2.09 [0.42, 10.32]</td>
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<tr>
<td>Clei 2002</td>
<td>12</td>
<td>43</td>
<td>47</td>
<td>0.87 [0.40, 1.86]</td>
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<tr>
<td>Duijverman 2011</td>
<td>9</td>
<td>31</td>
<td>35</td>
<td>0.85 [0.41, 1.73]</td>
</tr>
<tr>
<td>Kohnlein 2014</td>
<td>2</td>
<td>102</td>
<td>95</td>
<td>4.66 [0.23, 95.84]</td>
</tr>
<tr>
<td>McEvoy 2009</td>
<td>4</td>
<td>72</td>
<td>72</td>
<td>1.00 [0.26, 3.85]</td>
</tr>
<tr>
<td>Murphy 2017</td>
<td>5</td>
<td>57</td>
<td>59</td>
<td>0.40 [0.15, 1.04]</td>
</tr>
<tr>
<td>Struik 2014</td>
<td>25</td>
<td>101</td>
<td>100</td>
<td>1.03 [0.63, 1.68]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>455</td>
<td>458</td>
<td>100.0%</td>
<td>0.97 [0.72, 1.29]</td>
</tr>
</tbody>
</table>

Heterogeneity: Chisq = 7.65, df = 7 (P = 0.36); I² = 8%
Test for overall effect: Z = 0.23 (P = 0.82)