



Noninvasive Positive Pressure Ventilation in the Home in COPD

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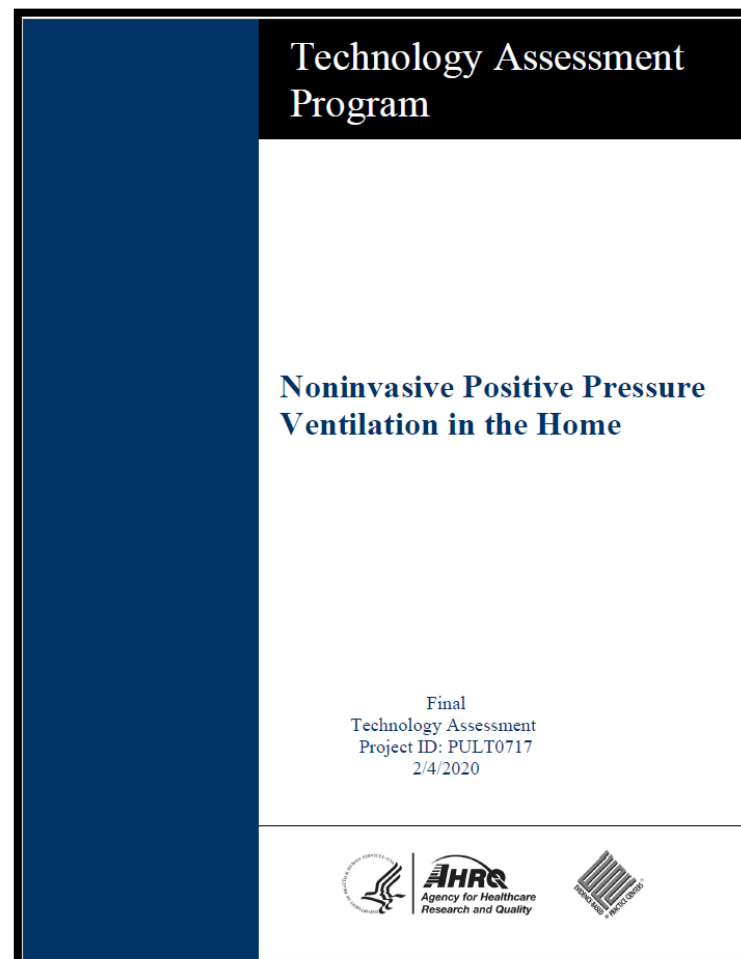
Full Report

AHRQ Report

- <https://www.ahrq.gov/sites/default/files/wysiwyg/research/findings/ta/hmv/hmv-ta-fullreport.pdf>

JAMA publication on COPD

- <https://jamanetwork.com/journals/jama/fullarticle/2760390>



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Background

Chronic Respiratory Failure

- Definition
 - Inability to maintain normal oxygen or carbon dioxide levels
 - Hypoxia (low oxygen)
 - Hypercapnia (high carbon dioxide)
 - Chronic (vs acute)
- Causes
 - Chronic obstructive pulmonary disease (COPD)
 - Thoracic restrictive disorders (e.g. kyphosis, scoliosis)
 - Neuromuscular disease (e.g. amyotrophic lateral sclerosis)
 - Obesity hypoventilation syndrome
- Adverse consequences
 - Sudden or gradual hypoxemia or hypercapnia
 - Poor quality of life, sleepiness, hospital admission, intubation, respiratory arrest, death
 - High cost

Noninvasive positive pressure ventilation (NIPPV)

- Setup
 - Machine, hose, mask (or mouthpiece)
 - In the home, usually (but not always) nocturnal
- Types of machines
 - **BPAP (Bilevel Positive Airway Pressure)**
 - BPAP S (spontaneous), no back up rate
 - BPAP ST (spontaneous/timed), back up rate
 - AVAPS (average volume assured pressure support)
 - Others
 - **HMV (Home Mechanical Ventilator)**
 - Pressure support
 - Pressure control
 - Volume assist control
 - Others
 - **CPAP (Continuous Positive Airway Pressure)**



Noninvasive positive pressure ventilation (NIPPV)

- Variability among machines:
 - interface (tracheostomy or mask)
 - mode of ventilation (e.g. pressure vs. volume targeted)
 - respiratory circuit (e.g. single vs. double limb)
 - monitoring capability
 - safety and alarm systems
 - internal battery life
 - level of oversight and servicing
 - device maneuvers (e.g. lung volume recruitment)



Clinical Dilemmas

- Marked variability in usage, prescribing patterns, policies, and guidelines
- Which devices are optimal for which patient populations?
- Which device modes are optimal for which patient populations?
- Which respiratory services impact outcomes?

Objectives

- To evaluate home NIPPV in adult patients with chronic respiratory failure in terms of:
 - Initiation / continuation
 - Effectiveness
 - Equipment parameters
 - Required respiratory services
 - Adverse events
- We evaluated respiratory failure due to:
 - Chronic obstructive pulmonary disease (COPD)
 - Thoracic restrictive disorders
 - Neuromuscular disease
 - Obesity hypoventilation syndrome

Key Questions

- KQ1: What characteristics/criteria were considered when initiating NIPPV?
- KQ2: What was the effect of HMV, BPAP, or CPAP on patient outcomes?
- KQ3: What equipment parameters were used?
- KQ4: What home services were provided?

Methods

Systematic Review and Meta-Analysis

- Defined study eligibility criteria
 - Stakeholder and key informant input
- Literature search (9 databases)
- Evaluated studies for possible inclusion
- Assessed risk of bias of individual studies
- Abstracted data
- Performed meta-analysis
- Assessed strength of evidence of four main outcomes
- Wrote report
 - Peer review and public commentary

PICOTS Elements Inclusion Criteria	
Populations	Adults ≥ 18 years
Interventions	Noninvasive mask or mouthpiece: <ul style="list-style-type: none"> • HMV • BPAP • CPAP
Comparators	<ul style="list-style-type: none"> • Usual care (i.e. no NIPPV) • Different type of NIPPV • Different mode same equipment
Outcomes	PRIMARY <ul style="list-style-type: none"> • Mortality • Hospitalization • Need for intubation • Quality of life SECONDARY <ul style="list-style-type: none"> • ICU admission • Outpatient visits • Emergency room visits • Disease exacerbations • Activities of daily living (ADL) • Dyspnea • Sleep quality • Exercise tolerance • Adverse events
Timing	≥ 1 month of treatment in home settings
Settings	<ul style="list-style-type: none"> • Home or assisted living
Study design	<ul style="list-style-type: none"> • Randomized controlled trials (RCTs) • Non randomized comparative studies (prospective and retrospective) • Relevant systematic reviews and clinical guidelines • Excluded: before and after studies
Publications	1995 to November 6, 2019

Strength of Evidence

Four primary outcomes (mortality, need for intubation, quality of life, hospital admissions)

Strength of Evidence (SOE)	Definition
High	Confident that the estimate of effect lies close to the true effect. The body of evidence has few or no deficiencies and judged to be stable.
Moderate	Moderately confident that the estimate of effect lies close to the true effect. The body of evidence has some deficiencies and is judged to be likely stable.
Low	Limited confidence that the estimate of effect lies close to the true effect. The body of evidence has major or numerous deficiencies and is likely unstable.
Insufficient	No evidence, were unable to estimate an effect, or had no confidence in the estimate of effect

Determinants

- Study limitations (i.e. risk of bias)
- Directness of evidence to the key questions
- Consistency of results
- Precision
- Publication bias

Results

All disease categories

Abstracts screened
N=6,180

Full text articles assessed
N=1,088

Articles included

N=68 original studies

(38 studies on COPD)

N=13 guidelines

- Studies were conducted in:
 - Europe (n=53)
 - United States (n=5)
 - Asia (4)
 - Australia (3)
 - Canada (n=1)
 - Africa (1)
 - South America (1)

KQ1: What characteristics/criteria were considered when initiating NIPPV?

- Criteria to start home NIPPV were variable
- Single criterion vs. combined criteria
- Common criteria:
 - Hypercapnia (PaCO₂ ranging from >45 to >56mmHg)
 - pH >7.35
 - Hypoxia (PaO₂ ranging from <55 to <60mmHg or long term oxygen use)
 - FEV1 <50% of normal
- Disease stability
 - 24 studies stable disease (no recent exacerbation)
 - 11 studies unstable disease (after hospitalization for acute exacerbation)
 - 2 studies both stable and unstable
 - 1 study not specified

KQ1: What characteristics/criteria were considered when initiating NIPPV?

- Processes used to titrate NIPPV
 - Variable
 - Common criteria
 - reduction in hypercapnia
 - reduction in hypoxia (including nocturnal hypoxia)
 - achievement of target tidal volumes
 - reduction in patient symptoms

KQ2: What was the effect of HMV, BPAP, or CPAP on patient outcomes?

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BPAP (compared with no device):

Primary Outcomes

Outcome	Direction	Study Design	Statistic (95% CI)	Strength of Evidence
Mortality	Lower	13 studies, 1423 patients (8 RCTs, 5 Observational)	OR: 0.66 (0.51 to 0.87) 55 fewer per 1000 patients	Moderate SOE
Hospital admissions	No difference	5 studies, 326 patients (3 RCTs, 2 Observational)	OR 0.91 (0.71-1.17)	Low SOE
Patients with hospital admission	Fewer	1 study, 166 patients	OR: 0.22 (0.11-0.43) 39.74% vs 75.00%	Low SOE
Need for intubation	Fewer	3 studies, 267 patients (1 RCT, 2 Observational)	OR: 0.34 (0.14 to 0.83) 80 fewer per 1000 patients	Moderate SOE
QOL	No difference	10 studies, 977 patients (9 RCTs, 1 Observational)	SMD: 0.15 (-0.03 to 0.32)	Insufficient SOE

KQ2: What was the effect of HMV, BPAP, or CPAP on patient outcomes?

BPAP (compared with no device):

Secondary Outcomes

Outcome	Study Design	Statistic (95% CI)	P value*
Number of emergency department visits	1 RCT (195 patients)	Rate Ratio=0.72 (0.60 to 0.85)	<0.001
Number of ICU admissions	1 RCT and 1 Observational study (81 patients)	Rate Ratio=0.43(0.18 to 1.05)	0.06
Number of patients with ICU admission	1 Observational study (166 patients)	7.69% vs. 31.82%; RD=-0.24(-0.36 to -0.13); OR=0.18(0.07 to 0.46)	0.001
Number of COPD exacerbations	3 RCTs and 1 Observational study (352 patients)	Rate Ratio=0.85(0.67 to 1.07)	0.17
Number of patients with COPD exacerbation	1 RCT (52 patients)	61.54% vs. 65.38%; RD=-0.04(0.30 to 0.22); OR=0.84(0.26 to 2.68)	0.17
Activities of daily living (ADL)	3 RCTs (318 patients)	SMD=0.09(-0.13 to 0.31)	0.41
Dyspnea (higher score represents better outcome)	6 RCTs (468 patients)	SMD=0.24(0.03 to 0.45)	0.02
Sleep quality (higher score represents better outcome)	2 RCTs (120 patients)	SMD=0.12(-0.06 to 0.30)	0.19
6-minute walk distance test	7 RCTs (271 patients)	23.83 meters(-12.44 to 60.10)	0.20
Shuttle walk test	1 RCT(45 patients)	72 meters(12.9 to 131)	0.01

KQ2: What was the effect of HMV, BPAP, or CPAP on patient outcomes?

HMV (compared with no device):

Outcome	Direction	Study Design	Statistic (95% CI)	SOE
Mortality	No difference	2 studies (2 observational)	OR: 0.56 (0.29 to 1.08)	Insufficient SOE
Hospital admissions	Fewer	1 study, 93 patients (1 observational)	Rate Ratio: 0.50 (0.35 to 0.71)	Low SOE
Need for intubation	-----	-----	-----	
QOL	-----	-----	-----	

HMV (compared with BPAP):

Outcome	Direction	Study Design	Statistic	SOE
Patients with hospital admission	Fewer	1 study, 9,471 patients (1 observational)	P<0.001	Low SOE

HMV (compared with CPAP):

Outcome	Direction	Study Design	Statistic	SOE
Patients with hospital admission	Fewer	1 study, 39,700 patients (1 observational)	P<0.001	Low SOE

KQ2: What was the effect of HMV, BPAP, or CPAP on patient outcomes?

Subgroup analysis

BPAP (compared with no device):

- In stable COPD:
 - lower mortality
 - higher activities of daily living
 - reduced dyspnea
- In unstable COPD (after hospitalization for recent exacerbation):
 - reduced need for intubation

KQ2: What was the effect of HMV, BPAP, or CPAP on patient outcomes?

Post-hoc analysis

To determine if PaCO₂ initiation threshold had an effect on outcomes

- PaCO₂ ≥45 to 49 mmHg
- PaCO₂ ≥50 to 51 mmHg
- PaCO₂ ≥52 mmHg or greater

No direct comparisons

Mortality and hospitalizations

- No statistically significant differences

Quality of life

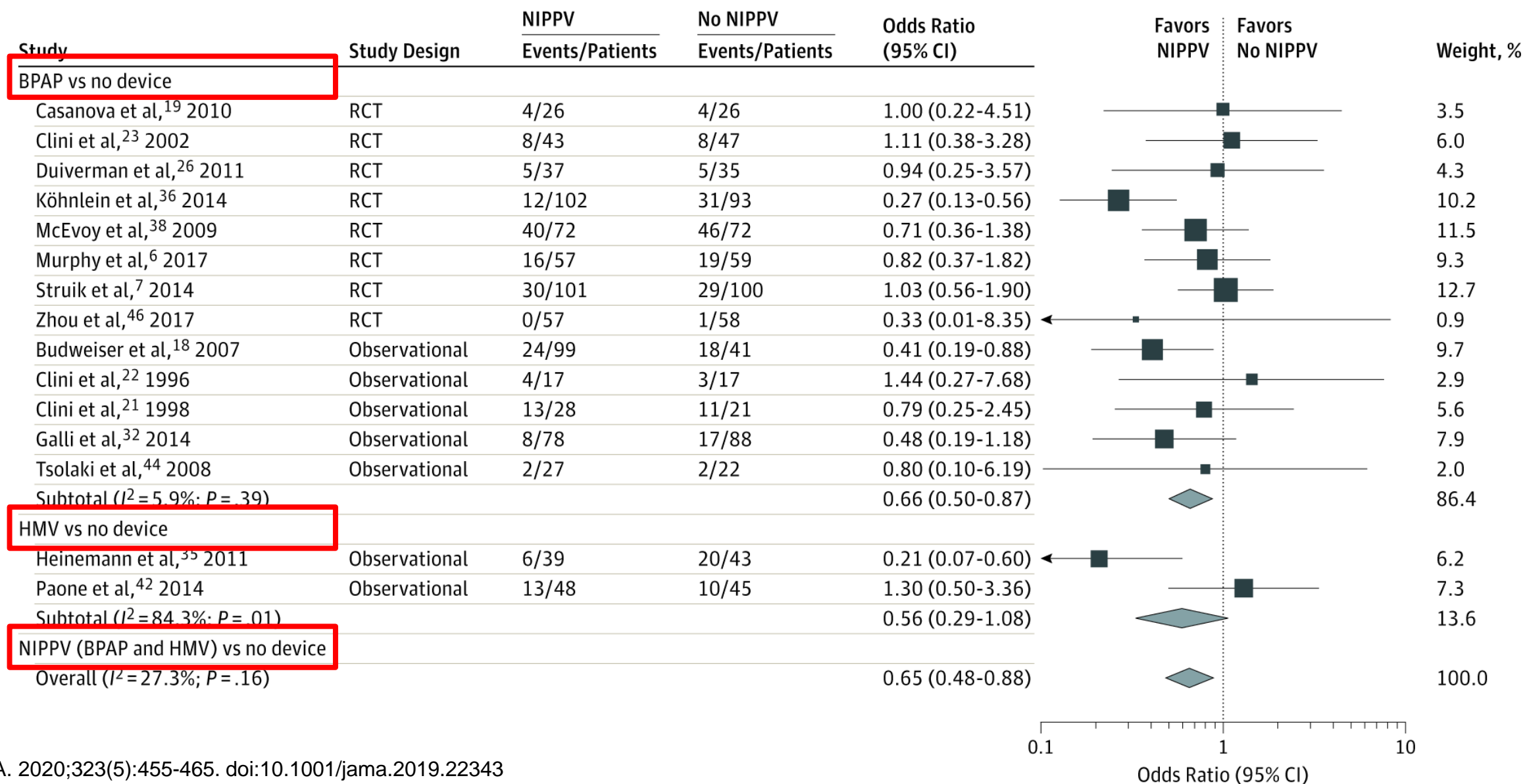
PaCO ₂ initiation threshold	Result	Studies
Paco ₂ ≥52 mm Hg	SMD, 0.18 (−0.05 to 0.40)	2 studies, 311 patients
Paco ₂ of 50 to 51 mm Hg	SMD, 0.97 (0.36 to 1.58)	1 study, 49 patients
Paco ₂ of 45 to 49 mm Hg	SMD, −0.06 (−0.28 to 0.17]	2 studies, 102 patients

KQ2: What was the effect of HMV, BPAP, or CPAP on patient outcomes?

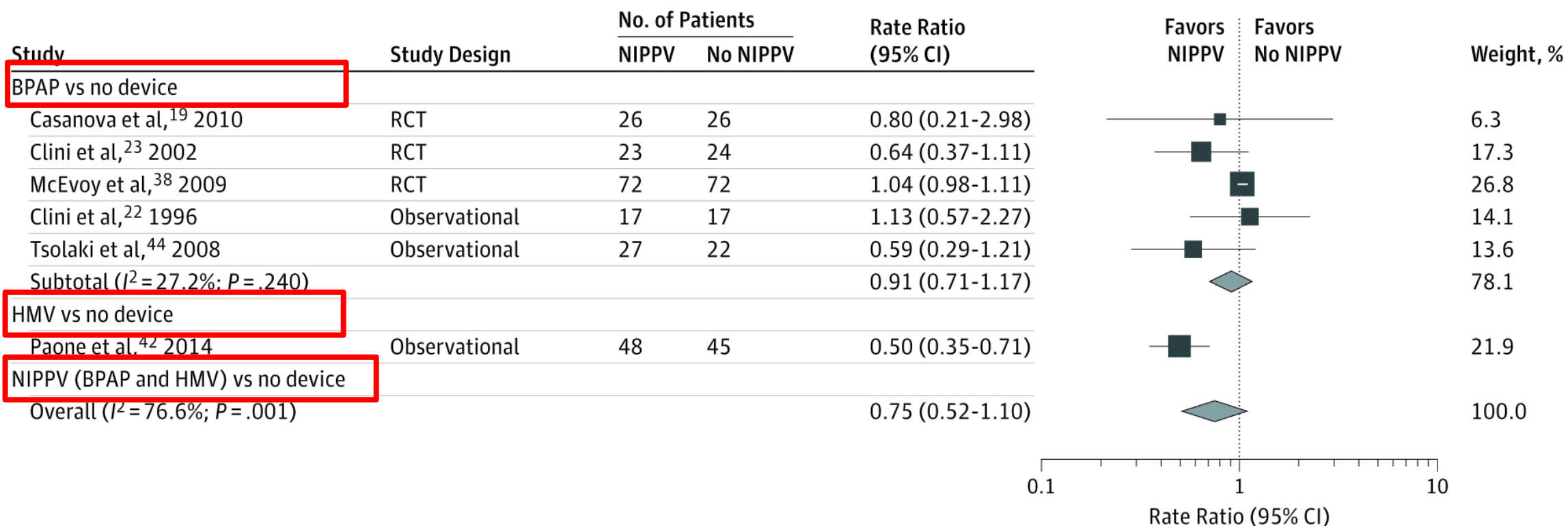
Other device comparisons

Comparison	Outcome	Study Design	Findings
BPAP vs. CPAP	Number of patients with exacerbations	1 RCT, 49 patients	30.43% vs. 53.85%; RD: -0.23 (-0.50 to 0.03)
BPAP volume assured pressure support ventilation vs. BPAP ST	Mortality	1 RCT	RD: -0.05 (-0.21 to 0.11)
	QOL	40 patients	WMD: -4.70 (-15.97 to 6.57)
	Shuttle Walk Test		WMD: -4.00 meters (-54.24 to 46.24)
	Sleep quality		WMD: -2.70 (-6.07 to 0.67)
	Dyspnea		WMD: -0.70 (-1.60 to 0.20)
HMV (pressure controlled ventilation) vs. HMV (pressure support ventilation)	QOL	1 RCT	WMD: -0.14 (-4.90 to 4.60)
	6-minute walk distance test (meters)	17 patients	WMD: 14 (-42 to 70)
BPAP for 6 months vs. BPAP for more than 6 months	6-minute walk distance test (meters)	1 RCT 26 patients	43% increase vs. 11% decrease, p=0.04
	QOL		57 vs. 53, p=0.80
	Number of patients with ICU admission		23.08% vs. 15.38%; RD: 0.08 (-0.23 to 0.38)
HMV/BPAP mix (pressure controlled ventilation) (high intensity) vs. HMV/BPAP mix (pressure support ventilation) (low intensity)	QOL	1 RCT 14 patients	WMD: 2.30 (-2.35 to 6.95)
BPAP S Treatment adherent (≥ 4 hours per day on $\geq 70\%$ of days) vs. BPAP S Treatment non-adherent	Number of all-cause hospital admissions	1 Obs	0.4 vs. 1.0 (p<0.01)
	Number of ICU admission	54 patients	0.6 vs. 1.2 (p=0.37)
BPAP ST started in the home using telemedicine vs. BPAP ST started in the hospital	Mortality	1 RCT 67 patients	6.06% vs. 2.94%; RD: 0.03 (-0.07 to 0.13)
	QOL		WMD: -1.20 (-9.92 to 7.52)
	Dyspnea		WMD: 0.10 (-0.50 to 0.70)
	6-minute walk distance test (meters)		WMD: -19.00 (-64.60 to 29.60)
	Number of all-cause hospital admissions		WMD: -0.10 (-0.60 to 0.40)
	Number of exacerbations		No significant difference

Mortality

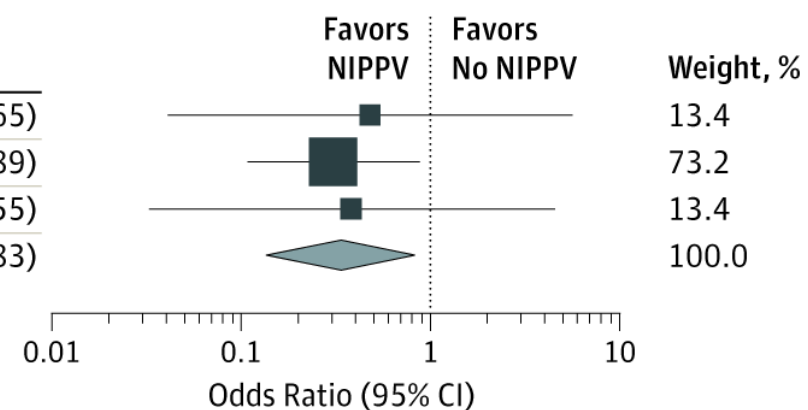


Hospital Admissions

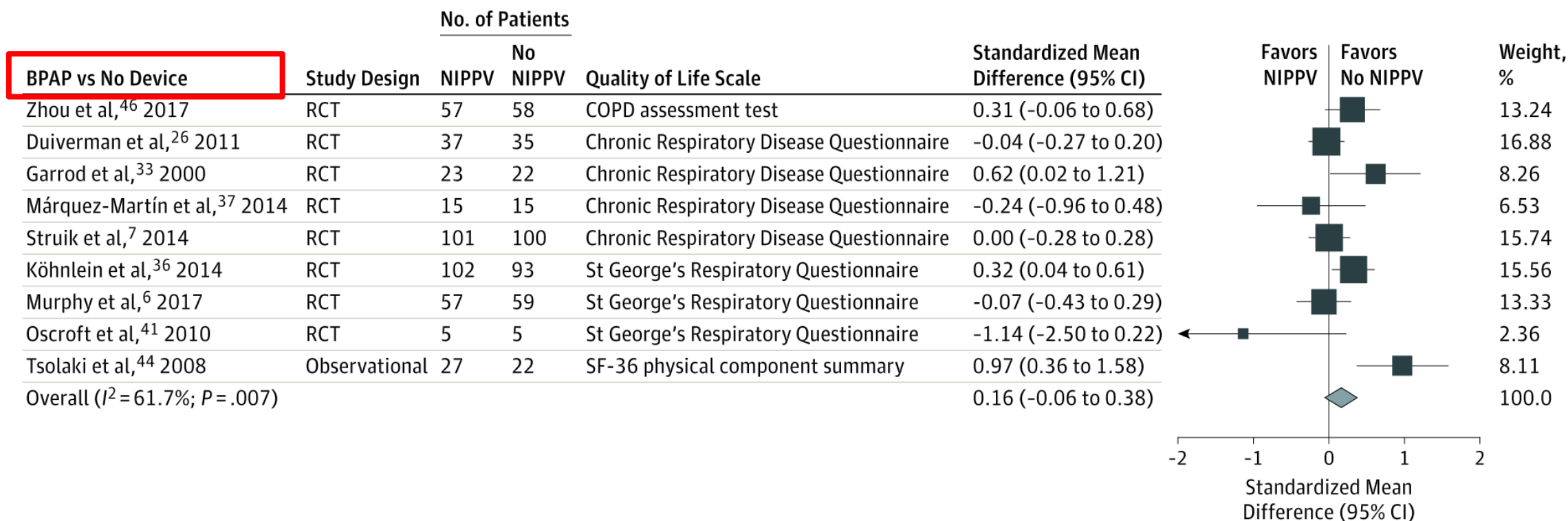


Intubations

BPAP vs No Device	Study Design	NIPPV	No NIPPV	Odds Ratio (95% CI)
		Events/Patients	Events/Patients	
Casanova et al, ¹⁹ 2010	RCT	1/26	2/26	0.48 (0.04-5.65)
Galli et al, ³² 2014	Observational	5/78	16/88	0.31 (0.11-0.89)
Tsolaki et al, ⁴⁴ 2008	Observational	1/27	2/22	0.38 (0.03-4.55)
Subtotal ($I^2 = 0.0\%$; $P = .94$)				0.34 (0.14-0.83)



Quality of Life



KQ2: What was the effect of HMV, BPAP, or CPAP on patient outcomes?

Summary

KQ2: What was the effect of HMV, BPAP, or CPAP on patient outcomes?

Summary

	Device	Comparator(s)	Findings (Strength of evidence)
COPD	HMV	No device	Fewer hospital admissions (low SOE)
	HMV	BPAP	Fewer hospital admissions (low SOE)
	HMV	CPAP	Fewer hospital admissions (low SOE)
	BPAP	No device	Lower mortality (moderate SOE) Reduced need for intubation (moderate SOE) Fewer hospital admissions (low SOE)

- Improved outcomes
 - Number of ED visits
 - Number of patients with ICU admission
 - Dyspnea
 - Shuttle walk test
- No difference
 - ICU admissions
 - COPD exacerbations
 - ADLs
 - Sleep quality
 - 6-minute walk distance test

KQ3: What equipment parameters were used?

	COPD
BPAP Modes	<ul style="list-style-type: none">• BPAP S• BPAP ST• BPAP volume assured pressure support• Pressure control• Not specified
HMV Modes	<ul style="list-style-type: none">• Pressure support• Pressure control
CPAP Modes	<ul style="list-style-type: none">• CPAP
Prescribed Usage (daily)	<ul style="list-style-type: none">• ≥5-8 hours (BPAP)• >12 hours (HMV)
Actual Usage (range of means)	<ul style="list-style-type: none">• 4.5-9.0 hours

Significant variability

KQ4: What home services were provided?

COPD	
Number of studies reporting home respiratory services	15 out of 38 studies
Home services provided	<ul style="list-style-type: none">• Telephone hotline staffed by nurses• Scheduled phone calls by respiratory therapists• Home visits by respiratory therapists• Smoking cessation• Comprehensive home care program with evaluation and treatment of physical, occupational, and dietary needs
Efficacy of home services assessed?	<ul style="list-style-type: none">• N/A

Adverse Events

Type of adverse events	Example
Serious adverse events	Death, hospitalization, and need for intubation were reported as primary efficacy outcomes. Acute respiratory failure Any life-threatening event/illness Any disability or permanent damage Any required intervention to prevent impairment (such as pacemaker) Any congenital anomaly/birth defect
Non serious adverse events	Skin symptoms (e.g. facial rash, nasal ulceration) Eye symptoms (e.g. dry eyes, conjunctivitis) Nose/mouth symptoms (e.g. nasal stuffiness, rhinorrhea, nosebleed, mucosal dryness, oral air leak) Gastrointestinal symptoms (e.g. gastric distension, aerophagia) Device/mask intolerance (e.g. claustrophobia, discomfort, noncompliance) Other

Adverse Events

- 28% of studies reported adverse events (19 out of the 68 included studies)
 - No consistent approach for evaluation and reporting

Device	Serious adverse events Incidence rate and 95% CI	Non-serious adverse events Incidence rate and 95% CI
HMV	IR: 0.00 (0.00 to 0.00)	IR: 0.35 (0.27 to 0.46)
BPAP	IR: 0.01 (0.00 to 0.05)	IR: 0.31 (0.16 to 0.58)
HMV/BPAP mix	Not reported/not evaluated	IR: 0.27 (0.15 to 0.50)
CPAP	IR: 0.09 (0.03 to 0.26)	IR: 0.39 (0.27 to 0.56)
No device	IR: 0.00 (0.00 to 0.01)	IR: 0.00 (0.00 to 0.00)

- Serious adverse events:
 - Mortality, hospitalization, and need for intubation classified as study outcomes

Device type	Serious adverse events (all disease states)	Number of cases, patients at risk, and studies
BPAP	Acute respiratory failure	29 cases out of 178 patients (5 studies)
	Treatment failure (combined endpoint of use<2h/night, hospital admission for respiratory failure, or PaCO ₂ >60)	4 cases out of 29 patients (1 study)
	Aortic dissection	1 case out of 37 patients (1 study)
	Transient ischemic attack	1 case out of 23 patients (1 study)
CPAP	Treatment failure (combined endpoint of use<2h/night, hospital admission for respiratory failure, or PaCO ₂ >60)	4 cases out of 31 patients (1 study)
HMV	Not reported/not evaluated	
HMV/BPAP mix	Not reported/not evaluated	
No device	Acute respiratory failure	13 cases out of 30 patients (2 studies)
	Ischemic stroke	1 case out of 35 patients (1 study)
	Arrhythmia requiring pacemaker	1 case out of 18 patients (1 study)

Adverse Events

- Non-serious adverse events:
 - Skin symptoms (e.g. facial rash, nasal ulceration)
 - Eye symptoms (e.g. dry eyes, conjunctivitis)
 - Nose/mouth symptoms (e.g. nasal stuffiness, rhinorrhea, nosebleed, mucosal dryness, oral air leak)
 - Gastrointestinal symptoms (e.g. gastric distension, aerophagia)
 - Device/mask intolerance (e.g. claustrophobia, discomfort, noncompliance)
- No difference in adverse events or treatment withdrawals
 - Device use vs no device use
 - Different device comparisons
- In COPD 6 studies directly compared adverse events in NIPPV vs no device
 - No difference in total adverse events

Limitations

- Variability and heterogeneity among included studies regarding devices used, modes used, duration of use, ancillary respiratory services provided, outcome definitions, measurement tools, followup lengths of time
- Conclusions based on low to moderate strength of evidence
- Limited evidence on HMV vs BPAP comparisons
- Limited evidence on impact on clinical outcomes of:
 - Device initiation criteria (KQ1)
 - Device parameters (KQ3)
 - Home respiratory services (KQ4)
- Lack of reporting of device type, device mode
- Lack of consistent approach to reporting of adverse events
 - 70% of studies did not report adverse events
- English studies only
- Majority of studies conducted in Europe (78%), home respiratory services may not be explicit
- Could not find studies where patients with COPD used significant daytime NIPPV
- Publication bias was unable to be statistically evaluated because of the number of studies included in a direct comparison

Future Research

- HMV vs BPAP
- Modes
- Respiratory services
- Initiation titration practices
- Consideration of patients who require daytime NIPPV support

Conclusions

- In patients with COPD
 - BPAP (compared to no device) was associated with lower mortality, intubations, hospital admissions, and dyspnea, no change in QOL.
 - HMV (compared individually with BPAP, CPAP, or no device) was associated with fewer hospital admissions.
- Low to moderate SOE
- Current comparative evidence is not available to assess the impact of many device capabilities on patient outcomes.
- Criteria to initiate home NIPPV and home respiratory services vary and are not validated in comparative studies.
- Significant variability in devices used and device modes used.

QUESTIONS