Appendix 2: detailed evaluation of the risk of bias.

Risk of bias – Nagata et al. 2017		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low	« Randomization was performed at Translational Research Informatics Center, Kobe, Japan, using permuted block method with block sizes of 2 and 4 »
Allocation concealment (selection bias)	Low	« Institution and patient registration will be performed using the centralized registration system following the procedure below. » complete data are available in online data supplement
Blinding : participant and personnel (performance bias)	High	« First, the subjects were not blinded to treatment, and therefore, those receiving the intervention may have overreported improvements in subjective outcomes, such as health-related QOL »
Blinding : outcome assessment (detection bias)	High	As above
Incomplete outcome data (attrition bias)	High	Intention-to-treat, flow chart According to the flow-chart, 13 patients were analysed out of the 14 patients included
Selective reporting (reporting bias)	Low	Important outcomes reported All outcomes are announced in NCT registration.
Other	Unclear	« Tomii K reports honoraria from Teijin Pharma Limited » « Primary Source of Funding: Teijin Pharma Limited » No washout period

Risk of bias – Storgaard et al. 2018		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear	« In this randomized, prospective trial a total of 200 patients were included from 4 outpatient clinics in the North Jutland Region of Denmark between December 2013 and July 2015 » but no more details
Allocation concealment (selection bias)	Low	« By the use of numbered sealed envelopes containing group allocations, patients were randomly assigned to either LTOT (controls) or LTOT plus HFNC home treatment »
Blinding : participant and personnel (performance bias)	High	No placebo treatment « A randomized blinded study could have been wished for, however, blinding the patients against the ow, the heat and the humidity is not realistic »
Blinding : outcome assessment (detection bias)	High	As above
Incomplete outcome data (attrition bias)	Low	Intention-to-treat, flow-chart « The analysis population was defined as all subjects randomized to treatment and who had no major protocol deviations affecting efficacy data, giving 100% inclusion of all 200 subjects enrolled. As such, data were included on patients who discontinued the study or paused treatment and those who discontinued HFNC but stayed in the study, in the HFNC group (intention-to-treat) »
Selective reporting (reporting bias)	Unclear	All outcomes are not reported in ClinicalTrials Data are not included in the text and tables of the study

Other	Unclear	« Hans-Ulrich Hockey received remuneration from Fisher & Paykel, who also contributed equipment and some administration costs »

Risk of bias – Fraser et al. 2016		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear	« After the baseline period the patient will be randomised using sealed opaque envelopes » no more information
Allocation concealment (selection bias)	Low	« The order of therapy was allocated using sequentially-numbered, sealed envelopes which were not prepared by study staff »
Blinding : participant and personnel (performance bias)	High	No placebo treatment
Blinding : outcome assessment (detection bias)	High	As above
Incomplete outcome data (attrition bias)	Low	Intention-to-treat, flow-chart
Selective reporting (reporting bias)	Low	Important outcomes reported All outcomes are announced in ANZCTR registration.
Other	High	« We studied only males thus the results seen cannot be generalised to women suffering COPD » « JFF has received a research fellowship from Queensland Health Office of Health and Medical Research. JFF received an unrestricted grant from Fisher & Paykel Healthcare in support of the current study. JFF and AC have received assistance from Fisher & Paykel Healthcare to support travel and accommodation costs to attend research meetings; neither has received honoraria or consultancy fees from Fisher & Paykel »

Risk of bias – McKinstry et al. 2018		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low	« The order of administration of the four treatments was randomized. The randomisation was computer- generated by the study statistician, who had no role in the recruitment, study visits or data collection »
Allocation concealment (selection bias)	Low	« Random allocations were sealed in sequentially numbered opaque envelopes before recruitment »
Blinding : participant and personnel (performance bias)	Unclear	« Our study was single-blinded in that although participants were blinded to the actual flow rate they received, they could feel the difference between low, medium and high flows »
Blinding : outcome assessment (detection bias)	Low	« The un-blinded investigator's role included manually counting the respiratory rate and controlling the settings on the NHF device. The blinded investigator recorded $PtCO_2$, heart rate and StO_2 from the SenTec display while seated behind a screen so that they could not see the participant or myAIRVO 2 display and wearing ear plugs to avoid hearing changes to the NHF flow-rate »
Incomplete outcome data (attrition bias)	Low	Intention-to-treat, flow-chart
Selective reporting (reporting bias)	Low	Important outcomes reported All outcomes are announced in ANZCTR registration
Other	Unclear	« The study was funded by Fisher and Paykel Healthcare New Zealand » Lack of staff calculation

Risk of bias – Nilius et al. 2013		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear	« The study design consisted of a randomized crossover design » but no more details
Allocation concealment (selection bias)	Unclear	Information not available
Blinding : participant and personnel (performance bias)	High	No placebo treatment
Blinding : outcome assessment (detection bias)	High	As above
Incomplete outcome data (attrition bias)	Unclear	Information not available
Selective reporting (reporting bias)	Unclear	No full-text available No registration number available
Other	High	No full-text available "This abstract is funded by: The study was supported by TNImedical Germany"

Risk of bias – Cirio et al. 2016		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear	« we performed a randomized crossover study » but no more details
Allocation concealment (selection bias)	Unclear	Information not available
Blinding : participant and personnel (performance bias)	Unclear	Single-blind but « Another limitation is the lack of blinding, difficult to be performed using the specific device for HFNC »
Blinding : outcome assessment (detection bias)	High	Single-blind for participants
Incomplete outcome data (attrition bias)	Low	Lack of flow-chart All participants inclued were analyzed
Selective reporting (reporting bias)	High	HR and blood pressure are not reported
Other	Low	No other bias seems to be present