



Supplementary Table 1: PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1/ Line 3-6
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 1-3/ Line 17-44
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 3-6/ Line 47-112
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 6/ Line 113-116
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 6-7/ Line 123-137
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 7-8/ Line 144-146
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page 7-8/ Line 141-146
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 8/ Line 150-154
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 8/ Line 157-158
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 7/ Line 128-131
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 8/ Line 158-162
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 9/ Line 168-176
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 8-9/ Line 185-188
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 6-7/ Line 123-131
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 9/ Line 180-185
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 9/ Line 179-180
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 9/ Line 179-184
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Page 10/ Line 194-201



Supplementary Table 1 (Continued)

Section and Topic	Item #	Checklist item	Location where item is reported
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Page 10/ Line 189-190
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 10/ Line 190-191
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	—
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 10-11/ Line 204-210
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Page 11/ Line 209-210
Study characteristics	17	Cite each included study and present its characteristics.	Page 11-12/ Line 213-233
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Page 12/ Line 235-245
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	—
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Page 11-12/ Line 213-245
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Page 13-17/ Line 247-331
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Page 17/ Line 333-339
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Page 17/ Line 341-343
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Page 17-18/ Line 343-345
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	—
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 18/ Line 347-354
	23b	Discuss any limitations of the evidence included in the review.	Page 22-23/ Line 444-457
	23c	Discuss any limitations of the review processes used.	—
	23d	Discuss implications of the results for practice, policy, and future research.	Page 23/ Line 466-448
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	—
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	—



Supplementary Table 1 (Continued)

Section and Topic	Item #	Checklist item	Location where item is reported
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	—
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 24/ Line 475
Competing interests	26	Declare any competing interests of review authors.	Page 24/ Line 486
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Page 25/ Line 489-490

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: <http://www.prisma-statement.org/>

Supplementary Table 2: Search strategy

	Search strategy (PubMed)	Results
#1	(randomized controlled trial [Publication Type] OR controlled clinical trial [Publication Type] OR randomized [Title/Abstract] OR placebo [Title/Abstract] OR clinical trials as topic [MeSH Terms:noexp] OR randomly[Title/Abstract] OR trial[Title]) NOT (animals[MeSH Terms] NOT (humans[MeSH Terms] AND animals[MeSH Terms]))	1,360,724
#2	(((((HFO OR HFNC OR HFNP OR HHFNOX OR HFNO OR NHF) OR (humidification oxygen)) OR (Humidication oxygen)) OR (humidified oxygen)) OR (High Flow Oxygen)) OR (nasal high flow)) OR (High flow nasal)	22,627
#3	(((((hypercapnic) OR (hypercapneic)) OR (hypercapnia)) OR (acidotic)) OR (AT2RF)) OR (type II respiratory failure)) OR (type two respiratory failure)	92,935
#4	#1 AND #2 AND #3	280
	Search strategy (Embase)	Results
#1	'Clinical trial (topic)'/exp	399,233
#2	'trial': ti	372,231
#3	'random': ab,ti OR 'placebo':ab,ti OR 'double-blind':ab,ti OR 'randomized':ab,ti OR 'randomly':ab,ti	1,825,315
#4	#1 OR #2 OR #3	2,211,694
#5	(hypercapneic:ab,ti OR hypercapnic:ab,ti OR hypercapnia:ab,ti OR acidotic:ab,ti OR at2rf:ab,ti OR (type AND ii AND respiratory AND failure:ab,ti) OR (type AND two AND respiratory AND failure:ab,ti)) AND ('high flow nasal cannula therapy'/exp OR 'high flow nasal cannula	694

	therapy' OR (humidication AND oxygen:ab,ti) OR (humidified AND oxygen:ab,ti) OR (high AND flow AND oxygen:ab,ti) OR (high AND flow AND nasal:ab,ti) OR (nasal AND high AND flow:ab,ti) OR hfo:ab,ti OR hfnc:ab,ti OR hfnp:ab,ti OR hhfnox:ab,ti OR hfno:ab,ti OR nhf:ab,ti)	
#6	#4 AND #5	140
	Search strategy (Cochrane Library)	Results
#1	(high flow): ti,ab,kw OR (high-flow):ti,ab,kw (Word variations have been searched)	13,564
#2	(Humidication oxygen): ti,ab,kw OR (humidified oxygen):ti,ab,kw OR (HFO):ti,ab,kw OR (hfnc):ti,ab,kw OR (hfnp):ti,ab,kw OR (hhfnox):ti,ab,kw OR (hfno):ti,ab,kw OR (NHF):ti,ab,kw (Word variations have been searched)	1,275
#3	#1 OR #2	13,864
#4	MeSH descriptor: [Hypercapnia] explode all trees	534
#5	(hypercapnic) OR (hypercapneic) OR (hypercapnia) OR (acidotic) OR (AT2RF) (Word variations have been searched)	2,085
#6	(type II respiratory failure) OR (type two respiratory failure) (Word variations have been searched)	5,540
#7	#6 OR #5 OR #4	7,284
#8	#7 AND #3	622

Supplementary Table 3: Results of risk assessment of bias in the included studies

Study	random sequence generation	allocation concealment	blinding of participants	blinding of outcome assessment	incomplete outcome data	selective reporting	other biases
Cortegiani A,2020	Low	Low	High	Low	Low	Low	Low
Li C,2019	Unclear	Unclear	High	Unclear	Low	Low	Low
Wang J,2019	Unclear	Unclear	High	Unclear	Low	Low	Unclear
Doshi PB,2020	Low	Low	High	Low	Low	Low	Unclear
Papachatzakis Y,2020	Unclear	Unclear	High	Unclear	Low	Low	Low
Tan D,2020	Low	Low	High	Low	Low	Low	Low
Jing G,2019	Low	Low	High	Unclear	Low	Low	Low
Yu Z,2019	Low	Low	High	Unclear	Low	Low	Unclear
Li X,2020	Low	Low	High	Low	Low	Low	Low
Xia J,2022	Low	Low	High	Low	Low	Low	Low