**Appendix Table 1.** Theoretical benefits and drawbacks of high-flow nasal cannula compared to other treatments for acute respiratory failure

| | Potential benefits of high-flow nasal cannula | Potential drawbacks of high-flow nasal cannula |
|---|---|---|
| Compared to noninvasive ventilation | • Improved dyspnea [1,2]<br>• Improved respiratory rate [1]<br>• Improved comfort [1,2]<br>• Improved mask tolerance (e.g. less claustrophobia, less anxiety)<br>• Improved ability to tolerate treatment for longer periods of time [3]<br>• Less adverse events (e.g. less skin breakdown) [4,5]<br>• Improved ability to communicate<br>• Improved ability to eat/drink<br>• Improved ability to sleep [6]<br>• Lower mortality rate [1]<br>• Does not need to be removed for airway procedures (e.g. laryngoscopy)<br>• Can be used in certain patient populations where noninvasive ventilation is contraindicated (altered mental status, claustrophobia, airway obstruction, facial injury, significant sputum production, unstable hemodynamics) | • Lower ability to improve hypercapnia [7]<br>• Lower ability to improve hypoxia [2,5]<br>• Lower ability to improve work of breathing [8] |
| Compared to conventional oxygen | • Improved dyspnea [2,9]<br>• Improved respiratory rate [1,9]<br>• Improved hypoxia [2,9] (fewer desaturations) [10]<br>• Improved comfort [11]<br>• Reduced mouth dryness [11]<br>• Lower mortality rate [1] | • More nasal dryness/discomfort<br>• Decreased mask tolerance [12] |
| Compared to palliative opioids | • Less opioid associated sedation (and therefore indirectly associated with improved ability to communicate, say good bye, continue to direct healthcare decisions) | • Less comfortable<br>• More nasal dryness/discomfort<br>• Cannot routinely be administered outside of the hospital<br>• Decreased ability to easily transport patient while connected to high-flow nasal cannula |

**Appendix Table 2.** Detailed Search Strategy

OVID MEDLINE

| | |
|---|---|
| 1 | ("high flow" adj3 (nasal or oxygen or cannula*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] |
| 2 | (optiflow or aquinox or vapotherm or "pari hydrate").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] |
| 3 | 1 or 2 |
| 4 | exp respiratory therapy/ or exp oxygen inhalation therapy/ |
| 5 | "high flow".mp. and 4 [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] |
| 6 | (hfnc or hhfnc or nhft or hhhfnc.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] |
| 7 | exp respiratory insufficiency/th |
| 8 | 7 and "high flow".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] |
| 9 | 3 or 5 or 6 or 8 |
| 10 | remove duplicates from 9 |

EMBASE

| | |
|---|---|
| 1 | exp intensive care/ or oxygen therapy/ or acute respiratory failure/ or exp noninvasive ventilation/ or exp respiratory failure/ |
| 2 | 1 and "high flow".mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading] |
| 3 | ("high flow" adj3 (nasal or oxygen or cannula*)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading] |
| 4 | (optiflow or aquinox or vapotherm or "pari hydrate").mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading] |
| 5 | (hfnc or hhfnc or nhft or hhhfnc).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading] |
| 6 | 2 or 3 or 4 or 5 |
| 7 | remove duplicates from 6 |
| 8 | 7 not case report/ |

CINAHL

1982 present

#QueryLimiters/ExpandersLast Run ViaResults
S4S1 OR S2 OR S3Search modes - Boolean/PhraseInterface - EBSCOhost Research Databases

Search Screen - Advanced Search
Database - CINAHL with Full Text 537
S3optiflow ORT aquinox OR vapotherm OR "pari hydrate"Search modes - Boolean/PhraseInterface - EBSCOhost Research Databases

Search Screen - Advanced Search
Database - CINAHL with Full Text 27
S2nhftSearch modes - Boolean/PhraseInterface - EBSCOhost Research Databases

Search Screen - Advanced Search
Database - CINAHL with Full Text0S1"high flow" OR hfnc OR hhfnc OR hhhfncSearch modes - Boolean/PhraseInterface - EBSCOhost Research Databases

Search Screen - Advanced Search
Database - CINAHL with Full Text 525

Scopus
( TITLE-ABS-KEY ( "high flow" W/3 ( oxygen OR nasal OR transnasal OR prong* OR therap* ) ) OR TITLE-ABS-KEY ( ( optiflow OR aquinox OR vapotherm* OR "pari hydrate" OR hfnc OR hhfnc OR hhhfnc OR nhft ) ) ) AND NOT ( PMID ( 1* OR 2* OR 3* OR 4* OR 5* OR 6* OR 7* OR 8* OR 9* ) ) 541

Web of Science
**TOPIC:** ("high flow" SAME (therap* OR oxygen* OR nasal OR cannula*)) *OR* **TOPIC:** (optiflow OR aquinox OR vapotherm* OR "pari hydrate" OR hfnc OR hhfnc OR hhhfnc OR nhft) 1965

**Appendix Table 3.** Modified Newcastle-Ottawa Risk of Bias Scoring Guide.

1—Sample representativeness
1 point: Multicenter
0 points: Single center

2—Sample size
1 point: "Do-not-intubate" or "comfort-measures-only" group sample size ≥50 patients
0 points: "Do-not-intubate" or "comfort-measures-only" group sample size <50 patients

3—Nonexposed cohort
1 point: The study provided mortality rates for a "full-code" comparison group
0 points: The study did not provide mortality rates for a "full-code" comparison group

4—Ascertainment of exposure No. 1
1 point: The study reported the process used to determine "do-not-intubate" or "comfort-measures-only" orders
0 points: The study did not report the process used to determine "do-not-intubate" or "comfort-measures-only" orders or the process reported was incomplete

5—Ascertainment of exposure No. 2
1 point: The study explicitly identified and analyzed separately "comfort-measures-only" patients (received treatment with palliative intent) from "do-not-intubate" patients (received treatment with curative intent)
0 points: The study did not identify, exclude, or analyze separately "comfort-measures-only" patients from "do-not-intubate" patients

Scoring
Low risk of bias: Total score, 3-5 points
High risk of bias: Total score, 0-2 points

## Appendix References


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12. Parke R, McGuinness S, Dixon R, Jull A. Open-label, phase II study of routine high-flow nasal oxygen therapy in cardiac surgical patients. *British journal of anaesthesia.* 2013;111(6):925-931.

# PRISMA 2009 Checklist

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 3-4 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 3-4 |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 4 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 4 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 4 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | Appendix |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 4-5 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 4-5 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | Table 1 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 5 and Appendix |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | N/A |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | N/A |

# PRISMA 2009 Checklist

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | N/A |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | N/A |
| **RESULTS** | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | Figure 1 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | Table 1 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | Table 2 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | N/A |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | N/A |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | N/A |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | N/A |
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 8-10 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 8-10 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 8-10 |
| **FUNDING** | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | Title page |

*From:* Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097