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Orientado por:

Ricardo Miguel Ribeiro Marques Fernandes, MD, PhD

Abstract:

Background: The quality of the reporting of interventions in health research is generally poor, limiting the utility of study results. High flow oxygen therapy (HFOT) is a relatively novel multicomponent intervention used in children with acute respiratory conditions without an established evidence base. **Objectives:** To evaluate the completeness and quality of the reporting of HFOT interventions across published studies. **Search method:** MEDLINE database was searched up to 31st July 2019. **Selection criteria:** Randomized controlled trials (RCTs) and observational studies of children with bronchiolitis, pneumonia or in acute respiratory failure, whose main respiratory support was HFOT. **Data collection:** One reviewer extracted data on general study characteristics and on HFOT interventions according to an adapted version of the Template for Intervention Description and Replication (TIDieR) checklist, with data verification by a second reviewer. We selected a priori a set of core TIDieR items (items 3 - What Materials, 4 - What Procedures, 8 - When and How much and 9 - Tailoring). **Data analysis:** We performed a descriptive synthesis and assessed the completeness and quality of the reporting of HFOT interventions. **Results:** Of the 48 studies (8139 participants) included, 11 studies (23%) were RCTs and 37 studies (77%) were observational studies. 19 studies (40%) reported the use of HFOT exclusively in patients with bronchiolitis and 29 studies (60%) in patients with different respiratory conditions. Only 6 studies (12.5%) correctly reported more than 50% of core items and no study correctly reported all these items. The least correctly reported component of HFOT was the item on Tailoring, found in 8% of published studies. **Conclusion:** The reporting of HFOT interventions in children with acute respiratory diseases is generally poor. An effort to improve the reporting of this intervention in future studies may result in better-quality evidence and ultimately lead to the optimization of care of children in acute respiratory distress.

Keywords: High flow oxygen therapy; Pediatrics; Respiratory diseases; Reporting of interventions

O Trabalho Final exprime a opinião do autor e não da FML

Resumo:

Introdução: A qualidade do reporte das intervenções na investigação em saúde é geralmente pobre, limitando a utilidade dos resultados obtidos. A oxigenioterapia de alto fluxo (OAF) é um método de suporte respiratório relativamente recente, utilizado em crianças com doenças respiratórias agudas, embora sem uma base de evidência claramente estabelecida. **Objetivos:** Avaliar a qualidade do reporte da terapêutica com OAF em estudos publicados. **Pesquisa:** A base de dados MEDLINE foi pesquisada até 31 de Julho de 2019. **Critérios de seleção:** Ensaios clínicos controlados e aleatorizados (ECAs) e estudos observacionais em crianças com bronquiolite, pneumonia e insuficiência respiratória aguda, cujo principal suporte respiratório foi a OAF. **Colheita de dados:** Um revisor extraiu os dados relativos às características gerais de cada estudo e à intervenção com OAF, de acordo com uma versão adaptada da *Template for Intervention Description and Replication* (TIDieR*),* com verificação dos dados extraídos por um segundo revisor. Selecionamos *a priori* um conjunto de items-chave da intervenção com OAF (items 3 - Materiais, 4 - Procedimentos; 8 – Quando e Quanto e 9 - Titulação). **Análise de dados:** Realizamos uma síntese descritiva e avaliamos a qualidade do reporte das intervenções com OAF. **Resultados:** Dos 48 estudos incluídos (8139 participantes), 11 estudos (23%) eram ECAs e 37 estudos (77%) eram observacionais. 19 estudos (40%) reportaram a utilização de OAF em doentes com bronquiolite e 29 estudos (60%) em doentes com outras doenças respiratórias. Apenas 6 estudos (12.5%) reportaram corretamente mais de 50% items-chave e nenhum estudo reportou corretamente todos estes items. O elemento da OAF menos corretamente reportado correspondeu ao item relativo à "Titulação" em apenas 8% dos estudos publicados. **Conclusão:** O reporte das intervenções com OAF em estudos com crianças com doenças respiratórias agudas é globalmente mau. Um esforço para melhorar o reporte desta intervenção em estudos futuros pode resultar na produção de evidência de maior qualidade e na otimização da terapêutica de crianças em *distress* respiratório agudo.

Palavras-Chave: Oxigenoterapia de alto fluxo; Pediatria; Doenças respiratórias; Reporte das intervenções

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Introduction

Background

It is essential to correctly report all the components of an intervention in a scientific study, in order to correctly translate research findings to clinical practice. Complete reporting also allows other researchers to replicate the intervention in new studies, and to adequately compare and aggregate their results in methodologically adequate systematic reviews. Studies have shown that the quality of the reporting of interventions in health research is generally poor, limiting the utility of study results and compromising the ethics of study participation (1).

Recently, there has been an increasing interest in the research on high flow oxygen therapy (HFOT) as a respiratory support intervention in acute respiratory conditions (2,3). HFOT has been studied as a treatment approach in children with acute respiratory diseases such as bronchiolitis, pneumonia or asthma exacerbations across different healthcare settings. One of its aims is to act in an early phase of moderate to severe respiratory distress, in order to reduce escalation of care to other more invasive and resource-intensive respiratory interventions, which often require admission to an Intensive Care Unit (ICU) (4). HFOT has also been studied as a potential de-escalation strategy to prevent reintubation in mechanically ventilated patients (5).

HFOT is provided through a medical device with multiple variable technological interacting components (ie humidifier, circuit, interface, receptors) (6). It is available from different manufacturers as stand-alone or built-in packages, with different settings that can be adjusted manually or automatically (eg air and O2 flow, targeted FiO2). This complexity has implications in the preparation and implementation of HFOT in distinct settings and may influence the safety and efficacy of the intervention across different conditions and participants.

Furthermore, devices used in pediatrics have specificities related to the anatomical, physiological and developmental features of children and adolescents (7,8). These features must be considered when designing and developing pediatric devices and protocols adapted to different children and pediatrics conditions (9). However, it has been shown that there is reduced investment and clinical research in this field, with few approved pediatric medical devices with validated protocols and clinical data (10).

Therefore, clinicians are often forced to use adult devices "off-label", and to extrapolate their use from the adult to the pediatric population (11). The HFOT devices are not an exception considering the lack of established validated protocols for their use concerning different pediatric age groups and clinical conditions (12–14).

There is potential variability of interventions in studies using medical devices to provide HFOT. Therefore, complete reporting is essential so that the interventions can be correctly replicated by researchers in other studies and possibly be used in clinical practice. The validated framework and checklist Template for Interventions Description and Replication (TIDieR) allows the assessment of the completeness of reporting of interventions in published studies (1). So far no studies have evaluated the quality of the reporting of HFOT interventions in children with bronchiolitis, pneumonia or in acute respiratory failure, using the TIDieR checklist.

Objectives

The objectives of this systematic review were:

- To characterize the description of HFOT interventions in published studies in children with acute respiratory conditions.
- To assess the completeness of the reporting on the *what* (materials and procedures), the *who* (provided), the *how, where, when, how* much and on the *tailoring* of HFOT interventions.
- To evaluate the quality of the reporting of HFOT interventions.

Methods

We designed a methodological systematic review according to previous examples of studies assessing the quality of the reporting of different interventions (15–18). This manuscript was reported according to the PRISMA guidance for reporting systematic reviews (19).

Eligibility criteria

Studies were selected according to the following criteria:

Study design

We included randomized controlled trials (RCTs) as well as prospective and retrospective observational studies, including cohort studies, case-control studies and case series. Time series and cross-sectional studies, including surveys, and case reports were not included. Systematic and narrative reviews were also excluded.

Participants

We included studies with children up to 18 years of age, diagnosed with bronchiolitis, pneumonia, asthma exacerbations or in acute respiratory failure, who were treated in the emergency department, as inpatients or in the pediatric ICU. Studies including newborns with conditions specifically related to prematurity or neonatal-related respiratory diseases were excluded. Studies including both children and adults were excluded, unless children data was reported separately. Animals studies were excluded, as well as those in which the main intervention had been tested in physiological human-like mechanical models.

Interventions

We included any study in which HFOT was administered as a main therapeutic intervention. The fact that patients undergoing HFOT were given additional pharmacological or non-pharmacological treatments as co-interventions was not an exclusion criterion. This included noninvasive positive pressure ventilation (NIPPV) through CPAP/Bi-level or invasive mechanical ventilation (IMV), if these were used as step-up treatments or in control/comparison groups. Studies using HFOT as a step-down approach to deescalate respiratory support with NIPPV or MV were also included.

The definition of HFOT has been used differently across studies (20). High flow (or fixed performance) devices are those capable of delivering gas at a flow rate that exceeds the patient peak inspiratory flow rate. Consequently, these devices deliver an almost constant oxygen concentration (FiO2). If the system fails to match the patient's ventilatory demand, then it is called a low flow system (21). We included high flow oxygen interventions using high flow nasal cannula (HFNC). Studies focused on testing other devices like Venturi masks, non-re-breather or partial re-breather masks, simple masks, face tents or low flow nasal cannula were excluded.

Comparators

We included experimental or observational studies in which HFOT was compared to 1.) another HFOT device or method, 2.) low flow oxygen or 3.) another respiratory therapy.

Outcomes

We only included studies whose primary outcomes were clinical outcomes. Studies which focused on physiological outcomes as primary outcomes were excluded unless those outcomes included: O2 saturation, respiratory rate, work of breathing or heart rate.

Setting

We included studies with patients in the emergency department, pediatric ward and ICU. Studies using HFOT in the context of pediatric transport were excluded.

Language and timing of publication

We included studies published in English, French, Spanish or Portuguese, if they were published until July 31st 2019.

Information Sources

We developed a search strategy using medical subject headings (MeSH) and text words related to Pediatrics and to High Flow Oxygen Therapy. We searched in one electronic database, MEDLINE, through the Pubmed interface. Whenever possible, our research was complemented by consulting reference lists and study protocols to determine whether additional information about the interventions could be obtained from other sources.

Search strategy

A systematic search was performed in MEDLINE database, up to 31st July 2019, with no study design or language restrictions. However, only English, French, Spanish and Portuguese published studies were included in this review. A specific search strategy with MeSH and free-text terms for Pediatrics and for High Flow Oxygen Therapy was performed by one researcher (MD) with the help of a Health Sciences Librarian. Our MEDLINE search strategy is reported in Appendix 1.

Study records

- Data management before Screening

After the literature search was performed, the titles and abstracts were uploaded manually to an Excel sheet. No systematic review data management software was used. Both authors developed the screening questions, based on the inclusion and exclusion criteria, which were also uploaded to the same Excel sheet.

- Piloting

Before the formal screening process and data extraction, a pilot study (n=8) was performed to refine the eligibility criteria, the extraction form and the extraction process.

- Selection process (Screening)

Both RF and MD proceeded to (1) screening of titles and abstracts, independently, according to the eligibility questions. Studies were classified as “Included”, “Excluded” or “Unclear”. This was followed by (2) a full text analysis of the “Unclear” and “Included” citations, to decide on their final eligibility. At the end of each stage (1) and (2) authors discussed their results and resolved disagreements about the eligibility through oral consensus. We also recorded the reasons for excluding studies. Review authors were not blinded to the study titles, authors or institutions.

- Collection process (Data extraction)

The extraction process was carried out by one author (MD) into a dedicated Excel sheet, with data verification by a second author (RF). The items in the extraction form consisted

of general paper and study characteristics, and an adapted version of the TIDieR checklist for HFOT which was developed a priori by both authors.

When there was missing information on the studies' interventions (HFOT methodology) in the original papers, we searched for published protocols and references, if they were cited in the main paper as having potentially relevant details on the study interventions. If relevant information was found, additional data extraction was performed. Attempts to retrieve any further information by contacting authors was not made.

Data items

We initially extracted general paper and study characteristics from the included articles, including the article title, authors, journal or magazine where it was first published, year of publication, language, study design, setting, aim of study, number of arms, the randomization method if applicable, blinding if applicable, inclusion and exclusion criteria, definition of the clinical condition studied (bronchiolitis, pneumonia, asthma and acute respiratory failure), number of patients included, active and control interventions and co-interventions.

We then extracted items related to an adapted TIDieR checklist. TIDieR - Template for Intervention Description and Replication - consists of a 12 items checklist which evaluates the completeness of interventions reporting (1). Items 1 and 2 cover the name and the rationale of the intervention. Items 3 to 9 pose several questions - what (materials and procedures), who (provided), how, where, when and how much and tailoring. The reporting of answers to these seven questions provides researchers and clinicians with detailed information about the procedures and the context. This information is essential for the replicability of interventions (1). Items 10 to 12 cover the modifications along the study and the fidelity (actual and to the planned intervention).

Considering that our research was focused on HFOT interventions, we chose to use an adapted version of TIDieR, which subdivides items 3 (What Materials), 4 (What Procedures), 8 (When and How much) and 9 (Tailoring) into subitems.

- **Item 3 (What - Materials)** was subdivided in:
    - **3.a) Brand(s)** (of the device(s) used to provide the HFOT);

- **3.b) Device(s)** (used to provide HFOT, specifying the model as complete as possible)**;**
- **3.c) Humidifier** (humidifier model in case it is not integrated in the device)**;**
- **3.d) Circuit** (circuit model in case it is not integrated in the device)
- **3.e) Cannula** (cannula model, outer diameter, maximum flow rate and grade of fitting to the child's nares);

- **Item 4 (What - Procedures)** is subdivided in:
  - **4.a) Main intervention performed** (reporting that High Flow Oxygen Therapy - HFOT - was performed);
  - **4.b) Baseline assessment** (physical and analytical parameters that were assessed immediately before the main intervention was started or in the moment the intervention started).
  - **4.c) Assessment during the intervention** (physical and analytical parameters that were assessed as well as the schedule of the assessment until the end of the intervention).
  - **4.d) Co-interventions performed** (if any therapeutic co-intervention was performed, including pharmacological and non-pharmacological interventions and intravenous hydration)
  - **4.e) Feeding** (the study must report if the children were or were not feed and the method used).

- **Item 8 (When and How much)** was subdivided in:
  - **8.a) When did the intervention start?** (clinical and/or analytical criteria that determined the beginning of the intervention);
  - **8.b) Initial and maximum FiO2**; (percentage (%) of FiO2 in the mixture of gases supplied in the beginning of the intervention and maximum FiO2 permitted)
  - **8.c) Initial and maximum Flow** (flow rate in L/min supplied in the beginning of the intervention and maximum flow permitted. The latter must be mentioned in the case of a "step up" approach in which the patient is not supplied with the maximum flow since the beginning);

- **8.d) Targeted Temperature** (temperature in ºC or ºF of the mixture of gases supplied, that was intended during the intervention);
- **8.e) Co-interventions** (scheduling and doses of the therapeutic co-interventions, the latter in case of pharmacological co-interventions, hydration or feeding)

- **Item 9 (Tailoring)** was subdivided in:
  - **9.a) FiO2 titration** (targeted SatO2 to which the FiO2 must be regulated as well as the method of FiO2 titration);
  - **9.b) Flow titration** (whether it consisted of starting with a lower flow and then "stepping-up" until a maximum flow or starting with a higher flow and then weaning, explanation of the method chosen);
  - **9.c) Criteria for weaning** (clinical and/or analytical criteria used to start weaning)**;**
  - **9.d) Timing for weaning** (minimum stability Period and/or interval between weaning trials);
  - **9.e) Weaning method** (process for stepping down, including FiO2 and Flow);
  - **9.f) "Switch down" from HFOT to LFOT** (flow rate, FiO2 and clinical and/or the analytical criteria to "switch down" from HFOT to LFOT)
  - **9.g) "Switch up" from HFOT to NIPPV or mechanical ventilation** (clinical and/or the analytical criteria to "switch up" from HFOT to NIPPV or mechanical ventilation)

These subitems intended to assess in detail the main components of oxygen therapy delivered by high flow systems.

The general items from 1.) to 12.) were classified as complete, incomplete or absent.

For subitems within items 3.), 4.), 8.) and 9.), the extracted data corresponding to each subitem was analyzed and scored as complete, incomplete or absent. If all the subitems of an item were reported as "complete", then the general item was considered: complete. If some but not all the subitems of an item were reported as "complete", then the general item was considered: incomplete. If all the subitems of an item were absent, then the general item was considered: absent.

The process of scoring each subitem and item as complete, incomplete or absent was performed by one author (MD) and then checked by a second author (RF). Disagreements were resolved through discussion.

Outcomes

The outcomes of this review were:

1) A description of HFOT interventions in included studies, according to an adapted version of the TIDieR checklist for HFOT;

2) The completeness and quality of the reporting of HFOT interventions in the selected studies.

We assessed:

1. The proportion of studies with complete reporting of each of the twelve TIDieR items, after consulting the primary papers, available study protocols and references with readily available details about the interventions;
2. The proportion of studies that correctly reported all the items 3.) to 9.), which were considered core items for study replicability;
3. The proportion of studies with complete reporting of each of the subitems of items 3.), 4.), 8.) and 9.);
4. The TIDieR items more often absent or incompletely described in the reporting of HFOT interventions;
5. The TIDieR items more often completely described in the reporting of HFOT interventions.

Risk of bias

Because we did not consider research of clinical outcomes, but rather the descriptive features of HFOT interventions and the completeness of their reporting, we did not assess the risk of bias of individual studies or outcomes included in this review.

Data synthesis

We performed a descriptive synthesis of all included studies (Table 1) followed by a quantitative analysis of the review's outcomes, using descriptive statistics methods.

Results were presented graphically to summarize the completeness of interventions description, as the proportion of studies with "complete", "incomplete" and "absent" description of each item and subitem.

Results

Figure 1 presents our study flow chart, based on the PRISMA flow diagram (22). A full list of included studies is shown in the Appendix 2.

Description of included studies

Table 1 presents a detailed description of the characteristics of included studies. There were 48 studies (8139 participants) included in our study analysis. Among these studies there were 11 RCTs (23%) and 37 observational studies (77%). There were 19 studies (40%) reporting the use of HFOT exclusively in patients with bronchiolitis. The remaining 29 studies (60%) reported the use of HFOT in patients with medical conditions different from bronchiolitis or in populations with multiple medical conditions including bronchiolitis and other diseases. A HFOT intervention was performed in all studies included in this review, either in the active intervention or in the comparator group. Among the included RCTs, HFOT was compared to another respiratory support therapy such as low-flow oxygen therapy (LFOT) using a nasal prong or another low-flow device in 5 studies (45%), to another high-flow device such as CPAP and Bi-level in 4 studies (36%) and to nebulized aerosol therapy in 2 studies (19%). Studies were restricted to the pediatric ICU in 30 studies (63%), to the emergency department in 9 studies (19%) and to the pediatric ward in 2 studies (4%). In the remaining 7 studies (14%), HFOT was used in more than one of these settings.

Description of the reporting of TIDieR items across included studies

Table 1 presents the completeness of reporting of general TIDieR items 3 to 9 (core items) across included studies. There were only 6 studies (12.5%) correctly reporting more than

50% of these items and no studies correctly reported all these items. There were 7 studies (14.5%) incorrectly reporting all items 3.) to 9.).

On Figure 2 we present the proportion of studies with complete, incomplete and absent reporting of all 12 items of our adapted version of the TIDieR checklist. The items more consistently and correctly reported were items 1.) *Brief name* in 96% and 2.) *Rationale* in 77% of the studies. If we consider exclusively the core items 3.) to 9.), the only item being correctly reported in at least 50 % of the times was item 7.) *Where* (in 67% of the studies). The remaining items 3.), 4.), 5.), 6.), 8.) and 9.) were correctly reported in proportions ranging from 8 % for Item 9: *Tailoring* and 29 % for Item 3: *Materials*.

Figures 3, 4, 5 and 6 represent results on the reporting of items 3.) *What Materials*, 4.) *What Procedures*, 8.) *When and how much* and 9.) *Tailoring*, respectively, with their subitems.

For item 3.) *Materials*, the subitem more often absent or incorrectly reported was the subitem 3.e) *Cannula/ Interface* in 60% of the studies. For item 3.) the subitem more often correctly reported was 3.a) *Brand* in 90 % of the studies (figure 3).

For item 4.) *What Procedures*, poorly described subitems were 4.d) *Co-interventions* and 4.e) *Feeding*. These subitems were absent or incorrectly reported in 69 % and 67 % of the studies, respectively. The most often correctly reported subitems were 4.a) *Baseline assessment* and 4.b) *Assessment along the intervention*. These subitems were correctly reported in 98% and 88% of the studies, respectively (figure 4).

For item 8.) *When and how much*, there were only 2 subitems reported correctly more than 50% of the times, 8.a) *When did the intervention start?* and 8.c) *Initial and targeted Flow*, in 77% and 67% of the studies, respectively. The subitems more often absent or incorrectly reported were the subitems 8.d) *Targeted Temperature* and 8.e) *Co-interventions (Schedule/Doses)* both absent or incorrectly reported in 73% of the studies (figure 5).

Finally, for item 9.) *Tailoring*, the most correctly described subitem was 9.b) *Flow titration*, in 65% of the studies. The most frequently absent or incorrectly reported subitems were 9.a) *FiO2 titration*, 9.c) *Criteria for weaning* and 9.d) *Timing for Weaning* which were absent or incomplete in 73%, 75% and 77% of the studies, respectively (figure 6).

The assessment of the reporting of all items and subitems for each included study is summarized using a color code on Table 2.

Discussion

In a systematic review focused on the reporting of HFOT interventions in trials and observational studies in pediatric acute respiratory conditions, we found that many HFOT intervention components were reported incorrectly or not reported at all. We used a validated framework to evaluate the completeness of reporting of interventions (TIDieR), and we focused on the proportion of studies that correctly reported a set of core items from an adapted TIDieR checklist (3.) to 9.). While there is no cut-off value to clearly establish the quality of the reporting of an intervention, adequate reporting of most of these items was inferior to 30% across included studies and no studies correctly reported all these seven items. This highlights that there is poor and inadequate reporting of HFOT interventions in pediatric studies.

The need for complete and adequate reporting of interventions is a core issue in medical research, with a fundamental role in the processes of reproduction, aggregation and implementation of clinical results as well as in the ethics of research development (1). Our results are consistent with results from previous studies assessing the quality of reporting of interventions in both adult (23–25) and pediatric populations (26), which was consistently poor. This can have a considerable impact in the production of evidence and its subsequent use in the elaboration of clinical guidelines and implementation in clinical practice. Inadequate reporting of interventions represents a flaw in the origin of this translational chain, which can compromise the use of evidence and the quality of future medical care.

In recent years several checklists and guidelines were developed in order to improve the quality of reporting of interventions across a range of study reports. These included the Consolidated Standards of Reporting Trials 2010 statement (CONSORT 2010) (27), Standard Protocol Items: Recommendations for Interventional Trials 2013 (SPIRIT 2013) (28) and more recently the Template for Interventions Description and Replication checklist (TIDieR) (1). Before the development of the TIDieR checklist, there was evidence that low quality of reporting of interventions was related, on the one hand, to

the lack of awareness of researchers to the core elements of an intervention that need to be reported and, on the other hand, to the fact that lack of reporting was not identified by peer reviewers and editors or was only detected and fixed after publication (1,25). Almost one decade after the publication of TIDieR, the poor quality of reporting shown in our study as well as results from others (23–26) demonstrates that the problem of poor reporting remains topical. This may relate to publication-related limitations, such as unawareness or lack of implementation by editors and peer reviewers (25) or restrictions in word counts (15,29).

Furthermore, the properties and the complexity of certain interventions may require detailed reporting of specific components. This is not straightforward, as it can entail adaptation within the TIDieR framework and could explain the poor reporting results obtained in our systematic review. On the one hand, medical devices used to provide HFOT have multiple technological interacting components and different settings that must be tailored throughout the intervention. Therefore, it becomes harder to correctly report all the components of this type of intervention when compared to less complex interventions. On the other hand, the TIDieR checklist provides authors with general guidelines and practical examples of reporting per item, trying to be as comprehensive as possible. However, for practical reasons, it is not extensive enough to cover all the components within each item for all existing interventions (1). In our systematic review, we tried to adapt the TIDieR checklist to assess the reporting of this specific intervention, developing subitems within the 12 general items that we considered to be core elements of HFOT to be reported. Although this was performed in the context of a methodological systematic review, we reckon that using this approach could be an important step when designing, performing and reporting studies with HFOT interventions.

Study limitations:

The two main limitations of our study are related to the search strategy and to our adapted version of the TIDieR checklist.

We followed a systematic search methodology with MeSH and free-text terms, not restricted to English language, with no time restrictions up to the 31st July of 2019, in MEDLINE, the largest existing medical database. However, our research was limited to only one database and it was not extended to another important databases such as

EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL) which could have affected our sample size.

As mentioned by the TIDieR checklist authors, this reporting tool might not be able to capture the full complexity of some interventions (1), as we thought might be the case of HFOT interventions. Thus, we needed to adapt this checklist adding some subitems to the main items. This adaptation was made by the review authors, without consultation of a larger panel of experts. Therefore, we might have been too strict or too flexible when we defined which core elements should be described to correctly report HFOT interventions., which might have influenced our results.

Implications of poor reporting of HFOT interventions for the future:

Poor reporting of HFOT interventions has a negative impact in the replicability of these interventions by different researchers, in the elaboration of methodologically correct systematic reviews and also in the translation of these interventions into the clinical practice, ultimately leading to a suboptimal care of children with bronchiolitis, pneumonia or in acute respiratory failure. The correct reporting of HFOT interventions is particularly important because this type of intervention has been the focus of recent research, eg of all studies included in our review 25 studies (52%) published between 2017 and 2019. However, there is not yet a clear and strong evidence about its benefit when compared to other techniques of non-invasive ventilation (30). Therefore, new studies that will be assessing this intervention should provide a more detailed and correct reporting of interventions, so that their results can be compared and aggregated, to produce better quality evidence.

In order to achieve better reporting of interventions in this field, we encourage researchers, peer reviewers and editors to take a major role in this process, guided by the validated TIDieR framework. This important methodological tool provides them with valuable and objective guidelines to correctly report interventions. Researchers could use these guidelines when designing their protocols and reporting their intervention details. The peer-reviewing process could focus on assessing the quality of this reporting by using the TIDieR checklist (1). Editors guidelines should require the correct reporting of interventions for publication, providing authors and peer-reviewers with more detailed instructions on the reporting of interventions (31). Despite restrictions on manuscript length, journals could also encourage authors to improve reporting quality by allowing

the publication of supplementary materials indexed to the primary paper or referring to readily accessible resources such as protocols with more detailed information about the methods and procedures.

We reckon that our recommendations are not limited to clinical research in HFOT, but instead can be applied to studies assessing other types of respiratory support interventions. We consider that for complex non-HFOT interventions, for which intervention protocols are not yet standardized, it would be useful to foster debate between experts which specific components of that intervention should be reported. This could lead to a list of essential TIDieR items and subitems to be reported when designing the study protocol and when describing the intervention in an original paper. We encourage researchers, peer reviewers and editors to engage in this coordinated effort to improve reporting of interventions, following TIDieR guidelines. This effort will probably lead to an increase in the quality of clinical evidence produced. It will ultimately lead to improved medical care not only of children in acute respiratory failure but also throughout other areas of research, known to have poor reporting of interventions.

Conclusions:

The reporting of HFOT interventions in children with acute respiratory diseases is generally poor. Across experimental and observational studies, the least correctly reported component of this intervention is the item on Tailoring, found in less than one in ten published studies. The poor reporting of HFOT interventions is a factor compromising the quality of evidence obtained from published studies. Because HFOT is an area of current research, we consider that an effort to improve the reporting of this intervention in future studies may result in stronger and better-quality evidence in this field. The use of the TIDieR checklist and guidance, besides providing guidelines for researchers to report their interventions, was a useful tool in assessing the quality of the reporting. There is a major role to be played by peer-reviewers and editors before study publication which may lead to better reporting of HFOT interventions and ultimately to the optimization of care in children with acute respiratory diseases.

Contribution of authors:

RM is the guarantor. RM and MD contributed to the conception and design of the study and developed the search strategy. SH provided support with the design and implementation of the search strategy. RM and MD contributed to the processes of the analysis and interpretation. RM and MD provided a critical revision and RM provided the final approval of the version to be published.

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Reference list:

1. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: Template for intervention description and replication (TIDieR) checklist and guide. BMJ. 2014;348(March):1–12.

2. Baudin F, Pouyau R. High-flow nasal cannula in the pediatric ICU: Popular or efficient? Respir Care. 2018;62(8):1116–7.

3. Miller AG, Gentle MA, Tyler LM, Napolitano N. High-flow nasal cannula in pediatric patients: A survey of clinical practice. Respir Care. 2018;63(7):894–9.

4. Franklin D, Babl FE, Schlapbach LJ, Oakley E, Craig S, Neutze J, et al. A randomized trial of high-flow oxygen therapy in infants with bronchiolitis. N Engl J Med. 2018;378(12):1121–31.

5. Hernández G, Vaquero C, González P, Subira C, Frutos-Vivar F, Rialp G, et al. Effect of postextubation high-flow nasal cannula vs conventional oxygen therapy on reintubation in low-risk patients: A randomized clinical trial. JAMA - J Am Med Assoc. 2016;315(13):1354–61.

6. Sinha IP, McBride AKS, Smith R, Fernandes RM. CPAP and high-flow nasal cannula oxygen in bronchiolitis. Chest. 2015;148(3):810–23.

7. Society AP. JAMA Network | JAMA Pediatrics | Lessons From Drugs to Devices: A Pediatric Perspective. 2015;169(11):10–1. Available from: http://archpedi.jamanetwork.com/article.aspx?articleid=2436540

8. Samuels-Reid JH, Cope JU. Medical devices and adolescents: Points to consider. JAMA Pediatr. 2016;170(11):1035–6.

9. Field M, Tilson H. Safe Medical Devices for Children [Internet]. Safe Medical Devices for Children. Washington, DC: The National Academies Press.; 2005. Available from: https://doi.org/10.17226/11313.

10. AAP brings need for pediatric medical devices to forefront [Internet]. 2018. Available from: https://www.aappublications.org/news/2018/08/17/fdadevices081718?utm_source=TrendMD&utm_medium=TrendMD&utm_campaign=AAPNews_TrendMD_0

11. Jenkins KJ, Beekman RH, Vitale MG, Hennrikus WL. Off-label use of medical devices in children. Pediatrics. 2017;139(1).

12. Shein SL, Slain KN, Rotta AT. High Flow Nasal Cannula Flow Rates: New Data Worth the Weight. J Pediatr [Internet]. 2017;189(October):9–10. Available from: https://doi.org/10.1016/j.jpeds.2017.06.077

13. Mikalsen IB, Davis P, Øymar K. High flow nasal cannula in children: A literature review. Scand

J Trauma Resusc Emerg Med [Internet]. 2016;24(1). Available from: http://dx.doi.org/10.1186/s13049-016-0278-4

14. Panciatici M, Fabre C, Tardieu S, Sauvaget E, Dequin M, Stremler-Le Bel N, et al. Use of high-flow nasal cannula in infants with viral bronchiolitis outside pediatric intensive care units. Eur J Pediatr. 2019;178(10):1479–84.

15. Abell B, Glasziou P, Hoffmann T. Reporting and Replicating Trials of Exercise-Based Cardiac Rehabilitation: Do We Know What the Researchers Actually Did? Circ Cardiovasc Qual Outcomes. 2015;8(2):187–94.

16. Bartholdy C, Nielsen SM, Warming S, Hunter DJ, Christensen R, Henriksen M. Poor replicability of recommended exercise interventions for knee osteoarthritis: a descriptive analysis of evidence informing current guidelines and recommendations. Osteoarthr Cartil [Internet]. 2019;27(1):3–22. Available from: https://doi.org/10.1016/j.joca.2018.06.018

17. Tew GA, Brabyn S, Cook L, Peckham E. The completeness of intervention descriptions in randomised trials of supervised exercise training in peripheral arterial disease. PLoS One. 2016;11(3).

18. Hoffmann TC, Walker MF, Langhorne P, Eames S, Thomas E, Glasziou P. What's in a name? The challenge of describing interventions in systematic reviews: Analysis of a random sample of reviews of non-pharmacological stroke interventions. BMJ Open. 2015;5(11).

19. Moher D, Liberati A, Tetzlaff J, Altman DG. PRISMA 2009 Checklist. Vol. 151, Annals of Internal Medicine. 2014. p. 264–9.

20. Cunningham S, Fernandes RM. High-flow oxygen therapy in acute bronchiolitis. Lancet [Internet]. 2017;389(10072):886–7. Available from: http://dx.doi.org/10.1016/S0140-6736(17)30192-7

21. A Ritesh and G Dheeraj. What Are High-Flow and Low-Flow Oxygen Delivery Systems? Stroke 2005;2066–7.

22. Moher D, Liberati A, Tetzlaff J et al. PRISMA 2009 Flow Diagram. Vol. 6, The PRISMA statement. 2009. p. 1000097.

23. Duff JM, Leather H, Walden EO, Laplant KD, George TJ. Adequacy of published oncology randomized controlled trials to provide therapeutic details needed for clinical application. J Natl Cancer Inst. 2010;102(10):702–5.

24. Hoffmann TC, Erueti C, Glasziou PP. Poor description of non-pharmacological interventions: Analysis of consecutive sample of randomised trials. BMJ [Internet]. 2013;347(7924):1–10. Available from: http://dx.doi.org/doi:10.1136/bmj.f3755

25. Schroter S, Glasziou P, Heneghan C. Quality of descriptions of treatments: A review of published randomised controlled trials. BMJ Open. 2012;2(6):1–7.

26. Yu AM, Balasubramanaiam B, Offringa M, Kelly LE. Reporting of interventions and "standard of care" control arms in pediatric clinical trials: a quantitative analysis. Pediatr Res [Internet]. 2018;84(3):393–8. Available from: http://dx.doi.org/10.1038/s41390-018-0019-7

27. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: Updated guidelines for reporting parallel group randomised trials. Int J Surg. 2011;9(8):672–7.

28. Chan A, Tetzlaff JM, Altman DG, Laupacis A, Gotzsche P, Krleža-Jerić K, et al. Declaración SPIRIT 2013: definición de los elementos estándares del protocolo de un ensayo clínico [SPIRIT 2013 Statement: defining standard protocol items for clinical trials]. Rev Panam Salud Publica. 2015;38(6):506–14.

29. Conn VS, Cooper PS, Ruppar TM, Russell CL. Searching for the intervention in intervention research reports. J Nurs Scholarsh. 2008;40(1):52–9.

30. Ramnarayan P, Schibler A. Glass half empty or half full? The story of high-flow nasal cannula therapy in critically ill children. Intensive Care Med. 2017;43(2):246–9.

31. Hoffmann T, English T, Glasziou P. Reporting of interventions in randomised trials: An audit of journal Instructions to Authors. Trials. 2014;15(1):1–6.

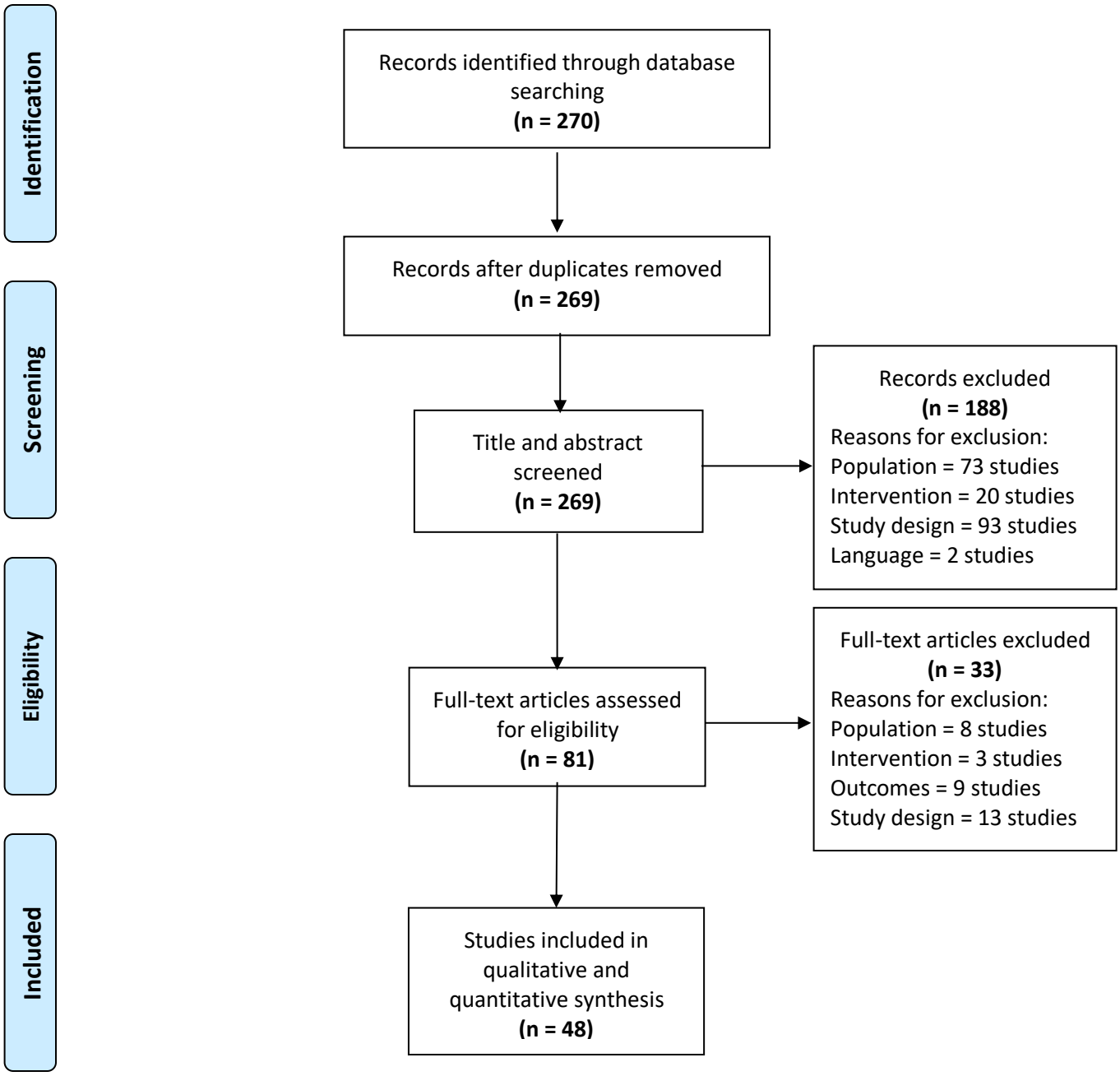

Figure 1: Study flow chart according to PRISMA flow diagram (22)

Table 1: Details and completeness of reporting of included studies.

Author, Year	Journal	Study design	Population	Intervention	Comparator	Setting	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Nº of items 3-9 correctly reported (%)
Hansen *et al.* (2019)	Pediatr Int.	Retrospective chart review	< 17 Y with acute respiratory distress (N=18)	HFNC oxygen therapy	Patients who did not require HFNC support	Pediatric ward + PICU	A	I	I	I	C	I	I	1 (14%)
Akyıldız *et al.* (2018)	Turk J Pediatr.	Single-centre RCT	1 M to 17 Y post-extubation (N=100)	HFNC oxygen therapy	LFOT delivered by a nasal prong or a simple face mask	PICU	I	I	I	I	I	I	I	0 (0%)
Dohna-Schwake *et al.* (2018)	Klin Padiatr.	Retrospective chart review	< 1 Y with acute viral bronchiolitis (N=146)	HFNC oxygen therapy, CPAP BiPAP or MV	NA	PICU	A	I	I	I	I	I	A	0 (0%)
Ergul *et al.* (2018)	Eur J Pediatr.	Single-center RCT	1 M to 24 M with moderate to severe acute viral bronchiolitis. (N=60)	HFNC oxygen therapy	Oxygen therapy from OxyMask® (Southmedic, Inc.)	PICU	C	I	I	A	C	I	I	2 (29%)
Ramnarayan *et al.* (2018)	Crit Care.	Multi-center RCT	> 36 WOG and < 16 Y with acute respiratory distress or post-extubation. (N=121)	HFNC oxygen therapy ("Step-up" and "Step down" support)	CPAP ("Step-up" and "Step down" support)	PICU + HDU	I	I	I	I	I	I	I	0 (0%)
Valencia-Ramos *et al.* (2018)	Respir Care.	Multi-center cross-over RCT	≤ 24 M with diagnosis of acute bronchiolitis (N=6)	HFNC oxygen therapy + aerosol therapy (integrated nebulization device)	Nebulized aerosol therapy	PICU	C	I	C	I	C	I	I	3 (43%)
Franklin *et al.* (2018)	N Engl J Med.	Multi-center RCT	> 36 WOG and < 12 M with acute viral bronchiolitis (N=1638)	HFNC oxygen therapy	Standard LFNC oxygen therapy	Emergency department + pediatric ward	I	I	C	I	C	I	I	2 (29%)
Guillot *et al.* (2018)	Arch Pediatr.	Prospective observational study	< 24 M with a diagnosis of severe acute viral bronchiolitis (N=61)	HFNC oxygen therapy	Nasal CPAP or Bi-level oxygen therapy	PICU	I	I	I	A	C	I	I	1 (14%)
Er *et al.* (2018)	Pediatr Pulmonol.	Retrospective, cohort study	Children with moderate/severe respiratory distress (N=154)	HFNC oxygen therapy	NA	Emergency department	I	I	I	C	C	I	I	2 (29%)
Ballestero *et al.* (2018)	J Pediatr.	Single-center Nonblinded RCT	1 Y to 14 Y with acute asthma exacerbation (N=62)	HFNC oxygen therapy	LFOT using a nasal prong, Venturi mask or non-rebreather mask	Emergency department	C	I	C	I	C	I	I	3 (43%)

Author, Year	Journal	Study design	Population	Intervention	Comparator	Setting	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Nº of items 3-9 correctly reported (%)
Can *et al* (2018)	J Crit Care.	Prospective observational study	1 M to 18 Y treated with HFNC as 1st RS post-extubation in patients with ARD/ARF (N=204)	HFNC oxygen therapy	NA	PICU	C	C	I	I	C	C	C	5 (71%)
Can *et al* (2017)	Indian Pediatr.	Retrospective chart review	1 M to 18 Y with ARD/ ARF (N=272)	HFNC oxygen therapy	LFOT using a nasal cannula, hood, simple face mask or non-rebreather mask.	PICU	C	I	I	A	C	I	I	2 (29%)
Coletti *et al.* (2017)	Respir Care.	Retrospective cohort study	Children requiring HFNC therapy during their PICU admission (N=620)	HFNC oxygen therapy	NA	PICU	I	I	A	A	C	I	A	1 (14%)
Goh *et al.* (2017)	J Paediatr Child Health.	Retrospective cohort study	<24 M with acute viral bronchiolitis. (N=166)	HFNC oxygen therapy	RS before HFNC oxygen therapy introduction	Outside the PICU + inside PICU	I	I	C	C	I	I	I	2 (29%)
Vitaliti *et al.* (2017)	Respir Care	Multi-center RCT	1 M to 24 M in ARF (N=60)	HFNC oxygen therapy	Helmet CPAP	Emergency unit + Intermediate Care Unit	I	I	I	I	C	I	I	1 (14%)
Betters *et al.* (2017)	Pediatr Crit Care Med.	Retrospective cohort study	Children treated with HFNC (regardless of age/diagnosis) (N=133)	HFNC oxygen therapy (weaning protocol)	NA	PICU	I	I	C	I	C	I	I	2 (29%)
Sochet *et al.* (2017)	Hosp Pediatr.	Prospective, cohort study	1 M to 2 Y with a diagnosis of acute viral bronchiolitis. (N=132)	HFNC oxygen therapy + concurrent enteral nutrition	NA	PICU	I	I	I	I	C	I	A	1 (14%)
Slain *et al.* (2017)	Hosp Pediatr.	Retrospective chart review	<24 M with a diagnosis of acute viral bronchiolitis (N=70)	HFNC oxygen therapy + concurrent enteral nutrition	NA	PICU	I	I	I	C	C	I	A	2 (29%)
Davison *et al.* (2017)	Emerg Med Australas.	Retrospective cohort study	1 M to 23 M with acute viral bronchiolitis. (N=61)	HFNC oxygen therapy	NA	Emergency department + pediatric ward	I	I	I	C	C	I	C	3 (43%)
Pilar *et al.* (2017)	Med Intensiva.	Retrospective cohort study	18 M to 14 Y with acute asthma exacerbation. (N=42)	HFNC oxygen therapy	NIV (bi-level or CPAP)	PICU	C	I	I	I	C	I	I	2 (29%)
Kepreotes *et al.* (2017)	Lancet.	Single center, phase 4, RCT	< 24 M with a clinical diagnosis of acute viral bronchiolitis (N=202)	HFNC oxygen therapy	Standard LFNC oxygen therapy	Emergency department	I	I	C	C	C	I	C	4 (57%)

Author, Year	Journal	Study design	Population	Intervention	Comparator	Setting	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Nº of items 3-9 correctly reported (%)
Milési *et al* (2017)	Intensive Care Med.	Multi-center, Cross-over RCT	< 6 M with acute viral bronchiolitis + moderate to severe respiratory distress. (N=142)	HFNC oxygen therapy then switched to nCPAP	nCPAP then switched to HFNC oxygen therapy	PICU	I	I	C	I	C	I	I	2 (29%)
Guimaraes *et al.* (2017)	Arch Pediatr.	Retrospective observational study	< 6 M with a diagnosis of acute viral bronchiolitis (N=89)	HFNC oxygen therapy	Standard LFNC oxygen therapy	Emergency department	C	I	C	I	I	I	I	2 (29%)
Betters *et al.* (2017)	Pediatr Pulmonol.	Retrospective chart review	Children who received HFNC for an acute respiratory or non-respiratory illness. (N=231)	HFNC oxygen therapy	NA	Outside the PICU ("on the floor")	I	I	I	C	C	I	I	2 (29%)
Baudin F *et al.* (2016)	Respir Care.	Retrospective observational study	< 18 Y admitted to the PICU and treated with HFNC. (N=145)	HFNC oxygen therapy	NA	PICU	I	I	I	A	C	I	I	1 (14%)
Milani *et al.* (2016)	Acta Paediatr.	Prospective observational study	>34 WOG and <12 M with moderate to severe acute viral bronchiolitis. (N=40)	HFNC oxygen therapy	Standard LFNC oxygen therapy	Emergency department	I	C	I	I	I	I	I	1 (14%)
Bermúdez *et al.* (2017)	An Pediatr. (Barc)	Ambispective cohort study	< 28 days of age with acute viral bronchiolitis. (N=112)	HFNC oxygen therapy	Standard LFNC oxygen therapy and/or NIV	NICU	I	C	A	A	I	I	I	1 (14%)
Long *et al.* (2016)	Emerg Med J.	Prospective observational study	Hypoxemic children (SatO2< 90%) despite LFOT (N=71)	HFNC oxygen therapy	NA	Emergency department	C	C	C	C	I	C	I	5 (71%)
Oto *et al.* (2016)	Turk J Pediatr.	Prospective observational study	1 M to 17 Y with hypoxemic respiratory failure (PaO2 < 55 mmHg in RA) (N=50)	HFNC oxygen therapy	NA	PICU	I	I	A	A	I	I	I	0 (0%)
Riese *et al.* (2015)	Hosp Pediatr	Observational pre-post intervention	< 24 M with URI, bronchiolitis, apnea, or unspecified viral illness. (ICD) (N=290)	HFNC oxygen therapy	HFNC initiated in different setting	PICU	A	I	A	A	C	I	I	1 (14%)
Wegner *et al.* (2015)	Rev Chil Pediatr.	Descriptive, prospective study.	Children with signs of respiratory distress requiring RS (regardless the age/ diagnosis). (N=109)	HFNC oxygen therapy	NA	PICU	C	I	I	C	I	I	I	2 (29%)

Author, Year	Journal	Study design	Population	Intervention	Comparator	Setting	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Nº of items 3-9 correctly reported (%)
Chisti *et al.* (2015)	Lancet.	Single-center RCT	<5 Y with a diagnosis of severe pneumonia and hypoxemia in RA. (N=255)	Bubble CPAP	HFNC or standard LFNC oxygen therapy	PICU	I	C	I	I	I	C	I	2 (29%)
Wraight *et al.* (2015)	Crit Care Resusc.	Descriptive, retrospective study.	Children < 20kg treated with HFNC therapy (regardless the diagnosis) (N=54)	HFNC oxygen therapy	NA	PICU	I	I	I	I	C	I	I	1 (14%)
Morgan *et al.* (2015)	Respir Care.	Case series	Infants with moderate to severe respiratory distress (N=5)	LFOT + aerosol (face mask + jet nebulizer) followed by HFNC + aerosol.	NA	Emergency department	I	I	A	A	C	C	I	2 (29%)
Mayfield *et al.* (2014)	J Paediatr Child Health	Prospective observational study.	Age <12 M with bronchiolitis + SpO2 < 94% in RA. (N=94)	HFNC oxygen therapy	Standard LFNC oxygen therapy	Emergency department	I	I	C	I	I	I	I	1 (14%)
Metge *et al.* (2014)	Eur J Pediatr.	Descriptive, retrospective study.	Infants with acute viral bronchiolitis. (N=34)	HFNC oxygen therapy	Nasal CPAP	PICU	C	C	I	I	C	I	I	3 (43%)
Bueno-Campaña *et al.* (2014)	Arch Dis Child.	Multi-center RCT	≤ 6 M with moderate acute viral bronchiolitis (N=74)	HFNC oxygen + nebulised epinephrine 1/1000 + 2 mL of NS (0.9%).	Nebulised epinephrine 1/1000 plus 2 mL of HS (3%)	Paediatric ward	C	I	I	C	C	I	I	3 (43%)
Kelly *et al.* (2013)	Pediatr Emerg Care.	Retrospective cohort study	≤24 M in respiratory distress who received HFNC (N=498)	HFNC oxygen therapy	NA	Emergency department	I	I	I	A	C	I	I	1 (14%)
Bressan *et al.* (2013)	Eur J Pediatr.	Prospective observational study	7 days to 12 M hospitalized for the 1st episode of moderate to severe acute bronchiolitis (N=27)	HFNC oxygen therapy	NA	Pediatric ward	C	C	C	I	C	C	I	5 (71%)

Author, Year	Journal	Study design	Population	Intervention	Comparator	Setting	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Nº of items 3-9 correctly reported (%)
Mayfield *et al.* (2013)	Aust Crit Care.	Case series	Children with a diagnosis of asthma bronchiolitis or cardiomyopathy. (N=3)	HFNC oxygen therapy	NA	PICU	A	I	A	A	C	I	I	1 (14%)
Brink *et al.* (2013)	Pediatr Crit Care Med.	Retrospective observational study	Children in whom either HFNC or NP-CPAP was started in PICU. (N=109)	HFNC oxygen therapy	Nasopharyngeal - CPAP	PICU	C	I	I	C	C	C	C	5 (71%)
Hegde *et al.* (2013)	Pediatrics	Case series	Children who developed air leaks related to HFNC therapy. (N=3)	HFNC oxygen therapy	NA	PICU	I	I	A	A	I	I	I	0 (0%)
Wing *et al.* (2012)	Pediatr Emerg Care.	Observational pre-post intervention	<18 Y in ARI (= any acute respiratory illness that required PICU admission) (N=848)	HFNC oxygen therapy	HFNC before the new guideline (and treatment before the own HFNC introduction)	PICU	C	I	C	C	C	I	I	4 (57%)
Abboud *et al.* (2012)	Pediatr Crit Care Med.	Retrospective chart review	≤12 M with acute bronchiolitis (N=113)	HFNC oxygen therapy	NA	PICU	I	I	I	A	C	I	I	1 (14%)
Schibler *et al.* (2011)	Intensive Care Med.	Retrospective chart review	<24 M treated with HFNC therapy due to respiratory and non-respiratory illness (N=298)	HFNC oxygen therapy	NA	PICU	I	I	I	I	C	I	I	1 (14%)
McKiernan *et al.* (2010)	J Pediatr.	Retrospective chart review	<24 M with acute bronchiolitis, respiratory distress or respiratory failure (N=115)	HFNC oxygen therapy	Blow-by O2, LFNC, Simple face mask, Non-rebreather mask or Nasal CPAP	PICU	I	C	I	I	I	I	I	1 (14%)
Spentzas *et al.* (2009)	J Intensive Care Med.	Retrospective obsevational study.	<12 Y with respiratory distress and treated with HFNC (N=46)	HFNC oxygen therapy	NA	PICU	I	I	A	A	I	I	I	0 (0%)

Author, Year	Journal	Study design	Population	Intervention	Comparator	Setting	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Nº of items 3-9 correctly reported (%)
Urbano *et al.* (2008)	An Pediatr. (Barc)	Prospective observational study	Children with moderate respiratory distress requiring a high O2 supplementation (N=16)	HFNC oxygen therapy	NA	PICU	I	I	I	A	I	I	I	0 (0%)

C = an item that is correctly reported; I = an item that is only partially/incompletely reported; A = an item that is absent. ARF = Acute respiratory failure; ARD = Acute respiratory distress; CPAP = continuous positive airway pressure; HDU = high dependency unit; HS = Hypertonic Saline; LFNC = Low-flow nasal cannula using a standard nasal prong; LFOT = Low flow oxygen therapy; M = months of age; NS = Normal Saline; NICU = Neonatal intensive care unit; PICU = Pediatric intensive care unit; RA = Room air; RS = Respiratory support; URI = Upper respiratory infection; WOG = weeks of gestation; Y = Years of age.

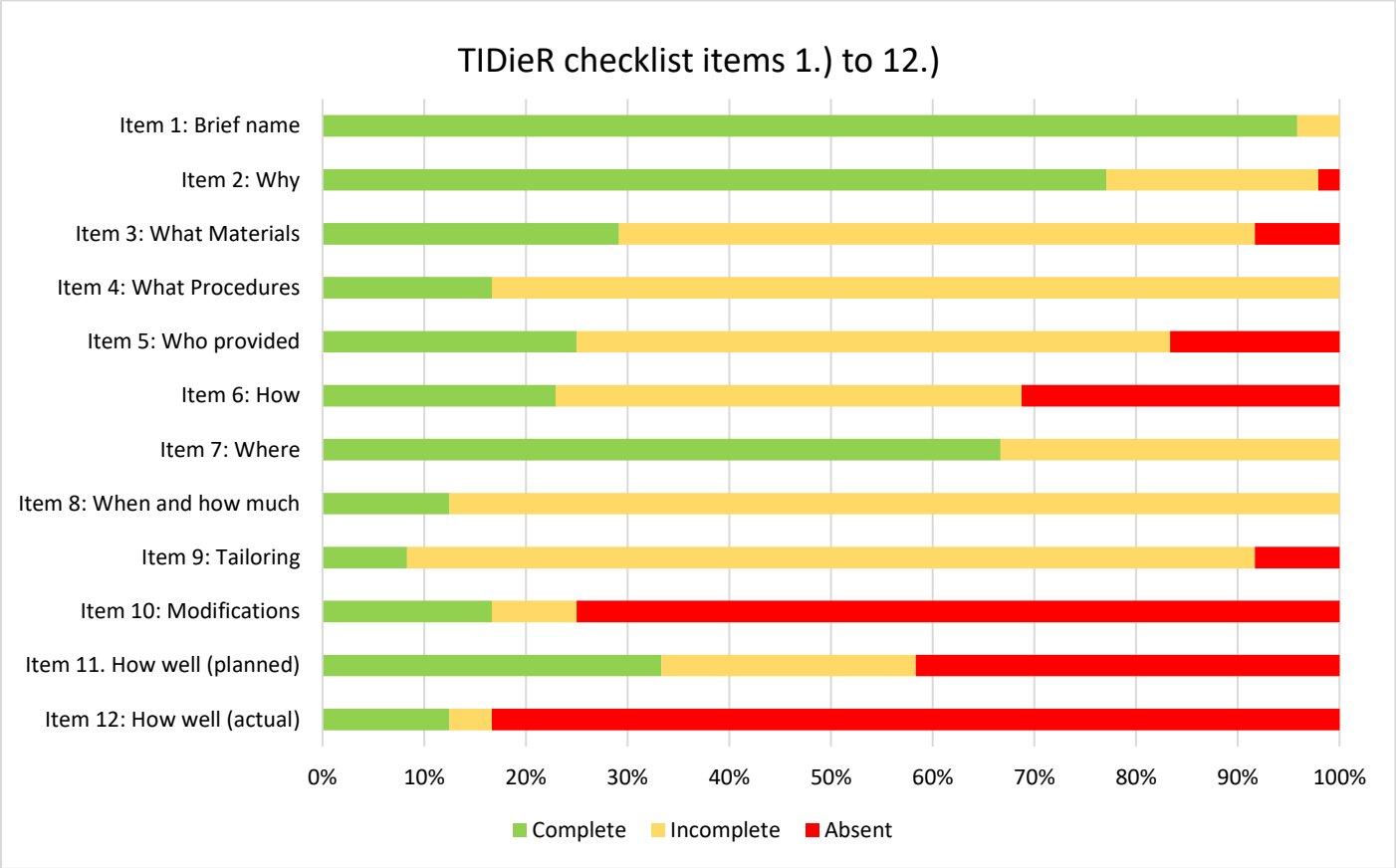

Figure 2: The proportion of studies with complete, incomplete and absent reporting of each of the items 1.) to 12.) of the TIDieR checklist.

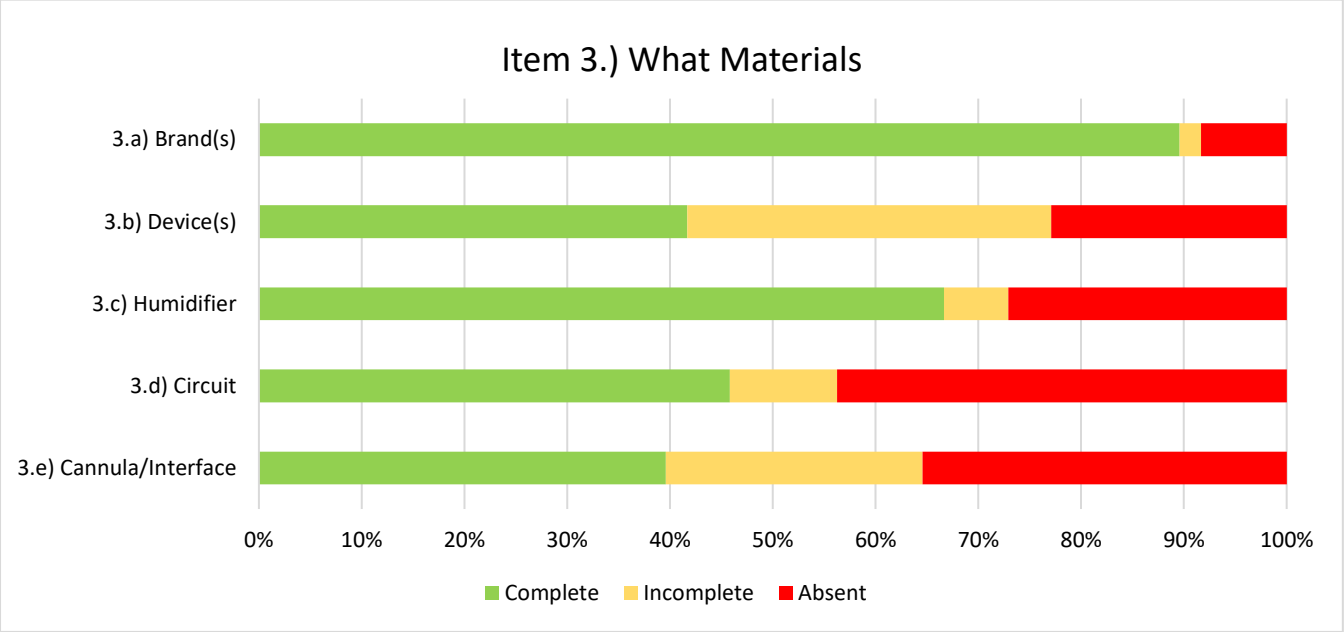

Figure 3: The proportion of studies with complete, incomplete and absent reporting of each of the subitems 3.a) to 3.e) of our model of the TIDieR checklist adapted to HFOT interventions.

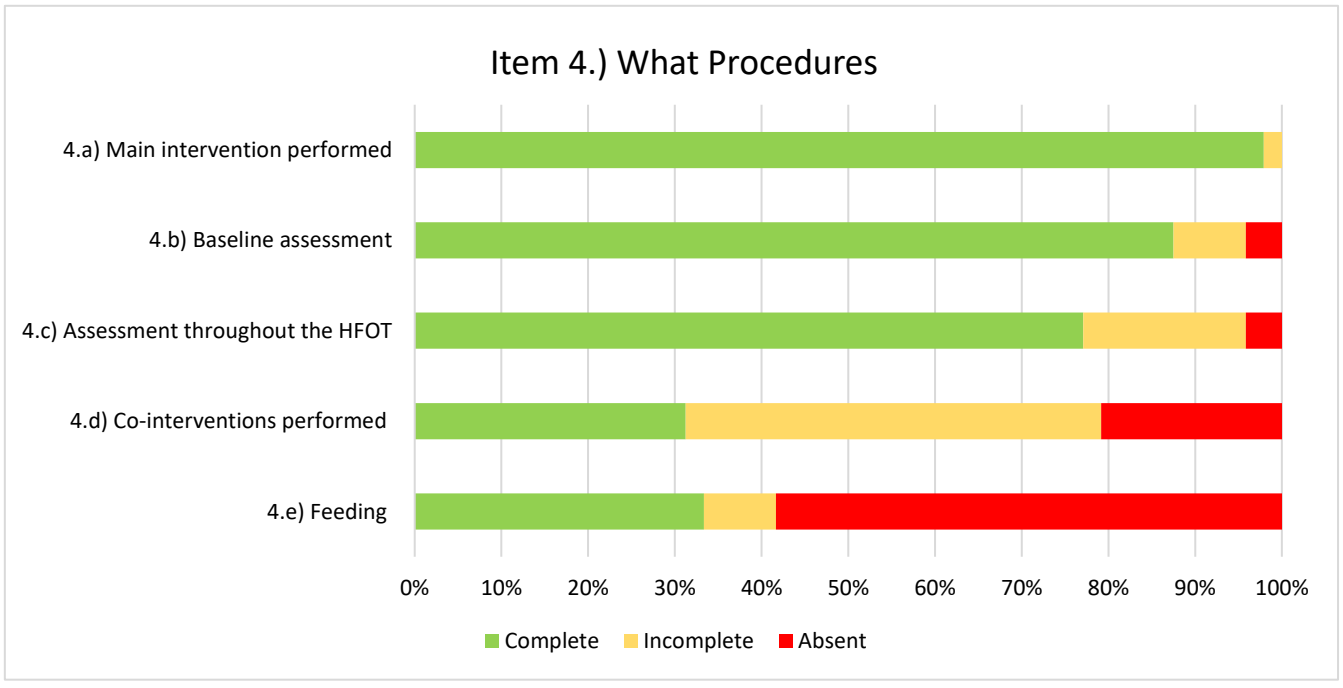

Figure 4: The proportion of studies with complete, incomplete and absent reporting of each of the subitems 4.a) to 4.e) of our model of the TIDieR checklist adapted to HFOT interventions.

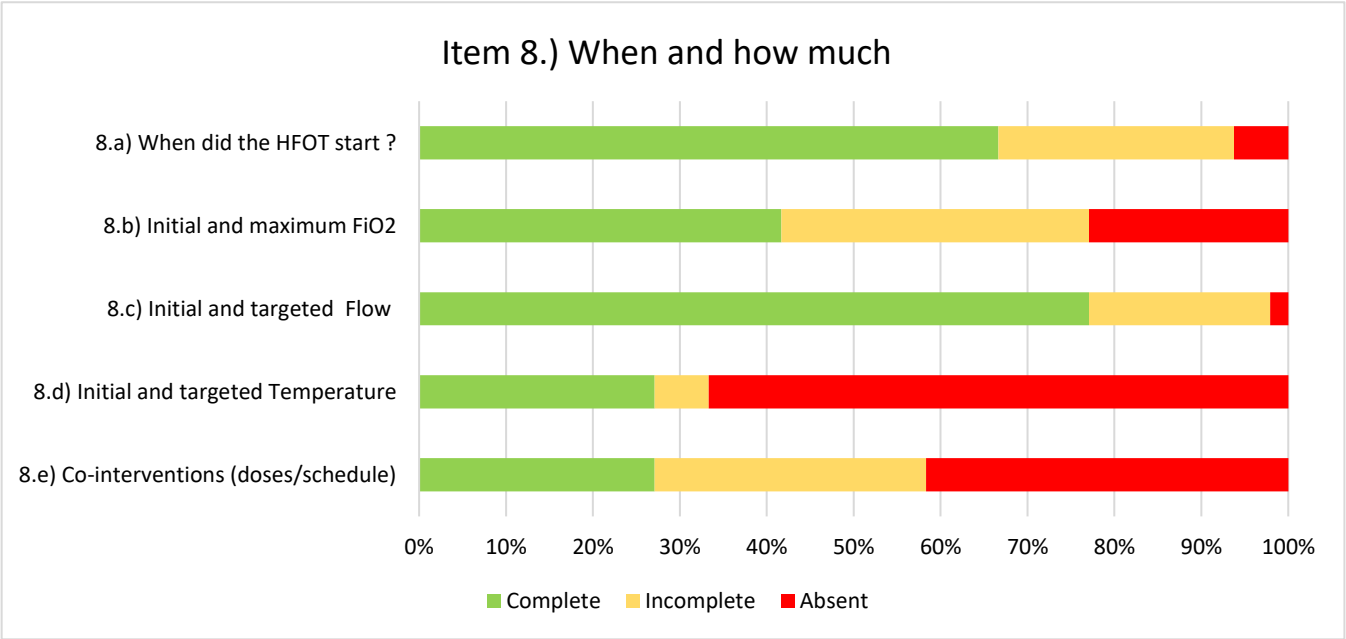

Figure 5: The proportion of studies with complete, incomplete and absent reporting of each of the subitems 8.a) to 8.e) of our model of the TIDieR checklist adapted to HFOT interventions.

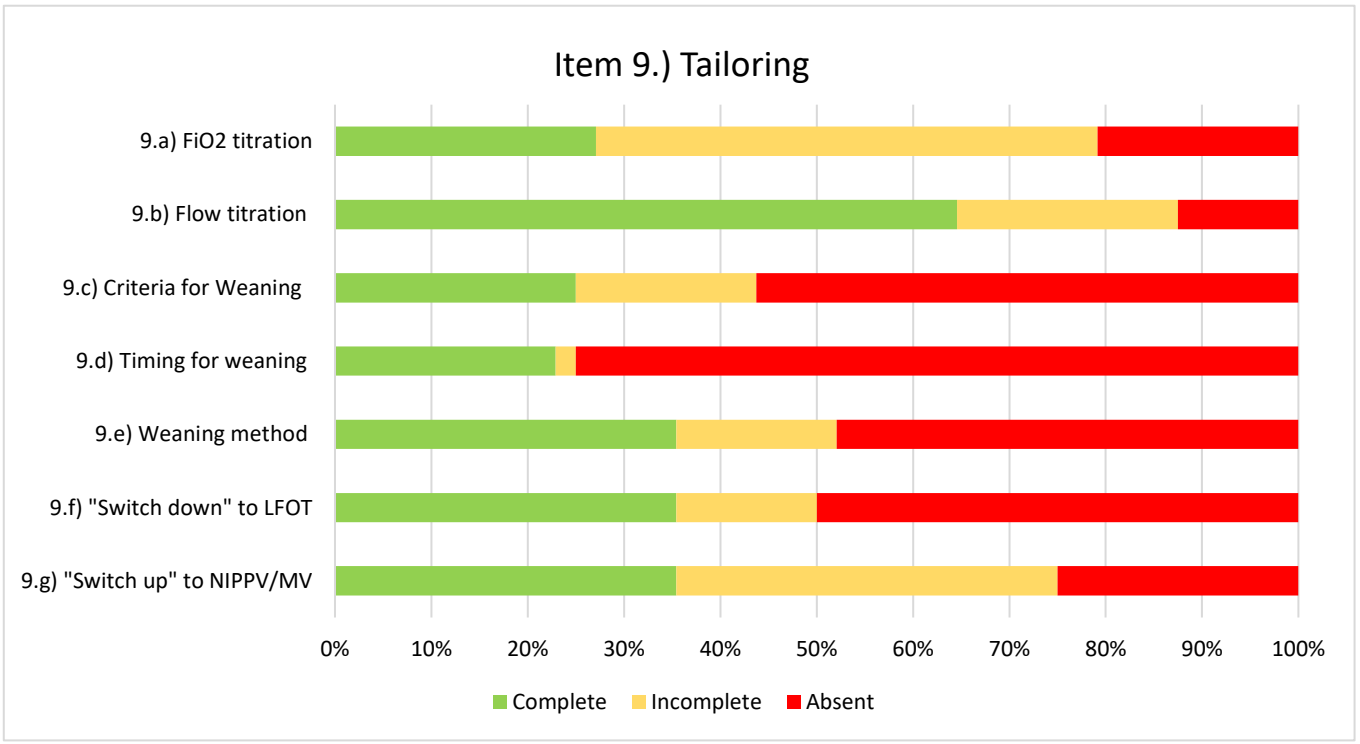

Figure 6: The proportion of studies with complete, incomplete and absent reporting of each of the subitems 9.a) to 9.g) of our model of the TIDieR checklist adapted to HFOT interventions.

Table 2: Scoring of all the items and subitems of our adapted checklist for the reporting of HFOT interventions across included studies.

Article's author and year of publication	Item 1) Brief name	Item 2) Why	Item 3) What (Materials)						Item 4) What (Procedures)						Item 5) Who provided	Item 6) How	Item 7) Where	Item 8) When and how much						Item 9) Tailoring								Item 10) Modifications	Item 11) How well (planned)	Item 12) How well (actual)
	1) General Item	2) General Item	3.a)	3.b)	3.c)	3.d)	3.e)	3) General item	4.a)	4.b)	4.c)	4.d)	4.e)	4) General item	5) General Item	6) General Item	7) General Item	8.a)	8.b)	8.c)	8.d)	8.e)	8) General Item	9.a)	9.b)	9.c)	9.d)	9.e)	9.f)	9.g)	9) General Item	10) General Item	11) General Item	12) General Item
Hansen *et al.* (2019)	C	I	A	A	A	A	A	A	C	C	C	I	A	I	I	I	C	C	C	C	A	A	I	C	C	A	A	A	A	I	I	A	A	A
Akyıldız *et al.* (2018)	C	C	C	I	C	I	I	I	C	C	C	I	A	I	I	I	I	C	I	C	A	I	I	I	C	A	A	A	A	I	I	A	A	A
Dohna-Schwake *et al.* (2018)	I	A	A	A	A	A	A	A	I	C	A	C	C	I	I	I	I	I	I	I	A	I	I	A	A	A	A	A	A	A	A	A	I	A
Ergul *et al.* (2018)	C	C	C	C	C	C	C	C	C	C	C	I	A	I	I	A	C	C	C	C	A	A	I	C	I	A	A	I	I	C	I	A	A	A
Ramnarayan *et al.* (2018)	C	C	I	I	I	I	A	I	C	C	C	I	A	I	I	I	I	C	I	C	A	I	I	I	C	C	A	C	C	C	I	A	C	C
Valencia-Ramos *et al.* (2018)	C	I	C	C	C	C	C	C	C	A	C	C	C	I	C	I	C	C	C	A	A	A	I	C	A	A	A	A	A	A	I	A	C	A
Franklin *et al.* (2018)	C	C	C	I	C	A	I	I	C	C	I	C	C	I	C	I	C	C	C	C	A	I	I	C	C	I	I	C	C	C	I	A	C	A
Guillot *et al.* (2018)	C	C	C	I	C	A	C	I	C	C	C	I	A	I	I	A	C	C	I	C	A	A	I	I	C	A	A	A	I	I	I	A	I	I
Er *et al.* (2018)	C	C	C	I	C	I	I	I	C	C	C	I	A	I	I	C	C	C	I	C	C	I	I	I	C	A	A	A	A	C	I	A	A	A
Ballestero *et al.* (2018)	C	C	C	C	C	C	C	C	C	C	C	I	A	I	C	I	C	C	A	I	A	I	I	C	I	C	A	I	I	I	I	A	C	A
Can *et al* (2018)	C	C	C	C	C	C	C	C	C	C	C	C	C	C	I	I	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	A	A	A
Can *et al* (2017)	C	C	C	C	C	C	C	C	C	I	I	A	A	I	I	A	C	C	I	C	A	A	I	I	C	A	A	C	A	C	I	A	I	A
Coletti *et al.* (2017)	C	I	C	A	A	A	A	I	C	I	I	I	A	I	A	A	C	I	C	C	A	I	I	A	A	A	A	A	A	A	A	C	C	A
Goh *et al.* (2017)	C	C	C	I	C	I	C	I	C	A	I	I	A	I	C	C	I	I	A	I	C	A	I	I	I	C	A	I	A	I	I	C	C	A
Vitaliti *et al.* (2017)	C	I	C	I	C	A	A	I	C	C	C	C	A	I	I	I	C	I	I	I	A	I	I	I	I	A	A	A	A	I	I	A	A	A
Betters *et al.* (2017)	C	I	C	C	C	C	I	I	C	C	C	A	A	I	C	I	C	C	I	I	A	A	I	A	A	C	C	C	C	A	I	A	I	A
Sochet *et al.* (2017)	C	C	C	A	A	A	A	I	C	C	C	I	C	I	I	I	C	A	A	I	A	I	I	A	A	A	A	A	A	A	A	A	A	A
Slain *et al.* (2017)	C	I	C	A	A	A	A	I	C	C	C	I	C	I	I	C	C	A	A	I	A	I	I	A	A	A	A	A	A	A	A	A	A	A
Davison *et al.* (2017)	C	C	C	I	C	A	A	I	C	C	I	C	C	I	I	C	C	C	C	C	A	I	I	C	C	C	C	C	C	C	C	A	I	A
Pilar *et al.* (2017)	C	I	C	C	C	C	C	C	C	C	I	C	A	I	I	I	C	C	I	C	A	C	I	I	C	A	A	A	A	I	I	A	I	A
Kepreotes *et al.* (2017)	C	C	C	I	C	A	I	I	C	C	C	I	I	I	C	C	C	C	C	C	A	C	I	C	C	C	C	C	C	C	C	C	C	A
Milési *et al* (2017)	C	C	C	A	A	A	I	I	C	C	C	I	A	I	C	I	C	C	I	C	C	C	I	I	C	I	C	C	A	C	I	A	C	A
Guimaraes *et al.* (2017)	C	C	C	C	C	C	C	C	C	C	I	A	A	I	C	I	I	C	I	C	A	A	I	I	C	A	A	C	C	I	I	A	C	A
Betters *et al.* (2017)	C	C	C	C	C	C	A	I	C	C	C	A	A	I	I	C	C	C	I	C	I	A	I	I	C	I	A	C	C	I	I	A	C	C
Baudin F *et al.* (2016)	C	C	C	I	A	C	I	I	C	C	C	A	A	I	I	A	C	I	C	C	A	A	I	A	I	A	A	A	A	I	I	I	I	C
Milani *et al.* (2016)	C	C	C	I	C	A	I	I	C	C	C	C	C	C	I	I	I	C	A	C	A	A	I	I	C	A	A	A	I	A	I	I	C	A
Bermúdez *et al.* (2017)	C	C	C	I	C	A	I	I	C	C	C	C	C	C	A	A	I	C	I	C	A	I	I	C	C	C	A	I	C	C	I	A	I	A

Article's author and year of publication	Item 1) Brief name	Item 2) Why	Item 3) What (Materials)						Item 4) What (Procedures)						Item 5) Who provided	Item 6) How	Item 7) Where	Item 8) When and how much						Item 9) Tailoring								Item 10) Modifications	Item 11) How well (planned)	Item 12) How well (actual)
	1) General Item	2) General Item	3.a)	3.b)	3.c)	3.d)	3.e)	3) General item	4.a)	4.b)	4.c)	4.d)	4.e)	4) General item	5) General Item	6) General Item	7) General Item	8.a)	8.b)	8.c)	8.d)	8.e)	8) General Item	9.a)	9.b)	9.c)	9.d)	9.e)	9.f)	9.g)	9) General Item	10) General Item	11) General Item	12) General Item
Long *et al.* (2016)	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	I	C	C	C	C	C	C	I	C	C	C	C	C	I	I	A	C	C
Oto *et al.* (2016)	C	C	C	A	A	A	C	I	C	C	C	A	A	I	A	A	I	C	C	C	C	A	I	I	I	A	A	A	A	I	I	A	A	A
Riese *et al.* (2015)	C	C	A	A	A	A	A	A	C	I	I	I	A	I	A	A	C	I	A	C	A	I	I	I	C	I	A	I	C	I	I	A	A	A
Wegner *et al.* (2015)	C	C	C	C	C	C	C	C	C	C	I	I	C	I	I	C	I	I	A	C	A	I	I	I	I	I	A	I	C	C	I	A	I	A
Chisti *et al.* (2015)	C	I	C	I	I	A	A	I	C	C	C	C	C	C	I	I	I	C	C	C	C	C	C	A	C	A	A	A	A	I	I	C	A	C
Wraight *et al.* (2015)	C	C	C	I	I	A	I	I	C	C	C	A	A	I	I	I	C	C	C	C	A	A	I	A	I	A	A	A	A	C	I	A	A	A
Morgan *et al.* (2015)	I	I	C	C	C	C	A	I	C	C	C	I	I	I	A	A	C	C	C	C	C	C	C	C	C	A	A	A	A	A	I	A	A	A
Mayfield *et al.* (2014)	C	C	C	C	C	C	I	I	C	C	C	I	A	I	C	I	I	I	I	C	C	I	I	I	C	I	C	C	C	C	I	A	C	A
Metge *et al.* (2014)	C	C	C	C	C	C	C	C	C	C	C	C	C	C	I	I	C	C	C	C	A	C	I	I	C	C	C	C	C	C	I	C	I	A
Bueno-Campaña *et al.* (2014)	C	C	C	C	C	C	C	C	C	C	C	C	A	I	I	C	C	C	A	C	A	C	I	I	I	C	A	A	A	A	I	I	I	A
Kelly *et al.* (2013)	C	C	C	C	C	C	A	I	C	C	A	I	A	I	I	A	C	I	I	I	I	A	I	I	I	A	A	A	A	I	I	A	A	A
Bressan *et al.* (2013)	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	I	C	C	C	C	C	C	C	I	C	I	C	C	C	C	I	A	C	I
Mayfield *et al.* (2013)	C	C	A	A	A	A	A	A	C	C	C	I	I	I	A	A	C	C	A	I	A	C	I	I	C	I	C	I	I	A	I	A	A	A
Brink *et al.* (2013)	C	C	C	C	C	C	C	C	C	C	C	I	C	I	I	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	A	C	C
Hegde *et al.* (2013)	C	C	C	A	A	A	A	I	C	C	C	I	I	I	A	A	I	I	C	C	A	C	I	C	C	A	A	A	A	I	I	A	A	A
Wing *et al.* (2012)	C	C	C	C	C	C	C	C	C	I	C	A	A	I	C	C	C	C	C	C	C	A	I	C	C	C	A	C	C	A	I	C	C	A
Abboud *et al.* (2012)	C	C	C	I	C	I	I	I	C	C	C	I	A	I	I	A	C	C	I	I	I	A	I	I	I	A	A	A	I	I	I	A	A	A
Schibler *et al.* (2011)	C	C	C	I	A	C	C	I	C	C	C	A	A	I	I	I	C	I	I	C	A	A	I	I	C	I	A	C	I	I	I	I	A	A
McKiernan *et al.* (2010)	C	C	C	I	C	A	C	I	C	C	C	C	C	C	I	I	I	I	A	C	A	A	I	A	C	A	A	A	A	C	I	C	A	A
Spentzas *et al.* (2009)	C	I	C	A	A	A	A	I	C	C	C	I	A	I	A	A	I	A	A	C	A	A	I	A	I	A	A	A	A	A	I	A	I	A
Urbano *et al.* (2008)	C	C	C	C	C	C	A	I	C	C	C	A	A	I	I	A	I	I	C	C	C	A	I	I	C	A	A	I	A	A	I	C	A	A

C = an item or subitem that is correctly reported; I = an item or subitem that is partially or incompletely reported; A = an item or subitem that is absent

Appendix 1: MEDLINE (Pubmed) search strategy

#1 ("lower respiratory tract infection" OR "lower respiratory tract infections" OR "lower respiratory infection")

#2 (("Oxygen Inhalation Therapy"[Mesh]) AND ("high flow" OR "high-flow"))

#3 "Respiratory Tract Diseases"[Mesh]

#4 (("nasal" AND ("cannula" OR "prong"))

#5 "high flow"

#6 1 AND 2 AND 3 AND 4 AND 5

#7 6 AND (infant[MeSH] OR child[MeSH] OR adolescent[MeSH])

#8 7 AND humans[MeSH]

Appendix 2: Full reference list of included studies

1. Hansen G, Hochman J, Garner M et al. Pediatric early warning score and deteriorating ward patients on high-flow therapy. Pediatr Int. 2019;61(3):278–83.

2. Akyıldız B, Öztürk S, Ülgen-Tekerek N, et al. Comparison between high-flow nasal oxygen cannula and conventional oxygen therapy after extubation in pediatric intensive care unit. Turk J Pediatr. 2018;60(2):126–33.

3. Dohna-Schwake C, Mücher K, Stehling F et al. Differences of Medical Care for Acute Severe Viral Bronchiolitis in Two Urban Areas in Europe. Klin Padiatr. 2018;230(5):245–50.

4. Betul-Ergul A, Calıskan E, Samsa H et al. Using a high-flow nasal cannula provides superior results to OxyMask delivery in moderate to severe bronchiolitis: a randomized controlled study. Eur J Pediatr. 2018;177:1299–307.

5. Ramnarayan P, Lister P, Dominguez T et al. FIRST-line support for Assistance in Breathing in Children (FIRST-ABC): A multicentre pilot randomised controlled trial of high-flow nasal cannula therapy versus continuous positive airway pressure in paediatric critical care. Crit Care. 2018;22(1):1–11.

6. Valencia-Ramos J, Mirás A, Cilla A et al. Incorporating a nebulizer system into high-flow nasal cannula improves comfort in infants with bronchiolitis. Respir Care. 2018;63(7):886–93.

7. Franklin D, Babl F, Schlapbach L et al. A randomized trial of high-flow oxygen therapy in infants with bronchiolitis. N Engl J Med. 2018;378(12):1121–31.

8. Guillot C, Le Reun C, Behal H et al. First-line treatment using high-flow nasal cannula for children with severe bronchiolitis: Applicability and risk factors for failure. Arch Pediatr [Internet]. 2018;25(3):213–8. Available from: https://doi.org/10.1016/j.arcped.2018.01.003

9. Er A, Çağlar A, Akgül F et al. Early predictors of unresponsiveness to high-flow nasal cannula therapy in a pediatric emergency department. Pediatr Pulm. 2018;53(6):809–15.

10. Ballestero Y, De Pedro J, Portillo N et al. Pilot Clinical Trial of High-Flow Oxygen Therapy in Children with Asthma in the Emergency Service. J Pediatr [Internet]. 2018;194:204-210.e3. Available from: https://doi.org/10.1016/j.jpeds.2017.10.075

11. Kamit-Can F, Anil A, Anil M et al. Predictive factors for the outcome of high flow nasal cannula therapy in a pediatric intensive care unit: Is the SpO2 /FiO2 ratio useful? J Crit Care. 2018;

12. Can F, Anil A, Anil M et al. Impact of high-flow nasal cannula therapy in quality improvement and clinical outcomes in a non-invasive ventilation device-free pediatric intensive care unit. Indian Pediatr. 2017;54(10):835–40.

13. Coletti K, Bagdure D, Walker L et al. High-flow nasal cannula utilization in pediatric critical care. Respir Care. 2018;62(8):1023–9.

14. Goh C, Kirby L, Schell D et al. Humidified high-flow nasal cannula oxygen in bronchiolitis reduces need for invasive ventilation but not intensive care admission. J Paediatr Child Health. 2017;53(9):897–902.

15. Vitaliti G, Vitaliti M, Finocchiaro M et al. Randomized comparison of helmet CPAP versus high-flow nasal cannula oxygen in pediatric respiratory distress. Respir Care.

2018;62(8):1036–42.

16. Betters K, Hebbar K, McCracken C et al. A Novel Weaning Protocol for High-Flow Nasal Cannula in the PICU. Pediatr Crit Care Med. 2017;18(7):e274–80.

17. Sochet A, McGee J, October T. Oral Nutrition in Children With Bronchiolitis on High-Flow Nasal Cannula Is Well Tolerated. Hosp Pediatr. 2017;7(5):249–55.

18. Slain K, Martinez-Schlurmann N, Shein S et al. Nutrition and High-Flow Nasal Cannula Respiratory Support in Children With Bronchiolitis. Hosp Pediatr. 2017;7(5):256–62.

19. Davison M, Watson M, Wockner L et al. Paediatric high-flow nasal cannula therapy in children with bronchiolitis: A retrospective safety and efficacy study in a non-tertiary environment. EMA - Emerg Med Australas. 2017;29(2):198–203.

20. Pilar J, Modesto-i-Alapont V, Lopez-Fernandez Y et al. High-flow nasal cannula therapy versus non-invasive ventilation in children with severe acute asthma exacerbation: An observational cohort study. Med Intensiva. 2017;41(7):418–24.

21. Kepreotes E, Whitehead B, Attia J et al. High-flow warm humidified oxygen versus standard low-flow nasal cannula oxygen for moderate bronchiolitis (HFWHO RCT): an open, phase 4, randomised controlled trial. Lancet [Internet]. 2017;389(10072):930–9. Available from: http://dx.doi.org/10.1016/S0140-6736(17)30061-2

22. Milési C, Essouri S, Pouyau R et al. High flow nasal cannula (HFNC) versus nasal continuous positive airway pressure (nCPAP) for the initial respiratory management of acute viral bronchiolitis in young infants: a multicenter randomized controlled trial (TRAMONTANE study). Intensive Care Med. 2017;43(2):209–16.

23. Guimaraes M, Pomedio M, Viprey M et al. Utilisation des lunettes nasales à haut débit chez les nourrissons hospitalisés en service d'accueil des urgences pédiatriques pour bronchiolite : étude observationnelle. Arch Pediatr. 2017;24(1):3–9.

24. Betters K, Gillespie S, Miller J et al. High flow nasal cannula use outside of the ICU; factors associated with failure. Pediatr Pulmonol. 2017;52(6):806–12.

25. Baudin F, Gagnon S, Crulli B et al. Modalities and complications associated with the use of high-flow nasal cannula: Experience in a pediatric ICU. Respir Care. 2016;61(10):1305–10.

26. Milani G, Plebani A, Arturi E et al. Using a high-flow nasal cannula provided superior results to low-flow oxygen delivery in moderate to severe bronchiolitis. Acta Paediatr Int J Paediatr. 2016;105(8):e368–72.

27. Bermúdez L, García N, López J et al. High flow nasal cannula oxygen therapy in the treatment of acute bronchiolitis in neonates. An Pediatría (English Ed.) 2017;86(1):37–44.

28. Long E, Babl F, Duke T. Is there a role for humidified heated high-flow nasal cannula therapy in paediatric emergency departments? Emerg Med J. 2016;33(6):386–9.

29. Oto A, Erdoğan S, Boşnak M. Oxygen therapy via high flow nasal cannula in pediatric intensive care unit. Turk J Pediatr. 2016;58(4):377–82.

30. Riese J, Fierce J, Riese A et al. Effect of a Hospital-wide High-Flow Nasal Cannula Protocol on Clinical Outcomes and Resource Utilization of Bronchiolitis Patients Admitted to the PICU. Hosp Pediatr. 2015;5(12):613–8.

31. Wegner A, Cespedes P, Godoy M et al. Cánula nasal de alto flujo en lactantes: Experiencia en una unidad de paciente crítico. Rev Chil Pediatr [Internet]. 2015;86(3):173–81. Available from: http://dx.doi.org/10.1016/j.rchipe.2015.06.003

32. Chisti M, Salam M, Smith J et al. Bubble continuous positive airway pressure for children with severe pneumonia and hypoxaemia in Bangladesh: An open, randomised controlled trial. Lancet [Internet]. 2015;386(9998):1057–65. Available from: http://dx.doi.org/10.1016/S0140-6736(15)60249-5

33. Wraight T, Ganu S. High-flow nasal cannula use in a paediatric intensive care unit over 3 years. Crit Care Resusc. 2015;17(3):197–201.

34. Morgan S, Mosakowski S, Solano P et al. High-flow nasal cannula and aerosolized β agonists for rescue therapy in children with bronchiolitis: A case series. Respir Care. 2015;60(9):e161–5.

35. Mayfield S, Bogossian F, O'Malley L et al. High-flow nasal cannula oxygen therapy for infants with bronchiolitis: Pilot study. J Paediatr Child Health. 2014;50(5):373–8.

36. Metge P, Grimaldi C, Hassid S et al. Comparison of a high-flow humidified nasal cannula to nasal continuous positive airway pressure in children with acute bronchiolitis: Experience in a pediatric intensive care unit. Eur J Pediatr. 2014;173(7):953–8.

37. Campanã M, Ortiz J, Muñoz C et al. High flow therapy versus hypertonic saline in bronchiolitis: Randomised controlled trial. Arch Dis Child. 2014;99(6):511–5.

38. Kelly G, Simon H, Sturm J. High-Flow Nasal Cannula Use in Children With Respiratory Distress in the Emergency Department. Pediatr Emerg Care. 2013;29(8):888–92.

39. Bressan S, Balzani M, Krauss B et al. High-flow nasal cannula oxygen for bronchiolitis in a pediatric ward: A pilot study. Eur J Pediatr. 2013;172(12):1649–56.

40. Mayfield S, Jauncey-Cooke J, Bogossian F. A case series of paediatric high flow nasal cannula therapy. Aust Crit Care [Internet]. 2013;26(4):189–92. Available from: http://dx.doi.org/10.1016/j.aucc.2013.05.004

41. Brink F, Duke T, Evans J. High-Flow Nasal Prong Oxygen Therapy or Nasopharyngeal Continuous Positive Airway Pressure for Children With Moderate-to-Severe Respiratory Distress?*. Pediatric Critical Care Medicine 2013;14(7).

42. Hegde S, Prodhan P. Serious air leak syndrome complicating high-flow nasal cannula therapy: A report of 3 cases. Pediatrics. 2013;131(3).

43. Wing R, James C, Maranda L et al. Use of high-flow nasal cannula support in the emergency department reduces the need for intubation in pediatric acute respiratory insufficiency. Pediatr Emerg Care. 2012;28(11):1117–23.

44. Abboud P, Roth P, Skiles C et al. Predictors of failure in infants with viral bronchiolitis treated with high-flow, high-humidity nasal cannula therapy. Pediatr Crit Care Med. 2012;13(6):343–9.

45. Schibler A, Pham T, Dunster K et al. Reduced intubation rates for infants after introduction of high-flow nasal prong oxygen delivery. Intensive Care Med. 2011;37(5):847–52.

46. McKiernan C, Chua L, Visintainer P et al. High Flow Nasal Cannulae Therapy in Infants with Bronchiolitis. J Pediatr [Internet]. 2010;156(4):634–8. Available from: http://dx.doi.org/10.1016/j.jpeds.2009.10.039

47. Spentzas T, Minarik M, Patters A et al. Children with respiratory distress treated with high-Flow nasal cannula. J Intensive Care Med. 2009;24(5):323–8.

48. Urbano J, Mencía S, Cidoncha E et al. Experiencia con la oxigenoterapia de alto flujo en cánulas nasales en niños. An Pediatr. 2008;68(1):4–8.

NOTE: This reference list follows the order of studies presented on Tables 1 and 2