Towards a harmonized bronchopulmonary dysplasia definition: a study protocol for an international Delphi procedure


ABSTRACT

Introduction Bronchopulmonary dysplasia (BPD) remains the most common complication of preterm birth with lifelong consequences. Multiple BPD definitions are currently used in daily practice. Uniformity in defining BPD is important for clinical care, research and benchmarking. The aim of this Delphi procedure is to determine what clinicians and researchers consider the key features for defining BPD. With the results of this study, we hope to advance the process of reaching consensus on the diagnosis of BPD.

Methods and analysis A Delphi procedure will be used to establish why, when and how clinicians propose BPD should be diagnosed. This semi-anonymous iterative technique ensures an objective approach towards gaining these insights. An international multidisciplinary panel of clinicians and researchers working with preterm infants and/or patients diagnosed with BPD will participate. Steering committee members will recruit potential participants in their own region or network following eligibility guidelines to complete a first round survey online. This round will collect demographic information and opinions on key features of BPD definitions. Subsequent rounds will provide participants with the results from the previous round, for final acceptance or rejection of key features. Statements will be rated using a 5-point Likert scale. After completing the Delphi procedure, an (online) consensus meeting will be organised to discuss the results.

Ethics and dissemination For this study, ethical approval a waiver has been provided. However, all participants will be asked to provide consent for the use of personal data. After the Delphi procedure is completed, it will be published in a peer-reviewed journal and disseminated at international conferences.

INTRODUCTION

Bronchopulmonary dysplasia (BPD) is one of the most common complications of preterm birth. BPD is associated with short-term in-hospital morbidity and long-term adverse respiratory, cardiovascular and neurodevelopmental outcomes. Accurate criteria to establish the diagnosis and severity of BPD are important in translational and clinical research, but also in daily clinical care to decide on the use of therapies for prevention and treatment and to inform parents of the possible problems their child may experience in the future. The internationally accepted 1988 Shennan- and the 2001 National Institute Health (NIH)-BPD definition are the most used BPD definitions over the last two decades, but have been recently challenged by the emergence of other BPD definitions. Several reasons underpin the development of these new BPD definitions. First, neonatal care has improved significantly resulting in more premature survivors being exposed to lung injurious conditions and interventions at a much younger stage of lung development. These developments may have changed the disease entity and thus the accuracy of diagnosing BPD.
and predicting long-term outcomes. Second, high flow nasal cannula (HFNC) was implemented in daily clinical care in recent years. HFNC is a mode of respiratory support that was not incorporated in the 2001-NIH definition as it was not in widespread use when the 2001-NIH definition was created. Therefore, it is unclear how infants treated with HFNC should be classified in terms of BPD severity in the 2001-NIH definition.

The newer BPD definitions use different parameters, timing of assessment and/or methods to diagnose BPD and its severity compared with the 2001-NIH definition. First, they do not incorporate the cumulative days of oxygen as a criterion and have different thresholds of respiratory support and supplemental oxygen for BPD severity classification at 36 weeks post-menstrual age (PMA). Second, in contrast to the adapted 2001 NIH definition, no oxygen reduction testing is required. Furthermore, one new definition suggests postponing the timing of the BPD diagnosis up to 40 weeks PMA. Finally, some authors suggest to move away from a diagnosis based on clinical treatment purposes, benchmarking, quality improvement as well as of reliable data comparison and data synthesis for clinical and research purposes. Uniformity in the definition for BPD is an essential part of the diagnosis (when), to assess the (minimal) parameters and/or procedures needed to establish the BPD diagnosis, to assess the optimal timing of the diagnosis (when), and to assess the (minimal) parameters and/or procedures needed to establish high accuracy (how), including the feasibility and effort of collecting those parameters. In preparation for an international consensus meeting, a Delphi procedure beginning with an online questionnaire is a widely used and effective method to gain insight and opinions on a specific topic from a multidisciplinary group of experts.

The aim of this Delphi procedure is to guide clinicians and researchers in reaching global consensus in defining BPD by acquiring information on which features of BPD definition are important.

METHODS AND ANALYSIS

Steering committee
A study team from the Amsterdam University Medical Centers (Amsterdam UMC) was formed to undertake this Delphi procedure. Next, an impartial expert on Delphi procedures working in a different field of medicine was invited to join the steering committee to moderate the procedure, with the goal of minimising bias and maintaining objectivity. After, BPD (definition) experts were identified through a literature search and invited to join the steering committee. These BPD experts were consulted on the design of the Delphi procedure and the questionnaires, and were asked to disseminate the survey invitation to potential participants in their own region or network. The steering committee reached agreement on participant selection, consensus thresholds and survey format.

Selection and identification of participants
Participants will be asked to complete the Delphi survey. To ensure sufficient diversity, we will include clinically oriented and/or research-oriented healthcare professionals with relevant backgrounds, for example; neonatologists, paediatricians (eg, providing outpatient clinical care of preterm infants), pulmonologists and ventilation practitioners or respiratory therapists. Administrators and regulators involved in neonatal care will also be invited to participate. We aim to achieve global coverage, by including participants from all continents. Participants will be recruited from all different levels of care (regional centres to specialised BPD referral centres). To prevent selection bias, initial survey invitations will be forwarded to national network list servers and no individual emails will be sent out. Lay experts and patients (representatives) will not be included as participants. The aim of this Delphi procedure is not to establish a core outcome dataset or other items that would benefit from patient or parental input.

Recruitment
Participants will be identified by the study team and the steering committee members (figure 1). The steering committee members will be asked to disseminate an open-link invitation to the survey to participants in their region and/or network while adhering to the guidelines for eligibility (box 1).

An email reminder to the steering committee will be sent 2 and 3 weeks after disseminating the primary invitation. In subsequent rounds, a group reminder will be sent after 2 weeks, and non-responders will receive a final reminder after 4 weeks. Participants who do not complete the surveys will be reminded via email 1 week after the final reminder. Recipients of the reminder email will be sent a reminder to complete the survey 1 week after sending the reminder email. The steering committee members, champions and an independent expert will be asked to disseminate the survey and remind participants to take part in the Delphi procedure. Participants will be asked to complete the Delphi survey within 4 weeks of receiving the survey invitation. The steering committee agreed on an initial survey reminder after 4 weeks, and participants who do not complete the survey will be sent a second reminder after 2 weeks. The steering committee will meet after the completion of the Delphi procedure to discuss the results and next steps.

Figure 1 Participants’ recruitment process.
Sample size and composition
Sample sizes in Delphi procedures are variable, ranging from 10 to over 1000 participants, with no agreement in the literature on the ideal size. No lower or upper limit will be set as larger panels increase the reliability of the outcomes.

Semianonymity
One of the key features of a Delphi technique is that the procedure is anonymous on group level, also known as semianonymity. However, the participant is not anonymous to the researcher. At the conclusion of the process, participants who have completed each round will be offered the choice to remain anonymous or receive acknowledgement in the publication.

Design and content of the survey
All electronic surveys will be developed in the electronic data capture (EDC) system Castor EDC 2019; online available at: https://castoredc.com. Each round of the survey will be accompanied by a cover sheet containing background information and aims. After the first round, the subsequent rounds will include results from the previous rounds. The participants will be asked to state the extent to which they agree on the different statements regarding features of the BPD definitions using a 5-point Likert scale (1: strongly disagree; 2: disagree; 3: neutral; 4: agree; 5: strongly agree). A 5-point Likert scale is commonly used in Delphi procedures. We chose this 5-point scale after careful consideration as studies show an increased response rate and quality along with reducing respondents’ dissatisfaction with a 5-point compared with a 3-point or 7-point scale.

Survey development
Statements/questions for the first-round survey will be developed with the study team’s expertise and partly based on key features from current BPD definitions (e.g., timing of diagnosis). The survey of the first round will be thoroughly revised by the steering committee members and discussed in an (online) meeting. Communication experts will be consulted on their expertise of interpretation and formulation of the questions and statements. The survey will also be tested by a research data manager to identify any technical or data management issues. Finally, a small pilot study will be performed inviting a group of neonatologists to fill in the survey. The survey will be adjusted based on their feedback before being finalized (see online supplemental material for the final first round survey).

Rounds
A minimum of two rounds will be undertaken to allow the participants to complete the Delphi process (figure 2). It is anticipated that between two and four rounds will be necessary to achieve consensus.

First round
The first-round questionnaire will consist of 20–30 questions, and it will take approximately 10–15 min to complete. First, demographic characteristics of the participants will be collected including region of practice, main field of practice, current position, years of experience in (neonatal) care, level of neonatal care at the current institute, amount of time spent on research and clinical work. Second, data on their current use of BPD definitions will be collected. Next, participants will be asked to respond to a series of statements on key features of a BPD definition using a 5-point Likert scale. Finally, the participants will be asked to suggest additional parameters for a BPD definition or other remarks regarding the survey itself in an open field box. These suggestions will be discussed by the study team for incorporation into subsequent rounds.

Subsequent rounds
Once again, participants will be asked to state the extent to which they agree with the newly suggested statements using a 5-point Likert scale. Statements with a median score ≥4 will be presented for final acceptance, and statements with a median score <4 will be presented for final rejection (figure 2). Parameters that do not reach consensus in the second round will be presented in subsequent rounds using a Best-Worst scale (figure 2).

Definition of consensus
Multiple cut-offs for consensus are reported in the literature. A minimum of 70% agreement is most frequently reported and will be used to define consensus.
in this Delphi procedure. If too many parameters reach acceptance/consensus during the procedure, the cut-off will be increased to 80% to achieve our objectives.

Statistical analysis
The quantitative data will be entered into SPSS (IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0., IBM) for analysis and descriptive statistics, such as medians and IQRs, will be reported for each statement to be fed back to the participants in subsequent rounds.

Data collection
After all participants have provided informed consent, only limited identifying information (name and email) will be registered. This identifiable information will be stored separately from the answers to the questionnaire and will only be used for the purpose of direct feedback, reminder emails, and if applicable, for acknowledgement of contribution.

Study status and dissemination
The steering committee members were identified and invited in the third quarter (Q3) of 2022, and all agreed to participate. The Delphi protocol was written and discussed in online meetings between Q3 of 2022 and Q1 of 2023. The development of the Delphi questionnaire started in Q3 of 2022 and the pilot study finalised in Q1 of 2023. The anticipated start of the online Delphi study is May 2023. We will finalise the procedure in Q4 2023, analyse the data in Q1 2024, and anticipate hosting an (online) meeting during an international conference in Q2 of 2024 to optimise the uptake of the results from this Delphi procedure. Dissemination of the results will be accomplished by publication in an international peer-reviewed journal and by presentations at (international) conferences.

DISCUSSION
Currently, clinicians and researchers around the world use different definitions of BPD. The heterogeneity in how BPD is defined makes comparison of the BPD incidence between different neonatal intensive care units, data collection in large databases and interpretation of study results difficult, if not impossible. To address this problem, neonatal caregivers and researchers should all use a harmonised BPD definition.

This Delphi procedure is the first step towards a harmonised BPD definition. It will provide insight in key features that, based on the opinion of clinicians and experts in BPD, should be used as criteria in a future, harmonised definition of BPD. In doing so, we will take differences between countries in clinical practices and resources use into account.

To ensure that the results of this Delphi procedure will find their way into a future practice, an online/in person meeting will be organised to discuss the results of the Delphi procedure. These results will provide a first step in guiding clinicians and researchers in reaching global consensus in defining BPD. Future steps may include coming to a consensus on which currently available BPD definition should be validated and implemented in current practice or a data-driven approach in designing a new BPD definition.

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Ethics approval This Delphi procedure seeks opinions and information from medical professionals and does not include patients. The medical research ethics committee of the Amsterdam University Medical Centers (Amsterdam UMC) was contacted and confirmed that the Dutch Medical Research Involving Human Subject Act does not apply to this study and that Institutional Review Board (IRB) review is not necessary. However, electronic informed consent will be obtained from all healthcare professionals/participants for the use of personal data. All data will be handled in accordance with privacy laws.

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