JPPT | Primer

Peer Review as a Professional Obligation: Steps and Tips to Becoming a High-Quality Reviewer

Peter N. Johnson, PharmD and Jamie L. Miller, PharmD

Peer review is an essential step in the publication process and dissemination for scientific information to improve patient care and future research in pediatric patients. It is a professional obligation to ensure high quality, reliable, and relevant information is published. Despite this, many journals face problems finding peer reviewers. Several journals and organizations have developed resources to aid in the training of peer reviewers. The purpose of this primer is to provide an overview of the steps of peer review and to emphasize key points on how to conduct a peer review.

ABBREVIATIONS COVID-19, 2019 novel coronavirus; JPPT, Journal of Pediatric Pharmacology and Therapeutics; NICU, neonatal intensive care unit; PGY2, post-graduate year 2

KEYWORDS peer review; editor; pediatric; pharmacy; manuscript review; publishing peer review

J Pediatr Pharmacol Ther 2024;29(6):570-577

DOI: 10.5863/1551-6776-29.6.570

Introduction

Publication of case reports/series, comprehensive, authoritative reviews, and original research manuscripts are essential to allow for the sharing of information and scientific works to improve patient care and to stimulate future research in pediatric patients.¹ An essential step in the publication process and dissemination of information is peer review. The purpose of peer review for research-based, scientific- and clinically-focused journals is to authenticate the integrity of research design, accuracy of data collection and analysis and applicability of results to improve the quality and readability of manuscripts.^{2–3} Journal editors are reliant upon reviewer feedback to assess the quality of submitted manuscripts and provide feedback to authors to improve their manuscripts for publication. Therefore, some have argued that serving as a peer reviewer is a professional obligation not only for those who submit manuscripts for publication, but for those who are readers of the scientific literature as well.⁴ In a sense, the professional obligation is to help ensure that high quality, reliable, and relevant information is published.

Even though peer reviewers are an essential part of the publication process, a few challenges exist with the peer review process. First, editors may have difficulty obtaining an adequate number of individuals with aligned expertise to accept the peer reviewer assignment. It has been reported that a mean of 4-7 invitations for peer review are sent per manuscript, and only 30-50% of invitations are accepted.^{5–6} Second, a number of journals have reported a 2 to 5-fold increase in the number of manuscript submissions during and after the 2019 novel coronavirus (COVID-19) pandemic.^{5,7–9} As a result of this increase in submissions, a greater number of reviewers are being called upon for service and some reviewers are being asked to review more articles per year. This increased need may result in the need for additional reviewers to be added to the reviewer pool, which could contribute to a third challenge of the peer review process, which is a new reviewer's unfamiliarity with expectations of peer review with subsequent submission of a poor-quality review. Most pharmacists, physicians, and clinicians have not received specific training for peer review; as a novice reviewer, they may be unfamiliar or lack confidence with the peer review process and provide a more superficial or less critical review that focuses on grammar and style instead of emphasis on critique of methodology, interpretative analysis, and provision of actionable suggestions. The purpose of this primer is to provide an overview of the steps of the peer review process and emphasize key points of how to conduct a peer review.

Steps of the Peer Review Process

Many authors and reviewers may not be familiar with the steps of peer review. It is essential to understand these steps to appreciate the role that the authors, editors, and reviewers play in shaping the manuscript through the peer review process. Below are eight steps of the peer review process. It is important to note that some journals may have additional steps required. An attempt is made to highlight considerations of the peer review process with a specific focus on the *Journal of Pediatric and Pharmacology and Therapeutics* (JPPT) with each step below.

Johnson, P et al

1. Peer reviewer registration. The most direct way to become a peer reviewer for a journal is to register as a reviewer in the journal's electronic database. For example, registration to become a peer reviewer for JPPT can be found at https://www.editorialmanager. com/jppt. When registering as a reviewer, include an email address that you check frequently, as requests for peer review will be sent to that email address. If there is a change in primary email address, this can be updated at any time in the system. Also, at the time of registration, prospective reviewers will be asked to select their areas of interest or expertise from a predetermined listing of expertise classifications. These peer-reviewer-linked classification selections are used by the editors to identify potential reviewers to align the reviewer's expertise with the submitted manuscript. If interest areas or expertise change over time, reviewers are encouraged to update these in the system.

Initial review by member of the Editor team. It is important that peer reviewers understand the general timelines from submission of a manuscript to publication. The first step after a manuscript is submitted to the journal is an initial review by a member of the Editor team. For JPPT, the initial desk review is conducted by the JPPT Editor-in-Chief. The purpose of this review is to determine if the manuscript aligns with the scope of the journal, would be of interest to the readers, adds to the body of literature, and is not similar to a manuscript that was recently published or is in-press. This part of the process is usually completed within 1-2 days to no longer than one week. After this review, the Editor-in-Chief can decide to reject (i.e., desk reject) or release the manuscript or proceed to Step 3 of the peer review process.

3. Review by Corresponding Editor and identification of peer reviewers. If the manuscript passes the initial review, the manuscript will be assigned to a Corresponding Editor. The title of this editor will be dependent upon the journal as some may refer to this individual as an Associate Editor, Section Editor, or Corresponding Editor. The role of the Corresponding Editor is to facilitate the peer review process and serve as the primary contact for the corresponding author. The Corresponding Editor will identify 2-6 potential content expert reviewers based on key words from the manuscript and reviewers' selected areas of interest or expertise or if a known reviewer has previous publications in the content area. The number of peer reviewers desired can vary based on the specific journal or the focus of the manuscript. For JPPT, the Corresponding Editor will attempt to identify 3 peer reviewers for each manuscript. Of note, many editors will try to include a mix of experienced and novice reviewers to avoid over-using established reviewers and to give novice reviewers an opportunity to establish themselves. Requests are emailed to the selected reviewers, and the Corresponding Editor awaits a response for the reviewer to accept or decline. Identification of additional potential reviewers will be sought depending upon the number of requests declined. Identification of peer reviewers can take 1-3 weeks, depending on how quickly the potential reviewers respond to the request.

4. Response to request for peer review. The email potential reviewers receive requesting their services will include the title and abstract of the manuscript as well as the due date for completion of the review. The provided title and abstract can be used by the potential reviewer to determine if the manuscript is in alignment with their areas of interest or expertise or if there is a potential conflict of interest. It is important to note that reviewers need to have familiarity with the topic, but they do not necessarily need to be an expert specific to the manuscript topic to provide a quality review. For example, with JPPT, reviewers may receive an invitation on a topic related to neonatal fungal infections. The Corresponding Editor may identify reviewers within the Pediatric Pharmacy Association, JPPT pool of reviewers or seek outside, non-registered experts that have experience in fungal infectious diseases, but not necessarily expertise in neonatology. In addition to determining if they are competent to serve as an expert reviewer for the submitted manuscript, the invited peer reviewer must assess if any possible/probable conflicts of interests may be present. Conflicts include financial interests, moral beliefs, or an extremely strong viewpoint on a topic that does not allow for unbiased consideration of other viewpoints. Close relationships with manuscript author(s) could also be a potential conflict of interest; however, the initial invite email may not include the name(s) of the author(s), but this may be identified because of familiarity with a colleague's research or identified when receiving the entire submission. There may also be times where a potential reviewer may identify that they have reviewed the manuscript for another journal. This is not necessarily a conflict of interest that would disgualify a reviewer. However, it should be disclosed to the Corresponding Editor, and the reviewer should not use the exact same review from the previous submission. It is important that any potential perceived conflict of interest be discussed with the Corresponding Editor prior to declining the request; this allows for the Corresponding Editor to determine if conflict exists. Last, before accepting the review, the reviewer should also determine if they can meet the expected deadline for review. Deadlines for review are typically 2-3 weeks from acceptance of the review invitation. However, if additional time may be needed, a request can be made to the Corresponding Editor for an extension of the deadline.

5. Conducting the peer review. Once accepted, the peer reviewer will need to schedule dedicated time

to complete the review. It has been proposed that a high-quality review will take between 3-6 hours to perform but could be longer for novice peer reviewers.¹⁰ Some experts recommend breaking this review process into three steps.¹¹ The first step would be an initial read-through to get a general understanding of the manuscript. The second step would be an in-depth review, where the reviewer would make notes and highlight areas of concern. The third step would include a final read through of the manuscript and preparation of formal comments for submission. An example of how to format formal comments for submission is included in the Appendix and will be discussed in more detail below. In addition, JPPT provides tips on reviewing a paper, which includes specific items to consider in each section of the manuscript (https://meridian.allenpress. com/DocumentLibrary/PPAG/Reviewer-Tips.pdf).12 The most important part of the review is that constructive comments are provided and are focused, detailed, supported by data/accepted practice, and actionable. This step of the process can take 1-3 weeks, depending on the time to accept the peer review invitations and if there is a need for a deadline extension. Prompt submission of your authoritative review is a cornerstone of the scientific publication process.

6. Decision on manuscript. Once the assigned reviewers have completed and submitted their review, the Corresponding Editor will consider all the overall and specific comments provided by the reviewers. Depending on the specific journal, the Corresponding Editor alone or the entire Editor team will determine the disposition of the manuscript (i.e., accept, minor revisions, major revisions, or reject). This decision is not only influenced by the assessments of the peer reviewers, but also by other factors including the focus of the manuscript (e.g., novelty of topic, similarity to other submissions/publications, and potential contribution to the literature), perceived acceptance by the readers of the journal, and the perception of the Corresponding Editor or the Editor team that the authors can make the revisions required if a fatal flaw with the manuscript is identified. This step of the process is typically completed within 1-2 weeks after receipt of the review comments.

7. Author revisions. If it is determined by the Corresponding Editor that minor or major revisions are needed and the manuscript be resubmitted, then reviewer comments are sent to the authors to direct them in making revisions. The authors are asked to make the necessary edits to their manuscript and to provide a point-by-point comprehensive yet succinct response to each comment offered by each peer reviewer. For JPPT, authors are typically asked to re-submit the revised manuscript within 4 weeks. However, other journals may provide different timeframes for a due date. It is important to note that authors could be provided with an extension of this deadline if requested. Once

revised and resubmitted, the Corresponding Editor may call upon the previous peer reviewers for a second review to ensure that their comments and concerns were adequately addressed. If these concerns were not adequately addressed, the reviewer may provide additional comments for the authors to address or can recommend that the manuscript be rejected. This step of the process can take approximately 2-4 weeks depending on the quantity and depth of revisions that are needed.

8. Final disposition of the manuscript. The Corresponding Editor or Editor team will take into consideration the reviewer comments and satisfaction with the authors' response to each reviewer comment and resultant revisions to the manuscript and will make a final decision on the disposition of the manuscript. This step of the process will take 1-2 weeks to complete.

The time from submission of an article by authors to determination of final disposition of the manuscript can take approximately 2.5-5 months, as outlined in the steps above. It is important for potential reviewers to understand the peer review process and timelines and to be aware of how they can contribute to a timely review and decision. In addition, it is important that reviewers know they are essential in the peer review process and their thorough review can ensure that high quality manuscripts are published. Key points and tips are included below to provide guidance on how reviewers can positively impact the timeline of manuscript review and provide constructive, actionable comments that will be beneficial for authors.

Key Points of Peer Review

1. Respond promptly to the request. To expedite the peer review process, it is important that potential reviewers respond as quickly as possible, accept or decline, to the invitation to review. Some reviewers may choose not to respond to the request, or an old email address may be in the system, or the request email may be re-directed by the email system to the junk folder. Therefore, it is important to ensure email addresses are periodically updated in the system and emails from the editorial manager are marked as "not junk". The corresponding editor may allow up to 1-2 weeks for a potential reviewer to respond; therefore, if no response is received, there can be a 1-2 week delay before the editor knows to move on to the next potential peer reviewer. Each time this occurs, the peer review timeframe gets extended.

2. Be professional. Professionalism in the peer review process can include following through on the commitment to perform the review, conducting the review in a timely manner (or communicating if timelines need to be extended), and using professional and courteous language in the comments and recommendations for the authors. Peer reviewers should make every effort to provide a professional review that demonstrates respect for the author's work. Comments that are sarcastic, antagonistic, or judgmental will not be well received and may not contribute to the improvement of the manuscript. It is important to try to identify the positive aspects of the manuscript when providing the review.

3. Use a systematic process to provide written feedback for peer review. A recommended format for peer review is included in the Appendix. This example in the Appendix includes a section for comments to the editor and comments to the author. Global and specific comments should be provided to the authors. The global comments should include the overall assessment of the article, identify major strengths or areas for improvement, and comment on the importance of the topic or potential interest to readers of the journal. Do not provide an opinion here regarding acceptance or rejection of the submission as this recommendation is corresponded directly to the editor as described in Key Point 7 below. Specific comments should be organized based on the section of the article. Organizing the comments by section will be helpful to the authors when making revisions, but is also helpful to the peer reviewer to ensure that sections were not overlooked. When providing comments, it is most helpful to provide authors with page and/or line numbers for each comment so they can easily determine where edits need to be made. Of note, the abstract and title are important sections to review because these are often the parts of a manuscript that would be viewed when literature reviews are performed. It is very important to ensure that the contents of the abstract provide an accurate reflection of the body of the manuscript.

4. Ensure comments are constructive and actionable. Peer reviewers should provide specific comments that are constructive and actionable about sentences or areas of concern. Vague comments from peer reviewers such as "this sentence is confusing" or "you need to add more detail here" can be frustrating to the authors because they may be unsure how to address those types of comments. Instead, peer reviewers should provide an explanation of why clarification is needed or what information appears to be missing. Some actionable feedback that peer reviewers can provide include suggestions for rephrasing a sentence that is confusing, eliminating a sentence that doesn't really add to the manuscript, reorganizing information to the appropriate section of the manuscript, identifying specific information that may be missing in a section (e.g., data is introduced in the discussion section, but was not discussed in the results section), or suggesting the authors consider citing a specific article in the introduction or discussion section. Recommendations for citing a specific article can be made to ensure the most recent or highest quality literature on the topic is included or could be

used when the reviewer disagrees with a statement in the manuscript. Comments or suggestions should be based on published evidence, guidelines, or accepted clinical practice when applicable. By providing specific recommendations for literature to include, the reviewer can potentially help authors strengthen the quality of the submitted manuscript.

There may be times when serving as a peer reviewer that the quality of a manuscript is perceived as very poor, and a peer reviewer may be inclined to dismiss the paper with minimal feedback. It is important that peer reviewers still attempt to provide useful feedback in these situations because the article may address a novel topic and could be publishable with revisions or the Corresponding Editor is seeking additional review because a previous decision was appealed by authors. In addition, authors will receive the reviewer comments even if the manuscript is rejected; therefore, providing constructive and actionable feedback can be beneficial if the authors choose to revise and resubmit to another journal.

5. Avoid focusing on grammatical issues. Comments to authors should not focus on grammatical issues as this will be addressed later during the copy-editing process. However, if grammatical errors are extensive, a global comment can be made at the beginning of the review. If grammatical errors make a sentence difficult to understand or a sentence is ambiguous, then the reviewer can provide a suggested example of how to rephrase the sentence.

6. Provide separate comments to Corresponding Editor. In addition to the global and specific comments to the authors, there is an opportunity to provide confidential comments to the Editor. This section of the review can be used to provide a summary of global comments to the Editor. Some examples of information that are recommended to be included in this section are potential interest to journal audience, major concerns (e.g., readability, flaws in study design, data analysis, incomplete components, etc.), perception of authors' abilities to address concerns, or recommendations to Editor. In addition, it could also be disclosed in this section if a trainee or colleague assisted with the review.

7. Provide a final assessment. In addition to the global and specific comments, reviewers will also be asked to provide a recommendation (e.g., accept, minor revision required, major revision required, or reject) in the peer review platform. The final assessment on the disposition of the manuscript should be shared only with the Corresponding Editor and not with manuscript authors. It is important that this overall recommendation align with the quantity and complexity of the specific comments provided. The Corresponding Editor or team of editors are ultimately responsible for determining the final disposition of the manuscript; therefore, reviewers should not put too much pressure on themselves with concerns about making the wrong recommendation.

The Corresponding Editors will consider all reviewers' comments and assessments, while taking into consideration additional factors when making their final decision.

Other Considerations for Peer Review

1. Don't hesitate to contact the corresponding editor. There are several time points where potential or assigned reviewers can utilize the Corresponding Editor as a resource. For example, prior to accepting the assignment to review, the potential reviewer could contact the editor for guidance on a potential conflict of interest or could express interest in reviewing. The peer reviewer could also request an extension in deadline due to schedule conflicts. In addition, some reviewers may be hesitant to accept the review assignment because they have never completed a peer review. Lack of experience should not be a reason to decline. Many Corresponding Editors may be willing to serve as a mentor or identify a mentor for a new reviewer to help them develop confidence in this skill. After accepting the review, reviewers may have conflicts in their schedule that prohibit submission of the review by the deadline. In this case, it is better to communicate with the Corresponding Editor and request and deadline extension versus giving half effort or not following through on this obligation.

2. Compare quality of review to other peer reviewers. After the completion of peer reviews from all assigned reviewers, the Corresponding Editor may provide a summary email or document to the reviewers that includes all reviewers' comments. This email or summary document may also provide the final decision from the Corresponding Editor, but this will depend upon the journal as some will not disclose the final decision to anyone outside the author team. This is an ideal opportunity for reviewers to compare the style, quality, and quantity of their comments to the other reviewers. Reviewers can use this opportunity to self-reflect on the quality of their review and determine if there are specific areas of focus that should be considered when accepting another review assignment.

3. Include trainees in the peer review process. The skill of performing a quality peer review is not innate, but rather a skill that must be learned and practiced. As noted above, many new reviewers have not received formal training on how to conduct a peer review. Experienced reviewers should consider creating opportunities for trainees or new practitioners to peer review an article with mentorship. A previous publication has provided recommendations on how to involve trainees in the peer-review process.¹³ This hands-on experience will allow the novice reviewer an opportunity to develop confidence and increase the likelihood of providing a high-quality review. This collaborative opportunity can be rewarding for the novice and experienced reviewer.

Conclusion

Serving as a peer reviewer can be an intimidating experience because many practitioners are not familiar with the steps of peer review and do not have formal training in how to perform a high-quality review. Peer reviewers should be knowledgeable about the steps of the peer review process and the expectations of peer review to have a better appreciation for their role in ensuring timely publication of high-quality articles.

Article Information

Affiliations. Department of Pharmacy: Clinical and Administrative Sciences (PNJ, JLM), College of Pharmacy, University of Oklahoma Health Sciences Center, Oklahoma City, OK.

Correspondence. Peter N. Johnson, Pharm.D.; peter-johnson@ouhsc.edu

Disclosure. The authors declare no conflicts or financial interest in any product or service mentioned in the manuscript, including grants, equipment, medications, employment, gifts, and honoraria. Dr. Miller serves a Section Editor with the *Journal of Pediatric Pharmacology and Therapeutics*. Dr. Johnson serves as an Associate Senior Editor with the American Journal of Health-System Pharmacists. The article reflects the opinions of Drs. Miller and Johnson and not the *Journal of Pediatric Pharmacology and Therapeutics* and *American Journal of Health-System Pharmacists*.

Acknowledgement. The authors would like thank Michael Reed, PharmD, FCCP, FCP, FPPA, Editor-in-Chief with the *Journal of Pediatric Pharmacology and Therapeutics*, for his assistance and feedback on this article.

Copyright. Pediatric Pharmacy Association. All rights reserved. For permissions, email: membership@pediatricpharmacy.org

References

- Nahata MC, Sorkin EM. Responding to manuscript reviewer and editor comments. *Ann Pharmacother*. 2019;53(9):959-961. doi: 10.1177/1060028019849941
- Janke KK, Bzowyckyj AS, Traynor AP. Editor's perspectives on enhancing manuscript quality and editorial decisions through peer review and reviewer development. *Am J Pharm Edu.* 2022;86(4):73. doi: 10.5688/ajpe81473
- Medina MS, Draugalis JR. "What if we all said now?": removing barriers to peer review. Am J Pharm Educ. 2022;86(4):8746. doi: 10.5688/ajpe8746
- Grainger DW. Peer review as professional responsibility: a quality control system only as good as the participants. *Biomaterials*. 2007;28(34):5199-5203. doi: 10.1016/j. biomaterials.2007.07.004
- Perlis RH, Kendall-Taylor J, Hart K, et al. Peer review in a general medical research journal before and during the COVID-19 pandemic. JAMA Network Open. 2023;6(1):e2253296. doi: 10.1001/jamanetworkopen.2022.53296
- Kowalczuk M, Samarasinghe M. Comparison of acceptance of peer reviewer invitations by peer review model: open, single-blind, and double-blind peer review. International Congress on Peer Review and Scientific

Publication. https://peerreviewcongress.org/abstract/ comparison-of-acceptance-of-peer-reviewer-invitations-by-peer-review-model-open-single-blind-anddouble-blind-peer-review/#:~:text=Results,peer%20review%20journals%20(Table). Accessed March 27, 2024.

- Kondziolka D, Couldwell WT, Rutka JT. Putting pen to paper during a pandemic: increased manuscript submissions to the JNS Publishing Group. *J Neurosurg*. 2020;133(4):947-949. doi: 10.3171/2020.7.JNS202691
- Jackson JL, Bates C, Asch SM. Peer review at JGIM. J Gen Intern Med. 2021:36(12):3657-3658. doi: 10.1007/ s11606-021-07250-1
- Bauchner H, Fontanarosa PB, Golub RM. Editorial evaluation and peer review during a pandemic: how journals maintain standards. *JAMA*. 2020;324(5):453-454. doi: 10.1001/jama.2020.11764

- Evans AT, McNutt RA, Fletcher SW, Fletcher RH. The characteristics of peer reviewers who produced goodquality reviews. *J Gen Intern Med.* 1993;8(8):422-428. doi: 10.1007/BF02599618
- DiDomencio RJ, Baker WL, Haines ST. Improving peer review: what reviewers can do. *Am J Health-Syst Pharm*. 2017;74(24):2080-2084. doi: 10.2146/ajhp170190
- Tips on reviewing a paper. Journal of Pediatric Phamacology and Therapeutics. https://meridian.allenpress.com/ DocumentLibrary/PPAG/Reviewer-Tips.pdf. Accessed March 27, 2024.
- Johnson PN, Parman A, Miller JL. Training the next generation of peer reviewers: steps for guiding pharmacy learners through the peer review process. *Am J Health Syst Pharm*. 2024;81(5):e137-e140. doi: 10.1093/ajhp/zxad277

Appendix: Template for Reviewer to Develop their Global and Specific Comments to the Authors

Confidential Comments to the Editors: [This section is for the peer reviewers to provide their overall confidential comments to the Corresponding Editor. These comments would be developed during Step 5 of the steps of peer review. Considerations for this section would include the following questions: Is the article appropriate for the journal? Does the manuscript include valid methods and results? Is the manuscript well written? What are the strengths of the manuscript? What are 2-3 major concerns with the manuscript?].

Thanks for the opportunity to revise this manuscript. I reviewed this article with a PGY2 Pediatric Resident. I commend the authors for their attempt to answer a question (i.e., use of ipratropium in neonates with chronic lung disease) that does come up in the neonatal intensive care unit (NICU) setting. Overall, I think the writing quality is marginal as I have some significant concerns about the description of the methods, results, and discussion section. There were some significant grammatical concerns that could be addressed by the Copy Editor if accepted for publication. However, these issues really do impact the overall readability of the manuscript. In addition to these concerns, I have some significant concerns with this manuscript that are related to the study design and analysis, which impacts the results and overall takeaway message of the manuscript.

Example:

- 1. Treatment pathway: In order to truly assess the impact of ipratropium on the NICU length of stay in patients with bronchopulmonary dysplasia, there is significant information missing in regards to the institution's treatment algorithm for patients with chronic lung disease. Specific missing details are noted below:
 - a. Ipratropium: There is no mention on the timing of the ipratropium with albuterol. Given that timing of interventions plays a significant role on the outcomes of chronic lung disease, the authors must include some sort of analysis to address this.
 - b. Corticosteroids: There is no specific information included on the dosing (mg/kg/day) or dosing frequency. There is considerable variability in the dosing utilized in the NICU for patients with chronic lung disease. In addition, there is no mention on what type of steroids were used. Therefore, it is truly difficult to determine the impact that corticosteroids may have had on the NICU length of stay.
 - c. Additional therapies: Considering that these patients were in the NICU setting, there is no mention of additional therapies that patients may have received like caffeine, inhaled corticosteroids, and sedative/ opioids. All of these medications may potentially directly or indirectly affect the NICU length of stay.
- 2. Analysis:
 - a. Power calculation: There is no mention of a power calculation. Was this performed?
 - b. Confounding variables: To me the fatal flaw of this manuscript is the lack of a multivariable analysis that controls for confounding variables. In neonates with chronic lung disease, there are a number of variables that may influence outcomes aside from the ipratropium. Therefore, it is really difficult to accept the findings of this study. I would recommend that the authors consult a biostatistician.

It is plausible that the authors could address some of the concerns I have highlighted in my comments to the authors. However, in order to address the methodological concerns, it would require a significant overhaul, and if those concerns are addressed, it would be a different manuscript. Therefore, I would recommend to release.

Comments to the Authors:

Global Comments to the Authors: [This section is where you would provide the overall assessment of the article. Would provide an assessment of the strengths and the major areas for improvement of the article. Make sure that the areas of improvement are in alignment with your specific comments below.]

Example:

I commend you and your colleagues for attempting to address this important clinical question. This question has come up in the care of patients at our facility as well. I have some concerns about the methodology and analysis of the present study. My major concerns include the following:

- 1. Power calculation: There is no mention of a power calculation. Was this performed? The sample size is small, and there is a potential for a type 2 error with the primary objective.
- 2. Confounding variables: Given the number of confounding variables in this study (e.g., gestational age, comorbidities, corticosteroid exposure, and additional medication therapies this patient received), I would recommend consultation with a biostatistician to determine the need for a multivariable analysis of the primary outcome. Without controlling for these variables, then it is difficult to accept the results of your bivariate analysis.

Specific Comments to the Authors:

[In this section, you should provide an assessment on each area of the manuscript. It is important that you utilize the line number or alternatively the page number/paragraph to highlight the specific sentence or sentences of concern.]

Example:

- 1. Title: No specific concerns noted.
- 2. Abstract:
 - General comment: Would revise and try to use complete sentences.
 - Methods:
 - Would add dates of inclusion of your study.
 - Would also add specifics of the data analysis plan.
 - Results:
 - Derivide one sentence to provide a general overview of baseline demographics.
 - De The data provided in line 15-16 does not match what you have in the results section of the manuscript.
- 3. Introduction:
 - Lines 36-39—Provide references for this statement as this would not be something that would be general knowledge of all practitioners. Also, there was a study published a few years ago that is applicable from the NICU setting (include specific reference citation).
 - · Recommend ending the introduction section with one sentence stating the purpose of the study.
- 4. Methods:
 - Lines 46-47: These data were obtained from 2012-2017, and the study seems to be outdated given the recent advances in the NICU. Please address if these dates of inclusion are correct.
 - Treatment pathway: In order to truly assess the impact of ipratropium on the NICU length of stay, there is significant information missing in regards to the institution's treatment algorithm for patients with chronic lung disease. Specific missing details are noted below:
 - Ipratropium: There is no mention on the timing of the ipratropium with albuterol. Given that timing of interventions plays a significant role on the outcomes of chronic lung disease, the authors must include some sort of analysis to address this.
 - Corticosteroids: There is no specific information included on the dosing (mg/kg/day) or dosing frequency. There is considerable variability in the dosing utilized in the NICU for patients with chronic lung disease. In addition, there is no mention on what type of steroids were used. Therefore, it is truly difficult to determine the impact that corticosteroids may have had on the NICU length of stay.
 - Additional therapies: Considering that these patients were in the NICU setting, there is no mention of additional therapies that patients may have received like caffeine, inhaled corticosteroids, and

sedative/opioids. All of these medications may potentially directly or indirectly affect the NICU length of stay.

- Statistical analyses:
 - Power analysis: Since you are comparing the NICU length of stay between patients with and without ipratropium, it is unclear if you performed a power calculation. Given that this is a small sample size, there could be a potential risk of a type 2 error since you did not find a difference between groups. Please clarify.
 - Multivariable analysis: Given the number of confounding variables, it is difficult for me to understand why you just performed a bivariate analysis between groups rather than a multivariable analysis that would include the impact of other concomitant factors. Would recommend you consult a biostatistician.
- 5. Results:
 - Lines 67-68: Would provide specific details on the use of corticosteroids including dosing frequency and total daily dose.
 - Global comment: Please address how many patients may have received 0.25 versus 0.5 mg q 6 hrs of ipratropium. Also please provide duration of albuterol and ipratropium.
- 6. Discussion:
 - Global comment: The discussion seems to be focused mostly on the role of ipratropium in the emergency department setting. There is really no mention from the authors on how these results could differ in the NICU setting. In addition, there is at least one study in the pediatric ICU population that assessed this therapy previously.
 - Lines 105-109: You mention some specific therapies that patients received. However, these details belong in the results section not in the discussion section as they were not introduced previously.
- 7. Conclusion: No specific concerns noted
- 8. References: No specific concerns noted
- 9. Tables/figures
 - Table 1: This table is not necessary since much of this data is summarized in the text.
 - Table 2: This table provides the median and interquartile range of the data. However, in the text, the authors provide the mean and standard deviation. Would suggest to be consistent in the description of the data.
 - Figure 1: Would suggest adding a legend to provide more description on what the lines represented mean.