Peer Review File

Article information: https://dx.doi.org/10.21037/tp-21-61

Reviewer A	Author comments
The authors have undertaken an important topic in pediatric critical care. The breadth of the review article is vast and while the authors have attempted to be comprehensive, the result is a manuscript that is not concise, has some redundancy, and lacks focus. For example, the first 2 paragraphs of the introduction are very similar in conveying that morbidity has increased among survivors.	We appreciate the reviewers comments, and have both generally attempted to refocus the article to be more concise and amended the introduction as recommended.
However, discussion of the fiber myelination of the infant brain is distracting as the concluding sentence of the first paragraph (lines 50-53).	Amended.
Similarly, the discussion of adult ICU and NICU guidelines is somewhat distracting as currently laid out (ex lines 222-225 and 232-234); it may be more helpful to have a section dedicated to lessons learned from other ICU experiences with long-term outcomes at the end of the manuscript.	Amended.
Similarly, the discuss of COVID-19 would be best served as a lesson learned from current use of digital health or something to this effect.	The brief mention of COVID-19 refers to the innovations that have come from this experience at some sites in establishing post-hospital follow-up clinics, both in person and virtually. We feel this is well-positioned.
The current organizational structure of the manuscript is also difficult to follow in terms of understanding challenges and barriers. It might be more helpful if the	Many thanks for these recommendations. Due to workload and timeline commitments, we are unable to make these structural changes at this time. We

authors restructured the manuscript to concisely outline considerations (why long-term outcomes are important globally, breadth of ages, appropriate domains/assessments, format), challenges (lack of resources, lack of access, time burden), and solutions (consideration of child factors, parent/family factors, and illness/treatment factors to prioritize/target efforts). As currently structured, the challenges are interspersed with the considerations making it a little difficult to get a sense of what the challenges are in totality (e.g. the limitation of a lack of baseline data is discussed in the section on Why ages are important). Consider subheadings for challenges and solutions within each section.	therefore have refined the title to 'considerations for clinical practice', as opposed to challenges and barriers. We believe this has led to a more focused, clinically oriented manuscript useful to the readers of Translational Pediatrics.
Having a section on "Other Challenges" is a bit overwhelming at the end of the manuscript. Consider reframing as suggested above with a section on considerations regarding retention with a subheading for challenges and solutions. Again, integrate lessons learned from adult and NICU experiences into its own section.	Amended
Consider eliminating the discussion about statistical considerations; it is distracting (lines 408-416).	Section has been removed.
Lines 416-420 would be better discussed in the section on parent/family factors (Beginning with Line 147).	We respectfully left this discussion in the current section as reasons for non-compliance with follow-up are multifactorial.

Similarly, consider eliminating the section on "Does follow-up care make any difference?" or making this more concise.	Deleted
The knowledge gaps and conclusions sections should also be shortened.	Have left knowledge gaps. Conclusions amended.
Throughout the manuscript, the authors have interjected subjective assessments more reflective of an editorial than an objective, unbiased review. There are some contradictions in the editorial comments that are interspersed throughout. For example, the final sentence of the 2nd paragraph (lines 66-67) acknowledges that pediatric literature has prioritized long-term outcomes but the final sentence of the subsequent paragraph (lines 80-83) discussed that most pediatric critical care trials focus on short-term outcomes and "continuing with this approach will be unfortunately insensitive…" Some of the language is stylistically more appropriate for a book chapter than a review article (e.g. line 288-290: Certainly, the African proverb of 'It takes a village…')	Amended
Ensure that acronyms (ex: CHD) are spelled out when first utilized (e.g. congenital heart disease (CHD)).	Amended.
Avoid colloquial language such as "fly under the radar" (line 239-240) and "perfect storm" (line 246) or "deep dive" (line 275).	Amended.
Reviewer B	**Author Comments**

The impact of the manuscript is limited by its broad topic review and many general statements that are not sufficiently specific and without clear evidence provided. If this article is meant to be a narrative review, please review reference article and checklist provided by the journal for further specifics related to methodology (e.g., methods section).	Whilst we appreciate the value of an unsystematic narrative review, this paper was not written as such. This paper has been written as a commentary (another type of narrative review) and as such is written with a particularly expressed opinion with the purpose of provoking scholarly dialog among readers. Unfortunately, we do not have the capacity to convert this paper to an unsystematic narrative review at this time.
The goal of the manuscript is stated as: "In viewing long-term outcome assessment through a complex intervention lens, this paper outlines the important considerations, challenges and barriers for implementing the current evidence and understanding on PICS-p and long-term outcomes into practice." A more focused approach with a clear methodology for collecting the key data to support the findings in the manuscript would be a more impactful addition to the literature.	With great respect, we were tasked with writing an unstructured review article on this important topic; thus, there are no search terms. However, as clinical and research experts in the field of PICU outcomes, our searches provided us with inclusive foundational knowledge to summarize and convey to readers.
Also, the mix of discussion related to clinical and research follow-up barriers and strategies without a clear delineation between the two environments results in confusion within the manuscript. Similarly, much of the manuscript describes "follow up" but this could be interpreted to mean a variety of interventions. The term "follow-up" should be defined or replaced with more specific descriptions to which the authors are referring. For example, does this universally mean a follow-up clinic or is	We appreciate your feedback in this area, however a lot of considerations for implementation are informed from research given that the idea of PICU follow-up is relatively new. Few reports of clinical follow-up are published, therefore information from research has been extrapolated.

it sometimes data collection for research follow-up and non-traditional clinic settings?	Definition of follow-up amended.
Additionally, there are many examples of colloquial terms that are not sufficiently specific for publication. Here are some examples: “In an ideal world” “for some time” “fly under the radar” “go so far as” Delphi “exercise” “cut-off” “deep dive” “hard-to-reach” “back-up” “wanting to get on with life” “been promising” “do not work”	Amended
Abstract: Lines 39-40 suggest that sequelae described in PICS-p must last the duration of the lifetime. Consider rewording as it is only important that sequelae last beyond the acute illness/injury period.	Amended
There is not a clear research question defined in the abstract.	Aim added.
Background The introduction could greatly benefit from editing to reduce redundancy. Much of paragraph 1 is restated paragraph 2.	Amended
Also, a more balanced presentation of the	Trials added. Information on

current attention to PICS-p in some studies (even RCTs) seems appropriate (e.g., RESTORE study, LAPSE, THAPCA, POCCA). This is mentioned later in the manuscript but omitted in earlier sections. Additionally, as the authors identify in lines 140-141, family and environmental factors can have more of an impact on long-term outcomes than PICU interventions, thus, limiting the utility of long-term outcomes to serve as primary outcomes in interventional trials. This challenge should be discussed more clearly related to the use of long-term outcomes in clinical trials.	socioeconomics and family functioning and its association with long term outcomes in included under the heading Parent/Family Factors.
Why are long-term outcomes important? Based on the stated goals of the manuscript, the section entitled, "Why are long-term outcomes important?" can be removed in order to focus and shorten this lengthy review. Key data elements can be added to the Background section, if indicated.	Amended.
Who should be followed up? Both the child and patient/family factors sections discuss SES factors related to poor outcomes- consider restructuring so that this point is not duplicated across multiple sections.	Amended
Illness and treatment factors: This section has important data related to sedation medications, however, omits key data related to the intensity of the ICU experience. It does not provide a broad overview of the literature	Amended

incorporating other ICU factors (severity of illness, procedures, etc.) associated with PICS-p in children and their families. (see recently published review by Woodruff and Choong [Children March 2021] for a more balanced review of the risk factors)	
Please provide a reference for the sentence beginning on line 189.	Amended
The authors refer to symptoms of PTSD and PTSS—they should modify to be consistent in their description as the differences in these definitions are important.	Amended
What ages are important? Line 239: "Additionally, once children develop literacy skills…" This sentence does not account for the important perspective of the parent/caregiver in assess the child's abilities. Given the proportion of patients with neurodevelopmental impairments in many PICU cohorts and the need for baseline assessments, the need for proxy report will not easily be avoided. Additionally, it does not address the necessity for the child to be able to comprehend time. For example, when you ask a young child to assess the prior month, it takes a certain developmental capacity to consider the last month versus state their assessment at the current time period.	Amended
Line 262: "too late for effective	

intervention" is a broad characterization and potentially incorrect for some impairments and/or interventions. Sweeping statements such as these would be more impactful if targeted to specific impairments and interventions. Similar comments related to the subsequent statement, "These minor morbidities are high prevalence, low severity…" During this section, the authors should consider highlighting the important work primary care physicians do to identify neurodevelopmental impairments and mental illness. As it currently reads, this paragraph could be alienating to that group of providers.	Amended Amended
Paragraph starting on line 269 does not directly address age of the patient.	Information from this paragraph was moved to Knowledge Gaps and Future Directions for the PICU population.
Most important domains and assessments Line 286: "The COS also offers important extended family outcomes…" While many of the domains in the COS-E are related to family outcomes, the majority of the COS-E domains are not directly to families. Consider revising this sentence to increase accuracy.	Amended
Line 294: "To date, research has either only addressed a singular domain or assessed overall function using crude measures." What is meant by crude measures? Also, the scoping review suggested that most manuscripts evaluated more than one domain and frequently not only overall health. Please clarify what is meant by this sentence.	Amended

Line 296: “While these methods may offer a deep dive into one area… huge insights and benefits to the PICU community.” This sentence is very general and not sufficiently specific to directly inform future work.	Amended
What is the best format for follow-up? Line 301: “While it may seem obvious to some…” This sentence is reflective of opinions. It would be more informative to more directly provide pros and cons of intensivists providing follow-up care versus follow-up care provided by other providers (rehabilitation medicine physician, pediatricians, etc.). Additionally, this section could be strengthened by a discussion related to the barriers of payers for post-PICU follow-up care as this is a primary obstacle in many settings. Describing payment structure of post-PICU follow-up across international settings with differing payer models would be highly informative and, in my opinion, is a necessary component to this discussion of barriers that is not adequately addressed in this manuscript.	Sentence removed. Cost-effectiveness studies and costs of initiating and maintaining post-ICU follow-up clinics are lacking; discussion on the critical importance of this topic was added.
The CHD population approach to follow-up care described beginning on line 334 is really helpful. Additional information about other examples of follow-up such as neonatal follow-up would directly address that stated goal of this work. For example, more details about “several levels of care” (line 341) would be	Amended

helpful.	
How do peer support groups fit into the structure of PICU follow-up? While I agree they have a valuable place in the holistic care of the patient and family, the discussion related to PICU support groups is a bit disconnected from the follow-up care. As stated above, a more specific definition of "follow-up" would be helpful. Is it meant to encompass all forms of post-ICU care even if not provided in a traditional clinic setting? If so, are there examples in pediatrics that can be provided?	Discussion of peer support groups removed. Amended
Line 378: Is there good evidence that digital technologies or ICU follow-up clinics can decrease hospital readmission rates? Also, how do these digital technologies remove financial and societal barriers to recovery? In fact, it may do the opposite as many families do not have reliable internet access with which they can access these services.	We agree with the reviewer remarks; however there are few data to support the impact – positive or negative – of technologies on ICU follow-up clinic impact and attendance. This idea was added to the
Line 389: I like this paragraph but what is a "just in case" intervention? Can the authors provide more specifics or examples?	Amended
Other Challenges Recommendations starting on line 397: Are these meant for clinical or research-related follow-up? Many of the recommendations don't seem to relate to clinical follow-up which has been the focus of the article up to this point.	Amended
Line 400: "Interim visits with consistent	Amended

staff…" Please clarify what is meant by this statement.	
Line 406: Even parents who don't have traditional work schedules, may require accommodations due to other responsibilities (other children or family members they care for, etc.).	Amended
Line 407: "no" outlay?	Amended
Line 424: It is not clear to me how Davies comment reaffirms the need to assure representativeness of the general PICU population. It would be more informative to cite relevant research in PICU outcomes and their enrollment and retention rates.	Amended
Much of the paragraph beginning on line 429 has been addressed in earlier sections.	Amended
Line 448: "Some PICUs now use…" can you cite this?	This information is unable to be referenced, as knowledge is based on personal communication and site visitation.
Knowledge Gaps and Future Directions Line 508: "In order to transform…" This sentence feels overly pessimistic. One could argue that many of our patients do not have poor outcomes, despite a lack of follow-up care.	Amended
Line 511: "To date, the research describing these outcomes has been limited to specific medical conditions…many studies assess	Amended

singular outcomes" the results of the scoping review suggest that many studies evaluate the general picu population and multiple domains.	
Conclusions The oncology follow-up model is introduced in the conclusion but not discussed in the main article. Are there key lessons from oncology follow-up clinics that could be useful?	Amended
Line 542: "In some interventions, direct treatment effects differ from short term versus long term outcomes." Is there direct evidence that can be cited to support this?	Amended
Figure 1: In the Follow-up Services box, some items are challenging to read as they do not remain within their intended text box. The meaning of "Profiles" at the bottom of the figure is not entirely clear.	We are unable to see the formatting difficulty in our files but will ensure original files are included in the re-submission. PDFs also provided.
Figure 2. Box to the left: words extend beyond the lower end of the box, the Parent/Family and Environmental factors focus heavily on maternal factors without attention to other caregivers.	We are unable to see the formatting difficulty in our files but will ensure original files are included in the re-submission. PDFs also provided.
Line 228: has◊ have	Amended.
Line 234: the 3) burden	Amended
Line 261: bought ◊ brought	Amended
Line 278 ◊ do you mean heterogeneity where it says homogeneity?	Yes, amended.

Line 345: recovery ◊ recovery	Amended.
Notation for HRQoL is not consistent- sometimes as QoL, sometimes written out and sometimes HRQoL.	Amended.
Line 487: moto-> motor	Amended.
Define terms: ECMO and CVVH	Amended.
Reviewer C	**Author comments**
Page 8, line 176: Please reword "poor health prevention''. It is difficult to understand this long sentence on first eye.	Amended.
Page 12, line 262: I think "bought" needs to be replaced with "brought".	Amended.
Authors recommend, keeping the school aged high risk children on surveillance screening even when initial screens are not concerning. Do we have a timeframe in mind? For how long this surveillance needs to be done? And how frequently? Is there a data form adult studies that can be extrapolated to pediatric population? It is possible that child may fail further grades but that could be unrelated to PICU course, specially so long out of the PICU stay. In these scenarios, it will be difficult to attribute it to PICU stay for this outcome. I understand there may not be a perfect answer to these questions at this point and a lot more research in this subject would be needed to have a much focused care.	Neonatal studies recommend follow-up at key transition timepoints, including 4-5 years (entering primary/junior school), 11-12 years (entering secondary/senior school) and 17-18 years (entering tertiary studies or workforce). Neonatal papers also advocate for later screening, even if earlier screens not concerning, as some skills are not developed until older ages. Eg executive function and social/behavioural concerns. Adult ICU studies do not provide time line data that can be extrapolated. Additional commentary was added for the PICU population.