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**Article Title:** The impact of the COVID-19 pandemic on routine childhood vaccination rates in an academic family health team: a pre-post analysis of a retrospective chart review

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**Reviewer: 1**

Dr. Patricia Cresswell Parkin, Hospital for Sick Children

Thank you for the opportunity to review this manuscript. The authors ask an important question and report some important findings. There are some limitations to the study, which the authors address. I may have arrived at a different interpretation of the results. The following are some comments for consideration:

1. Abstract – Results section – could the authors provide data for this section?

**Thank you. The manuscript has been revised accordingly.**

2. Study Objective – page 16 line 45 – should the setting be described as two-site rather than multi- site?

**Thank you for this suggestion. The manuscript has been revised accordingly.**

3. Methods – the authors could consider adding as the first subheading a section describing Study Design.

**We have added this heading and include a basic description of our design.**

4. Methods – Study Setting – the authors provide an excellent description of the study setting and highlight the facilitators to providing “uninterrupted routine childhood vaccinations”. Since the primary objective is to report rates, representativeness of the setting and population is important, and the authors appropriately address this in their Discussion.

Thank you!

5. Methods – Participants – in Methods, the authors report that they collected DOB and sex (M/F). Was it possible to collect other participant characteristics to further address representativeness?

**We have added additional available demographic information to the results section as detailed above from lines 171-182.**

6. Methods – Outcome Measures – the authors write: “We estimated pre-post COVID-19 differences in the proportion of patients...”. Since the authors describe this further in the Statistical Analysis section, it may not be needed here.

**We will address this in the below comment.**

7. Methods – Outcome Measures – the sentences providing definitions for the pre and post groups could be included in a separate section with a

separate subheading since these are not outcome measures. This section could be placed before the Outcome Measures section. Table 1 is very helpful.

**Noted. Thank you!**

8. Methods – Design – The use of a before-after study design to address this question seemed appropriate. However, I struggled with the complexities. If I understand correctly, data from some children could be included in more than one of the 10 immunizations? Was the unit of analysis the immunization or child? For the post-group, is it possible that some children received earlier immunizations pre-Covid19?

Thank you for highlighting this confusion. In this study, the unit of measure was each individual vaccine and not the child. There are a number of children who straddle both the pre- and post- pandemic time periods but each vaccine will be considered in the time period in which it was scheduled to be given.

9. Results – Participant Characteristics for the combined groups are described in the text (age and sex). Would it be meaningful to describe the two groups separately? As per a comment above, are there any additional characteristics that could be included in a Table of Participant Characteristics? The Table could include columns for each group and a column for the combined groups.

**Thank you for the suggestion. We have addressed this in a prior comment. Please see response to comment #13 for extended demographic data. We combined the groups because of the study design where we analyze events at the vaccine level. Thus, there may be children in the group with vaccination events in both the pre and post-COVID period, rather than two distinct cohorts of children.**

10. Table 2 – there is a typo in the header “Delated”

instead of “Delayed” **Thank you for catching this.**

**This has been fixed.**

11. Table 2 – it might be helpful to use terms consistently such as vaccinated-immunized; timely-on time; no immunization-not vaccinated.

**We have revised the heading to standardized our terms.**

12. Table 3 – median time to vaccination – consider adding

units in brackets eg (days) **We have added the units in**

**brackets.**

13. Results – In Results, the authors write: “For the later vaccines administered at 12, 15, and 18 months, the results were suggestive of modest declines in timeliness of vaccination and up-to-date

14. vaccination status in the post-COVID-19 period compared to the pre-

COVID-19 period.” A similar sentence is written in Discussion and could be removed from Results. The Results section could focus on the data rather than the interpretation.

**The sentences interpreting vaccination differences have been removed and will be incorporated into interpretations.**

15. Discussion – Following the recommendations of Docherty (BMJ 1999;318:1224–5) the first paragraph could be a “statement of principal findings”.

**We have added a paragraph stating our findings found from lines 207-212.**

16. Discussion – Canadian Pediatrics Society should be changed to Canadian Paediatric Society.

**Thank you for noting the error. It has been corrected.**

17. Discussion – the authors write: “However, we found that vaccine completion rates at the 12- month, 15-month and 18-month ages were modestly lower in the post pandemic period.” And “it may be clinically significant that there was an increase in the delayed vaccination rate (ranging from 5-15%) in the post COVID-19 period depending on the age group analyzed...” However, the between-group differences appear to be clinically (and statistically) meaningful at almost all time points, for the 12-month, 15-month, and 18-month immunizations. For example, at the 12 month Men C-C (Meningococcal Conjugate C) the percent immunizations on-time was 80% vs 66% (OR 2.0). The percent no-immunization was 5.6% vs 13.4% (OR 2.6). This magnitude may not be interpreted as “modest” by many readers.

**Thank you, we have revised this as suggested. Edits are found on line 222.**

18. Discussion – In Discussion, the authors write: “...childhood National Vaccination Coverage Survey (cNICS) and declares a national vaccination goal of 95% for each childhood vaccine (11). Our FHT vaccination rates seemed on par with cNICS's Ontario data for 2017...”. Could the authors report cNIC's Ontario data for comparison with their no-immunization rate of 5-15% for the 12-18-month immunization rates?

The cNICS data for Ontario does not specify immunization rates at the 12 month or 18-month mark. Rather, that report presents data for each vaccine, as well as a non-immunized rate for Ontario, for up to 2 years of age - there is no breakdown of vaccine coverage they provide for specific age milestones less than 2 years of age.

19. Discussion – “Some jurisdictions have reported declining early childhood vaccination rates as a result of COVID-19...”. The authors may consider modifying this sentence to ensure the reader knows that these are non-Canadian jurisdictions, especially as a previous sentence highlights that this is the “...first study to examine childhood vaccination data in the time of COVID-19 from an Ontario primary care perspective.”

**Thank you. The manuscript has been revised to clarify that the other reported data is from the United States. Please see edits on line 248.**

20. Discussion – The authors cite reference #5 which includes over 23,000

children in a US primary care network (Bode et al. COVID-19 and Primary Measles Vaccination Rates in a Large Primary Care Network, Pediatrics 2021). Bode et al write: “From March 2017 to March 2020, the average proportion of 16-month-old children with MMR vaccination was 72.0%, which decreased to 66.8% in April to May 2020 ( $P < .001$ ) and then to 62.4% ( $P = .02$ ) from June to August 2020...” and in their Discussion interpret their findings as: “Given the baseline low vaccination rates even before the pandemic and the subsequent decline, we face a critical need to improve timely vaccination and provide catch-up opportunities...”. This study setting and population is very different from the current study. However, both demonstrate clinically meaningful declines. This could be considered in the interpretation of the current study.

**Thank you for your helpful suggestion. Please see revisions in this paragraph emphasizing the similar trend in a different setting on line 250.**

21. Discussion – The authors acknowledge an important limitation: “This retrospective chart review shows the rate of vaccination during COVID-19 in two settings where service-provision factors were not significantly changed; therefore, our data likely under-estimated the effect of the COVID-19 pandemic on vaccination rates and may not be representative of the broader context.” Considering the previous comment, perhaps another interpretation is that despite optimal circumstances (the academic FHT study setting and population) meaningful declines were observed in immunization rates.

Thank you for pointing this out. We will include a revision in this paragraph to present the balanced interpretation you have suggested.

## **Reviewer: 2**

Dr. Zulfiqar Bhutta, The Hospital for Sick Children

This is an important study of the impact of COVID-19 mitigation strategies early on in the pandemic on disruption of childhood immunizations. It shows what has been demonstrated from other countries that there was an impact. In this instance, the findings of the disruption being greater for older infants post 6 months, are important and merit further discussion. Do families differ in their perception of boosters and second tier vaccines such as Meningococcal and Varicella vaccines?

I wonder if the authors could have provided further information on inequities in vaccinations by data reflecting maternal age, gender, residence and if available ethnicity/immigration status. There is now enough data available on these disparities in Ontario post-COVID-19 and any study of this nature is incomplete without these qualifiers, especially as remedial measures would need to take all of these elements into account.

**Thank you for this suggestion. Unfortunately, our EMR does not link infant charts to maternal charts in a way that would allow us to easily pull these maternal characteristics for our study population. We do agree however that this would be a valuable data set to explore.**

How do the data compare with global experience especially from the USA, UK and the European Union? It would be interesting to see commonalities

and temporality of impacts, if any.

**Thank you for your reflections. These are interesting points that are brought up regarding the need to examine the multiple factors affecting these different jurisdictions across the world. For brevity, we did include a review of some reported findings from the USA in our discussion. We believe appropriately addressing the global experience behind vaccination rate declines may necessitate a larger undertaking, which we feel is beyond the intended scope of this article.**

**Reviewer: 3**

Dr. Joanna Merckx, McGill University Faculty of Medicine, Biomérieux Canada Inc

The authors estimate the difference in childhood vaccination coverage between the pre and post- pandemic period, up until November 2020, in a primary care health care practice group in the province of Ontario, Canada. They calculate both the effect on coverage and timeliness of vaccination for 10 recommended vaccines in eligible children up to 2 years old.

The inclusion of timeliness is an asset for the manuscript and has been less described in the published literature so far. Data from Canada are lacking and this is a start.

Thanks to the authors for their efforts to collect the data and publish on this important topic. The article is clearly written and reads easily.

**MAJOR COMMENTS:**

-The setting is prone to be minimally representative to report on the average impact of the pandemic on childhood vaccination coverage, both in Canada and moreover globally. The main question remains if this can however be transportable to other settings. The answer seems yes, conditioning on reporting more in detail on the (more favourable) setting and population included in this study.

**Thank you for the thoughtful reflection around generalizability and feedback on our study setting. Please see comment above on: overall comment #13 which includes additional demographic information for our cohort.**

The setting of the clinic is, as described in the discussion, indeed a best-case scenario. It would be informative to reflect this early in the manuscript, including in the abstract. How does the clinic compare to vaccination coverage in the rest of Canada? Is the population different? How unique is the group dealing with vaccination? The fact that this group publishes on vaccine uptake shows already an interest from the team and its clientele will also differ. Additional information is warranted. Are there waiting times to get into the practice as a patient? Is this based on closeness or how do families become patients at the clinic? Are there provincial waiting lists? Is there free choice of clinician? And further: Neighbourhood characteristics? Patients general characteristics, more related to SES factors.

**Thank you! We have noted this and attempted to address these thoughts in our manuscript edits.**

The period described has also been far from the worst period of the epidemic in Ontario. In this sense this is also an underestimation of the impact of the pandemic. Investigation of the vaccination rates over a longer period plus comparison with a different province (and better more than one) would largely improve the value of the article, but is not feasible for this manuscript.

**Thank you for the suggestion. We have included further emphasis on this issues of sampling in a less severe phase of the pandemic. Please see lines 284-286**

How can this manuscript more clearly inform the need to collect and analyse data of those settings and groups with the largest impact from the pandemic indirect effects? An effort to include those data (in further research) is warranted.

This is an interesting reflection. We agree that there are important matters to consider and have added a comment in the end of our interpretation section to inspire direction for future research. (burden on preventative care?)

The article is very Canadian centered – which is as such (and given the venue) of course ok. This is however also the case for the referenced work in the manuscript. More in dept analysis is performed on the impact on decreased childhood immunization during the pandemic. How do these result stand taking global data in perspective?

**Thank you for the suggestion again. We would love to learn more about the global perspective, but given the scope of our paper, we feel that this is beyond the message we are trying to convey.**

What do we learn about the differences (and absence of differences) between the vaccines given at the same moment for this rather small group?

We interpret this question to be inquiring about vaccines that are grouped in one visit versus parents deciding to separate the same vaccines over different visits. We believe the sample size of these potential groups in our study are likely too small to draw any meaningful conclusions.

If access and consultation (health care services use) are to be measured: one can take and analyse the vaccines given at the same moment together to have a larger sample size. CI are very wide and thus the data of this study miss precision. The aim of the study is less to investigate specific hesitancy patterns for different types of vaccines, so this can be an option. Was there any sample size calculated?

There was no sample size calculation to determine power given that we accepted all patients that met inclusion criteria within our practice (ie. All of our available patients).

Can the vaccines given at 2-4-12 months not be taken together? The separate vaccines can be added in the supplementary as a separate/sensitivity analysis. There is little additional value in the separate analysis of these vaccines.

**Yes, we recognize that technically this is possible. In our practice, most parents opt to separate vaccines into multiple visits in a catch-up scenario. Thus, we believe the clearest method of analysis remains to analyze the specific vaccine events.**

MMR always remains a specific vaccine which 1. can be given earlier in pre-pandemic times where there is travel to regions with measles outbreaks and 2. is given its history within the context of specific vaccine hesitancy the most separate – specific vaccine. However: if in the supplement separate curves can be added: this is clear. The main objective shifts then mildly towards vaccination moments instead of specific vaccines.

**Thank you for this suggestion. We have**

**included separate curves. MINOR**

COMMENTS

Abstract:

-Adding the date of the start of the pandemic: which date was chosen – is informative.

**We chose March 17, 2020 (the day the province of Ontario declared the COVID-19 pandemic a state of emergency).**

-guideline recommended vaccines: NACI recommended? Globally recommended? In which province? – is provincial.

**The abstract was revised to clarify that we were looking at the vaccinations in Ontario's publicly funded immunization schedule.**

-what with those that did not get their vaccine: time as indefinite? In the manuscript it is clear that this is handled as a fraction of not-vaccinated, however in the abstract this is not understood.

**Please see our edits in methods clarifying this.**

-quantification needed in the results section of the abstract

**Thank you, noted.**

-Best to add in the abstract that these are results from a clinic that prioritized and kept vaccination clinics/appointments open at all times during the pandemic and is the best case scenario as per structural and organizational provision of vaccination.

**Thank you. Please see responses to above reviewer's comments and**

**edits in the "Limitations" section. Introduction:**

-line 52 – p16: to complete routine vaccination, to routine for ....that age or by vaccines? Please see line 135. These are the vaccines administered in the routine publicly funded vaccine schedule in Ontario.

Methods:

Study setting:

-line 41 – p

17: typo

Sources:

-sources: you checked validity of absence of vaccination, but not of correct application of vaccination: did you check how valid your registration system is and what the misclassification rate is in those with full and timely vaccination? There is created some type of partial verification bias.

**Based on our EMR and clinical workflow, it would be highly unlikely that a timely vaccination would have been entered incorrectly. We verified the veracity of our vaccination strings for a small sample of patients with timely vaccinations as an extra precaution. We could have manually reviewed every single patient, but we believe the risk of verification bias to be minimal.**

Outcome measures:

-If they were not old enough for vaccination they were excluded: unclear if all children vaccinated prior to their bd-month mark were excluded. Not all, given MMR prior to age 1yo were included (or was here the 6mo mark used?) Are children vaccinated the week prior to the completion of the e.g. 4mo of age all excluded? How many children were excluded? A flow chart would make this more clear. (as written above)

**For our patients who received early MMR for reasons like travel, we still offer a booster 12 months based on our provincial recommendations. For the purpose of this study, these patients would be flagged by our statistical scripting as delayed for further review as our window in the programming was defined as +/- 28 days.**

-Why is rotavirus not included in the analysis? Thank you to have this explained. The difference schedules indeed make this more complicated. Good to leave your explanation in.

**Thank you for the comment. We have**

**included in line 136. Results:**

-line 12 – page 21: not necessary to report the months of oldest and youngest child – is visual in the tables

**Thank you for your suggestion. We have considered your helpful advice and after re-reading, we elected to keep the section to summarize this information in the text in order to ensure clarity for a variety of readers.**

-line 19-33: this is already half interpretation – half results: is it possible to quantify in the text as well this finding?

**Thank you for your feedback. We have addressed this comment**

**in a prior reviewer's comment.**

Discussion:

-immunization is a cornerstone of primary care: it is the cornerstone of all



preventive medicine – independent of the level of care. If Ontario has a larger proportion of generalists included in vaccination compared to other provinces then this can be added. How does Ontario differ from the rest of Canada, from elsewhere?

**We have considered the wording of this sentence and agree. We revised this for clarity on lines 217-218.**

-Other Canadian data are also available for Quebec where timeliness of vaccination was assessed and estimates include mean time not vaccinated: O'Donnell S, Dubé E, Tapiero B, Gagneur A, Doll MK, Quach C. Determinants of under-immunization and cumulative time spent under-immunized in a Quebec cohort. *Vaccine*. 2017 Oct 13;35(43):5924-31.

**Thank you for your suggestion. We have considered this in our reflection of our analysis and we believe that our reported median time to vaccination is a good surrogate for the mean time not vaccinated.**

-Is another conclusion of your work also not that you would prefer to have data readily available from all jurisdictions and a vaccine coverage database on a country or at least provincial level? Is it up to clinicians to find how they want to register vaccination? Is this not crucial health data to be collected in a rigorous and uniform way? How do you propose improvement of data collection and analysis?

**There is no shared vaccination registry for infants in Ontario. Toronto Public Health does collect vaccination information from parents for school-aged children to identify completeness, but the information source would come from primary care physician offices. For our studied population, data is collected and stored by primary care physicians.**

**We recognize this varies by province. For example, in Alberta, where childhood vaccinations are performed by public health clinics, there is a province-wide registry recording these vaccinations. Unfortunately, this does not exist in Ontario at the moment.**

-"clear division...": why is this not clear: it depends if you want to assess the uptake as such or differential by patients already patients in the practice. Not sure what the message of this limitation is: can this be clarified? Mainly because your patients are part of the practice prior and now – a more in detail description of your general study population can help to define if and to which extent the results would be found back in other Canadian patient populations.

**Noted, thank you. We believe our revisions overall aimed to address this point.**

-Table 1:  
DOB intervals pre- post do not need to be

repeated every time. **Noted.**

-Table 2:  
-Add the details of the vaccines in the footnotes of the table. It takes up unnecessary space and the reader with content knowledge is very aware about the diseases included in the vaccines.

**Thanks.**

-Figure one: maybe move to appendix the graphs of the separate vaccines – include those taken together and make larger and improve readability.

**We have included separate tables.**

-Appendix 1: the article only looks at the first vaccines – not those in older children – the table might be shortened. (this is an official reference, however only up to 2yo is on topic with the manuscript).

**We have made changes to the presentation of this table as noted in above comments.**