

Global caregiver concerns of SARS-CoV-2 vaccination in children with cancer: a cross-sectional mixed-methods study

Authors

Gumy, J.M., PhD¹, Silverstein, A., MD², Kaye, E.C., MD², Caniza, M. A., MD³, Homsy, M. R., MPH⁴, Pritchard-Jones, K., PhD⁵, Bate, J., PhD^{6*} on behalf of St Jude/SIOP Parent and Carer Advisory group

* Corresponding author

Affiliations

¹ School for Policy Studies, University of Bristol, 8 Priory Road, BS8 1TZ, UK

² Department of Oncology, St. Jude Children's Research Hospital, 262 Danny Thomas Place, Memphis, TN, USA, 38105

³ Departments of Global Pediatric Medicine and Infectious Diseases, St. Jude Children's Research Hospital, Memphis, 262 Danny Thomas Place, TN, USA, 38105

⁴ Department of Global Pediatric Medicine, St. Jude Children's Research Hospital, 262 Danny Thomas Place, Memphis, TN, USA, 38105

⁵ Developmental Biology and Cancer Department, University College London Great Ormond Street Institute of Child Health, 30 Guilford St, London, UK

⁶ Department of Paediatric Oncology, Southampton Children's Hospital, Tremona Road, Southampton, UK

Abstract

The objective of this study was to understand global caregiver about SARS-CoV-2 vaccination for children with cancer and to provide healthcare providers with guidance to support parental decision-making. A co-designed cross-sectional mixed-methods survey was distributed to primary caregivers of children with cancer globally between April and May 2021 via several media. Caregivers were asked to rate the importance of vaccine-related questions and the median scores were ranked. Principal Component Analysis was conducted to identify underlying dimensions of caregiver concerns by World Bank income groups. Content analysis of free-text responses was conducted and triangulated with the quantitative findings. 627 caregivers from 22 countries responded to the survey with 5.3% (n = 67) responses from low-and-middle-income countries (LMIC). 184 caregivers (29%) provided free-text responses. Side effects and vaccine safety were caregivers' primary concerns in all countries. Questions related to logistics were of concern for caregivers in LMIC. A small minority of caregivers (n = 17) did not consider the survey questions important; free-text analysis identified these parents as vaccine hesitant, some of them quoting safety and side effects as main reasons for hesitancy. Healthcare providers and other community organizations globally need to provide tailored information about vaccine safety and effectiveness in pediatric oncology settings. Importantly, continued efforts are imperative to reduce global inequities in logistical access to vaccines, particularly in LMIC.

Keywords: Global child health; immunization; pediatric oncology; SARS-CoV-2; vaccine

Introduction

SARS-CoV-2 is a relatively mild disease for healthy children^{1,2}. However, there is an increase in the risk of morbidity and mortality in paediatric cancer patients, particularly from low-and middle-income countries (LMIC)³. In this regard, the clinical value of SARS-CoV-2 vaccination in adult oncology patients has been ascertained as a vital measure to reduce hospitalisation, development of severe disease and death⁴⁻⁶. Although trial data in paediatric oncology groups is lacking, data demonstrating high efficacy of vaccines in children^{7,8} have led to recommendations from global healthcare authorities to vaccinate paediatric oncology children, with formal guidance issued alongside vaccination protocols^{6,9-11}. However, vaccination uptake depends primarily on caregivers' perceptions of acceptability, which are often guided by perspectives about risk – already heightened by exposure to cancer and SARS-CoV-2¹²⁻¹⁴ - governmental and healthcare professional recommendations, and the advice of oncology healthcare professionals¹⁵. A recent study conducted in the U.S., which aimed to understand SARS-CoV-2 vaccine acceptability and hesitancy, showed that vaccine acceptability amongst parents of children with cancer aligned to that of the general adult cancer population¹⁶, with expressed concerns about vaccine safety and efficacy and ongoing need for guidance and education to support decision-making¹⁷.

In this study, we aimed to understand what specific aspects of SARS-CoV-2 vaccination are of concern for paediatric oncology caregivers across 22 countries representing low- (LMIC), middle- (UMIC) and high-income groups (HIC), with the goal of better tailoring guidance and education worldwide.

Methods

Survey design and participants

A primary caregiver survey was co-designed by the COVID-19 Vaccine Working Group on Paediatric Oncology - a collaboration between St Jude Children's Research Hospital and the International Society of Paediatric Oncology (SIOP) - and a parent advisory group representing cancer patients and their families worldwide in March 2021. The survey contained 19 Likert-type questions where respondents were asked to rate on a scale of 1 (not important) to 5 (very important) the importance of vaccine-related questions. The survey also asked closed questions about country of residence, type of cancer, and timing of cancer experience. A free-text question was included asking respondents to report any additional questions or comments regarding the COVID-19 vaccine in children with cancer.

The survey was disseminated between April and May 2021 by each member of the parent advisory group to respondents in their own country via several online media. A small proportion of respondents in South Africa and Ghana were approached directly in the clinic setting with paper forms of the survey due to limited access to the online version. A version of the survey was translated into Spanish for wider access. Survey responses were anonymous, no identifiable information was requested and informed consent was obtained. Institutional Review Board approval was not required as the study was classified as informational by St Jude and therefore exempt. The involvement of Patients and Public advisers was not deemed subject to ethical approval by the U.K. National Research Ethics Services.

Statistical Analysis

Descriptive statistics were conducted to characterise the sample and to assess central tendency (median) and dispersion measures (interquartile range (IQR)) of the Likert scales. Principal Component Analysis (PCA) was run on the 19 items to reduce the dimensionality of the data and to identify main themes. A correlation matrix (Supplementary Appendix 1) revealed a high degree of correlation between groups of items. The Kaiser-Meyer-Olkin measure for sampling adequacy confirmed that the data were suitable for PCA ($KMO = 0.899 > 0.5$). Observation of Eigenvalues (Supplementary Appendices 2 and 3) revealed four components explaining 63% of the variation in the data. An oblique Promax rotation achieved the simple structure (Supplementary Appendix 4). Cronbach's Alpha (α) measure of internal consistency was used to assess the reliability of the dimensions. Selected variables, each representing a latent construct, were averaged into scales measuring 'Safety and Effectiveness', 'Acute Side Effects', 'Eligibility' and 'Logistics' (See Supplementary Appendix 5). Group comparison tests for non-parametric data, such as Kruskal Wallis and Mann Whitney tests, were conducted to test statistical significance between World Bank (WB) income groups. Statistical analyses were conducted with Stata/MP version 17.0.

Inductive content analysis was conducted on free-text responses by three investigators using MAXQDA software to organize coding. Rigorous content analysis processes were followed, including iterative memoing to identify salient concepts, subsequently informing codebook development. Two investigators coded the responses independently, with third-party adjudication to facilitate reconciliation and achieve consensus. Frequency of codes were reported.

Results

The survey achieved a total sample size of 627 parents from 22 countries (Table 1). 89.1% of the sample ($n = 559$) belonged to a country classified by the WB as high-income, 6.54% of the sample ($n = 41$) belonged to a country classified as upper-middle-income, and 4.15% ($n = 26$) belonged to a country classified as lower-middle-income. 51.8% of parents ($n = 325$) reported having a child diagnosed with leukaemia, 24.7% ($n = 155$) with solid tumour, 12.9% ($n = 81$) with brain or spinal tumour, 9.2% ($n = 58$) with lymphoma, and 0.48% ($n = 3$) with other cancers. Most caregivers reported that their child began cancer treatment more than a year prior to taking this survey: 12.6% ($n = 79$) within a year from the survey, 34.9% ($n = 219$) between 1-3 years from the survey, 23.9% ($n = 150$) between 3-5 years from the survey, and 28.5% ($n = 180$) more than 5 years from the survey date. 184 parents (29%) provided a free text response, resulting in a total of 271 codes applied. No significant bias from the general sample survey was observed in the distribution of this sample (Supplementary Appendix 6).

Table 1: Sample description

	Frequency	Percentage
N	627	
WB income group		
Lower Middle Income (LMIC)	26	4.15%
Upper Middle Income (UMIC)	41	6.54%
High Income (HIC)	559	89.15%
<i>missing values</i>	1	0.16%
WHO Region		
African Region	46	7.34%
European Region	62	9.89%
Region of the Americas	493	78.63%
South East Asian Region	18	2.87%
Western Pacific Region	7	1.12%
<i>missing values</i>	1	0.16%
Type of Cancer		
Leukaemia (such as ALL, AML)	325	51.83%
Lymphoma (such as B-NHL, Hodgkins Disease)	58	9.25%
Brain or Spinal tumour (such as Ependymoma, Medulloblastoma)	81	12.92%
Solid tumour outside the brain (such as Wilms, Neuroblastoma, Sarcoma)	155	24.72%
Other	3	0.48%
<i>missing values</i>	2	0.32%
Timing of Cancer experience		
Within last 12 months	79	12.60%
Between 1 and 3 years ago	219	34.93%
Between 3 and 5 years ago	150	23.92%
More than 5 years ago	179	28.55%

Analysis of the 19 survey items (Figures 1a and 1b) showed little variation in responses across survey questions with a median score of 5 for most items, indicating a high degree of concern (i.e. high importance) towards most questions. 75% (n = 470) of participants reported a score of 5 for questions related to safety and severe side effects. The cost of the vaccine was reported to be the least important question (median = 3; IQR = 1, 4), followed by the brand (median = 4; IQR = 3, 5) and the number of doses required (median = 4; IQR = 3, 5). No statistically significant differences were found between WB income groups in most items, except in the cost of the vaccine item, where caregivers in lower and upper-middle-income countries were more likely to consider the cost highly important, compared to caregivers in high-income countries ($H(2) = 25.156, p < 0.001$).

Figure 1a: Box plot of survey items by importance (1 not important and 5 very important)

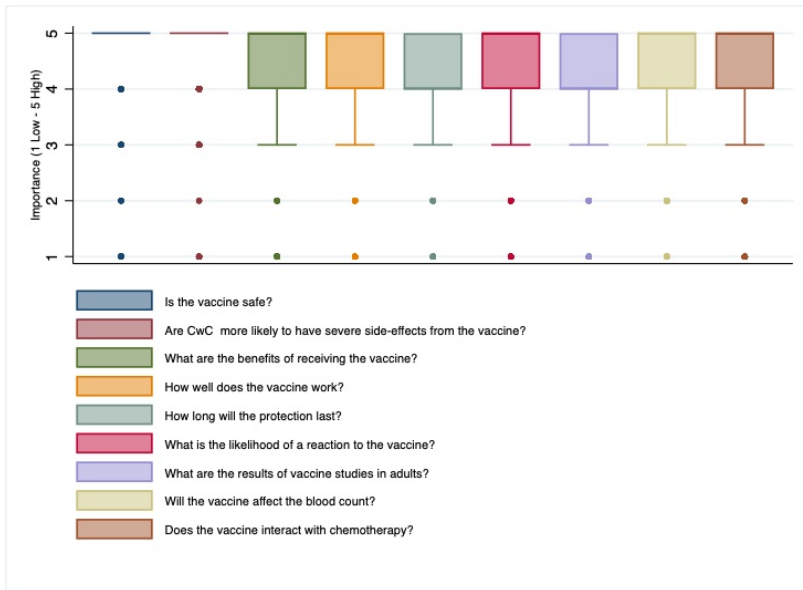
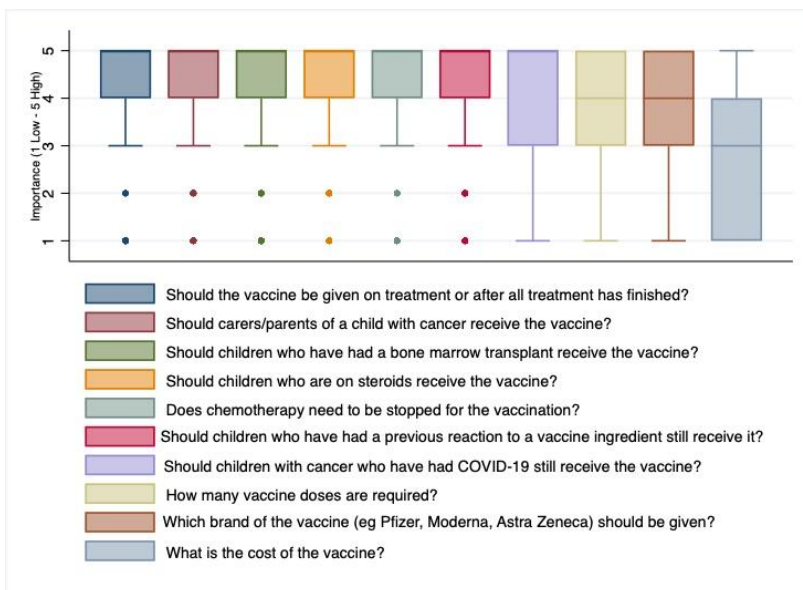
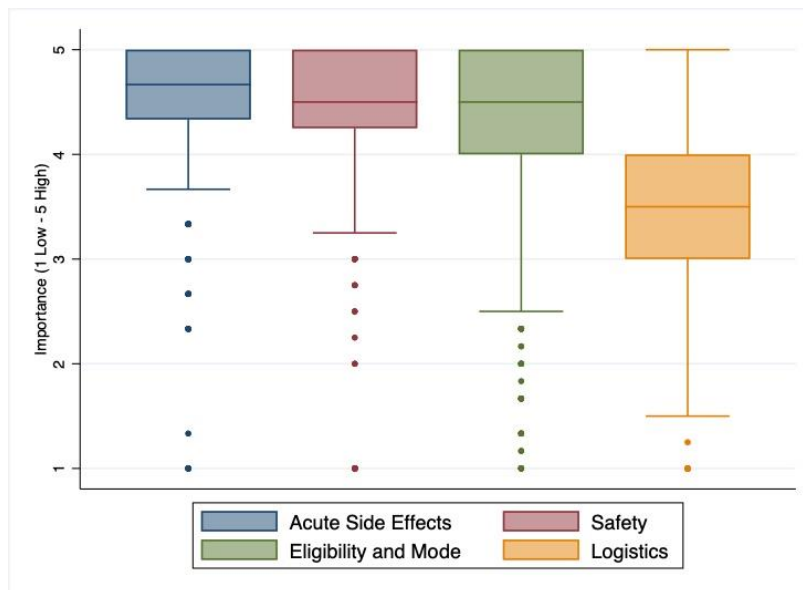


Figure 1b: Box plot of survey items by importance (1 not important and 5 very important)



Using the four PCA dimensions, caregivers rated the vaccine’s acute side effects (median = 4.75; IQR = 4.25, 5), the vaccine’s safety and effectiveness (median = 4.5; IQR = 4.25, 5) and the eligibility of the vaccine (median = 4.5; IQR = 4, 5) as very highly and equally important but rated the logistics of administering the vaccine of lower importance (median = 3.5; IQR = 3, 4) (Figure 2).

Figure 2: Box plot of PCA dimensions by importance (1 not important and 5 very important)



A small group of outliers (2.7%, $n = 17$) from North America and the African region indicated that ‘Safety and Effectiveness’ was ‘not important’. While these caregivers also rated ‘Eligibility and Mode’ and ‘Logistics’ as not being very important (median = 1; IQR = 1, 1.75), questions related to ‘Acute Side Effects’ scored on average slightly higher (median = 4; IQR = 1, 5), which indicates concern regarding the immediate effects of the vaccine on their children (Supplementary Appendix 7).

Scores by WB income groups aligned with the overall distribution, with ‘Acute Side Effects’ and ‘Safety and Effectiveness’ scoring on average higher than ‘Eligibility and Mode’ and ‘Logistics’ for all income groups (see Figure 4). Kruskal Wallis test showed statistically significant differences only in the ‘Logistics’ dimension ($H(2) = 18.39, p < 0.001$). Post-hoc Mann-Whitney tests showed differences to lie between the upper-middle- and high-income groups ($M_{UMIC} = 4, M_{HI} = 3.5, z = 1.99, p < 0.05$) and between lower-middle- and high-income groups ($M_{LMIC} = 4.25, M_{HI} = 3.5, z = 3.91, p < 0.001$), indicating that parents from lower- and middle-income groups were slightly more likely to consider questions related to logistics more important than parents from high-income groups. No other statistically significant differences were found.

Free text responses

Results from content analyses of free text responses aligned with quantitative themes identified by PCA and revealed that ‘Safety and Effectiveness’ were primary concerns for caregivers. Out of 271 codes applied, 35.1% of codes ($n = 94$) related to the vaccine’s safety, including acute and chronic side effects; 25.5% of codes ($n = 67$) related to logistics and mode of administration of the vaccine including where it should be administered, which vaccine, who should receive it and contraindications; and 13% ($n = 35$) were requests for more information about the vaccine and guidance, including requests for more research. 20.3% of codes ($n = 55$) were expressions in favour or against the vaccine. Specifically, 19 caregivers indicated they would refuse to vaccinate themselves or their child, 20 were in

favour of receiving a vaccine and 16 indicated they were hesitant, showing uncertainty on whether to vaccinate. The caregivers who expressed favourable attitudes quoted the importance to vaccinate vulnerable children. Many of them indicated they had already vaccinated themselves or their children. One caregiver said: *“I think that a vaccine for children before chemotherapy is critical. Parents should receive a vaccine too”*. (See Supplementary Appendix 8 for all quotes).

Analysis of free-text responses of caregivers who were against a COVID-19 vaccine (n = 19) indicated safety, side effects, and insufficient knowledge of long-term side effects as main reasons for refusal. Triangulation with the quantitative survey questions showed that 17 of these 19 caregivers had indicated in the Likert scales that ‘Safety and Effectiveness’ were ‘not important’ questions to consider. However, several of their comments showed concern about safety, particularly in the context of children already experiencing a highly medicalised childhood. One caregiver quoted: *“It should not be given. Not enough knowns and absolutely zero longevity studies. Our kids suffer enough without added man made chemicals and concoctions”* (See Supplementary Appendix 9 for all quotes).

Conclusions

In this study, we investigated global caregiver concerns regarding SARS-CoV-2 vaccination for children with cancer, with a focus on gathering caregivers’ views on what aspects about vaccines are most important for decision making.

The findings show that, across all countries, pediatric oncology caregivers rated most items of the survey as highly important, indicating that numerous aspects related to the vaccine factor into decision-making, specifically safety, effectiveness, and acute side effects. While these findings may not appear, in principle, to be substantially different to that of the general child and adult population¹⁸⁻²¹, they should be interpreted in the context of the pediatric oncology community. Importantly, the negative impact of the pandemic in this subgroup should be considered¹²⁻¹⁴ as it may influence vaccine decision making. In particular, the perception of risk of pediatric oncology caregivers may be heightened due to the already increased levels of medicalisation of their children¹⁷ and the need to protect the child from additional illness²². Vaccine guidance should, therefore, be sensitive to these circumstances.

A combination of behavioural interventions, reduction of socio-economic inequities and public communication strategies have been recommended as the way forward to increase vaccine uptake^{23,24}. From a behavioural perspective, healthcare providers need to work with caregivers of children with cancer to instil trust¹⁷, but also to provide effective and tailored communication on the safety, effectiveness and side effects of the vaccine to promote informed choices²³. The abundance of information generated about the vaccine since the start of the pandemic and multiple sources of disinformation in social media²⁵ hindered this task, highlighting the need to increase the dissemination of evidence-based messages²³. Indeed, numerous caregivers mentioned the need for more research in this area to reduce uncertainties related to the vaccine and aid decision-making.

The cost and brand of the SARS-CoV-2 vaccine or, more generally, the logistics of administering the vaccine elicited less concern from caregivers overall. However, caregivers from lower- and upper-middle income countries considered the logistics of administering the vaccine as important. The increased concern about logistics found amongst these caregivers

may reflect the inequities oncology families in these countries experience in terms of access to healthcare and delays in treatment³, which have adversely impacted the morbidity and mortality rates of COVID-19 in children with cancer in these regions^{26,27}. The development of strategies to minimize barriers to care in low- and middle-income settings may lower concern towards logistics, which could in turn lead to increased vaccine uptake³.

Findings from the quantitative survey were mirrored by the qualitative open-ended question, where comments related to safety and effectiveness appeared more frequently than other comments. A small minority of caregivers were identified as vaccine hesitant revealing strong feelings against the vaccine, and quoting safety, side effects and lack of sufficient evidence for the vaccine and expressing misinterpretation of vaccine science (e.g. toxic ingredients). This aligns with limited prior publications related to COVID-19 vaccine hesitancy in this population subgroup²⁸. Opportunities exist for healthcare providers and public health organisations to increase confidence in the vaccine through education and communication campaigns aimed at addressing these concerns^{29,30}. Oncology teams worldwide have an important responsibility to initiate discussions with families of the patients to provide accurate vaccine messaging that respects the circumstances of the child and their family²³.

This study has a number of limitations. The cross-sectional survey was disseminated in March 2021 when the vaccine roll out had recently started in most Western countries and limited studies and trials had been conducted. With more information available presently, some caregiver views may have changed. As the aim of the study was to characterise caregivers' concerns regarding the COVID-19 vaccine, the survey did not explicitly ask whether caregivers were in favour or against the vaccine. Hesitancy was inferred from qualitative analysis of free text comments, particularly in caregivers who questioned the need for a vaccine given the low risk of COVID-19 in children or those who explicitly indicated refusal to vaccinate. Notably, absence of negative perceptions towards the vaccine cannot be interpreted as support for the vaccine. The study also attempted to understand differences between WB income groups. The use of convenience sampling resulted in unequal sample sizes amongst WB income groups with an important bias towards high income groups (i.e. 89% of the sample) which may affect the statistical reliability of group comparisons. More effort should be done in future to represent low and upper-middle income country voices in light of the possible healthcare inequities identified. Lastly, to retain anonymity the survey did not include questions related to the demographic and socio-economic status of respondents, so we were unable to assess whether vaccine concerns varied by socio-economic groups.

To our knowledge, this study is the first to present a global perspective on caregivers' concerns towards the SARS-CoV-2 vaccine, providing crucial information to healthcare providers and public health messengers when advising families of children with cancer during the SARS-CoV-2 pandemic.

Acknowledgements

Members of the COVID-19 vaccine global parent/carer advisory group as below contributed to the concept for this study and to the evaluation of its findings:

- **Brian Regan**, United States, Dana Farber/Boston Children's Pediatric Patient/Family Advisory Committee
- **Meghan Shea**, United States, Dana Farber/Boston Children's Pediatric Patient/Family Advisory Committee
- **Julie Chessell**, Canada, AC20RN
- **Kim Buff**, United States, Momcology
- **Carmen Auste**, Philippines, Childhood Cancer International
- **Pinta Manullang-Panggabean**, Indonesia, Yayasan Anyo Indonesia
- **Poonam Bagai**, India, Can Kids India
- **John Ahenkorah**, Ghana, Ghana Parents Group

We thank Dr José Luis Copado (Paediatric Infectious Diseases Specialist, Mexico) for translating the survey into Spanish.

We thank Professor Carlos Rodriguez-Galindo, for the support of the St Jude Global Alliance programme.

We would like to thank the caregivers for taking their time to participate in our survey and for sharing their views on the COVID-19 vaccine. We would also like to thank all those who helped to disseminate the survey globally.

Declaration of Interest Statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Contributorship statement

JB had the concept for the study and led the co-design with KPJ and MC. JG, EK and JB developed the methodology. MH provided project administration and resources. JG and AS undertook the formal analysis and investigation of data. JG wrote the original draft of the paper supervised by JB. All authors revised the paper critically and approved the final version.

Funding

This study was supported by ALSAC/St. Jude 10.13039/100012524.

Data availability statement

The data that support the findings of the study are available on reasonable request from the corresponding author.

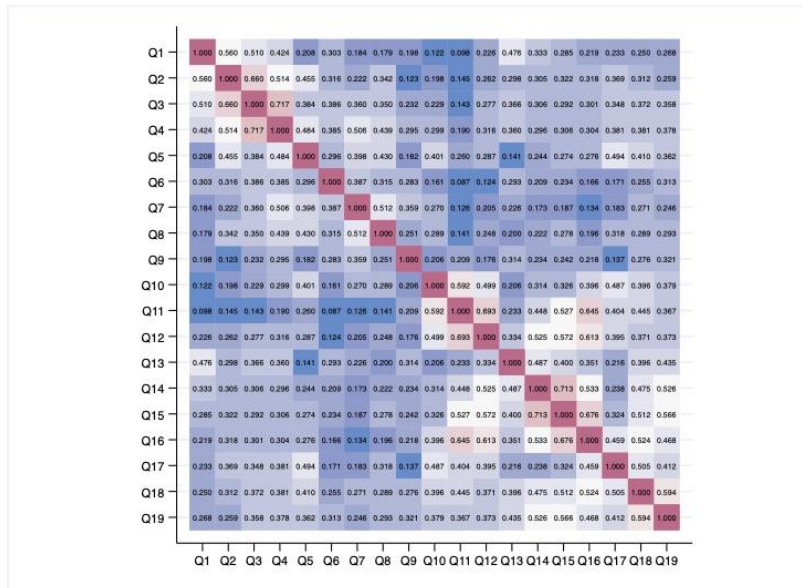
References

1. Molteni E, Sudre CH, Canas LS, et al. Illness duration and symptom profile in symptomatic UK school-aged children tested for SARS-CoV-2. *Lancet Child Adolesc Health*. Oct 2021;5(10):708-718. doi:10.1016/S2352-4642(21)00198-X
2. Swann OV, Holden KA, Turtle L, et al. Clinical characteristics of children and young people admitted to hospital with covid-19 in United Kingdom: prospective multicentre observational cohort study. *BMJ*. Aug 27 2020;370:m3249. doi:10.1136/bmj.m3249
3. Graetz D, Agulnik A, Ranadive R, et al. Global effect of the COVID-19 pandemic on paediatric cancer care: a cross-sectional study. *Lancet Child Adolesc Health*. May 2021;5(5):332-340. doi:10.1016/S2352-4642(21)00031-6
4. Pino MS, Cheli S, Perna M, et al. The National COVID-19 Vaccination Campaign Targeting the Extremely Vulnerable: the Florence Medical Oncology Unit Experience in Patients with Cancer. *European Journal of Cancer*. 2022;0(0)
5. Aznab M, Eskandari Roozbahani N, Moazen H. Value of influenza vaccines in cancer patients during the coronavirus (COVID-19) pandemic: a cross-sectional study. *Support Care Cancer*. Nov 2021;29(11):6225-6231. doi:10.1007/s00520-021-06204-x
6. Corti C, Crimini E, Tarantino P, et al. SARS-CoV-2 vaccines for cancer patients: a call to action. *Eur J Cancer*. May 2021;148:316-327. doi:10.1016/j.ejca.2021.01.046
7. Wallace M, Woodworth KR, Gargano JW, et al. The Advisory Committee on Immunization Practices' Interim Recommendation for Use of Pfizer-BioNTech COVID-19 Vaccine in Adolescents Aged 12-15 Years - United States, May 2021. *MMWR Morb Mortal Wkly Rep*. May 21 2021;70(20):749-752. doi:10.15585/mmwr.mm7020e1
8. Walter EB, Talaat KR, Sabharwal C, et al. Evaluation of the BNT162b2 Covid-19 Vaccine in Children 5 to 11 Years of Age. *N Engl J Med*. Jan 6 2022;386(1):35-46. doi:10.1056/NEJMoa2116298
9. Agency UHS. COVID-19 vaccination programme for children and young people: guidance for schools (version 2). Accessed 14 December, 2021. <https://www.gov.uk/government/publications/covid-19-vaccination-resources-for-schools/covid-19-vaccination-programme-for-children-and-young-people-guidance-for-schools>
10. Administration UFaD. FDA Authorizes Pfizer-BioNTech COVID-19 Vaccine for Emergency Use in Children 5 through 11 Years of Age. Accessed 14 December, 2021. <https://www.fda.gov/news-events/press-announcements/fda-authorizes-pfizer-biontech-covid-19-vaccine-emergency-use-children-5-through-11-years-age>
11. Charla Y, Kalra M, Chopra N, Choudhury S. COVID-19 vaccination in pediatric cancer patients: A high priority. *Pediatr Blood Cancer*. Dec 2021;68(12):e29397. doi:10.1002/pbc.29397
12. Darlington AE MJ, Wagland R, Sodergren SC, Culliford D, Gamble A, Phillips COVID-19 and children with cancer: Parents' experiences, anxieties and support needs. *Pediatr Blood Cancer*. 2021;68(2)doi:10.1002/pbc.28790
13. Davies J, O'Connor M, Halkett GKB, Kelada L, Gottardo NG. Parents' Experiences of Childhood Cancer During the COVID-19 Pandemic: An Australian Perspective. *J Pediatr Psychol*. Feb 14 2022;47(2):148-157. doi:10.1093/jpepsy/jsab125
14. Wimberly CE, Towry L, Caudill C, Johnston EE, Walsh KM. Impacts of COVID-19 on caregivers of childhood cancer survivors. *Pediatr Blood Cancer*. Apr 2021;68(4):e28943. doi:10.1002/pbc.28943
15. Doherty M, Schmidt-Ott R, Santos JI, et al. Vaccination of special populations: Protecting the vulnerable. *Vaccine*. Dec 20 2016;34(52):6681-6690. doi:10.1016/j.vaccine.2016.11.015

16. Kelkar AH, Blake JA, Cherabuddi K, Cornett H, McKee BL, Cogle CR. Vaccine Enthusiasm and Hesitancy in Cancer Patients and the Impact of a Webinar. *Healthcare (Basel)*. Mar 19 2021;9(3)doi:10.3390/healthcare9030351
17. Wimberly CE, Towry L, Davis E, Johnston EE, Walsh KM. SARS-CoV-2 vaccine acceptability among caregivers of childhood cancer survivors. *Pediatr Blood Cancer*. 2021;1-9. doi:<https://doi.org/10.1002/pbc.29443>
18. Brodziak A, Sigorski D, Osmola M, et al. Attitudes of Patients with Cancer towards Vaccinations-Results of Online Survey with Special Focus on the Vaccination against COVID-19. *Vaccines (Basel)*. 2021;9(5)doi:10.3390/vaccines9050411
19. Goldman RD, Krupik D, Ali S, et al. Caregiver Willingness to Vaccinate Their Children against COVID-19 after Adult Vaccine Approval. *Int J Environ Res Public Health*. Sep 28 2021;18(19)doi:10.3390/ijerph181910224
20. Schilling S, Orr CJ, Delamater AM, et al. COVID-19 vaccine hesitancy among low-income, racially and ethnically diverse US parents. *Patient Educ Couns*. 2022;
21. Bell S, Clarke R, Mounier-Jack S, Walker JL, Paterson P. Parents' and guardians' views on the acceptability of a future COVID-19 vaccine: A multi-methods study in England. *Vaccine*. Nov 17 2020;38(49):7789-7798. doi:10.1016/j.vaccine.2020.10.027
22. Carlsson T, Kukkola L, Ljungman L, Hovén E, von Essen L. Psychological distress in parents of children treated for cancer: An explorative study. *PLOSone*. 2019;doi:<https://doi.org/10.1371/journal.pone.0218860>
23. Omer SB, Benjamin RM, Brewer NT, et al. Promoting COVID-19 vaccine acceptance: recommendations from the Lancet Commission on Vaccine Refusal, Acceptance, and Demand in the USA. *Lancet*. Dec 11 2021;398(10317):2186-2192. doi:10.1016/S0140-6736(21)02507-1
24. Geoghegan S, O'Callaghan KP, Offit PA. Vaccine Safety: Myths and Misinformation. *Front Microbiol*. 2020;11(372)
25. Viswanath K, Bekalu M, Dhawan D, Pinnamaneni R, Lang J, McCloud R. Individual and social determinants of COVID-19 vaccine uptake. *BMC Public Health*. Apr 28 2021;21(1):818. doi:10.1186/s12889-021-10862-1
26. Mukkada S, Bhakta N, Chantada GL, et al. Global characteristics and outcomes of SARS-CoV-2 infection in children and adolescents with cancer (GRCCC): a cohort study. *Lancet Oncol*. Oct 2021;22(10):1416-1426. doi:10.1016/S1470-2045(21)00454-X
27. Corso MCM, Soares VJ, Amorim AMP, et al. SARS-CoV-2 in children with cancer in Brazil: Results of a multicenter national registry. *Pediatr Blood Cancer*. Dec 2021;68(12):e29223. doi:10.1002/pbc.29223
28. Razai M S, Chaudhry U A R, Doerholt K, Bauld L, A M. Covid-19 vaccination hesitancy. *BMJ*. 2021;(373)doi:<https://doi.org/10.1136/bmj.n1138>
29. Cooper DM, Afghani B, Byington CL, et al. SARS-CoV-2 vaccine testing and trials in the pediatric population: biologic, ethical, research, and implementation challenges. *Pediatr Res*. Nov 2021;90(5):966-970. doi:10.1038/s41390-021-01402-z
30. Edwards KM, Hackell JM, Committee On Infectious Diseases TCOP, Ambulatory M. Countering Vaccine Hesitancy. *Pediatrics*. Sep 2016;138(3)doi:10.1542/peds.2016-2146

Supplementary Appendix

Appendix 1: Correlation Matrix



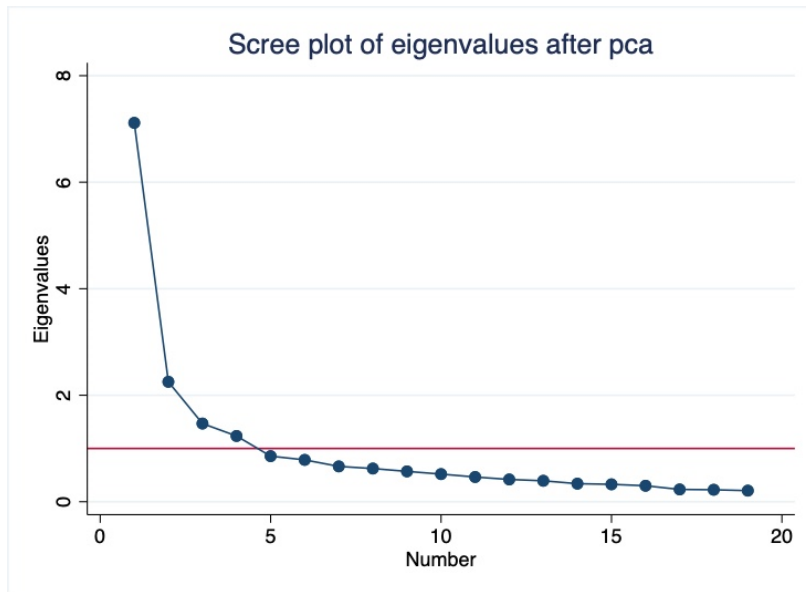
Legend

- Q1 What are the benefits of receiving the vaccine
- Q2 Is the vaccine safe
- Q3 How well does the vaccine work
- Q4 How long will the protection from the vaccine last
- Q5 What is the likelihood of a reaction from the vaccine
- Q6 What are the results of the vaccine in adults
- Q7 How many vaccine doses are required
- Q8 Which brand of the vaccine should be given
- Q9 What is the cost of the vaccine
- Q10 Will the vaccine affect the blood count
- Q11 Does the vaccine interact with chemotherapy
- Q12 Should the vaccine be given on treatment or after all treatment has finished
- Q13 Should carers/parents of a child with cancer receive the vaccine
- Q14 Should children who have had a bmt receive the vaccine
- Q15 Should children who are on steroids receive the vaccine
- Q16 Does chemotherapy need to be stopped for vaccination
- Q17 Are children with cancer more likely to have severe side effects
- Q18 Should children who have had a previous reaction still receive the vaccine
- Q19 Should children with cancer who have had covid still receive the vaccine

Appendix 2: Principal Component Models

Principal components/correlation			Number of observations	605
			Number of components	19
Rotation: (unrotated = principal)			Rho	1
Component	Eigenvalue	Difference	Proportion	Cumulative
Comp1	7.115	4.863	0.375	0.375
Comp2	2.252	0.784	0.119	0.493
Comp3	1.468	0.233	0.077	0.570
Comp4	1.235	0.379	0.065	0.635
Comp5	0.856	0.070	0.045	0.680
Comp6	0.786	0.122	0.041	0.722
Comp7	0.664	0.041	0.035	0.757
Comp8	0.624	0.053	0.033	0.790
Comp9	0.570	0.051	0.030	0.820
Comp10	0.519	0.055	0.027	0.847
Comp11	0.465	0.046	0.024	0.871
Comp12	0.419	0.025	0.022	0.893
Comp13	0.394	0.054	0.021	0.914
Comp14	0.340	0.012	0.018	0.932
Comp15	0.327	0.027	0.017	0.949
Comp16	0.301	0.069	0.016	0.965
Comp17	0.231	0.006	0.012	0.977
Comp18	0.225	0.017	0.012	0.989
Comp19	0.209	.	0.011	1.000

Appendix 3: Scree plot van Cattell



Appendix 4: Oblique Promax Rotation

Variable	Eligibility	Safety	Side effects	Logistics	Unexplained
What are the benefits of receiving the vaccine		0.500			0.329
Is the vaccine safe		0.546			0.243
How well does the vaccine work		0.467			0.269
How long will the protection from the vaccine last		0.307			0.320
What is the likelihood of a reaction from the vaccine			0.433		0.367
What are the results of the vaccine in adults				0.366	0.542
How many vaccine doses are required				0.551	0.318
Which brand of the vaccine should be given				0.373	0.462
What is the cost of the vaccine				0.514	0.444
Will the vaccine affect the blood count			0.419		0.396
Does the vaccine interact with chemotherapy	0.336				0.265
Should the vaccine be given on treatment or after all treatment has finished	0.321				0.367
Should carers/parents of a child with cancer receive the vaccine	0.304				0.392
Should children who have had a bmt receive the vaccine	0.417				0.319
Should children who are on steroids receive the vaccine	0.414				0.294
Does chemotherapy need to be stopped for vaccination	0.370				0.306
Are children with cancer more likely to have severe side effects			0.455		0.377
Should children who have had a previous reaction still receive the vaccine					0.470
Should children with cancer who have had covid still receive the vaccine					0.451

Appendix 5: Reliability Analysis of PCA dimensions

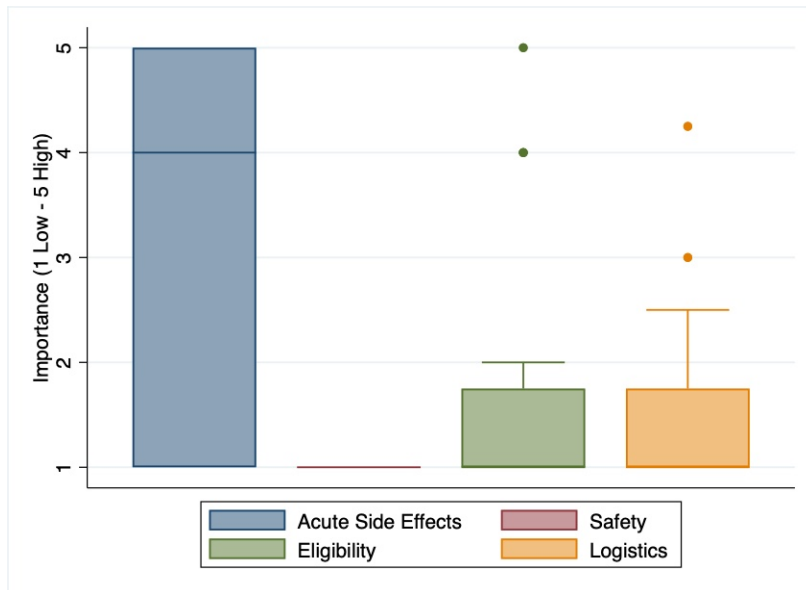
<p>What are the benefits of receiving the vaccine</p> <p>Is the vaccine safe</p> <p>How well does the vaccine work</p> <p>How long will the protection from the vaccine last</p>	<p>Safety and Effectiveness ($\alpha = 0.827$)</p>
<p>What is the likelihood of a reaction from the vaccine</p> <p>Will the vaccine affect the blood count</p> <p>Are children with cancer more likely to have severe side effects</p>	<p>Acute Side Effects ($\alpha = 0.704$)</p>
<p>What are the results of the vaccine in adults</p> <p>How many vaccine doses are required</p> <p>Which brand of the vaccine should be given</p> <p>What is the cost of the vaccine</p>	<p>Logistics ($\alpha = 0.680$)</p>
<p>Does the vaccine interact with chemotherapy</p> <p>Should the vaccine be given on treatment or after all treatment has finished</p> <p>Should carers/parents of a child with cancer receive the vaccine</p> <p>Should children who have had a bmt receive the vaccine</p> <p>Should children who are on steroids receive the vaccine</p> <p>Does chemotherapy need to be stopped for vaccination</p>	<p>Eligibility and Mode ($\alpha = 0.863$)</p>

Note: the 'Logistics' dimension presents a Cronbach's Alpha marginally below the threshold for internal consistency of $\alpha = 0.7$. Removing any of the items does not increase α . Two items were unclassified as they did not load on any component (See Appendix 4).

Appendix 6: Sample distribution

	Free text comments		Total Sample	
	Frequency	Percentage	Frequency	Percentage
N	184	29.35%	627	
WB income group				
Lower Middle Income	8	4.35%	26	4.15%
Upper Middle Income	15	8.15%	41	6.54%
High Income	161	87.5%	559	89.15%
WHO Region				
African Region	18	9.78%	46	7.34%
European Region	15	8.15%	62	9.89%
Region of the Americas	145	78.80%	493	78.63%
South-East Asian Region	4	2.17%	18	2.87%
Western Pacific Region	2	1.09%	7	1.12%
Type of Cancer				
Leukaemia (such as ALL, AML)	91	49.46%	325	51.83%
Lymphoma (such as B-NHL, Hodgkins Disease)	17	9.24%	58	9.25%
Brain or Spinal tumour (such as Ependymoma, Medulloblastoma)	23	12.50%	81	12.92%
Solid tumour outside the brain (such as Wilms, Neuroblastoma, Sarcoma)	49	26.63%	155	24.72%
Other	1	0.54%	3	0.48%
Timing of Cancer experience				
Within last 12 months	19	10.33%	79	12.60%
Between 1 and 3 years ago	60	32.61%	219	34.93%
Between 3 and 5 years ago	52	28.26%	150	23.92%
More than 5 years ago	53	28.80%	179	28.55%

Appendix 7: Box plot of PCA dimensions by importance of caregivers who consider ‘Safety and Effectiveness’ as ‘Not Important’ (n = 17) (1 not important and 5 very important)



Appendix 8: Free text responses of caregivers who are coded as being favourable towards a COVID-19 vaccine (n = 20)

- *My only other comment would be that children undergoing cancer treatment and bone marrow transplants should be prioritised for vaccinations as quickly and safely as possible due to the unknown consequences of long Covid as they already have long term treatment side effects to manage.*
- *Children with cancer and in certain stages of treatment should get their vaccine first, my child has finished treatment less than 1 year ago butte would be happy for him to wait until more vulnerable children to have theirs first*
- *All of the questions above are so important. My son is 5 and is undergoing treatment for ALL so I am not sure if/when he can get the vaccine during treatment. It is also difficult convincing grown humans who are healthy to get the vaccine to protect kids like my son. It is frustrating. I don't care how many booster doses I would need, getting the vaccine certainly outweighs the "newness" and "inconvenience" it, plus the chance effects of COVID.*
- *Research and answers need to happen immediately- pediatric cancer patients have not had the chance to live full lives & if they beat cancer shouldn't then die from covid? They should have been vaccinated with first group like essential workers instead of last?*
- *I did not answer questions that did not apply to our situation such as children that have already had Covid 19 or have had a bone marrow transplant. I have already received the vaccine and know that it is very important for all adults that are eligible to get it.*
- *My daughter was diahnsosed with Stage 3 C Eptheial Ovarian Cancer at 14yrs old she is now 22yrs old and had both of the Moderna Vaccinations without complications.*
- *I think that a vaccine for children before chemotherapy is critical. Parents should receive a vaccine too*
- *In understanding the questions above, I have assumed that I am saying it is very important to have answers (research)to the questions before a child with cancer is given the vaccine. As chemotherapy destroys immunity two things can happen 1. The benefits of the vaccine are null and void if followed by chemo 2. The child can have a severe reaction to the vaccine as they don't have an immune system to ilearn from the vaccine. Family members and health care providers around the child should receive the vaccine.*
- *Let's start vaccinating!*
- *My daughter has CML since 2014 and she is now 16. She received two doses of the Pfizer vaccine as recommended by her oncologist here in [omitted for anonymity]*
- *Thanks for doing this! If adults with cancer can get vaccine then kids should be able to get it too!*
- *I think it's imperative that we know as much as we can about the vaccines for kids with cancer, and we administer them as soon as possible for these children (and other kids and adults in the same household).*
- *When can we make this available*
- *I think it is important for kids who have or have had cancer to get the Covid Vaccine as long as it has been proven safe. My daughter has had it and is 6 years out of treatment.*
- *My 21-year-old with leukemia got the vaccine done and did very well with vaccine, he was diagnosed May 2018 and still has 6 months left in treatment*
- *I would definitely want my child to receive the vaccine and he is off treatment over a year and his Dr. said that he can get it so we have him scheduled for an appointment*
- *I think the COVID_19 vaccine will be good for children with cancer since their immune system is not strong and easily get the virus.*

- *My husband and I look at the Covid-19 vaccine just like any other vaccine including flu shots which we get every year. My son had bone marrow transplant so he had to have shots of all the vaccines he had when he was little all over again.*
- *As children with cancer are vulnerable to severe disease, the safer vaccine without interfering with chemotherapy is important to administer*
- *My child has been vaccinated with no serious side effects*

Appendix 9: Free text responses of caregivers who are coded as refusing a COVID-19 vaccine (n = 19)

- *It should not be given. Not enough knowns and absolutely zero longevity studies. Our kids suffer enough without added man made chemicals and concoctions*
- *We won't be getting the Vaccine*
- *We did not take any covid 19 vaccine*
- *This vaccine must be tested on animals before and studied long term before even being considered for our vulnerable children who are NOT seeing serious illness with this virus. The unknown risks are vast and complex in this population. No carcinogenic/mutagenic effects unknown as well as other systemic and cellular effects have been studied on this unique or other event general populations - it could have devastating effects that would implicate this industry in massive harm. My child would not be volunteering for this study.*
- *We will not be getting the vaccine nor will any of our children.*
- *I will never allow my child to get the covid-19 vaccine.....if childhood cancer really wants to find a cure , they should stop injecting METAL into these poor children. [curse word] who ever approved putting metal into these innocent children. & [curse word] the covid vaccine - Sincerely, an angry mother.*
- *My daughter is a survivor for a long time. She will not be getting the vaccine. Too many unknowns and she wants to get pregnant. We whole heartily support her. She is extremely healthy, no health issues, exercises daily, eats extremely healthy and is rarely ill. Covid would not be any more harmful to her than a cold. The vaccine may be harmful . She's had plenty of poison in her body from 1+ years of treatment.*
- *My son along with myself, and husband all had Covid in November 2020. We will not be getting the vaccine as our body has the natural antibodies. When our son, whose immune system is low as he's actively on treatment, had a stuffy nose for a day. Our family will not be getting the vaccine.*
- *I do not support giving children with or without cancer the covid-19 vaccine*
- *My husband and I are totally against getting this particular vaccine for ourselves. I also have a hard time with seeing the necessary information stating that we should even begin injecting children with this, I wasn't aware children were at risk of even getting covid. And furthermore, my child will have to survive the treatment that is meant to save her life first. And even IF she survives she will most likely have lasting side effects from the chemo she received including infertility! How can I make the decision for her to be injected with god knows what then later having it cause all sorts of complications.....nope not signing up for that, I'm already carrying a heavy burden!!*
- *I would not ever give my child the vaccine. It has not been around long enough to know of valid side effects. Nor will I as a parent take it.*
- *We will NOT be getting the vaccine.*
- *It is my opinion that our children should not receive this vaccine. It was approved for emergency use only. There are not nearly enough studies or research to determine what the side effects could be.*
- *I don't think any child should get this vaccine. Let alone a child with cancer. NO ONE SHOULD BE RECEIVING THIS VACCINE*
- *Isn't it too early to tell if the vaccine is really worth the risk? the vaccine be a personal choice and not one forced upon you. Isn't it critical important to understand whether or not a person has had Covid or not before stating they should or should not get a vaccine that we still don't fully understand. Isn't the vaccine still a clinical trial and not fully approved by the FDA? If so why aren't we telling people those facts?*

- *My daughter will not be receiving the vaccine until more studies have been done. It makes me extremely uncomfortable that her cancer was caused by her cells and that the vaccine goes into the cell. She finished treatment less than a year ago. I do not want her to have anything that could potentially affect her cells and cause a relapse.*
- *The medication for cancer children is more than ok and its chronic so i dont see any importance for children to be vaccinated.rmb this kids dont take any medications but prescribed ones.covid 19 no to this children*
- *Covid is being used as a trojan horse to take over parts of our lives government has no business with. This "vaccine" is a scam and only time will tell the long-term affects of this vaccine for which the sickness has a 99.9% recovery rate. How dare anyone try to subject kiddos with cancer to this. Please stop this nonsense right now and get onto fighting cancer.*
- *No children should be getting this vaccine*