Answers to Common Questions about COVID-19 Vaccines in Children with Cancer

Miguela A. Caniza, [1,2,3,*] Maysam R. Homsi[1], Jessica Bate,[4] Riyadi Adrizain,[5] Tarek Ahmed,[6] Sarah Alexander,[7] Arpita Bhattacharyya,[8] Jose Luis Copado-Gutierrez,[9] Ivan Gutierrez,[10,11] Yan Yin Lim,[12] Lisa Morrissey,[13] Gita Naidu,[14] Vivian Paintsil,[15] Nita Radhakrishnan,[16] Sheena Mukkada[1,2], Robert Phillips,[17,18] Kenneth A. Alexander,[19] and Kathy Pritchard-Jones[20]

Departments of [1]Global Pediatric Medicine and [2]Infectious Diseases, St. Jude Children's Research Hospital, Memphis, TN, USA; [3]Department of or Pediatrics, University of Tennessee Health Science Center, Memphis, TN, USA; [4]Department of Paediatric Oncology, Southampton Children's Hospital, Southampton, United Kingdom; [5]Department of Child Health, Faculty of Medicine Universitas Padjadjaran Dr. Hasan Sadikin General Hospital, Bandung, Indonesia; [6]Children's Cancer Hospital Egypt 57357, Cairo, Egypt; [7]Division of Haematology/Oncology, Hospital for Sick Children, Department of Pediatrics, University of Toronto, Toronto, Canada; [8]Tata Medical Center, Kolkata, India; [9]Universidad Anahuac Queretaro – División Ciencias de la Salud, Queretaro, Mexico; [10]Colsubsidio Investiga Research Group, Clinical Infantil Colsubsidio; Bogotá, Colombia [11]Division of Pediatric Infectious Diseases, Clinica Infantil Santa María del Lago, Bogotá, Colombia; [12]KK Women's and Children's Hospital, Singapore; [13]Boston Children's Hospital, Boston, MA, USA; [14]Chris Hani Baragwanath Academic Hospital, University of the Witwatersrand, Johannesburg, South Africa; [15]Department of Child Health, School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana; [16]Department of Pediatric Hematology Oncology, Post Graduate Institute of Child Health, Noida, India; [17]Regional Department of Haematology and Oncology, Leeds

Children's Hospital, Leeds, United Kingdom; [18]Centre for Reviews and Dissemination, University of York, York, United Kingdom; [19]Nemours Children's Hospital-Florida, Orlando, Florida, USA; [20]Developmental Biology and Cancer Research and Teaching Department, UCL Great Ormond Street Institute of Child Health, London, UK

[*]**Address correspondence to:** Dr. Miguela A. Caniza, Department of Global Pediatric Medicine, MS 721, St. Jude Children's Research Hospital, 262 Danny Thomas Place, Memphis, TN 38105-3678. Tel: 901-595-4194; Fax: 901-595-2099; E-mail: miguela.caniza@stjude.org

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Abbreviations

Abbreviation	**Definition**
AAP	American Academy of Pediatrics
CAR	Chimeric antigen receptor

CDC	Centers for Disease Control and Prevention
CI	Confidence interval
CLL	Chronic lymphocytic leukemia
EUA	Emergency Use Authorization
FDA	Food and Drug Administration
HCT	Hematopoietic cell transplantation
HIC	High-income country
LIC	Low-income country
LMIC	Low middle–income country
WHO	World Health Organization

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ORCIDs

Miguela A Caniza: https://orcid.org/0000-0002-7846-9605

Maysam Homsi: https://orcid.org/0000-0002-0665-246X

Jessica Bate: https://orcid.org/0000-0003-4933-9497

Riyadi Adrizain: https://orcid.org/0000-0001-6939-3306

Tarek Ahmed: https://orcid.org/0000-0002-0780-5106

Sarah Alexander: https://orcid.org/0000-0002-9695-1702

Arpita Bhattacharyya: https://orcid.org/0000-0003-3705-0995

Jose Luis Copado-Gutierrez: https://orcid.org/0000-0002-6011-542X

Ivan Gutierrez: https://orcid.org/0000-0002-9614-2040

Lisa Morrissey: https://orcid.org/0000-0001-5524-203X

Gita Naidu: https://orcid.org/0000-0002-4412-3825

Vivian Paintsil: https://orcid.org/0000-0002-8965-0549

Nita Radhakrishnan: https://orcid.org/0000-0002-7941-5641

Sheena Mukkada: https://orcid.org/0000-0001-5435-3707

Robert Phillips: https://orcid.org/0000-0002-4938-9673

Kathy Pritchard-Jones: https://orcid.org/0000-0002-2384-9475

Abstract

Background. The SARS-CoV-2 outbreak in 2020 evolved into a global pandemic, and COVID-19 vaccines became rapidly available, including for pediatric patients. However, questions emerged that challenged vaccine acceptance and use. We aimed to answer these questions and give recommendations applicable for use in pediatric patients with cancer by healthcare professionals and the public.

Methods. A 12-member global COVID-19 Vaccine in Pediatric Oncology Working Group made up of physicians and nurses from all world regions met weekly from March to July 2021. We used a modified Delphi method to select the top questions. The Working Group, in 4-member subgroups, answered assigned questions by providing brief recommendations, followed by a discussion of the rationale for each answer. All Working Group members voted on each recommendation using a scale of 1 to10, 10 being complete agreement. A "pass" recommendation corresponded to an agreement ≥7.5.

Results. We selected 15 questions from 173 suggested questions. Based on existing published information, we generated answers for each question as recommendations. The overall average agreement for the 24 recommendations was 9.5 (95% CI 9.4 to 9.6).

Conclusion. Top COVID-19 vaccine–related questions could be answered using available information. Reports on COVID-19 vaccination and related topics have been published at record speed, aided by available technology and the priority imposed by the pandemic; however, all efforts were made to incorporate emerging information throughout our project. Recommendations will be periodically updated on a dedicated website.

Introduction

The SARS-CoV-2 outbreak in Wuhan, China, in late 2019 rapidly evolved into a global pandemic, and vaccines emerged, as expected, to effectively control the disease.[1] Pharmaceutical companies quickly completed all steps for regulatory approval of several COVID-19 vaccines that were then made available to the public under the Emergency Use Authorization (EUA) of supervisory and regulatory agencies.[2,3,4,5] Despite compelling evidence indicating their effectiveness, multiple questions about the vaccines arose. These questions came from healthcare providers, patients, and families, including concerns about the safety of COVID-19 vaccines for children with cancer, hematopoietic cell transplant (HCT) or cellular therapy.

We aimed to review and select common, relevant questions about COVID-19 vaccines; answer those questions with the available evidence and information; and provide summary recommendations for healthcare providers, caregivers, and patients. Here we share how we selected the questions and our method for answering them by summarizing the available scientific literature and expert opinions.

Methods

Working Group selection. In March 2021, the multidisciplinary COVID-19 Vaccine in Pediatric Oncology Working Group was formed to answer emerging questions about the use of COVID-19 vaccines in children with cancer and/or HCT. The Working Group, composed of 12 individuals, including oncologists, infectious diseases physicians, and nurses from all World Health Organization (WHO) regions (Table 1), shared a global and multidisciplinary perspective. Members were nominated by the International Society of Pediatric Oncology regional leadership. Members were organized into four three-person subgroups, and consultants provided additional methodology and content expertise support. A parent/caregiver advisory group from around the world, established concurrently with our Working Group, has independently reported their findings of a survey of COVID-19 vaccine questions relevant to parents and caregivers.[6]

Targeted audience. We targeted healthcare providers, patient caregivers, families, and patients who need information to guide their recommendations and decisions about COVID-19 vaccines. Healthcare institutions, organizations' leaders, and decision makers for children with cancer, including families and healthcare providers, were also considered.

Virtual meetings and data management. Working Group coordinators and subgroup members held weekly meetings from March to July 2021 to communicate and discuss their progress. Project methods, including voting processes and literature review strategies, were shared; meeting notes and recordings were circulated among Working Group members. Surveys were anonymous; data were cleaned and managed by a coordinator.

Question selection. Questions about COVID-19 vaccines from professional healthcare organizations' websites ~~(including websites of the World Health Organization, U.S. Centers for~~

~~Disease Control and Prevention (CDC), American Cancer Society, MD Anderson Cancer Center, and St. Jude Children's Research Hospital (St. Jude)) (Box 1),~~ were reviewed. These websites were the American Cancer Society; Cancer Connect; Centers of Disease Control and Prevention (CDC); Fred Hutchinson Cancer Research Center; MD Anderson Cancer Center; The National Academies of Sciences, Engineering, and Medicine; Pancreatic Cancer Action Network; Tennessee Department of Health; St. Jude Children's Research Hospital; and the WHO. After collating 173 questions, we employed a modified Delphi method to identify the most relevant ones for our target audience (Figure 1). The list of questions was prepared through an electronic survey platform and distributed to 12 voting members to determine the importance of each question by using a Likert Scale (1 = Not at all important, 5 = Extremely important). Members also had the option to vote "0 = Beyond the scope" for questions unrelated to vaccinating children with cancer. Finally, Working Group members contributed to the list of questions for the panel to vote on during succeeding rounds. All voting was conducted anonymously.

Three voting sessions, as collective decision venues of the Working Group, were organized to select the top questions. Each panelist received a link to the electronic survey platform. In the first round, the panelists ranked an initial list of 132 questions selected from professional healthcare organizations' websites. After this initial vote, 30 top-scoring questions and 37 additional questions proposed by the subgroups were combined for the next round of voting. These added questions reflected the members' professional medical experiences, and the panel ranked the 67 questions during the second round of voting. The rankings were shared at a virtual meeting and displayed using the digital online whiteboard platform (MURAL® [https://www.mural.co/]). Over the subsequent two sessions, the panel completed the third round

of voting through open discussion until a consensus was reached on the 15 most essential questions (**Q1**-**Q15**) to answer (Table 2; Figure 1).

Literature review. The search strategy was developed in collaboration with the St. Jude Biomedical Library. For the search in PubMed, a combination of keywords, medical subject headings terms, and filters was used. Because of the rapidly evolving evidence base for SARS-CoV-2, new publications that became available after the search strategy was completed were included in the review of evidence by members.

Review of the evidence. Each subgroup had three members, at least one of whom was an infectious diseases specialist or had training in infectious diseases. They prepared recommendations (**R1**-**R15**) for three to five questions by evaluating the citations generated by the search for relevance and study quality. Quality was assessed using the Oxford Levels of Evidence method,[7] chosen for its relatively simple application and transparency.

Agreement with the recommendations. Each question, answer, and rationale were presented and discussed at Working Group meetings. Each member anonymously graded the recommendations on a 10-point Likert Scale (0 = complete disagreement, 5 = neutral position, 10 = complete agreement). The level of agreement for each recommendation was represented by the mean score and 95% confidence interval (CI).

Statistical analyses. To summarize the demographics of the Working Group, we used descriptive statistics; this included members' medical specialty and the World Bank designations of their countries:[8] high-income countries (HIC), upper-middle-income countries (UMIC), lower-middle-income countries (LMIC), and low-income countries (LIC) (Table 1). An average Likert score ≥7.5 corresponded to a "pass" recommendation and was considered an agreement. We provided

a mean score and 95% confidence interval (CI) for each recommendation. CIs were constructed using a bias-correct bootstrap method with 5000 iterations per estimate and R software.[9]

Results

Q1. Is the vaccine safe for pediatric patients with cancer and other underlying immunocompromising conditions?

R1: The vaccine appears to be safe for patients with cancer and other underlying immunocompromising conditions.

Level of agreement: 9.4 (95% CI 9-9.8).

Q2. What are the indications and contraindications for receiving the COVID-19 vaccine?

R2a: Indications for receiving a COVID-19 vaccine include any individual with cancer undergoing treatment, any patient whose anticancer treatment has ended, and any patient who is at least 100 days post-HCT and chimeric antigen receptor (CAR) T–cell therapy.

Level of agreement: 9.2 (95% CI 8.5-9.8).

R2b: Contraindications for receiving a COVID-19 vaccine include any individual with a history of allergy to vaccine components, or any individual with a history of an anaphylactic reaction following the first dose of a COVID-19 vaccine. Vaccine may consist of mRNA, protein antigens, replication-defective adenovirus, toxoids, stabilizers, adjuvants, antibiotics, and preservatives.

Level of agreement: 9.8 (95% CI 8.6-10).

R2c: Those living in the same household as a person with cancer, caregiver, and close contacts should be vaccinated as soon as possible.

Level of agreement: 10 (95% CI 10-10).

Q3. What considerations should be made for vaccinating patients during anticancer treatment? Does receiving the COVID-19 vaccine require altering anticancer treatment?

R3a: If possible, COVID-19 vaccination should be completed at least 14 days before starting cancer-directed therapy.

Level of agreement: 9.4 (95% CI 8.9-9.8).

R3b: If anticancer therapy cannot be delayed, COVID-19 vaccination should be given outside of the period of anticipated anticancer therapy–induced cytopenia.

Level of agreement: 9.4 (95% CI 8.6-9.9).

R3c: For recipients of HCT and CAR T–cell therapy, COVID-19 vaccination is recommended a minimum of 100 days after completion of transplantation therapy.

Level of agreement: 9.2 (95% CI 8.07-9.76).

Re3d: There is no indication for altering anticancer treatment after COVID-19 vaccination.

Level of agreement: 9.6 (95% CI 9.2-9.9).

Q4. After anticancer treatment has been completed, is COVID-19 re-vaccination required if the patient was vaccinated while immunosuppressed?

R4a: An additional dose is indicated for the primary vaccine series to increase the immune response in patients who received BNT162b2 mRNA or mRNA-1273 SARS-CoV-2 vaccines.

Level of agreement: 8.8 (95% CI 7.9-9.5).

R4b: A booster dose is indicated to enhance or re-establish the protection by the primary series of COVID-19 vaccine doses.

Level of agreement: 9.5 (95% CI 9-9.9).

Q5. After bone marrow transplantation, when should the child receive a COVID-19 vaccine?

R5a: Current recommendations by leading international professional organizations support vaccinating patients as early as 100 days after HCT and CAR T–cell therapy.

Level of agreement: 9.3 (95% CI 8.5-9.9).

R5b: Patients who received COVID-19 vaccination prior to HCT should be re-vaccinated with a complete COVID-19 vaccine series at least 100 days after HCT and CAR T–cell therapy.

Level of agreement: 9.4 (95% CI 8.7-9.9).

Q6. What is the recommendation for COVID-19 vaccination for children younger than 16 years of age, including infants?

R6a: All children (≥5 years), including those with cancer and receiving anticancer treatment or who recently completed anticancer treatment, should be vaccinated against COVID-19 by using an approved dosage for the age group.

Level of agreement: 9.3 (95% CI 8.6-9.8).

R6b: All survivors of childhood cancer should be vaccinated.

Level of agreement: 9.8 (95% CI 9.5-10).

R6c: All children (≥5 years) with certain nonmalignant hematologic disorders (e.g., aplastic anemia, sickle cell disease, Evans syndrome, Schwachman diamond syndrome, Fanconi anemia) should be vaccinated with an approved dosage for the age group.

Level of agreement: 9.4 (95% CI 8.7-9.9).

Q7. Can children with cancer receive a COVID-19 vaccine if they are participating in a clinical trial?

R7: The decision to administer a COVID-19 vaccine to a pediatric patient participating in a therapeutic clinical trial must be based on the individual patient, the underlying disease severity/stage of progression, and the criteria of the clinical trial in which the child is enrolled.

Level of agreement: 9.2 (95% CI 8.4-9.9).

Q8. What are the findings of clinical trials testing the COVID-19 vaccine in the pediatric population?

R8: The BNT162b2 vaccine is safe and effective in children 5 years or older.

Level of agreement: 9.1 (95% CI 8.2-9.8).

Q9. Which COVID-19 vaccines are approved for use in immunocompromised patients? Does it matter which type of vaccine they receive?

R9: Patients should receive the COVID-19 vaccine for which they are eligible and have access. However, live-attenuated virus vaccines and replicating viral–vectored vaccines are not recommended for patients with immunosuppression.

Level of agreement: 9.8 (95% CI 9.5-10).

Q10. Should caregivers and family members of patients with cancer receive the COVID-19 vaccine?

R10: Caregivers, family members, close contacts, and household members of patients with cancer should be vaccinated against COVID-19.

Level of agreement: 10 (95% CI 10-10).

Q11. Is it safe for patients with cancer who have received the COVID-19 vaccine to go back to school?

R10: In-person school attendance for children receiving anticancer therapy during the COVID-19 pandemic requires individualized decision-making; however, vaccination should be considered.

Level of agreement: 9.1 (95% CI 8.3-9.8).

Q12. What can healthcare providers do to address vaccine hesitancy?

R12: Healthcare providers should initiate conversations with caregivers and family members of patients with cancer at an early stage to understand and address their underlying concerns about getting vaccinated against COVID-19 and promote vaccination acceptability.

Level of agreement: 9.8 (95% CI 9.5-10).

Q13. Should a previously infected patient (asymptomatic or symptomatic) receive a COVID-19 vaccine? How soon after SARS-CoV-2 infection should the patient receive the vaccine?

R13: Children with a history of SARS CoV-2 infection should be offered vaccination whenever feasible. Children can safely wait for 2 to 3 months after infection before getting vaccinated.

Level of agreement: 9.3 (95% CI 8.7-9.8).

Q14. What is known about the long-term protection provided by the currently available COVID-19 vaccines?

R14: COVID-19 vaccines do not provide lifelong protective antibody levels; the antibody level wanes after several months, requiring a COVID-19 vaccine booster dose to maintain a protective level of immunity.

Level of agreement: 9.6 (95% CI 8.9-10).

Q15. Can a vaccinated person still transmit COVID-19?

R15: Fully vaccinated people can experience a breakthrough infection and transmit COVID-19 to others.

Level of agreement: 9.8 (95% CI 9.4-10).

Discussion

A Working Group, representing healthcare workers of children with cancer from all world regions, identified and selected 15 questions about COVID-19 vaccines in children with cancer and HCT. Questions addressed the safety and efficacy of COVID-19 vaccines for the pediatric population, including those with cancer; COVID-19 vaccines indications and contraindications in relation to the treatment of cancer and HCT; vaccination for care providers and family members to protect the patient with cancer; and patient protection when attending schools. Finally, questions about COVID-19 vaccination hesitancy were also identified.

Safety information about COVID-19 vaccines in pediatric patients with active cancer or receiving anticancer treatment was extrapolated from data obtained from adult patients and immunocompetent children.[10-12] None of the current COVID-19 vaccines are "live" vaccines (Table 3), which is important because vaccines that contain agents that actively replicate in the recipient should be avoided in immunocompromised individuals, including patients with

malignancies undergoing treatment.[13] Despite a milder manifestation of COVID-19 among children,[14] the severity in selected pediatric populations of some ethnic backgrounds, low socioeconomic status,[15] or those with co-morbidities[16] was unacceptable. Among children with cancer, the severity of COVID-19 was associated with age older than 11 years, pulmonary co-morbidities, obesity, cytopenia, and certain malignancies.[17] As efficacy data became available,[11,12] public health and global health agencies and professional organizations have recommended pediatric vaccination.[18-20] Multiple COVID-19 vaccines are currently available, but for children and adolescents, the efficacy and safety data are available only for BNT162b2[11,12] and mRNA-1273.[21,22] Clinical trials in adolescents (12–17 years old)[11] and children (5–11 years old)[12] showed that BNT162b2 is safe, immunogenic, and efficacious. Similarly, clinical trials of mRNA-1273 vaccine among adolescents[22] and children[21] demonstrated safety and efficacy. Both vaccines are currently indicated for these age groups in many regions of the world.[19,23-25] Small myocarditis risk documented in children and adolescent outweighs the benefit of COVID-19 vaccine.[26 27] Although the safety should be similar in age-matched children with cancer, vaccine efficacy will likely be lower in immunocompromised children. The best information would be gained by a clinical trial of COVID-19 vaccination in children with cancer. Until such trial is conducted, a surveillance of the safety and immunogenicity of vaccine administered to any child or adolescent, especially those with cancer, could provide valuable information. In agreement with Hwang et al.,[28] we advocate creating national reporting systems for pediatric patients receiving anticancer treatment and COVID-19 vaccines. Such reports would facilitate safety, immunogenicity, and efficacy studies of patients with cancer.

Although the immune response to vaccination in patients with cancer may be lower than that of healthy individuals, vaccination may still prevent or decrease the severity of infections, including in those with specific medical conditions (Figure 2). Thus, public health agencies and professional societies broadly recommend vaccination, including for children with cancer and those receiving HCT/cellular therapy.[29-35] The **recommendations** of the National Cancer Institute and the CDC are that all patients with cancer receive a COVID-19 vaccine.[18,33] Those who have undergone HCT or received CAR T–cell therapy should delay the COVID-19 vaccine until 100 days after completion of treatment.[36] A systematic review [37] of patients with solid tumors in remission, myeloproliferative neoplasia, myelodysplastic syndromes without treatment, and those receiving endocrine treatment or noncytotoxic agents showed no restrictions or time window for vaccination. However, for patients with lymphoid malignancies requiring B-cell–depleting agents and those with solid tumors requiring cytotoxic agents, COVID-19 vaccines should be given before the planned anticancer regimen, if feasible. If not, vaccine doses should be timed to avoid coinciding with expected chemotherapy-induced cytopenia. Anti-CD20 antibody therapy produces a blunted immune response to vaccines, including a COVID-19 vaccine, especially in those patients on active treatment (less than 3 months after receiving anticancer therapy).[38] The pre-exposure prophylaxis product tixagevimab co-packaged with cilgavimab received EUA approval for situations in which COVID-19 vaccination might not be effective or persons may experience severe reaction to the COVID-19 vaccines.[39] Knowledge of vaccine components can guide selection of alternative products for those who exhibit an allergic reaction.[18]

Children receiving chemotherapy have lower seroconversion and seroprotection rates after vaccination than do healthy children.[40] The rate of COVID-19 vaccine seroconversion in adult

patients with cancer is lower than that in immunocompetent patients.[37] Similarly, seroconversion rates are low in patients with hematologic malignancies and patients receiving highly immunosuppressive therapies and HCT.[10] The level of immunity achieved depends on the underlying diagnosis, the intensity of chemotherapy received, the timing of treatment, and any pre-existing immune dysfunction.[10,37] Higher or additional vaccine doses[41 42] are frequently used when immunizing oncology patients against influenza. An additional dose of vaccine is recommended for immunosuppressed patients, if they were vaccinated while immunosuppressed (Table 4).[29-31,33] This additional COVID-19 vaccine dose is expected to maximize protection. Surveillance of children with cancer receiving COVID-19 vaccines should assess the duration of immune response to ascertain the frequency of booster doses required to extend protection. Data from COVID-19 vaccine studies in adults indicate waning immunity over time.[43,44] Experience and relevant data suggest that immunization could be started 6–12 months after HCT and CAR T–cell therapies.[13] Surveillance data suggest that COVID-19 vaccination of patients post-HCT can mount a preliminary immune response to COVID-19 and other vaccinations and that vaccination should begin 3 months after transplantation.[45,46] Based on these data, professional societies recommend vaccinating patients as early as 100 days post-HCT and CAR T–cell therapy.[29] The efficacy of primary vaccination and boosters regimen[30,34] in immunocompromised patients should be studied and reported. These additional doses and booster indications include those with HCT and CAR T–cell therapy.[18,25,34] Moreover, like influenza, the SARS-CoV-2 transmission rate in the community and the emergence of new variants[47] should be considered when deciding on additional vaccine composition and doses for any individual. COVID-19 vaccines are considered investigational agents and their use could complicate clinical trial eligibility or vaccine administration for an enrolled participant, if the protocol prohibits the

concomitant use of other investigational agents. To address this, the FDA clarified that COVID-19 vaccines should not be considered investigational agents for patients in cancer clinical trials.[48] The European Medicines Agency, and other organizations have provided guidance for using COVID-19 vaccines in cancer therapy trials.[49,50]

Decisions about **school attendance** for children with cancer, regardless of the COVID-19 pandemic, are complex.[51] Medical recommendations vary widely by geography, the type and phase of therapy, and parental choice. Even within the same oncology program, providers may offer varied guidance. Regardless of the vaccination status, children with cancer should adhere to local COVID-19–related public measures for school safety.[52] Decisions about in-person school attendance could be guided by local, ongoing COVID-19 epidemiology and family preferences. During anticancer treatment, attending school in person might not increase the risk of infections if the patient adheres to immunization recommendations (e.g., influenza and COVID-19), uses respiratory barrier precautions (e.g., masks), and practices heightened hand hygiene.[53] Factors that could inform and influence the decision to attend school include the patient's age, the grade in which the patient is enrolled, vaccination against COVID-19 and other viruses (e.g., influenza), and the child's medical condition and treatment plans. Adolescents attending high school may prefer returning to school if their stage of disease permits. In contrast, parents of younger children may opt to withhold in-person schooling for a limited period.[51] Currently, professional organizations and agencies, including the WHO and the American Academy of Pediatrics (AAP) endorse in-person school attendance.[20 52] To render school attendance safe during the COVID-19 pandemic, the AAP recommends that all eligible individuals, including children with cancer, receive COVID-19 vaccine. Also, for the 2021 – 2022 school year, the AAP recommended that all school staff and students older than 2 years wear face masks at

school, regardless of vaccination status, especially during indoor activities.[54] Furthermore, schools should follow local public health agencies' guidelines for quarantine and isolation protocols. COVID-19 transmission rates in local schools should be reviewed periodically, and that information should guide school policies (e.g., implementing virtual learning).[20]

The Advisory Committee on Immunization Practices and other guidelines recommend that **close contacts** of immunosuppressed patients receive all routine immunizations for vaccine-preventable communicable diseases.[13] Household spread of COVID-19 infection is well documented, and a recent meta-analysis showed secondary infection rates to be 17% in households.[55] Caregivers and household members have a unique opportunity to protect immunocompromised patients with cancer. Immunizing caregivers, so-called "cocoon vaccination,"[56] is a highly effective strategy for children with cancer who are not able to be vaccinated and should include household members and other close contacts. The National Comprehensive Cancer Network and the American Cancer Society both recommend this approach. These entities support using any of the available FDA- or EUA-approved vaccines (BNT162b2, mRNA-1273, and Ad26.COV2.S vaccine) in eligible patients.[29,57]

Acceptance rates of COVID-19 vaccination among parents and caregivers range from 52% to 89% across multiple studies.[58-65] In congruence with the WHO vaccine-hesitancy model, the 3Cs,[66] safety and efficacy of vaccine (Confidence), perceived lower risk of contracting and severity of disease among children (Complacency), and vaccine literacy (Convenience) were the major deterrents for families/caregivers in accepting COVID-19 vaccine for their child/children.[58-65,67] No study has reported the effectiveness of interventions that address hesitancy for COVID-19 vaccination among the pediatric population. Communication remains an essential tool for the success of any immunization program.[59,68] Open, transparent

communication from trusted sources about the rationale for vaccination can significantly increase the confidence and uptake of vaccines. Healthcare providers are commonly described as the trusted source of information. Parents/caregivers are more likely to vaccinate their children if information and recommendations are given by their healthcare provider.[58-61,69] Healthcare providers should use clear, comprehensible communication tailored to their audience's literacy level, relevant to minority and underprivileged groups. Initiating conversations with parents/caregivers at an early stage to understand the underlying concerns about vaccine acceptability may allay anxiety and mitigate misinformation.[59-61] Targeted educational efforts are required to clarify information about COVID-19 vaccination for parents or caregivers of a child with a chronic illness. Health communication messages should also emphasize the risk and consequences of the disease and the importance of COVID-19 vaccination for herd immunization, which could contribute to overall COVID-19 control.[58,60,65,69] Training healthcare professionals to make recommendations using presumptive language and positive framing can increase vaccine acceptability among parents.[70,71]

Study Limitations

COVID-19 is a new disease, and information about the disease, vaccination, and immune responses is evolving rapidly. Although efforts were maximized to include new information reported after the inception of our project and the best available evidence was applied to each answer, new findings have inevitably been published since manuscript preparation. Another potential limitation is that the websites used for selecting questions in Round 1 were primarily from North America. Nevertheless, more than half of the questions in the final 15-question list were provided by the global Working Group members. Early in the pandemic, a limited number

of websites contained questions about COVID-19 vaccines, but more emerged as the pandemic unfolded. We reviewed two such websites[31,32] and compared their questions with our 15-question list and found that we had addressed most questions on those sites.

Conclusion

We identified 15 key COVID-19–related questions and answered them with the available information we carefully extracted from the growing body of literature. Similar recommendations to our study were reached by other professional associations, validating our findings.[72,73] Reports addressing COVID-19 vaccines and related topics have been produced at record speed, aided by available technology and the priority imposed by the pandemic. As new information emerges, group members affiliated with professional networks, including the St. Jude Global Infectious Diseases Network, will continue to update recommendations on our dedicated website.[74]

Figure 1. Flow chart for the selection of the top questions (N=number of questions)

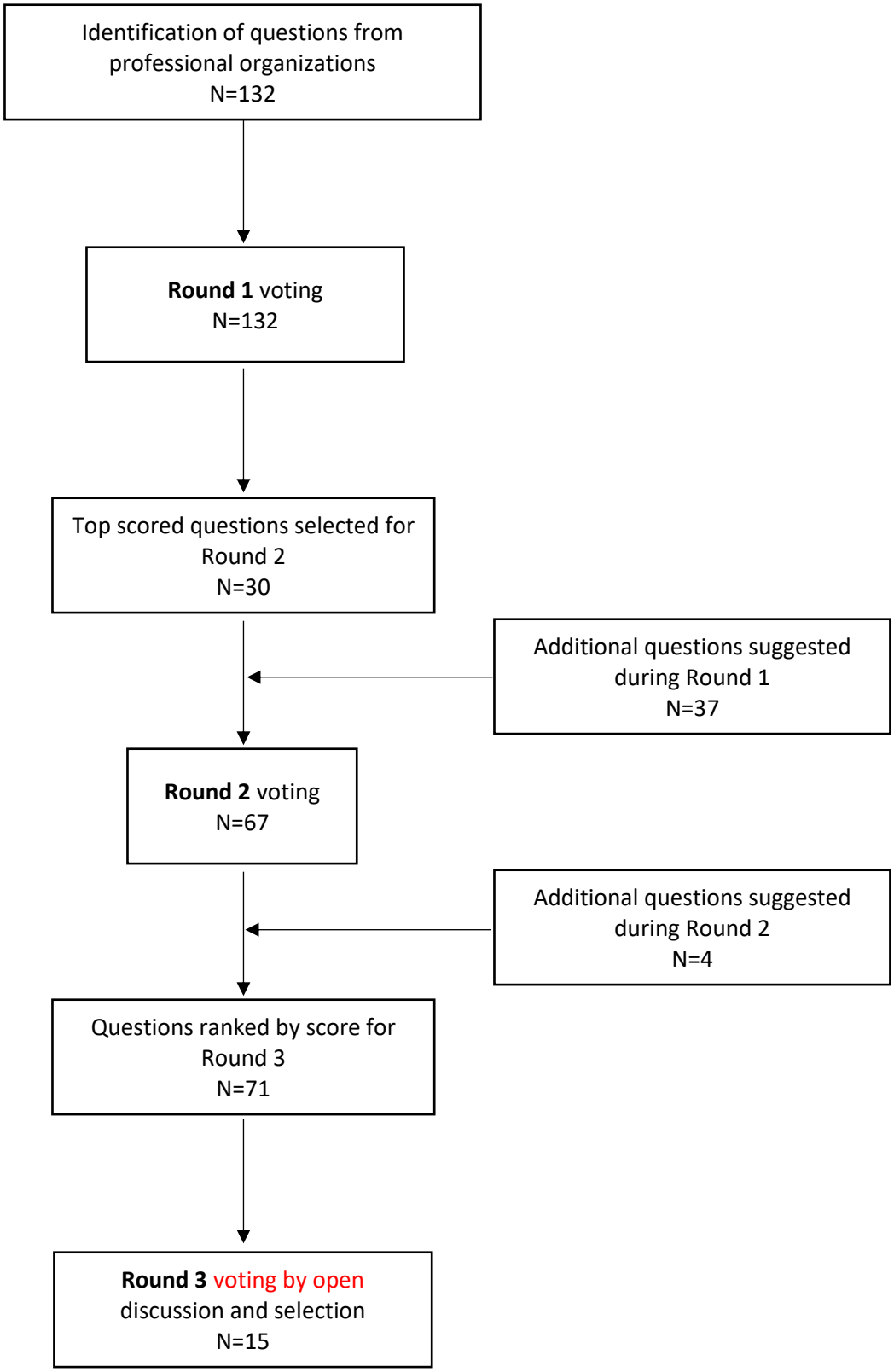

Figure 2. Medical conditions that can result in severe COVID-19[a]

- Immunosuppressive states (humoral and cellular). These states can occur during cancer, organ transplantation, HCT and CAR T–cell therapies, and HIV infection. Situations applying to children with hematologic and/or oncologic disease are listed below (the list is not exhaustive).
    - Severe: Primary or inherited immunodeficiencies, such as X-linked agammaglobulinemia, SCID, and CGD; secondary or acquired immunodeficiency caused by a disease process or its therapy, such as HCT (<100 days post-HCT and ALC <100 or severe GvHD), ALL on induction with ALC <100, or relapsed or refractory ALL with ALC <100, recent T-cell therapy (ATG <90 days, alemtuzumab <6 months); HIV with CD4+ T-cell count <100.
    - Moderate: ALL on induction with ALC 100-300; other malignancies with ALC <100; bone marrow failure with ALC <100; other high doses of immunosuppressant (example steroids); HIV infection with CD4+ T-cell count 100-200.
- Sickle cell disease or thalassemia
- Chronic organ diseases: kidney disease, liver disease, lung disease, heart disease
- Cystic fibrosis
- Neurologic disease
- Type 1 or 2 diabetes
- Down syndrome
- Obesity
- Tuberculosis

[a]A COVID-19 infection is considered severe when a person with COVID-19 is hospitalized, needs intensive care, requires a ventilator for breathing, and/or dies from COVID-19.[75]

Abbreviations: ALC, absolute lymphocyte count; ALL, acute lymphoblastic leukemia; ATG, anti–thymocyte globulin; CAR, chimeric antigen receptor; CGD, chronic granulomatous disease; GvHD, graft-versus-host disease; HCT, hematopoietic cell transplantation; SCID, severe combined immunodeficiency disease

Table 1. Question assignments and Working Group members' countries and specialties

Question assignments	Members' initials	Country (WHO regional groupings of countries)	Country economic classification			Specialty
			LIC/LMIC	UMIC	HIC	
1-3	AB	India (SEAR)	X			PO
	VP	Ghana (AFR)	X			PO
	LM	United States (AMR)			X	N
4-6	JB	United Kingdom (EUR)			X	PO
	JLC	Mexico (AMR)		X		PID
	GN	South Africa (AFR)		X		PO
7-11	NR	India (SEAR)	X			PO
	RA	Indonesia (SEAR)	X			PID
	SA	Canada (AMR)			X	PO
12-15	TA	Egypt (EMR)	X			PO
	IG	Colombia (AMR)		X		PID
	YYL	Singapore (WPR)			X	N

Abbreviations: AFR=African region; AMR=American region; EMR=Eastern Mediterranean region; EUR=European region; N=nursing; PID=pediatric infectious diseases; PO=pediatric oncology; SEAR=South-East Asian Pacific region; WHO=World Health Organization; WPR=Western Pacific region

Table 2. Most relevant and frequent COVID-19 vaccine questions selected by the panel

Number	Question
1	Is the vaccine safe for pediatric patients with cancer and other underlying immunocompromising conditions?
2	What are the indications and contraindications for receiving the COVID-19 vaccine?
3	What considerations should be made for vaccinating patients during anticancer treatment? Does receiving the COVID-19 vaccine require altering anticancer treatment?
4	After anticancer treatment has been completed, is COVID-19 re-vaccination required if the patient was vaccinated while immunosuppressed?
5	After bone marrow transplantation, when should the child receive a COVID-19 vaccine?
6	What is the recommendation for COVID-19 vaccination for children younger than 16 years of age, including infants?
7	Can children with cancer receive a COVID-19 vaccine if they are participating in a clinical trial?
8	What are the findings of clinical trials testing the COVID-19 vaccine in the pediatric population?
9	Which COVID-19 vaccines are approved for use in immunocompromised patients? Does it matter which type of vaccine they receive?
10	Should caregivers and family members of patients with cancer receive the COVID-19 vaccine?
11	Is it safe for patients with cancer who have received the COVID-19 vaccine to go back to school?
12	What can healthcare providers do to address vaccine hesitancy?
13	Should a previously infected patient (whether asymptomatic or symptomatic) receive a COVID-19 vaccine? How soon after SARS-CoV-2 infection should the patient receive the vaccine?
14	What is known about the long-term protection provided by the currently available COVID-19 vaccines?
15	Can a vaccinated person still transmit COVID-19?

Table 3. Information about COVID-19 vaccines[a]

Vaccine Name	Platform	Manufacturer/Location	Minimum Age	No. Doses for Primary Series
BNT162b2 COMIRNATY Tozinameran[b]	mRNA	Pfizer and BioNTech/USA	6 months	3 (6 months–4 years) 2 (≥ 5 years)
mRNA-1273 SPIKEVAX[b]	mRNA	Moderna/USA	6 months	2
NVX-CoV2373 Novavax[b]	Adjuvanted SARS-CoV-2 recombinant spike protein	Novavax/USA	18 years	2
AZD1222 Vaxzevria	Nonreplicating chimp adenovirus-vector encoding the spike protein gene of SARS-CoV-2	SK BIO Oxford-AstraZeneca/UK	18 years	2
Sinopharm/BIBP COVID-19 vaccine BIBP Covilo	Inactivated SARS-CoV-2	Beijing Institute of Biological Products Co., Ltd./China	18 years	2
Sinopharm (Wuhan)	Inactivated SARS-CoV-2	Sinopharm's Wuhan Institute of Biological Products/China	18 years	2
CoronaVac	Inactivated SARS-CoV-2	Sinovac Biotec/China	18 years	2
BBV152 Covaxin	Inactivated SARS-CoV-2	Bharat Biotech and Indian Council of Medical Research/India	18 years	2
Ad26.COV2.S[b]	Replication-incompetent recombinant adenovirus serotype 26, vector for SARS-CoV-2 spike protein gene	Janssen (Johnson & Johnson)/USA	18 years	1
Sputnik V	Human nonreplicative Ad26 (in first dose) and Ad5 (in second dose) adenovirus vector modified for SARS-CoV-2 spike protein gene	The Gamaleya Research Institute of Epidemiology and Microbiology/Russia	18 years	2

Sputnik Light	Nonreplicating recombinant adenovirus Ad26 vector for spike protein gene of SARS-CoV-2	The Gamaleya Research Institute of Epidemiology and Microbiology/Russia	18 years	1
Soberana 2	Recombinant SARS-CoV-2 receptor-binding domain–conjugated to tetanus toxoid	The Finlay Vaccine Institute and The Centre of Molecular Immunology/Cuba	19 years	2
Soberana Plus[c]	Dimeric SARS-CoV-2 receptor-binding domain adsorbed on 1250-µg alumina	The Finlay Vaccine Institute and The Centre of Molecular Immunology/Cuba	19 years	1

[a]The information presented here was extracted from: Status of COVID-19 Vaccines within WHO EUL/PQ Evaluation Process.[76]
[b] COVID-19 vaccines approved or authorized by the FDA under EUA (06/27/2022).[30]
[c]Soberana Plus vaccine is administered as a booster for individuals with pre-existing immunity to SARS-CoV-2.

Table 4. COVID-19 vaccines for children, pre-teens, teens, and adults who are moderately or severely immunocompromised, following the Centers for Disease Control and Prevention guidelines[a]

Vaccine	Age indication	Primary Dose[b]	No. of doses in PS	Interval between doses	Additional dose for immunocompromised people	BD recommendation and interval between previous dose and 1st BD	BD recommendation and interval between 1st BD and 2nd BD
BNT162b2	6 mos–4 y	3	3	3 wks between Dose 1 and Dose 2 ≥8 wks between Dose 2 and Dose 3	NR	BD NR	BD NR
BNT162b2	5–11 y	10	2	3 wks (21 days)	Recommended (≥28 days)	BD recommended ≥3 months for immunocompromised (If primary is BNT162b2)	BD NR
BNT162b2	12–17 y	30	2	3 wks (21 days)	Recommended (>28 days)	BD recommended ≥3 months for immunocompromised (If primary is BNT162b2)	BD recommended ≥4 months for immunocompromised (If primary is BNT162b2)
BNT162b2	≥18 y	30	2	3 wks (21 days)	Recommended (>28 days)	BD recommended ≥3 months for immunocompromised (If primary is BNT162b2)	BD recommended ≥4 months for immunocompromised (If primary is BNT162b2)
mRNA-1273	6 mos–5 y	25	2	1 month (28 days)	Recommended (>28 days)	BD NR	BD NR
mRNA-1273	6–11 y	50	2	1 month (28 days)	Recommended (> 28 days)	BD NR	BD NR
mRNA-1273	12–17 y	100	2	1 month (28 days)	Recommended (> 28 days)	BD NR	BD NR
mRNA-1273	≥18 y	100	2	1 month (28 days)	Recommended (> 28 days)	BD recommended ≥3 months for immunocompromised (If primary is mRNA-1273; BD 50 µg)	BD recommended ≥4 months for immunocompromised (If primary is mRNA-1273; BD 50 µg)

Ad26.COV2.S	≥18 y	5×10^{10} viral particles	1	N/A	Recommended (> 28 days)	Recommended mRNA vaccine dose ≥2 months (If primary is J&J/Janssen)	BD recommended mRNA vaccine dose ≥4 months for immunocompromised (If primary is Ad26.COV2.S)
NVX-CoV2373	≥18 y	5	2	3–8 wks (3 wks in immunocompromised)	NR	BD NR	BD NR

[a]The information presented here was extracted from COVID-19 Vaccines for Moderately to Severely Immunocompromised People.[30]
[b]The primary dose of vaccine is given in micrograms, unless otherwise indicated.
Abbreviations: BD=booster dose; J&J=Johnson & Johnson; N/A=not applicable; NR=not recommended; PS=primary schedule; wks=weeks; y=years
Note: BNT162b2 product is the Pfizer-BioNTech or COMIRNATY® vaccine; mRNA-1273 product is the SPIKEVAX or Moderna; and the Ad26.COV2.s product is the Janssen vaccine. NVX-CoV2373 product is the Novavax.
https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/immuno.html
https://www.cdc.gov/vaccines/acip/recs/grade/covid-19-moderna-pfizer-children-vaccine-etr.html

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