

Title: Is There a Secondary Vaccine Hesitancy? Parental Attitudes Toward Revaccination of Childhood Cancer Survivors

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Short Running Title: Secondary Vaccine Hesitancy

Keywords: Immunology, Pediatric hematology/oncology, Vaccines, Cancer biology, Late effects of cancer treatment, Chemotherapy

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Abbreviation Key	
Advisory Committee on Immunization Practices	ACIP
Infectious Disease Society of America	IDSA
Primary Care Physician	PCP
Centers for Disease Control	CDC

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26 Target Journal: Pediatric Blood and Cancer

27 Article Type: Research Article

28 Parameters: 1200-word main text, 250-word abstract, 2 figures, unlimited references

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30 **Contributors' Statements:**

31 Dr. Ezeoke drafted the interview tool, conducted the interviews, analyzed and interpreted the
32 data, drafted and revised the manuscript, and approved the final version as submitted.

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34 Dr. Goteti assisted with data analysis, drafted and revised the manuscript, and approved the final
35 version as submitted.

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37 Dr. Cashell drafted and revised the manuscript, and approved the final version as submitted.

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39 Dr. Caruso Brown conceived and designed the study, drafted and revised the interview tool,
40 analyzed and interpreted the data, drafted and revised the manuscript, and approved the final
41 version as submitted.

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43

44 ABSTRACT

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46 **Introduction:** Many children and adolescents who were vaccinated prior to cancer treatment
47 lose humoral immunity after completion of therapy. Pediatricians and pediatric oncologists often
48 recommend re-immunization, although there is little consensus on timing and approach to
49 serologic testing. However, vaccine hesitancy in the U.S. is a growing problem. It is not known
50 whether parents who initially permitted vaccination might demonstrate secondary hesitancy
51 regarding re-immunization.

52 **Methods:** We conducted a qualitative study to explore parental attitudes toward re-immunization
53 after completion of cancer therapy. Twenty primary caregivers of current pediatric cancer
54 patients participated in structured interviews exploring knowledge and understanding of
55 immunity and vaccination; previous experiences with vaccines; and attitudes toward vaccines
56 and revaccination.

57 **Results:** Of those interviewed, 80% were female and 90% were White Non-Hispanic. Of
58 interviewees' children with cancer, 60% were male, 75% had been diagnosed within the past 6
59 months, and 45% had leukemia or lymphoma. All caregivers demonstrated a basic understanding
60 of vaccination, but only 65% understood that it was possible to lose immunity even with
61 previous vaccination. All caregivers were willing to have their children immunized if tests
62 showed lack of humoral immunity, with 85% expressing a preference for testing prior to
63 revaccination.

64 **Conclusions:** Primary caregivers of children with cancer are willing to consider re-immunization
65 interest but do express some secondary hesitancy and strongly prefer that the need for re-
66 immunization be established via serologic testing, rather than performed empirically. Caregivers'

beliefs and preferences regarding re-immunization in pediatric oncology should be considered in the development of post-treatment guidelines.

INTRODUCTION

Vaccine hesitancy – defined as an active desire to defer or omit a vaccine recommended by the Advisory Committee on Immunization Practices (ACIP) – is a growing problem in the U.S.^{1,2} Although exact rates of vaccination are difficult to measure, proxy measures, such as requests for school vaccine exemptions and pediatrician reports, suggest that vaccine uptake has declined steadily in some regions.^{3,4} A study of measles outbreaks in the U.S. determined that more than half and as many as 93% of victims of such outbreaks were intentionally unvaccinated.⁵

Children receiving chemotherapy for cancer are particularly susceptible to these diseases; however, some risks persist even after completion of therapy due to loss of humoral immunity.⁶ Humoral immunity and cell-mediated immunity are affected during chemotherapy. Current research is aimed at developing re-immunization guidelines, including considerations of optimal timing of re-immunization.^{9,10} While Infectious Disease Society of America (IDSA) Clinical Practice Guideline exist for stem cell transplant patients, no widely accepted standardized re-immunization protocol exists for non-transplant patients.^{11,12} Multiple countries, including Italy and the United States, have formulated individual guidelines, where revaccination is recommended three to six months post chemotherapy without serologic testing.¹³⁻¹⁶

In our clinical experience, some vaccine-hesitant parents faced with a recommendation to re-immunize automatically after therapy, simply requested serologic testing from another provider, such as their children's primary care physicians (PCP). Most PCPs readily granted such a

request, and, although the cost of a serologic test typically exceeds the cost of a dose of the vaccine, many or most private insurance companies do pay for these tests. Such experiences raised ethical questions about the potential for conflict between clinical practice guidelines rooted in cost-effectiveness and parents' perceptions of their children's best interests. We sought to describe the attitudes of parents of children with cancer regarding re-immunization after completion of therapy in order to understand their preferences with regard to possible clinical practice guidelines.

METHODS

We conducted structured interviews with twenty guardians of children with cancer who were admitted to the inpatient pediatric oncology service. Parents and guardians were approached on five separate days over the course of six-months and invited to participate. All families of children with a cancer diagnosis who were inpatient on a given interview day were approached, with the exception of children deemed clinically unstable by the attending physician. Otherwise, there were no exclusions for admitting diagnosis, cancer diagnosis, stage of treatment, or prognosis.

The content of the structured interview tool was developed by the first and senior authors, in consultation with a pediatric infectious disease specialist, and reviewed by two other pediatric oncologists for content validity and three parents of former pediatric oncology patients (none of whom had a background in science or medicine) for comprehension and construct validity. Interviews were divided into nine sections: participant demographics; characteristics of each

participant's child with cancer; participant's understanding of immunization and immunity; previous experience with pediatric immunizations; experience with immunizations during or after treatment; attitudes toward re-immunization after treatment *for the participant's child*; attitudes toward immunization *in general*; attitudes toward re-immunization *in general*; and changes in attitudes over time (as perceived by participants).

Interviews lasted approximately 45-60 minutes. Responses were entered in a database in REDCap, a secure web-based data capture application, during the interview.¹⁶ Open-ended responses were recorded as accurately as possible. Families were not compensated for participation. Data was stored in a REDCap database and did not include patient identifiers; the study was submitted to the SUNY Upstate Institutional Review Board and deemed exempt from review.

Descriptive statistics were generated for all survey items. Qualitative analysis was undertaken for the ten open-ended questions. The first four of these related to parents' understanding of concepts such as myelosuppression and loss of immunity; these were first coded as "medically accurate" or "medically inaccurate." The next five related to concerns regarding vaccines. The last was an opportunity to share any final thoughts regarding the interview. A thematic analysis of these was performed.

RESULTS

Of twenty-one families eligible to participate, 20 were agreed to participate and were interviewed and one was unable to participate for logistical reasons. Several families expressed appreciation for the opportunity to discuss their views on this subject. Demographic features of participants are summarized in Fig 1.

Experience with Immunizations Prior to and During Therapy

All participants (20/20) reported that they had previously permitted their children to receive all recommended immunizations (based upon the CDC vaccination schedule), and half (10/20) had also permitted their children receive the influenza vaccine while receiving treatment for cancer. Although 35% (7/20) reported that their children had experienced minor adverse events after immunization; none reported serious adverse events or events lasting longer than seven days post-immunization. Three stated that they expected their children to receive more vaccines after completion of therapy, 11 did not expected further vaccines to be administered, and six stated that they were uncertain, although less than half (9/20) of children were old enough to have completed the primary vaccination series. 80% (16/20) felt that they had a choice to vaccinate, while 20% (4/20) did not. Of the four who felt that vaccinating their children was not a choice, two felt this was due to school requirements, one did not feel adequately informed to choose, and one felt that vaccines were necessary, and therefore not a choice.

Attitudes Toward Immunization and Reimmunization

Seven participants had thought about reimmunization after therapy prior to the interviews. Four had discussed it with their primary oncologist previously. Almost half (9/20) stated that they neither agreed nor disagreed with the statement, "My child should be re-immunized after

completing chemotherapy,” based on available information, and the remaining participants were divided. Although six had concerns that their children would be adversely affected by vaccines after treatment for cancer, 13 felt that childhood vaccines were more important now that their children had been treated for cancer. Of the former, four had expressed concerns with vaccines prior to their child being diagnosed with cancer: two parents felt they had not been provided with a comprehensive enough review of the literature on vaccine side effects, one parent expressed concerns about allergic reactions and one parent cited online information about links to autism. All caregivers were willing to re-immunize if testing showed their children had lost immunity to previously administered vaccines, but fewer (12/20 or 60%) stated that they would agree to re-immunization without serologic testing and most (17/20) stated that they would like such tests done. Three said their opinions on vaccines had changed after their children’s diagnosis and specifically that their understanding of the immunosuppressive effects of chemotherapy made them see vaccines as more important for their child with cancer than they had previously. Participant views on vaccine safety and vaccine choice are shown in Fig 2.

DISCUSSION

This was an exploratory, qualitative study, and its generalizability may be limited by the small sample size and single-institution setting. In this population, we found that, while parents are open to re-immunization and respect their physicians’ recommendations, they are inclined to prefer that their children be tested prior to receiving additional vaccines. Caregivers’ concerns and preferences regarding re-immunization in pediatric oncology should be considered in the

181 development of post-treatment guidelines and of future studies regarding post-chemotherapy
182 immunological assessment and re-immunization.

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184 **CONFLICT OF INTEREST STATEMENT**

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186 The authors have no conflicts of interest to disclose. No external funding was provided for this study.

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188 **ACKNOWLEDGMENTS**

189 The authors wish to thank Manika Suryadevara, MD, for her assistance developing the interview tool.

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239 **LEGEND:**

240 **Figure 1:** Parent/Care-Giver Demographic Data

241 **Figure 2:** Safety and Choice of Vaccinations