Identifying the Barriers and Facilitators to Complete Revaccination in Adult Hematopoietic Stem Cell Transplant Survivors in the United States

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Abstract

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Abstract

Background: Comprehensive hematopoietic stem cell transplant (HSCT) survivorship care includes revaccination after transplant to restore immunity to vaccine-preventable diseases (VPDs). Revaccination after HSCT to restore VPD immunity is a complex undertaking for HSCT survivors, and current revaccination uptake is sub-optimal. As HSCT survivors are at higher risk for morbidity and mortality from infectious causes, efforts to reduce infectious risk in this population, such as improving the rate of fully revaccinated survivors, are imperative. No existing published studies have reported comprehensive barriers and facilitators to complete revaccination among adult HSCT survivors in the US.

Purpose: The overall objective of this dissertation is to advance understanding of the factors influencing revaccination uptake among adult HSCT survivors living in the US. This dissertation had three specific aims: 1a) Determine the prevalence of adult HSCT survivors who are

completely, partially, or not revaccinated 2-8 years after HSCT using a well-characterized and geographically diverse sample, 1b) Examine associations between demographic variables, social determinants of health, clinical variables, past vaccine behaviors, vaccine hesitancy (Vaccine Confidence Scale), and revaccination status in adult HSCT survivors, 2) Explore vaccine hesitancy in the context of revaccination among adult HSCT survivors by describing the level of agreement between quantitative results of vaccine hesitancy (Vaccination Confidence Scale) and qualitative results (open-ended survey items regarding vaccine confidence), and 3) Identify barriers and facilitators to complete revaccination using fixed and open-ended responses and describe the extent to which these factors explain the three revaccination status categories (completely, partially, or not revaccinated) among adult HSCT survivors.

Methods: This dissertation comprised one quantitative analysis and two convergent mixed methods analyses of a cross-sectional revaccination survey of adult HSCT survivors between 2-8 years after transplant and living in the US. The survey was sent to eligible survivors in the Fred Hutchinson Cancer Center (FHCC) Long-term Follow-up (LTFU) research cohort. The first analysis (quantitative, n=338) determined the point prevalence of revaccination outcomes with descriptive statistics and examined associations between revaccination outcomes and predictors using logistic regression. The second analysis (quantitative, n=332 and qualitative, n=189) determined the point prevalence of vaccine confidence, examined relationships between vaccine confidence levels and revaccination outcomes and intent to complete revaccination using the Fisher's exact test, and associations between vaccine confidence levels and predictors using logistic regression. Additionally, open-ended responses related to benefits, trust, and harms (the constructs of the Vaccine Confidence Scale) were analyzed using inductive thematic analysis. Lastly, a merged analysis to compare quantitative and qualitative findings was completed. The

third analysis (quantitative and qualitative=194) determined the prevalence of barriers and facilitators using descriptive statistics, examined the association between the number of barriers and facilitators and revaccination outcome using logistic regression, and tested relationships between the most frequent specific barriers and facilitators and revaccination using the Fisher's exact test. Additionally, open-ended responses were analyzed using deductive content analysis using the *WHO behavioural and social drivers of vaccination framework*. Finally, a merged analysis was conducted to compare quantitative and qualitative findings.

Results: In the first analysis, the point prevalence of revaccination outcomes was 62% completely revaccinated, 33% partially revaccinated, and 4% not revaccinated. Factors associated with incomplete revaccination were shorter time from transplant, inadequate immune reconstitution, and not having received all childhood vaccines as a child. In the second analysis, the point prevalence of vaccine confidence was 69% high confidence, 20% medium confidence, and 11% low confidence. Revaccination outcomes and intent to revaccinate were significantly different across vaccine confidence levels. Factors associated with high vaccine confidence included: living in a zip code that voted for the Democratic presidential candidate in 2020, having means to pay out-of-pocket or health insurance coverage for vaccines, receiving all pre-HSCT adult vaccines, and receiving all the recommended COVID-19 vaccines. Themes were categorized as 1) *Physical and mental benefits* and *beliefs about benefits* (Benefits); 2) *Existing factors for trust, prerequisites for trust*, and *impeding factors to trust* (Trust); 3) *Vaccine quantity, vaccine side effects, vaccines and harm*, and *not all vaccines are the same* (Harms); and 4) *Uniqueness of HSCT vaccinees* and *revaccination motivation and behavior* (Other). The merged analysis showed congruence between Vaccine Confidence Scale scores and overall vaccine confidence coding from open-ended responses. Finally, the merged analysis created a narrative about the relative importance of the

constructs when approaching revaccination by vaccine confidence level: the low confidence group relayed (dis)trust>harm>benefits, the medium confidence group relayed trust>benefits~harm, and the high confidence group relayed benefits>trust>harm. In the third analysis, the most frequent barriers were the inability to receive live vaccines because of continued immunosuppression, finding a place in the community that would give childhood vaccines to adults, and delayed immune system recovery. The most frequent facilitators were having healthcare insurance covering vaccines and having a clear calendar of what vaccines to receive and when. Further, with each additional reported barrier, the odds of being completely revaccinated were lower, OR=0.58 (95% CI 0.459-0.722), and with each additional reported facilitator, the odds of being completely revaccinated were higher, OR=1.31 (95% CI 1.05-1.63), $p < 0.001$. Two of the five most reported barriers were significantly associated with no or partial revaccination: taking immunosuppressive therapy so not eligible for live vaccines ($p = 0.001$) and immune system not recovered enough for vaccines ($p < 0.001$). Three of the five most reported facilitators were significantly associated with being fully revaccinated: having a clear calendar of what vaccines to get when ($p = 0.032$), being able to contact LTFU for vaccine questions ($p = 0.018$), and getting vaccines at FHCC ($p = 0.041$). Content analysis suggested that most barriers were in the "practical issues" construct, especially service quality and availability. A surprising, but important theme was *the transplant center as vaccination site*, with 15% of all respondents commenting in free text that they believed that is where revaccination should be offered. The merged analysis mostly indicated convergence. Overall, the barriers seemed to outweigh the facilitators as influencing factors in the no and partial revaccination groups. Conversely, the facilitators seemed to outweigh the barriers as influencing factors in the complete revaccination group.

Discussion: As few factors were associated with revaccination outcomes, interventions to increase revaccination uptake do not need to be targeted to certain survivors. Since many survivors cannot be revaccinated promptly due to delayed immune recovery, clinicians must extend the period to evaluate for revaccination readiness and ensure eventual revaccination. We can no longer ignore that HSCT survivors experience vaccine hesitancy and that vaccine hesitant HSCT survivors are less likely to complete revaccination. We must develop population-specific interventions to help vaccine-hesitant survivors choose to revaccinate. Reducing barriers and enhancing facilitators associated with poor revaccination outcomes is required. Clinicians can assess patients for barriers and facilitators and formulate individual plans towards complete revaccination. Novel programs for reducing system barriers, such as a vaccine clinic co-located within the HSCT survivorship clinic, should be designed and tested.

Conclusions: In these studies, revaccination outcomes were associated with few factors, only 69% of survivors had high vaccine confidence which significantly affected revaccination intent and outcome, and practical barriers and facilitators played a consequential role in revaccination uptake. Taken together, these findings significantly expand our knowledge of the factors influencing revaccination uptake among US HSCT survivors. Future research that builds on these findings should focus on prospective methods and intervention testing.

Dedication

I dedicate this dissertation to Dr. Mary Flowers and Judy Campbell, RN, trailblazers in HSCT survivorship care, for teaching me how to care for survivors.

I also dedicate this work to the survivors I have had the privilege of supporting over the years. You have inspired me daily with your resilience and taught me to treasure what really matters. To the survivors who participated in this research study, I especially thank you for sharing your experience so that together, we can generate new knowledge about the challenges of revaccination to make this process easier for future HSCT survivors.

Acknowledgments

Word counts have been a near-constant enemy throughout my academic career. For the dissertation acknowledgment section, there is no word count limit (I checked). So be warned, this section will be longer than is typical. If you grow weary reading the acknowledgments, I invite you to skip ahead. But the depths of my gratitude run deep, and it is important to my process to extend thanks where thanks are due.

Perhaps a fitting place to start is to thank my parents, Don and Mareth, for instilling a love of learning at a tender age and for making great sacrifices so that I could attend university. I appreciate both, for these gifts were foundational for eventually pursuing advanced degrees. To my in-law parents, Mike and Cheryl, thank you for your words of encouragement throughout the past four years. Your belief in my ability to do this difficult thing has meant a great deal to me. To my brother Dayn, thank you for your interest in my studies over the past four years. I have loved telling you about all that I was learning. To my sister, Shawna, thank you for all the book recommendations. I have loved reading books that have held your attention to divert mine from all my required readings—I have a few more on my stack to read after I graduate. To my in-law siblings Melanie, Lars, Leslie, LeAnne, Martin, and Dave, thank you for your kind words of support and eagerness to celebrate the academic milestone of earning my PhD with me. I am also grateful to my grandma Jean for encouraging me to become a nurse and my great-grandma Margaret for being my first student. I wish you were here to celebrate with me.

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When I started the PhD program, it was the fall of 2020. My three children were being homeschooled against their will due to pandemic safety requirements. We had learned with the school shutdowns in the spring of 2020 that I was ill-suited to be their teacher, and with me starting a program that demanded 60+ hours of my time weekly, we needed a creative solution. It is no exaggeration to say that I would not have been able to succeed in the program had Ria, our home school manager extraordinaire, not stepped into our lives at just the right time. Ria, thank you for being the ideal employee and for sticking with us even though it was challenging at times. You fulfilled all aspects of your role beautifully, especially the “other duties as assigned.” I am grateful for the sense of order you brought to the Wickline Academy. You felt like a sixth Wickline that year as we continued to isolate during the pandemic, and I hope you realize what an important role you played in all our lives. I am also indebted to Ripe Catering for the delicious meals you delivered each week during the first year of my program. There were not

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days when school seemed too much. But mostly, I loved being with you, working side by side with the best group of professionals that I have had the privilege of calling co-workers during my nursing career. To Stephanie, thank you for allowing me to be the first nurse to write a supplemental module to pair with the annual Patient Recovery Questionnaire, and thank you for your advice and mentorship over the life of the project. To Kevin, thank you for cheerfully answering COUNTLESS emails with random questions about the annual survey process and for always finding the answers.

To basketball, I know, reader, you are now in disbelief, she is THANKING BASKETBALL? Yes, to basketball, thank you for being my happiest diversion during the past four years. Being a PhD student requires a lot of time, energy, and headspace. I was rarely able to disconnect entirely from the constant buzzing in my brain as I balanced coursework, teaching, and research. My best chance of taking a break from the work was as a spectator in the bleachers or stands. I have many happy memories from the hundreds of games I have attended in the past four years, such as watching the Seattle Storm, NCAA March Madness, Lincoln High School, Hamilton Middle School, and many AAU teams. To my all-time favorite player, Sue Bird, you have inspired me as you have retired from the sport to step into a new chapter in your life, using your wisdom, experience, and influence to do the next good thing. I am taking notes from your playbook and will apply them as I step away from clinical nursing into my next good thing.

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grateful for Ken, who was always incredibly patient and kind as I learned how to use Stata and perform the statistical tests required for this dissertation.

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my schoolwork to help you with yours. I have enjoyed extra snuggle time in the evenings, focused time on the weekends, and undivided attention on family vacations as I have tried to set boundaries between work and family time. I hope you forget the lack of homemade meals! This season has certainly been one where "Seek and Eat" played the most prominent role as the dinner entrée on our weekly menus. I think we are all wondering if I will ever cook again! Thank you for all your small acts of kindness and grace as I devoted so much energy to my schoolwork. Ellie, thank you for reading every paper I wrote over the past four years—totaling hundreds of pages! You are an outstanding scholar and writer, and I appreciate all the time you invested in improving my papers. I am glad my final collegiate journey is ending as we are on the precipice of yours beginning. Sera, thank you for constantly inspiring me to try new things, even when they are scary. Thanks for also helping me view the world through alternative lenses. Luke, thank you for all the sweet ways you have encouraged me by leaving little notes and Lego creations on my desk. I treasure your pranks and sense of humor almost as much as our routines, like connecting every night with our joint effort on the Wordle. To Ellie, Sera, and Luke, I hope you all found a small measure of inspiration from watching me pursue my academic dreams despite many challenges that you can take with you to your most difficult pursuits in the future.

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Dissertation Haiku

Revaccination…

Difficult? Yes. Hopeless? No.

Time for improvement!

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Chapter One | Introduction

Hematopoietic Stem Cell Transplant Survivors and Vaccine Preventable Disease

An estimated half a million hematopoietic stem cell transplant (HSCT) survivors will be living in the United States by 2030.[1] HSCT survivors typically experience multiple late complications, one of the more common is increased infection risk due to immune impairment from the transplant process.[2,3] Infection is a factor in up to 30% of late deaths in HSCT survivors, despite significant advances in infectious disease prevention and management.[4] Although vaccine-preventable disease (VPD) remains rare in society, Dyer et al. reported a 41.7% self-reported incidence of VPDs in adult HSCT survivors.[5] Additionally, several authors have reported greater morbidity, more long-term sequelae, and higher mortality from VPDs in HSCT survivors than would be expected in a healthy population.[6-13] Given the higher rates of VPDs among HSCT survivors,[7,8,10,13] VPDs are an important target for infection prevention in this population.

Hematopoietic Stem Cell Transplant Survivors and Revaccination

After HSCT, 30-100% of patients lose immunity to previously administered vaccinations by one year after transplant due to damage to vaccine memory cells with the transplant process.[14] Revaccination with childhood vaccines to restore immunity to VPDs is an essential component of comprehensive survivorship care for patients who have undergone HSCT. Revaccination is a cost-effective method of achieving and sustaining immunity to VPDs that can reduce the risk of severe and sometimes fatal infections in this vulnerable patient population.[15] One Australian and three US studies contribute to our understanding of revaccination uptake. The four studies that captured complete revaccination uptake reported rates of 31.8%- 67% (sample sizes ranging from 111-663).[5,15-17] Two of these studies reported partial revaccination uptake of 24%[16] and

40%.[15] The same two studies reported that 23%[15] and 38%[16] of HSCT survivor participants had not been revaccinated. Another study from Australia reported that 7.2% of their adult survivors were not revaccinated.[18] Taken together, these data illustrate that revaccination is not currently optimized.

Revaccination Challenges for Hematopoietic Stem Cell Transplant Survivors

The revaccination series follows a multi-year schedule, with a prescribed order of vaccines (inactivated first and live later) that are given at different intervals, requiring many clinic visits. Given the inherently complicated schedule and other factors, survivors who start the revaccination series may only achieve partial revaccination. True clinical contraindications to revaccination are relapse, certain ongoing maintenance therapies, and inadequate immune reconstitution (severe hypogammaglobulinemia or insufficient T-cell or B-cell recovery) as these conditions limit vaccine effectiveness (inactive vaccines) or could potentially cause the same infection they are meant to prevent (live vaccines).[14,19,20] Chronic graft-versus-host disease (cGVHD) and ongoing immunosuppressive therapy (IST) are not reasons to withhold inactivated vaccines; however, in clinical practice, survivors with cGVHD on IST are sometimes not revaccinated with inactivated vaccines due to provider reluctance, effectively withholding vaccines from the survivors who may benefit from them most.[16,17,20-27]

Barriers to Complete Revaccination

Barriers to revaccination have been partially documented through various publications and abstracts, most of which surveyed providers on behalf of patients, not patients themselves, about revaccination barriers. Social determinants of health that serve as barriers to revaccination include inability to pay for vaccines,[5,17,28-30] lack of knowledge,[17,24,31,32] language barriers,[16,28] and loss to follow-up.[17,22,26] Further, lower revaccination rates have been observed in African-

American and Hispanic HSCT survivors.[16] Systems barriers are weaknesses of the decentralized vaccination model,[18,24,25,27,29,31,33] provider knowledge gap,[25] and provider discomfort with the guidelines.[21] These data provide evidence that many factors negatively impact successful revaccination.

Vaccine hesitancy is a conceivable and understudied barrier to revaccination in the HCST population.[34] Vaccine hesitancy, according to Larsen in 2020, is "a state of indecisiveness regarding a vaccine decision."[35, page 1609] Although a few HSCT publications refer to vaccine hesitancy,[20,34,36] studies have not explored vaccine hesitancy in the context of revaccination among adult HSCT survivors. In the general population, estimates of vaccine hesitancy are elusive and are often reported by subpopulation (e.g., parents, healthcare providers, etc.) or vaccine type (e.g., Human Papilloma Virus, Influenza, etc.).[37] A recent population-based study of 8,737 adults in Quebec discovered a vaccine hesitancy prevalence of 32.2%.[37] With the COVID-19 pandemic, three papers reported vaccine hesitancy specific to the COVID-19 vaccine in the range of 21-39% among adult and childhood cancer survivors.[38-40] These recent reports provide preliminary evidence that the cancer survivor community is not immune to vaccine hesitancy and that their levels of hesitancy around the COVID-19 vaccine mirrored that of the general population. Whether vaccine hesitancy is a factor in revaccination uptake among HSCT survivors is unknown.

Facilitators of Complete Revaccination

Facilitators of complete revaccination among adult HSCT survivors have been explored, with several papers describing driving factors for revaccination. However, none of this body of literature invited survivor participation; instead, all the publications are based on samples of provider informants. Two effective programs to increase revaccination uptake have been

described, one in Brazil that implemented a dedicated vaccination nurse[24] and another in Australia that developed a revaccination service within the transplant center.[31] An efficacy study of the pneumococcal vaccine in HSCT patients from the US described a nurse-led protocolized vaccine program that resulted in a >95% vaccine uptake.[33] Vaccination cards and reminder phone calls have been studied as an intervention to increase vaccine uptake, but their effect is unknown as the authors did not report baseline data.[17] A recent paper describing a quality improvement initiative in autologous adult HSCT survivors used an informational packet that increased uptake.[29] Many papers and abstracts have described system-level changes to support revaccination efforts such as updating policies and procedures, [16,41-44] writing standardized order sets, [42,45,46] automating vaccine reminders, [16,42] providing patient and provider education, [16,42,44,45,47] and improving communication between the transplant center and primary care.[47,48] These findings support the need for research to understand the drivers of complete revaccination from HSCT survivor voices.

Overarching Purpose of this Dissertation

The overall objective of this dissertation is to advance understanding of the factors influencing revaccination uptake among adult HSCT survivors living in the US. We currently lack evidence about the survivor experience with revaccination and, therefore, are ill-suited to test and scale appropriate interventions to improve uptake. There are presently more questions than answers on this topic. Who gets completely revaccinated? How do they achieve this difficult status? Who doesn't get completely revaccinated? Why are they not being revaccinated—is it due to vaccine hesitancy, clinical contraindications, financial hardship, or system barriers? Most importantly, what can we learn from current survivors to apply to future

survivors to make the revaccination process easier? This work will provide foundational knowledge that may eventually improve uptake.

Philosophical Paradigm

The pragmatic philosophical approach guided this project. The pragmatic paradigm centers the research questions and invites the researcher to match the best-suited methods to answer them. A complex real-world problem, such as the under-vaccination of HSCT survivors, may have some components that can be explored using a post-positivist worldview and others that can be explored using a constructivist worldview and is therefore well-suited for pragmatism.[49] Pragmatism's embrace of the objective and subjective, as well as the individual and collective, makes it a natural fit for mixed methods studies.[50] Knowing in a complex reality requires that multiple perspectives are considered, and the pragmatic viewpoint acknowledges that emerging knowledge may not converge but present with diverse, nonetheless legitimate, truths.[51] By bringing together various sources of knowledge, a deeper understanding of a complex phenomenon can be appreciated. The main goal of pragmatic nursing research is to access the human experience as the means for creating actionable knowledge about clinical problems.[52] This dissertation started with a complex, real-world problem and aimed to discover practical knowledge to improve the health of HSCT survivors.

Theoretical Foundation: The World Health Organization Behavioural and Social Drivers of Vaccination Framework

Existing research that has studied revaccination after HSCT has not been explicit about any utilized frameworks. This lack of precedent paved the way for finding the most suitable model to support revaccination uptake nursing research. To be most useful, the proposed model needed to incorporate vaccination outcomes in addition to intention, and practical and system-

level factors known to affect uptake. The model also needed to include vaccine hesitancy as one component. The World Health Organization behavioural and social drivers of vaccination framework, or "The BeSD Framework," is a model that depicts the many factors involved in vaccine uptake and is helpful for exploring the factors that drive and inhibit revaccination among HSCT survivors (see Figure 1).[53] The BeSD Framework acknowledges that the motivation for vaccination comprises what individuals think and feel as well as social processes. Notably, the model recognizes that motivation is not the sole driver in vaccination behavior, considering the practical issues that heavily influence uptake. Finally, the model ends with the various vaccine behaviors of accepting, delaying, or refusing vaccination, making it more valuable than models that describe intent only. The model is comprehensive yet simple.

The BeSD Framework was a good fit for this dissertation as there is evidence that practical barriers play a meaningful role in poor revaccination uptake among HSCT survivors. Additionally, there is reason to believe that HSCT survivors are not immune to vaccine hesitancy. Finally, since the study aimed to correlate various factors with revaccination outcomes (complete, partial, and no revaccination), a model that ended with vaccination behavior was needed. The BeSD Framework served as an organizing framework for questionnaire development, data analysis, and interpretation of the findings. Questionnaire items salient to the specific aims were derived from each of the model's five constructs. The five constructs guided the qualitative data analysis and quantitative and qualitative data integration. Interpretation and dissemination of the findings were structured using the model.

Specific Aims

This dissertation had three specific aims: 1a) Determine the prevalence of adult HSCT survivors who are completely, partially, or not revaccinated 2-8 years after HSCT using a well-

characterized and geographically diverse sample, 1b) Examine associations between demographic variables, social determinants of health, clinical variables, past vaccine behaviors, vaccine hesitancy (Vaccine Confidence Scale), and revaccination status in adult HSCT survivors, 2) Explore vaccine hesitancy in the context of revaccination among adult HSCT survivors by describing the level of agreement between quantitative results of vaccine hesitancy (Vaccination Confidence Scale) and qualitative results (open-ended survey items regarding vaccine confidence), and 3) Identify barriers and facilitators to complete revaccination using fixed and open-ended responses and describe the extent to which these factors explain the three revaccination status categories (completely, partially, or not revaccinated) among adult HSCT survivors.

To meet the study aims, three analyses are included. In chapter two, the prevalence of revaccination was determined, and factors associated with complete revaccination were explored using quantitative methods. In chapter three, vaccine hesitancy was explored using mixed methods. In chapter four, the barriers and facilitators to complete revaccination were examined using mixed methods. Together, these three analyses contribute to the current evidence regarding the complexities of revaccination for US HSCT survivors.

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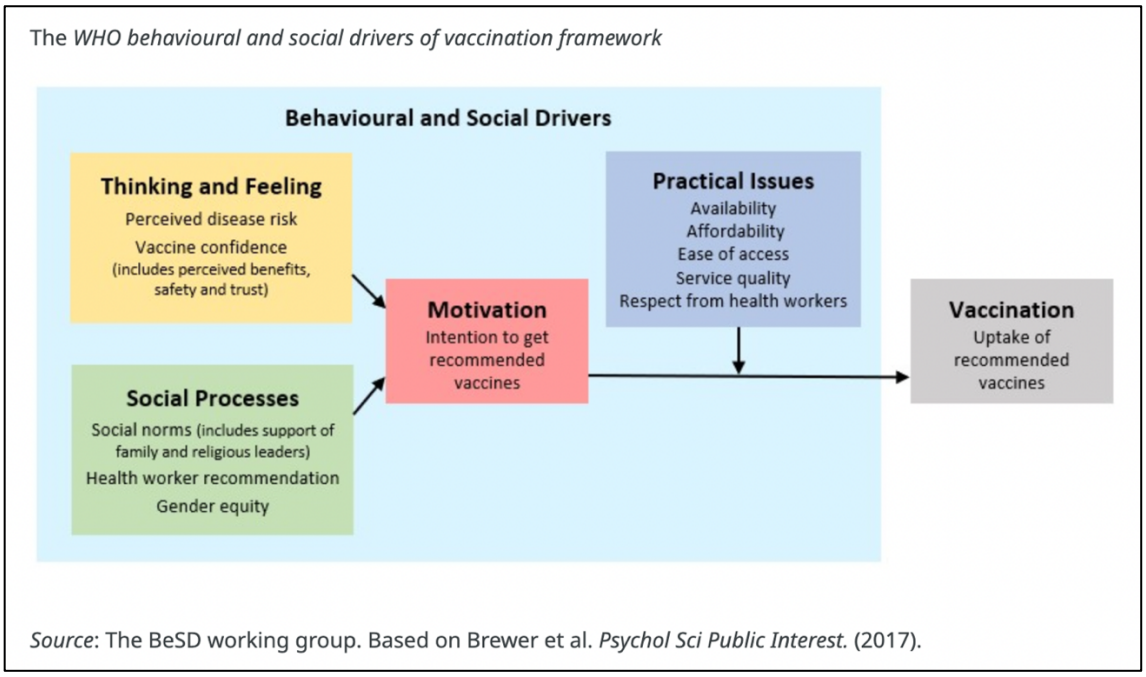
Figure 1. The BeSD Framework



Chapter Two |Associations between demographic factors, clinical variables, social determinants of health, vaccine hesitancy, vaccine behavior, and revaccination status in adult HSCT survivors in the United States

Background and Significance

Comprehensive hematopoietic stem cell transplant (HSCT) survivorship care includes revaccination with childhood vaccines to restore immunity to vaccine-preventable diseases (VPDs). Revaccination can help survivors achieve and sustain immunity to VPDs, thereby reducing the risk of serious and sometimes fatal infections in this vulnerable patient population.[1] Infection remains a primary or contributing factor in up to 30% of late deaths in HSCT survivors, despite significant advances in infectious disease prevention and management.[2] Therefore, efforts to reduce infectious risk such as vaccination are critical in this population. Revaccination after HSCT is a complex undertaking for HSCT survivors, and current revaccination uptake is sub-optimal. Several authors have reported complete revaccination among HSCT survivors from 31.8% to 67%.[1,3-5] HSCT survivors suffer higher rates of VPDs compared to healthy controls,[6-9] and they risk worse morbidity when they experience a VPD.[10] This, combined with an increase in vaccine hesitancy and decreased uptake of routine vaccines in the general population, which has increased the number of community VPD outbreaks, renders inadequate revaccination uptake among HSCT survivors a clinically significant problem.

Revaccination with childhood vaccines is recommended for all survivors beginning within the first year post-transplant. The revaccination series follows a multi-year schedule, with vaccines given at different intervals requiring many vaccine center visits.[11] Inactivated vaccines are given once a survivor meets initial criteria, and live vaccines can be given when further criteria are met.[10,12,13] Patients remaining on immunosuppressive medications, up to half of survivors who had an allogeneic HSCT,[14] may take significantly longer to complete the

revaccination series. However, most patients meet eligibility for complete revaccination within the first posttransplant decade. Given the inherently complex schedule, survivors who initiate the revaccination series may not successfully obtain all the needed vaccines and may only achieve partial revaccination.

Vaccine hesitancy is a potential and understudied barrier to revaccination in the HCST population.[15] Vaccine hesitancy, according to the World Health Organization (WHO), "refers to delay in acceptance or refusal of vaccination despite availability of vaccination services. Vaccine hesitancy is complex and context-specific, varying across time, place and vaccines."[16] Although a few HSCT publications allude to this phenomenon,[12,15,17] studies have not included measures of vaccine hesitancy for revaccination among adult HSCT survivors. One way to measure vaccine hesitancy is with vaccine confidence. People with high levels of vaccine confidence (lower vaccine hesitancy) have higher vaccine uptake than those with lower vaccine confidence.[18,19] Whether vaccine hesitancy is a factor in sub-optimal revaccination uptake among HSCT survivors remains unknown.

The WHO behavioural and social drivers of vaccination framework (The BeSD Framework) details the drivers of vaccination and can serve as an organizing framework for studying vaccine uptake in special populations (Figure 1).[20,21] The five constructs of the BeSD Framework include *thinking and feeling, social processes, motivation*, and *practical issues*, which all contribute to *vaccination*. The BeSD Framework includes influences particular to vaccination, measurable, and mutable. While this model is not specific to post-transplant revaccination uptake, it is suitable for this population as there is evidence that practical barriers play a meaningful role in preventing successful revaccination among HSCT survivors. Additionally, there is reason to believe that HSCT survivors experience vaccine hesitancy like

the general population. Finally, since revaccination outcomes are paramount, a model that ends with vaccination behaviors, not just intent, is needed to explore successful versus unsuccessful revaccination in HSCT survivors.

A recent scoping review about the facilitators and barriers to revaccination in adult HSCT survivors highlighted how little we know about this problem.[22] The present study applied a cross-sectional survey design to estimate the point prevalence of completely, partially, and not revaccinated HSCT survivors and examine factors associated with revaccination in a large sample of HSCT survivors from the Fred Hutchinson Cancer Center's (FHCC) Long-term Follow-up Research Cohort. To address limitations of prior research, factors previously unexplored (such as prior vaccine behaviors, vaccine hesitancy, and social determinants of health) were included with demographic and clinical measures as potential associated factors for incomplete revaccination. In this study, we aimed to 1) determine the prevalence of adult HSCT survivors who are completely, partially, or not revaccinated 2-8 years after HSCT using a well-characterized and geographically diverse sample, and 2) examined associations between demographic variables, social determinants of health, clinical variables, past vaccine behaviors, vaccine hesitancy (Vaccination Confidence Scale[19,23]), and revaccination status in adult HSCT survivors.

Methods

Participants

Adult participants were drawn from the LTFU Research Cohort, comprised of approximately 4,500 allogeneic and autologous HSCT survivors between 1 year and more than 40 years post-transplant at FHCC. People in this cohort have consented to receive lifelong annual surveys, including an institution-specific standard self-reported health status questionnaire called

the Patient Recovery Questionnaire (PRQ) and novel questionnaires addressing survivorship topics within supplemental modules. Inclusion criteria for receiving the one-time LTFU Revaccination Module were survivors between 2-8 years after allogeneic or autologous HSCT who reside in the US and can read and write English. Exclusion criteria were age <18 years and a multiple myeloma diagnosis. The range of time after transplant was selected to capture those at the beginning stages of revaccination and to provide a large enough range whereby most patients would have met clinical parameters to get all their vaccines, even if they needed a prolonged period of immunosuppressive therapy after transplant. The multiple myeloma patients were excluded to reduce survey burden, as they were selected for a different supplemental module measuring a distinct survivorship topic. After approval by the FHCC IRB, the survey was sent to 1,117 eligible patients via paper (if preferred) or online using REDCap electronic data capture tools hosted at Fred Hutchinson Cancer Center,[24,25] between July 1, 2022-June 30, 2023. REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies, providing 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources.[26] Patients received one reminder email a month after receipt of the survey, and completed surveys were accepted through September 30, 2023.

Survey Instrument

Because no validated questionnaires about revaccination after HSCT exist, the LTFU Revaccination Module was iteratively developed and tested. Development of the novel module relied on the BeSD Framework, published literature, and an unpublished anonymous clinician

survey about barriers and facilitators to revaccination (n=10). Six clinician-researchers with expertise in the population and survey design reviewed the survey and it was modified according to their extensive feedback. After IRB approval for pilot testing, the questionnaire was further evaluated anonymously by two LTFU patients for content validity, readability, and understandability and was revised accordingly. The final version contains questions about revaccination status, social determinants of health, clinical status, vaccine confidence, vaccine behaviors, and barriers and facilitators of complete revaccination. It has between 41-44 items, depending on branching logic. In addition to survey items from the LTFU Revaccination Module, items from the PRQ, and sociodemographic data (stored in a separate database), were extracted for the analysis.

The Vaccine Confidence Scale (VCS) was used to measure vaccine hesitancy (Figure 2).[19,23] The VCS is an 8-item scale validated for use in parental respondents for teens and children with three sub-scales (benefits, harms, and trust) that measure a person's confidence in vaccination. The coefficient alpha of the VCS was reported from a prior study of parental respondents for their teen vaccinees (n=9623) of α=0.77 (overall), α=0.78 (benefits), α=0.56 (harms), and α=0.55 (trust).[23] The scale was modified to be appropriate for self-respondents by changing language such as "your child" to "you" with permission from the scale's creator. None of the scale's items were altered in a way as to change the substance of each item. The scale has validated cut-points for low, medium, and high confidence.

Outcome and Predictor Variables

The outcome variable of interest was revaccination status, that is, being completely revaccinated, partially revaccinated, and not revaccinated. Complete revaccination was defined as receiving all recommended childhood vaccines after HSCT. No revaccination was defined as

having received no vaccines. Partial revaccination was defined as having received some but not all vaccines. Participants who were completely, partially, or not revaccinated were identified through self-report. These outcome variables were examined at various time points post-transplant as it is expected that the prevalence of fully revaccinated survivors will increase as time from transplant increases. The predictor variables were categorized as demographic (age, gender, diagnosis, type of transplant, time from most recent transplant), social determinants of health (race, ethnicity, educational attainment, distance from the transplant center, rurality, political environment, income, insurance status, ability to pay out of pocket revaccination expenses, LTFU clinic access), clinical (chronic graft versus host disease, current immunosuppressive therapy, history of inadequate immune reconstitution, healthcare access related anxiety), vaccine hesitancy (low, medium and high confidence according to the VCS), and usual vaccine behaviors (completion of primary vaccine series as a child, receipt of recommended adult vaccines before transplant, and COVID-19 vaccine uptake).

Statistical Analyses

Data were analyzed for missingness, with no discernible patterns. For the Vaccine Confidence Scale, scores were imputed by taking the mean of the items available within that construct for all constructs that had at least 50% completion of other items (n=20). Respondents with more than 50% missing items within constructs were not scored for those constructs and, therefore, did not have a mean Vaccine Confidence Scale score to analyze (n=15). The number and percent of participants who were completely, partially, and not revaccinated were stratified by characteristics and reported using descriptive methods. Intent to complete revaccination was reported for individuals who had not yet completed revaccination. The associations between the outcome variables and predictor variables were explored using logistic regression, after

collapsing the outcome into a binary variable: not or partially revaccinated versus completely revaccinated.[27] The selection of variables used in the final models was determined using the Chi-Square test to test whether an association existed between predictor variables and revaccination status. The multivariate analysis used a series of initial univariable and subsequent multivariable logistic regression models to estimate the association between predictor variables and revaccination status. Using a p-value cut-point of $\leq$0. 25,[28] relevant and potentially associated variables were selected for fitting the models. In the final models, odds ratios were reported with 95% confidence levels, and significance was set at p-values <0.05. Descriptive and inferential analyses were conducted using STATA statistical software (version 18.0 BE, StataCorp, College Station, TX).[29]

Results

While 454 people (41% of eligible) responded to the PRQ, 338 (74%) completed the additional LTFU Revaccination Module and reported their revaccination status, so the analysis is based on these 338 respondents. The 116 people who completed the PRQ but did not complete the LTFU Revaccination Module were compared to the 338 respondents who did both surveys on all available factors (age, gender, diagnosis, transplant type, time from transplant, race, ethnicity, distance from transplant center, rurality, vote in 2020 election by zip code, median household income, chronic GVHD, and current immunosuppressive status). The only statistically significant difference between the two groups was age (p-value = 0.024), with more people in the older age groups completing both surveys. Of the 338 respondents who completed both surveys, 164 (41.5%) completed them on paper, and 231 (58.5%) completed them online.

Ten percent of the sample (35/338 respondents) left one or more items missing on the 8-item Vaccine Confidence Scale. Given the importance of measuring vaccine hesitancy for the

first time in this population and in an effort not to “lose” the voices of people with missingness on this scale, scores were imputed for each construct that had at least 50% completion of other items within that construct and a mean VCS score was computed (n=20). Respondents with more than 50% missing items within any construct(s) were not scored for those constructs and, therefore, did not have a mean VCS score to analyze (n=15). With a sensitivity analysis restricted to those without missingness on the VCS, results were similar, with no meaningful differences. Outside of the VCS score, no imputations were made, and analyses of all other factors were completed by omitting missing values.

The 338 respondents resided in 28 of the 50 states in the US, although 192 (57%) were from the state where the transplant center is located. Only 14/338 (4.1%) of the respondents were not at all revaccinated. Partially revaccinated respondents comprised 113/338 (33.4%) of the respondents. The remainder of the respondents, 211/338 (62.4%) were completely revaccinated. The demographic, social determinants of health, clinical, and vaccine-related characteristics of the respondents were explored by revaccination status and are presented in Table 1. Fisher’s exact test was used to evaluate differences among the three revaccination status groups. Statistically significant between-group differences were seen in many factors.

Survivors who were not completely revaccinated were asked to report what vaccines (inactive versus live) they had received to date. Of the 133 respondents who answered this question, 30 (22.6%) were yet incomplete on inactive vaccines, 69 (51.9%) had completed inactive vaccines but had not yet completed live vaccines, and 34 (25.6%) did not know. Additionally, survivors who were not yet completely revaccinated were asked about their revaccination intentions. Table 2 displays revaccination intention by current revaccination status. Between-group differences in intention to completely revaccinate by current revaccination status

were significant (p-value = 0.032). This subset of respondents was also asked about the effect of COVID-19 on their revaccination plans, with 117 (79.1%) reporting that COVID-19 had no effect, 15 (10.1%) reporting that COVID-19 had somewhat of an effect, and 7 (4.7%) reporting that COVID-19 had a large effect on their revaccination plans.

As this is the first time vaccine hesitancy has been explored in this population, it is worth noting that vaccine hesitancy, as measured by the VCS, was present in this cohort of HSCT survivors. While 226 (70%) of the respondents reported high vaccine confidence, 64 (19.8%) and 33 (10.2%) reported medium and low vaccine confidence, respectively. Additionally, respondents were asked about their prior vaccine behaviors, including primary vaccination in childhood, usual adult vaccine uptake prior to transplant, and uptake of the COVID-19 vaccine. Most of the sample reported complete uptake of childhood vaccines (290/329, 88.1%), recommended adult vaccines before transplant (273/336, 81.3%), and the COVID-19 vaccines series (268/334, 80.2%).

As there were too few people who reported no revaccination (n=14) to do an ordinal regression with the three outcome variables as was intended, those reporting no revaccination and those reporting partial revaccination (n=113) were combined (n=127) and compared with those reporting complete revaccination (n=211) using binary logistic regression. Univariate logistic regressions were first undertaken to evaluate associations between revaccination status and the demographic, social determinants of health, clinical, and vaccine-related factors within the sample, detailed in Table 3a. We could not look for associations between primary vaccination status and revaccination uptake for survivors unvaccinated in childhood as all the survivors (n=4) who reported that they had not received any of their childhood vaccines also reported they had not received any vaccines after transplant. Factors brought forward to the multivariate model had

to meet a p-value threshold of <0.25. Factors meeting this threshold were demographic (age, time from most recent transplant, ethnicity), social determinants of health (insurance status, ability to pay for vaccines out of pocket), clinical (inadequate immune reconstitution, current immunosuppression, healthcare access-related anxiety), and vaccine behaviors (primary vaccination status, and COVID-19 vaccine uptake). Of these threshold-meeting factors, three were not included in the multivariate model. Ethnicity was not included in the multivariate model as the sample was 98% non-Hispanic or Latino, and only one Hispanic or Latino-identifying survivor reported being completely revaccinated. Additionally, insurance status was not included since only 3% of the sample was under or uninsured post-transplant. Lastly, current immunosuppression was not included since the response rate on that item (n=114) severely reduced the number of participants that could be included in the model, limiting interpretation and generalizability.

A multivariate logistic regression (n=292) was then undertaken to test which associations held after including selected associated factors in the model, detailed in Table 3a. Factors that remained statistically significant in the multivariate model were time from transplant, inadequate immune reconstitution, and primary vaccination status. Time from transplant was significant with an odds ratio of being completely revaccinated of 3.33 (CI 1.60-6.90) for survivors 3-5 years out from transplant and 7.75 (CI 3.31-18.17) for survivors 6-8 years out from transplant compared to the referent group of survivors two years out from transplant. Immune reconstitution also was significant with an odds ratio of being completely revaccinated of 0.14 (0.06-0.34) for survivors with inadequate immune reconstitution compared to the referent group of survivors who did not report inadequate immune recovery. Lastly, primary childhood vaccination status was significant with an odds ratio of being completely revaccinated of 0.04

(0.01-0.13) for survivors who reported they had received some childhood vaccines compared to the referent group of survivors who reported they had received all their childhood vaccines.

To explore the effect of current immunosuppression on revaccination uptake, a subset multivariate model (n=103) was undertaken to add current immunosuppression to the model and is detailed in Table 3b. Some covariates were dropped from the model due to positivity violations. Time from transplant remained significant for the group who were 6-8 years post-transplant with an odds ratio of being completely revaccinated of 3.54 (CI 1.07-11.75) as compared to the referent group of survivors two years out from transplant. Immune reconstitution also remained significant with an odds ratio of being completely revaccinated of 0.26 (CI 0.09-0.79) for survivors with inadequate immune reconstitution as compared to the referent group survivors who did not report inadequate immune recovery.

Discussion

Respondents were 2-8 years after HSCT from a well-characterized longitudinal survivor cohort associated with an NCI-designated Cancer Center and represented all US geographic regions. Most survivors in this sample were completely revaccinated. Reassuringly, of the survivors who were not yet fully revaccinated, the majority planned to achieve full revaccination. Our analysis detailed several factors associated with revaccination uptake. Associations with revaccination outcomes were observed for demographic variables such as time from most recent transplant; clinical variables such as inadequate immune reconstitution; and past vaccine behaviors such as primary vaccination status. An association between vaccine hesitancy and revaccination uptake was not observed, although 29% of the respondents indicated some degree of vaccine hesitancy ~~and between-group differences in revaccination outcome by vaccine confidence were seen with the Fisher's exact test.~~

The prevalence of fully and partially revaccinated HSCT survivors in the present study are within the range of what others have observed. However, our sample had fewer non-revaccinated survivors than prior studies have reported. Three US and one Australian study have included revaccination prevalence with sample sizes ranging from 111-663. The four studies that captured complete revaccination uptake reported rates of 31.8%-67%.[1,3,5,30] Two of these studies reported partial revaccination uptake of 24%[3] and 40%.[1] The same two studies reported that 23%[1] and 38%[3] of HSCT survivor participants had not been revaccinated. Another study from Australia reported that 7.2% of their adult survivors were not revaccinated.[31]

Two prior reports have reported associations between various factors and revaccination uptake in adult HSCT survivors (n=441) in Australia[30] and pediatric HSCT survivors (n=63) in Brazil.[32] Dyer et al. explored age, gender, income strata, rurality, marital status, education, presence of cGVHD, and early post-transplant status, comparing survivors who had received all vaccines (n=136) with those who had received no vaccines (n=31). They found that those who were early post-transplant were significantly less likely to have been fully revaccinated (p-value = <0.001), which aligns with the current study findings. They also found a trend of lower income negatively affecting complete revaccination (p-value = 0.09), differing from the present study where ability to pay for vaccines was not associated. Of the other overlapping factors between the Dyer and present study, associations were similarly not seen in gender, income, rurality, educational background, or chronic GVHD status.[30] Gouveia-Alves et al. explored underlying disease, transplant type, acute GVHD, chronic GVHD, living in the transplant center city, living in the transplant center state, and presence of a special immunization center in the town of residence, comparing survivor adherence to the revaccination schedule by vaccine type (diphtheria and tetanus, Hib, HAV, HBV, MMR, and VZV). The associations varied based on

the vaccine type but taken together, they noted the existence of a special immunization center in the city of residence was positively associated with a completed vaccine schedule, and chronic GVHD was negatively associated with revaccination adherence. The association between chronic GVHD was not found in our analysis, although there was a signal that perhaps continuing immunosuppression, a potential surrogate for chronic GVHD, may be associated, with an odds ratio of being completely revaccinated of 0.42 (p-value = 0.064, approaching significance) for those still on immunosuppression as compared to the referent group who were not on immunosuppression, and the response rate for this question (n=114) was much smaller than all the other factors studied. Of the other overlapping factors between the Gouveia-Alves and this study, associations were similarly not seen in underlying disease, transplant type, or living in the transplant center city or state (which would be analogous to closer distance to the transplant center).[33]

Factors associated with revaccination uptake were present in 8/15 (53%) sources from a scoping review we published.[22] From this review, the most commonly represented factors were clinical, then SDoH, and then demographic.[22] This differs slightly from the present study, where clinical and demographic factors were seen but SDoH factors were not.

Two surprising results were the lack of associations between SDoH factors and vaccine hesitancy with revaccination uptake. Prior research regarding the SDoH and vaccine uptake in adults has shown that non-white/non-Asian race, Hispanic ethnicity, poverty, lower educational background, conservative political views, rurality, and low healthcare utilization rates adversely affect routine vaccine uptake in adults.[34-38] Perhaps the numbers of survivors in this study who fell into these groups were not high enough to detect associations, particularly given the large number of non-Hispanic, white, well-educated, non-impoverished survivors primarily residing in

urban centers that made up this sample. Another explanation could be that while these associations exist for routine adult vaccination, revaccination after transplant with childhood vaccines is a different enough process that the SDoH are less critical in predicting successful uptake in this context. The lack of an association between vaccine hesitancy and vaccine uptake may be more difficult to explain. It is possible that the low numbers of non-revaccinated people in this study made it difficult to find a true association between hesitancy and uptake. Add qual results here to back this idea up. Or it may be that HSCT survivors revaccinate despite vaccine hesitancy. Past researchers have presented similar findings in a parental-adolescent context,[39] although most have reported a link between measured vaccine hesitancy and poorer vaccine uptake with routine adult vaccines.[40-43] However, in the context of the relationship between hesitancy and uptake for adult vaccines among high-risk health status adults, the association between hesitancy and uptake was lower as compared to adults without high-risk health status, as well as among parents on behalf of child vaccinees with or without high-risk health status according to a recent review of 34 articles on the topic.[44] Although it seems logical that people who express vaccine hesitancy would be less apt to get vaccines, it is essential to acknowledge that thinking and feeling (vaccine confidence) and motivation (intention to receive vaccines) are discrete from vaccine behavior and that many people do indeed get vaccines despite hesitancy, especially if their personal risk-benefit assessment favors vaccination. Perhaps in the population of HSCT survivors, who have likely experienced infections post-transplant and understand their higher risk for infectious morbidity and mortality, the personal risk-benefit assessment more often is tipped towards revaccination despite vaccine hesitancy.

The study findings presented here should be examined considering several limitations related to methods, sample diversity, various biases, and timing. Firstly, the lack of validation of

the study questionnaire may raise doubts about the reliability and accuracy of the data collected. However, we attempted to mitigate this through expert review and pilot testing during the iterative questionnaire development process. Further, the cross-sectional design limits causality and creates time- and context-bound results, especially given evidence of people's capacity to change their vaccine intentions and behaviors over time. Future studies on this topic might use a prospective study design to mitigate these concerns. Additionally, the need for more diversity across many demographic factors limits generalizability. The lack of diversity in Hispanic or Latino ethnicity limits the ability to draw associations between ethnicity and revaccination outcomes. Nevertheless, the findings in the present study were aligned with prior research that shows worse revaccination among Hispanic or Latino-identifying people. Moreover, although 28 states were represented by respondents, over half the respondents lived in the state where the transplant center was located, a state that typically has higher than average vaccine uptake across most populations and vaccines. Future studies on this topic may employ a multi-center approach to gather data from across all regions in the US. Also, since multiple myeloma patients were excluded from the questionnaire, there were fewer autologous transplant patients than would be anticipated. Therefore, differences in revaccination uptake across transplant types noted by other studies[22] potentially were missed. Furthermore, selection bias may have existed, with those who chose to respond to the questionnaire potentially having fundamental differences from those who decided not to respond. Future research could be incentivized to encourage higher participation. Recall bias also may have compromised the findings, as patients were asked to self-report on some items that required recall of vaccines that may have been administered months to years prior. A prospective approach may lessen recall bias in future studies. Another limitation is the missing data on the Vaccine Confidence Scale, which created an incomplete data set around

vaccine hesitancy. Despite attempts to mitigate missing data by imputation, the imputed scores may have misrepresented what individuals may have scored had they not skipped items despite a sensitivity analysis that did not reveal any meaningful statistical differences. The missing data on current immunosuppressive medications was substantial, with only about one-third of the sample completing that item, which was from the PRQ rather than the revaccination survey. It is unknown why this item was so poorly completed, but this created challenges in the multivariate model as current immunosuppressive therapy is a clinically important factor in delaying complete revaccination, but low numbers made it difficult to determine associations. Missing data could be moderated by requiring answers to all items, but this could lead to lower overall participation, especially for sensitive items. Another important limitation is the diversity within the partially revaccinated group, as this could include survivors who might have received only a few vaccines as well as survivors who had received all but the final live vaccines. Lastly, the timing of this study set within the COVID pandemic, when the vaccine landscape was forever changed, likely created unforeseen challenges as the research questions were first conceived before the commencement of the pandemic and subsequent COVID-19 vaccine roll-out.

Future studies might utilize a prospective design and a larger sample size to validate these findings. Further exploration of the relationship between vaccine hesitancy and revaccination uptake would be prudent to better understand if collecting vaccine hesitancy measures in a clinical context is helpful in changing vaccination outcomes. As only a few associated factors in the present study (time from transplant, inadequate immune reconstitution, current immunosuppression, and primary vaccination status) were important in revaccination outcomes, limited targeted interventions to increase revaccination uptake can be explored and tested. Continued follow-up and monitoring of post-HSCT patients in a prospective late effects clinic

with attention to meeting criteria for inactive and live vaccines based on time from transplant, immune recovery, and cessation of immunosuppression may be effective in increasing the number of HSCT survivors who achieve complete revaccination. A brief screening tool may identify people who were under or unvaccinated as children as these survivors may need more support and encouragement to get vaccines after transplant. In addition to these targeted interventions, clinicians can proceed with general evidence-based vaccination interventions (such as a strong vaccine recommendation with each clinical encounter, presumptive language when introducing the need for vaccines, and automatic reminders via text, email, or patient-medical record interface) to encourage revaccination after transplant.

Conclusion

Although VPDs remain rare events, HSCT survivors are more at risk of contracting a VPD and experience worse outcomes than those who have not undergone HSCT. With the rise of vaccine hesitancy among the general populace and the subsequent amplified threat of VPDs in the community, supporting revaccination efforts is a worthy endeavor to decrease late morbidity and mortality in HSCT survivors. Improving revaccination uptake requires clinicians to monitor those who are at the highest risk for missing vaccines, namely survivors who have impaired immune recovery and remain on immunosuppression, and intervene to improve adherence to the revaccination schedule.

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Tables and Figures

Figure 1. The BeSD Framework

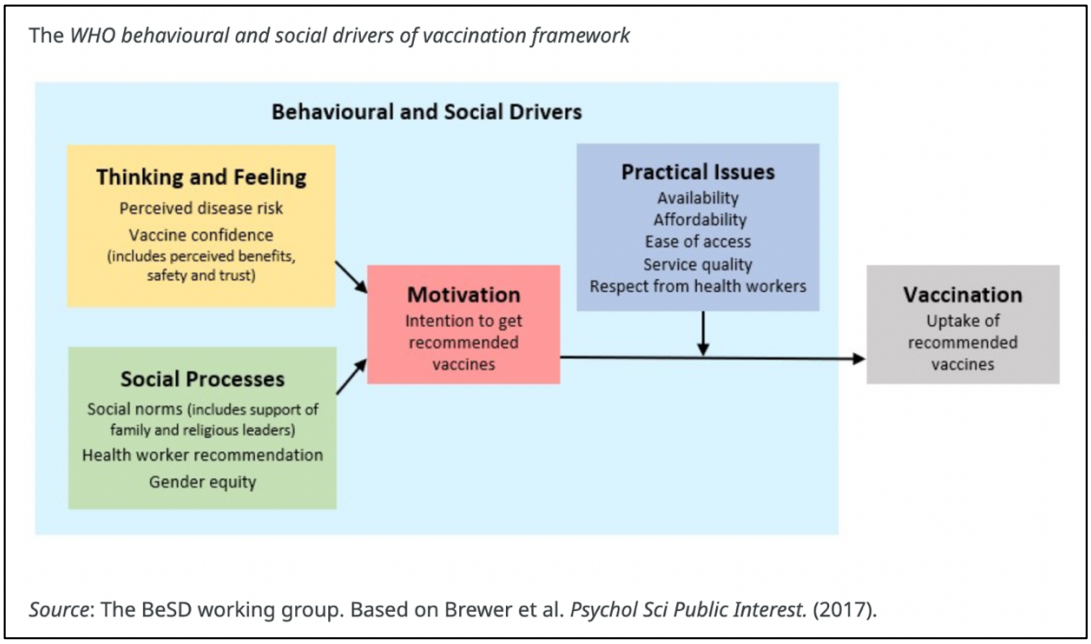

Figure 2. Modified Vaccination Confidence Scale

1. People receive too many vaccines	0 *	1	2	3	4	5	6	7	8	9	10 **
2. If I get vaccinated, I may have serious side effects	0 *	1	2	3	4	5	6	7	8	9	10 **
3. Vaccines are necessary to protect my health	0 *	1	2	3	4	5	6	7	8	9	10 **
4. Vaccines do a good job in preventing the diseases they are intended to prevent	0 *	1	2	3	4	5	6	7	8	9	10 **
5. Vaccines are safe	0 *	1	2	3	4	5	6	7	8	9	10 **
6. If I do not get vaccinated, I may get a disease and can cause others also to get the disease	0 *	1	2	3	4	5	6	7	8	9	10 **
7. In general, medical professionals in charge of vaccinations have my best interest at heart	0 *	1	2	3	4	5	6	7	8	9	10 **
8. I have a good relationship with my health care provider	0 *	1	2	3	4	5	6	7	8	9	10 **

*Strongly disagree = 0
**Strongly agree = 10
Constructs measured: Yellow = Harms, Green = Benefits, Blue = Trust
Items 1 and 2 (Harms) are reverse-coded
Based on: Gilkey, MB. Et el. (2016). Validation of the Vaccination Confidence Scale: A brief measure to identify parents at risk for refusing adolescent vaccines. *Academic Pediatrics* 16(1): 42-49

Table 1. Demographic, Social Determinants of Health, Clinical, and Vaccine-related Characteristics of Respondents by Revaccination Status (n=338) Collapse this table to Binary outcome to match logistic regression to follow (see how many p-values change when doing this) Consider adding what we lose to narrative… sensitivity analysis

	Revaccination Status			
	Not revaccinated	Partially revaccinated	Completely revaccinated	Test
N	14 (4.1%)	113 (33.4%)	211 (62.4%)	
Age				
Age 18-29	0 (0.0%)	6 (5.3%)	6 (2.8%)	0.026
Age 30-49	5 (35.7%)	24 (21.2%)	23 (10.9%)	
Age 50-69	6 (42.9%)	64 (56.6%)	127 (60.2%)	
Age 70+	3 (21.4%)	19 (16.8%)	55 (26.1%)	
Gender				
F	5 (35.7%)	52 (46.0%)	87 (41.2%)	0.638
M	9 (64.3%)	61 (54.0%)	124 (58.8%)	
Diagnosis				
Lymphoid Malignancy	5 (35.7%)	47 (41.6%)	81 (38.4%)	0.749
Myeloid Malignancy	7 (50.0%)	57 (50.4%)	112 (53.1%)	
Non-Malignant	2 (14.3%)	5 (4.4%)	13 (6.2%)	
Other/Multiple Diagnoses	0 (0.0%)	4 (3.5%)	5 (2.4%)	
Transplant Type				
Autologous	3 (21.4%)	27 (23.9%)	56 (26.5%)	0.877
Allogeneic	11 (78.6%)	86 (76.1%)	155 (73.5%)	
Time from Transplant				
2 years	6 (42.9%)	43 (38.1%)	28 (13.3%)	<0.001
3-5 years	5 (35.7%)	45 (39.8%)	94 (44.5%)	
6-8 years	3 (21.4%)	25 (22.1%)	89 (42.2%)	
Race				
Non-white/Non-Asian	0 (0.0%)	3 (2.7%)	7 (3.3%)	0.986
Asian	0 (0.0%)	7 (6.2%)	13 (6.2%)	
White	13 (92.9%)	96 (85.0%)	180 (85.3%)	
Unavailable	1 (7.1%)	7 (6.2%)	11 (5.2%)	
Ethnicity				
Hispanic or Latino	1 (7.1%)	5 (4.4%)	1 (0.5%)	0.042
Not Hispanic or Latino	12 (85.7%)	101 (89.4%)	200 (94.8%)	
Unavailable	1 (7.1%)	7 (6.2%)	10 (4.7%)	
Educational Background				
Never attended	0 (0.0%)	1 (0.9%)	0 (0.0%)	0.086
Grades 9 through 11	1 (7.1%)	1 (0.9%)	2 (1.0%)	
Grade 12 or GED	4 (28.6%)	11 (9.9%)	27 (12.9%)	
College 1 to 3 years	5 (35.7%)	30 (27.0%)	64 (30.5%)	
College 4 years or more	4 (28.6%)	68 (61.3%)	117 (55.7%)	
Distance from Transplant Center				
<100 miles	2 (14.3%)	66 (58.4%)	130 (61.6%)	0.009
101-300 miles	6 (42.9%)	24 (21.2%)	38 (18.0%)	
>300 miles	6 (42.9%)	23 (20.4%)	43 (20.4%)	
Residential Location				
Urban	10 (71.4%)	92 (81.4%)	173 (82.0%)	0.538

Rural	4 (28.6%)	21 (18.6%)	38 (18.0%)	
Vote in 2020 Presidential Election by Zip Code				
Republican	10 (71.4%)	36 (31.9%)	69 (32.7%)	0.015
Democrat	4 (28.6%)	77 (68.1%)	142 (67.3%)	
Household Median Income by Zip Code				
<$50,000	1 (7.1%)	2 (1.8%)	5 (2.4%)	0.558
$50,001 to $75,000	7 (50.0%)	39 (34.5%)	70 (33.2%)	
$75,001 to $100,000	3 (21.4%)	37 (32.7%)	78 (37.0%)	
>$100,000	3 (21.4%)	35 (31.0%)	58 (27.5%)	
Health Insurance Since Transplant				
No insurance	1 (7.1%)	0 (0.0%)	5 (2.4%)	0.057
Insured the whole time	13 (92.9%)	108 (96.4%)	203 (96.7%)	
Insured part of the time	0 (0.0%)	4 (3.6%)	1 (0.5%)	
Ability to Pay for Vaccines Out of Pocket				
No	4 (28.6%)	10 (9.2%)	7 (3.4%)	0.011
Yes	2 (14.3%)	27 (24.8%)	39 (18.8%)	
N/A, insurance pays	8 (57.1%)	65 (59.6%)	151 (72.9%)	
Don't know	0 (0.0%)	7 (6.4%)	10 (4.8%)	
Visits to Long-term Follow-up at Transplant Center				
No LTFU clinic visits	5 (35.7%)	26 (24.1%)	48 (24.0%)	0.021
One LTFU clinic visit	7 (50.0%)	21 (19.4%)	39 (19.5%)	
Two or more LTFU clinic visits	2 (14.3%)	61 (56.5%)	113 (56.5%)	
Chronic Graft versus Host Disease Since Transplant				
No	3 (33.3%)	24 (27.3%)	39 (28.5%)	0.990
Yes	6 (66.7%)	60 (68.2%)	91 (66.4%)	
Don't Know	0 (0.0%)	4 (4.5%)	7 (5.1%)	
Current Immunosuppressive Therapy				
No	1 (16.7%)	15 (31.9%)	30 (47.6%)	0.284
Yes	5 (83.3%)	31 (66.0%)	32 (50.8%)	
Inadequate Immune Reconstitution				
No	6 (42.9%)	88 (78.6%)	190 (91.8%)	<0.001
Yes	6 (42.9%)	21 (18.8%)	11 (5.3%)	
Don't know	2 (14.3%)	3 (2.7%)	6 (2.9%)	
Negative Reactions with Health Care Access				
Often	2 (14.3%)	8 (7.3%)	4 (1.9%)	0.049
Sometimes	4 (28.6%)	28 (25.5%)	61 (29.0%)	
Never	8 (57.1%)	74 (67.3%)	145 (69.0%)	
Vaccine Confidence Levels (VCS Mean Score)				
Low	6 (42.9%)	9 (8.2%)	23 (11.1%)	0.023
Medium	2 (14.3%)	24 (21.8%)	40 (19.2%)	
High	6 (42.9%)	77 (70.0%)	145 (69.7%)	
Primary Vaccination Status				
All childhood vaccines	8 (57.1%)	77 (68.1%)	205 (97.6%)	<0.001
Some childhood vaccines	2 (14.3%)	34 (30.1%)	3 (1.4%)	
No childhood vaccines	4 (28.6%)	0 (0.0%)	0 (0.0%)	
Don't know	0 (0.0%)	2 (1.8%)	2 (1.0%)	
Pre-HSCT Adult Vaccine Uptake				
Always got recommended vaccines	6 (42.9%)	90 (80.4%)	177 (84.3%)	<0.001
Sometimes got recommended vaccines	3 (21.4%)	19 (17.0%)	27 (12.9%)	
Never got recommended vaccines	5 (35.7%)	3 (2.7%)	6 (2.9%)	

COVID-19 Vaccine Uptake				
All recommended doses	8 (57.1%)	88 (78.6%)	172 (82.7%)	
One or more but not all doses	0 (0.0%)	15 (13.4%)	26 (12.5%)	
Did not receive	6 (42.9%)	9 (8.0%)	10 (4.8%)	0.001

Fisher's Exact Test Used

Table 2. Intent to Revaccinate for those not yet Completely Revaccinated (n=126)

Current Revaccination Status	What best describes your plans for completing revaccination?		
	Plan to be fully revaccinated	Do not plan to be fully revaccinated	Don't know
Not revaccinated (n=14)	7 (50%)	4 (29%)	3 (21%)
Partially revaccinated (n=112)	90 (80%)	11 (10%)	11 (10%)
Totals (n=126)	97 (77%)	15 (12%)	14 (11%)

Fishers exact = 0.032

Table 3a. Factors Associated with Revaccination Uptake Comparing Not Revaccinated or Partially Revaccinated Survivors with Fully Revaccinated Survivors: Univariate and Multivariate Analysis

Associated Factors	**Univariate Analysis**		**Multivariate Analysis (n=292)**	
	Odds Ratio (95% CI)	**P-value**	**Odds Ratio (95% CI)**	**P-value**
Age (n=338)				
18-49	1.0 (referent)		1.0 (referent)	
50-69	2.19 (1.24-3.88)	**0.007***	1.56 (0.70-3.48)	0.272
70+	3.01 (1.50-6.06)	**0.002***	1.86 (0.71-4.86)	0.208
Gender (n=338)				
Female	1.0 (referent)			
Male	1.16 (0.74-1.81)	0.511		
Diagnosis (n=338)				
Lymphoid Malignancy	1.0 (referent)			
Myeloid Malignancy	1.12 (0.71-1.79)	0.623		
Non-Malignant	1.19 (0.45-3.19)	0.726		
Other or Multiple Malignancies	0.80 (0.21-3.13)	0.751		
Type of transplant (n=338)				
Autologous	1.0 (referent)			
Allogeneic	0.85 (0.51-1.43)	0.551		
Time from most recent transplant (n=338)				
2 years	1.0 (referent)		1.0 (referent)	
3-5 years	3.29 (1.85-5.86)	**<0.001***	3.33 (1.60-6.90)	**0.001***
6-8 years	5.56 (2.96-10.44)	**<0.001***	7.75 (3.31-18.17)	**<0.001***
Race (n=319)				
Non-white/Non-Asian	1.0 (referent)			
Asian	0.80 (0.16-4.08)	0.784		
White	0.71 (0.18-2.79)	0.622		
Ethnicity (n=320)				
Hispanic or Latino	1.0 (referent)		Not included despite p-value <0.25 due to only 2% of sample being Hispanic or Latino	
Not Hispanic or Latino	10.62 (1.26-89.32)	**0.030***		
Educational background (n=335)				
Grade 11 or less	1.0 (referent)			
Grade 12 or GED	2.70 (0.40-18.00)	0.305		
College 1 to 3 years	2.74 (0.44-17.20)	0.281		
College 4 years or more	2.44 (0.40-14.94)	0.335		
Distance from transplant center (n=338)				
Less than 100 miles	1.0 (referent)			
101-300 miles	0.66 (0.38-1.16)	0.151		
>300 miles	0.78 (0.45-1.35)	0.369		
Rurality (n=338)				
Urban	1.0 (referent)			
Rural	0.90 (0.51-1.57)	0.702		
Vote in 2020 election by zip code (n=338)				
Republican	1.0 (referent)			
Democrat	1.17 (0.74-1.86)	0.509		
Median household income (n=338)				
Less than $50,000	1.0 (referent)			
$50,001 to $75,000	0.91 (0.21-4.01)	0.904		
$75,001 to $100,000	1.17 (0.27-5.15)	0.835		
More than $100,000	0.92 (0.21-4.06)	0.908		

Insurance status (n=335)			Not included despite	
Insured the whole time since HSCT	1.0 (referent)		p-value <0.25 due to	
Insured part of the time since HSCT	0.15 (0.02-1.35)	0.090	only 3% being under-	
No insurance since HSCT	2.98 (0.344-25.81)	0.321	or uninsured	
Ability to pay for revaccination (n=313)				
Unable to pay out of pocket if needed	1.0 (referent)		1.0 (referent)	
Able to pay out of pocket if needed	2.69 (0.96-7.51)	0.059	1.65 (0.38-7.25)	0.504
Not applicable since insurance pays	4.13 (1.60-10.69)	**0.003***	2.14 (0.54-8.59)	0.281
LTFU clinic access (n=322)				
No LTFU clinic visit	1.0 (referent)			
One LTFU clinic visit	0.90 (0.46-1.75)	0.754		
Two or more LTFU clinic visits	1.16 (0.67-2.00)	0.598		
Chronic GVHD (n=223)				
Never had chronic GVHD	1.0 (referent)			
Ever had chronic GVHD	0.95 (0.53-1.71)	0.876		
Current immunosuppression (n=114)			Not included despite	
Not currently on IST for GVHD	1.0 (referent)		p-value <0.25 due to	
Currently on IST for GVHD	0.47 (0.22-1.03)	0.058	only 114 respondents for this item	
Inadequate immune reconstitution (n=322)				
Not told inadequate immune recovery	1.0 (referent)		1.0 (referent)	
Told inadequate immune recovery	0.20 (0.10-0.42)	**<0.001***	0.14 (0.06-0.34)	**<0.001***
Healthcare access related anxiety (n=334)				
Never	1.0 (referent)		1.0 (referent)	
Sometimes	1.07 (0.65-1.79)	0.771	0.85 (0.44-1.67)	0.645
Often	0.23 (0.07-0.74)	**0.014***	0.34 (0.08-1.40)	0.136
Vaccine confidence (n=323)				
Low $\leq$ 6	1.0 (referent)			
Medium > 6 to $\leq$ 8	0.95 (0.40-2.24)	0.907		
High >8	1.16 (0.55-2.46)	0.692		
Primary vaccination status (n=329)				
All childhood vaccines in childhood	1.0 (referent)			
Some childhood vaccines in childhood	0.03 (0.01-0.12)	**<0.001***	0.04 (0.01-0.13)	**<0.001***
No childhood vaccines in childhood	Too few to regress			
Pre-HSCT adult vaccine uptake (n=336)				
All recommended adult vaccines	1.0 (referent)		1.0 (referent)	
Some recommended adult vaccines	0.67 (0.36-1.23)	0.195	0.64 (0.26-1.56)	0.325
No recommended adult vaccines	0.41 (0.14-1.21)	0.105	0.59 ().10-3.40)	0.554
COVID-19 vaccine uptake (n=334)				
All recommended COVID-19 vaccines	1.0 (referent)		1.0 (referent)	
Some recommended COVID-19 vaccines	0.97 (0.49-1.91)	0.924	0.87 (0.34-2.24)	0.777
No recommended COVID-19 vaccines	0.37 (0.16-0.86)	**0.021***	1.55 (0.40-6.03)	0.528

* p-value $\leq$ 0.05

Table 3b. Factors Associated with Revaccination Uptake comparing not Revaccinated or Partially Revaccinated Survivors with Fully Revaccinated Survivors: Multivariate Analysis on Subset of Patients Reporting Current Immunosuppression Status (n=103)

Associated Factors	**Multivariate Analysis**	
	Odds Ratio (95% CI)	**P-value**
Age		
18-49	1.0 (referent)	
50-69	1.15 (0.35-3.80)	0.821
70+	1.51 (0.39-5.80)	0.547
Time from most recent transplant		
2 years	1.0 (referent)	
3-5 years	2.71 (0.86-8.54)	0.087
6-8 years	3.54 (1.07-11.75)	**0.039***
Current immunosuppression		
Not currently on IST for GVHD	1.0 (referent)	
Currently on IST for GVHD	0.42 (0.17-1.05)	0.064
Inadequate immune reconstitution		
Not told inadequate immune recovery	1.0 (referent)	
Told inadequate immune recovery	0.26 (0.09-0.79)	**0.017***
Healthcare access related anxiety		
Never	1.0 (referent)	
Sometimes	0.56 (0.21-1.46)	0.236
Often	0.13 (0.01-1.43)	0.096

*p-value $\leq$ 0.05

Chapter Three | Vaccine hesitancy and routine revaccination among adult HSCT survivors in the United States: A convergent mixed methods analysis

Background and Significance

Vaccines have become victims of their own success. Their perceived value has diminished, given their effectiveness in erasing formerly problematic diseases from the collective modern memory. When vaccines work, *nothing* happens (the desired effect); therefore, it is difficult to discern vaccine benefits. However, in the process of working, *something* happens, commonly predictable vaccine side effects such as sore arm and fever, although occasionally over-sensationalized adverse events, leading to the idea that vaccines cause harm.[1] Adding to the inaccurate risk-benefit calculation is the global decline in people's trust in science, healthcare providers, and institutions that promote vaccination.[2-4] The trust problem extends to health care providers, with trust in vaccinations declining even among nurses and physicians.[5] Despite evidence that vaccines have saved more lives in the last 50 years than any other health intervention, the continued ability of vaccines to protect individual and public health is at risk if we cannot sustain vaccine uptake.[6] Even before the COVID-19 pandemic that further eroded vaccine confidence, the WHO listed vaccine hesitancy as one of the top ten threats to global health.[7] Vaccine hesitancy as a detrimental influence on vaccine uptake requires further exploration, especially among at-risk populations such as hematopoietic stem cell transplant (HSCT) survivors.

Vaccine hesitancy is a dynamic and multi-dimensional phenomenon. It is no longer thought to be a binary phenomenon—one is either vaccine hesitant or not—but exists on a continuum of non-static beliefs and resultant behaviors.[6] The World Health Organization's 2015 SAGE working group definition of vaccine hesitancy is "a delay in acceptance or refusal of

vaccination despite availability of vaccination services. Vaccine hesitancy is complex and context specific, varying across time, place and vaccines. It is influenced by factors such as complacency, convenience, and confidence."[8] This classic WHO definition combined beliefs and behaviors. A 2022 definition described vaccine hesitancy as "a state of indecisiveness regarding a vaccine decision,"[9] that more appropriately disentangles vaccine beliefs (hesitancy) from vaccine behaviors (uptake). Figure 1 is a visual representation (not-to-scale) of the spectrum and possible relationships of vaccine beliefs and behaviors. While presented as a linear model given the confines of the two-dimensional page, this spectrum should be imagined as more nuanced than presented, with the overlay of vaccine behaviors and beliefs less fixed. This paper defines vaccine hesitancy as *uncertainty regarding vaccine decision-making*, and vaccine confidence is defined as *patients' and healthcare providers' trust in the recommended vaccines and vaccination schedule*. These definitions have been selected as they are consistent with beliefs, not behaviors, and will be used as divergent (but not quite opposite) ideas throughout the paper.

Revaccination with childhood vaccines after HSCT is essential, with many authors describing waning immunity and the increased risk of vaccine preventable diseases (VPDs) in this population as compared to healthy controls.[10-20] Revaccination with childhood vaccines is a safe and effective mechanism to reestablish immunity to VPDs via both serologic and clinical measures in HSCT survivors.[21-28] Despite the evidence supporting revaccination, complete revaccination uptake is sub-optimal, with ranges between 31.8% to 67% from three US and one Australian study with sample sizes ranging from 111-663.[29-32] In a recent study of 338 participants from the Fred Hutchinson Cancer Center (FHCC) Long-term Follow-up (LTFU) survivorship cohort, the prevalence of complete revaccination was 62.4%.[(unpublished data)] The potential role of vaccine hesitancy in HSCT revaccination uptake has not yet been elucidated.

There are few mentions of vaccine hesitancy in the HSCT population in the current literature. Conrad et al. described the lack of data on vaccine hesitancy in HSCT patients. They reported that none of their ongoing cohort of survivors have refused the whole series of post-transplant vaccines, although 2.5% of their survivors had refused the hepatitis B vaccine.[33] Carpenter and Englund acknowledged vaccine hesitancy in this population in their "How I vaccinate blood and marrow transplant recipients" paper when they offered advice on addressing vaccine-hesitant patients/parents.[34] Our 2023 scoping review described this problem among HSCT survivors as a likely possibility, given signals for potential vaccine hesitancy in the available evidence.[35]

As a yet unexplored phenomenon in this population, there are many unknowns about vaccine hesitancy in HSCT survivors. What is the prevalence of vaccine hesitancy in HSCT survivors, and how does that compare to the general population? What effect does vaccine hesitancy have on vaccine uptake in this population? In other words, does vaccine hesitancy lead to vaccine avoidance or refusal, or do survivors get vaccinated despite hesitancy? Are there demographic factors, clinical variables, social determinants of health, or vaccine behaviors that predict vaccine confidence levels in HSCT survivors? What do survivors have to say about vaccine confidence as it relates to revaccination? As a first step toward answering these essential questions, the aim of this study was to explore vaccine hesitancy in the context of revaccination among adult HSCT survivors using a convergent mixed methods design, by describing the level of agreement between quantitative results of vaccine hesitancy (Vaccination Confidence Scale[36,37]) and qualitative results (open-ended survey items regarding vaccine confidence).

Methods

Positionality of the First Author

Positionality describes where one stands in relation to the other and encompasses how your identity influences, and potentially biases, how you see the world. In the research context, positionality influences what questions are asked, how they are asked, and how the answers are interpreted. The desire to understand vaccine hesitancy in HSCT survivors was borne out of my clinical practice in the LTFU Telemedicine service at FHCC, where about 10% of the patient and local health care provider queries are about revaccination. It is important to note that my interest in this topic comes from the healthcare vantage point of the revaccination narrative, not the survivor vantage point. I have not experienced a life-threatening illness that necessitated a treatment so intense as a transplant, or that resulted in lifelong changes to my health. I was vaccinated as a child, have sought all eligible adult vaccines for myself, and have chosen to vaccinate my children. As someone confident in the revaccination protocol, I encourage HSCT survivors to be fully revaccinated according to available guidance.

Philosophical Framework

The pragmatic paradigm was adopted as the philosophical framework for this project. The tenets of pragmatism, namely the commitment to what works in practice, appreciation of plurality, and desire for integrated results, create a natural foundation for the proposed research questions.[38] The pragmatic paradigm centers the research questions and summons mixed methods when suited for the research aims. I used the underlying ontological assumption that scientific reality comprises multiple perspectives. My epistemological stance put me in the position to make meaning of the data by balancing my experiences providing nursing care to vaccine hesitant patients with intentional open-mindedness to see the data as a fresh source of knowledge.

Mixed Methods Research Design

Following guidance from the text Designing and Conducting Mixed Methods Research by Creswell and Plano Clark[39] and using A Checklist of Mixed Methods Elements in a Submission for Advancing the Methodology of Mixed Methods Research by Fetters and Molina-Azorin[40], we used a cross-sectional, parallel convergent mixed methods design to explore vaccine hesitancy in HSCT survivors. The intent of this design was to compare quantitative and qualitative results and discover if they correspond, with an overall goal of creating a richer understanding of the phenomenon than using either method alone. The quantitative and qualitative data measuring the same constructs were collected simultaneously via a questionnaire, and analysis followed.[41] The analysis started with quantitative, then qualitative, and finally jointly using integrated analysis.[42] This project was designed with quantitative and qualitative integration from the philosophical paradigm through the design, methods, interpretation, and dissemination of findings.[43]

Measures

As vaccine hesitancy among HSCT survivors needing revaccination has not yet been studied, existing measures suited to this context were unavailable. Therefore, the Vaccine Confidence Scale (VCS)[36,37] was modified for his study. The VCS is an 8-item scale validated for parental respondents for teens and children with three sub-scales (benefits, harms, and trust) that measure a person's confidence in vaccination. The coefficient alpha of the VCS was reported from a prior study of parental respondents for their teen vaccinees (n=9623) of α=0.77 (overall), α=0.78 (benefits), α=0.56 (harms), and α=0.55 (trust).[36] The scale was adapted to be appropriate for self-respondents by changing language such as "your child" to "you" with permission from the scale's creator. None of the scale's items were altered in a way as to change the substance of each item. The scale has validated cut-points for determining high, medium, and

low vaccine confidence. Open-ended questions were written to capture qualitative data on benefits, harms, and trust. Participants were invited to provide an optional response with a 65,000-character limit. One additional open-ended item was provided for respondents to provide any information they wanted to share with the researchers. The measures about vaccine hesitancy were part of a more extensive survey about revaccination in HSCT survivors. The revaccination survey was iteratively designed and modified with feedback from six clinician-researchers with expertise in the population and survey design. After IRB approval for pilot testing, the questionnaire was further evaluated anonymously by two LTFU patients for content validity, readability, and understandability and was revised accordingly. See Figure 2 for the aligned quantitative and qualitative measures.

Participants

Adult participants were drawn from the LTFU Research Cohort, comprised of approximately 4,500 allogeneic and autologous HSCT survivors between 1 year and more than 40 years post-transplant at FHCC. People in this cohort have consented to receive lifelong annual surveys, including an institution-specific standard self-reported health status questionnaire called the Patient Recovery Questionnaire (PRQ) and novel questionnaires addressing survivorship topics within supplemental modules. Inclusion criteria for receiving the one-time revaccination survey were survivors between 2-8 years after allogeneic or autologous HSCT who reside in the US and can read and write English. Exclusion criteria were age <18 years and a multiple myeloma diagnosis. The range of time after transplant was selected to capture those at the beginning stages of revaccination and to provide a large enough range whereby most patients would have met clinical parameters to get all their vaccines, even if they needed a prolonged period of immunosuppressive therapy after transplant. The multiple

myeloma patients were excluded to reduce the survey burden, as they were selected for a different supplemental survey measuring a distinct survivorship topic. After approval by the FHCC IRB, the survey was sent to 1,117 eligible patients via paper (if preferred) or online using REDCap electronic data capture tools hosted at Fred Hutchinson Cancer Center,[44,45] between July 1, 2022-June 30, 2023. REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies, providing 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources.[46] Patients received one reminder email a month after receipt of the survey, and completed surveys were accepted through September 30, 2023.

Quantitative Analysis

Data were analyzed for missingness, with no discernible patterns. Thirty-five of the 347 respondents had at least one item missing from the 8-item VCS. To retain as many of these participants as possible for the analysis, VCS scores were imputed by taking the mean of the items available within that construct for all constructs with at least 50% completion of other items (n=20). Respondents with more than 50% missing items within constructs were not scored for those constructs and, therefore, did not have a mean Vaccine Confidence Scale score to analyze (n=15). This resulted in a final sample size of 332 for the quantitative measure. Of those with a complete or imputed VCS score, 189 also responded to the open-ended questions. We calculated descriptive statistics for the entire sample (n=332) and the subset of respondents who answered open-ended questions (n=189). The characteristics of the participants were stratified by vaccine confidence level and reported using descriptive methods. Revaccination status and intent

to complete revaccination for individuals who had not yet completed revaccination by vaccine confidence level was reported using the Fisher's Exact test. The associations between vaccine confidence level and demographic factors, clinical variables, social determinants of health, and vaccine behavior were explored using logistic regression.[47] The multivariate analysis used initial univariable and subsequent multivariable logistic regression models to estimate the association between predictor variables and vaccine confidence levels. Using a p-value cut-point of $\leq$0. 25,[48] relevant and potentially associated variables were selected for fitting the models. In the final models, odds ratios were reported with 95% confidence levels, and significance was set at p-values <0.05. Descriptive and inferential analyses were conducted using STATA statistical software (version 18.0 BE, StataCorp, College Station, TX).[49]

Qualitative Analysis

The open-ended vaccine confidence items were analyzed using thematic analysis with the assistance of NVivo 14 software[50]. This software program facilitates labeling text segments into codes, which can then be organized and analyzed. The Braun and Clarke six-step process for thematic analysis was used.[51] After familiarization with the data by reading it several times in multiple sittings, codes were identified inductively by reading, re-reading, and interpreting the free-text responses. An initial set of codes were identified. The initial codes were iteratively refined and combined to make a final set. The final codes were then combined conceptually by constructs (benefits, harm, trust) and "other" before themes were identified. The themes were then reviewed and defined. Finally, a matrix of constructs, themes, codes, and exemplar quotes was developed to organize and present the thematic analysis. Additionally, each participant who provided open-ended responses was assigned a code of "vaccine hesitant," "mixed confidence," or "vaccine confident" based on the gestalt of their responses.

Merged Analysis

The overall gestalt of the themes by construct was integrated with the VCS overall and subset scores in a mixed methods analysis by comparing the quantitative and qualitative results and examining the level of convergence and divergence. Additionally, the overall codes of "vaccine hesitant," "mixed confidence," or "vaccine confident" were compared to each corresponding participant's VCS scores for congruence. Finally, a joint display graphic with exemplar quotes was created to visually present the merged analysis.

Results

Participant Characteristics

There were no significant differences in demographic factors, clinical variables, social determinants of health, or vaccine behaviors between the entire sample (n=332) and the subset of respondents who answered open-ended questions (n=189). Although 59% of the sample lived within 100 miles of the transplant center, 21% lived more than 300 miles away, and there were respondents from over half of the 50 states in the US. Respondents were mainly from urban or suburban areas, with only 19% living in rural areas. Only 23% of patients had never returned for a follow-up visit after discharge from the transplant center. The demographic, social determinants of health, clinical, and vaccine-related characteristics for the 332 respondents with a complete or imputed VCS score are presented in Table 1, stratified by vaccine confidence level. In this sample, 69% of survivors had high vaccine confidence, 20% had medium vaccine confidence, and 11% had low vaccine confidence. Fisher's exact test was used to evaluate differences among the three vaccine confidence level groups. Statistically significant between-group differences were seen for age, educational background, distance from transplant center,

vote by zip code in 2020 election, household median income, ability to pay for vaccines out of pocket, and prior vaccine behaviors.

Quantitative Results

Table 2a displays the revaccination status by level of vaccine confidence, with significant differences between revaccination outcomes by vaccine confidence scores (p-value 0.043) Add narrative describing relationship (more confident = more revax). Table 2b displays the intent to revaccinate among survivors not completely revaccinated by the level of vaccine confidence, again with significant differences between intent to complete revaccination and vaccine confidence scores (p-value <0.001).

We did a sensitivity analysis comparing the logistic regression with the entire sample (n=332) and the subset of respondents who answered open-ended questions (n=189) and there were no significant differences. However, the regression model fit better with the larger sample size, and thus it is reported. The low and medium vaccine confidence groups were combined and compared with the high vaccine confidence group using binary logistic regression. Univariate logistic regressions were first undertaken to evaluate associations between vaccine confidence levels and the demographic, social determinants of health, clinical, and vaccine-related factors within the sample, detailed in Table 3. Factors brought forward to the multivariate model were those with a p-value <0.25. Factors meeting this threshold were demographic (age), social determinants of health (educational background, distance from the transplant center, vote in 2020 election by zip code, median household income, ability to pay for vaccines out of pocket), clinical (current immunosuppression) and vaccine behaviors (pre-HSCT adult vaccine uptake, and COVID-19 vaccine uptake). Of these threshold-meeting factors, four were not included in the multivariate model. Race was not included in the multivariate model as the sample was 93%

white. Time from the most recent transplant was not included due to a lack of scientific plausibility for association with vaccine hesitancy. Additionally, current immunosuppression was not included since the response rate on that item (n=109) severely reduced the number of participants that could be included in the model, limiting interpretation and generalizability. Lastly, primary vaccination status was not included, as only four people reported not receiving any routine childhood vaccines.

A multivariate logistic regression (n=282) was then undertaken to test which associations held after including selected associated factors in the model, detailed in Table 3. Factors that remained statistically significant in the multivariate model were vote in the 2020 election by zip code, ability to pay for revaccination out of pocket, pre-HSCT adult vaccine uptake, and COVID-19 vaccine uptake. The vote in the 2020 election by zip code was significant, with an odds ratio of having high vaccine confidence of 2.28 (CI 1.05-4.97) for survivors living in Democratic zip codes compared to the referent group of survivors living in Republican zip codes. The ability to pay for vaccines out of pocket was also significant, with an odds ratio of having high vaccine confidence of 7.26 (1.58-33.30) for survivors who could pay out of pocket if needed and 6.50 (1.67-25.35) for survivors who had insurance that covered vaccines compared to the referent group of survivors who were unable to pay for vaccines out of pocket if needed. HSCT survivors who did not get all their vaccines prior to transplant had lower confidence than those who received them all, with an odds ratio of having high vaccine confidence of 0.18 (CI 0.08-0.44) for survivors who got some of the recommended vaccines as compared to the referent group of survivors who got all recommended adult vaccines. Lastly, COVID-19 vaccine uptake was significant, with an odds ratio of having high confidence of 0.25 (CI 0.10-0.62) for survivors who reported they had received some COVID-19 vaccines and 0.13 (CI 0.004-0.84) for survivors

who reported they had not received any COVID-19 vaccines compared to the referent group of survivors who reported they had received all their COVID-19 vaccines.

Qualitative Results

There were 189 participants who responded to one or more of the three open-ended items on the survey. Elucidated themes were 1) *Physical and mental benefits* and *Beliefs about benefits* (Benefits); 2) *Existing factors for trust, Prerequisites for trust*, and *Impeding factors to trust* (Trust); 3) *Vaccine quantity, Vaccine side effects, Vaccines and harm*, and *Not all vaccines are the same* (Harms); and 4) *Uniqueness of HSCT Vaccinees* and *Revaccination motivation and behavior* (Other). The themes, organized by construct and presented with codes and exemplar quotes, are shown in Table 4. There were many comments from participants that led to the codes within these themes about vaccine hesitancy from the unique lens of having survived a life-threatening illness and subsequent transplant. Additionally, 179 participants were assigned a code of "vaccine hesitant," "mixed confidence," or "vaccine confident" based on the gestalt of their responses, with ten responses being insufficient to assign a code.

Merged Results

The first step in the merged analysis was assessing the congruence between the vaccine confidence level (VCS score) and the overall coding of the responses, presented in Table 5. For the most part, congruence was observed, especially in the low (VCS score $\leq$6) and high vaccine confidence (VCS score >8) groups. The medium confident group had more participants coded as "vaccine confident" (62%) than would be expected, with "vaccine hesitant" (19%) and "mixed confidence" (19%) being assigned to less than half the people with VCS scores >6 to 8.

The second step of the merged analysis is presented in Table 6 in a joint display. The mapping of the qualitative analysis onto the quantitative VCS scores thoroughly evaluates

vaccine confidence in HSCT survivors. The quantitative and qualitative results are presented alongside conclusions for each construct. Following are quantitative and qualitative results for overall confidence, with information about the relative importance of the constructs by vaccine confidence level and overall divergence and convergence. The quantitative and qualitative results were largely complementary, with the qualitative results deepening and broadening the understanding of the quantitative results. A few respondents had seemingly divergent results between quantitative and qualitative, but this was limited to less than 5% of the sample.

The final step of the merged analysis is presented in Figure 3 as a joint display graphic with exemplar quotes. Quotes from respondents are overlayed on a heat map with the VCS scale. Each quote is accompanied by the respondent's age, gender, VCS score, and revaccination status. This graphic provides a snapshot of the range of responses from people with low, medium, and high vaccine confidence.

Discussion

Respondents were 2-8 years after HSCT from a well-characterized longitudinal survivor cohort associated with an NCI-designated Cancer Center and represented all US geographic regions. Most survivors in this sample had high vaccine confidence, although 31% had medium or low vaccine confidence. In this sample, statistically significant differences were seen in revaccination outcomes X and intention X to complete revaccination by vaccine confidence levels (add p-values). Reassuringly, of the survivors who were not yet fully revaccinated, the majority planned to achieve full revaccination, especially those with high confidence. Our analysis detailed several factors associated with vaccine confidence levels. Associations with vaccine confidence levels were observed for the vote in the 2020 election by zip code, ability to pay for vaccines out of pocket, and prior adult (but not childhood) vaccine uptake of general and

COVID-19 vaccines. Nine themes related to benefits (physical and mental benefits, beliefs about benefits), trust (existing factors for trust, prerequisites for trust, impeding factors to trust), and harms (vaccine quantity, vaccine side effects, vaccines and harm, not all vaccines are the same) were identified, along with two additional themes not related to these constructs (uniqueness of HSCT vaccinees, revaccination motivation and behavior). There was congruence between the quantitative and qualitative analysis, with the open-ended responses adding a deeper understanding to the VCS scores. The three vaccine confidence level groups differed in the relative importance they placed on the constructs examined.

The prevalence of vaccine hesitancy in this study aligns with reports looking at vaccine hesitancy among healthy adults. A recent publication from a population-based study in Quebec (n=8737) reported an adult vaccine hesitancy rate of 32.2%.[52] Influenza-specific vaccination hesitancy among adults in the US in 2018 (n=4,286) was reported as 36.9%.[53] Additionally, vaccine hesitancy in adult advanced cancer patients has been reported as 42% for general vaccines[54] and from a recent review of 18 studies, between 3.9%-76.7%, with a mean of 38.4% for the COVID-19 vaccines.[55] Taken together, this provides evidence that HSCT survivors are about as likely to be vaccine hesitant as the general population.

Several respondents commented that they were concerned the vaccines would not work for them, given their impaired immune systems. Additionally, many voiced the opinion that they wanted a specialized program of revaccination that considered their unique recovery after transplant. These types of concerns have also been seen in the literature. Several authors have reported the unique fears related to being a cancer survivor and receiving vaccines, such as concerns about safety since new vaccines are rarely tested on cancer patients,[56,57] lower vaccine

efficacy in cancer patients,[56] interactions between cancer medications and vaccines,[55] and the effect of vaccine delivery on timing of cancer therapy.[55]

One surprising result from this study is how few patients in this sample avoided revaccination altogether (4%) or planned to avoid complete revaccination (4.2%), compared to the level of low confidence (11.4%). If vaccine hesitancy were a better predictor of vaccine refusal or avoidance, those numbers would be more closely aligned. So, why do vaccine hesitant HSCT survivors get revaccinated despite their hesitancy? A recent meta-analysis of 34 observational studies examining the relationship between vaccine hesitancy and vaccine behaviors reported that high-risk adult vaccinees have the lowest association between vaccine hesitancy and vaccine avoidance as compared to healthy adults, high-risk children, and healthy children.[58] It may be that adults at higher risk for morbidity and mortality from infectious disease due to their health status end up choosing to vaccinate even with hesitancy after decisional analysis. If vaccine hesitant survivors typically end up completing revaccination, why must we better understand HSCT vaccine hesitancy and design interventions to support increased vaccine confidence? Vaccine hesitant people can be seen as the "moveable middle." While they are not yet confident enough in vaccines that they will seek out vaccines, neither are they vaccine refusers. There is evidence that the "moveable middle" is amenable to interventions to nudge them towards uptake despite their hesitancy.[59-61] These interventions may be making vaccination receipt lower barrier, positively influencing motivation, or building trust in vaccine safety.[59] Additionally, vaccine hesitancy is not static in the population at large, and it is possible that it continues to grow among HSCT survivors.

Strengths and Limitations

The present study is the first to examine vaccine hesitancy in HSCT survivors, and as such, is a significant beginning contribution to this complex topic. The mixed methods approach was a considerable strength as the different data types about the same constructs could be merged to provide a more comprehensive examination of the issue. While critical to understanding the metrics about vaccine hesitancy in this population, the quantitative results would have painted a narrow picture of the phenomenon had they been presented in isolation. The qualitative responses added richness, and integrating the two methods creates a solid foundation for knowledge on this topic for HSCT clinicians. The findings are compelling, given the overall convergence of quantitative and qualitative data. The sample size and geographic spread of respondents is another strength, as it provides more faith in the potential generalizability of the findings. Finally, while the primary phenomenon was vaccine hesitancy, the respondents' revaccination outcomes and intent to complete revaccination were helpful for examining the link between vaccine beliefs and behaviors.

While this study provides novel and compelling findings, it is essential to acknowledge its limitations. First, the overall response rate was low, with only 332/1,117 (30%) of eligible participants answering the survey. The non-responders may have had different rates of revaccination uptake and vaccine hesitancy. Next, the sample was homogenous regarding race and ethnicity. This is not fully explained by the lack of racial and ethnic diversity at the transplant center as 8.5% of eligible participants were non-white/non-Asian, and only 3.3% of respondents were non-white/non-Asian. Also, 6.8% of eligible participants were Hispanic or Latino, and only 2.2% of respondents were Hispanic or Latino. This lack of racial and ethnic diversity is disappointing and limits interpretation. Although there was geographic representation from all regions of the US, most of the respondents were from Washington State, so vaccine

confidence levels may be more reflective of HSCT survivors living in Washington. These participants may be influenced by the socio-political climate in the region. All the patients were from a single center located in a generally pro-vaccine region and had access to revaccination guidance from LTFU clinicians, conceivably influencing vaccine confidence. The VCS was adapted for self-respondents, and the scale's validity has only previously been tested in parental respondents on behalf of dependent child vaccinees. Ten (35/332) of the respondents did not complete all eight items on the VCS. To include as many participants as possible, VCS scores were imputed for twenty of these participants. A sensitivity analysis was done for these respondents and there was no change in the results. However, imputation likely did not capture exactly how respondents would have answered the items. While the qualitative data came from 189/332 (57%) respondents, the responses were often brief, and a few were insufficient for interpretation. Although the VCS scale, open-ended items, and intention to complete revaccination asked patients to respond based on present beliefs, views, and plans, the revaccination outcome (not revaccinated, partially revaccinated, or completely revaccinated) question may have been influenced by recall bias. An additional limitation is that this was cross-sectional data, and there is some evidence that people's views on vaccines change over time. Also, the 2020 vote was by zip code and may not have aligned with how the survivor voted, so better reflects the political environment. Lastly, but critically important, is the effect of the timing of this study amid a global pandemic when vaccine hesitancy became a part of everyday conversation. Researching vaccine hesitancy in the context of revaccination in HSCT survivors at a time when discussions about vaccines could be as divisive as politics or religion likely served as a strength *and* a limitation of this study. While the dust may settle on the polarization

of vaccines as we are further from the beginning of the COVID-19 pandemic, it seems safe to say the historical narrative about vaccines and vaccine hesitancy has been forever altered.

Clinical and Research Implications

Our results imply that clinicians caring for HSCT survivors should learn more about vaccine hesitancy as they will undoubtedly encounter survivors who are hesitant to get revaccinated. In the absence of HSCT-specific interventions for working with vaccine-hesitant patients, clinicians can employ methods used for the general population when working with vaccine hesitant survivors to encourage revaccination. As many studies (including this one) have shown, clinicians are the preferred and most trusted source of vaccine information and can, therefore, positively impact both intention and uptake.[62-65] Evidence-based communication for vaccine uptake centers on three concepts:

Be careful when debunking myths.

Deliver an effective pro-vaccination message.

Keep the door open.[65,66]

When you encounter a myth, identify it as a myth, state it is false, state the correct information succinctly, and move on. Spending too much time on myths can backfire and reinforce the myth. An effective pro-vaccination message uses presumptive language and bundles vaccines to be given, “Today you are due to start the revaccination protocol, and there are six important childhood vaccines planned for this afternoon.” If resistance is encountered, provide a strong recommendation again, “I believe these vaccines are necessary to prevent disease and are safe for you to receive today,” and address any specific concerns. Motivational interviewing is an effective tool for communication with vaccine hesitant patients.[65,67] Keeping the door open for hesitant patients maintains clinician-patient trust and allows for further conversation about

vaccines. Getting into a heated exchange with a patient about vaccines may close the door on the therapeutic relationship and rarely ends in vaccination.[66] Additionally, clinicians should mitigate non-hesitancy barriers to revaccination to minimize other causes of poor uptake. These barriers may include affordability, availability, ease of access, and service quality.[68]

The findings presented, and the limitations described, can prompt several research questions for future exploration. To capture more diverse voices about HSCT survivor vaccine hesitancy, a similar study might be reasonable using multi-center research collaboratives to increase geographical representation, sample diversity, and overall sample size. Additionally, interventions to reduce HSCT-specific vaccine hesitancy could be developed and tested. These might be clinician-focused, such as training in motivational interviewing or communication methods with vaccine hesitant survivors. Or, they may be patient-focused, modified after existing interventions for the general population, or de novo interventions targeted to HSCT-specific concerns.

Conclusion

Vaccine hesitancy, while not new, has evolved into an increasingly problematic cause of reduced vaccine uptake. The results of this study have shown that HSCT survivors are not immune to this problem. While there is some evidence that many HSCT survivors choose to revaccinate despite their hesitancy, some do not. This phenomenon lends itself to future research to target interventions for this population. The risk of increased morbidity and mortality from VPDs is already concerning in HSCT survivors. This risk is due to the increased chance of developing late infections with increased VPDs in society due to reduced vaccine uptake in the healthy population. We cannot afford to ignore the additive risk of HSCT survivor vaccine hesitancy. We must be creative and work together to help vaccine hesitant survivors move

towards vaccine confidence and be able to echo the words of this fully revaccinated, 54-year-old female, “I avoided disease during childhood by being fully vaccinated and protected. I am glad I have accomplished a similar status now as an adult, post-transplant.”

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Tables and Figures

Figure 1. Continuum of Vaccine Beliefs and Behaviors

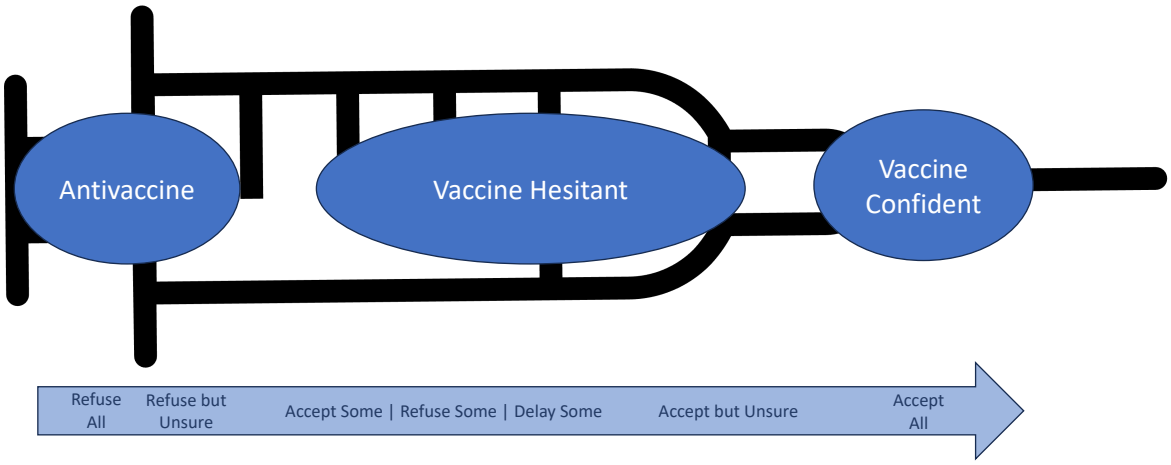

Figure adapted from authors Dube and MacDonald, chapter Vaccine Acceptance, in The Vaccine Handbook, 2nd Edition, 2016

Figure 2. Aligned Quantitative and Qualitative Measures

<table>
<tr><th colspan="2">**Quantitative:**
Modified Vaccine Confidence Scale*</th><th>**Qualitative:**
Open-ended Vaccine Confidence Questions</th></tr>
<tr><td>1. People receive too many vaccines**</td><td>0-10***</td><td rowspan="6">**Benefits/Harms** Describe your thoughts about the benefits and harms of getting revaccinated.</td></tr>
<tr><td>2. If I get vaccinated, I may have serious side effects**</td><td>0-10</td></tr>
<tr><td>3. Vaccines are necessary to protect my health</td><td>0-10</td></tr>
<tr><td>4. Vaccines do a good job in preventing the diseases they are intended to prevent</td><td>0-10</td></tr>
<tr><td>5. Vaccines are safe</td><td>0-10</td></tr>
<tr><td>6. If I do not get vaccinated, I may get a disease and can cause others also to get the disease</td><td>0-10</td></tr>
<tr><td>7. In general, medical professionals in charge of vaccinations have my best interest at heart</td><td>0-10</td><td rowspan="2">**Trust** What factors are important for you to be able to trust the process of getting revaccinated?</td></tr>
<tr><td>8. I have a good relationship with my health care provider</td><td>0-10</td></tr>
<tr><td colspan="3">**Other** If there is anything else you would like to tell us about your revaccination experience after transplant, please write it here.</td></tr>
</table>

*Constructs: Harms (yellow), Benefits (green), Trust (blue)
**Items 1 and 2 (Harms) are reverse coded
***Strongly disagree=0, Strongly agree=10

Table 1. Demographic, Social Determinants of Health, Clinical, and Vaccine-related Characteristics of Respondents Stratified by Vaccine Confidence Level (n=332)

	Vaccine Confidence Levels According to VCS Mean Score			
	Low*	Medium**	High***	p-value
N	38 (11.4%)	66 (19.9%)	228 (68.7%)	
Age				
Age 18-29	2 (5.3%)	3 (4.5%)	6 (2.6%)	**<0.001**
Age 30-49	11 (28.9%)	10 (15.2%)	29 (12.7%)	
Age 50-69	25 (65.8%)	40 (60.6%)	129 (56.6%)	
Age 70+	0 (0.0%)	13 (19.7%)	64 (28.1%)	
Gender				
F	13 (34.2%)	31 (47.0%)	98 (43.0%)	0.452
M	25 (65.8%)	35 (53.0%)	130 (57.0%)	
Diagnosis				
Lymphoid Malignancy	14 (36.8%)	22 (33.3%)	94 (41.2%)	0.804
Myeloid Malignancy	22 (57.9%)	37 (56.1%)	114 (50.0%)	
Non-Malignant	2 (5.3%)	4 (6.1%)	14 (6.1%)	
Other/Multiple Diagnoses	0 (0.0%)	3 (4.5%)	6 (2.6%)	
Transplant Type				
Autologous	9 (23.7%)	14 (21.2%)	62 (27.2%)	0.646
Allogeneic	29 (76.3%)	52 (78.8%)	166 (72.8%)	
Time from Transplant				
2 years	8 (21.1%)	12 (18.2%)	55 (24.1%)	0.539
3-5 years	13 (34.2%)	31 (47.0%)	99 (43.4%)	
6-8 years	17 (44.7%)	23 (34.8%)	74 (32.5%)	
Race				
Non-white/Non-Asian	0 (0.0%)	1 (1.6%)	9 (4.2%)	0.652
Asian	2 (5.4%)	5 (8.1%)	11 (5.1%)	
White	35 (94.6%)	56 (90.3%)	194 (90.7%)	
Ethnicity				
Hispanic or Latino	2 (5.4%)	1 (1.6%)	4 (1.9%)	0.327
Not Hispanic or Latino	35 (94.6%)	62 (98.4%)	210 (98.1%)	
Educational Background				
Grade 11 or less	2 (5.4%)	0 (0.0%)	3 (1.3%)	**<0.001**
Grade 12 or GED	13 (35.1%)	10 (15.2%)	18 (7.9%)	
College 1 to 3 years	9 (24.3%)	29 (43.9%)	59 (26.0%)	
College 4 years or more	13 (35.1%)	27 (40.9%)	147 (64.8%)	
Distance from Transplant Center				
<100 miles	13 (34.2%)	33 (50.0%)	151 (66.2%)	**<0.001**
101-300 miles	14 (36.8%)	20 (30.3%)	31 (13.6%)	
>300 miles	11 (28.9%)	13 (19.7%)	46 (20.2%)	
Residential Location				
Urban	28 (73.7%)	51 (77.3%)	191 (83.8%)	0.204
Rural	10 (26.3%)	15 (22.7%)	37 (16.2%)	
Vote in 2020 Election by Zip Code				
Republican	23 (60.5%)	29 (43.9%)	61 (26.8%)	**<0.001**
Democrat	15 (39.5%)	37 (56.1%)	167 (73.2%)	
Household Median Income by Zip Code				
<$50,000	5 (13.2%)	1 (1.5%)	2 (0.9%)	**0.001**
$50,001 to $75,000	17 (44.7%)	26 (39.4%)	72 (31.6%)	
$75,001 to $100,000	11 (28.9%)	18 (27.3%)	86 (37.7%)	
>$100,000	5 (13.2%)	21 (31.8%)	68 (29.8%)	
Health Insurance Since Transplant				
No insurance	3 (7.9%)	0 (0.0%)	3 (1.3%)	0.078

Insured the whole time	35 (92.1%)	64 (97.0%)	221 (97.4%)	
Insured part of the time	0 (0.0%)	2 (3.0%)	2 (0.9%)	
Ability to Pay for Vaccines Out of Pocket				
No	9 (24.3%)	6 (9.4%)	5 (2.2%)	**<0.001**
Yes	4 (10.8%)	14 (21.9%)	49 (21.9%)	
N/A, insurance pays	22 (59.5%)	39 (60.9%)	161 (71.9%)	
Don't know	2 (5.4%)	5 (7.8%)	9 (4.0%)	
Visits to LTFU at Transplant Center				
No LTFU clinic visits	10 (27.8%)	13 (21.3%)	55 (25.0%)	0.161
One LTFU clinic visit	12 (33.3%)	15 (24.6%)	39 (17.7%)	
Two or more LTFU clinic visits	14 (38.9%)	33 (54.1%)	126 (57.3%)	
Chronic GVHD Since Transplant				
No	7 (28.0%)	15 (30.0%)	43 (27.7%)	0.931
Yes	17 (68.0%)	34 (68.0%)	103 (66.5%)	
Don't Know	1 (4.0%)	1 (2.0%)	9 (5.8%)	
Current Immunosuppressive Therapy				
No	6 (42.9%)	12 (54.5%)	26 (33.8%)	0.180
Yes	7 (50.0%)	10 (45.5%)	50 (64.9%)	
Inadequate Immune Reconstitution				
No	30 (78.9%)	60 (90.9%)	190 (84.4%)	0.123
Yes	4 (10.5%)	5 (7.6%)	29 (12.9%)	
Don't know	4 (10.5%)	1 (1.5%)	6 (2.7%)	
Negative Reactions with Health Care Access				
Often	3 (7.9%)	3 (4.5%)	8 (3.5%)	0.126
Sometimes	12 (31.6%)	24 (36.4%)	54 (23.9%)	
Never	23 (60.5%)	39 (59.1%)	164 (72.6%)	
Primary Vaccination Status				
All childhood vaccines	29 (76.3%)	60 (90.9%)	197 (86.8%)	**0.015**
Some childhood vaccines	6 (15.8%)	4 (6.1%)	27 (11.9%)	
No childhood vaccines	3 (7.9%)	0 (0.0%)	1 (0.4%)	
Don't know	0 (0.0%)	2 (3.0%)	2 (0.9%)	
Pre-HSCT Adult Vaccine Uptake				
Always got recommended vaccines	18 (47.4%)	46 (69.7%)	206 (90.4%)	**<0.001**
Sometimes got recommended vaccines	11 (28.9%)	18 (27.3%)	19 (8.3%)	
Never got recommended vaccines	9 (23.7%)	2 (3.0%)	3 (1.3%)	
COVID-19 Vaccine Uptake				
All recommended doses and boosters	16 (42.1%)	41 (63.1%)	208 (91.6%)	**<0.001**
One or more but not all doses or boosters	6 (15.8%)	20 (30.8%)	15 (6.6%)	
Did not receive	16 (42.1%)	4 (6.2%)	4 (1.8%)	

Fisher's Exact Test Used, bold denotes significant at p-value <0.05
*Vaccine Confidence Scale score $\leq$ 6
**Vaccine Confidence Scale score > 6 to 8
***Vaccine Confidence Scale score >8

Table 2a. Revaccination Status by Level of Vaccine Confidence (Quantitative, n=323) Try to combine first two columns and then check same test, make sure NOT significant to jive with first paper, also compare no and complete (forget partial group)

Current Revaccination Status	No Revaccination (n=13)	Partial Revaccination (n=107)	Complete Revaccination (n=203)	Total (n=323)
Low Confidence*	5 (38%)	8 (7%)	20 (10%)	33 (10%)
Medium Confidence**	2 (15%)	24 (22%)	38 (19%)	64 (20%)
High Confidence***	6 (46%)	75 (70%)	145 (71%)	226 (70%)

*Vaccine Confidence Scale score $\leq$ 6
**Vaccine Confidence Scale score > 6 to 8
***Vaccine Confidence Scale score >8
Fisher's exact p-value = 0.043

Table 2b. Intent to Revaccinate by Level of Vaccine Confidence for Survivors not yet Completely Revaccinated (Quantitative, n=119)

Revaccination Plan	Plan to complete revaccination (n=93)	Do not plan to complete revaccination (n=12)	Don't know (n=14)	Total (n=119)
Low Confidence*	5 (5%)	5 (42%)	3 (21%)	13 (11%)
Medium Confidence**	19 (20%)	5 (42%)	2 (14%)	26 (22%)
High Confidence***	69 (74%)	2 (17%)	9 (64%)	80 (67%)

*Vaccine Confidence Scale score $\leq$ 6
**Vaccine Confidence Scale score > 6 to 8
***Vaccine Confidence Scale score >8
Fisher's exact p-value = <0.001

Table 3. Factors Associated with Vaccine Confidence comparing HSCT Survivors with Low or Medium Vaccine Confidence with HSCT Survivors with High Vaccine Confidence: Univariate and Multivariate Analysis

Associated Factors	**Univariate Analysis**		**Multivariate Analysis (n=282)**	
	Odds Ratio (95% CI)	**P-value**	**Odds Ratio (95% CI)**	**P-value**
Age (n=323)				
18-49	1.0 (referent)		1.0 (referent)	
50-69	1.42 (0.77-2.61)	0.261	1.32 (0.55-3.19)	0.538
70+	3.33 (1.5-7.39)	**0.003***	2.56 (0.82-8.05)	0.107
Gender (n=323)				
Female	1.0 (referent)			
Male	0.99 (0.62-1.61)	0.992		
Diagnosis (n=323)				
Lymphoid Malignancy	1.0 (referent)			
Myeloid Malignancy	0.77 (0.47-1.28)	0.317		
Non-Malignant	0.87 (0.31-2.44)	0.789		
Other or Multiple Malignancies	1.12 (0.22-5.80)	0.895		
Type of transplant (n=323)				
Autologous	1.0 (referent)			
Allogeneic	0.82 (0.47-1.43)	0.487		
Race (n=305)				
Non-white/Non-Asian	1.0 (referent)			
Asian	0.17 (0.02-1.70)	0.132*		
White	0.25 (0.03-2.01)	0.193*		
Ethnicity (n=306)				
Hispanic or Latino	1.0 (referent)			
Not Hispanic or Latino	0.56 (0.06-5.07)	0.605		
Educational background (n=321)				
High school graduate or less	1.0 (referent)		1.0 (referent)	
College 1 to 3 years	1.72 (0.83-3.55)	0.145	1.43 (0.54-4.51)	0.539
College 4 years or more	4.00 (1.99-8.02)	**<0.001**	2.69 (0.89-8.12)	0.080
Distance from transplant center (n=323)				
Less than 100 miles	1.0 (referent)		1.0 (referent)	
101-300 miles	0.30 (0.17-0.55)	**<0.001**	0.48 (0.19-1.25)	0.135
>300 miles	0.66 (0.36-1.22)	0.188	0.75 (0.31-1.82)	0.519
Rurality (n=323)				
Urban	1.0 (referent)		1.0 (referent)	
Rural	0.63 (0.35-1.13)	0.122	1.07 (0.42-2.72)	0.892
Vote in 2020 election by zip code (n=323)				
Republican	1.0 (referent)		1.0 (referent)	
Democrat	2.54 (1.55-4.17)	**<0.001**	2.28 (1.05-4.97)	**0.038**
Median household income (n=323)				
Less than $50,000	1.0 (referent)		1.0 (referent)	
$50,001 to $75,000	4.50 (0.83-24.26)	0.080	5.93 (0.82-42.86)	0.078
$75,001 to $100,000	8.08 (1.48-11.12)	**0.016**	5.95 (0.77-45.70)	0.086
More than $100,000	6.54 (1.19-35.83)	**0.030**	4.17 (0.50-35.00)	0.189
Insurance status (n=321)				
No insurance since HSCT	1.0 (referent)			
Insured the whole time since HSCT	2.38 (0.47-12.01)	0.294		
Insured part of the time since HSCT	1.00 (0.08-12.56)	>0.999		
Ability to pay for revaccination (n=300)				
Unable to pay out of pocket if needed	1.0 (referent)		1.0 (referent)	
Able to pay out of pocket if needed	9.33 (2.71-32.13)	**<0.001**	7.26 (1.58-33.30)	**0.011**
Not applicable since insurance pays	10.25 (3.24-32.44)	**<0.001**	6.50 (1.67-25.35)	**0.007**

LTFU clinic access (n=308)				
No LTFU clinic visit	1.0 (referent)		1.0 (referent)	
One LTFU clinic visit	0.65 (0.32-1.32)	0.234	0.58 (0.21-1.56)	0.280
Two or more LTFU clinic visits	1.23 (0.62-2.06)	0.697	0.90 (0.40-2.05)	0.804
Chronic GVHD (n=213)				
Never had chronic GVHD	1.0 (referent)			
Ever had chronic GVHD	0.96 (0.51-1.80)	0.896		
Inadequate immune reconstitution (n=309)				
Not told inadequate immune recovery	1.0 (referent)			
Told inadequate immune recovery	1.31 (0.59-2.91)	0.506		
Healthcare access related anxiety (n=321)				
Never	1.0 (referent)		1.0 (referent)	
Sometimes	0.63 (0.37-1.07)	0.204	0.74 (0.34-1.64)	0.463
Often	0.49 (0.16-1.47	0.089	2.78 (0.50-15.56)	0.245
Primary vaccination status (n=318)				
All childhood vaccines in childhood	1.0 (referent)			
Some childhood vaccines in childhood	1.10 (0.51-2.39)	0.807		
No childhood vaccines in childhood	0.21 (0.19-2.37)	0.208**		
Pre-HSCT adult vaccine uptake (n=323)				
All recommended adult vaccines	1.0 (referent)		1.0 (referent)	
Some recommended adult vaccines	0.22 (0.11-0.42)	**<0.001**	0.18 (0.08-0.44)	**<0.001**
No recommended adult vaccines	0.09 (0.02-0.34)	**<0.001**	0.20 (0.04-1.13)	0.069
COVID-19 vaccine uptake (n=321)				
All recommended COVID-19 vaccines	1.0 (referent)		1.0 (referent)	
Some recommended COVID-19 vaccines	0.16 (0.8-0.32)	**<0.001**	0.25 (0.10-0.62)	**0.003**
No recommended COVID-19 vaccines	0.07 (0.02-0.21)	**<0.001**	0.13 (0.004-0.84)	**0.008**

Bold denotes significant at p-value <0.05

*Race not included in multivariate analysis despite p-value <0.25 due to 93% of sample being white

**No childhood vaccines in childhood not included in multivariate analysis despite p-value <0.25 due to only 4 people reporting no childhood vaccines

Table 4. Themes, Codes, and Exemplar Quotes from Open-Ended Vaccine Confidence Questions (Qualitative, n=189)

Benefits	Physical and mental benefits	Getting revaccinated reduces worry	"Getting revaccinated decreased worry about getting sick from preventable diseases."
		Vaccines prevent disease	"Prefer the vaccine to the disease every time."
		Vaccines benefit the vaccinee and others around them	"I am and always have been pro-vaccination, both for my protection and the protection of those around me."
	Beliefs about benefits	Revaccination is important	"Vaccinations are important, and I get all of them that are recommended by my healthcare provider."
		Vaccines are beneficial	"I work in the school system, so I believe it is beneficial to get vaccinations to prevent getting any childhood illnesses."
		Revaccination is necessary	"I believe it is necessary to get revaccinated."
		Benefits of revaccination outweigh potential harms	"I did not have any concerns about getting revaccinated as I believe the benefits greatly outweigh any small risks associated with being vaccinated."
Trust	Existing factors for trust	Vaccines themselves are trustworthy	"I have complete faith in the application of proper, careful, and scientific methodology in the development and delivery of vaccines in the US, and especially in this region."
		Trust myself and my experience	"I avoided disease during childhood by being fully vaccinated and protected."
		Trust the process	"I have not really had super bad reactions - other than what might be expected - so this is why I trust the process."
		Enjoy relationships with my doctors, nurses, and institutions	"Before and after receiving a transplant requires many appointments with nurses and doctors. During this time, you establish relationships with them. Because of these personal interactions I have come to trust them."
		US resources like CDC and FDA	"As long as it has been cleared by the CDC."
		Have faith in Fred Hutch	"I gave complete faith to follow what Fred Hutch recommended."
	Prerequisites for trust	Clear revaccination schedule	"Having a clear schedule of what is needed, and when."
		Health care access and quality	"The quality of my medical support team is paramount."
		Information or more information	"I think just giving all of the information possible is the best way to earn trust."
		Science-backed data	"Sufficient research to support recommendation."
		An understanding of why vaccines are needed	"A better understanding of why I should get the shots."
		Confidence in my provider	"I tend to trust the health providers and hope for the best."
		Truth and transparency from doctors, politicians, and pharmaceutical industry	"Politicians and doctors that don't lie."
		Vaccinators to instill confidence	"The person giving the vaccination knows what they are talking about."
		Provider recommendation	"My doctor telling me my immune system was ready."
		Don't like coercion to get vaccines	"That bothered me, when I was pushed to get certain vaccines I didn't want."

	Impeding factors to trust	Lost trust in institutions	"Don't trust the CDC now."
Harms	Vaccine quantity	There are so many required vaccines	"I feel the amount of vaccines and the ingredients contribute to a weakened immune system over time."
		Don't like getting so many shots at once	"It's just that getting so many vaccines is scary to me, and it's uncomfortable. I'm fatigued for several days."
	Vaccine side effects	Vaccines can cause temporary side effects	"I don't like the side effects that come with being revaccinated."
		Vaccines can make you sick	"I am glad there were only 2 doses of Shingrix. I had a serious reaction 2 weeks post the 2nd dose. I had pericardial fluid buildup and was hospitalized. The cardiologist/radiologist removed almost a liter of fluid. Very scary."
	Vaccines and harm	Vaccines do not cause harm	"I don't believe they harm you."
	Not all vaccines are the same	Covid and flu vaccines are more problematic than childhood vaccines	"Please do not conflate the covid with the typical vaccines post-transplant. There is no comparison. In many respects the covid vaccine (more of a flu shot that missed the mark like some seasonal flu shots) just did not have the advertised efficacy. The other vaccines do and a mildly sore arm once in a while was all I suffered."
Other	Uniqueness of HSCT vaccinees	Hope the vaccines work for me	"My only concern about revaccination post-transplant while on immune suppressant medications is how well my body mounted a response to the vaccines."
		Revaccination is an obvious choice after HSCT	"Why wouldn't I get vaccinated? I just survived cancer. I didn't come this far including a stem cell transplant to die from not getting vaccinated."
		Want a personalized approach to revaccination	"Confirmation that it is safe for me to receive the vaccine given my current medical condition."
	Revaccination motivation and behavior	Am not at all revaccinated	"I have not had any vaccination currently."
		Have been revaccinated	"I feel lucky to be revaccinated."
		Have no problem with getting revaccinated	"I'm all for getting revaccinated."
		Haven't kept up with revaccination	"I have lost track, not sure which one I need."
		Want to complete revaccination	"Wanted to get all of them once I was ready to receive them."

Spelling and capitalization errors have been corrected in the participant quotes

Table 5. Congruence between Vaccine Confidence Score (Quantitative) and Overall Vaccine Confidence Coding in Open-Ended Responses (Qualitative) (Mixed, n= 179)

Quantitative Level of Confidence (VCS Score)		**Qualitative** Coding of participant's comments	
Low Confidence VCS score ≤ 6	n=16 (9%)	Coded as "Vaccine Hesitant"	n=10 (63%)
		Coded as "Mixed Confidence"	n=5 (31%)
		Coded as "Vaccine Confident"	n=1 (6%)
Medium Confidence VCS score > 6 to 8	n=37 (21%)	Coded as "Vaccine Hesitant"	n=7 (19%)
		Coded as "Mixed Confidence"	n=7 (19%)
		Coded as "Vaccine Confident"	n=23 (62%)
High Confidence VCS score >8	n=126 (70%)	Coded as "Vaccine Hesitant"	n=1 (<1%)
		Coded as "Mixed Confidence"	n=4 (3%)
		Coded as "Vaccine Confident"	n=121 (96%)

Table 6. Vaccine Confidence Joint Display Table (Mixed, n=189)

Construct	Quantitative Results	Qualitative Results	Conclusions
Harms	Range 0-10 Median 9 Mean 7.87 SD 2.45	Low Confidence Group: Worried about potential harms from vaccines Medium Confidence Group: Do not care for uncomfortable temporary side effects High Confidence Group: Stated vaccines cause no harm and potential side effects were mild at most	The harms construct had the lowest mean and median scores and widest standard deviation on the VCS. This aligns with the qualitative responses that were more heavily weighted with concerns about harm in the low and medium groups, and less so in the high group, painting a picture of a diversity of ideas about harm within the sample.
Benefits	Range 0-10 Median 9.5 Mean 8.57 SD 1.92	Low Confidence Group: No mention of potential benefits Medium Confidence Group: Vaccines prevent disease in self and protect others High Confidence Group: Vaccines prevent disease in self, protect others, and reduce worry	The benefits construct was in the middle with its quantitative measures on the VCS and was reassuringly high. While the low confidence group did not describe benefits of revaccination, the other two much larger groups described the many benefits of revaccination and provided qualitative evidence that the sample overall finds revaccination beneficial.
Trust	Range 0-10 Median 10 Mean 9.06 SD 1.56	Low Confidence Group: Mentioned distrust of government, healthcare, and pharma; coercion; too many vaccines; and health care errors regarding vaccines Medium Confidence Group: Described needing accurate and honest information from a trusted healthcare provider High Confidence Group: Described existing trust in healthcare providers and institutions, reliance on scientific data, desire for information, and a clear revaccination schedule	The trust construct had the highest mean and median scores and the narrowest standard deviation on the VCS. Given the wide range of qualitative responses about trust, this is more unexpected. People from the sample described everything from deep mistrust in healthcare providers, the government, and the pharmaceutical industry all the way to extreme trust in the same.
Overall Confidence	Range 1.67-10 Median 9 Mean 8.52 SD 1.74	**Relative importance of constructs by confidence level:** Low Confidence Group: **(dis)trust>harms>benefits** People in this group indicated worries about harm from vaccines, did not see benefits of revaccination, and described challenges with trust. Medium Confidence Group: **trust>benefits~harm**	**Divergence and convergence by respondents:** Low Confidence Group: The quantitative and qualitative data converged for all but one respondent who had a low VCS score (5.42) but indicated they had been revaccinated after transplant and all had gone well

		People in this group were worried about side effects of vaccines, saw benefits of revaccination for themselves, and provided factors that could increase trust. High Confidence Group: **benefits>trust>harm** People in this group were not worried about harm and were minimally worried about side effects from vaccines, saw benefits of revaccination for themselves and others, and described existing factors for trust.	with the revaccination in the open-ended responses. Medium Confidence Group: The quantitative and qualitative data converged for all but three respondents who had confident responses but lower scores within the range (6.33, 6.42. 6.58) and for one respondent who had hesitant responses but had a higher score (7.42) within the range. High Confidence Group: The quantitative and qualitative data converged for all but three respondents who had mixed confidence responses (expressed hesitancy and confidence) despite high confidence VCS scores (8.12, 8.42, 9.17) with one of these respondents indicating high confidence overall but a desire to let others choose for themselves without mandates as vaccines are personal. Additionally, one respondent with a VCS score 9.75 indicated distrust in the COVID vaccine.

SD: Standard Deviation
VCS: Vaccine Confidence Scale

Figure 3. Joint Display Graphic with Exemplar Quotes (Mixed)

Chapter Four | Barriers and facilitators to routine revaccination among adult HSCT survivors in the United States: A convergent mixed methods analysis

Background and Significance

Comprehensive hematopoietic stem cell transplant (HSCT) survivorship care includes revaccination after transplant to restore immunity to vaccine-preventable diseases (VPDs).[1] After HSCT, 30-100% of patients lose immunity to prior vaccinations by one year post-transplant, and current guidance recommends revaccination with childhood vaccines for all survivors.[2] Revaccination after HSCT is a complex undertaking for HSCT survivors, and current revaccination uptake is sub-optimal, with reported complete revaccination rates between 32-67% based on four studies.[3-6] As HSCT survivors are at higher risk for morbidity and mortality from infectious causes, efforts to improve the rate of fully revaccinated survivors are crucial.[7] The risk of VPDs in HSCT survivors may increase given COVID-19 pandemic-related disruptions to routine maternal, infant, and child vaccination, resulting in losses to overall routine vaccination uptake.[8,9] Understanding the inhibitors and drivers of vaccine uptake in specialized populations is critical to improving uptake:

> While public health organizations strive to provide interventions to promote vaccination at the population level, these are not always based on data about the vaccination drivers and barriers and may instead reflect entrenched practices. Accordingly, there is a need for effective strategies, based on the best possible evidence regarding drivers and barriers to enhance vaccine demand, acceptance, and uptake in all settings. Drivers and barriers include logistics, as well as complex psychological, social, political, and cultural factors.[10] (p. 189)

To date, no reports have been published describing research that has sought to systematically elucidate the barriers and facilitators to complete revaccination among adult HSCT survivors in the US.

The WHO behavioural and social drivers of vaccination framework, or "The BeSD Framework," can serve as a helpful model to understand the potential barriers and facilitators of revaccination uptake among HSCT survivors (Figure 1).[11,12] The five constructs of The BeSD Framework are *thinking and feeling, social processes, motivation*, and *practical issues*, which all lead to *vaccination*. These constructs are individual-level and system-level factors influencing potential vaccinees that are quantifiable and mutable. This model is more comprehensive than frameworks that merely focus on hesitancy as it recognizes that motivation is not the sole driver in vaccination behavior; rather, practical issues also heavily influence uptake. The model ends with the desired behavior of vaccination (uptake of recommended vaccines), making it more useful than models that describe intent only.

We conducted a scoping review[13] describing the barriers and facilitators to complete revaccination among adult HSCT survivors that included 15 data sources (10 quality improvement and five original research papers) written by authors from seven countries.[13] The majority of these sources used chart review and provider surveys to collect data; few included HSCT survivors as informants. Most of the barriers and facilitators described in these reports fell into the practical issues construct of The BeSD Framework. The most frequent barriers were the cost of vaccines, lack of systemization, poor communication, and problematic care coordination between the HSCT center and primary care. The most common facilitators were system-level quality improvement initiatives. The main takeaways from this scoping review were that we currently do not have enough evidence about what hinders and helps revaccination to develop

and test interventions and that more research incorporating HSCT survivor voices on the topic is needed.

This paper describes our mixed methods study with HSCT survivor informants to better understand the barriers and facilitators to complete revaccination as a preliminary step toward interventions that drive uptake. The objective of this study was to identify barriers and facilitators to complete revaccination using fixed and open-ended responses and describe the extent to which these factors explain the three revaccination status categories (completely, partially, or not revaccinated) among adult HSCT survivors who wanted to be or were, completely revaccinated. Specifically, the quantitative strand aimed to describe the extent to which pre-determined barriers and facilitators affected the survivors' revaccination experience; the qualitative strand aimed to see which of the pre-determined barriers and facilitators were expanded upon, explore patterns and themes in participant responses about barriers and facilitators, and amass new barriers and facilitators from survivors' perspectives; and the merged analysis aimed to understand this phenomenon more comprehensively, taking into account the areas of convergence and divergence.

Methods

Mixed Methods Research Design

We used a cross-sectional, parallel convergent mixed methods design to explore barriers and facilitators to revaccination in HSCT survivors. The text, Designing and Conducting Mixed Methods Research, by Creswell and Plano Clark[14] and the article, A Checklist of Mixed Methods Elements in a Submission for Advancing the Methodology of Mixed Methods Research, by Fetters and Molina-Azorin[15] guided this project. Qualitative methods in isolation are ill-suited to uncover the prevalence of barriers and facilitators, whereas quantitative methods alone lack

context for nuance regarding experienced barriers and facilitators. Therefore, this design intended to compare quantitative and qualitative results and discover where they converged or diverged, with the overall goal of creating a deeper understanding of the phenomenon. The quantitative and qualitative data were collected simultaneously via a novel questionnaire.[16] The quantitative and qualitative analyses were conducted separately and then jointly using integrated analysis.[17] This project was planned with quantitative and qualitative integration from the design through the methods, interpretation, and dissemination of findings.[18] The integrative findings can potentially improve our knowledge of this topic more thoroughly than quantitative or qualitative analysis alone.

Measures

As barriers and facilitators to revaccination among HSCT survivors have not yet been studied, existing measures suited to this context were unavailable. Therefore, novel quantitative and qualitative items addressing this topic were developed. We provided eleven drop-down barriers and six drop-down facilitators on the survey. Participants were asked to assign a ranking for how much of a problem (barriers) or how much of a help (facilitators) these factors were or are in their pursuit of complete revaccination on a three-point scale. These barriers and facilitators were selected based on the extant literature and an anonymous survey of ten Long-term Follow-up (LTFU) physicians, advance practice providers, and registered nurses from the Fred Hutchinson Cancer Center (FHCC), formerly known as the Seattle Cancer Care Alliance (SCCA), who routinely counsel patients regarding revaccination, order revaccination, and administer vaccines to adult HSCT survivors. Additionally, three open-ended items collected information about barriers, facilitators, and "anything else you would like to tell us about your revaccination experience." Participants were invited to respond to these three items with a

65,000-character limit. These measures were part of a more extensive survey about revaccination in HSCT survivors. The revaccination survey was iteratively designed and modified with feedback from six clinician-researchers with expertise in the population and survey design. After IRB approval for pilot testing, the questionnaire was further evaluated anonymously by two LTFU patients for content validity, readability, and understandability and was revised accordingly.

Participants

Participants were drawn from the FHCC LTFU Research Cohort, a pool of approximately 4,500 allogeneic and autologous HSCT survivors between 1 year and more than 40 years post-transplant. People in this cohort have consented to receive lifelong annual surveys, including an institution-specific standard self-reported health status questionnaire called the Patient Recovery Questionnaire (PRQ) and novel questionnaires addressing survivorship topics within supplemental modules. Inclusion criteria for receiving the one-time revaccination survey were people between 2-8 years after allogeneic or autologous HSCT who live in the US and can read and write English. Exclusion criteria were people aged <18 years or a multiple myeloma diagnosis. The multiple myeloma patients were excluded from this survey as they were selected for a different supplemental survey measuring a distinct survivorship topic. After approval by the FHCC IRB, the survey was sent to 1,117 eligible patients via paper, per pre-existing preference, or online using REDCap electronic data capture tools hosted at Fred Hutchinson Cancer Center,[19,20] between July 1, 2022-June 30, 2023. REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies, providing 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data

downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources.[21] Patients received one reminder email a month after receipt of the survey, and completed surveys were accepted through September 30, 2023.

Quantitative Analysis

Data were analyzed for missingness, with no discernible patterns. The quantitative data were analyzed in three different ways. First, descriptive statistics were used to present the frequencies of all the barriers and facilitators queried in the survey. Secondly, a multivariate logistic regression was performed to evaluate the association between the number of barriers and facilitators and the odds of being completely revaccinated. Odds ratios were reported with 95% confidence levels, and significance was set at p-value <0.05. Finally, associations were tested between the five most common barriers and the five most common facilitators and revaccination outcomes using Fisher's exact test. Factors for these final tests were dichotomized due to small cell quantities. Therefore, the revaccination outcomes were either no revaccination or partial revaccination compared with full revaccination, the reported barriers were either a big problem or somewhat of a problem compared with no problem, and the reported facilitators were either a big help or somewhat of a help compared with no help. Descriptive and inferential analyses were conducted using STATA statistical software (version 18.0 BE, StataCorp, College Station, TX).[22]

Qualitative Analysis

The open-ended items were analyzed with the assistance of NVivo 14 software.[23] This software program facilitates labeling text segments into codes, which can then be organized and analyzed. Deductive (directed) content analysis[24,25] was used, using pre-determined codes from The BeSD Framework. After familiarization with the data by reading it several times in multiple

sittings, codes were assigned by reading, re-reading, and interpreting the free-text responses. New codes were developed when no suitable a priori code existed. These new codes were organized within the appropriate constructs of The BeSD Framework. The a priori and de novo codes in The BeSD Framework were counted to quantify the responses. Constructs and codes also were mapped to exemplar quotes and presented.

Merged Analysis

Barriers and facilitators were studied by revaccination outcome (no revaccination, partial revaccination, complete revaccination), comparing the quantitative and qualitative results and examining the level of convergence and divergence. Using merged analysis, we created a "narrative" about the barriers and facilitators common to each of the three groups. Finally, a joint display graphic was generated to present the merged analysis visually.

Results

Participant Characteristics

The demographic factors, clinical variables, social determinants of health, and vaccine behaviors of the 194 respondents are presented in Table 1. The majority of respondents were non-Hispanic, white survivors greater than 50 years of age and 3-5 years out from allogeneic transplants. Most respondents were college-educated, insured, and lived within 300 miles of the transplant center in urban settings. Slightly more than half had visited the LTFU clinic at the transplant center two or more times, and the same proportion were still on immunosuppressive therapy for chronic GVHD. Around 80% of the respondents received all the recommended childhood vaccines in their youth and all the recommended adult vaccines pre-HSCT. Slightly less, around 75%, had received all the recommended COVID-19 vaccines.

Quantitative Results

The self-reported barriers and facilitators to revaccination along with the level of the problem and level of help are listed in Table 2. The three most influential barriers were taking immunosuppressive medications so they were not yet eligible for live vaccines, trouble finding a place in their community that would give childhood vaccines to adults, and delayed immune system recovery. The two most influential facilitators were having healthcare insurance covering vaccines and a clear calendar of what vaccines to receive and when. On multivariate regression, the number of self-reported barriers and facilitators was strongly associated with revaccination outcome (n=178). With each additional reported barrier, the odds of being completely revaccinated were lower, OR=0.58 (95% CI 0.459-0.722), and with each additional reported facilitator, the odds of being completely revaccinated were higher, OR=1.31 (95% CI 1.05-1.63) with a p-value <0.001. Of the five most reported barriers (Figure 2a), two were significantly associated with being not or partially revaccinated: taking immunosuppressive therapy so not eligible for live vaccines (p-value 0.001) and immune system not recovered enough for vaccines (p-value <0.001). Of the five most reported facilitators (Figure 2b), three were significantly associated with being fully revaccinated: having a clear calendar of what vaccines to get when (p-value 0.032), being able to contact LTFU for vaccine questions (p-value 0.018), and getting vaccines at FHCC (p-value 0.041).

Qualitative Results

While all the constructs of The BeSD Framework (thinking and feeling, social processes, motivation, and practical issues) were represented in the open-ended responses, several of the codes within three of the constructs were not observed in comments from this sample: perceived disease risk, social norms, gender equity, and respect from healthcare workers (Figure 3). Most open-ended responses were coded within the practical issues (82.2%) construct. Of the nine de

novo codes created from the comments, seven (77.8%) fit within the practical issues construct. Of the nine de novo codes, six were unique to HSCT survivor revaccination (difficult finding childhood vaccines for adults, continued immunosuppression, impaired immune system, relapse or new cancer, revaccination schema, and transplant center as a vaccination site). In contrast, three could also apply to other populations (too many vaccines, allergic or significant reaction, and hate needles). More than 20% of the comments from the practical issues construct fell within the service quality code, with people describing both poor service quality that served as a barrier and excellent service quality that served as a facilitator. Some examples of participant experience regarding service quality are found in these comments:

> *I questioned why I had not received the rest of my vaccines but did not get a satisfactory answer.* (Barrier, 69-year-old female, fully revaccinated)
>
> *My doctor- Oncologist has never follow(ed) through. Last time I call(ed) they did not call me back.* (Barrier, 69-year-old male, unknown if fully revaccinated)
>
> *Pharmacists pushed back about pneumonia vaccines and extra Covid vaccines needed due to my transplant. I had to stand my ground and prove my need to be vaccinated. I always anticipated a battle going into vaccination sites and clinics. There is no standard documentation to provide to make this process easier.* (Barrier, 54-year-old female, fully revaccinated)
>
> *Since I live in XX all of my care has been at XX. The nurse navigator at the clinic has been very helpful. I know she has been in contact with LTFU several times concerning vaccines.* (Facilitator, 77-year-old female, partially revaccinated)
>
> *My provider at XX planned everything for me. I just had to show up for appointments.* (Facilitator, 50-year-old female, fully revaccinated)

> *It was very helpful having my oncologist and LTFU team be on top of my vaccine schedule and checking my immunization records according to schedule. It always got a little confusing when I was told I wasn't ready to receive vaccines, but they always followed up and checked to see if I was ready.* (Facilitator, 39-year-old male, partially revaccinated)

The second most frequent comments related to a new code, "transplant center as a vaccination site." Nearly 15% of the respondents commented about receiving vaccines or wishing they could receive vaccines at FHCC. While the LTFU clinic routinely provides vaccines as part of the revaccination protocol, vaccines must be given in conjunction with a planned visit, which is every 3-6 months most frequently (but is often only annually or one time). There is no vaccination-only clinic for HSCT survivors where patients can get needed vaccines outside of an LTFU consult visit. Some of the respondents in this survey received their post-HSCT oncology care at FHCC, so even though they had been discharged from the transplant service, they benefitted from vaccine availability within the system and received vaccines with oncology visits (which are often more frequent than LTFU visits and are easier to align with the revaccination cadence). Given these system constraints, some respondents were able to get some or all their vaccines from FHCC, and some were not able to get any. However, all the responses were in support of the FHCC offering an expanded vaccine service:

> *I have had SCCA/LTFU do all of my vaccines except covid, for me this was probably the biggest reason I have received and am on track to receive all.* (38-year-old male, fully revaccinated)
>
> *Having the SCCA do it all in one place makes all the differen(ce) in my opinion.* (32-year-old male, partially revaccinated)

> *I'd LOVE if SCCA did the vaccinations part - it would help immensely!* (47-year-old female, partially revaccinated)
>
> *I would prefer to conclude re-vaccination to be performed at SCCA / Fred Hutch / LTFU, mostly because of familiarity.* (68-year-old male, partially revaccinated)
>
> *I found when I went through my primary care provider, her office didn't have childhood vaccinations. I went to my local pharmacy and they needed to know specific details like the manufacturer of a vaccine (which I didn't know). It seemed like pharmacies needed specifics on letterhead from a doctor, which I didn't have. It was easier to wait to go back to SCCA than it was to find my vaccines elsewhere.* (59-year-old female, fully revaccinated)

Additional exemplar quotes from each code are presented in Table 3, categorized by the constructs of The BeSD Framework.

Merged Results

Data integration explored the barriers and facilitators by revaccination outcome: no revaccination, partial revaccination, and complete revaccination (Table 4). The three groups differed in their experience of barriers and facilitators to successful revaccination. Overall, the barriers seemed to outweigh the facilitators as influencing factors in the no and partial revaccination groups. Conversely, the facilitators seemed to outweigh the barriers as influencing factors in the complete revaccination group. While this study sought to include only those who wanted to be or were completely revaccinated, vaccine hesitancy was noted in the comments of the people in the no revaccination and partial revaccination groups but not in the complete revaccination group. Areas of convergence and expansion for barriers were delayed immune recovery, continued immunosuppression, lack of insurance coverage, finding vaccines in the

community, and finding places that would give childhood vaccines to adults. Complementary data were noted in the following barriers: taking maintenance therapy (quantitative only), avoidance of healthcare settings due to bodily or emotional reactions (quantitative only), vaccine hesitancy (qualitative only), local healthcare provider issues (qualitative only), and unclear or missing guidance about revaccination (qualitative only). Areas of convergence and expansion for facilitators were insurance coverage, LTFU support, local healthcare provider help, and a clear calendar of what vaccines to get and when. Complementary data were noted in the following facilitators: provider recommendation (qualitative only), patient education (qualitative only), and local pharmacies as a resource (qualitative only). A complete list of the barriers and facilitators with frequencies is presented by revaccination outcome in Table 5. New barriers were plentiful and often were related to local healthcare provider issues, unclear guidance about revaccination, or relapse/new cancer. New facilitators were less abundant, but provider recommendation and helpful local pharmacies were the most common.

Discussion

This study is the first to our knowledge to use a mixed methods design to understand the barriers and facilitators to complete revaccination among adult HSCT survivors living in the US. Considering the elevated risk of VPDs and the currently inadequate revaccination uptake among HSCT survivors, it is critical to understand the factors that inhibit or drive revaccination. Respondents were 2-8 years after HSCT from a well-characterized longitudinal survivor cohort associated with an NCI-designated Cancer Center and represented all US geographic regions. The most common barriers were related to clinical contraindications and local access to vaccines. The most common facilitators were related to insurance coverage and having a clear calendar of

what vaccines to get and when. Overwhelmingly, the barriers and facilitators in this study fell within the practical issues construct of The BeSD Framework.

Previous studies and quality improvement reports have described barriers to post-HSCT revaccination.[4-6,26-37] Similar to the results of this study, most of the barriers described fell into the practical issues construct of The BeSD Framework. Barriers previously described in the literature that were not evident in this study were loss to follow-up,[4,26,27,35] missed opportunities to vaccinate,[26] being inpatient when vaccines are due,[5] inconsistent orders,[31] long wait time for vaccines,[4] patient refusal.[4,36] Previous studies and quality improvement reports have also described facilitators to post-HSCT revaccination.[5,27-33,35,36,38] Again, as with this study, most facilitators fell within the practical issues construct of The BeSD Framework. Facilitators described in earlier papers yet not seen in this study were standard operating procedures for revaccination[5,30,31,33], nurse screening tool[5], provider education[5,29,31], prospective monitoring of patients needing revaccination[27], a nurse-led vaccine program/clinic at the transplant center[27,33,35], standard order-set[29,31,32], and automatic alerts when vaccines due.[5,29] These barriers and facilitators are mainly at the system level; this difference could be explained by the fact that most previous research that has described the barriers and facilitators to revaccination has queried clinicians, not patients.

The main unexpected result of this study was how pervasive the theme of wanting to get revaccinated at the transplant center was in patient comments. Twenty-seven respondents (15%) described that this would be the ideal option for post-transplant revaccination, despite over 40% of the respondents living more than 100 miles away from the transplant center, many of whom are in adjacent or distant states. The quantitative and qualitative data regarding the difficulty in finding vaccines locally, as well as the added difficulty in finding places that would give

childhood vaccines to adults locally, also support this theme. For a motivated survivor who wishes to be revaccinated, the take-home message from this group of respondents was that it is less burdensome to travel to the transplant center than to fight an uphill battle locally with systems ill-equipped to support revaccination for adults.

Strengths and Limitations

The current study is the first to examine barriers and facilitators to routine revaccination in HSCT survivors, offering valuable insights into the barriers and facilitators to revaccination. The mixed methods approach was a considerable strength as the different data types provided more comprehensive results. The findings are valuable, given the overall convergence of quantitative and qualitative data and the expansion of quantitative results with qualitative data. The sample size of almost 200 people in the study is another strength, especially for a mixed methods design, as it provides more confidence in the prospective generalizability of the findings. Finally, using The BeSD Framework was a strength as this conceptual model for organizing and interpreting the results was beneficial in the revaccination setting.

It is important to acknowledge limitations to the findings. While the study was conceived before the COVID-19 pandemic, data were collected and analyzed in the pandemic era, and may have limited its generalizability in more ordinary times. The cross-sectional design limits interpretation as the barriers and facilitators and revaccination outcomes were collected at one point, making it difficult to assess these factors' influence on eventual revaccination outcomes. The lack of diversity within the sample across various social determinants of health, such as race, ethnicity, rurality, household income, and educational background is another major limitation, especially as barriers and facilitators may be disparate according to these factors. Selection bias may have resulted in less generalizable findings as people who chose to complete the survey may

have significant differences from those who were unable or unwilling to take the survey. Additionally, recall or social desirability bias may have affected revaccination outcomes which were self-reported and not validated by medical record review. Moreover, some participants did not answer all the questions in the survey, resulting in missing data that may have affected some of the analyses. Additionally, issues with vaccine confidence are likely underrepresented as a barrier in these results as we limited the data collection to people who wanted to be or were fully revaccinated, potentially limiting the number of vaccine hesitant or vaccine resistant people. Since this study excluded multiple myeloma patients, the barrier of continuing to take maintenance therapy was likely underrepresented. Finally, this study was conducted with patients from a single transplant center, and although they are geographically dispersed in their survivorship, they may have a unique set of characteristics based on their transplant experience at FHCC that have influenced their particular barriers and facilitators. While all geographic regions of the US were represented in the sample, the number of patients from some regions far from the transplant center was too small for us to analyze whether there were unique barriers based on geography.

Research, Advocacy, and Clinical Practice Implications

The findings presented, and the limitations described, prompt several areas for future study. Interventions to improve revaccination uptake should be developed, piloted, and tested based on the evidence from this study. As many of the barriers are related to lingering clinical effects from HSCT that preclude initiating or completing revaccination, it is essential to look at interventions that will follow patients longitudinally to ensure eventual revaccination. One option is a prospective trial with an intervention of every 6-month check-ins with patients to evaluate readiness for vaccines and support local revaccination. Additionally, an on-site, nurse-led

vaccine clinic could be explored for both feasibility and effectiveness in improving institutional uptake.

The US has a program called Vaccines for Children (VFC) which provides free vaccines through most pediatricians and state or territory health departments to children who are uninsured or under-insured, Medicaid eligible, or American Indian or Alaska Native.[39] This safety net has helped vaccinate children who would otherwise not be able to receive their routine childhood vaccines. Given the expense of repeating the entire childhood vaccine series for adults who lack insurance, expanding this program to anyone needing routine childhood vaccines, not just people aged 19 and under, would be reasonable. Clinicians can advocate for policy change to expand this program to adults.

The clinical implications of this study center around removing barriers, whether individual- or system-level, and reinforcing the facilitators. To help survivors find vaccines in their community, nurses can use government vaccine finders such as the US Department of Health and Human Services> Get Vaccinated>Where to Go website[40] or the CDC>Adult Vaccination Home>Where to Find Vaccines website.[41] Nurses and pharmacists can also help uninsured patients connect with medical insurance and write appeal letters to insurance companies if they deny coverage for revaccination. Appeal letters should include HSCT-related ICD-10 codes, an explanation of medical necessity, and links to the Advisory Committee on Immunization Practices (ACIP) Altered Immunocompetence document, which contains information regarding the need to administer vaccines out of routinely recommended age groups in the context of post-HSCT revaccination.[42] All clinicians caring for HSCT survivors can offer pro-vaccination messages and make specific recommendations for what vaccines are needed and when. An easy-to-follow written map of the revaccination protocol should be provided to

patients and caregivers in an online and printable format. All patients and lay caregivers should receive written and verbal patient education about revaccination in their preferred language before discharge from the transplant center. Patients should know who to contact if they have questions about revaccination after discharge. Patients should have access to a written and digital vaccine record that keeps track of all vaccines received after transplant. Additionally, clinicians must learn evidence-based strategies for working with vaccine-hesitant individuals. Transplant center clinicians must work with referring providers to support revaccination by providing clear guidance and rationale for revaccination and being available to field questions, as providing revaccination is generally an infrequent endeavor for oncologists and PCPs. Finally, transplant center staff should be prepared with written guidance to provide to local pharmacies willing to provide revaccination but need more information to support doing so.

Conclusion

The results of this convergent, mixed methods, cross-sectional survey of 194 adult HSCT survivors living in the US have exposed the myriad barriers HSCT survivors face when attempting to complete revaccination. Impaired immune recovery, continuing immunosuppressive therapy, and difficulty finding needed vaccines in the community are important barriers. Additionally, this study has identified several major facilitators that support revaccination uptake. Having healthcare insurance that covers vaccines, clear guidance from the transplant center about what vaccines are needed and when, and getting vaccines at the transplant center are important facilitators. This evidence can serve as the launching point for future research activities. Additionally, our findings are presently helpful for developing interventions to increase revaccination uptake. We must find novel ways to support survivor-centered

revaccination efforts, which can potentially decrease the risk of morbidity and mortality from VPDs among HSCT survivors.

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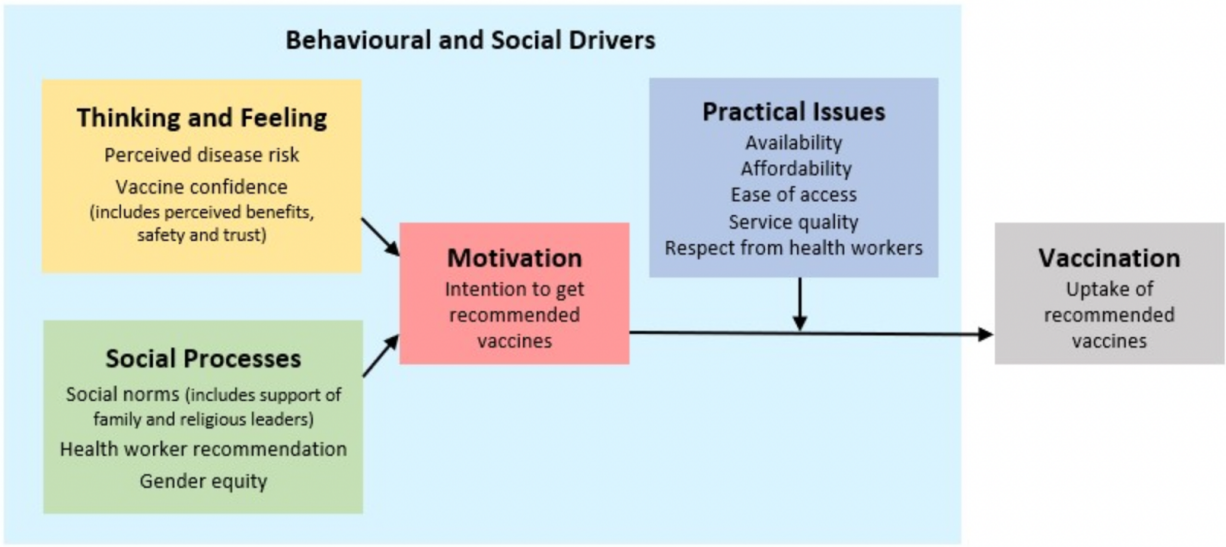
Tables and Figures

Figure 1. The BeSD Framework

The *WHO behavioural and social drivers of vaccination framework*



Source: The BeSD working group. Based on Brewer et al. *Psychol Sci Public Interest.* (2017).

Table 1. Demographic, Social Determinants of Health, Clinical, and Vaccine-related Characteristics of Respondents (n=194)

Characteristic	Number (percent)
Transplant Type	
Autologous	54 (27.8%)
Allogeneic	140 (72.2%)
Time from Transplant	
2 years	37 (19.1%)
3-5 years	92 (47.4%)
6-8 years	65 (33.5%)
Age	
Age 18-29	8 (4.1%)
Age 30-49	33 (17.0%)
Age 50-69	104 (53.6%)
Age 70+	49 (25.3%)
Gender	
F	94 (48.5%)
M	100 (51.5%)
Diagnosis	
Lymphoid Malignancy	85 (43.8%)
Myeloid Malignancy	93 (47.9%)
Non-Malignant	9 (4.6%)
Other/Multiple Diagnoses	7 (3.6%)
Race	
Non-white/Non-Asian	4 (2.2%)
Asian	13 (7.2%)
White	164 (90.6%)
Ethnicity	
Not Hispanic or Latino	182 (100.0%)
Educational Background	
Grade 11 or less	3 (1.6%)
Grade 12 or GED	21 (10.9%)
College 1 to 3 years	48 (25.0%)
College 4 years or more	120 (62.5%)
Distance from Transplant Center	
<100 miles	113 (58.2%)
101-300 miles	40 (20.6%)
>300 miles	41 (21.1%)
Residential Location	
Urban	155 (79.9%)
Rural	39 (20.1%)
Vote in 2020 Presidential Election by Zip Code	
Republican	71 (36.6%)
Democrat	123 (63.4%)
Household Median Income by Zip Code	
<$50,000	6 (3.1%)
$50,001 to $75,000	61 (31.4%)
$75,001 to $100,000	69 (35.6%)
>$100,000	58 (29.9%)
Health Insurance Since Transplant	
No insurance	2 (1.0%)
Insured the whole time	185 (95.4%)
Insured part of the time	6 (3.1%)

Don't know	1 (0.5%)
Ability to Pay for Vaccines Out of Pocket	
No	16 (8.4%)
Yes	40 (20.9%)
N/A, insurance pays	124 (64.9%)
Don't know	11 (5.8%)
Visits to Long-term Follow-up Clinic at Transplant Center	
No LTFU clinic visits	44 (23.8%)
One LTFU clinic visit	42 (22.7%)
Two or more LTFU clinic visits	99 (53.5%)
Chronic Graft versus Host Disease Since Transplant	
No	36 (26.3%)
Yes	92 (67.2%)
Don't Know	9 (6.6%)
Current Immunosuppressive Medications or Treatments	
No	30 (44.1%)
Yes	37 (54.4%)
Don't know	1 (1.5%)
Inadequate Immune Reconstitution	
No	163 (84.0%)
Yes	24 (12.4%)
Don't know	7 (3.6%)
Experience Negative Reactions with Health Care Access	
Often	11 (5.7%)
Sometimes	53 (27.6%)
Never	128 (66.7%)
Primary Vaccination Status	
All childhood vaccines	159 (82.4%)
Some childhood vaccines	26 (13.5%)
No childhood vaccines	2 (1.0%)
Don't know	6 (3.1%)
Pre-HSCT Adult Vaccine Uptake	
Always got recommended vaccines	159 (82.4%)
Sometimes got recommended vaccines	27 (14.0%)
Never got recommended vaccines	7 (3.6%)
COVID-19 Vaccine Uptake	
All recommended doses and boosters	145 (75.9%)
One or more doses but not all doses or boosters	33 (17.3%)
Did not receive	13 (6.8%)
Revaccination Status	
Not revaccinated	8 (4.3%)
Partially revaccinated	71 (38.0%)
Completely revaccinated	108 (57.8%)

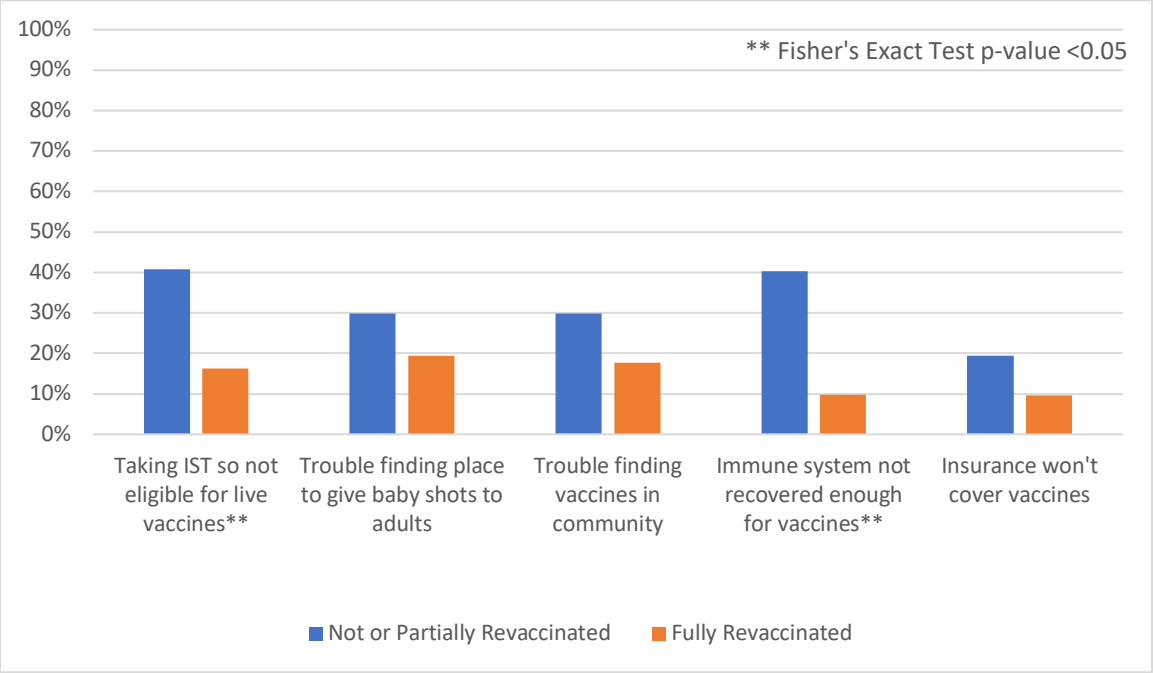
Table 2. Self-Reported Barriers and Facilitators to Complete Revaccination (Quantitative, n=194)

Barriers*	A Problem		Not a Problem
	A Big Problem	Somewhat of a Problem	
Taking immunosuppressive medications so not eligible for live vaccines	11%**	15%	74%
Trouble finding a place in the community that gives childhood vaccines to adults	9%	15%	76%
Immune system not recovered enough for vaccines	9%	15%	77%
Trouble finding a place in the community that carries all the needed vaccines	7%	16%	78%
Healthcare insurance won't cover vaccines	3%	11%	86%
Taking maintenance therapy so not eligible for vaccines	4%	5%	90%
Trouble paying for vaccines	4%	5%	91%
Strong fear of needles	2%	7%	92%
Avoidance of medical settings because of bodily or emotional reactions to seeking healthcare	2%	4%	95%
Local provider advising against vaccines	2%	3%	95%
Trouble with transportation to get vaccines	1%	3%	96%
Facilitators*	**A Help**		**Not a Help**
	A Big Help	Somewhat of a Help	
Having healthcare insurance that covers vaccines	83%**	9%	9%
Having a clear calendar of what vaccines to receive when	78%	13%	9%
Ability to call or email the LTFU Telemedicine team for questions about vaccines	60%	26%	15%
Getting vaccines at the Fred Hutch during an oncology clinic or LTFU clinic visit	65%	13%	23%
Having a non-Fred Hutch healthcare provider help with getting vaccines	49%	22%	29%
Having a caregiver (family or friend) help with getting vaccines	42%	23%	35%

*Listed in order of frequency, with the most encountered barriers and facilitators at the top of each list, and the least encountered barriers and facilitators at the bottom of each list

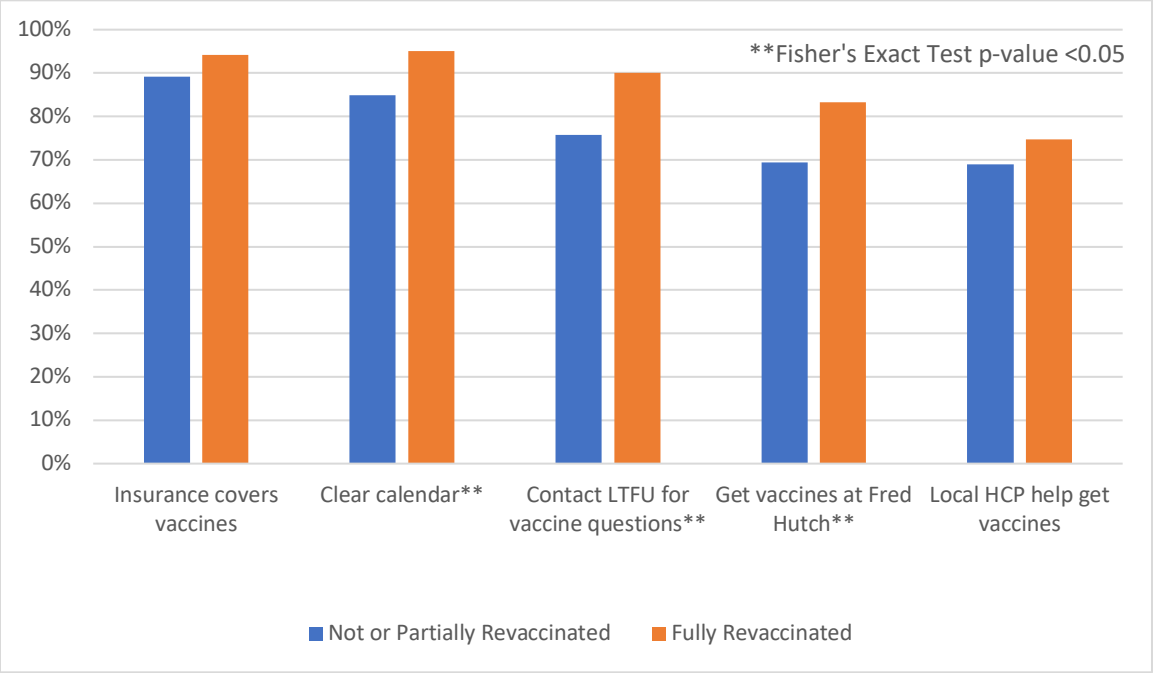
**May not add to 100% due to rounding

Figure 2a. Association Between Experiencing Most Common Barriers ("A big problem" or "Somewhat of a problem") and Full Revaccination (Quantitative, n=174-184*)



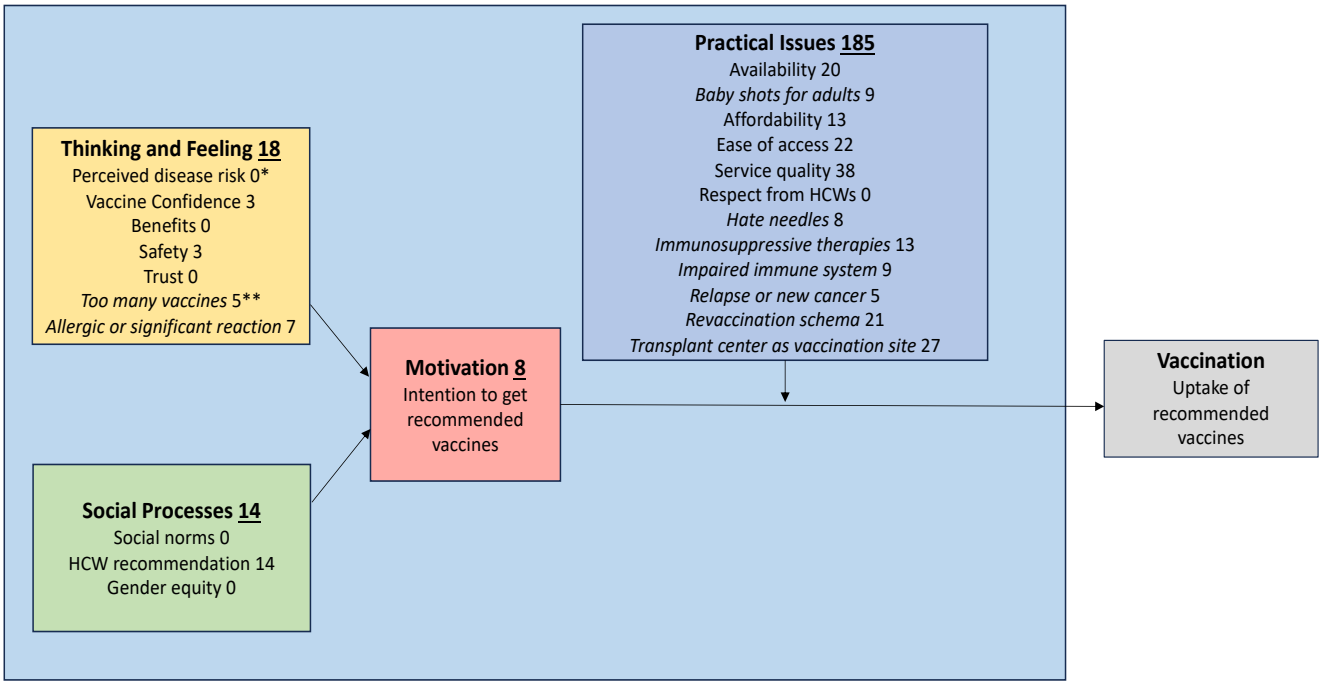
*Range in sample size is due to not all respondents completing each item

Figure 2b. Association Between Experiencing Most Common Facilitators ("A big help" or "Somewhat of a Help") and Full Revaccination (Quantitative, n=168-178*)



*Range in sample size is due to not all respondents completing each item

Figure 3. BeSD Framework with Additional Codes and Content Analysis Counts Regarding Barriers and Facilitators to Revaccination for Survivors who Want to be or are Fully Revaccinated (Qualitative, n=194)



*Codes from original BeSD model in regular font
**Additional codes from study data in italic font

Table 3. Codes and Exemplar Quotes from Open-Ended Responses about Barriers and Facilitators to Revaccination for Survivors who Want to be or are Fully Revaccinated (Qualitative, n=194)

BeSD Framework Construct	Codes*	Exemplar Quotes
Thinking and Feeling	Perceived disease risk	N/A
	Vaccine confidence (includes perceived benefits, safety, and trust)	Be disappointing to not finish the journey after you've come such a long way right? So, you might as well get the stupid shots for your own protection.
	Too many vaccines	I've been poked so many times. Getting so many vaccines at one time is horrible.
	Allergic or significant reaction	Clinic did a great job responding to potentially life-threatening complication. Epi pen worked but I will admit to being worried about what will happen when we restart/complete the vaccination process.
Social Processes	Social norms (includes support of family and religious leaders)	N/A
	Health worker recommendation	I am simply waiting for my team to tell me when and what additional vaccines to take and then administer them. It's been a wild ride for sure. I follow their directions to the letter (and am extremely thankful for them all).
	Gender equity	N/A
Motivation	Intention to get recommended vaccines	I had to get revaccinated twice because I had two transplants. Time consuming but not a problem.
Practical Issues	Availability	My local doctor and pharmacies did not have some of the vaccines I needed.
	Baby shots for adults	I had to hunt down someone that would give me my shots because I was an adult. They may have had the drug on hand but would not give it to an adult.
	Affordability	They made me pay out of pocket & submit to insurance, but insurance never paid me back $440.
	Ease of access	I had to get one of my vaccinations at the local healthcare center. No one else had the vaccine I needed that week. I had to wait in line with the methadone clinic folks for my turn.... I felt unsafe. I wished there had been a better option. It was hard going place to place to get all the vaccines needed. I would have preferred having a single provider/facility.
	Service quality	My oncologist Dr. XX, has been amazing making sure I have gotten all my vaccinations.
	Respect from HCWs	N/A
	Hate needles	
	Immunosuppressive therapies	When I was on immunosuppressants, was told I couldn't have MMR or Chicken Pox (live) vaccines, but I have never been told when it was or would be okay to have them.

	Impaired immune system	Vaccine titer levels are at or below normal for some vaccines due to compromised immune system. My individual response to vaccines is the problem (lack of response).
	Relapse or new cancer	I am now not able to get caught up on my vaccines as I am being treated for AML again and going in for transplant soon.
	Revaccination schema	With needing to take so many, knowing which ones and when to take them was confusing. It would have been good to have a clear chart.
	Transplant center as vaccination site	I would appreciate SCCA doing the vaccinations - in one place and keeping me on track. It is all way too scattered currently and it isn't efficient nor organized.

*Codes from original BeSD model in regular font, additional codes from study data in italic font
Quotes have been edited for spelling and grammar

Table 4. Visual Data Display of Merged Findings by Revaccination Outcome (Mixed, n=187*)

Outcome	Most Reported Barriers (Quantitative)	Most Reported Facilitators (Quantitative)	Relative Frequencies of Barriers and Facilitators (Quantitative)	Open-Ended Barrier Responses (Qualitative)	Open-Ended Facilitator Responses (Qualitative)	Merged Findings
No Revaccination n=8	Immune system not recovered enough for vaccines 58% On maintenance therapy 50% On IST so no live vaccines 33% Avoidance of medical settings 25% Insurance does not cover vaccines 17%	Insurance covers vaccines 100% Can contact LTFU for vaccine help 100% Local health care provider helps with vaccines 100%	9/11 barriers reported by >10% of respondents 3/6 facilitators reported by > 90% of respondents	*Qualitative expansion on provided barriers (2/11):* Healthcare insurance won't cover vaccines Immune system not recovered enough for vaccines *New barriers (5):* Vaccine hesitancy No provider recommendation Too busy Healthy so did not come up with provider Wants titer-based revaccination	*Qualitative expansion on provided facilitators (1/6):* Having healthcare insurance that covers vaccines *New facilitators (2):* Provider recommendation Self-advocacy	Most of the people in the no revaccination group reported many different barriers quantitatively, and a couple of these were further expanded in qualitative responses. New barriers were common, with five identified among only eight people in this group. Many barriers were clinical contraindications for either starting or completing revaccination. This was the only group where avoidance of medical settings due to bodily or emotional responses to seeking healthcare was an important barrier. Additionally, insurance coverage was a barrier. Facilitators were relatively common in this group by both quantitative and qualitative responses. Insurance coverage and health care provider recommendations and assistance were important facilitators. **Barriers > Facilitators**
Partial Revaccination n=71	On IST so no live vaccines 41% Immune system not recovered enough for vaccines 39% Trouble finding vaccines in the community 31%	Insurance covers vaccines 88% Clear calendar of what vaccines to get when 85% Can contact LTFU for vaccine help 74%	7/11 barriers reported by >10% of respondents 0/6 facilitators reported by > 90% of respondents	*Qualitative expansion on provided barriers (8/11):* Taking immunosuppressive medications so not eligible for live vaccines Trouble finding a place in the community that gives childhood vaccines to adults	*Qualitative expansion on provided facilitators (4/6):* Having a clear calendar of what vaccines to receive when Ability to call or email the LTFU Telemedicine team for questions about vaccines	More than half of the people in the partial revaccination group reported many barriers quantitatively, and most of the barriers were further expanded in qualitative responses. New barriers were relatively less common when compared to the no revaccination group but more common when compared

	Trouble finding pediatric vaccines for adults 31% Insurance does not cover vaccines 20%			Immune system not recovered enough for vaccines Trouble finding a place in the community that carries all the needed vaccines Healthcare insurance won't cover vaccines Taking maintenance therapy so not eligible for vaccines Trouble paying for vaccines Strong fear of needles *New barriers with multiple responses** (8):* Local healthcare provider issues Unclear guidance or did not receive guidance about revaccination Cancer got in the way Vaccine hesitancy Fred Hutch not helpful or did not know Fred Hutch LTFU could be contacted for help Calendar from LTFU is confusing Can't find titers locally GVHD	Getting vaccines at the Fred Hutch during an oncology clinic or LTFU clinic visit Having a non-Fred Hutch healthcare provider help with getting vaccines *New facilitators with multiple responses** (2):* Local pharmacy was helpful Patient education about revaccination	to the complete revaccination group, with 15** identified among 71 people in this group. The most common barriers were clinical contraindications for either starting or completing revaccination, but almost as common were trouble finding the needed vaccines in the community and places that would give pediatric vaccines for adults. Additionally, insurance coverage was a barrier. The experience of facilitators in this group is divergent between the strands. Although facilitators were highlighted in qualitative responses, they were rarer in the quantitative responses. Transplant center support (guidance, availability for questions, and a site for vaccine administration) were important facilitators as was local health care provider support and local pharmacy as a site for vaccine administration. **Barriers > Facilitators**
Complete Revaccination n=108	On IST so no live vaccines 27% Trouble finding pediatric vaccines for adults 19% Trouble finding vaccines in the community 18%	Clear calendar of what vaccines to get when 95% Insurance covers vaccines 94% Can contact LTFU for vaccine help 90%	3/11 barriers reported by >10% of respondents 3/6 facilitators reported by > 90% of respondents	*Qualitative expansion on provided barriers (5/11):* Taking immunosuppressive medications so not eligible for live vaccines Trouble finding a place in the community that gives childhood vaccines to adults	*Qualitative expansion on provided facilitators (All 6):* Having healthcare insurance that covers vaccines Having a clear calendar of what vaccines to receive when	Less than half of the people in the complete revaccination group reported many barriers quantitatively, and less than half of the barriers were further expanded in qualitative responses. New barriers were less common when compared to both other groups, with 16** identified among 108 people in

	Immune system not recovered enough for vaccines 10% Insurance does not cover vaccines 10%			Trouble finding a place in the community that carries all the needed vaccines Healthcare insurance won't cover vaccines Strong fear of needles *New barriers with multiple responses** (9):* Unclear guidance or did not receive guidance about revaccination Local healthcare provider issues Calendar from LTFU was confusing Pharmacist reluctant or refused to give vaccines So much time and effort to get revaccinated Too many shots at once Hard to get vaccine appointments during pandemic Serious side effects after vaccines Got a VPD before vaccinated against that VPD	Ability to call or email the LTFU Telemedicine team for questions about vaccines Getting vaccines at the Fred Hutch during an oncology clinic or LTFU clinic visit Having a non-Fred Hutch healthcare provider help with getting vaccines Having a caregiver (family or friend) help with getting vaccines *New facilitators with multiple responses** (4):* LTFU kept track of needed and received vaccines Provider recommendation Local pharmacy was helpful Patient education about revaccination	this group. The most common barriers were the same as the partial revaccination group, although each barrier was reported by less people in this group. People in this group reported many facilitators both quantitatively and qualitatively. New facilitators identified in this group were far more plentiful than in the other groups. The same facilitators as identified in the partial revaccination group were reported in this group, with one expansion of transplant center facilitators being LTFU keeping track of needed and received vaccines. This group was the only group that identified having a supportive caregiver (family or friend) help with getting vaccines as an important facilitator. **Facilitators > Barriers**

*Seven respondents selected "I don't know" for revaccination status, thus total is not 194 for this table
** For complete list of all new barriers and facilitators, see Table 5

Table 5. Expansion and Divergence of Barriers and Facilitators by Revaccination Outcome (Quantitative and Qualitative)

No revaccination (total discrete Barriers=7, total discrete Facilitators=3)

Two of the listed barriers matched drop-down barriers:
- 1 Healthcare insurance won't cover vaccines
- 1 Immune system not recovered enough for vaccines

New barriers:
- 1 Vaccine hesitancy
- 1 No provider recommendation
- 1 Too busy
- 1 Healthy so did not come up with provider
- 1 Wants titer-based revaccination

One of the listed facilitators matched drop-down facilitators:
- 1 Having healthcare insurance that covers vaccines

New facilitators that were or would be helpful:
- 1 Provider recommendation
- 1 Self-advocacy

Partial revaccination (total discrete Barriers=29, total discrete Facilitators=9)

Most of the listed barriers matched drop-down barriers at least once, often more frequently (listed in original order):
- 6 Taking immunosuppressive medications so not eligible for live vaccines
- 6 Trouble finding a place in the community that gives childhood vaccines to adults
- 4 Immune system not recovered enough for vaccines
- 7 Trouble finding a place in the community that carries all the needed vaccines
- 2 Healthcare insurance won't cover vaccines
- 1 Taking maintenance therapy so not eligible for vaccines
- 2 Trouble paying for vaccines
- 2 Strong fear of needles

New barriers:
- 14 Local healthcare provider issues
  - 4 Provider did not recommend vaccines
  - 4 Provider did not understand need for revaccination
  - 4 Provider is reluctant or not helpful
  - 1 Don't have a provider
  - 1 Not a priority for provider
- 5 Unclear guidance or did not receive guidance about revaccination
- 5 Cancer got in the way
  - 4 Relapse needing more treatment
  - 1 New malignancy requiring treatment
- 4 Vaccine hesitancy
- 3 Fred Hutch not helpful or did not know Fred Hutch LTFU could be contacted for help
- 3 Calendar from LTFU is confusing
- 2 Can't find titers locally
- 2 GVHD
- 1 Inefficient to get locally
- 1 Mistakes made at local pharmacy
- 1 Anaphylaxis to last set of vaccines so must meet with allergist before next round
- 1 Lost vaccine record
- 1 Vaccines should be free
- 1 Illness and emergency surgery delayed revaccination
- 1 Survivor procrastinated

Most of the listed facilitators matched drop-down barriers at least once, often more often (listed in original order):
- 1 Having a clear calendar of what vaccines to receive when
- 8 Ability to call or email the LTFU Telemedicine team for questions about vaccines
- 10 Getting vaccines at the Fred Hutch during an oncology clinic or LTFU clinic visit
- 3 Having a non-Fred Hutch healthcare provider help with getting vaccines

New facilitators that were or would be helpful:
- 5 Local pharmacy was helpful
- 2 Patient education about revaccination
- 1 An online vaccine record that you could always reference/could not lose!
- 1 Provider recommendation
- 1 An easy way to schedule vaccines

Complete revaccination (total discrete Barriers=23, total discrete Facilitators=14)

Less than half of the listed barriers matched drop-down barriers multiple times (listed in original order):
- 7 Taking immunosuppressive medications so not eligible for live vaccines
- 2 Trouble finding a place in the community that gives childhood vaccines to adults
- 7 Trouble finding a place in the community that carries all the needed vaccines
- 7 Healthcare insurance won't cover vaccines
- 5 Strong fear of needles

New barriers:
- 8 Unclear guidance or did not receive guidance about revaccination
- 4 Local healthcare provider issues
  - 2 Local provider used a different revaccination schedule than LTFU
  - 1 Lack of transition to adult providers
  - 1 Provider is reluctant
- 3 Calendar from LTFU was confusing
- 3 Pharmacist reluctant or refused to give vaccines
- 3 So much time and effort to get revaccinated
- 2 Too many shots at once
- 2 Hard to get vaccine appointments during pandemic
- 2 Serious side effects after vaccines
- 2 Got a VPD before vaccinated against that VPD
- 1 Felt sick after getting vaccines
- 1 Blanks in the vaccine record
- 1 Had to re-revaccinate because of low titers
- 1 Mistakes made at local pharmacy
- 1 Pharmacist did not understand revaccination guidance
- 1 Sorting out shingles vaccine for person aged <50
- 1 Hard to miss work/income to get vaccines

All of the listed facilitators matched drop-down barriers at least once, often more frequently (listed in original order):
- 1 Having healthcare insurance that covers vaccines
- 5 Having a clear calendar of what vaccines to receive when
- 2 Ability to call or email the LTFU Telemedicine team for questions about vaccines
- 14 Getting vaccines at the Fred Hutch during an oncology clinic or LTFU clinic visit
- 14 Having a non-Fred Hutch healthcare provider help with getting vaccines
- 1 Having a caregiver (family or friend) help with getting vaccines

New facilitators that were or would be helpful:
- 3 LTFU kept track of needed and received vaccines
- 3 Provider recommendation
- 2 Local pharmacy was helpful
- 2 Patient education about revaccination
- 1 Getting vaccines at regularly scheduled visits
- 1 Spacing out vaccines so less shots at once
- 1 Customized patient calendar
- 1 Letter on Fred Hutch letterhead to pharmacy with instructions

Chapter Five | Conclusion

Synopsis

Childhood vaccines are arguably one of the most important interventions for infectious disease prevention, control, and elimination, preventing four million premature deaths worldwide each year.[1] However, vaccines in vials on a shelf or in a refrigerator can do nothing to protect individuals or the public. Many Hematopoietic Stem Cell Transplant (HSCT) survivors are not starting or completing their revaccination series after transplant, which puts them at higher risk of vaccine-preventable diseases (VPDs). Additionally, we are amid a worldwide under-vaccination crisis, putting HSCT survivors further at risk for post-transplant infectious morbidity and mortality with waning herd immunity in the community. It is time to change the narrative on the post-HSCT revaccination story and intervene to help survivors access protective vaccines. Taken together, the evidence from this dissertation provides immediate opportunities for clinicians and researchers.

Chapter Two Summary

For chapter two, I aimed to determine the point prevalence of completely, partially, or not revaccinated adult HSCT survivors and to examine associations between demographic variables, social determinants of health, clinical variables, past vaccine behaviors, vaccine hesitancy, and revaccination status from a cohort who were between 2-8 years after transplant. Regarding revaccination outcomes, 62% were completely revaccinated, 33% were partially revaccinated, and 4% were not revaccinated. Most survivors (77%) who were not yet completely revaccinated wanted to achieve full revaccination. On multivariate analysis, the only three factors significantly associated with incomplete (no or partial) revaccination were shorter time from transplant, inadequate immune reconstitution, and not having received all childhood vaccines as a child.

While this may partly be due to sample size (n=338), which could have limited associations between more variables and revaccination outcomes, it can also be seen as a promising finding for clinicians. The goal of determining if there were certain variables associated with poorer revaccination uptake would be to target interventions to groups of survivors with similar characteristics. Given the few associations, revaccination uptake interventions can be broadly applied.

Chapter Three Summary

For chapter three, I aimed to explore vaccine hesitancy in the context of revaccination among adult HSCT survivors by describing the level of agreement between quantitative results of vaccine hesitancy (Vaccination Confidence Scale[2,3]) and qualitative results (open-ended survey items regarding vaccine confidence). The point prevalence of vaccine confidence was 69% high, 20% medium, and 11% low confidence. Revaccination outcomes and intent to revaccinate significantly differed by vaccine confidence levels more here on relationship. The four factors associated with high vaccine confidence included living in a zip code that voted for the Democratic presidential candidate in 2020, having means to pay out-of-pocket or health insurance coverage for vaccines, receiving all pre-HSCT adult vaccines, and receiving all recommended COVID-19 vaccines. The themes from the open-ended responses were categorized as 1) *Physical and mental benefits* and *beliefs about benefits* (Benefits); 2) *Existing factors for trust, prerequisites for trust*, and *impeding factors to trust* (Trust); 3) *Vaccine quantity, vaccine side effects, vaccines and harm*, and *not all vaccines are the same* (Harms); and 4) *Uniqueness of HSCT vaccinees* and *revaccination motivation and behavior* (Other). The merged analysis showed congruence between the Vaccine Confidence Scale scores and overall vaccine confidence coding from open-ended responses. Finally, the merged analysis created a

narrative about the relative importance of the constructs when approaching revaccination by vaccine confidence level: the low confidence group relayed (dis)trust>harms>benefits, the medium confidence group relayed trust>benefits~harm, and the high confidence group relayed benefits>trust>harm. These findings suggest that HSCT survivors experience vaccine hesitancy that can affect revaccination uptake. It is possible to predict which survivors may have lower hesitancy based on their political environment, financial means, and past vaccine behaviors. The relative importance of harm, trust, and benefits based on vaccine confidence level provides information for tailoring pro-revaccination messages based on vaccine confidence level.

Chapter Four Summary

For chapter four, I aimed to identify the barriers and facilitators to complete revaccination using fixed and open-ended responses and describe the extent to which these factors explain the three revaccination status categories (completely, partially, or not revaccinated) among adult HSCT survivors. The most frequent barriers were the inability to receive live vaccines because of continued immunosuppression, finding a place in the community to give childhood vaccines to adults, and delayed immune system recovery. The most frequent facilitators were having healthcare insurance covering vaccines and having a clear calendar of what vaccines to receive and when. On multivariate analysis, with each additional reported barrier, the odds of being completely revaccinated were lower, OR=0.58 (95% CI 0.459-0.722), and with each additional reported facilitator, the odds of being completely revaccinated were higher, OR=1.31 (95% CI 1.05-1.63), $p < 0.001$. Further, two of the five most reported barriers were significantly associated with no or partial revaccination: taking immunosuppressive therapy so not eligible for live vaccines ($p = 0.001$) and immune system not recovered enough for vaccines ($p < 0.001$). Three of the five most reported facilitators were significantly associated with being fully revaccinated:

having a clear calendar of what vaccines to get when (p= 0.032), being able to contact LTFU for vaccine questions (p= 0.018), and getting vaccines at FHCC (p= 0.041). Content analysis suggested that most barriers were in the "practical issues" construct of the World Health Organization Behavioural and Social Drivers of Vaccination Framework, especially service quality and availability. A surprising but important theme was *the transplant center as vaccination site*, with 15% of all respondents commenting in free text that they believed that is where revaccination should be offered. The merged analysis mainly indicated convergence. Additionally, it illustrated the difference between fully revaccinated people and those who were not. Overall, the barriers seemed to outweigh the facilitators as influencing factors in the no and partial revaccination groups. Conversely, the facilitators seemed to outweigh the barriers as influencing factors in the complete revaccination group. The evidence from this analysis should be carefully reviewed as the first comprehensive set of barriers and facilitators from HSCT survivor informants. These findings are helpful in directly addressing efforts to reduce barriers and expand facilitators for HSCT survivors.

Clinical Implications

Prospectively monitoring HSCT survivors for revaccination readiness would help all survivors to know when they are due to start vaccines. In the case of HSCT survivors who do not meet parameters for timely revaccination, continued prospective monitoring for vaccine readiness could catch survivors who are many years out before they can be revaccinated, decreasing the chance of missed vaccines after transplant. On a systems level, the transplant center should implement policies and procedures to support revaccination. These will look different depending on whether the transplant center is the primary revaccination site, a hybrid revaccination site (some vaccines at the transplant center and some in the community), or refers

all revaccination to the community. These systems-level interventions may include automated vaccine order sets, clinic visit templates that include a prompt for revaccination, and scheduling reminders. Additionally, revaccination education for clinicians should be provided on a routine basis. On an individual level, clinicians can proceed with general evidence-based vaccination interventions (such as a strong vaccine recommendation with each clinical encounter, presumptive language when introducing the need for vaccines, and automatic reminders via text, email, or patient-medical record interface) to encourage revaccination after transplant. Patients and caregivers should all receive education about the need for revaccination in their preferred language before they leave the transplant center. They should also be able to verbalize the plan for what vaccines they are to receive and when.

Clinicians caring for HSCT survivors must learn about vaccine hesitancy, as they will undoubtedly encounter patients who are vaccine hesitant. At this time, targeted interventions that support vaccine hesitant HSCT survivors are not available; therefore, interventions for the general vaccine hesitant population should be used. Studies have repeatedly shown that patients prefer to get vaccine information from their providers. This means that transplant and oncology clinicians have an essential role in encouraging uptake for HSCT survivors. Presumptive language, a pro-vaccine message with every encounter, and willingness to talk openly about vaccine hesitancy are indispensable tools for clinicians.

Assessing for barriers and working to eliminate them should be a focus for clinicians working with patients due for revaccination. Nurses can use available resources to help patients find vaccines in their communities and work with pharmacists to write appeal letters when insurance denies coverage for revaccination. Nurses can help uninsured or underinsured patients get matched with resources to gain insurance coverage or free or low-cost vaccines. Transplant

center clinicians must keep open lines of communication with oncology and primary care clinicians to support their efforts towards revaccination locally. Transplant clinicians can also ensure that patients have written education about revaccination, a clear and patient-friendly calendar of what vaccines to receive and when, and access to paper and online vaccine records so they can check their progress toward complete revaccination. Where transplant centers are equipped to provide prospective revaccination, this practice should be supported as it offers the greatest likelihood of successful revaccination.

Policy Implications

These findings have both "little p" and "big P" policy implications. Transplant centers should ensure that their institutional guidance is robust concerning revaccination. Clear guidance for the revaccination protocol, and procedures that outline how to implement revaccination, are critical. On a larger scale, US policy should be addressed to mitigate the financial burden of revaccination. The Vaccines for Children program should be expanded to cover ALL childhood vaccines given to people of any age for people who cannot afford them.[4] This program exists as a stopgap to help children get their vaccines if they cannot afford them and is a vital public health safety net that ensures that vaccine gaps do not exist due to inability to pay. It is time to expand this program to adults.

Research Implications

A potential targeted set of interventions for HSCT survivors who are not clinically cleared for timely revaccination due to maintenance therapy, continued immunosuppression precluding live vaccines, or delayed immune recovery should be developed and tested. Tracking patients prospectively to help them start revaccination when their situation allows will improve uptake, as it will bring revaccination back to mind for patients who are so many years from

transplant that it may no longer be at the forefront of patient or clinician memory. A short and simple screening tool could be created and trialed that could identify vaccine hesitant survivors or survivors who had not been vaccinated as children or had not followed adult pre-HSCT vaccine guidance may prove helpful to targeting efforts to survivors who may be less inclined to seek revaccination. Further research to identify what interventions support vaccine uptake in vaccine hesitant HSCT survivors is also necessary. There may be HSCT-specific factors that modify vaccine confidence in HSCT survivors that require specialized interventions. Therefore, this topic should be further explored. The feasibility and acceptability of an on-site revaccination clinic co-located with the transplant clinic could also be explored. In addition to studying whether such a clinic would improve revaccination uptake compared to baseline levels, cost-efficiency would need to be studied. With all these potential avenues for further research into what can improve revaccination rates, multiple methods could be used to determine what interventions work best and are most cost-efficient.

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