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Association of Self-Reported COVID-19 Vaccination Status with COVID-19 Infection among Adult Long-Term Hematopoietic Cell Transplantation Survivors

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A B S T R A C T

Hematopoietic cell transplantation (HCT) recipients experience significant morbidity and mortality from coronavirus disease 19 (COVID-19) infection. Data are limited regarding long-term HCT survivors' uptake of and experiences with COVID-19 vaccination and infection. This study aimed to characterize COVID-19 vaccination uptake, use of other prevention measures, and COVID-19 infection outcomes in adult HCT recipients at our institution. Between July 1, 2021, and June 30, 2022, long-term adult HCT survivors were surveyed regarding overall health, chronic graft-versus-host (cGVHD) status, and experiences with COVID-19 vaccinations, prevention measures, and infections. Patients reported COVID-19 vaccination status, vaccine-related adverse effects, use of nonpharmaceutical prevention measures, and infections. Comparisons by response and vaccination status were performed using the chi-square test and Fisher exact test for categorical variables and the Kruskal-Wallis test for continuous variables. Of 4758 adult HCT survivors who underwent HCT between 1971 and 2021 and consented to participate in annual surveys, 1719 (36%) completed the COVID-19 module, and 1598 of 1705 (94%) reported receiving ≥1 dose of COVID-19 vaccine. Severe vaccine-related adverse effects were infrequent (5%). Among respondents receiving an mRNA vaccine, completion of doses according to the Centers for Disease Control and Prevention's vaccine recommendations at the time of survey return was 2 doses in 675 of 759 (89%), 3 doses in 610 of 778 (78%), and 4 doses in 26 of 55 (47%). Two hundred fifty respondents (15%) reported COVID-19 infection; 25 (10%) required hospitalization. Vaccinated respondents reported significantly higher uptake of household vaccination (1284 of 1404 [91%] versus 18 of 88 [20%]; $P < .001$) and the use of nonpharmaceutical interventions ($P < .001$). Vaccinated respondents were significantly less likely to have contracted COVID-19 (85 of 1480 [6%] versus 130 of 190 [68%]; $P < .001$), as were their household members (149 of 1451 [10%] versus 85 of 185 [46%]; $P < .001$). Receipt of additional COVID-19 vaccine doses beyond the first dose was associated with a reduced risk of COVID-19 infection (odds ratio, .63; 95% confidence interval, .47 to .85; $P = .002$). Vaccination was well tolerated and associated with a lower risk of COVID-19 infection among HCT survivors and their household contacts. Vaccination and booster doses should be encouraged as part of a multifaceted approach in this high-risk population.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has caused >100 million infections and >1 million deaths in the United States to date [1]. Hematopoietic cell transplantation (HCT) recipients are at increased risk of severe disease and adverse outcomes from COVID-19 infection, with reported mortality rates between 17% and 40% [2–6]. Older age, male sex, development of COVID-19 infection within 12 months of HCT, active graft-versus-host disease (GVHD), and steroid use are risk factors for worse outcomes [2–6]. Strategies to reduce exposure and prevent infection are critical to optimizing outcomes in this vulnerable population.

COVID-19 vaccines are highly effective in reducing infection, morbidity, and mortality [7–10]. Although HCT recipients

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may have reduced protection following COVID-19 vaccination compared to the general population [11], seroconversion rates of approximately 80% have been observed in HCT recipients after 2 doses of mRNA vaccine [12,13]. Consensus guidelines recommend initiating the COVID-19 vaccination series at 3 to 6 months after HCT, with a preference for mRNA vaccines [14]. As part of a multifaceted approach to prevention, household contact/caregiver vaccination and nonpharmaceutical interventions, including wearing masks, social distancing, avoiding crowded settings, and performing hand hygiene, are also recommended to mitigate the risk of exposure in HCT recipients [15].

To our knowledge, there are no published data on long-term HCT survivors' adherence to and experiences with COVID-19 vaccination or uptake of other prevention strategies. In this study, we surveyed a long-term adult HCT survivor population to characterize the use of COVID-19 vaccination, other nonpharmaceutical prevention measures, and COVID-19 infection outcomes.

METHODS

As part of Fred Hutchinson Cancer Center's long-term follow up of HCT recipients, starting 1 year after HCT we administer an annual survey regarding overall health and cGVHD status, including immunosuppressive treatment. Between July 1, 2021, and June 30, 2022, the annual survey included an additional module on COVID-19 vaccinations, infection, and precautions (Supplementary Data). This study included responses to the annual survey and COVID-19 module that were returned between July 1, 2021, and September 30, 2022. This study was approved by the Fred Hutchinson Cancer Center's Institutional Review Board.

Vaccinated respondents were defined as those who reported receipt of ≥1 COVID-19 vaccine dose. Given the heterogeneity of immunocompetence in our cohort and the evolving vaccination recommendations, in this study we defined the primary series of COVID-19 vaccination as 1 dose of the Janssen/Johnson & Johnson vaccine or 2 doses of either mRNA vaccine (Moderna or Pfizer). The NovaVax vaccine was not approved for use at the time of this study. When defining adherence to Center for Disease Control and Prevention (CDC) vaccination recommendations, we allowed for a 6-week window after a recommendation update. A timeline of CDC vaccination recommendations for immunocompetent and immunocompromised individuals is shown in Figure 1.

Comparisons by response and vaccination status were performed using the chi-square test and Fisher exact test for categorical variables and the Kruskal-Wallis test for continuous variables. Analyses were performed using SAS/STAT version 9.4 (SAS Institute, Cary, NC).

RESULTS

Respondent Vaccination Status

Of 4758 HCT survivors who underwent transplantation HCT between 1971 and 2020 and consented to receive annual surveys, 2060 (43%) completed the core survey, and 1719 (36%) answered the COVID-19 module (Supplementary Table S1). Compared to nonrespondents, core survey respondents were more likely to be older, female, and non-Hispanic white ($P <$ .001 for all). Among module respondents, the median time since HCT was 11.9 years (range, .9 to 50.0 years), with a median age at HCT of 50.4 years (range, .9 to 77.6 years), and 902 (53%) were male. The most common indication for HCT in this group was acute myeloid leukemia/myelodysplastic syndrome (n = 465; 27%), followed by multiple myeloma (n = 316; 18%) and lymphoma (n = 315; 18%). Most underwent allogeneic HCT with myeloablative conditioning, had a matched donor, and received a peripheral blood stem cell graft.

Of the 1705 module respondents who provided vaccination status, 1598 (94%) received ≥1 doses of COVID-19 vaccine. Of 1577 respondents who received ≥1 vaccine dose and who provided vaccination information, uptake of the primary series was 97% (1535 of 1577), and most respondents (n = 1485; 94%) received an mRNA vaccine only. Eight hundred fifty-six respondents (54%) received the Pfizer vaccine, 589 (37%) received the Moderna vaccine, and 42 (3%) received the Janssen/Johnson & Johnson vaccine. Sixty-four respondents (4%) received ≥1 type of vaccine, and vaccine type was unknown for 47 respondents (3%). Regardless of type of vaccine, 1496 of 1579 respondents (95%) received ≥2 vaccine doses, 910 (58%) received ≥3 doses, and 176 (11%) received 4 doses.

The percentage of respondents who reported completion of COVID-19 mRNA vaccine doses according to the CDC vaccine recommendations for the general US population at the time of survey return are shown in Figure 2A. Between July 1 and December 31, 2021, 675 of 759 respondents (89%) reported receipt of ≥2 vaccine doses, including 237 (31%) who had 3 doses and 1 (.1%) who had 4 doses. After CDC guidelines changed to recommend a third dose or first booster dose of mRNA vaccine, between January 1 and June 30, 2022, 610 of 778 respondents (78%) reported receipt of ≥3 doses of mRNA vaccine, including 148 (19%) who had 4 doses. Between July 1 and September 30, 2022, 26 of 55 respondents (47%) reported receiving 4 doses of mRNA vaccine following the CDC's recommendation of a second booster for those age ≥50 years or those age ≥12 years and immunocompromised. Most

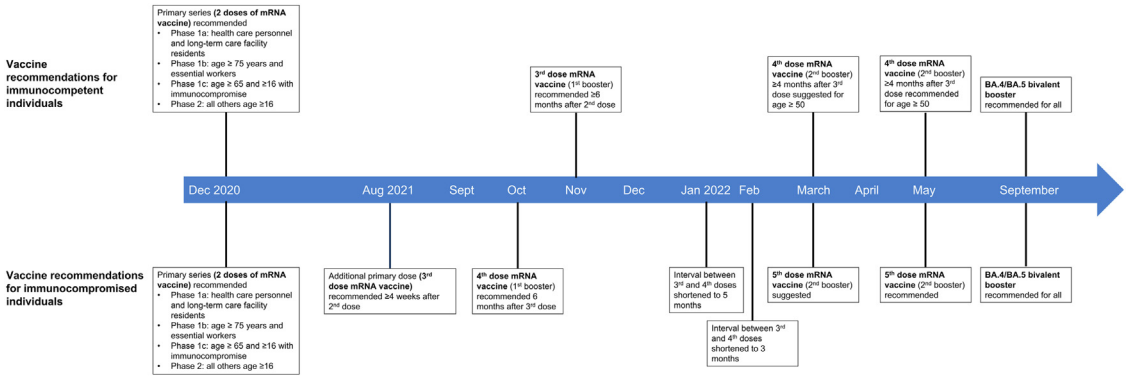

Figure 1. Timeline of CDC vaccination recommendations for immunocompetent and immunocompromised individuals.

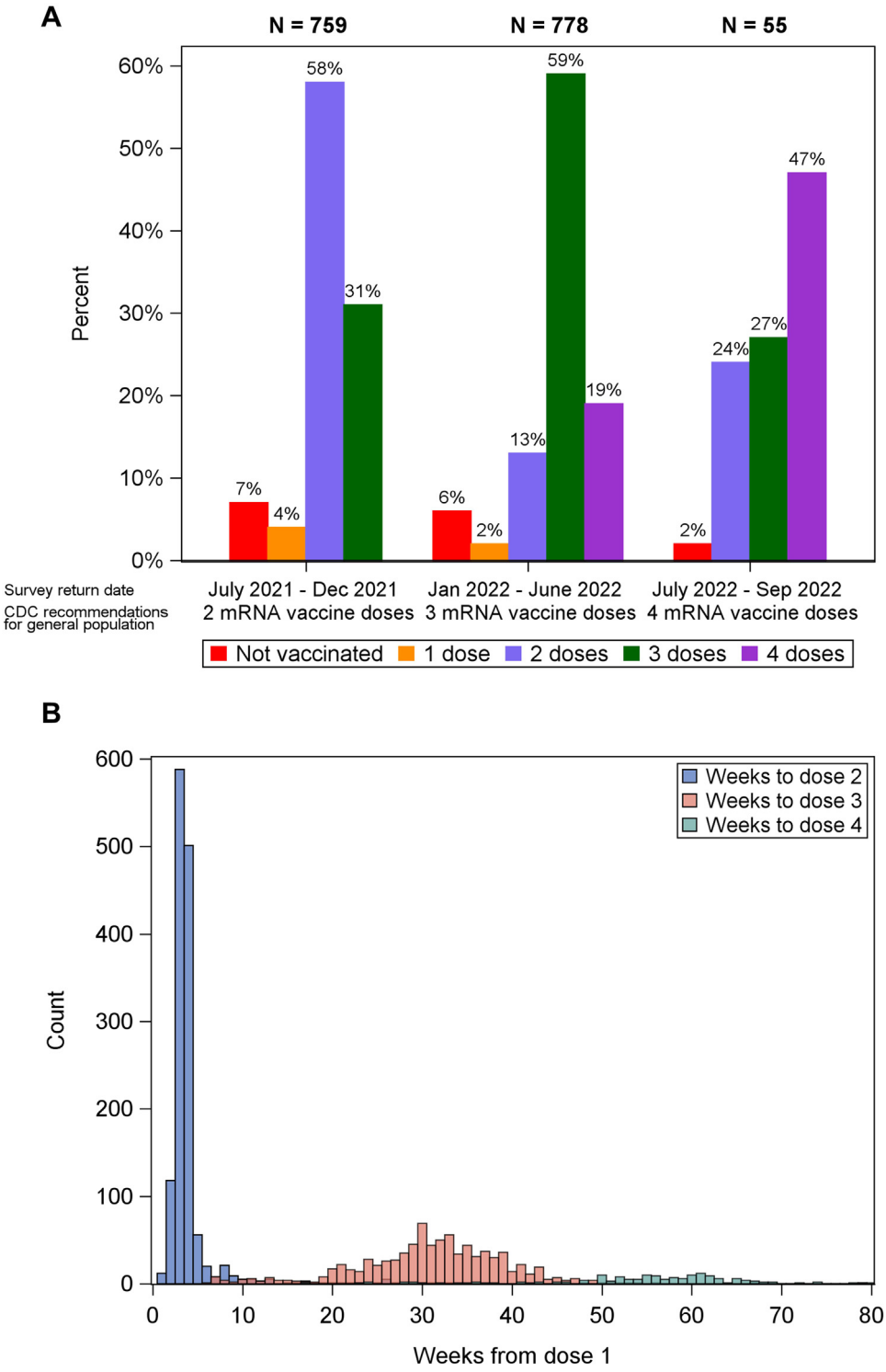

Figure 2. (A) Percentage of respondents reporting completion of COVID-19 mRNA vaccine doses in accordance with CDC vaccine recommendations for the general population at the time of survey return. (B) Time between first and subsequent mRNA vaccine doses.

respondents received their second mRNA vaccine dose within 4 weeks of their first dose (Figure 2B). The times to third and fourth mRNA vaccine doses were more widely distributed, ranging from 6 to 96 weeks and from 17 to 109 weeks after the after the first dose, respectively. Baseline characteristics of respondents by vaccination status are summarized in Table 1.

Vaccinated respondents were older (median age, 65 years versus 59 years; $P < .001$), and a greater proportion had active cancer (351 of 1504 [23%] versus 12 of 101 [12%]; $P = .008$) and were not currently working (820 of 1578 [52%] versus 40 of 101 [40%]; $P = .02$) compared to unvaccinated respondents. One or more vaccine doses were received by 372 of 1466 (94%) non-Hispanic white respondents, 193 of 200 (97%) non-Hispanic/nonwhite respondents, and 33 of 39 (85%) of Hispanic/Latino respondents.

Vaccination status also varied geographically. While uptake of ≥1 vaccine doses was ≥90% among survey

Table 1
Respondent Characteristics by Vaccination Status*

Characteristic	Total (N = 1705)	Vaccinated (N = 1598)	Nonvaccinated (N = 107)	*P* Value†
Current age, yr, median (range)	64.7 (18.7-89.9)	65.1 (18.7-89.9)	59.4 (23.0-83.3)	<.001
Time since HCT, yr, median (range)	11.9 (.9-50.0)	11.9 (.9-50.0)	11.9 (.9-47.9)	.57
Sex, n (%)				.07
Female	814 (47.7)	772 (48.3)	42 (39.3)	
Male	891 (52.3)	826 (51.7)	65 (60.7)	
Race/ethnicity, n (%)				<.001
Non-Hispanic white	1466 (86.0)	1372 (85.9)	94 (87.9)	
Hispanic/Latino	39 (2.3)	33 (2.1)	6 (5.6)	
Asian	78 (4.6)	77 (4.8)	1 (.9)	
Black or African American	15 (.9)	15 (.9)	0 (0)	
Other/unknown	107 (6.3)	101 (6.3)	6 (5.6)	
Transplant type, n (%)				.18
Allogeneic	1125 (66.0)	1048 (65.6)	77 (72.0)	
Autologous	580 (34.0)	550 (34.4)	30 (28.0)	
Active cancer, n (%)				.008
No	1242 (77.4)	1153 (76.7)	89 (88.1)	
Yes	363 (22.6)	351 (23.3)	12 (11.9)	
Missing	100	94	6	
cGVHD, n (%)‡				.44
Never	373 (40.9)	344 (40.4)	29 (48.3)	
Former	290 (31.8)	272 (32.0)	18 (30.0)	
Current	248 (27.2)	235 (27.6)	13 (21.7)	
Work status, n (%)				.02
Working/school full- or part-time	819 (48.8)	758 (48.0)	61 (60.4)	
Not working/disabled due to health	860 (51.2)	820 (52.0)	40 (39.6)	
Missing	26	20	6	

Respondents with cGVHD, n (%)‡	N = 248	235	N = 13	
cGVHD severity				.69
Mild	145 (58.9)	137 (58.8)	8 (61.5)	
Moderate	78 (31.7)	73 (31.3)	5 (38.5)	
Severe	23 (9.3)	23 (9.9)	0 (0)	
Missing	2	2	0	
Currently on steroids for GVHD				.39
No	156 (64.2)	146 (63.5)	10 (76.9)	
Yes	87 (35.8)	84 (36.5)	3 (23.1)	
Missing	5	5	0	
Currently on nonsteroid immunosuppressive therapy for GVHD				.01
No	132 (55.5)	121 (53.5)	11 (91.7)	
Yes	106 (44.5)	105 (46.5)	1 (8.3)	
Missing	10	9	1	
Currently on any immunosuppressive therapy for GVHD				.02
No	110 (45.5)	100 (43.7)	10 (76.9)	
Yes	132 (54.5)	129 (56.3)	3 (23.1)	
Missing	6	6	0	

* Percentages represent column percentages and do not include missing values.
† Based on the chi-square test or Fisher exact test for categorical variables and the Kruskal-Wallis test for continuous variables.
‡ Limited to allogeneic HCT survivors.

respondents in most states, lower uptake was seen in residents of Midwestern and Southern states (Supplementary Figure S1). The presence of cGVHD, chronic medical conditions, autologous versus allogeneic transplantation, sex, and time since HCT were not associated with vaccination status. The most common reasons for declining vaccination among the 107 unvaccinated respondents were concerns about side effects (n = 75; 70%), rapidity of vaccine development (n = 74; 69%), and lack of testing in HCT recipients (n = 57; 53%).

Of the 1581 vaccinated respondents who provided information about adverse effects after vaccination, 947 (60%) did not report any adverse effects and 634 (40%) reported adverse effects, most commonly fatigue, injection site pain, and muscle/body aches (Figure 3A). The median number of reported adverse effects was 3 (range, 1 to 13). Among the 626 respondents who reported the severity of their adverse effects, most indicated minimal or moderate symptoms (Figure 3B). Overall, severe adverse effects were reported by 72 of 1573 (5%). The frequency of reported adverse effects was 252 of 1598 patients

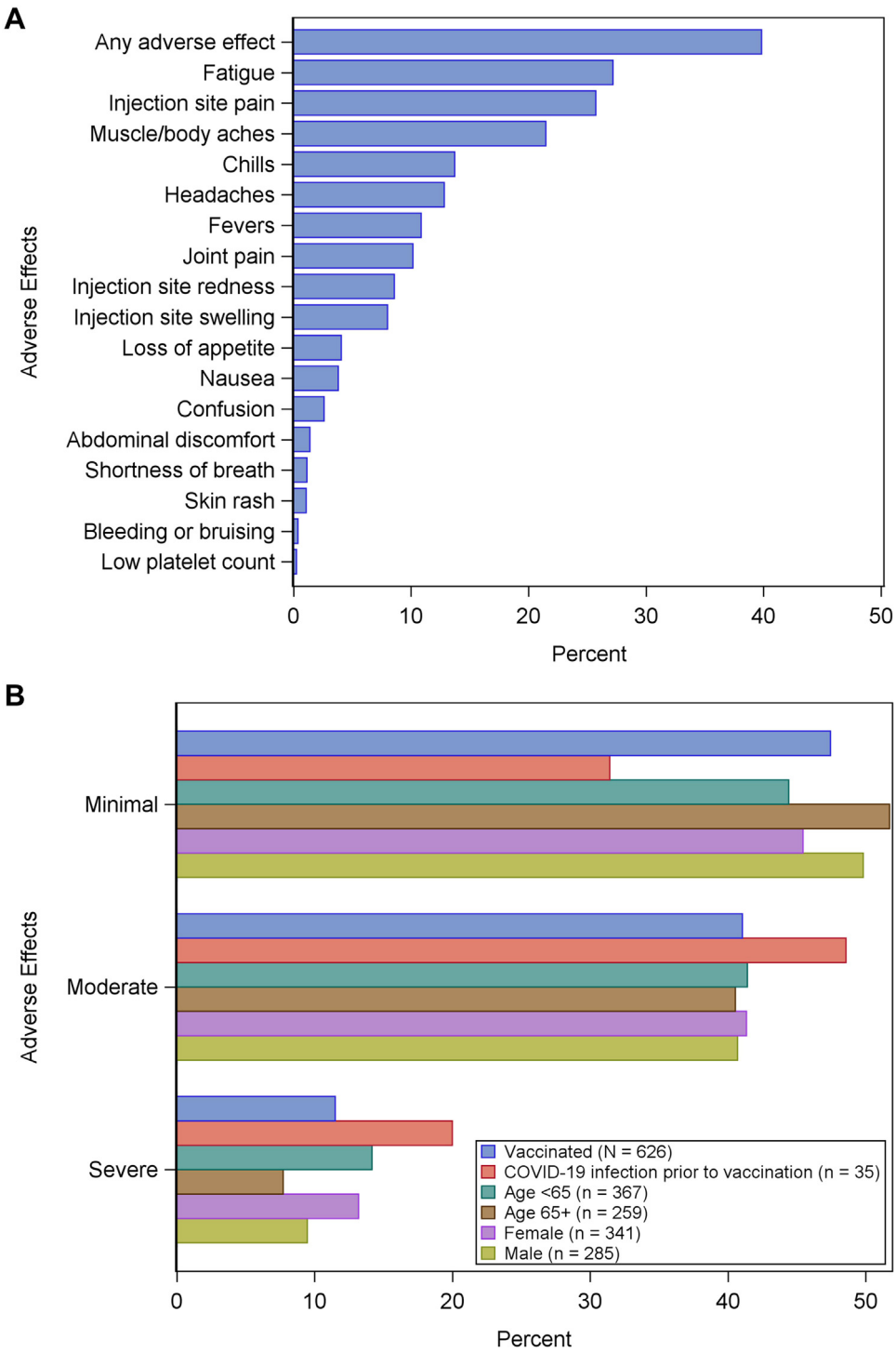

Figure 3. (A) Reported adverse effects following COVID-19 vaccination in vaccinated respondents who provided information about specific adverse effects after vaccination (n = 1574). (B) Severity of adverse effects following COVID-19 vaccination among respondents who reported adverse effects severity (n = 626).

(16%) after the first dose, 312 of 1496 (21%) after the second dose, 250 of 910 (27%) after the third dose, and 46 and 176 (26%) after the fourth dose.

Among 98 vaccinated respondents with current cGVHD who reported adverse effects following vaccination, 87 (89%) did not report any changes in their cGVHD symptoms after vaccination; 10 (10%) had worsening symptoms, and 1 experienced improved symptoms. Information on the type of symptoms, duration of symptoms, and concurrent tapering of immunosuppression was not captured in this survey. Current nonglucocorticoid immunosuppressive therapy was associated with vaccination in respondents with cGVHD ($P = .01$) (Table 1). Current glucocorticoid use, cGVHD severity, and type of organ involvement were not associated with vaccination status.

Experience with COVID-19 Infection

Among survey respondents, 250 (15%) reported having a COVID-19 infection. Infections occurred between January 2020

and June 2022 at a median of 224 days (range, 0 to 905 days) prior to survey response. Of the 242 respondents who provided information regarding diagnostic method, 171 (71%) were diagnosed by a positive antigen or polymerase chain reaction test and 57 (24%) reported infection based on symptoms only, including 15 (6%) who had symptoms and negative test results. Most infections (13 of 16 [81%]) reported between January through May 2020, before testing was widely available, were based on symptoms only. The patterns of COVID-19 infections in our cohort are consistent with trends observed in the general US population, with surges during the winters of 2020 and 2021 (Supplementary Figure S2).

A total of 244 respondents reported illness severity; 20 (8%) had asymptomatic COVID-19 infection, 173 (71%) had mild or moderate symptoms, and 51 (21%) reported severe symptoms. Of the symptomatic respondents, 129 (58%) had symptoms lasting ≤7 days, and 23 (9%) reported persistent symptoms related to COVID-19 infection ≥4 weeks after the initial diagnosis. The most common persistent symptoms were fatigue (n = 11; 48%), headaches (n = 7; 30%), and loss of taste/smell (n = 7; 30%) Supplementary Figure S3). Of 242 respondents who reported hospitalization status, 25 (10%) required hospitalization; the most commonly reported symptoms were fatigue (n = 20; 80%), fever (n = 17; 68%), and cough (n = 17; 68%). Among 134 respondents who were vaccinated within 1 year of HCT, 12 (9%) reported COVID-19 infection, including 4 who were hospitalized.

Of 168 vaccinated respondents who developed a COVID-19 infection and whose vaccination and infection dates were available, 83 (49%) received their first dose of COVID-19 vaccine after COVID-19 infection. Among those who were vaccinated after infection, nearly all (n = 78; 94%) reported infection prior to May 2021, prior to the widespread availability of vaccines [16]. According to vaccination status prior to infection, vaccinated respondents and their household members were significantly less likely to have contracted COVID-19 compared with unvaccinated respondents and their household members (85 of 1480 [6%] versus 130 of 190 [68%; $P < .001$] and 149 of 1451 [10%] versus 85 of 185 [46%; $P < .001$], respectively). Among 923 respondents with no active cancer following allogeneic HCT, vaccinated respondents were significantly less likely to experience COVID-19 infection (51 of 813 [6%] versus 75 of 110 [68%]; $P < .001$). In respondents with active cGVHD, those who were vaccinated were less likely to develop COVID-19 infection than those who were unvaccinated (14 of 219 [6%] versus 18 of 23 [78%]; $P < .001$). In respondents who were receiving steroids for active cGVHD, those who were vaccinated were also less likely to develop COVID-19 infection than those who were unvaccinated (6 of 219 [8%] versus 6 of 23 [75%]; $P < .001$).

In an analysis of vaccinated respondents restricted to the number of doses prior to any reported COVID-19 infection, receipt of additional COVID-19 vaccine doses beyond the first dose was associated with a reduced risk of COVID-19 infection (odds ratio, .63; 95% confidence interval, .47 to .85; $P = .002$). The rate of COVID-19 infection by number of vaccine doses was as follows: 1 dose, 15% (12 of 80); 2 doses, 7% (36 of 544); 3 doses, 4% (29 of 681); 4 doses, 5% (8 of 159). Among the respondents who had COVID-19 infection, there were no significant differences in self-reported symptom severity, symptom duration, or hospitalization between those who were vaccinated and those who were not vaccinated prior to COVID-19 infection. Although the numbers were small, we also did not observe differences in COVID-19 infection rates and hospitalization status between respondents who had received allogeneic HCT without cGVHD and respondents with cGVHD on immunosuppressive therapy.

Nonpharmaceutical Interventions to Prevent COVID-19 Infection

Nonpharmaceutical COVID-19 prevention measures reported by survey respondents are shown in Figure 4. Compared to unvaccinated respondents, vaccinated respondents took significantly more precautions against COVID-19 both while the CDC's mask mandate was in effect (July 1, 2021, to February 28, 2022: median, 5 [range, 0 to 11] versus 2 [range, 0 to 9]; $P < .001$) and after the mandate ended (March 1 to June 30, 2022: median, 4 [range, 0 to 11] versus 1 [range, 0 to 9]; $P < .001$). Vaccination of household contacts was more frequent in vaccinated respondents than in unvaccinated respondents (1284 of 1404 [91%] versus 18 of 88 [20%]; $P < .001$). Among vaccinated respondents, COVID-19 infection was significantly less frequent in those with vaccinated household contacts than in those with unvaccinated household contacts (157 of 1283 [12%] versus 23 of 120 [19%]; $P = .03$).

DISCUSSION

In this large survey study, we report the most comprehensive data to date on COVID-19 vaccination, prevention strategies, and infection among long-term HCT survivors. We found a high uptake of COVID-19 vaccine among survey respondents, with a majority receiving 1 or more doses of COVID-19 vaccine. Approximately 1 in 6 respondents experienced COVID-19 infection. Vaccinated respondents and their household contacts were significantly less likely to have experienced COVID-19 infection compared to those who were unvaccinated. Most respondents reported minimal to no adverse effects following vaccination, and the majority with cGVHD did not experience any worsening of symptoms.

According to the CDC, as of April 2023, 92% of US adults age ≥18 years have received at least 1 COVID-19 vaccine dose, with 79% having completed the primary series, 20% having received the bivalent Omicron BA.4/BA.5-targeting booster, and 43% of adults age ≥65 years having received the bivalent booster [1]. Compared to the general US adult population, vaccine uptake was higher in our cohort of HCT long-term survivors (at least 1 dose, 94% versus 92%; primary series, 97% versus 79%) [1].

Similar to studies of the general US population [17,18], we found that older age and coastal residence were associated with higher rates of vaccine uptake among respondents. Consistent with other studies that have observed lower rates of vaccine uptake among racial and ethnic minorities [18–22], we observed lower levels of vaccination among our Hispanic/Latino respondents (85%) compared to non-Hispanic white (94%) and non-Hispanic/nonwhite respondents (97%). The presence of cGVHD and/or other chronic medical conditions was not associated with vaccination status in our cohort.

We found that COVID-19 vaccine was well tolerated by most respondents, with only 5% reporting a severe adverse effect from vaccination, similar to what has been reported in studies conducted in the general adult population [7–9] and HCT recipients [12,13,23,24]. Although there have been some reports of cGVHD exacerbation after vaccination [25,26], only a small proportion of our respondents (10%) reported cGVHD exacerbation after vaccination, similar to findings reported by others [12,13]. We did not collect data on the specific cGVHD symptoms or duration of symptoms that these respondents experienced. Because we did not have data on immunosuppressive regimen dosing at the time of COVID-19 vaccination,

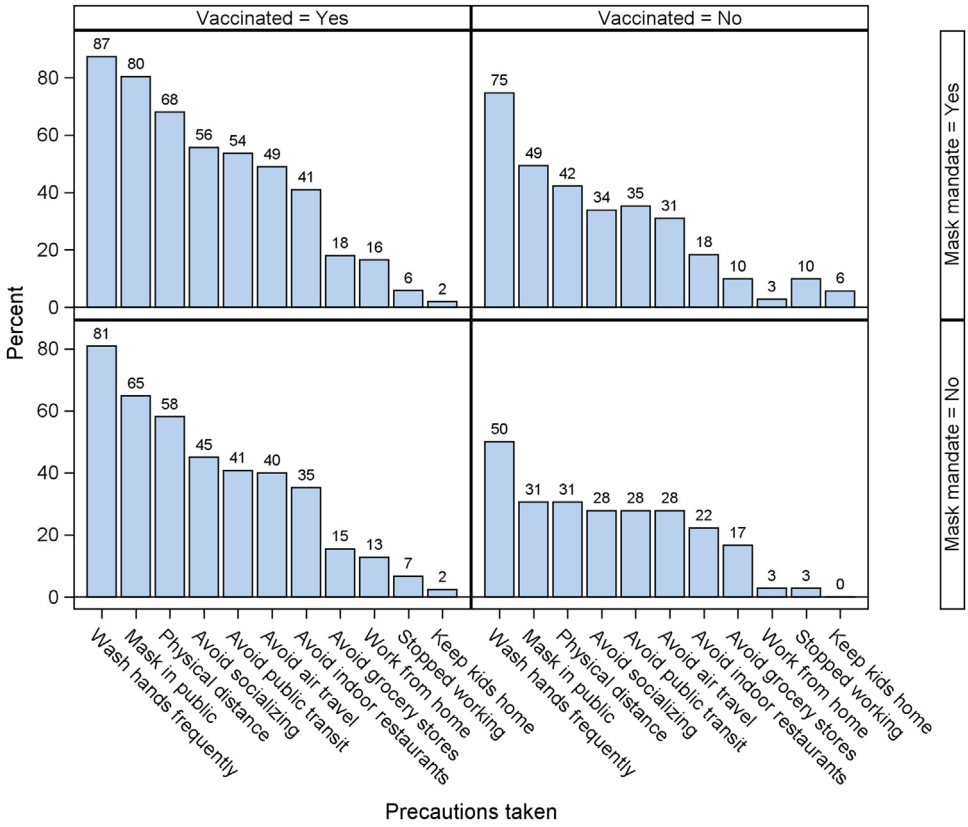

Figure 4. Precautions against COVID-19 infection taken by vaccinated respondents and nonvaccinated respondents during and after CDC mask mandate.

we were unable to discern any effect of tapering immunosuppressives from an adverse effect of COVID-19 vaccination. Future studies would benefit from incorporating transplantation team evaluations and objective measures of cGVHD flares with self-reported symptoms.

Although the majority of respondents received at least 2 doses of mRNA vaccine, uptake of booster doses was more limited. Within the periods specified in the CDC's guidelines for immunocompetent individuals, 78% of eligible patients received a third dose of mRNA vaccine, but only 47% received a fourth dose. We found that additional vaccine doses were associated with reduced risk of COVID-19 infection; this finding is consistent with prior studies showing that vaccine effectiveness, which wanes after 6 months [27], can be augmented by booster doses [28]. Efforts to enhance uptake of the bivalent booster, which appears to be effective against the currently circulating BQ.1 and BQ.1.1 variants [29], in HCT recipients are critical to reducing future COVID-19-related morbidity and mortality in this population.

The pattern of COVID-19 infections in our cohort over the course of the pandemic was similar to the trends observed in the general US population (Supplementary Figure S2). The proportions of survey respondents reporting symptomatic COVID-19 infection (92%) and hospitalization (10%) are higher than what have been reported for the general US population [30]. Compared to prior studies of HCT recipients [3,4,6], we observed lower rates of hospitalization. This lower rates seen in our study may reflect the lower immunosuppression in long-term HCT survivors compared to other studies, which focused on those who underwent transplantation more recently. Persistent COVID-19-related symptoms were similar in our cohort and the general US population [31].

We found that infection was more common in unvaccinated recipients than in vaccinated recipients. However, we did not detect any significant differences in self-reported symptom severity, illness duration, or hospitalization status between vaccinated and unvaccinated respondents. These findings may be limited by recall bias, the subjective nature of self-reported symptom severity and illness duration, and a lack of statistical power owing to the low incidence of COVID-19 infection in our cohort. It is also possible that there may have been differences by vaccination status in objective measures of disease severity, such as the need for supplemental oxygenation, admission to the intensive care unit, mechanical ventilation, and death, which were not captured in this survey.

Household vaccination was more common among vaccinated respondents who also used a greater number of nonpharmaceutical prevention measures. Even among vaccinated respondents, those with household contact vaccination were less likely to experience COVID-19 infection than those without household contact vaccination. These findings highlight the importance of encouraging household vaccination as part of a multifaceted approach to prevention in this population. Compared to the general US population, respondents to our survey reported similar rates of handwashing (84% versus 88%) and mask wearing (73% versus 50% to 83%), but lower rates of social distancing (63% versus 85% to 87%) and avoidance of indoor dining (38% versus 95%) [32–34]. Some differences are likely due to later administration of our survey (2021 to 2022 versus spring/summer 2020) and reflect pandemic-related restrictions around indoor gatherings and dining/restaurant capacity during different time periods [35].

Limitations of this study include those inherent to surveys, namely response rate (36%), self-reported data, recall and response biases, and no data from nonrespondents, including those who died of COVID-19. It is possible that there may be differences in vaccination status among survey respondents and nonrespondents. In addition, one-fourth of respondents reported COVID-19 infection based on symptoms alone, which could have inflated our study's infection rates. This aspect highlights the importance of reducing barriers to COVID-19 testing, which can facilitate access to timely treatment. Furthermore, given the colinear relationship between vaccination status and nonpharmaceutical interventions, we could not discern the magnitude of the effect of each factor on COVID-19 infection.

This large real-world study provides insight into how we can target efforts to improve vaccine uptake, especially for booster doses, in this immunocompromised population. Importantly, we found that COVID-19 vaccination was well tolerated with a low risk of cGVHD exacerbation, and that COVID-19 vaccination status in HCT survivors and their household contacts was significantly associated with decreased COVID-19 infection. Providers should continue to recommend that HCT recipients and their household members receive the COVID-19 vaccine as part of a multifaceted approach to prevent infection. The lower intake of boosters compared to primary series highlights an important opportunity for providers to continue to encourage vaccination including the bivalent booster in this vulnerable population, especially as new variants emerge.

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Conflict of interest statement: C.L. has served as an investigastor for a clinical trial sponsored by Pfizer.

Data availability: For original data, please contact catherine.liu@fredhutch.org.

Authorship statement: E.C.L., L.E.O., S.J.L., and C.L. had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: S.J.L. and C.L. Acquisition, analysis, or interpretation of data: E.C.L., L.E.O., S.J.L., and C.L. Drafting of the manuscript: E.C.L., L.E.O., S.J.L, and C.L. Critical revision of the manuscript for important intellectual content: E.C.L., L.E.O., P.C., S.A.P., M.E.F., S.J.L., and C.L. Statistical analysis: L.E.O.. Administrative, technical, or material support: S.J.L. and C.L. Supervision: S.J.L. and C.L.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jtct.2023.06.017.

REFERENCES

1. Centers for Disease Control and Prevention. CDC COVID data tracker. Available at: https://covid.cdc.gov/covid-data-tracker/#datatracker-home. Accessed April 17, 2023.
2. Sharma A, Bhatt NS, St Martin A, et al. Clinical characteristics and outcomes of COVID-19 in haematopoietic stem-cell transplantation recipients: an observational cohort study. *Lancet Haematol*. 2021;8:e185–e193. https://doi.org/10.1016/s2352-3026(20)30429-4.
3. Shah GL, DeWolf S, Lee YJ, et al. Favorable outcomes of COVID-19 in recipients of hematopoietic cell transplantation. *J Clin Invest*. 2020;130:6656–6667. https://doi.org/10.1172/jci141777.
4. Piñana JL, Martino R, García-García I, et al. Risk factors and outcome of COVID-19 in patients with hematological malignancies. *Exp Hematol Oncol*. 2020;9:21. https://doi.org/10.1186/s40164-020-00177-z.
5. Passamonti F, Cattaneo C, Arcaini L, et al. Clinical characteristics and risk factors associated with COVID-19 severity in patients with haematological malignancies in Italy: a retrospective, multicentre, cohort study. *Lancet Haematol*. 2020;7:e737–e745. https://doi.org/10.1016/s2352-3026(20)30251-9.
6. Varma A, Kosuri S, Ustun C, et al. COVID-19 infection in hematopoietic cell transplantation: age, time from transplant and steroids matter. *Leukemia*. 2020;34:2809–2812. https://doi.org/10.1038/s41375-020-01019-x.
7. Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med*. 2021;384:403–416. https://doi.org/10.1056/nejmoa2035389.
8. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med*. 2020;383:2603–2615. https://doi.org/10.1056/nejmoa2034577.
9. Sadoff J, Gray G, Vandebosch A, et al. Safety and efficacy of single-dose Ad26.COV2.S vaccine against Covid-19. *N Engl J Med*. 2021;384:2187–2201. https://doi.org/10.1056/nejmoa2101544.
10. Dunkle LM, Kotloff KL, Gay CL, et al. Efficacy and safety of NVX-CoV2373 in adults in the United States and Mexico. *N Engl J Med*. 2022;386:531–543. https://doi.org/10.1056/nejmoa2116185.
11. Embi PJ, Levy ME, Naleway AL, et al. Effectiveness of 2-dose vaccination with mRNA COVID-19 vaccines against COVID-19–associated hospitalizations among immunocompromised adults— nine states, January–September 2021. *MMWR Morb Mortal Wkly Rep*. 2021;70:1553–1559. https://doi.org/10.15585/mmwr.mm7044e3.
12. Bourgeois AL, Coste-Burel M, Guillaume T, et al. Safety and antibody response after 1 and 2 doses of BNT162b2 mRNA vaccine in recipients of allogeneic hematopoietic stem cell transplant. *JAMA Netw Open*. 2021;4. https://doi.org/10.1001/jamanetworkopen.2021.26344. e2126344-e2126344.
13. Ram R, Hagin D, Kikozashvilli N, et al. Safety and immunogenicity of the BNT162b2 mRNA COVID-19 vaccine in patients after allogeneic HCT or CD19-based CART therapy—a single-center prospective cohort study. *Transplant Cell Ther*. 2021;27:788–794. https://doi.org/10.1016/j.jtct.2021.06.024.
14. American Society of Hematology. ASH-ASTCT COVID-19 vaccination for HCT and CAR T cell recipients. 2022. Available at: https://www.hematology.org/covid-19/ash-astct-covid-19-vaccination-for-hct-and-car-t-cell-recipients. Accessed October 19, 2022.
15. Recommendations of the National Comprehensive Cancer Network (NCCN) Advisory Committee on COVID-19 Vaccination and Pre-exposure Prophylaxis, version 7.0. Available at: https://www.nccn.org/docs/default-source/covid-19/2021_covid-19_vaccination_guidance_v7-0.pdf?sfvrsn=b483da2b_119. Accessed October 22, 2022.
16. Cochran NW, Secretary of US Department of Health and Human Services. Secretarial directive on eligibility to receive COVID-19 vaccines. March 17, 2021. Available at: https://www.hhs.gov/sites/default/files/secretarial-directive-eligibility-for-covid-19-vaccines.pdf. Accessed December 8, 2022.
17. Ozdenerol E, Seboly J. The effects of lifestyle on COVID-19 vaccine hesitancy in the United States: an analysis of market segmentation. *Int J Environ Res Public Health*. 2022;19:7732. https://doi.org/10.3390/ijerph19137732.
18. McLaughlin JM, Khan F, Pugh S, Swerdlow DL, Jodar L. County-level vaccination coverage and rates of COVID-19 cases and deaths in the United States: an ecological analysis. *Lancet Reg Health Am*. 2022;9: 100191. https://doi.org/10.1016/j.lana.2022.100191.
19. Kriss JL, Hung MC, Srivastav A, et al. COVID-19 vaccination coverage, by race and ethnicity—National Immunization Survey Adult COVID Module, United States, December 2020–November 2021. *MMWR Morb Mortal Wkly Rep*. 2022;71:757–763. https://doi.org/10.15585/mmwr.mm7123a2.
20. Kaiser Family Foundation. COVID-19 vaccinations by race/ethnicity. Available at: https://www.kff.org/coronavirus-covid-19/. Accessed December 8, 2022.
21. Siegel M, Critchfield-Jain I, Boykin M, et al. Racial/ethnic disparities in state-level COVID-19 vaccination rates and their association with structural racism. *J Racial Ethn Health Disparities*. 2022;9:2361–2374. https://doi.org/10.1007/s40615-021-01173-7.
22. Reitsma MB, Goldhaber-Fiebert JD, Salomon JA. Quantifying and benchmarking disparities in COVID-19 vaccination rates by race and ethnicity. *Jama Netw Open*. 2021;4: e2130343. https://doi.org/10.1001/jamanetworkopen.2021.30343.
23. Ali H, Ngo D, Aribi A, et al. Safety and tolerability of SARS-CoV2 emergency-use authorized vaccines for allogeneic hematopoietic stem cell transplant recipients. *Transplant Cell Ther*. 2021;27:938. https://doi.org/10.1016/j.jtct.2021.07.008. e1-938.e6.
24. Bergman P, Blennow O, Hansson L, et al. Safety and efficacy of the mRNA BNT162b2 vaccine against SARS-CoV-2 in five groups of immunocompromised patients and healthy controls in a prospective open-label clinical trial. *EBioMedicine*. 2021;74: 103705. https://doi.org/10.1016/j.ebiom.2021.103705.
25. Trunk AD, Shewan SK, Lee CJ, Parker CJ, Couriel DR. Chronic graft-versus-host disease exacerbation after SARS-CoV-2 vaccination. *Bone Marrow Transplant*. 2022;57:502–503. https://doi.org/10.1038/s41409-021-01543-z.
26. Manjappa S, Phi HQ, Lee LW, et al. Humoral and cellular immune response to Covid-19 vaccination in patients with chronic graft-versus-host disease

on immunosuppression. *Transplant Cell Ther*. 2022;28:784.e1–784.e9. https://doi.org/10.1016/j.jtct.2022.08.026.
27. Feikin DR, Higdon MM, Abu-Raddad LJ, et al. Duration of effectiveness of vaccines against SARS-CoV-2 infection and COVID-19 disease: results of a systematic review and meta-regression. *Lancet*.. 2022;399:924–944. https://doi.org/10.1016/s0140-6736(22)00152-0.
28. Link-Gelles R, Levy ME, Gaglani M, et al. Effectiveness of 2, 3, and 4 COVID-19 mRNA vaccine doses among immunocompetent adults during periods when SARS-CoV-2 Omicron BA.1 and BA.2/BA.2.12.1 sublineages predominated—VISION Network, 10 States, December 2021–June 2022. *MMWR Morb Mortal Wkly Rep*. 2022;71:931–939. https://doi.org/10.15585/mmwr.mm7129e1.
29. Zou J, Kurhade C, Patel S, et al. Improved neutralization of Omicron BA.4/5, BA.4.6, BA.2.75.2, BQ.1.1, and XBB.1 with bivalent BA.4/5 vaccine. *Biorxiv* [preprint]. Published online November 17, 2022. doi: 10.1101/2022.11.17.516898.
30. Centers for Disease Control and Prevention. Estimated COVID-19 burden. Available at: https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/burden.html. Accessed December 3, 2022.
31. Kompaniyets L, Bull-Otterson L, Boehmer TK, et al. Post–COVID-19 symptoms and conditions among children and adolescents — United States, March 1, 2020–January 31, 2022. *MMWR Morb Mortal Wkly Rep*. 2022;71:993–999. https://doi.org/10.15585/mmwr.mm7131a3.
32. Park CL, Russell BS, Fendrich M, Finkelstein-Fox L, Hutchison M, Becker J. Americans' COVID-19 stress, coping, and adherence to CDC guidelines. *J Gen Intern Med*. 2020;35:2296–2303. https://doi.org/10.1007/s11606-020-05898-9.
33. Anderson KM, Stockman JK. Staying home, distancing, and face masks: COVID-19 prevention among US women in the COPE study. *Int J Environ Res Public Health*. 2020;18:180. https://doi.org/10.3390/ijerph18010180.
34. Czeisler MÉ, Tynan MA, Howard ME, et al. Public attitudes, behaviors, and beliefs related to COVID-19, stay-at-home orders, nonessential business closures, and public health guidance—United States, New York City, and Los Angeles, May 5–12, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69:751–758. https://doi.org/10.15585/mmwr.mm6924e1.
35. MultiState COVID-19 state and local policy dashboard. Available at: https://www.multistate.us/research/covid/public. Accessed October 22, 2022.