Cocooning Against COVID-19: The Argument for Vaccinating Caregivers of Patients With Cancer

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The allocation of the coronavirus disease 2019 (COVID-19) vaccines has been a true Gordian knot: difficult to unravel, impossible to get right for all communities, and challenging even for experts. One can construct a rational argument justifying the prioritization of nearly any group of Americans. Rationing health care is never comfortable but has become necessary while vaccine availability remains an issue. For many health care workers, our most vulnerable patients are at the front of our minds.

As the next phases of vaccine distribution begin, oncologists argue that patients with cancer should be a priority population to receive COVID-19 vaccines.[1-3] This approach makes sense because severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a systemic infection, and patients with cancer are at high risk for COVID-19 complications.[4] Early pandemic data showed 13% mortality among a cohort of patients with cancer,[5] nearly 10 times higher than the current 1.7% case fatality reported in the United States. Mortality among hematopoietic cell transplant recipients is even more concerning, reaching 32% within 30 days after COVID-19 diagnosis.[6] The vulnerabilities of patients with cancer are clear: therapies for their treatments leave them significantly immunosuppressed, many are elderly and chronically ill, and most have multiple comorbidities placing them at risk for severe COVID-19. The National Comprehensive Cancer Network's guidelines argue that newly diagnosed patients with cancer, those on active treatment, or those having recently completed therapy should be targeted for early vaccination.[2] Spearheaded by the American Association for Cancer Research, over 130 organizations representing researchers, health care providers, patients, and patient advocates signed a letter to prioritize patients with cancer for COVID-19 vaccinations.[7] Even the most ardent antilockdown or antimasking proponents would likely agree that we must protect this vulnerable population.

However, where do informal caregivers and family members, the people cancer patients count on for social support, lie on this priority continuum? Prioritizing patients with cancer for vaccination while not accounting for the contexts of their lives is myopic. This strategy only considers a cancer patient's individual risk for complications and does not address the modifiable risk for transmission in their social network and often isolated environment. Instead, we propose that priority access to vaccination also extend to immediate family members and informal caregivers who regularly interact with these high-risk patients to strengthen SARS-CoV-2 prevention and protection.

Offering early COVID-19 vaccinations to patients with cancer is undoubtedly a logical and ethical strategy. However, efficacy of current vaccines for patients with cancer are unknown because most were excluded from phase 3 clinical trials.[8,9] Patients with cancer, many of whom are immunosuppressed from their treatment or disease, may not respond to vaccines like those with fully functioning immune systems. Studies on the effectiveness of other common vaccines like influenza demonstrate that antibody protection may be limited, particularly among those with hematologic malignancies who have poor, short-lived, and often insufficient immunity after vaccination.[10] It will be several months before we have conclusive findings that delineate the effectiveness of COVID-19 vaccines in these populations, obfuscated by the panoply of and heterogeneity in sociodemographic characteristics, diseases, and treatment approaches.

Clearly, clinical guidance and decision-making regarding "optimal" vaccine allocation will be approximations at best. Most argue that any immunity is better than none, hoping that even limited responses will lead to reduction in clinically significant complications—we agree. Options such as additional booster vaccinations or higher dose vaccines may be more effective in the long run,[11,12] however, studying such approaches is incompatible with competing priorities in the midst of a pandemic. Vaccine efficacy studies and those addressing postvaccination immune responses in these

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populations are crucial, but results will not be available before we must make decisions. We believe additional creative strategies to prevent COVID-19 must complement vaccination of patients with cancer, particularly as we wait for vaccines to become more readily available and as new SARS-CoV-2 variants threaten to undermine the realized effectiveness of our current first-generation vaccines. Addressing the theoretical risk that patients with cancer could play in the development of these viral variants is even more important.[13]

Herd immunity, sometimes called community or population immunity, prevents transmission of communicable diseases by limiting an infected person's susceptible contacts. Reaching thresholds high enough to achieve herd immunity stops spread within larger populations; immune or even partially immune community members protect the nonimmune. Measles, a disease that is more infectious than SARS-CoV-2, was eliminated from the United States as high community seroprevalence demonstrated this effect by eliminating local transmission.[14] Unfortunately, as measles, mumps, and rubella vaccination rates have waned, measles outbreaks have become more frequent.[15] In the midst of our current COVID-19 pandemic, our limited vaccine supply means that reaching herd immunity by vaccinating a significant proportion of the population remains a distant goal; worryingly, this herd immunity "finish line" is moving further away in our vaccination race, as more contagious SARS-CoV-2 variants emerge in our communities. However, deliberate use of our current vaccine supply could leverage herd immunity concepts to protect our most vulnerable community members. Moving the caregivers and household contacts of patients with cancer higher in vaccine prioritization would create a protective layer of vaccinated family and household contacts buffering patients with cancer from exposure. This approach, so-called "cocooning," has been used to protect newborns[16] and other immunosuppressed populations[17,18] who either cannot receive live-virus vaccines or are known to have poor immunologic responses to other recommended vaccines. A classic example of this strategy has been to revaccinate adults to prevent late acquisition and transmission of the bacterial pathogen that leads to life-threatening pertussis (whooping cough) in newborns.[16]

A cocooning vaccination strategy seems particularly appropriate for COVID-19 because households remain one of the most common sources of transmission. A recent meta-analysis showed secondary attack rates to be 17% in households.[19] Patients with cancer require significant support from caregivers, relying on them to go out in the community for medications, food, and other necessities. A patient with cancer who follows protective behavioral measures such as social distancing and masking may be put at undue risk to SARS-CoV-2 exposure because their critical support members and close contacts must enter the community. The Advisory Committee on Immunization Practices and other guidelines recommend close contacts of immunosuppressed patients receive all routine vaccines for other communicable diseases,[20,21] but their current COVID-19 vaccination recommendations do not call-out informal caregivers or household contacts of high-risk individuals in their prioritization schema.[22]

The potential benefits of this strategy warrants strong consideration, but cocooning is not without its own weaknesses. This approach, in part, assumes that COVID-19 vaccines reduce viral transmission. Although this is highly possible, clinical trial data have not currently provided conclusive evidence whether vaccinated individuals are less likely to acquire and transmit SARS-CoV-2. However, studies have shown that symptomatic household members are more likely to transmit infection,[19] and available vaccines have been shown to be exceptionally efficacious at limiting moderate to severe COVID-19. Furthermore, if ongoing limits to the vaccine supply prevent all caregivers and household contacts from receiving vaccines, we may need to prioritize those caring for the highest risk patients with cancer such as those undergoing active chemotherapy, hematopoietic cell transplantation, or cellular therapy.

Beyond changing prioritization schema, mobilizing a cocooning approach for caregivers and household contacts of cancer and other immunosuppressed patients will require investment in vaccine education and targeted messaging to these groups to assure high-level vaccine uptake. Previous surveys have shown patients with cancer strongly believe it is important for their caregivers to receive seasonal flu vaccines,[23] yet 32% of US residents polled in a recent Centers for Disease Control and Prevention study reported they were not likely to get a COVID-19 vaccine.[24] Vaccine acceptance drops even more among Blacks and African Americans, one of the populations hardest hit by the pandemic.[24] Yet, despite the importance of vaccines in preventing infectious complications in patients with cancer, a recent study of National Cancer Institute–designated cancer centers showed only 11% of vaccine education on their websites specifically targeting caregivers.[25] Medical systems who care for high-risk patients—namely cancer and transplant centers—are ideally suited to identify these close contacts and to ensure vaccine education and appropriate distribution reaches them in a timely manner. By allowing cancer centers to

provide vaccines, clinic visits could easily double as vaccine appointments for both the patient and their eligible caregiver. The oncology community has a responsibility to both advocate for patient and caregiver vaccinations and support efforts to assure equitable vaccine distribution among their patient populations.

Over the last year, the power of creative scientific thinking has generated many innovative and effective pandemic mitigation strategies. We should be similarly as open-minded when developing our vaccine allocation strategies. The approach of vaccinating only high-risk patients cannot be the lone solution we rely on to protect our country's most vulnerable. Instead, the cancer community should target vaccines and vaccine education to caregivers and household contacts as one of our major pillars of COVID-19 prevention. We recognize that our proposal is not without its implementation challenges, however, it does offer opportunities for multidisciplinary collaboration and problem solving that could lead to sustainable vaccination models for major communicable pathogens, especially if COVID-19 becomes another endemic disease in our society.[26] It is time we ensure that the home of a patient with cancer remains a refuge for their therapy and not an epicenter of transmission.

CONFLICT OF INTEREST DISCLOSURES

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