

## ORIGINAL ARTICLE

# Caregiver COVID-19 vaccination for solid organ transplant candidates

Bob Z. Sun<sup>1</sup>  | Aaron Wightman<sup>1,2</sup>  | Douglas S. Diekema<sup>1,2</sup> 

<sup>1</sup>Department of Pediatrics, University of Washington, Seattle, Washington, USA

<sup>2</sup>Treuman Katz Center for Pediatric Bioethics, Seattle Children's Hospital, Seattle, Washington, USA

**Correspondence**

Bob Z. Sun, Department of Pediatrics, University of Washington, Seattle, WA, USA.

Email: [bobzsun@uw.edu](mailto:bobzsun@uw.edu)

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**Abstract**

An increasing proportion of transplant centers have implemented a mandate for vaccination against COVID-19 for solid organ transplant candidates. There has been comparatively little exploration of the ethical considerations of mandating vaccination of a candidate's primary caregiver, despite a high risk of transmission given the close nature of contact between the candidate and caregiver. We examine how a caregiver mandate can improve overall utility in organ allocation, particularly in circumstances where vaccine effectiveness at preventing transmission and serious disease is low among recipients but high in caregivers. Our analysis reveals how sensitive such mandates must be to the evolving circumstances of disease severity, transmissibility, and vaccine effectiveness: as the facts change, the degree of benefit gained and therefore the degree of infringement on access to transplant and caregiver choice that is tolerated will likewise change.

**KEYWORDS**

ethics, ethics and public policy, organ allocation, organ procurement and allocation, solid organ transplantation, vaccine

## 1 | INTRODUCTION

Solid organ transplant (SOT) recipients continue to be particularly vulnerable during the ongoing COVID-19 pandemic. Mortality from COVID-19 has been consistently higher among SOT recipients compared to the general population.<sup>1-4</sup> Since vaccines against COVID-19 became available at the end of 2020, there has been ongoing debate about encouraging, mandating, or otherwise accounting for COVID-19 immunization in the SOT allocation process. Nearly half of American transplant centers have mandated COVID-19 vaccination for transplant candidates.<sup>5,6</sup> These mandates have generally been justified by appealing to risk of harms to unvaccinated recipients from severe complications of COVID-19 or of transmission of the virus from an unvaccinated recipient to a healthcare provider or to other immunosuppressed transplant recipients at greater risk for severe complications of COVID-19. Though others have discussed

the ways in which the prevailing ethical framework for SOT allocation are applied to a rationale for a vaccination mandate for SOT candidates,<sup>7-9</sup> there has been limited consideration of how to account for the COVID-19 vaccination status of the SOT candidate's supporting caregivers, despite social support being a requirement for candidacy in many transplant programs.<sup>10</sup> It is beyond the scope of this article to evaluate claims of net benefit associated with social support criteria, which are themselves controversial. We confine ourselves to recognizing the reality that programs require various forms of social support, including identification of a primary caregiver or support person (or persons), asserting that such a person is necessary for support in areas such as transportation, wound care, and assistance with activities of daily living; such assertions are based on assumptions that they will improve adherence to transplant care and ultimately improve patient and graft survival.<sup>11</sup> By necessity, such caregivers will be in close, prolonged contact with

Abbreviation: SOT, solid organ transplant

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the transplant recipient—including living together, in many cases—and potentially with other immunosuppressed transplant recipients when accompanying the recipient to clinic visits or laboratory assessments. Centers with such social support requirements will need to consider not only how a SOT candidate's COVID-19 vaccination status impacts their candidacy, but whether the vaccination status of the caregiver should also impact transplantation candidacy. As Ben Hippen notes, “Centers electing for a vaccine-requirement policy will inevitably need to consider extending a vaccine requirement to the candidate's caregiver.”<sup>8</sup> Indeed, a nationwide survey of US transplant centers found that 10% of centers currently require caregiver vaccination and 5% additionally require it for all members of the same household.<sup>6</sup> Kuczewski and colleagues recommend mandating vaccination for a SOT candidate's primary support person, analogizing it to requiring a lung transplant recipient's primary caregiver to not smoke.<sup>12</sup> Arguing against a caregiver vaccination mandate in pediatric transplant, Ross and Opel assert that it would be unfair to tie SOT candidacy to a prerequisite not readily modifiable by the candidate, particularly in the setting of low pediatric morbidity from COVID-19.<sup>9</sup> We provide an in-depth examination of the ethics of mandating SOT caregiver vaccination against COVID-19, starting with a summary of the utility-based framework for SOT allocation in general and its application to mandates for SOT candidate vaccination before extending this reasoning to caregiver vaccination mandates. We find that such a mandate may be justifiable, contingent on the still-evolving data on COVID-19 prevalence, severity in the SOT population, and vaccine effectiveness. Finally, we investigate a special population of SOT candidates that are unambiguously reliant on their caregivers—children.

The Ethics Committee of the US Organ Procurement and Transplantation Network identifies three principles underlying the equitable allocation of solid organs: “(1) utility; (2) justice; and (3) respect for persons (including respect for autonomy).”<sup>13</sup> When there are competing considerations across the principles that underlie organ allocation, there is not a predefined priority of principles that automatically trump one another; rather, each consideration should be weighed in relation to the degree it conflicts with the other, with a goal of finding solutions that minimally infringe on competing principles.<sup>13</sup> A vaccine mandate, whether for candidate or caregiver, plainly infringes upon individual autonomy, and, as elaborated below, may be problematic from the standpoint of justice as well, so it must strongly support utility to avoid being dismissed at first glance as unethical. In general, to mandate a vaccine in a given setting—in other words, to require acceptance of an intervention that may not otherwise be desired—the harms of the vaccine should be low, it should be effective, and it should improve safety in that setting.<sup>14</sup> We can apply these criteria to vaccination against COVID-19 in the transplant setting. The COVID-19 vaccines authorized or approved by the Food and Drug Administration (FDA) for use in the U.S. are widely accepted as safe; they reduce the risk of severe illness or death in the general population as well as in SOT recipients<sup>15</sup>; and they reduce acquisition and transmission of COVID-19 (including to other SOT recipients who share the same healthcare settings) at a time when

community transmission is high in the United States.<sup>16-18</sup> Given those facts, a COVID-19 vaccine mandate for candidates should improve outcomes for SOT recipients and thus improve the utility of the graft.<sup>19</sup>

The potential utility of a vaccine mandate for caregivers must be considered complementary, or in addition to, the utility of a mandate for candidates. Most directly, a vaccinated caregiver could improve utility by reducing the risk of transmitting COVID-19 to the SOT recipient they are caring for. Similarly, they may reduce the risk of COVID-19 infection among other SOT recipients in shared spaces such as in the waiting room of a transplant clinic. Though physical distancing and use of personal protective equipment are less intrusive methods of achieving the latter, the frequent, prolonged, close contact that a SOT recipient and their caregiver experience is not easily overcome by less restrictive means. The benefit of caregiver vaccination is contingent on vaccination providing a high degree of protection against infection and transmission. If new COVID-19 variants are able to escape vaccine-provided immunity and cause serious disease, the magnitude of this potential benefit would decrease. Conversely, if vaccination provided perfect immunity against COVID-19 among SOT recipients, there would be no added benefit to reducing transmission by mandating caregiver vaccination. In fact, the benefit provided by caregiver vaccination would be greatest in a scenario where the vaccine provided minimal protection against serious illness in SOT recipients, but vaccination of caregivers significantly reduced disease severity and transmission. The present reality of the pandemic sits somewhere between these two hypothetical extremes, but closer to the latter, given evidence for decreased immunogenicity among SOT recipients and uncertainty about optimal timing for vaccination of SOT candidates.<sup>20-22</sup> Potential harm from COVID-19 may also vary by specific organ transplanted: lung transplant recipients have worse outcomes from COVID-19 compared to other SOT recipients.<sup>23</sup> The level of community spread is likewise important in determining the benefit a caregiver vaccine mandate confers through decreased transmission to the SOT recipient and others: in a setting with little to no baseline risk of infection, such as New Zealand prior to the Delta variant,<sup>24</sup> a caregiver mandate provides relatively little added utility. Likewise, in a community where herd immunity has been achieved, whether through infection or immunization or some combination, the risk of COVID-19 infection will be, by definition, negligible. Even if morbidity among SOT recipients remained high in the event of infection, the added benefit of preventing what would be a vanishingly rare event is not likely to be significant.

Perhaps less obviously, a vaccinated caregiver's reduced risk of serious illness (including hospitalization or death) in and of itself provides a benefit to the SOT recipient and the utility of the graft. Though the necessity of having identified caregivers—of social support—for SOT candidacy is itself controversial, many transplant programs do deem it important in allocation decision-making, with increased utility as the justification.<sup>25</sup> It must follow that taking away a primary caregiver, for instance due to hospitalization from COVID-19, causes the SOT recipient harm. In addition to loss of psychosocial support, harms to the transplant recipient might include

loss of transportation, assistance with medication management, or financial resources. Even if the contingencies we outlined above became reality—if a vaccine did not meaningfully reduce transmission, or if it were extremely effective at preventing serious infection in SOT recipients—preventing serious COVID-19 infection in a caregiver may still significantly benefit the SOT recipient.

Novel antiviral therapies may, at first glance, seem like an alternate means of providing similar protection against COVID-19 to SOT recipients—of providing similarly increased utility without the need for a mandate. However, limitations on their availability, efficacy, and use in the transplant population make them an imperfect substitute for vaccination. Most generally, there are limited data on their effectiveness among SOT recipients, compared to information on vaccine efficacy in the general population or indeed in SOT candidates and recipients. In fact, the American Society of Transplantation recommends against the use of oral antiviral therapies: molnupiravir has low efficacy overall; nirmatrelvir/ritonavir (Paxlovid) has the potential to significantly alter the levels of crucial transplant medications including immunosuppressive agents and antibiotics.<sup>26</sup> The FDA has suspended the use of most monoclonal antibody treatments out of concern for lack of efficacy against current COVID-19 variants such as Omicron. Finally, tixagevimab plus cilgavimab (Evushield), the only monoclonal antibody therapy authorized for pre-exposure prophylaxis in the United States, is not widely available.<sup>27</sup> Antiviral therapies may be a substitute for caregiver vaccination only in so far as they are taken by the caregiver and reduce the risk that the caregiver will be incapacitated from severe COVID-19 and unable to support the SOT recipient.

One important aim of a caregiver vaccine mandate should be to reduce injustice in transplant allocation: any vaccine requirement must be accompanied by active efforts by the transplant program to make it equitable. For instance, a mandate should be contingent on reducing barriers to access to vaccination. In a setting of vaccine scarcity, such as in the first few months of 2021, transplant programs that set vaccine mandates should ensure they are able to provide vaccines for candidates and caregivers with minimal added burden to the recipients. Mandates should also recognize socio-cultural reasons for vaccine hesitancy that are deeply rooted in harms and injustice, particularly in the context of human experimentation and novel therapies; institutions that perform SOT should actively engage these historically disenfranchised communities to reduce vaccine hesitancy, even if individual caregivers from these communities must ultimately abide by the institutional mandate.<sup>28,29</sup> It would similarly be unfair to limit access to a transplant waiting list based on initial caregiver hesitancy in the face of a mandate without an opportunity for education and shared decision-making, perhaps after some time for reconsideration. Transplant programs should explore a candidate's or caregiver's individual reasons for hesitancy and regularly revisit a caregiver's initial decision to decline vaccination, should that be the case. A caregiver vaccine mandate can therefore promote justice in organ allocation if it reduces structural barriers to vaccination.

All the considerations we have discussed thus far apply to pediatric SOT candidates, who universally must rely on caregivers

in the form of parents or guardians. They will certainly remain in close contact with their caregiver and must be accompanied by their caregiver to clinic or laboratory testing, potentially also increasing the risk of infectivity from caregiver to their child or another transplant recipient. Parent vaccination may especially improve utility among young SOT candidates who are not themselves eligible for COVID-19 vaccination, such as those less than 5 years old, as this is effectively an extreme case of the scenario we posited above where vaccines are highly effective in caregivers but not in SOT recipients. However, the overall increase in the utility of the graft may still be smaller compared to vaccination for caregivers of adult SOT candidates, as children overall, including SOT recipients, suffer substantially less morbidity and mortality from COVID-19.<sup>30,31</sup> Conversely, compared to adults, children suffer more harm from delayed or deferred organ transplant. End-stage organ failure causes impairment in cognitive, socio-emotional, and physical development in children that may be irreversible. A child at the same level of disease progression as an adult may have decreased access to bridging measures such as mechanical circulatory support due to size, safety, and efficacy limitations. Survival is also substantially higher after pediatric SOT.<sup>32</sup> Excluding a child from organ transplant would therefore cause greater harm than excluding a comparable adult. We noted above that a caregiver vaccination mandate must provide substantially increased overall utility to avoid being rejected out of hand: as a parental vaccination mandate for children undergoing SOT provides dubious net benefit, it fails this initial test.

In settings where a COVID-19 vaccine mandate has been instituted for transplant candidates, the utility provided by reducing the risk of severe COVID-19 among adult SOT recipients, as well as the lessened chance of a significant loss of social support, may indeed justify the infringement on respect for persons that a caregiver vaccine mandate necessitates. However, the degree of utility, and thus the degree of infringement tolerated, is not fixed but changes with the facts of the COVID-19 pandemic. Mandates cannot be “set and forget”—institutions that choose to impose them should have a systematic process for reviewing their appropriateness at regular intervals and be prepared to remove them if they are no longer found to be justifiable. Applications of transplant ethics, such as in decisions on caregiver vaccine mandates, must be prepared to evolve as quickly as the virus does.

## DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

## DATA AVAILABILITY STATEMENT

Data sharing not applicable – no new data generated.

## ORCID

Bob Z. Sun  <https://orcid.org/0000-0001-9029-8178>

Aaron Wightman  <https://orcid.org/0000-0003-0167-0420>

Douglas S. Diekema  <https://orcid.org/0000-0002-1703-5176>

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