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PERSONAL VIEWPOINT

Mandating COVID-19 vaccination prior to kidney transplantation in the United States: No solutions, only decisions

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The question of whether transplant clinicians should mandate COVID-19 vaccination as a condition of transplant candidacy is complex. A vaccine mandate may be defensible on the grounds that transplant clinicians are obligated to ensure transplantation is conducted safely, and in a manner that entails the best use of a scarce public good. However, mandate proponents will inexorably predicate their arguments on contingent clinical judgments that meliorate rather than resolve core value disagreements. Vaccine mandates are conceivably defensible on narrow grounds, but may prove to be purchased at the expense of an attenuation of shared decision-making, proffering claims of risk reduction from a vaccine mandate beyond what the current evidence base supports, and unintentionally exacerbating durable inequities in access to transplantation.

KEYWORDS
editorial / personal viewpoint, ethics and public policy, infectious disease, kidney transplantation / nephrology, vaccine, patient safety

1 | OVERVIEW

The COVID-19 pandemic has extinguished the lives of more than 745,000 Americans and counting.[1] An mRNA-derived vaccine against the virus has proven to be highly effective against the duration and severity of infection. Hospital systems and health care workers have been pushed to the breaking point,[2] overwhelmed by infected patients, the vast majority of whom are unvaccinated. Patients with chronic kidney disease, end-stage kidney disease, and kidney transplants are all more vulnerable to severe infections. Despite widespread availability of the vaccine, and widespread promulgation of the social costs of unchecked spread, vaccination rates in the United States remain relatively static. More than a third of our fellow citizens remain unvaccinated, and in some states, more than 50% of citizens are unvaccinated.

In the midst of this global public health crisis, focusing on how vaccine mandates affect a narrow category of patients with kidney disease seeking a transplant may seem parochial. Furthermore, for many public health professionals, the *prima facie* case in favor of a vaccine mandate for immunosuppressed transplant recipients may be so widely held and painfully obvious as to render doubts on some spectrum between tedious and exasperating. But, the ethical tensions and challenges at work for transplant centers currently considering a vaccine mandate for patients with kidney disease underscores an existing tension between practicing clinicians and public health professionals: Unlike public health authorities, whose decisions affect large populations, clinicians make judgments and decisions about the care of individual patients, and clinician leaders are primarily responsible for making sound medical judgments and decisions for health care institutions that provide care to local communities.

While the ends of public health professionals and clinicians are typically aligned, the particular obligations of clinicians to individual patients (or to local communities) require additional circumspection

when considering the exclusion of certain categories of patients from life-extending therapies such as kidney transplantation. In enacting a vaccine mandate policy, transplant center leaders render value-laden clinical judgments, contingent on an incomplete and evolving evidence base which offers directional but not dispositive guidance regarding the relative risk reduction afforded by a mandate. Mandate proponents relying on the obligation to promote "safe" transplant practices do so not by "balancing" competing obligations to promote shared decision-making, but by enacting exceptions to the "shared" part of decision-making in this instance, demarcating where the respect for patient autonomy ends and the policy-making authority of center leaders begins. Unintentionally, a vaccine mandate may exacerbate longstanding inequities in access to transplantation, and may entail extending policy authority in novel, intrusive, and tendentious ways. In each of these circumstances, mandate proponents test the durability of the public consensus from which their policy-making authority is derived. Elucidating how these competing ethical obligations on clinicians work in the case of kidney transplant candidates may illuminate how clinicians should proceed in analogous circumstances.

2 | THE NECESSITY AND PRECARIOUSNESS OF EXERCISING CLINICAL JUDGMENT

Kidney transplantation generally conveys both a longer duration and better quality of life for most patients with end stage kidney disease, making transplantation the preferred treatment for advanced kidney disease or end-stage kidney disease. However, the availability of kidney transplantation is limited by both an insufficient supply of organs and an array of clinical strictures and requirements necessary for successful post-transplant management. All transplant centers in the United States have written clinical criteria for accepting a patient as a candidate for transplantation. However, no list of selection criteria is all-encompassing, so in many instances the sound application of selection criteria is a matter of exercising clinical judgment.

Judgment, by definition, is a process of inductive reasoning: The exercise of *clinical* judgment is a matter of inference and decision, often under conditions of empirical uncertainty, employing an amalgam of observation, past experiences, and reference to germane empirical data, ultimately culminating in a decision. Clinical judgments are subject to framing and bias,[3] and thereby, to criticism. But, they are also ubiquitous, and often necessary to function in a clinical setting. Properly deployed,[4] the use of clinical judgment to form and execute a decision fuses the didactic and inductive expertise of the clinician with the ethical responsibilities and prerogatives of being entrusted with the care of individual patients, and with the responsibility for guidance and oversight of institutions delivering clinical care for entire communities.

Clinicians entrusted with the oversight of kidney transplant programs are obliged to make individual and programmatic clinical judgments that inexorably privilege some competing values and obligations over others. There is no method available for a grand ethical synthesis that definitively resolves intractable ethical disagreements.[5] Instead, what is typically available is a *modus vivendi*, an agreement which permits peaceful co-existence in the face of unwavering disagreement, rather than the harmony of robust moral agreement. This point is worth remembering, given the durability of beliefs among vaccine refusers.[6] The stakes of exercising judgment poorly, unwisely, or arrogantly include an erosion of the social support for investing that authority in clinicians, which from time to time will cause other sources of authority to step in.[7]

2.1 | Applying clinical judgment to the question of COVID-19 vaccine mandates for transplant candidates

Transplant clinicians have a fiduciary obligation, mirrored in Federal law,[8] to ensure that organ transplantation is conducted in a manner that is "safe" for patients, and that organs are allocated in a manner that comprises the "best" use of a public good. "Safe" and "best" are judgments. Some judgments of safety are minimally controversial: Administering global T-cell immunosuppression to a patient with an active bacterial or tubercular infection is generally understood to be unsafe. The fact that this or that patient in that circumstance might survive unscathed does not undercut the soundness of the judgment or the reasoning behind avoiding these clinical scenarios. Judgments of safety are sometimes expanded to cover matters where the cause-and-effect relationship with unsafe practices or bad outcomes is less clear, or even inconsistent with other accepted and extant practices and policies.

Translating this fiduciary obligation into public policy, centers are routinely held to objectively measured and publicly reported standards (such as patient and graft survival rates), and are held to account if they fall short. Transplant center leaders have agency, and are not obligated to cooperate with requests for non-emergency care they judge to be outside their endorsed standards for safety and quality.[9] (I stipulate that, given the widespread availability of dialysis, the need for a kidney transplant does not constitute a medical emergency.) Therefore, if center leaders are accountable for the outcomes of the patients they transplant and care for, and there are no regulatory or clinical best-practice exceptions to this standard for candidates who elect not to be vaccinated prior to transplant and then suffer a COVID-19 related adverse outcome, then center leaders could be justified in declining to list and transplant candidates who elect not to be vaccinated. By extension, if center leaders judge that the accommodations in care delivery for an unvaccinated transplant patient, to avoid exposing the patient to COVID-19 in the hospital or clinic, or exposing other patients, family members, and staff to COVID-19 from an unvaccinated and infected patient, are either too onerous or are likely to fall below the center's standards of care delivery, then the center could also be justified on these grounds to decline to list or transplant an unvaccinated candidate. Too, instituting a vaccine mandate for transplant candidates *may* prove to be a necessary (if not sufficient) condition for avoiding tort liability.[10]

However, centers contemplating this approach should be prepared to address the obvious counterfactual: In the United States, after a brief pause early in the pandemic, and prior to the availability of COVID-19 vaccines, organ transplant rates returned to previous levels, and in the case of kidney transplantation, actually exceeded pre-pandemic levels,[11] indicating an evolved consensus on the safety of transplantation during the pandemic. Transplantation has continued during the availability and use of COVID-19 vaccines, despite a preponderance of evidence showing that most transplanted patients on immunosuppression have either a negligible or reduced response[12] to a two-dose regiment of the vaccine. So, if transplanting unvaccinated patients is outside the standards of quality and safety *now*, why wasn't it also outside those same standards prior to the availability of the vaccine?

One answer might be that the assessment of the risks and benefits of continued dialysis versus receiving a transplant prior to the availability of a vaccine are now different with the wide availability of a vaccine. With demonstrated evidence of safety and efficacy (sometimes after more than two vaccine doses), the appropriate consideration has shifted to comparing risks and benefits with or without clinically sufficient vaccination. The skeptic has recourse to the argument that the infection fatality rate for SARS-CoV-2 infection in kidney transplant recipients is not known, because the total number of SARS-CoV-2 cases is not known, since an unknown number of patients develop infection without ever being tested. (*Infection* fatality rates require knowledge of the total number of patients infected; *Case* fatality rates use confirmed total cases as a denominator.[13]) Reports of a high risk of morbidity and mortality in infected kidney transplant recipients are limited only to patients requiring hospitalization, rather than all infected (tested or otherwise) recipients.[14] Furthermore, both the infection fatality rate and case fatality rate for SARS-CoV-2 infection will vary by location and over time, and both will likely decrease as prevalent vaccination rates and primary infection rates converge. The pro-mandate contingent may rejoin that pre-vaccination norms are not desirable norms for running a transplant program in the vaccine era, the widespread availability of vaccines, the very low adverse event rate from vaccination, and the high efficacy of vaccination to prevent serious complications from infection limits the appeal of the skeptic's concerns, and so on.

Center leaders may well decide to institute a vaccine mandate as a binary choice, without room for clinical exception, based on the low risk of receiving a COVID-19 vaccine combined with the likely benefit of lowering the risk (albeit from an unknowable *baseline* risk) of a severe infection. Center leaders choosing this "binary" path should offer clear justifications for their approach, and they should consider suggesting evidence-based conditions under which the policy should either be revisited or optionally modulated by clinical judgment in individuated circumstances. Ultimately, vaccine mandate proponents must inexorably contend with limits on their ability to quantify the risk reduction realized by a vaccine mandate, whereas skeptics must contend with the extent to which their insistence on evidentiary scrupulousness requires a high threshold of empirical proof rarely available in any facet of clinical medicine.

While the responsibilities for safety and quality placed upon center leaders provide wide latitude for acting on considered clinical judgments made in service to those responsibilities, center leaders should anticipate and be prepared to respond to questions and criticism from dissenters asking after data to justify more restrictive measures. Again, the terminus of this back and forth will not be a dissolution of disagreement, but only a policy decision more or less successfully executed by those invested with the authority to decide.[5] Continuing to be invested by society with the authority to make these decisions is contingent in part on exercising clinical judgment with precision, humility, transparency, and good faith. Which is to say, an updated version of the Oslerian virtue of equanimity.[15]

3 | VACCINE REFUSAL, SHARED DECISION-MAKING, AND CONSENT TO IMMUNOSUPPRESSION

Another answer for center leaders inclined to a vaccine mandate policy, in the vein of "shared decision-making," relates hesitancy or outright refusal of the COVID-19 vaccine to the question of whether such a patient fully understands the risks of long-term immunosuppression,[16] apart from the risks of developing COVID-19 infection. Connecting the dots in this fashion for a patient may result in a patient determining that the requirements for transplant immunosuppression also is not commensurate with their considered desires and values, or at least highlights a tension in the patient's stated values worth further consideration. A shared decision-making approach should not be instrumentalized; the clinician's decision not to offer transplantation to an unvaccinated patient should not be a subterfuge. If a center's considered policy is not to transplant unvaccinated patients, there is no decision-making to "share" in this instance. Clinicians practicing in a center with a vaccine requirement for transplant should engage a patient's values and how they align with the requirements of transplantation generally, without a pretense that the conclusion of that conversation will lead to alterations in the center's policy.

3.1 | Does a vaccine mandate require vaccine responsiveness?

Centers electing for a vaccine-requirement policy should take care to narrow their clinical judgments to a patient's discrete decisions about whether or not to accept the vaccine, and aggressively discourage conflating the rationale for that narrow policy with broader judgments about the constellation of values that animate a patient's decision to decline a vaccine. If a center endorses a vaccine requirement, the policy should be specific, precise, and tailored to the unique clinical features of the patient population in question. This may entail not just a vaccine requirement, but also require sufficient vaccine dosing to achieve a high antibody threshold, or some other evidence-based surrogate marker of clinical responsiveness. Early studies in patients with end stage kidney disease suggested a lower

likelihood of antibody responsiveness to vaccination,[17,18] though more recent studies suggesting responsiveness more comparable to the general population.[19,20] Furthermore, there have been concerns raised regarding the reliability of clinical interpretations of both the presence and absence of post-vaccine antibodies, as well as antibody titers.[21] Additionally, some patients with advanced chronic kidney disease or end stage kidney disease are maintained on medications, such as mycophenolate mofetil or rituximab, which demonstrably reduced responsiveness to the COVID-19 vaccine, and may require several vaccine doses to elicit clinically significant responsiveness (however defined).[22,23] No policy can be sufficiently granular to account for all clinical scenarios, but precision and specificity provides greater support to a center's arguments in favor of endorsing a requirement under the rubric of safe clinical practice. While is it probable that a hypo-responsive vaccine recipient has more protection against severe COVID-19 infection compared to no vaccination due to elicited T-cell mediated immunity, centers with a vaccine mandate should specify whether the mandate requires that transplant candidates demonstrate threshold antibody titers (or some other validated surrogate measure of responsiveness) after vaccination, before deemed eligible to receive an organ offer.

3.2 | Vaccine exemptions, patient caregivers, health inequities, and unintended consequences of a vaccine mandate

Exemptions from vaccine requirements pose additional challenges for center leaders. Though rare, anaphylaxis from administration of the COVID-19 vaccine has been reported.[24] Center leaders proposing a vaccine mandate, but still inclined to accept transplant candidates with clinical contraindications to additional vaccine doses will need to defend distinctions between these patients and patients who are hypo-responsive (however defined) after a two-dose regimen. For centers reasoning under the rubric of "safety," neither category of patient should receive organ offers. Non-clinical exemptions from vaccine requirements, such as "religious" exemptions, pose a similar challenge. Though some hospital systems have tried,[25] in general, judging the veracity or sincerity of religious convictions is outside the professional competence and authority of clinicians. So stipulated, respecting religious- or other conscience-based refusals of vaccination does not impose an obligation on center clinicians, operating within the narrow rubric of safe practices, to accept candidates who refuse vaccines.

The above considerations extend beyond the patient as well. For example, as most centers require that transplant candidates have a "caregiver" to assist the patient on a regular basis after transplant, centers electing for a vaccine-requirement policy will inevitably need to consider extending a vaccine requirement to the candidate's caregiver. Absent a vaccine requirement, the caregiver could not safely perform any of the caregiving functions required for the candidate. *De facto*, a candidate who complies with a vaccine mandate, but is without a caregiver willing to be vaccinated, would be excluded as a transplant candidate. Though, requirements for a caregiver and other social support criteria have been a source of controversy since the early days of dialysis, criticized as a cipher for social worth considerations in allocation.[26]

Arguments for excluding candidates solely based on the absence of social support might be tenuous enough, but it is additionally complicated by the fact that absence of social support overlaps substantially with being a member of vulnerable, marginalized groups. Recent studies have found that candidates having to take on a "self-advocacy" role to find a living donor often do not succeed, and are disproportionately Black, female, and unmarried.[27] Kidney disease disproportionately affects vulnerable and marginalized groups in the United States, and around the world. A recent study by Schold and colleagues highlights a lack of access to kidney transplantation among Black Americans and those living in the poorest zip codes which has persisted for two decades.[28] Given the high rate of non-vaccination among these populations, and the complex nexus of mistrust of institutions[29] that drive non-vaccination, it is likely that a vaccine-requirement policy will at least *not help* in alleviating durable structural health inequalities in access to transplantation among these populations. It doesn't follow that centers that choose to implement a vaccine mandate are indifferent to these concerns and unintended consequences. But, centers choosing to implement a vaccine mandate on "safe practice" and "standard of care" grounds are not excused from realizing these policies may unintentionally exclude patients that have long been subject to durable inequities in access to kidney transplantation.

Center leaders concerned about the extent to which patients may be excluded from access to transplantation as a consequence of hewing to a narrowly tailored conception of "safe practices," will be faced with either (a) identifying an ethical argument or principle which is more permissive in accepting non-vaccinated/non-responsive patients and excluding others, or (b) abandoning a vaccine mandate policy altogether. Special pleading to gerrymander the boundaries of safe practices for one out-group will inevitably spawn similar appeals from others. Consequentialist arguments are vulnerable to core disputes about the very possibility of interpersonal comparisons of utility. Refuge sought in principle-based arguments like beneficence, non-maleficence, and justice must content with the elasticity with which these principles can be employed to justify incompatible ends, disagreements regarding the superiority of one principle-based argument over competing contenders, and the extent to which such reasoning culminates (non-exclusively) in *ad hoc* assertions, circular reasoning, or dependence on false premises.[5]

4 | CONCLUSION

None of what I've argued for here should be conflated with disputing the truth of some key premises: Widespread vaccination combined with masking and social distancing is our *best* path out of the worst pandemic of our generation. Transplant professionals are right to be concerned about the clinical wisdom of transplanting unvaccinated patients, both for the sake of the patient themselves, for other transplant patients and caregivers, and for the safety of the community at

large. Whether or not a center chooses to enact a vaccine mandate policy, the importance of zealously encouraging patients and caregivers to get vaccinated is not in dispute. Centers enacting a vaccine mandate may be justified in doing so, but a mandate will not be cost-free, will inevitably test an already-tenuous *modus vivendi* in our fractured country, will come at some expense to shared decision-making, will have to disposition a raft of proposed non-clinical exceptions and special pleadings for exemptions, may entail extending vaccine requirements to patients' caregivers and cohabitants, may entrench existing inequities in access to transplantation, and should be designed for reconsideration and revision as the evidence base evolves. Clinician leaders should temper the courage of their decisions with humility in the face of questions and criticism, and a frank acknowledgement of the unstable justifications and unintended consequences of their policy decisions. If there is a chance to maintain the *modus vivendi*, it is by showing our communities that we are struggling (and sometimes failing) to get it right.

DISCLOSURE

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