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Ethical Issues in Kidney Transplant and Donation during COVID-19 pandemic

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#### **ABSTRACT**

The Covid-19 pandemic caused by the severe acute respiratory syndrome coronavirus (SARS-CoV-2) has faced the transplant community with unprecedented clinical challenges in a highly vulnerable patient category. These were associated with many uncertainties for patients and healthcare professionals and prompted many ethical debates regarding safe delivery of kidney transplantation. In this paper, we highlight some of the most important ethical questions that were raised during the pandemic and attempt to analyse ethical arguments in the light of core principles of

medical ethics to either suspend or continue kidney transplantation, to mandate vaccination in transplant patients and transplant candidates, and finally healthcare providers. We have come up with frameworks to deal responsibly with these ethical challenges, and formulated recommendations to cope with the issues imposed on patients and transplant professionals.

## INTRODUCTION

The Covid-19 pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been causing disruptions of an unprecedented magnitude in clinical practice in all areas including organ transplantation. The public health emergency poses ethical challenges for organ donation and transplantation healthcare professionals.<sup>1</sup> As in other areas of healthcare, the crisis of Covid-19 calls into question how to maintain the welfare of patients based on the ethical principles of justice, autonomy, beneficence, non-maleficence and accountability.

The objective of this article is to summarize ethical issues associated with kidney transplantation during the Covid-19 pandemic. An ethical framework to address different questions will be provided. Key issues for kidney transplantation during the time of Covid-19 include keeping kidney and kidney transplant patients safe, the need to ration scarce medical resources and make recommendations for suspending or continuing transplant activity, and recommendations towards advising or mandating vaccination.

## ETHICAL CHALLENGES

The challenging issues of kidney transplant patients and those on the waiting list for kidney transplantation have surfaced since the first wave before availability of the COVID-19 vaccine but remain critical following the delta and omicron waves.

Data from the Scientific Registry of Transplant Recipients (SRTR) have illustrated the magnitude of impact. During the early part of the pandemic, there was a 2.2-fold increase in mortality for patients on the kidney transplantation waitlist in the United States.<sup>2</sup> At the same time, total mortality rate observed in kidney transplant recipients during the Covid-19 era has also been shown to exceed the expected deaths by 1.4-fold according to the SRTR data.<sup>3</sup> The ratio of observed to expected deaths varied substantially by race or ethnicity even within the national study of the United States, being highest (82% above expected) among Hispanic solid organ transplant recipients.<sup>3</sup>

Based on meta-analyses of observational studies, the 30-day mortality of Covid-19 was 19% among kidney transplant recipients.<sup>4,5</sup> There was a trend towards lower mortality with time, approaching 14%<sup>6</sup> during the second half of 2020 and as low as 2%<sup>7</sup> during the omicron surge in 2022. The mortality of kidney transplant recipients from Covid-19 in low- and middle-income countries, such as Latin America, was higher, ranging from 14.3 to 35.4%.<sup>8</sup> Although Covid-19 vaccines are effective in curtailing cases and reducing mortality, ethical challenges come from the issue

of vaccine equity. In many low-resource countries, critical shortages of vaccine fell short of achieving herd immunity to allow preparedness for sustaining kidney transplantation activity, or even dialysis service. Such an ongoing mismatch between demand and supply of vaccines would likely cause controversy and divided opinion whether booster dosing should wait until global distribution of vaccines is better achieved.<sup>9</sup>

**Challenge 1: Should kidney transplantation be continued or suspended during the pandemic?**

Of note, the pandemic has imposed significant stress on healthcare systems, requiring a shift of resources to combat the infection and temporary cessation of elective clinical activities.<sup>10</sup> A substantial reduction in organ donation and transplantation has been reported worldwide<sup>11-13</sup>, and not necessarily restricted to regions with the highest infection rates. Based on a nationwide analysis in the United States, there was a reduction of over 50% in deceased donor transplantation since the Covid-19 outbreak, mostly driven by reduced kidney transplantation.<sup>12</sup> Another survey in the United States reported that 72% of transplant institutions had completely suspended living donor kidney transplantation in early 2020, where restrictions to deceased donor kidney transplantation was imposed in 84% of centers.<sup>13</sup> A decrease in kidney retrieval was also evident in regions with low caseloads, indicative of a global and nationwide effect beyond the local Covid-19 incidence and prevalence.<sup>12</sup> To quantify the impact of Covid-19 on solid organ transplantation, international data should be collected. The most comprehensive international data leverage on the

transplant activity from 22 countries, starting from the onset of the 100<sup>th</sup> cumulative Covid-19 cases through to the end of 2020.<sup>14</sup> Despite variation between countries, the most pronounced reduction was in kidney transplantation, with an overall decrease of 19%. Deceased and living kidney donor transplantation was decreased by 12% and 40% respectively.<sup>14</sup> The trend of reduced transplantation after 2020, including burnout in transplant workforces and the impact of increase in incidence of infection in kidney transplant recipients secondary to omicron variant, remains to be evaluated and monitored.<sup>15,16</sup>

Deferring elective surgical or medical procedures during the Covid-19 crisis is justified ethically to protect patients and healthcare workers (non-maleficence and distributive justice as resources and staff were not available for elective and even many emergency services). There was an unknown risk in the beginning of Covid-19 infection (pre-vaccination era) for immunosuppressed patients. We cannot ascertain if Covid-19 could be transmitted from donors to recipients. The fact that many hospitals were overwhelmed and operation theatres were converted to intensive care unit beds has substantial consequences. Anaesthetists and many other specialists had been deployed to work in intensive care units, dialysis units or areas other than the transplant programme. This could have implications for decision to keep or suspend transplant programme, and in many cases dictated by hospital directors.

The rationale underscores the need to balance individual patients' need and that of the community (again distributive justice). We have a duty to the communities, hospital employees and patients, in addition to the responsibility to individual waitlisted kidney transplant candidates. It amounts to

an estimation of the reserve of personal protective equipment (PPE) availability and the utilization of PPE for kidney transplantation surgery and perioperative transplant care. Other factors include the population density and incidence of Covid-19 cases in the community, hospital bed and ICU bed surge capacity, in addition to staffing availability. When high-filtration N-95 masks are in short supply, suspending elective surgery or endoscopy is considered more appropriate than contingency measures such as reusing masks or downgrading protective gear requirements. Blood product availability is not a major concern for kidney transplantation (but still needs to be reserved for every case even though there rarely is a need to transfuse), as opposed to liver transplantation. Although blood donation rate is expected to be reduced during a pandemic (due to fear of being infected while donating blood and restricted freedom of blood collection teams to attend public places<sup>17</sup>), the demand for blood products may well turn out to be lower as the number of trauma patients falls secondary to lockdown-related travel restrictions. The same applies to the consideration of ventilator capacity, which should not be too much affected by kidney transplantation; most kidney transplant recipients do not require ventilator support postoperatively, although we might argue that there should always be an intensive care bed for ventilation standby.

To aid in the decision making as to whether deceased and living donor kidney transplantation should be deferred/suspended during a region or hospital's Covid-19 response, there are several consequences to be considered. The first and foremost factor is the patients who need and benefit from kidney transplantation. That ethical principle is to strike a balance between equity and clinical results. While ethical values might inform the choice, one should distinguish between the situations when the position of a center is at the peak of the incidence curve versus those at the



downslope stage<sup>18</sup>, and between the pre-vaccination and post-vaccination era. Transplant programs should definitely also include patient factors regarding clinical risk. The question to address, in other words, is whether – and how long – the end-stage kidney disease (ESKD) patients can wait without transplantation. The waitlisted kidney transplant patients' views should be given a prominent place in the decision-making process, as we learned that communication with kidney transplant candidates is of the utmost importance.<sup>19</sup> The majority of surveyed patients favor receiving a kidney transplant despite the ongoing COVID-19 pandemic. Reactivation of candidates on the waitlist cannot be assumed, however, and should take an individualized approach, incorporating clinical risk with patient perspectives.<sup>20</sup>

Given the imbalance between supply and demand for medical resources, the pertinent question is not whether to set priorities, but how to do so ethically and consistently.<sup>21,22</sup> The need to be consistent by no means implies a fixed answer because the risk-benefit ratio can be highly dynamic during different stages of kidney disease and the varying Covid-19 incidence in the community and disease burden. The best framework for pandemic resource allocation during Covid-19 has been constructed by medical ethicists previously (Table 1). In essence, four fundamental pillars appear in the proposed ethical considerations: maximizing the benefits produced by scarce resources, treating people equally, promoting and rewarding instrumental value, and giving priority to the worst off.<sup>21,23</sup>

Intuitively, one of the reasons for kidney transplantation to be the most affected by Covid-19 pandemic among all solid organ transplantation, is the perceived effective alternative to transplantation for managing kidney failure. Although dialysis is perceived as a reasonable alternative, it is

important to note that there is an exceptionally high SARS-CoV-2 infection attack rate (the proportion of patients who become infected) among hemodialysis patients.<sup>24,25</sup> Owing to difficulty for dialysis patients to self-isolate and practical challenges of implementing social distancing in the dialysis units<sup>26</sup>, hemodialysis patients are subjected to an exceptionally high likelihood of infection. Furthermore, urgency of kidney transplantation varies between patients. Many patients can afford to wait longer when transplantation has to be suspended, whereas less fortunate patients need a kidney transplant within a short time to survive. Examples are those who have limited access to dialysis, who have exhaustion or imminent lack of vascular access and either have absolute contraindications to or technique failure of peritoneal dialysis.<sup>27</sup> Highly sensitized patients with high percentage panel reactive antibodies and impending dialysis technique failure could also be given priority status for kidney transplantation. Adoption of a broad-brush approach stopping all kidney transplantation could have significantly disadvantaged these high-priority waitlisted transplant candidates who will have the lowest life expectancy in the absence of a kidney transplant. Instead, priority setting is a more reasonable approach, even though priority-setting also entails trade-offs to be made.<sup>22</sup> While acknowledging that priority is inherently a value-laden process, we should make decisions on the premise that fair and transparent priority setting would address both population health needs and an individual patient's urgency. As outlined in Table 1, it is highly justified to give priority to maximizing the number of patients that survive treatment with a reasonable life expectancy<sup>21</sup>. If we simply consider "save the most lives," we should always save five lives rather than one. However, prognosis allocation is relevant too. That means incorporating estimated life-years into benefit estimation. The concept or metric of life-years, as initially introduced as epidemiological and economic indicator of disease burden, is now often

used by bioethicists to assign priority. In other words, we should not simply aim to save the most lives and should aim to save the most life-years. Although not all appear to champion life-year approach<sup>28</sup>, this approach is receiving most support from prognosis-based allocation perspective. Based on the estimation of reduced transplant activity during the Covid-19 pandemic compared with 2019, it has translated into a negative effect of 37,664 life-years lost for patients waitlisted for kidney, much higher than 7370 life-years lost for patients waitlisted for liver.<sup>14</sup>

There is a certain logic to have different policies for kidney transplantation programme suspension and resumption. Within the domain of kidney transplantation, most patients with ESKD can wait until an organ becomes available. However, some patients cannot wait too long. Live kidney donation can be rescheduled, whereas deceased donor kidneys will be wasted (as they will also likely not be retrieved, not just discarded) if transplant services are suspended. Should a deceased donor kidney be considered suitable for an immunologically high-risk patient awaiting transplant, that kidney could have been the one and only chance for this challenging cohort of often long-waiting patients. Outcome studies of highly sensitized kidney transplant candidates<sup>29,30</sup> further argues for prioritizing the transplant for them despite the pressures of the Covid-19 pandemic. A key finding of safety in using lymphocyte-depleting agents (associated with decrease in rejection and without increase in mortality) even during the pandemic era<sup>31,32</sup> supports the argument to prioritize highly sensitized transplant candidates. The policy of complete cessation of transplant surgery for highly sensitized patients would have precluded the precious chance of getting a compatible kidney; they may not get a chance to get another suitable offer. Consideration of relevant factors in deciding the policy should include the supply-to-demand gap of organs.

That means we should evaluate the impact of stopping kidney donation and transplantation. When stratifying urgency of resuming transplantation, it is reasonable to give higher priority to regions with lower organ donation rate.

In the face of ethical dilemmas surrounding decision conundrums regarding deferring versus maintaining transplantation, a simulation of the outcomes using a Markov decision process model and probabilities can give additional information. That means an estimation of risk and benefit for different phenotype patients in different geographies, the latter referring to Covid-19 acquisition risks and case fatality rates. Besides the characteristics of the pandemic, the length of delay should be factored in, because the length of the pandemic could influence the waitlist and post-transplant mortality. According to simulation calculator developed for this purpose ([http://www.transplantmodels.com/covid\\_sim](http://www.transplantmodels.com/covid_sim)), the best immediate survival benefits of kidney transplantation occur in areas where the case fatality rate from Covid-19 among the general population is low. On the other hand, kidney transplantation will result in harm only when case fatality rates are substantially higher for kidney transplant recipients (such as 50% or greater) than for waitlist patients (e.g. 30% or lower), and when the community risk of Covid-19 acquisition is medium or high.<sup>33</sup> When the survival probability is assessed for waitlist patients, we have to also consider the survival benefit for patients receiving home dialysis.<sup>34,35</sup>

Increasingly concerned that patient autonomy should be respected, surveys should be conducted to assess transplant waitlisted patients' attitudes and concerns toward transplantation during different periods of Covid-19. During the peak of Covid-19 and before availability of vaccination in Singapore, when safe distancing measures were strictly enforced and activities around the country were limited to essential activities only, a standardized telephone survey of patients awaiting transplant was conducted.<sup>36</sup> Nearly half of the respondents were waiting for kidney transplant. While most patients had initially responded that transplantation services should continue despite Covid-19, the opinion changed after the series of questions designed to introduce thoughts on the risk of infection to a transplanted patient. Careful consideration on the pre- and post-transplant care and the potential harm from donor-derived infection had influenced the willingness of patients to proceed with transplantation; the proportion of patients keen to proceed decreased by half.<sup>36</sup> A similar survey conducted in the United Kingdom, also before the era of SARS-CoV-2 vaccine, showed that the majority of kidney transplant candidates would like to be reactivated immediately on the transplant waitlist when transplant activity is resumed.<sup>19</sup>

Ideally, centers should decide the pragmatism and prioritising of living versus deceased donor transplantation.<sup>18</sup> Some transplant centers tend to defer deceased donor transplantation because the hospitalisation tends to be lengthier than for living donor transplant patients, and even more so if extended criteria donor kidneys are accepted. Resource utilisation and demands for deceased donor kidney transplant are also of concern when the

recipient hospitals are heavily affected by the shortage of manpower including nursing staff, PPE, bed and testing capacity. Key consideration for proceeding with living donor kidney transplantation is particularly relevant in regions where dialysis capacity is constrained or not affordable.<sup>37</sup>

Last but not least, we need to consider the ethical principle of accountability and safety of healthcare professionals, in addition to the benefit to the society and the transplant candidates. Even when a waitlisted candidate accepts the risk of infection and transplant, we have to be considerate of the risk for the medical team. This is even more relevant in the situations when PPE shortage occurs and the lack of resources to have universal screening.<sup>38</sup> Under such constraints, the rate of contagion among health-workers has been reported to increase, leading to a vicious circle of in-hospital nosocomial spread to patients and staff.<sup>38</sup>

All in all, the ethical considerations would favour a “phased approach” rather than “all-or-none” approach.<sup>39</sup> That could either be a stepwise decreasing or stepwise ramping up transplant activity according to (clinical) risk assessments (Table 2). The varying degrees of reduction would therefore depend on risk stratification, namely, resource availability and medical urgency (Figure 1). In the United Kingdom, NHS Blood and Transplant has supported organ donation and transplantation with up-to-date national guidance and data collection.

**Challenge 2: Should vaccination of kidney transplant candidates be mandatory during pandemic?**

The concern about pandemic spread and transmission risk from donor to recipient and nosocomial transmission has been calling into question whether or not mandating Covid-19 vaccination was justified. Are there ethical, legal and scientific reasons for mandatory vaccination before candidates can be waitlisted or accepted for kidney transplantation? One important factor that should caution the decision is that vaccine-hesitant populations are often hard hit by Covid-19 itself in terms of ethnicity, socio-economic background and comorbidities, and in other words, a vulnerable group. By mandating vaccines, we would have fueled an act of discrimination.

Before the spread of the delta variant of SARS-CoV-2, there have been optimistic indications that vaccines could eliminate transmission of the virus. With more data and experience with the vaccine efficacy especially in kidney patients and transplant patients, as well as the parade of variants, their transmissibility and antigenic changes affecting protection by vaccination, the vaccination landscape has changed. It is now believed that SARS-CoV-2 vaccines should be relied to prevent symptomatic infection, reduce Covid-19-associated morbidity and mortality, rather than a panacea.<sup>40</sup> As compared with previous variants, omicron variant demonstrates substantial immune-evasion capability, and more so among kidney

transplant recipients.<sup>41</sup> That being said, vaccination can still provide reasonably satisfactory reduction in viral shedding and infectivity, especially in vulnerable population in hospitals<sup>42</sup> and elderly care facilities.<sup>43,44</sup>

For the sake of protecting transplant candidates from Covid-19 infection, vaccinations should preferably be administered before transplantation. To draw the analogy with seasonal influenza vaccination, vaccination before kidney transplantation would confer better protection to patients than those who do not receive vaccine (or defer until after transplantation). The same phenomenon is even more pronounced for humoral response to SARS-CoV-2 vaccine.<sup>45</sup> Pooled estimate of antibody response after two doses of mRNA vaccines was 35% for transplant recipients, much lower than that of 89% for dialysis patients.<sup>46</sup>

A detailed ethical framework to argue for or against mandating vaccination in kidney patients prior to activation or reactivation on transplant waiting list has previously been published (Table 3).<sup>47,48</sup> One of the arguments against mandating vaccination is the uncertain vaccine efficacy, especially in transplant candidates or transplant recipients on immunosuppression.<sup>47</sup> On the other hand, this is exactly the reason to strongly recommend for vaccination before and not after kidney transplantation, in order to ensure the optimal protection. Registry data have suggested reduced mortality risk from Covid-19 infection for vaccinated kidney transplant recipients when compared to unvaccinated patients.<sup>49,50</sup> Furthermore, the protection conferred by vaccination among transplant candidates and recipients can be enhanced by accelerated or fourth booster



doses messenger RNA vaccines<sup>51,52</sup>, even the fifth dose<sup>53</sup>, and ring vaccination<sup>54</sup> (priority and booster dosing of close household contacts of kidney transplant recipients).

The controversy of vaccine mandate<sup>55,56</sup> has been shown in an electronic survey of 141 transplant centers in the United States<sup>57</sup>, where mandatory vaccination before solid organ transplant was implemented only in 36% of the centers. The most commonly cited justifications for a mandate included stewardship (64%), public health obligations (52%), and desire to reduce transmission risks to healthcare personnel (40%), other patients, and family members (40%).<sup>57</sup> Almost none of the centers required clinical evidence demonstrating vaccine responsiveness such as measurement of anti-SARS-CoV-2 spike protein antibodies (which are not universally available and not easy to interpret). To a certain extent, these results suggest that the predominant view is strong recommendation of vaccination as opposed to a mandatory policy. Most bioethicists oppose to mandatory vaccination as eligibility for transplant waitlisting<sup>58</sup>; this is to uphold patient autonomy and avoid forced medical treatment. To align with the principle of informed consent, waitlisted transplant candidates should be allowed time and room for decision, even when the current evidence favours vaccination. There is no doubt that when mentally competent patients decline to receive vaccine, compulsory vaccination before allowing kidney transplant violates the principle of autonomy. Although vaccination is in line with the principle of beneficence, denying transplantation has been considered to be in conflict with the principle of non-maleficence toward an individual transplant candidate who does not want to receive vaccination.<sup>59</sup> Respect for autonomy requires holding patients responsible for the consequences of their conscientious choice, which occasionally

conflicts with other important ethical principles such as public interest and other patients' safety concerns. The imperative to respect a transplant candidate's right of informed consent, however, is not necessarily violating the public interest. In fact, patients can opt for regular surveillance to be allowed hospitalisation for transplant surgery. Part of the problem for this argument justifying equal candidacy for organ transplantation irrespective of the SARS-CoV-2 vaccination status, of course, is the lack of evidence to support that regular surveillance can mitigate risk of infection to the hospital. Because the level of protection and optimal frequency of surveillance remains unknown, vaccination remains the safest and primary strategy to prevent SARS-CoV-2 (poor clinical outcomes of) infections from the patients awaiting transplantation.<sup>60</sup> In that case, respecting the personal choice to forego vaccination could have violated the principle of non-maleficence because of the potential harm to the other patients.<sup>61</sup>

To turn the decision making from transplant centers to a transplant candidate: should he or she decline a kidney transplant offer and delay the transplantation in order to allow time for pre-transplant vaccination optimization? A similar strategy of deferring rituximab B-cell depletion therapy for 4 weeks after SARS-CoV-2 vaccination has been proposed.<sup>62</sup> As opposed to drug therapy, a kidney transplantation will be more complicated. To assess the benefit or harm of delays in transplantation to facilitate pre-transplant vaccination, a Markov microsimulation model has been created.<sup>63</sup> In general, scenario analysis suggested a benefit to short delays in deceased donor transplants to receive the SARS-CoV-2 vaccine in waitlisted patients older than 55 years. In fact, delaying transplants for 6 months before living donor transplant is estimated to yield

effectiveness of 22.83 quality-adjusted life years (QALYS).<sup>63</sup> However, caution should be exercised when delay to access of transplantation is expected to exceed 3 years (as in the case for deceased donor transplantation), or with high Kidney Donor Risk Index of the eventual deceased donor transplantation.<sup>63</sup> Notably, this Markov model<sup>63</sup> included unadjusted probability of Covid-19 deaths (when the probability of dying from Covid-19 is more than two times higher in transplant recipients compared to dialysis patients). Another major criticism for the study is the (inappropriate) assumption that the probability of Covid-19 death in transplant recipients does not change according to vaccination status. In other words, the model could have underestimated the mortality in non-vaccinated transplant recipients.

Another argument against a vaccine mandate for kidney transplant candidates, as a result of recent drug development, is the emergence of therapeutic monoclonal antibodies. The current monoclonal antibodies (casirivimab and imdevimab, cilgavimab and tixagevimab), however, have limited neutralizing activity against BA.1 and BA.2 omicron variants after administration to immunocompromised patients.<sup>64</sup> Based on the suboptimal protection to protect kidney transplant recipients against infection, the arguments of moving from vaccine to monoclonal antibody as pre-exposure prophylaxis remain speculative. Regarding the use of monoclonal antibody such as cilgavimab and tixagevimab, another ethical issue would be the controversy of granting these drugs for transplant candidates who decline vaccination. Policy makers, transplant pharmacists and doctors need to make decisions concerning the appropriate prevention measures. In other words, should transplant candidates get priority for the monoclonal antibody treatment if they decline SARS-CoV-2 vaccines? To address this issue, consideration should be given to the supply of

monoclonal antibodies, effectiveness of the monoclonal antibodies for the predominant variants circulating in the community, immune response of the patients to vaccines. From the standpoint of distributive justice, the weight assigned to the fair distribution of monoclonal antibodies to transplant candidates should be given due consideration of the inequalities that have already existed among this cohort of patients who have higher infection rates, higher mortality, and less access to the healthcare. According to the National Institutes of Health guidelines in the United States, however, the monoclonal antibodies should not be considered a substitute for Covid-19 vaccination and, in particular, should not be used in unvaccinated individuals in whom Covid-19 vaccination is recommended and who are anticipated to have an adequate response. On the other hand, many transplant candidates face significant emotional and existential threats; emotional support and dedicated pre-transplant patient education are fundamental to prepare and equip them with knowledge.<sup>65</sup>

One ultimate and useful solution would be moving away from the language of mandated treatments and, instead, aiming to assess the risks and benefits on an individual basis.<sup>47</sup> That would entail exploration and understanding the reasons behind any transplant candidates' vaccine hesitancy. Vaccine acceptance has been found to decrease with financial hardship, lower age and education, and among those with suspected past Covid-19 infection.<sup>66</sup> Rather than a blanket policy of mandatory vaccination, doctors and transplant healthcare workers should aim to encourage, and not enforce vaccination. In tandem with respect for autonomy, mutual trust plays a key role in doctor-patient relationship, and more so in long term dialysis or transplant care. A growing body of literature suggests that one of the most effective means of communicating vaccine information to

parents is through sharing anecdotes and nudging, in contrast to coercion.<sup>67,68</sup> A more caring approach has been proposed. The approach, called patient-centered trauma-informed (PTCI) approach<sup>55</sup>, refers to the need to acknowledge patient's past trauma and its impact on patient interactions and treatment decision-making. Instead of informing patients in terse letters that they were ineligible to receive kidney transplant until getting vaccinated, PTCI calls for compassion, trustworthiness, collaboration and dignity.<sup>55</sup> As such, transplant healthcare workers and health authorities should work to improve health literacy of kidney transplant candidates, and should listen actively to patients regarding their concerns and vaccine hesitancy.<sup>69</sup> The bottom line is for the patients to meet trained clinicians and discuss their concerns. Other measures of protecting against infection, including proper hygiene and social distancing, should also be encouraged.

### **Challenge 3: Should vaccination of transplant healthcare workers be mandatory during pandemic?**

The issue of mandating Covid-19 vaccination is less controversial for healthcare workers than patients, although such policy could have been in tension with the healthcare workers' autonomy.<sup>70</sup> As previously signed by more than 80 organizations, a joint statement representing physicians, nurses, pharmacists, physician assistants, nurse practitioners, epidemiologists, public health workers and long-term care workers, has called for universal vaccination of health workers.<sup>71</sup> The rationale for such mandate is based on three important reasons.<sup>71,72</sup> First, that is considered a general ethical duty of healthcare workers to protect others. Second, getting vaccinated is considered a special duty to achieve professional objective and be committed to putting patients first. Mandating health workers to have vaccine, in short, implies a policy of mandatory

assignment to different tasks within the hospital. Whether it is ethically acceptable to dismiss the health workers because they refuse vaccination is another issue. Third, this is not new but an extension of well-established and historical practices such as getting vaccinated against influenza, hepatitis B and other infectious diseases. Indeed, large-scale longitudinal analysis of national data over 23 years has recently showed that state laws promoting influenza vaccination for hospital workers were associated with reductions in annual pneumonia and influenza mortality by 1.92 deaths per 100,000 persons in the general population.<sup>73</sup> The magnitude of population mortality reduction was especially obvious among elderly persons. Mandating SARS-CoV-2 vaccination for transplant healthcare workers is expected to protect the lives of vulnerable populations and build trust with the public. Genomic and epidemiological investigation has previously confirmed rapid nosocomial outbreaks of SARS-CoV-2 dissemination within the hospital setting triggered by asymptomatic healthcare workers, amplified by healthcare worker transmission to healthcare workers and patients.<sup>74</sup> Healthcare workers have been repeatedly demonstrated to be the previously hidden link between contact clusters in hospital environments.<sup>75</sup>

In addition to the abovementioned argument for healthcare workers to receive vaccination to protect the patients, we should also be mindful of the workers' autonomy and concerns. Efforts should be made to address the vaccine hesitancy (and more so when this overlaps with other disadvantages in the workplace). Flexibility of implementation, including time frame for different types of employees (clinical staff versus clerical staff), grace period before enhanced education and vaccine acceptance, re-deployment of employees, could be considered and subjected to the difference in cultural and legal settings.

## CONCLUSIONS

The guiding principles for resource allocation including the delivery of kidney transplantation during the Covid-19 pandemic are relatively well established and supported by an ethical framework (Table 1). The dichotomy of continuation versus suspension of transplant activity should best be replaced by a stepwise approach (Table 2). Decision to continue or suspend transplant activity during the Covid-19 pandemic requires a risk-stratified approach strongly incorporating patient views. The decision on mandatory vaccination for kidney transplant candidates (Table 3) is much more controversial, partly due to concerns regarding autonomy and violation of human rights. Arguments to mandate vaccination before transplant waitlisting are outweighed by arguments in favor of strongly recommending vaccination to patients but respecting their autonomous choices. We recommend moving away from coercion to encouragement of vaccination. After documented risk-benefit discussions are held, based on trusted patient-clinician relationships, and on individual risk assessment of morbidity and mortality risk after transplantation, kidney transplantation should not be declined for people who do not wish to be vaccinated. In contrast, we found a stronger, but not necessarily agreed by all, ground for mandatory vaccination for transplant healthcare workers. The mandate for healthcare workers seems indisputable given the need to protect themselves and others. The debate is contentious, however, if this is associated with loss of jobs and when perceived as coercion and loss of autonomy.

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Table 1. Ethical framework for guiding kidney transplantation management during Covid-19 pandemic.

Ethical Values and Guiding Principles	Application to kidney transplantation and Covid-19 pandemic
<b>Maximize total benefits: Utilitarianism</b> Save the most lives Save the most life-years – maximize prognosis	Receives the highest priority Receives the highest priority
<b>Treat people equally: Egalitarianism</b> First-come, first-served Random selection	Should not be used Used for selecting transplant recipients with similar HLA matching to donor
<b>Promote and reward social usefulness</b> (reciprocity or benefit to others) Retrospective – priority to those who have made relevant contributions  Prospective – priority to those who are likely to make relevant contributions	Gives priority to previous organ donors when other factors such as maximizing benefits are equal Gives priority to vaccinated patients when other factors such as maximizing benefits are equal
<b>Give priority to the worst off: Prioritarianism</b> Sickest first Youngest first	Used when it aligns with maximizing benefits Used when it aligns with maximizing benefits such as preventing spread of the virus

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Table 2. One of the proposed frameworks for phased approach to kidney transplantation activity during Covid-19 pandemic.

Kidney transplant activity level	Priority level description	Examples (include but not limited to)
25% reduction in transplant activity	Elective cases: patients whose conditions is not life threatening or can be managed with dialysis and for whom services can be deferred until the end of a pandemic wave (around 6 to 8 weeks)	No living donor activity Deceased donor activity allowed
50% reduction in transplant activity	Urgent cases: patients who are deemed urgent and who need service within 14 days Services can be deferred for a few days, but not for the length of a pandemic wave	No activity except highly sensitized cases (such as panel reactive antibody of 95% or above with suitable donor offer and negative donor specific antibody)
75% reduction in transplant activity	Emergency cases: patients who are deemed critical, whose condition is immediately life-threatening	No activity unless for medically urgent status (such as lack of dialysis access, uraemic cardiomyopathy) Combined kidney-pancreas transplant is not suggested
100% reduction in transplant activity	Health system is overwhelmed with Covid-19 No intensive care unit or other capacity available Severe shortage of health personnel	Complete cessation of all living and deceased donor transplant activity

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Table 3. Ethical arguments for or against mandatory vaccination before transplant waitlisting.

Arguments for mandating vaccination in transplant waitlisted candidates	Arguments against mandating vaccination in transplant waitlisted candidates
<b>Duty to protect patients: first do no harm</b> High mortality of Covid-19 in transplant recipients Additional risk of mortality in immediate post-transplant period	<b>Autonomy and human rights</b> Respect patient decision Clear difference between vaccination passport for tourism and access to life-saving transplantation Unfairness to less educated or health illiterate populations who are

	more likely to be misinformed by “fake news”
<b>Potential harm to others</b> Ensure safety of others and the hospital as a whole	<b>Equity of access</b> Damage to trust in medical profession
<b>Inappropriate use of a scarce resource</b> Maximize the benefit derived from the scarce resource of donated organs Damage to public perceptions of organ donation	<b>Practical uncertainties</b> Efficacy of SARS-CoV-2 vaccine Uncertain efficacy to limit infectivity and virus transmission, especially new virus variants
<b>Possible precedents</b> Predicating transplantation listing on aspects of patient choice or behavior such as abstinence from alcohol for liver transplant Poor compliance behaviour before transplantation as a predictor for non-adherence after kidney transplant	

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Figure 1. Schematic diagram of factors in favor or against of maintaining kidney transplantation during Covid-19 pandemic Table 1. Ethical framework for guiding kidney transplantation management during Covid-19 pandemic.

