Controversies in Living Kidney Donation

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Summary: The most precious gift that can be given is, arguably, a living organ to a person in need of replacement because of failure of that organ. Kidney transplantation remains the best modality of renal replacement therapy and there is an ever-increasing demand for organ donation. The inability of cadaveric organ donation to meet the needs of the increasing numbers of patients on global waiting lists highlights the important needs for alternate sources for kidneys such as those from living kidney donation. However, living donor kidney transplantation has been a focus of intense debate, with ethical concerns and controversies emanating from operating on an individual who does not need, and is put at a small but quantifiable risk from, the surgical intervention. Furthermore, health care systems across the world also are funded with different levels of national and individual affordability, leading to health inequalities for the sick and risks of exploitation for the poor, especially through commercialization of transplantation. This article highlights some of these contemporary ethical concerns and controversies in living organ donation.

Keywords: Kidney transplant, organ donation, living kidney donor, ethics, controversies

Kidney transplantation remains the best modality of renal replacement therapy. There is an ever-increasing demand for organ donation, especially given that the global burden of chronic kidney disease is increasing and it is projected to become the fifth most common cause of years of life lost globally by 2040.[1] It is estimated that approximately 850 million people currently are affected by different types of kidney disorders.[2]

The inability of cadaveric organ donation to meet the needs of the increasing numbers of patients on global waiting lists highlights the important needs for alternate sources for kidneys, such as those from living kidney donation. Living donor kidney transplantation also has the best outcome and, if available, is the treatment of choice for patients with end-stage kidney failure.[3]

Because the identification of a living donor largely is dependent on the prerequisite ad hoc actions of a potential recipient, the oversight and promotion of living organ donation by national organizations is limited as compared with cadaveric donation. Instead, it is usually the individual transplant center that largely is responsible for the whole process of living kidney donation.[4]

Living donor kidney transplantation has been, since the original identical twin donation in 1954 in Boston,[5] a focus of intense debate, with ethical concerns and controversies emanating from performing surgery on an individual who does not need, and is put at a small but quantifiable risk from, the surgical intervention. Health care systems across the world are funded with different levels of national and individual affordability, leading to health inequalities for the sick and risks of exploitation for the poor (Table 1[6-8]). Despite the call for "Kidney health for everyone everywhere and equitable access to care" by the World Kidney Day Steering Committee in their advocacy paper in 2020,[9] there remain significant differences in practice globally. This article highlights some of these contemporary ethical concerns and controversies.

CLASSIFICATION OF LIVING KIDNEY DONORS AND THEIR ETHICAL CONCERNS

The most precious gift that can be given is, arguably, a living organ to a person in need of replacement because of failure of that organ. The living organ from a deceased person can provide the needs of many different types of organs, but with limitations in availability compared with the need, the source of most kidney transplants in many countries is the living donor. The absence of deceased organ donor availability is the driving force behind the desperation of the recipient who must have a kidney transplant, especially if dialysis is unavailable or unaffordable. This also drives the emotional forces for kidney donors and provides the leverage for brokers and commercial organ sellers to make money. It is important to understand that the word *must* is, in many environments, not a truthful description of the alternatives that

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Table 1. Variable Model of Health Care and their Funding Across the World[6-8]

Countries/ Regions	Health Care System Model	Current Health Expenditure as % Gross Domestic Product in 2019	Current Public Health Expenditure as a % of Total Tax Revenue	Living Donation Rate in 2020, People per Million
Australia	Beveridge model	10	23.3	7.0
Brazil	Beveridge model	10	Not available	2.1
Canada	National health insurance model	11	23.7	10.42
China	Out-of-pocket model	5	17.1	1.14
Germany	Bismarck model	12	25.5	5.4
Hong Kong	Beveridge model	6.5	27.2	1.33
India	Out-of-pocket model	3	Not available	3.6
Japan	Bismarck model	11	28.1	12.29
New Zealand	Beveridge model	10	Not available	18.13
South Korea	National health insurance model	8	17.5	27.63
United Kingdom	Beveridge model	10	24.2	8.7
United States	Variable	17	58.8	15.81

The health care system models are as follows: Beveridge model: health care both paid for and provided by the government, financed through taxation; Bismarck model: health care paid for by nonprofit insurance firms and provided by public and private service, financed by employees and employers through payroll deduction; National health insurance model: health care paid for by government-run insurance programs and provided by public and private service, financed through taxation; and out-of-pocket model: health care paid for by consumers to public and private care providers, little to no insurance.

face a recipient with end-stage kidney failure. Dependent on age and availability of long-term dialysis treatment as well as comorbidities, it may well be that a transplant is actually not the best alternative available.

The factors that drive a recipient's perceived need for a transplant should be evaluated carefully and dispassionately, before accepting the argument for living donation. These factors are individual and are as follows: age; comorbidities; human leukocyte antigen sensitization; personal treatment preferences; environmental: availability and affordability of dialysis; and availability and affordability of deceased organ donation. At one end of the spectrum there is the 30 year old with polycystic kidney disease and no comorbidities living in a high-income country where deceased organ donation is available with a waiting time of 2 or 3 years, who would have a better long-term outcome from a living donor transplant. At the other end of the spectrum is the same person living in a low-income country, able to afford either only 6 months of dialysis or a kidney transplant surgery. Who will come forward to donate and save his life?

Living kidney donors usually are either family members, spouses, or close friends with a motive to improve or save the individual recipient's life. The best outcomes are from human leukocyte antigen−matched siblings, but with available modern therapies each of these donors is acceptable—if medically suitable to donate and as long as the recipient has no donor-specific antibodies. Few individuals in society believe it incumbent upon themselves to donate to someone who they do not know, but there are a few who, after careful medical and psychosocial evaluation, prove determined to donate. Such altruistic donors do not have the benefit of seeing someone they love heal from the effects of end-stage kidney failure, but live with the knowledge that they have helped another person in extraordinary ways. Some have argued that an individual should have the right to sell their kidney to a recipient in a commercial transaction, an issue that is considered further in this article.[10]

Donors are faced with a variable degree of pressure to donate and it is important to dissect the issues and understand them for each individual. At a simplistic level one simply can regard this as a routine part of gaining informed consent, but neither the information nor the consent are straightforward. There is a naïve belief that family member donation is emotionally safe and simple from an ethical perspective. The imbalance of female donors to male family members across the world is either a testament to the greater altruism shown by females than males, or relates to a power imbalance between family members.[11,12] In many societies this imbalance seems to be driven by the need to maintain the health of the breadwinner. In other situations, one has the always-unproven suspicion that a wealth imbalance between the recipient and donor drives the donation. Trying to understand the true driving forces for a donor offer is an important part of any living donor program and at the very least requires independent evaluation of donor motivation, unimpeded by the presence of the recipient. The degree to which the burden of proof rests with the transplant program, an independent individual, or a specially constituted ethical review committee varies between nations, and to a certain extent reflects the different pressures for commercial kidney transplantation in different countries.

A successful living donor transplant, in which both the donor and recipient live happily ever after, is a reasonably frequent occurrence[13] and provides a justification for the risks that both individuals have taken.

Unfortunately, there are occasions when this does not work out for either the donor or the recipient, or both. Adverse donor consequences usually, but not always, occur early after donation and are resolved satisfactorily.[14] Long-term donor consequences may take 30 years to play out, with a small proportion of donors developing end-stage kidney failure themselves.[15,16] Recipients are subject to the vagaries of post-transplant complications and events that should have been understood by both donor and recipient as part of informed consent. It is when the information process is inadequate, or when events are related to donor-derived disease, that the adverse events are felt most severely.

THE ETHICAL–LEGAL IMPACT OF PAIRED KIDNEY EXCHANGE PROGRAMS

Many patients have willing live donors who cannot donate to them because they are biologically incompatible, either they are blood group ABO incompatible or the recipients have preformed donor-specific antibodies, putting them at risk of hyperacute rejection.[17] Paired kidney exchange is an option in which the donor kidneys are exchanged with another prospective donor-recipient pair who also are biologically incompatible. This exchange program offers both parties an opportunity for a living donor transplant in a mutual beneficial way, sparing them the long waiting time for a cadaveric donor or the need for the riskier, costly, and sophisticated technique of desensitization.[18]

The idea of paired kidney exchange was first proposed in 1986,[19] but it was not until 1991 that the first paired kidney exchange transplantation was performed in South Korea, gaining international recognition.[20] Currently, several countries, such as Australia, Canada, South Korea, the United States, and many European countries, have developed a robust paired kidney exchange program involving two or even more pairs.[21-24] However, the approval of this practice is not universal and many countries (eg, Japan) prohibit live organ donations to strangers, rendering the implementation of the paired kidney exchange illegal in their locality.[25] Paired kidney exchange, however, is not without significant ethical concerns, in particular concerning the protection of live donors.

The most simple form of a paired kidney exchange is a two-way exchange among two incompatible pair within a single center (Fig. 1A[26]). However, there are now more advanced ways with increasing complexity to arrange the exchange to maximize the number of potential beneficiaries (Fig. 1B,[26]). For example, a domino paired kidney exchange involving a non-directed altruistic donor may initiate a large donation chain similar to a domino (Fig. 2A).

One caveat of these exchanges is that, in most countries, they are performed simultaneously, which makes

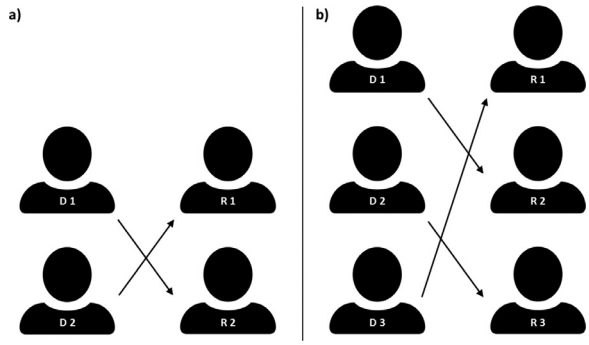

Figure 1. Different types of simple paired kidney exchanges. (A) Two-way exchanges, and (B) three-way exchanges (can be more than three-way; ie, n-way exchange). Adapted from Kher et al.[26]

multiple simultaneous surgeries and the logistics of such exchanges technically challenging. This is partly owing to the perceived risk of the donor reneging on their promise to donate once their recipient receives a kidney. However, there have been successful, nonsimultaneous, extended, altruistic donor chains, in which the final donor, instead of donating to a wait-listed patient, waits until a suitable match is found with a new incompatible pair, thus becoming a bridge donor to initiate another chain of donation[27] (Fig. 2B). Although arguably the risk of the bridge donor reneging is potentially higher, especially if there has been a poor outcome for their recipient. Despite that, the rate of reneging bridge donors appears to be small, and it has been argued that the benefits from nonsimultaneous, extended, altruistic donor chains outweigh these risks.[28]

Paired kidney exchange has several ethical limitations. First, it often is not possible to match all the pairs depending on the size of the pool of pairs. Second, blood group O recipients are disadvantaged and accumulate on the list, given group O donors are universal donors.[29] Similarly, AB donors also accumulate on the list. The donors themselves are also at greater pressure to donate as the excuse of incompatibility is removed.

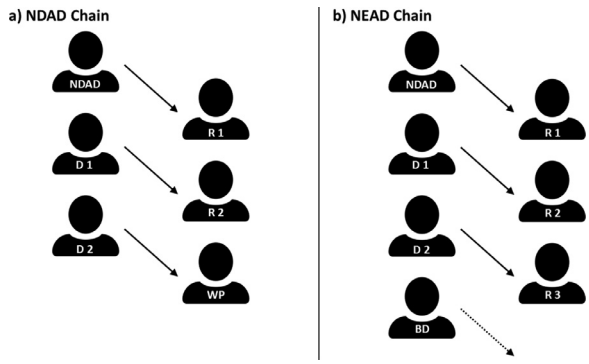

Figure 2. Matching strategies with nondirected altruistic donors (NDAD). (A) NDAD starting chain ending up with the final kidney to a recipient on the waiting list (WP); (B) nonsimultaneous extended altruistic donor (NEAD) chain ending up as a bridge donor (BD) who can start a new chain. Adapted from Kher et al.[26]

Table 2. Arguments for and Against Absolute Anonymity for Donor and Recipient

		Before Transplantation	After Transplantation
Donor	For	Donor privacy Maintaining the perception of an altruistic act Protection against pressure to donate Avoid prejudice against donor and possible withdrawal	Donor privacy Maintaining the perception of an altruistic act Allow closure for the donor to move on Protect against idealization of recipient or poor recipient outcome
	Against	Paternalistic and lack of autonomy if donor wishes to break anonymity	Paternalistic and lack of autonomy if donor wishes to break anonymity May lead to donor having anxiety or obsession about recipient outcomes No opportunity for positive experience (eg, gratitude from recipient)
Recipient	For	Recipient privacy Avoid the risk of the donor attempting to seek reward/commercialization of transplantation Protect against idealization of donor Avoid prejudice against recipient and possible withdrawal	Recipient privacy Allow closure for the recipient to move on Protect against idealization of donor and psychologic rejection Avoid the risk of the donor attempting to seek reward Avoid the recipient feeling in debt to the donor
	Against	Paternalistic and lack of autonomy if recipient wishes to break anonymity	Paternalistic and lack of autonomy if recipient wishes to break anonymity Unable for recipient to express gratitude Need for medical information about donor (eg, transmissible disease)

There are also the issues of anonymity in living donor kidney transplantation. Traditionally, the anonymity of both the donor and recipient is absolute and there are compelling reasons for and against such practice (Table 2).[30] However, there are emerging concepts of conditional anonymity, in which the altruistic donor −recipient pair are allowed to break anonymity after the transplantation. Indeed, a previous survey performed in The Netherlands and Sweden, where it is not allowed to break anonymity after transplantation, showed that although donors and recipients usually were satisfied with anonymity, the majority viewed a strict policy on anonymity as unnecessary and were open to meeting the other party if the desire was mutual.[31]

Pronk et al[32] recently published a study on the UK policy of conditional anonymity for living donors. A total of 207 recipients and 354 donors participated in a questionnaire on their experiences with and attitudes toward anonymity. Pronk et al[32] reported that anonymity was relinquished among 11% of recipients and 8% of donors, with their experiences being positive upon meeting the other party. Those participants who remained anonymous were content with anonymity, but 38% of them would have liked to meet post-transplant, and this number further increased to 64% if the other party also would have liked to meet. Overall, these results support the expansion of conditional anonymity to other countries that allow anonymous living donor transplantation. Thus, although the anonymity before and after the transplantation should be maintained with good reasons, the anonymity can be revoked conditionally after the transplantation if both the donor and recipient agree, after adequate counseling and support.

Other new and bolder modalities, along with a greater clinical and ethical risk, were conceptualized. One such example is the trans-organ paired exchange, wherein a donor who is ruled out for donating a kidney for some reasons still is able to donate another organ for exchange of a kidney from another pair who required a donation of the other organ.[33] Although this is an attractive proposition, one must note the surgical risk of donation is imbalanced between the different organs.[34] Another example is the advanced donation program, in which the potential recipient receives a voucher if his/her donor donates their kidney in advance as a nondirected donor to initiate a chain. The potential recipient may not yet be in need of a transplant, but the voucher can be redeemed at a later date when indicated. This may be helpful for donors who may become too old to donate by the time the recipient is in actual need of a transplant kidney.

Finally, global kidney exchange is postulated as a strategy whereby the kidneys are exchanged between a pair from a high-income country (HIC) and one from a low- or middle-income country (LMIC). It is suggested that the pair from the LMIC may even be compatible biologically but financially unable to proceed to transplantation, while the pair from the HIC is biologically incompatible. These exchanges may enable the pair from the LMIC to receive the financial aid required for a transplantation using funds saved from the cost of dialysis from the HIC pair.[35] This concept, of course, is fraught with ethical concerns because the advantage is skewed toward the HIC pair. There is a risk of exploitation of vulnerable LMIC pairs and post-transplant care of recipient−donor pairs from a LMIC cannot be guaranteed once they return home.[36]

MINORS AS LIVING KIDNEY DONORS

More contentious ethical concern is the consideration of using minors as potential donors. To what extent shall minors be allowed to donate a kidney to a sibling or even his/her much beloved grandparent? From whom is consent required or is the consent even valid? The child may feel coerced by parents to donate the kidney because they worry that they may lose parental love by refusing to donate. The surgical procedure also is not without short- or long-term risk and may subject the child to harm, both physically and mentally. The surgery, along with the postoperative recovery phase, may disrupt the child's development and daily activities such as school and sporting commitments. Furthermore, even if the surgery is successful, there will be risks to the child's remaining kidney (including the development of kidney disease, injury to the kidney, and others), which may alter the child's future, such as career options and also insurance premiums.[37]

In many countries, donation of a nonregenerative organ by a minor is banned by law, but in some countries there is no legal cut-off age for donation. Some physicians argue that most children aged 14 or older may have the competent thought process of an adult with regard to making decisions about their health. In fact, several states in the United States have granted adolescents age 14 years and older the right to consent to medical treatment intended for their benefit.[38] However, this is certainly not practiced worldwide and some countries, such as Australia, only allow a competent minor to donate regenerative tissue, such as bone marrow.[39]

Before accepting the minor's consent, his or her competency must be assessed by a skilled psychiatrist, similar to that in an adult. The parents also should be consulted and agree to the donation. In addition, the court should be involved to confirm the minor's competence and that "the donation could provide a clear benefit to the donor (one scenario can be a child, who is the only available organ source, donating his kidney to his father who is the sole carer for the child).[40] In particular, several conditions should be met[41]:

- The child donor is the only available organ source;
- The transplant procedure has a very high possibility of success, and the risk to the donor is extremely small;
- Both the donor and the recipient will benefit from the procedure;
- The recipient is a close family member;
- The minor freely assents to donate without coercion (established by an independent advocacy team); and
- The emotional and psychological risks to the donor are minimized.

The benefit also should be taken into account of the longer-term consequences for the child donor and the recipient. For example, the psychological benefit for the child donor to extend the life of his elderly grandfather for a few years as a result of his kidney donation may pale into insignificance if his grandfather dies of a heart attack a few years later nonetheless, or when the child donor becomes diabetic in his 30s and has end-stage kidney disease by his 40s. Regardless of these conditions, many serious ethical concerns remain unresolved and minor donations surely only should be considered in the most exceptional circumstances.[42,43]

THE ROLE OF THE TRANSPLANT TEAM

It is imperative that the transplant team serves as a gatekeeper in assessing whether to proceed with the transplantation, both clinically and ethically. In addition, there should be an independent assessor in parallel to the transplant team, given the inherent conflict of interest of the transplant team in the whole process of transplantation. The concept of an independent living donor advocate, a medical third party to ensure the protection of living donors and prospective donors, has been promoted and practiced in countries such as the United States.[44] This ensures an impartial assessment of the donor with regard to their understanding of the pros and cons of donation and that the decision is made voluntarily without any undue pressure or coercion, ultimately securing informed consent from the potential donor.

It also is important for both the donor and the recipient to understand the risks of donation, weighing the risks versus the benefits of such a self-sacrificial act. A recent review by Mamode et al[45] highlighted that one of the common errors in considering the risks of donation is to focus on relative, rather than absolute, risk. Instead, the use of absolute risk has been recommended specifically for living donors.[46] Nevertheless, this discussion of risk and benefit should be individualized and objective. Some physicians have argued that potential donors may not require extensive information and time for reflection to decide whether to donate because the initial decision made by a close relative of the recipient often is genuine and ethically acceptable.[47,48] However, adequate information always should be provided to the potential donor, and the donor's comprehension of his role in transplantation should be established and well documented. Furthermore, there have been novel tools to improve the donor's understanding of the risks of donation. One such example includes the donor-specific risk questionnaire, a dot matrix visual aid to improve patient engagement and to assess the donor's willingness to accept kidney failure risk.[49] Thiessen et al[49] showed that the visual aid can provide the transplant teams with individualized donor perspectives on risk thresholds, which potentially can facilitate greater patient-centered care for living donors.

Another important principle the transplant team should adhere to and is enshrined in the Hippocratic Oath is as

follows: first, do no harm. For example, should the surgical team remove a kidney through a high-risk procedure from a donor on request, in his bid to save his beloved, even though the donor accepted the high risk willingly? Apart from acting in the best interest of their patient, the transplant team also is responsible for the potential donor's well-being and to do no harm. Although the risk of morbidity and mortality in the organ's donor is low, it is an unnecessary surgery from the donor's health point of view and it would be unethical to conduct harmful medical interventions deliberately. One such example was the rejection of a donor, who wanted to donate his sole kidney to his daughter after having donated the other kidney to her a few years earlier.[50] If the transplant team deemed a potential donor unsuitable, the team should inform that donor of the reasons for rejection and offer a referral for a second opinion.

COMMERCIALIZATION OF ORGAN TRANSPLANTATION

The World Health Organization (WHO) recognized and prohibited commercial trade in human organs in the 1991 WHO Guiding Principles on Organ Donation and Transplantation.[51] "Organs should be donated freely, without any monetary payment or other monetary reward." It has been repeated in the revised WHO Guiding Principles, which was endorsed in 2010. It also is embodied within the 2008 Declaration of Istanbul.[52,53] The latter defines transplant commercialism as "a policy or practice in which an organ is treated as a commodity, including by being bought or sold or used for material gain." The WHO commentary associated with the 2010 guiding principles explains the rationale (Box 1), as does the subsequent 2016 Council of Europe Convention,[54] which takes the next step by creating a legally binding and enforceable international treaty. National laws prohibiting transplant commercialism and human organ trafficking stemming from these international instruments now are enacted in most countries with transplantation programs.

Two issues are more complex than one might imagine. The first is the precise definition of commercialism. Can a recipient reimburse a donor for the costs of travel to the hospital and pay for the health care costs involved in medical assessment and the donor surgery? This clearly does not contravene the various statements and is widely permitted. What about lost wages for the period of the evaluation, surgery, and recovery? Also usually deemed acceptable, but if the recipient were to fund health care insurance to cover future health care for the donor, ostensibly to cover any adverse events arising from the donation, this now extends to being a valuable consideration.

The second problem is that to break most national organ transplant laws, an individual actually has to do something (ie, the donor has to undergo surgery and the recipient actually has to pay money). It thus is not illegal to plan; it only becomes illegal after the event. For this reason, a number of countries have amended legislation to include intent to undertake commercial transplantation as illegal to prevent proactively any commercial transplants and provide a clear disincentive for those planning to broker such transplants.

Despite the international and national jurisdictional and professional frameworks designed to protect both donor and recipients from commercialism and human trafficking, it is disturbingly common across the world. In nations with affordable and high-quality dialysis and transplant programs, commercial transplants are rare. There is very limited incentive to pay for and perform an illegal procedure. A few wealthy people consider the option when barred by an absence of a voluntary living donor and a long waiting time for deceased donor transplantation, or a medical evaluation that precludes listing for transplantation. Illegal commercial transplant programs pay scant heed to medical suitability for transplantation and no attention to the origin of the organ, as long as all bills are paid before the procedure.

The most common dilemma globally is faced by potential recipients living in countries with absent or low-quality transplantation and unaffordable chronic dialysis. For these patients with end-stage kidney failure, death is a real likelihood if they do not have a voluntary donor in the family. It is these patients that the organ brokers prey on, seeking large amounts of money to arrange for a paid kidney donor. The brokers also prey on the poor to supply the kidney, often defrauding them of most of the money that they promise. Research in such countries has shown that the poor do not extract themselves from poverty, as they hope, and recipient outcomes are commensurately bad.

The Declaration of Istanbul Custodian Group monitors and publicizes, through their website, the ongoing toll of organ trafficking and commercialism.[55] It remains a responsibility of all renal programs to remain vigilant for signs of an unwilling donor unrelated to the recipient and with a marked disparity in wealth between people proposed to be closely related. Brokers and the ethics committees they try to delude are both becoming more sophisticated and while the transplant surgeons in heavily regulated but highly commercial health care systems try to absolve themselves of responsibility, in the final analysis it is their responsibility to use the knife ethically, wisely, and legally.

Living kidney donation provides one of the most precious gifts possible. It is truly invaluable to a person in need of a transplant and therein lies the unrelenting pressure for commercial transplantation. We, as kidney transplant professionals, should exercise our highest discretion in assisting kidney failure patients to find a suitable donor, albeit deceased or living. The protection of

the rights and welfare of the kidney donor is of utmost importance for the transplant team. As mentioned, an independent living donor advocate would serve well to maintain the donor selection process to be impartial and protect the interest of the donor without regard for the recipient. It is impossible as a transplant physician or surgeon to act on behalf of both the donor and the recipient without a conflict of interest. The enhancement of the paired kidney donation program would be able to allow more kidney failure patients' access to suitable kidneys for transplantation. The altruism of live kidney donation should be honored and promoted to the public to facilitate the growth of the program for kidney failure patients.

Box 1 WHO Guiding Principles on Human Cell, Tissue, and Organ Transplantation[53]

"Payment for cells, tissues and organs is likely to take unfair advantage of the poorest and most vulnerable groups, undermines altruistic donation, and leads to profiteering and human trafficking. Such payment conveys the idea that some persons lack dignity, that they are mere objects to be used by others.

In addition to preventing trafficking in human materials, this Principle aims to affirm the special merit of donating human materials to save and enhance life. However, it allows for circumstances in which it is customary to provide donors with tokens of gratitude that cannot be assigned a value in monetary terms. National law should ensure that any gifts or rewards are not, in fact, disguised forms of payment for donated cells, tissues, or organs. Incentives in the form of rewards with monetary value that can be transferred to third parties are not different from monetary payments.

Although the worst abuses involve living organ donors, dangers also arise when payments for cells, tissues, and organs are made to the next of kin of deceased persons, to vendors or brokers, or to institutions (such as mortuaries) in charge of dead bodies. Financial returns to such parties should be forbidden."

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