Global Kidney Exchange: opportunity or exploitation? An ELPAT/ESOT appraisal

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Abstract

This paper addresses ethical, legal and psychosocial aspects of Global Kidney Exchange (GKE). Concerns have been raised that GKE violates the non-payment principle, exploits donors in low and middle-income countries, and detracts from the aim of self-sufficiency. We review the arguments for and against GKE. We argue that while some concerns about GKE are justified based on the available evidence, others are speculative and do not apply exclusively to GKE but to living donation more generally. We posit that concerns can be mitigated by implementing safeguards, by developing minimum quality criteria and by establishing an international committee that independently monitors and evaluates GKE's procedures and outcomes. Several questions remain however that warrant further clarification. What are the experiences and views of recipients and donors participating in GKE? Who manages the escrow funds that have been put in place for donor and recipients? What procedures and safeguards have been put in place to prevent corruption of these funds? What are the inclusion criteria for participating GKE-centers? GKE provides opportunity to promote access to donation and transplantation but can only be conducted with the appropriate safeguards. Patients' and donors' voices are missing in this debate.

Glossary

Alliance for Paired Kidney Donation (APD):a charitable foundation that aims to establish a universal system that pairs living persons willing to donate a kidney with those needing kidney transplants, in order to increase the number of living donor kidney transplants; improve outcomes for kidney transplant recipients; and significantly reduce public and private costs incurred by chronic kidney disease

Council of Europe (CoE): an international organization whose aim is to uphold human rights, democracy and the rule of law in Europe.

Council of Europe Committee on Organ Transplantation (CD-P-TO): the steering committee in charge of organ transplantation activities at the European Directorate for the Quality of Medicines & Healthcare

Council of Europe Convention against Trafficking in Human Organs (CoEConvention): a treaty that calls on governments to establish the illegal removal of human organs from living or deceased donors as a criminal offence. Legally binding for governments that ratify the convention. Ratified by 9 member states at time of writing.

Declaration of Istanbul on Organ Trafficking and Transplant Tourism 2018 Edition (DoI): statement that defines and prohibits organ trafficking, trafficking in persons for organ removal and transplant tourism. Calls upon transplant professionals to endorse ethical transplant practices. Not legally binding**.**

Declaration of Istanbul Custodian Group (DICG): a group of professionalsthat promotes, implements and upholds the Declaration of Istanbul so as to combat organ trafficking, transplant tourism and transplant commercialism and encourages adoption of effective and ethical transplantation practices around the world.

European Network for Collaboration on Kidney Exchange Programmes (ENCKEP): a network supported by European Cooperation in Science and Technology. Brings together policy makers, clinicians, economists, social scientists and optimisation experts in Europe in order to establish and foster a channel for a transnational European kidney exchange program.

European Society for Organ Transplantation (ESOT): the umbrella organization under which transplant activities are structured and streamlined in Europe and worldwide.

Ethical, Legal and Psychosocial Aspects of Transplantation (ELPAT): European platform that brings continuity and progress in European research and dialogue on Ethical, Legal and Psychosocial Aspects of organ Transplantation. Section of ESOT.

European Union's National Competent Authorities on Organ Donation and Transplantation (NCA): bodies within the governments of the European Union member states that transpose European Union requirements related to organ donation and transplantation into national law.

Global Kidney Exchange (GKE): an international kidney exchange program that facilitates cross-border exchanges between immunologically incompatible donor-recipient pairs in high income countries.

Kidney exchange programs (KEP): programs that enable transplantation for recipients who have a willing living donor but are blood- and/or HLA incompatible with this donor. These incompatible pairs join a pool of recipient-donor pairs and compatible matches are made using an algorithm. Also referred to as kidney sharing schemes.

World Health Organization (WHO): an international organization that directs international health within the United Nations' system and leads partners in global health responses. Its Guiding Principles on Human Cell, Tissue and Organ Transplantation outline principles that are intended to provide an orderly, ethical and acceptable framework for the procurement and transplantation of human cells, tissues and organs for therapeutic purposes.

Introduction

In 2017, Rees et al. introduced 'Global Kidney Exchange' (GKE), an international kidney exchange program that facilitates cross-border exchanges between immunologically incompatible donor-recipient pairs in high income countries (HIC) and biologically compatible but financially impoverished donor-recipient pairs in low to middle income countries (LMIC) (1). GKE aims to overcome immunologic barriers in the developed world and poverty barriers in the developing world. The underlying rationale is that financial barriers prevent transplantation much more frequently than organ scarcity. The number of patients dying annually worldwide from end-stage kidney disease due to inadequate financial resources far exceeds the number of patients in developed countries placed on kidney transplantation waitlists (1-3). GKE has the potential to expand the genetic diversity of the donor pool which may help to transplant difficult–to-transplant, highly immunized patients (1).

In GKE, the health insurance company of the HIC recipient funds both transplants from the costs saved from avoiding or ceasing dialysis. This way, barriers are removed for patients who have a willing living donor but cannot afford the operation or do not have health insurance to cover the costs of donation and transplantation. For national health systems in HIC, global exchange is more cost-effective than continued dialysis. For example, a recent analysis of renal replacement therapy costs in The Netherlands indicates that after a successful transplantation, costs are annually approximately 14%-19% of annual dialysis costs (4). In addition, a new donor-recipient pair in the pool facilitates the transplantation for HIC incompatible pairs and increases the potential to make new chains. At the time of writing, Rees et al. have performed 7 GKE exchanges with The Philippines, Denmark and Mexico, enabling 36 transplantations (5).

GKE has received criticism and opposition from the Council of Europe Committee on Organ Transplantation (CD-P-TO), the European Union's National Competent Authorities on Organ Donation and Transplantation (NCA), the Declaration of Istanbul Custodian Group (DICG) and a number of transplant professionals (6-11). Their concerns are that GKE:

- violates the principle of non-payment for organs and constitutes organ trafficking;
- is exploitative;
- is coercive;
- may be undermined by corruption;

- cannot guarantee proper care for living donors and transplant recipients in LMIC;
- detracts from countries becoming self-sufficient.

In this paper, we discuss the concerns raised against GKE, but also discuss the potential merits of GKE by providing an overview of ethical, legal and psychosocial considerations. In doing so, we aim to offer a balanced, evidence-based view of arguments for and against GKE.

Does GKE violate the principle of non-payment for organs and does it constitute 'organ trafficking'?

GKE provides funding for a kidney transplant procedure (surgery and related medical treatment) to recipients from a LMIC in exchange for a living donor who facilitates a chain of transplants in HIC (1). According to the DICG, the CD-P-TO and others, this funding violates the non-payment principle and constitutes "organ trafficking" (6-9, 12). The principle of non-payment stipulates that "the human body and its parts shall not give rise to financial gain or comparable advantage" (13, 14). The definition of organ trafficking has been laid down in the 2015 Council of Europe Convention against Trafficking in Human Organs (15) (CoE Convention) and in the 2018 edition of the Declaration of Istanbul on Organ Trafficking and Transplant Tourism (DoI) (16). According to these instruments, virtually all commercial dealings in organs constitute "organ trafficking" (17, 18). Consequently, whereas organ trafficking was initially only associated with exploiting persons for their organs (19, 20), it is now also considered to include the removal of organs for financial gain or comparable advantage (7, 9, 21).

Rees at al. claim that GKE does not violate the non-payment principle, but that it is consistent with the altruistic exchanges in kidney exchange programs (KEP) that are accepted practice in many countries. According to them, donors participating in GKE do not "sell" their organ, but "trade" one healthy kidney for another, similar to donors in KEP (1). The authors further emphasize that GKE removes disincentives for those who would gladly donate a kidney to a friend or family member but cannot due to financial barriers (1).

Removing financial barriers to organ donation is an internationally agreed objective, enshrined, amongst others, in the World Health Organization's (WHO) Guiding Principles on Human Cell, Tissue and Organ Transplantation and in the CoE Convention (13, 15). These organizations highlight that prohibition of organ payments does not preclude reimbursing expenses incurred by the donor, including the costs of medical procedures (13, 17). Given that countries' legislation vary in their approach to what constitutes illicit payment versus legitimate reimbursement, it is doubtful whether GKE violates the non-payment principle under all circumstances. For example, the University of Minnesota's legal team vetted GKE and agreed to proceed. Other hospital legal teams have followed suit (1). However, given the CoE Convention's rather broad definition of "organ trafficking" and the vagueness of the

term, "comparable advantage", it is possible that GKE might be considered unlawful in countries that have ratified the CoE Convention (22).[1]

Whether GKE is considered illegal is however, in our view, not the most critical issue. The prohibition of payment for organs and organ trafficking has received considerable critique, amongst others for conflating payments with "trafficking", for failing to eradicate the crime, and for exposing victims to further harm (20, 23-28). Furthermore, laws are known to follow changing transplant practices (29). A more relevant question is therefore, whether GKE will help to *induce* or *prevent* organ trafficking. While organizations such as the DICG and CD-P-TO fear that allowing GKE will induce the crime, empirical research suggests that what drives organ trafficking more than scarcity is the global inequity in access to donation and transplantation and the growing divide between the rich and poor (28, 30-32). On the one hand, GKE has the potential to reduce global disparities in access to donation and transplantation, in particular, to prevent that only the rich patients have access to transplantation (1, 33). On the other hand, this aim can only be achieved if GKE is carried out on a larger scale. Currently, GKE only offers access to transplantation to a select few (1). If GKE succeeds in reducing disparities in access to donation and transplantation, GKE may contribute to preventing organ trafficking rather than being a constituent of it. If this turns out to be the case, GKE will fulfil the same objectives that the Council of Europe, the DICG and other international bodies have (until now unsuccessfully) been trying to achieve.

Is GKE exploitative?

One criticism of GKE is that it is exploitative, and in order to assess the strength of this claim one must be clear about what one means by exploitation. There is disagreement over where the wrongness of exploitation lies, and it may differ from case to case. It has variously been suggested that exploitation is wrong because it takes advantage of and fails to protect the vulnerable, because it uses people solely as a means to an end, and because it fails to benefit a disadvantaged person in the way that fairness requires (34). The DICG alludes to some of these aspects when it states that "[e]xploitation occurs when someone takes advantage of a vulnerability in another person for their own benefit, creating a disparity in the benefits gained by the two parties" (9). It is hard to see, however, that this description of exploitation can be readily applied to GKE. Primarily, it is not clear that there is a significant disparity in

[1] As of the beginning of 2020, the CoE Convention has been ratified by Albania, Croatia, Czech Republic, Latvia, Malta, Montenegro, Norway, Portugal and Moldova. For further details, see https://www.coe.int/en/web/conventions/full-list/-/conventions/treaty/216/signatures?p_auth=p6Mz9GHQ

benefits between recipients. Each patient receives a kidney transplant, and as Minerva et al point out, benefits are arguably *greater* for LMIC recipients, who get the additional benefit of their follow-up care being paid for (33). The same is true for the donors, who each obtain the desired benefit of their intended beneficiary receiving a transplant. Rather than there being a morally troubling disparity in benefit, GKE appears to offer either roughly equal benefit, or greater benefit for those who are allegedly exploited.

It is also unconvincing to consider GKE exploitative on other grounds. Rather than failing to protect the vulnerable, it seems that GKE addresses specific vulnerabilities by offering protection to those who are a) vulnerable to death from kidney failure or b) vulnerable to losing a loved one due to kidney failure. It is similarly unconvincing to suggest that GKE treats people merely as a means to an end. Instead, one can see that participants in LMIC are respected as individuals, with measures put in place to protect their welfare and to ensure that their participation is voluntary.

Another concern raised by Wiseman & Gill, the DICG and the CD-P-TO is that GKE is not based on humanitarian criteria but instead on the usefulness of the donor from a LMIC for a recipient in a HIC (9, 11). GKE could therefore be considered to be 'people in HIC' taking "advantage of a vulnerability in another person for their own benefit". While this means that the motives of those in HIC may not be purely altruistic, and that the ultimate reason for GKE's existence may be to provide those in HIC with transplants, it does not make GKE necessarily exploitative. Instead, it emphasizes the importance of careful implementation of GKE: if implemented poorly and with inappropriate safeguards to prevent an unfair disparity in benefits, GKE could become exploitative. If implemented with more caution, however, with stringent safeguards and monitoring to ensure that the rights and welfare of involved parties are protected, GKE can provide a fair distribution of benefits and burdens thereby avoiding a charge of exploitation.

Is GKE coercive?

The claim that donors and recipients in LMIC are too poor or vulnerable to voluntarily engage in GKE is also debatable and could be seen as paternalistic. First of all, the risk that voluntariness is undermined does not apply specifically to GKE or to LMIC alone, but applies to living donation more generally (35). The argument that a LMIC donor may feel compelled to donate is equally as relevant to the HIC donor candidate: both are willing but for different reasons cannot help their intended recipient. The potential for pressure to donate is thus present in all KEP. A recent study amongst professionals demonstrated that

safeguarding against coercion is a primary concern during screening in HIC (36). Furthermore, while costs incurred and loss of wages during the living donation process may deter lower income donor candidates (37), (low) economic status is not, and should not, be a contraindication for living donation.

Whether or not participants in GKE feel coerced or that they made a voluntary decision requires investigation. This speaks to the need for a qualitative evaluation of views and experiences of those who participate in GKE. Risks arising from potential pressure or coercion can be mitigated by standardized education, psychosocial assessment by mental health professionals and informed consent procedures that are already in place in countries that have formalized living donation procedures according to universally recognized standards (38-43).

Will corruption undermine GKE?

Rees et al. present a carefully regulated living donation and transplantation program involving a couple from The Philippines, supported by the Alliance for Paired Donation (APD). They reportedly plan to continue the program with transplant centers in Kenya, India, and Ethiopia (6). APD has created a $50.000 escrow account to ensure funding for follow-up care for the Filipino donor and recipient. Although Rees et al. state that they aim to rule out malpractices, they do not describe how they aim to prevent and alleviate possible corruption of GKE (7, 8).

Paradoxically, countries that are most likely to benefit from GKE are those who are the least likely to have safeguards in place to prevent corruption. Research into global financial flows has revealed that more funds leave certain countries than enters them (44, 45). If lump sums resulting from GKE are deposited for donors' and recipients' medical fees upon their return to their country, the questions arise: who has oversight and access to these funds? How are they audited? How is long-term protection of these funds guaranteed? What are the criteria for using the funds (what can the money be used for and what not)?

Another concern is the inability of some countries to protect transplant recipients and donors from transplant abuses (6, 9). GKE seeks to protect and uphold the rights of individual donors and recipients, however, this is not a certainty in countries where a black market of organ trade exists. An increasing number of studies reveal that some governments have been unable to prevent criminal networks from infiltrating into their transplant centers, turn a blind eye to the practice or wittingly facilitate illegal transplants (28, 46-51). In these countries, exploitation of recipients and donors is most often reported (28, 52, 53). In The Philippines,

Egypt, Bangladesh and India for instance, researchers have repeatedly demonstrated that despite these countries' laws banning organ trafficking, vulnerable individuals continue to sell kidneys, do not receive appropriate pre- and postoperative aftercare and are not recognized or treated as victims (52, 54-56). Only a few successful prosecutions of brokers, recruiters, doctors and other facilitators of illegal transplants have been reported from both LMIC and HIC (57-59). The concern therefore arises whether and how governments would address corruption or other violations of GKE if these were to arise.

Rees et al. do not explain how they plan to address possible issues of corruption of GKE and exploitation of donors and/or recipients participating in GKE. They may wish to develop criteria that (prospective) collaborating transplant centers need to satisfy. For example, they may wish to include only those centers that have a transparent and long-term track-record of successful, legitimate transplantation and donation procedures, including standardized donorscreening and follow-up care. All countries participating in GKE, including HIC, should carry equal responsibility to do what is necessary to ensure that patients and donors involved in GKE are adequately protected from the risks associated with corruption, given the need for GKE to avoid venturing into the realms of exploitation.

Can GKE guarantee proper care for living donors and transplant recipients in participating countries?

Another argument against GKE is that participating LMIC are incapable of providing long-term care for transplant recipients and donors (6, 9). This is however not an argument against GKE, but a critique of countries that lack appropriate conditions and safeguards for living donation, registries and follow-up. It can be argued that countries that are unable to implement basic safeguards for living donation, should not be conducting living organ transplants in the first place. It has also been argued that transplant medicine should not come at the expense of primary health-care (60). For this reason, some countries have prohibited transplantation altogether (59).

The claim that these issues only apply to LMIC also warrant careful consideration. First of all, problems with follow-up care of donors and transplant recipients are not exclusively reported from LMIC. Also HIC struggle to ensure that donors do not get lost to follow-up (61-64). While the international transplant community agrees upon the necessity of registration of long-term outcomes (64-67), rates of completion are typically low (62, 63). Moreover, even in HIC, low income recipients experience higher rates of rejection and graft failure than high income recipients (68-70). What's more, it is accepted practice in many

countries to accept living kidney donors (usually relatives) who travel from abroad (71). After their donation, these donors typically return to their country of origin, often without guarantee of post-operative and long-term follow-up care. The focus within GKE therefore on low income patients in LMIC may seem inappropriate when there are also low income patients (and donors) in HIC who are in need of improved care. All recipients and donors should be guaranteed proper aftercare, whether or not they participate in GKE.

Ultimately, the concern that GKE lacks the (financial) capacity to guarantee long-term care for donors and recipients may be somewhat overstated. We believe that such issues can be mitigated by APD and/or by an independent committee that monitors and evaluates GKE and that ensures that the escrow funds are not depleted or abused.

Does GKE detract from countries becoming 'self-sufficient'?

According to the DICG and NCA, GKE may undermine local efforts to develop transplant programs in both LMIC and HIC. More specifically, they claim that GKE "distracts from efforts to develop sustainable transplant programs within LMICs such as promoting ethical living donation, developing deceased donation, or addressing the financial barriers to immunosuppression" (8, 9). According to these bodies, the fairest and most effective way to address the transplant needs of patients in LMICs is to develop transplant services in their own countries (72).

The proclamation that countries have to be self-sufficient was first declared by the 2008 DoI and the WHO (73, 74) and has rapidly gained momentum since (75-77). The argument to ban GKE because of the need to achieve self-sufficiency raises various implications however. First of all, it implies that the need for countries to become self-sufficient is more important than the lives that can be immediately saved through GKE. Is achievement of self-sufficiency so important that it overrides life-saving alternatives? Who has the authority to decide which approach should get priority? Why is it required that countries become self-sufficient in organ donation and transplantation, while it is universally accepted for countries to rely on global exchanges of all other types of goods and services? Is it realistic to expect that countries will ever achieve self-sufficiency? Given these considerations, it is striking that the proclaimed importance of achieving self-sufficiency receives no criticism and scrutiny from within the transplant community.

Nonetheless, the concern that GKE impedes self-sufficiency is highly speculative. It implies that without GKE, countries are more likely to become self-sufficient. Yet, there is no evidence that supports this assumption. One could also argue that achieving successful kidney transplantation through GKE could serve as a positive model to boost the status and reputation of transplantation and to promote trust in transplant services across all countries. This may contribute towards achieving self-sufficiency.

Some transplant professionals have pointed out that rather than conducting GKE, countries should focus their efforts on optimizing KEP nationally or regionally.[2] Only several countries have established national KEP, namely the USA, South Korea, the UK, Australia, The Netherlands, Czech Republic, Austria and Canada (78). A number of countries including Greece, Sweden, Switzerland, Poland and India have been preparing and exploring KEP but

[2] These statements have been made, e.g. at the 10th ELPAT Working Group Meeting in Nice, France in 2018, at the 5th ELPAT Conference in Krakow, Poland in April 2019 and at the EDTCO conference in November 2018 in Munich, Germany.

haven't (yet) implemented a full-running program (79, 80). Most KEP are however not conducted optimally and report a range of problems. Examples include lack of knowledge, small pool sizes, ethical concerns, lack of adequate software, legal barriers and lack of central coordination (38, 79, 81). Some countries such as Romania and Turkey only run single-center KEP. The USA has 3 separate KEP, however, many of its transplant centers are not involved in any of these programs (79). Rather, numerous regional and single-center programs exist among approximately 250 living donor transplant centers (79). One of the implications of this fragmented system is that the KEP programs do not wait to build up their pools, as is common practice in other countries with national KEP (79). Consequently, the success rate of the USA's KEP is only 10% (79). The Netherlands, Australia and the UK by contrast report higher success rates due to leveraged national registries, an oversight body and frequently run matching cycles (78).

To optimize KEP, the European Network for Collaboration on Kidney Exchange Programmes (ENCKEP), has recommended that countries merge their national pools through regional cooperation (81). Several countries have started merging their pools with neighboring countries to perform KEP, including Spain, Italy and Portugal; Denmark, Norway and Sweden (79, 82). In its forthcoming handbook, ENCKEP presents the criteria that regional KEP should adhere to:

- countries should experience similar economical and societal development,
- countries should have comparable ethical and cultural values;
- a robust and sustainable framework with legal certainty for donors, patients and professionals should be in place;
- there should be comparable conditions and access to health care for patients (83).

Thus, ENCKEP favors regional KEP over GKE. On the one hand, it can be argued that optimizing KEP within countries and with neighboring countries is a more sustainable solution than engaging in expensive and potentially controversial intercontinental exchanges such as GKE. The high genetic diversity in the USA and Europe, for example, already offers great potential for optimizing national/regional KEP. This in turn is likely to diminish the need for GKE. On the other hand, it can be argued that national/regional KEP, GKE and

other alternatives can co-exist. Multiple strategies that complement one another may result in better all-round results.

GKE: opportunity or exploitation?

In sum, while some concerns about GKE are justified based on the available evidence, others are speculative or do not apply exclusively to GKE but to living donation more generally. We posit that many concerns about GKE can be mitigated by implementing safeguards, by developing minimum quality criteria for participating transplant centers and by establishing an international committee that independently oversees GKE's activities. This committee could be established under the umbrella of an international organization such as the WHO. Its tasks could include: screening participating GKE-transplant centers, collaborating in defining inclusion criteria for donor-recipients pairs, monitoring adherence to procedures, supervising matching algorithms, overseeing escrow accounts and evaluating the necessity and suitability of GKE. It could have the authority to visit and inspect transplant centers participating in GKE and provide support and remedies in case of complaints by donors, recipients and others participating in GKE. Monitoring and evaluating GKE can provide the data necessary to assert –in an evidence-based manner- whether GKE is a safe and successful strategy for improving access to donation and transplantation in both HIC and LMIC. Meanwhile, Rees et al. might wish to consider providing clarifications to some remaining questions:

- What are the perspectives, opinions and experiences of recipients and donors who have participated in GKE?
- Who manages the escrow fund(s) that has/have been put in place for donor and recipient pairs? What safeguards have been put in place to prevent corruption of these funds?
- What are the inclusion criteria for participating GKE-centers? Who initiates the GKE-exchanges?
- What are the inclusion criteria of donor-recipient pairs in both LMIC and HIC?
- What is the income level of participating donor-recipient pairs?
- How, where and by whom is pre-transplant assessment and evaluation of donors and recipients conducted? If the donor and recipient travel to a HIC and are found not to be able to proceed, for instance because of a new infection, who pays for the costs

incurred by both the health care system and the pair thus far? If the reason the transplant can't proceed is temporary, do the pair remain in the HIC until the transplant can be carried out?

- How, where and by whom is post-transplant care and long-term follow-up carried out? For how long is long-term donor and recipient follow-up care guaranteed?
- What impact does GKE have on transplant activity in participating countries?

Regular updates of GKE case are warranted, including data on follow-up. GKE may provide a much-needed opportunity to promote access to donation and transplantation but must coincide with close monitoring, evaluation and appropriate safeguards. Patients' and donors' voices are noticeably missing in this debate.

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Authors' statement

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