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Global Kidney Exchange Should Expand Wisely

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We read with great interest and appreciation the careful consideration and analysis by Ambagtsheer et al. of the most critical ethical objections to Global Kidney Exchange (GKE). Ambagtsheer et al. conclude that implementation of GKE is a means to increase access to transplantation ethically and effectively.^{1,2} These conclusions by their European Society of Transplantation (ESOT) committee on Ethical, Legal and Psychological Aspects of Transplantation (ELPAT) represent a step forward toward a greater understanding and an open, honest debate about GKE. Taken together with the strong endorsement of GKE by Minerva et al. in *Lancet*³ and the positive position statement of the American Society of Transplant Surgeons (ASTS)⁴, Ambagtsheer et al. successfully dispel previously raised doubts⁵⁻¹³ to which we have previously responded.^{2,14-17}

One previous argument against GKE that Ambagtsheer et al (and Minerva et al³) reject is that the general populations of some involved countries are not in support of this construct.^{18,19} We have recently published new data to refute this argument as well. In surveys in Germany, Spain, United States (U.S.) and Philippines asking whether GKE should be legal, following a detailed description of GKE, 79%, 74%, 87%, and 85% answered “legal” to the question “should this exchange be legal or illegal?”²⁰

Ambagtsheer et al. posed several questions to which we respond below.

As of February 2020, 16 international donors and recipients from the Philippines, Mexico, and Denmark participated in GKE and all enthusiastically support the concept. For these exchanges, international participating centers were chosen because the U.S.-based team had established relationships with trusted, well-trained transplant physicians at those centers. Participating U.S. centers evaluated and approved the financial and ethical aspects of the proposed exchanges. Six of the eight GKE recipients were identified by local physicians and presented to the Alliance for Paired Kidney Donation (APKD) for potential participation in GKE. Two patients directly contacted APKD. Five of the eight international patients transplanted through GKE were highly sensitized and had waited years in their respective countries without a match; however, they were matched within months by GKE which offered a different genetic diversity of HLA. We believe that any pair that wishes to participate in GKE should be able to if a match is found and the resultant exchanges and transplants are possible, considering medical suitability, logistics, and finances.

Pre-transplant evaluation was initially performed at the international transplant center and then confirmed at the center actually performing the transplant, seven in the U.S., and one in Antigua. In three instances, the expenses caused by longer stays in the U.S. than originally intended were financed by the APKD. The first three to six weeks of post-operative care were provided by the healthcare providers in the country where the transplant took place, after which all post-transplant care was managed by the healthcare partners in the patients’ country.

The APKD managed escrow funds in the U.S. and works with international physician partners to distribute the funds as needed. These physician partners purchased medications or paid for local hospital/laboratory/professional services and submit receipts to APKD accountants. International accounts were replenished in \$5,000 increments as necessary. As an example, we reserved \$50,000 for our first patient in the Philippines in January 2015, and for the first five years post-transplantation he and his wife (his paired donor) required less than \$5,000/year of APKD financial support. Escrow funds

were never dispersed directly to participating patients or donors. Our escrow accounts were modeled to pay for post-transplant medications and aftercare indefinitely, expecting an average graft survival of ten years with some patients requiring support for longer and some patients losing their kidney prior to ten years. Reserved funds for GKE aftercare were designed to provide transplant-specific healthcare; yet including comprehensive healthcare coverage would be even better if financially achievable. Nevertheless, as noted in Bozek et al., we believe that GKE will increase transplant activity in low and middle income countries (LMIC) by a net flow of financial resources from high income countries (HIC) to LMIC to pay for pre-transplant evaluation and post-transplant aftercare for patients who would not otherwise have had access to this resource.

Six of the eight GKE recipients required financial support (two full and four partial) to pay for evaluation, travel, transplantation, complication risk, follow-up medications, and aftercare for donor and recipient. Two participating pairs (one Danish and one Mexican) had private funds for the transplantation and government support to pay for aftercare. Thus, our actuarial analysis did not require APKD to reserve escrow funds for Mexican and Danish patients, in contrast to the three patients (all from the Philippines) where government support was absent. Even when working with patients in Denmark, where a single healthcare payer provides universal access to in-country healthcare for all citizens, financial barriers prevented access to transplantation through GKE.

GKE has made possible transplantation for patients who face a variety of immunological, regulatory, and financial barriers, to the benefit of all participants. Interestingly enough, some critics, who raise no objections when GKE is used to help highly sensitized patients in LMIC with sufficient financial resources to use GKE without financial subsidy, object when similar mechanisms are deployed to benefit poor patients who require subsidization.⁶ We are glad that Ambagtsheer et al. agree that GKE should also be carefully constructed to help patients from LMIC overcome financial barriers that just as surely prevent access to transplantation.

The 1,000 kidney exchange transplants accomplished per year in the U.S. are due in part to continued exploration of matching strategies, including non-simultaneous chains.²¹⁻²⁹ GKE can be expected to benefit from continued exploration and refinement as well.

Ambagtsheer et al. suggest international regulation and supervision, perhaps by the World Health Organization (WHO). Once a variety of GKE options have been explored so that standard practices begin to develop, we would welcome the establishment of international standards that would allow GKE to be

widely and wisely adopted. It is worth noting that we initially proposed WHO oversight⁵, and Italy's WHO Executive Board representative formally introduced such a motion.³⁰ However, the WHO also produced statements condemning GKE.¹² And, as Ambagtsheer et al. note, the WHO's longstanding policy that each country must develop self-sufficiency in transplantation has, unfortunately, the side effect of severely limiting the availability of transplants in LMICs. Since one of the main motivations of GKE is to make transplantation more available in LMICs, WHO regulation and supervision of GKE would require that the organization revisit the ethics of GKE, ideally with an open discussion involving representatives of all the WHO countries interested in this procedure. In other words, we strongly wish for WHO involvement exactly for the values used by the WHO to define itself: "These values are inspired by the WHO vision of a world in which all peoples attain the highest possible level of health, and our mission to promote health, keep the world safe and serve the vulnerable, with measurable impact for people at country level. We are individually and collectively committed to put these values into practice."³¹

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