



Transgenic pigs for human transplant – An imminent challenge

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Abstract. The purpose of this paper is to review the shortage of organs for renal transplantation, as well as the solution that the transgenic pig promises for the biomedical future. One of the topics of great relevance to urology is research in the field of transplantation and tissue compatibility between the donor source and the recipient of the transplanted kidney. This year, a kidney, with donor-specific tissue from thymus, from a transgenic pig ($\alpha 1$, 3-galactosyltransferase gene-knockout (GTKO)) was transplanted into the groin area (with anastomoses to the femoral vessels) of a brain-dead human subject by a group of surgeons at New York University Langone Health. The kidney was reported to function immediately after transplantation, excreting creatinine and passing urine. Genetic engineering and molecular biology will have a hard say in the future of human medicine. The transgenic pig appears to be a first case solution for patients in need of organs for transplantation.

Key Words: GTKO, kidney, *Sus scrofa*, transgenic pig, transplantation.

Introduction. One of the topics of great relevance to urology is research in the field of transplantation and tissue compatibility between the donor source and the recipient of the transplanted kidney (Popitean et al 2021; Horciag et al 2021; see Figure 1-8). This year, a kidney, with donor-specific tissue from thymus, from a transgenic pig ($\alpha 1$, 3-galactosyltransferase gene-knockout (GTKO)) was transplanted into the groin area (with anastomoses to the femoral vessels) of a brain-dead human subject by a group of surgeons at New York University Langone Health (Cooper 2021). The kidney was reported to function immediately after transplantation, excreting creatinine and passing urine (Cooper 2021).

The purpose of this paper is to review the shortage of organs for renal transplantation, as well as the solution that the transgenic pig promises for the biomedical future.

The current need of organs for urology. Such very important news for people suffering from kidney diseases was long awaited by directly interested patients, but also by urological optimists. Although this reality sounds grim, a huge number of dialysis-dependent patients "await the death" of a potential donor (Figure 9-10). The future that can be seen from this experiment is promising and life-giving.

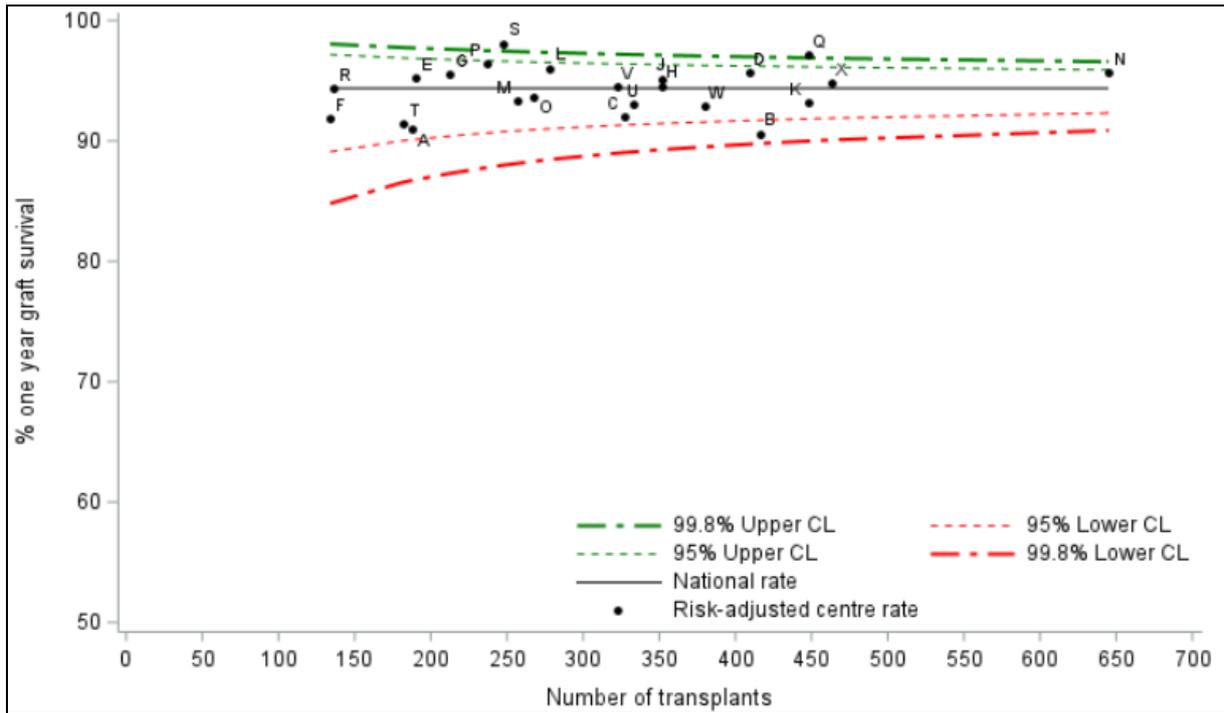


Figure 1. Risk-adjusted one year graft (death censored) survival rates for first deceased donor kidney transplants in adult patients, between 1 April 2015 and 31 March 2019, in UK (NHS 2020).

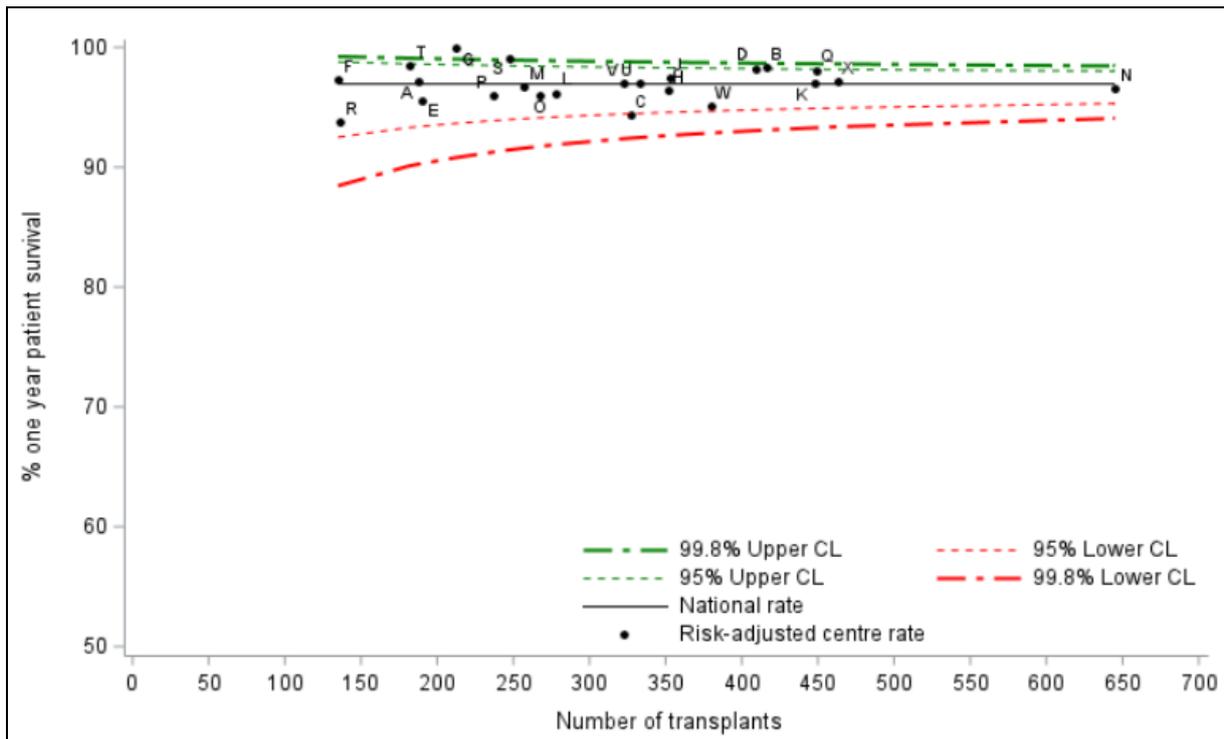


Figure 2. Risk-adjusted one year patient survival rates for first deceased donor kidney transplants in adult patients, between 1 April 2015 and 31 March 2019, in UK (NHS 2020).

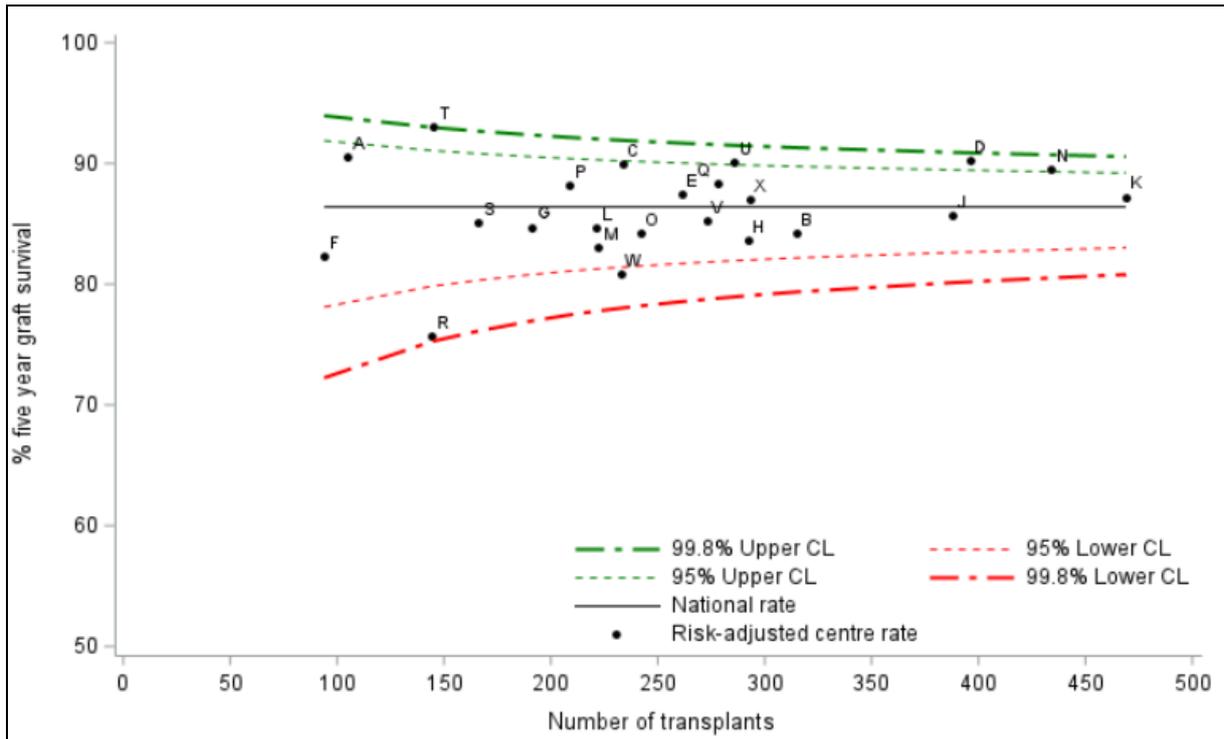


Figure 3. Risk-adjusted five year graft (death censored) survival rates for first deceased donor kidney transplants in adult patients, between 1 April 2011 and 31 March 2015, in UK (NHS 2020).

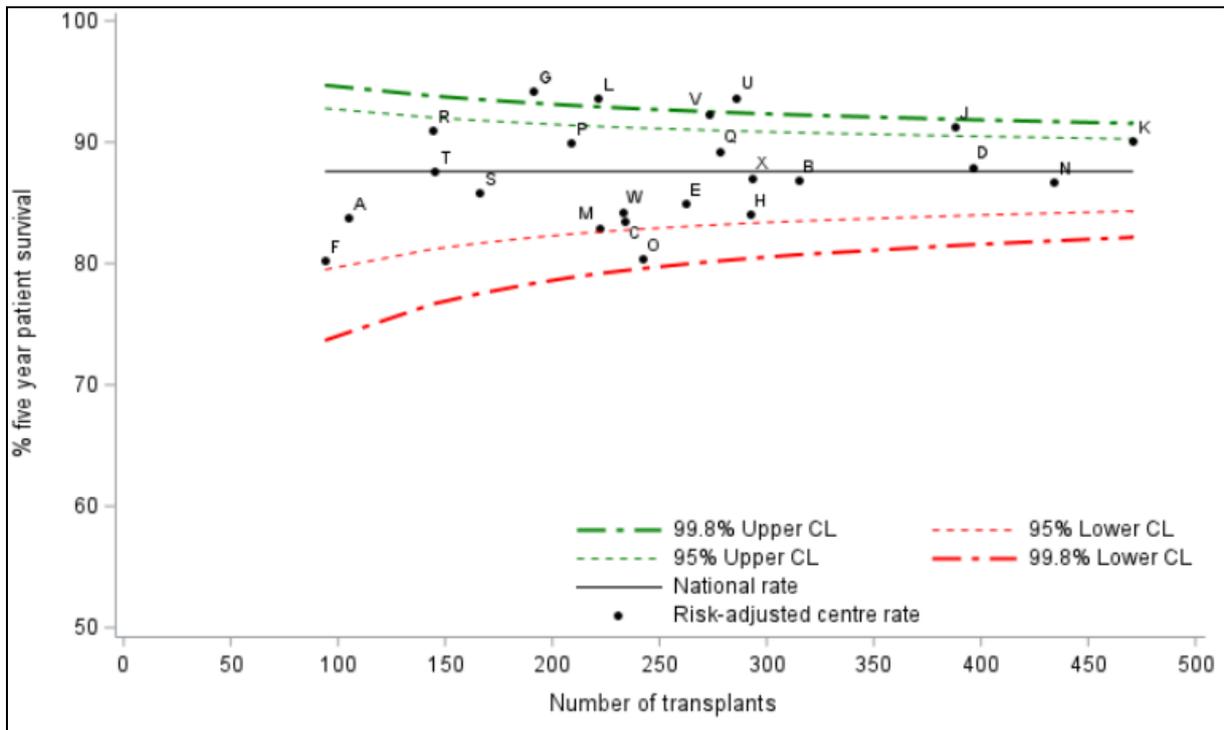


Figure 4. Risk-adjusted five year patient survival rates for first deceased donor kidney transplants in adult patients, between 1 April 2011 and 31 March 2015, in UK (NHS 2020).

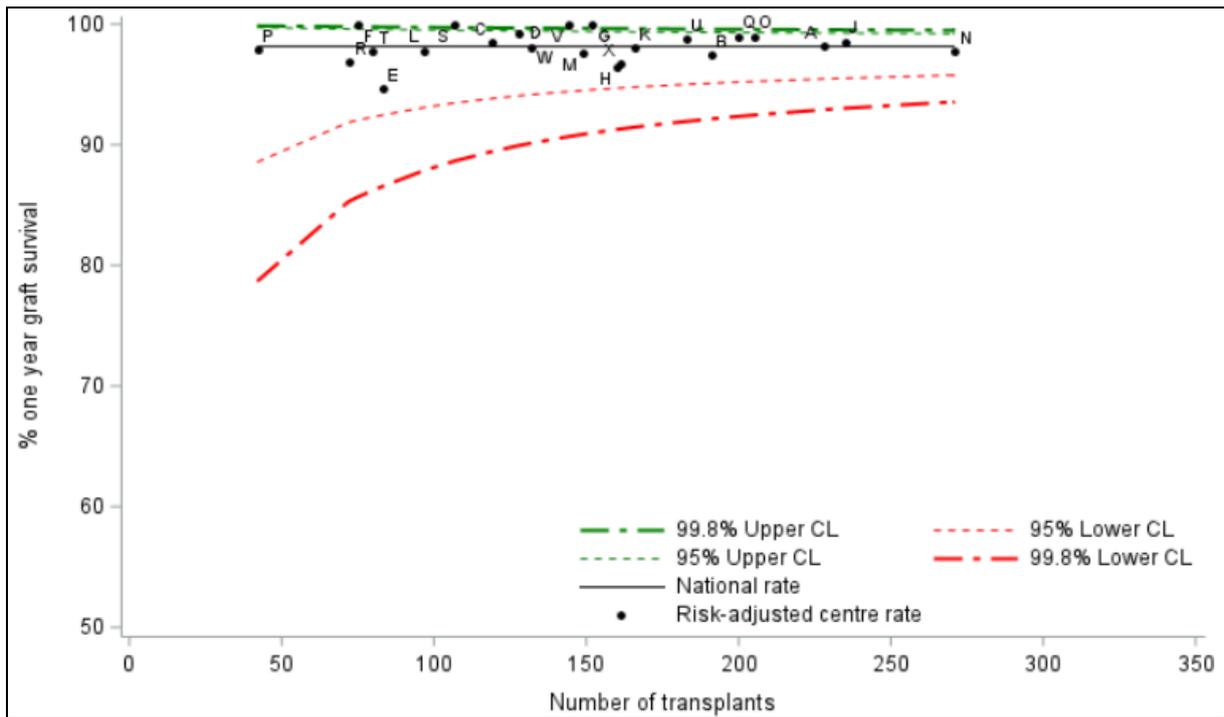


Figure 5. Risk-adjusted one year graft (death censored) survival rates for first live donor kidney transplants in adult patients, between 1 April 2015 and 31 March 2019, in UK (NHS 2020).

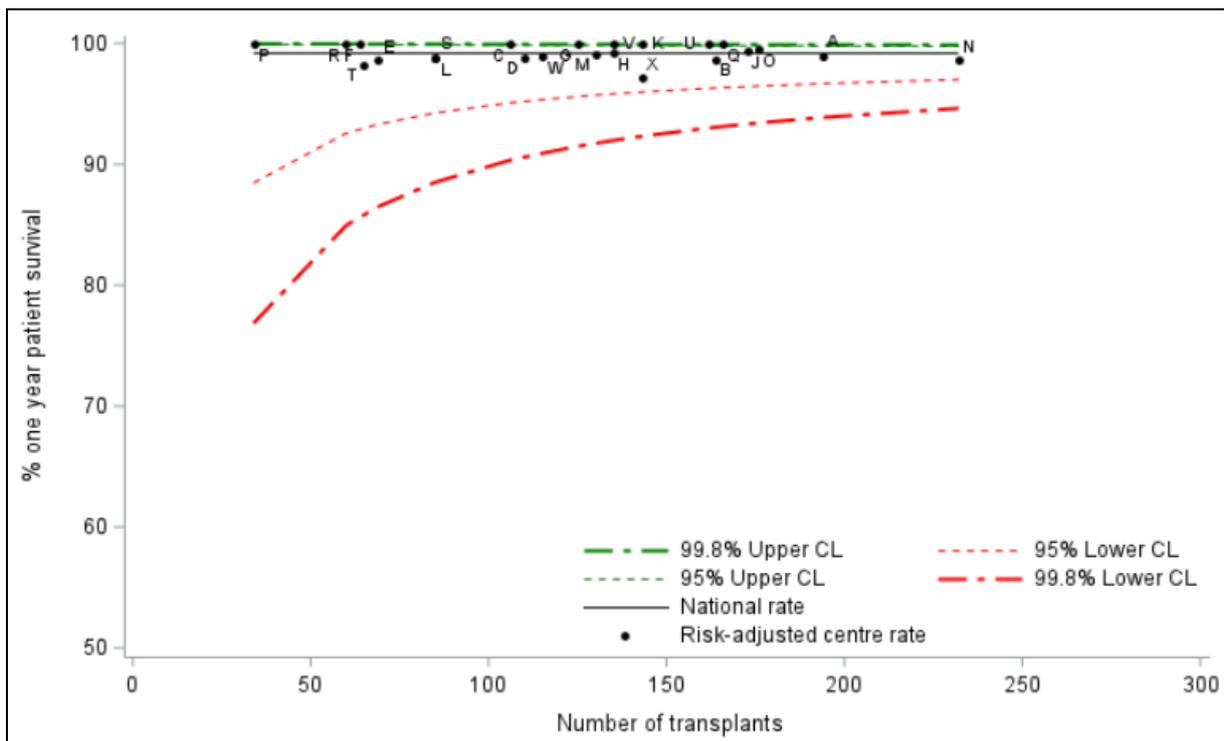


Figure 6. Risk-adjusted one year patient survival rates for first live donor kidney transplants in adult patients, between 1 April 2015 and 31 March 2019, in UK (NHS 2020).

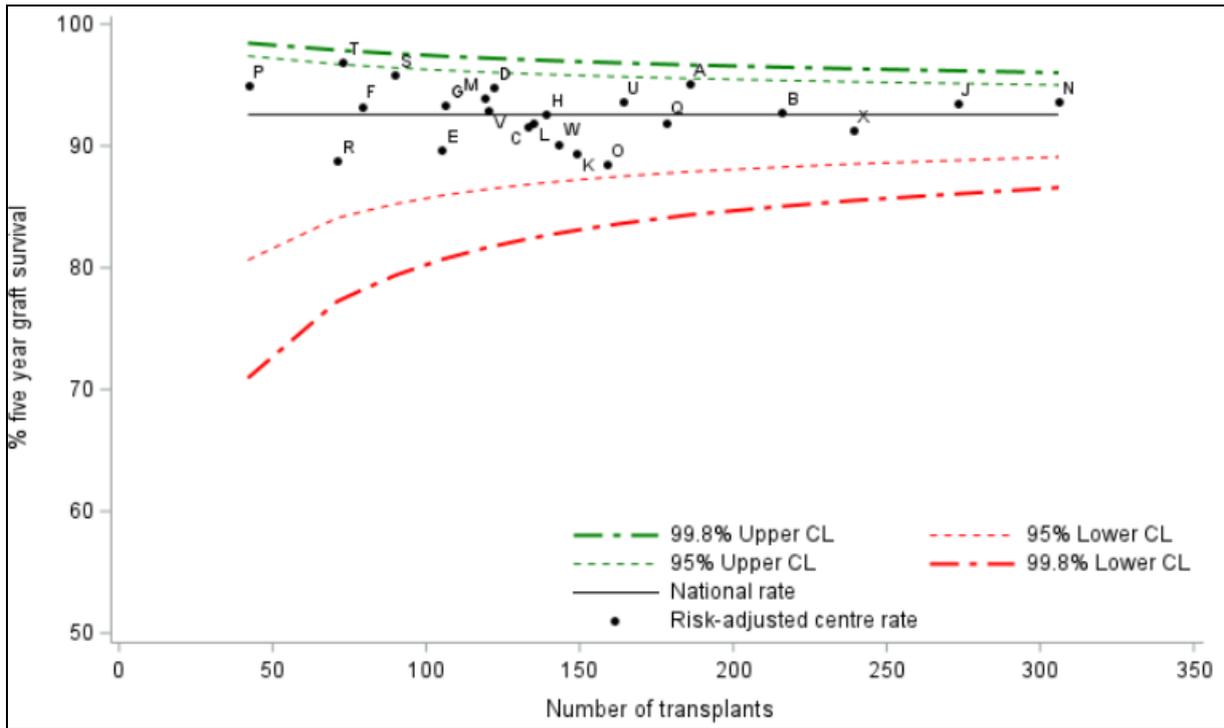


Figure 7. Risk-adjusted five year graft (death censored) survival rates for first live donor kidney transplants in adult patients, between 1 April 2011 and 31 March 2015, in UK (NHS 2020).

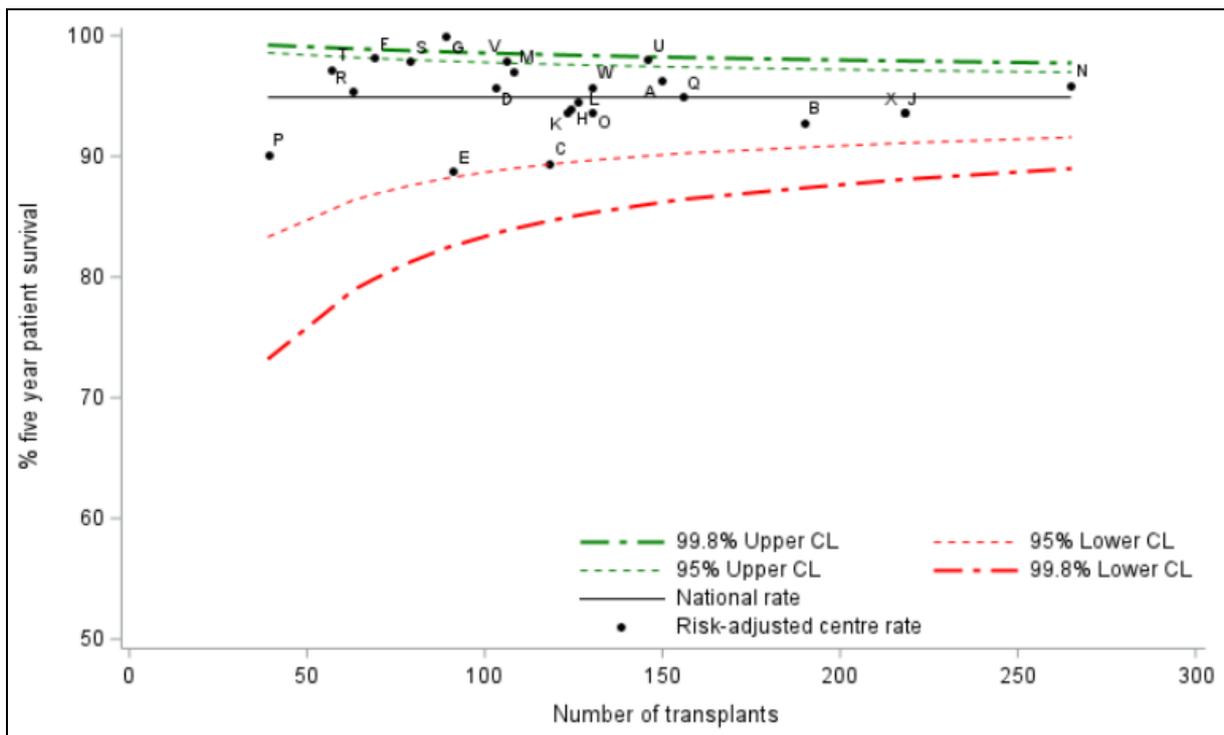


Figure 8. Risk-adjusted five year patient survival rates for first live donor kidney transplants in adult patients, between 1 April 2011 and 31 March 2015, in UK (NHS 2020).

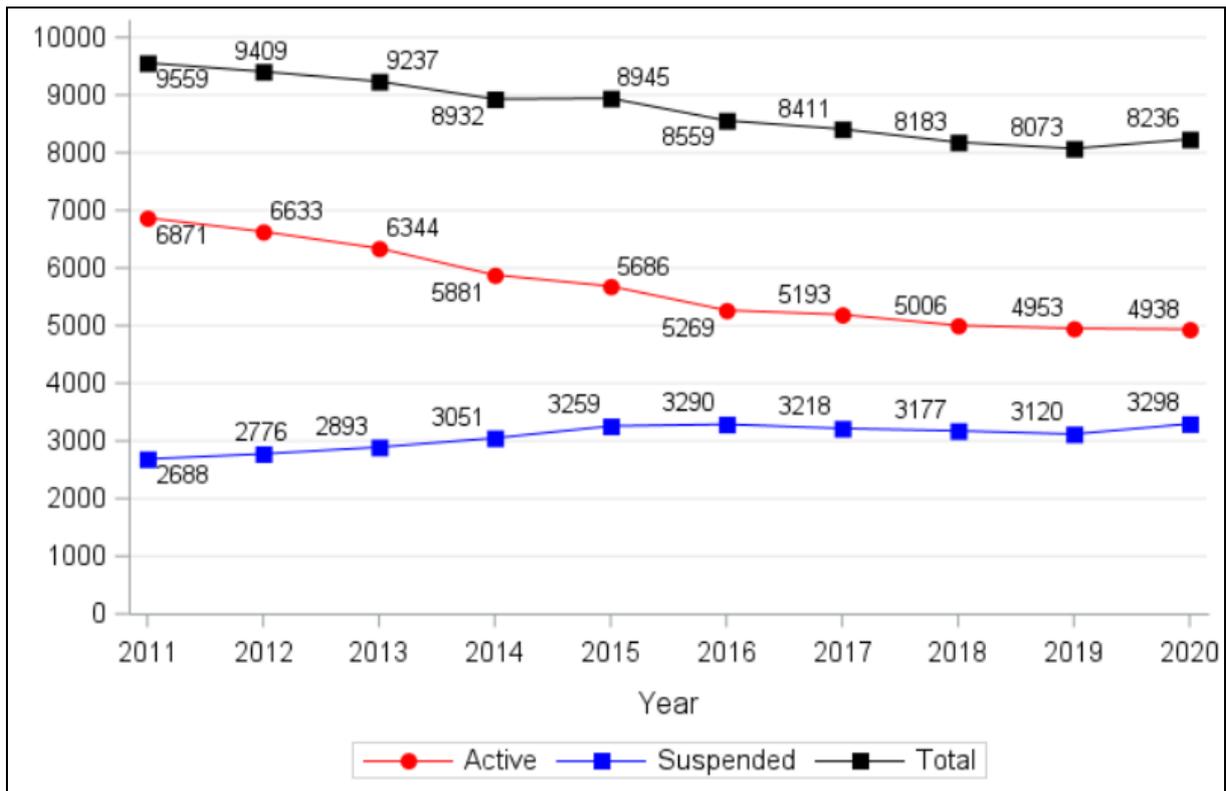


Figure 9. Patients on the kidney transplant list at 31 March 2011-2019 and at 29 February 2020 in UK (NHS 2020).

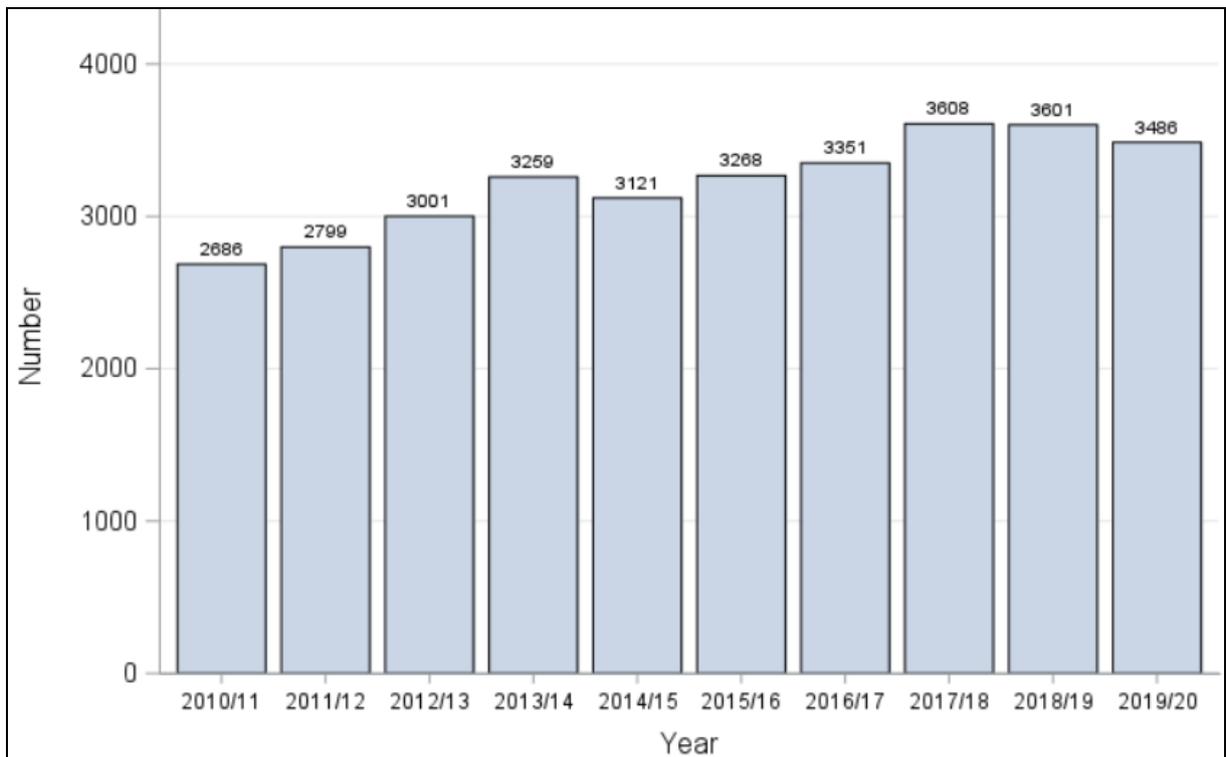


Figure 10. Kidney transplants in UK, during 1 April 2010 – 31 March 2020 (NHS 2020).

The promising solution. The experiment presented by Cooper (2021) (pig to human kidney transplant) was executed in a number of 54 hours and, during the surgical operation, the kidney did not show any macroscopic signs of rejection (Cooper 2021). Cooper (2021) summarizes in his paper some very important ideas about the significance of this remarkable scientific event: 1) No surprise: earlier research in nonhuman

primates has predicted that the transgenic pig kidney would function immediately (Yamada et al 2020). 2) Other research (in vitro investigation) has predicted that a GTKO pig kidney would not be rejected within the first few days after transplantation into a human subject (Cooper et al 2020; Iwase et al 2017). 3) GTKO kidneys are not the best solution for clinical transplantation, and the transplantation of a triple-knockout (TKO) pig kidney would have been more suitable for this purpose. 4) There was no purpose in transplanting a "thymokidney" without pre-transplant conditioning therapy and follow-up for several months. 5) The weaker part: because the native kidneys were retained, it is difficult to determine whether the function of the graft was sufficient to support life. 6) The experiment was announced to the media rather than published in a peer-reviewed medical journal (although hopefully this will follow), suggesting that it was primarily carried out to gain attention to the great potential of xenotransplantation (and possibly to New York University Langone Health). In this respect the experiment was successful, Cooper stated (Cooper 2021).

Because of the very short period of time for which a brain-dead human subject can be kept in a metabolically and hemodynamically stable state, the value of experiments in such subjects will remain very limited (Cooper 2021). It is hoped that any future similar experiments will be calculated to be more relevant to the clinical situation. Nevertheless, the report has stimulated public attention towards xenotransplantation which, unless there is an adverse response to what some might consider to be a bizarre experiment, should be of significant benefit to future development of medical practices (Cooper 2021).

Conclusions. Genetic engineering and molecular biology will have a hard say in the future of human medicine. The transgenic pig appears to be a first case solution for patients in need of organs for transplantation.

Conflict of Interest. The authors declare that there is no conflict of interest.

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