Kidney transplantations in the United States: A System Dynamics approach to reduce the waiting list and illegal trafficking

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***Abstract* — The increasing need for kidney transplants and the structural gap between kidney donation and demand is virtually a universal problem, and has been challenging policy makers in the US and worldwide for years. Although improvements for kidney procurement have been made over the years, still, on average 13 people on the waiting list die every day while awaiting a kidney transplant. At the same time, illegal kidney transplants are flourishing. In this study, an attempt was made to explore the various dynamics involved in the kidney transplant system by means of System Dynamics simulation, to identify leverage points for policy interventions and explore various policies and their effectiveness under highly uncertain conditions. Key focus was on the transplant waiting list, donor registrations, and both legal and illegal transplants performed. The model was validated in accordance with Organ Procurement and Transplantation Network Data. Simulation results showed that without intervention, problems are expected to worsen. Complementary, uncertainty analysis confirmed these results. The only policy which was found to have large enough impact to reverse the up going trend of the waiting list, is to provide financial compensation for unrelated living donors. However this policy is accompanied with many ethical issues.**

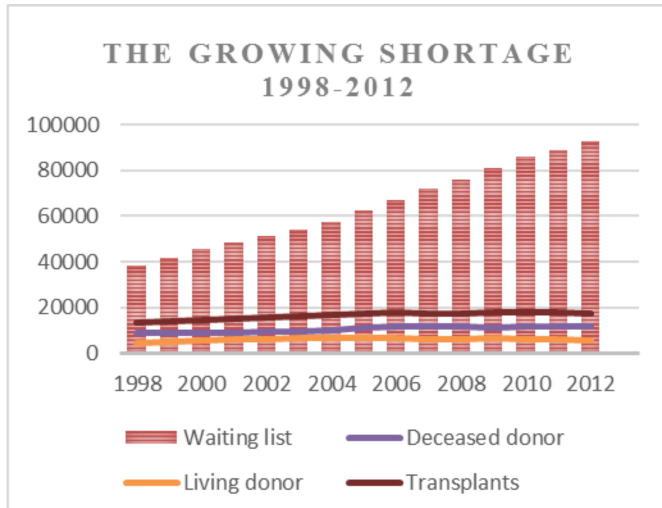
***Index Terms*—*Kidney transplantation, illegal organ trafficking, deceased and living donor, system dynamics, uncertainty analysis.*

Word count: *5152*

I. Background

Kidney shortage is a growing problem for patients in need for kidney transplants. In the United States alone, nearly 100,000 patients with end-stage renal disease (ESRD) were registered on the national waiting list for kidney transplantations in 2012. As Fig. 1 illustrates, the shortage for kidneys has been increasing every year. Demand structurally exceeds the supply by far; each year there are more waiting list additions than removals. For example, in 2012, about 34,000 people were added to the waiting list, but only 11,033 patients actually received a kidney (Organ Procurement and Transplant Network 2013). Consequently, currently waiting patients on the list wait on average (median) more than four years before they receive a kidney transplant (OPTN, 2012). More transplantations are not possible due to insufficient donors. The consequences of this shortage are dramatic; every year more than 4,000 patients in the US die while waiting for a kidney transplant and many more suffer from degrading health condition and are therefore dropped from the list, unlikely to ever be resumed (United States Renal Data System 2010).

Fig. 1: The growing shortage



Legal kidneys are obtained from both living donors (people willing to donate one of their kidneys by life) and deceased donors (people willing to donate their organs after death).
Many potential kidneys of deceased persons are lost for mainly the following reasons; 1. The person did not register in the national donor register (currently only 38% of US citizens are registered (U.S. Department of Health & Human Services , 2015)), 2. The circumstances of death were not suitable for donation, 3. When the conditions for donation are optimal, but the decedent is not registered as a donor, the related family often decides to decline donation, since the persons lack of registration is in case of doubt rather seen as an objection.

Meanwhile, the failure of effective organ procurement policies to meet the rising demand for kidneys in the US, causes flourishing in illegal kidney trafficking (Glazer, 2011, pp. 341 - 366). Desperate waiting patients in need for a kidney are tempted to participate in illegal organ transplantations provided by international organized crime. So far, little is known about the size and the structure of this sordid business which typically takes place in less developed countries. However, patients are reportedly willing to pay up to $200,000 for an illegal kidney transplant, a kidney for which the donor often receives as little as $1000 to $5000 (World Health

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Organization, 2015). Often transplantations takes place under bare, suboptimal conditions (World Health Organization, 2015) and endangers the health of donor as well as recipient.

Some previous System Dynamics research with regard to organ shortage has been performed. A similar scope as ours was chosen by (Hirsch, McCleary, Saeed, & Myer, 2012), who modelled the (kidney) donor potential in the US and identified in particular feedback loops within the organ procurement and transplant center capacity. However, their approach differs, as they have a particular strong focus on data calibration rather than on policy exploration and behavioral change. Moreover, they focus solely on the donor potential of deceased donor, overlooking the potential of living donors.

Another study by (Azar, McDonnell, & White, 2013) modelled the dynamics of the renal system as a whole, incorporating many aspects relevant regarding dialysis. Whereas a purely forecasting approach was performed by (Prasanna Devi, Suryaprakasa Rao, Krishnaswamy, & Wang, 2010), who modelled the development of corneal transplants for a transplant center in India. Finally, kidney transplantation system characteristics were explored regarding the optimal geographic allocation to recipients across the country with both a system dynamics approach by (Fernandez, 2014) and with a purely discrete modeling approach by (Davis, Mehrotra, & John Friedewald, 2013).

For our study we chose a holistic approach to identify dynamics in the kidney transplantation sector, represented by numerous interrelated feedback loops. The model incorporates also the interactions between the illegal kidney transplantations and the legal kidney transplantations system. The main purpose of the model, is on exploring the relative performance of diverging policy options that influence the systems' behavior. Though, in this study, OPTN and other data source were used for quantification of the model's initial values, flow rates and fractions, the main focus is on system behavior.

In the remainder of this paper, a description of the model is given, along with the chosen policies for increasing the legal transplants performed along with a reduction of the waiting list and illegal kidney trafficking. First, the methodology that was applied to obtain the results is addressed. Second, the conceptual model is presented, which illustrates the modelers' line of thought and important modelling decisions. Third, a detailed description of the model and its sub-systems is provided. Then, base case simulation results are discussed for this model. These results express the behavior of the hypothetical model. Following, different policies are addressed that were explored for this model. Finally, an uncertainty analysis was performed to address the deep uncertainty in the models' parameters, delays and explored policies. These results are discussed in the last chapter.

II. Methodology

In this study, a model was made by the use of System Dynamics, with the purpose of exploring different policy options to decrease the kidney transplant waiting list and fight the illegal kidney trafficking business. A simulation time frame from 2012 until 2030 was applied.

System dynamics is a methodology for studying complex feedback systems and makes use of stock flow diagrams to simulate system behavior over time (Forrester, 1961; Sterman, 2000). SD models allow to identify generic structures and behaviors that can be used to search for policies that influence the systems behavior in different scenarios (Azar, McDonnell, & White, 2013).

First, a conceptual model was made by means of a Causal Loop Diagram (CLD), in which the main feedback loops and the different subsystems were identified. In addition, a bull's eye diagram was created that expresses which variables were included or excluded from the model and to which detail modelled (Pruyt, 2013). The actual modelling of the system was started with several Stock Flow Diagram (SFD) which are explained in later paragraphs. After developing enough confidence in the model in an iterative process, policies were developed and implemented, and as a result the SFD's structure and/or parameter values were adjusted. This included an extensive uncertainty analysis to test the explored policies and the models parameters for deep uncertainty.

The model initial values, stocks and fractions are calibrated according to OPTN data, which contains data of every organ donation and transplantation event in the US since 1987 and other sources: (OPTN, 2012), (Centers for Disease Control and Prevention, 2015) and (National Kidney Foundation, 2015). These extensive databases provided all reference data needed for donor characteristics, transplantations, waiting list size, and survival rates etc.

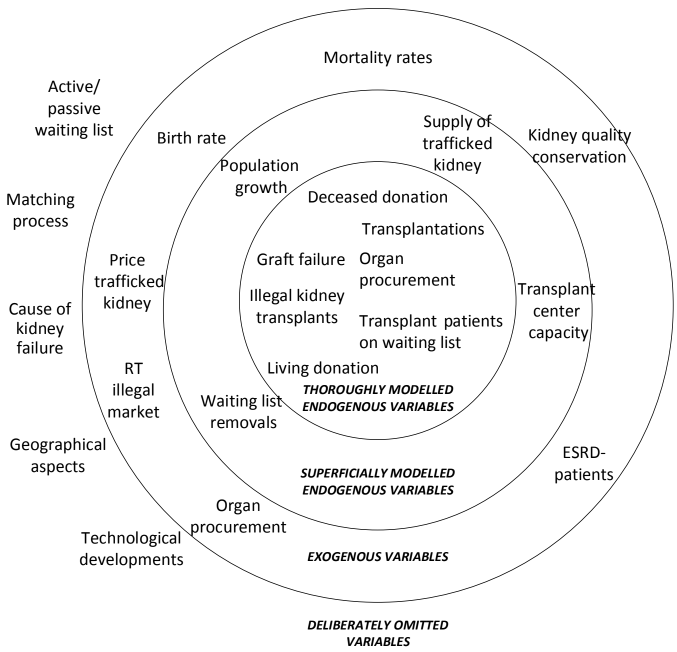
III. Model Description

A. *Model boundaries*

During the modelling process, decisions were made for the level of detail on which certain parameters/issues should be modelled. The bull's-eye diagram in Fig. 2 provides a general overview of the elements that were modelled thoroughly endogenously, superficially endogenously, exogenous or deliberately omitted from the model. Only the deliberately omitted elements and the exogenous elements will be addressed in this section.

An important exclusion was made for the donor-recipient matching process that is essential in real-life organ transplantation. In this process, important characteristics (mainly blood type and human leukocyte antigens) for both the donor and the possible recipient are taken into account in order to determine the best match. However, since the amount of patients on the waiting list is so large, a match is always found. Thus, this process is not of particular interest in this research, as the amount of kidney donors are the main problem, rather than their specific matching characteristics.

Fig. 2: Bull's-eye diagram



Another element that was deliberately omitted from the model are possible future technological improvements that might affect the kidney transplantation system. For example, the creation of kidneys with use of genetic modification. Although such developments could radically change the models behavior, they are not included within the timeframe of the model.

Moreover, as the authors applied a holistic approach to understand the general behavior for the US as a whole, geographical aspects, such as transplant center locations or kidney distribution networks, are excluded from the model as well.

Furthermore, the model omits the difference between passive and active waiting list, as only the later people are eligible to receive transplants.

A large potential to tackle the root cause of the problem are the causes for kidney failure, particularly obesity and hypertension. Nevertheless they were not included in the model.

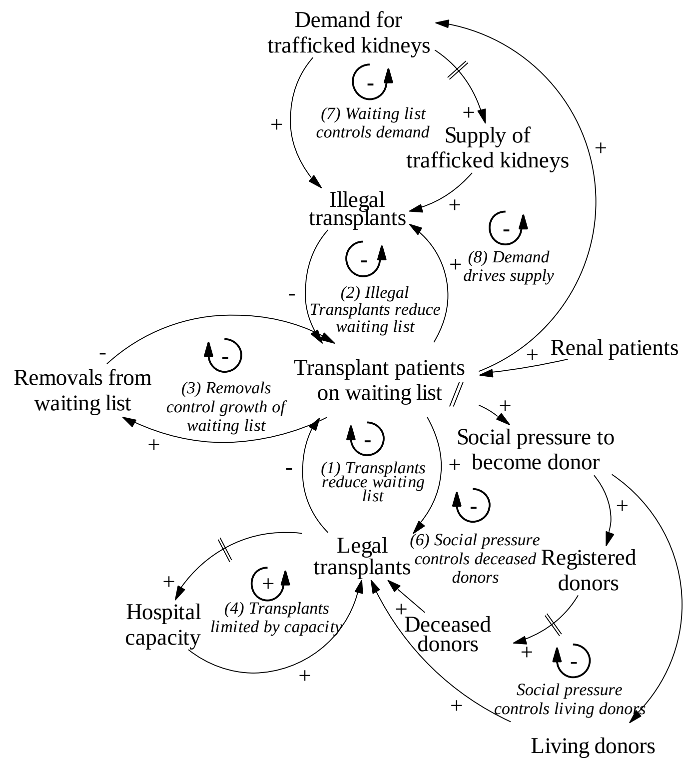
B. Conceptual Model

The model is centered around the transplant waiting list and focuses on the identification of reinforcing and balancing feedback loops that influence its length. Fig. 3 provides an overview that shows, which loops drive the system and which loops are rather balancing.

The flow of renal patients in need of a kidney transplant entering the waiting list is indicated by the arrow at the right towards the waiting list. Over the last decades the number of ESRD has shown a rising rapidly trend.

It is triggered by the dynamics of the population in terms of age structure, death rates and the fractions of new cases of end-stage renal disease. In addition, the population variables originates also how many kidneys are available from both deceased and living donor. Notice, the development of the population is incorporated in the model and described in more detail in the next chapter, but not displayed in the highly aggregated causal loop diagram.

Fig. 3: Highly aggregated causal loop diagram



Furthermore, the CLD provides an overview of the eight main feedback loops that can be identified:

(1) Transplants reduce waiting list: patients are removed from the waiting list after transplantation;

(2) Illegal transplants reduce waiting list: patients are removed from the waiting list after transplantation with trafficked kidney;

(3) Removals control growth of the waiting list: the growth of the waiting list is dampened by the patients that are removed from the waiting list, because their health condition has deteriorated or they died while waiting to receive a transplant.

(4) Transplants limited by capacity: transplant capacity restraints the legal transplants that can be carried out. This is not problematic under normal development, since capacity is delayed adaptive to the legal transplants performed. However it is expected to be a limitation if overall kidney supply increases suddenly, for instance because of a policy action.

(5) Social pressure controls deceased donors: increasing social pressure stimulates the number of transplants from deceased donors;

(6) Social pressure controls living donors: increasing social pressure stimulates the number of legal transplants performed with kidneys from unrelated or related living donors. In turn the length of the waiting list depends on the number of kidney donors.

(7) Waiting list controls demand: increasing length of the waiting list triggers demand for transplantations with trafficked kidneys;

(8) Demand drives supply: the waiting list or more precise the average waiting time triggers the demand for trafficked kidneys. Criminal organizations respond to this demand for trafficked kidneys and expand supply channels.

In the next chapter the model structure is presented in more detail. Four main subsystems have been modelled (1) Population development; (2) Transplantation; (3) Illegal kidney trafficking and (4) Kidney transplant capacity.

IV. Detailed Model Structure

A. Sub-system Population

As can be seen in the stock flow diagram in Fig. 4, the population is classified broadly into three age categories; pediatric, adult and senior population. In addition, two other stock variable were added to distinguish living donors (both related and unrelated) from the rest of the population.

At first, population aging, was modelled with regular first order material delays. However, since aging dynamics are actually rather discrete events, in Vensim they are often modelled by using conveyors. This function was implemented in the model for maturing and retiring, and it was found that with the same set of parameters the behavior correspond closer with far more complex population projection models such as those published by the U.S. Census Bureau (United States Census Bureau, 2009).

Finally, there is also no link between the senior population and the senior living donors since, only a negligible percentage of 2.1% of living donors is at the time donating aged 65 and older (National Kidney Foundation, 2015).

B. Sub-system Transplantation

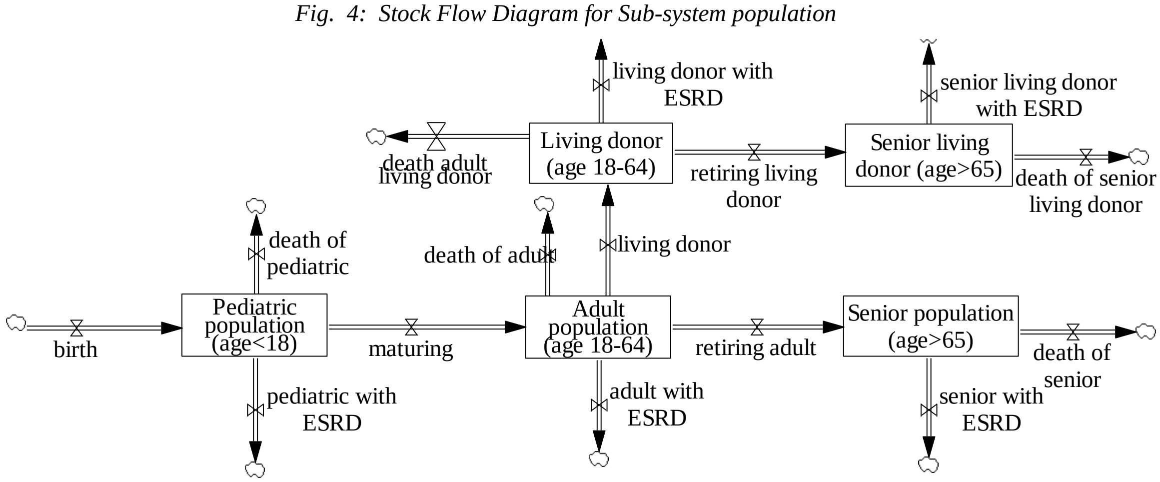
Fig. 5 provides an overview of the stocks and flows within the transplantation sub-system. Patients only leave this system when they die, for example due to renal failure or as consequence of surgery.

The inflow to the transplantation sub-system are new cases of ESRD, which accumulate in a stock. At present, in the US alone, over 700,000 patients are affected by ESRD (United States Renal Data System, 2012), which require compulsory routine kidney dialysis or transplantation. The main causes for ESRD are diabetes and hypertension (OPTN, 2012; United States Renal Data System, 2012), however in this model only simplified represented as fractions of new cases per year of the population.

A fraction of ESRD patients move further each year to the waiting list as their health status is acute and requires as soon as possible transplantation. Anyhow, since the United States lacks a universal health insurance for all citizens, access to the waiting list is further restricted and the real scarcity of kidneys is rather underestimated. Since transplantation and post-hoc medication is extremely expensive it can usually not be afforded by uninsured patients. Consequently out of fear that that their financial circumstances will cause kidney failure, uninsured persons are likely to be declined by transplant centers (Laurentine & Bramstedt, 2010); among others, possible changes at this leverage point were addressed in the uncertainty analysis.

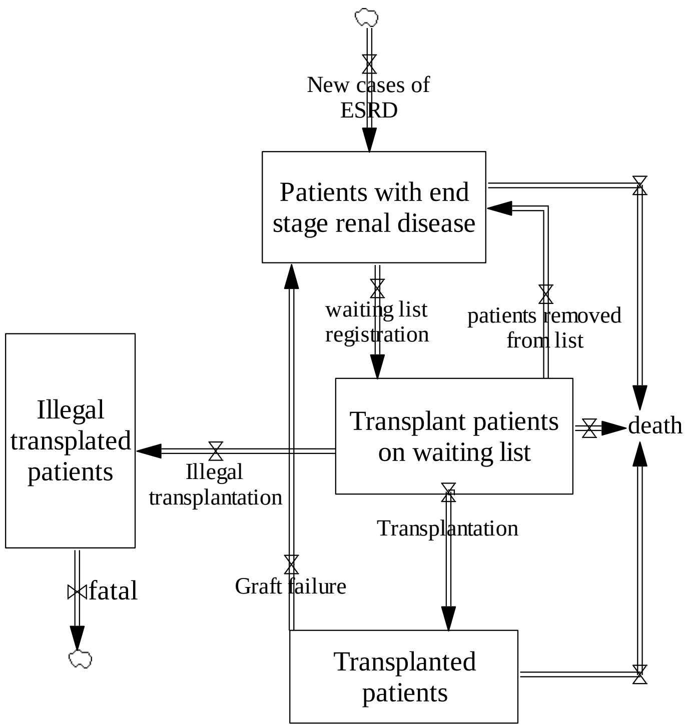
While waiting to receive a transplant a fraction of patients is removed from the list, usually because their health status deteriorates and make transplant impossible. As mentioned in the introduction the average waiting time for a kidney transplant is more than four years, and in 2012 only 11,033 patients received a kidney transplant. Transplants are limited by the availability of kidneys and at least theoretically also by the transplant center capacity.

Fig. 4: Stock Flow Diagram for Sub-system population



The transplants performed each year utilize organs approximately half each from living and from deceased donors. The number of transplants from living donors that can be performed is naturally limited by the number of people willing to become living donors. The motivation to become a living donor, is influenced by the social pressure to become a donor, triggered by the length of the waiting list and may be also influenced by policy making.

Fig. 5: Stock Flow Diagram Sub-system Transplantation



In terms of deceased kidney donation, the underlying reasons for the supply shortage is that only a small fraction of deaths each year occur in a manner that the kidney can be obtained before kidney taint, since removed kidneys require immediate and adequate conservation. If the death does not occur in hospital there is little chance that the organ can be transplanted. Furthermore, only a small fraction of potential donors is generally medically suitable, which further diminishes with ageing (OPTN, 2012).

Only in addition to this the fraction of people registered as donors and the consent from donors' families may pose two leverage points for policy makers.

Transplantation is nowadays initially almost always successfully. However transplanted patients face the risk that the foreign organ is rejected and the graft fails, though the patient intake of immunosuppressant a medicines that lower the body's ability to reject a transplanted organ. In case of graft failure, the patient moves back to the stock of patients with end stage renal disease and may again register on the waiting list for re-transplantation.

Little is known about illegal transplantations since of its very nature. However, it is estimated that around 5% of all recipients, obtain a transplant from grey sources each year, usually transplantation takes place outside the country (Shimazono, 2007). The simplified underlying mechanism is presented in the next paragraph. Anyhow, if the transplantation is not-successful the patient may remain on the waiting list and does not have to re-register.

C. Sub-system Illegal kidney trafficking

Because the organ supply cannot meet the rising demand a flourishing global black markets for illegal kidney trafficking has emerged. Potential recipients are out of hopelessness willing to take the risk and travel abroad to obtain kidneys through commercial transaction, the price of a renal transplant ranges from US$ 70 000 to 160 000 (Shimazono, 2007).

In the model, the demand for illegal trafficked kidneys is believed to be proportional to the transplant patients on the waiting list, and the reference price paid for the illegal kidney is assumed to be US$ 100,000.

The stock "supply of trafficked kidneys" is fed by the supply response to markets (organizations that are active in illegal organ trading react to demand from the ESRD patient side). This supply response is controlled by the relative profitability of organ trafficking which captures the supply and demand mechanism based on an average kidney price, the effective chance of being caught for trading, and the response time of the supply to react on market demand.

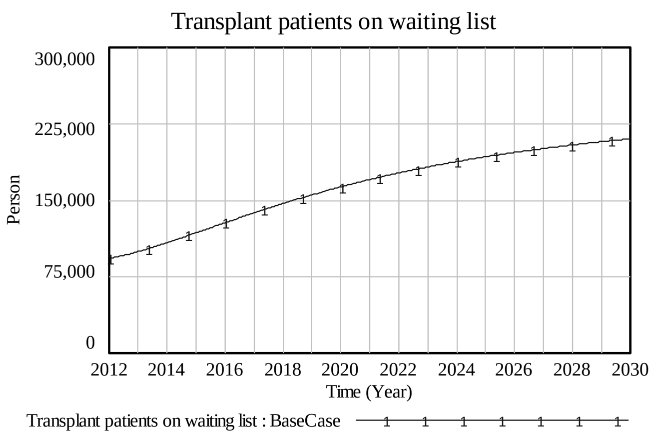
The supply and demand ratio determines the average price compared to the reference price for trafficked kidney. This effect is reflected by a lookup function following an exponentially declining graph. The smaller the supply relative to the demand, the higher is the average price paid and vice versa. This market supply demand effect is smoothed to take into account information delay time to price changes.

This average price has a twofold effect. First, it drives the demand from the ESRD patient side by an exponential declining relation between the average price paid and the demand, reflected by a lookup function: demand for trafficked kidney is higher when the average price is low and vice versa. Second, it influences the relative profitability of organ trafficking which controls the response of supply to market. Finally, demand for trafficked kidneys is affected by both the risk of illegal transplantations and the average price paid for a trafficked kidney. Hence, mutual interaction between supply from kidney supply channels and demand from the ESRD patient side determine market prices and thus the transplantations performed with trafficked kidneys.

V. Base Case Simulation Results

The base case is a hypothetical scenario, simulated with the models default values and assumptions. The base case behavior displayed in Fig. 6 suggests that the transplant patients on the waiting list more than double until 2030. This waiting list growth corresponds well to comparative System Dynamics studies, such as (Hirsch, McCleary, Saeed, & Myer, 2012).

Fig. 6: Base case simulation result for waiting list



Moreover, this behavior met the expectation, since it follows the current trend and is driven by the rising number of ESRD patients each year (United States Renal Data System, 2012). The ESRD growth is a result of the US population dynamics combined with an unhealthy nutrition and lifestyle. While the number of donations remains relatively constant and does not rise along with the demand, see also Fig. 1.

Fig. 7: Base case simulation result for registered donors

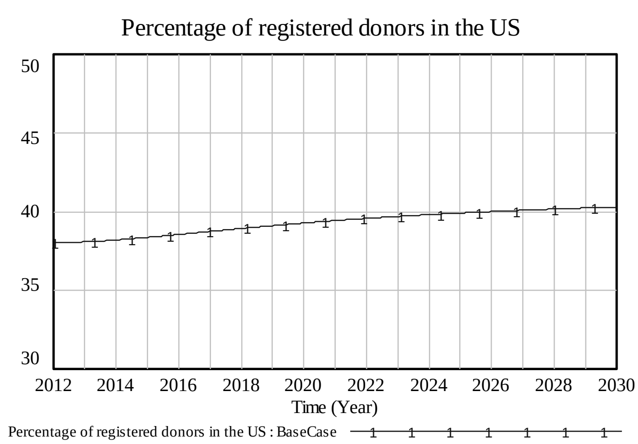


Fig. 7 shows the base case behavior for the potential donor population that is registered as a donor, which is only 38 percent at the model's initial time. A slight increase is seen within the simulation timeframe, driven by the increasing social pressure to become a donor. In general, this social pressure restrains the increase of the waiting list to some extent, however the balancing effect is not enough to flatten the waiting list growth.

Fig. 8: Base case simulation result for transplants

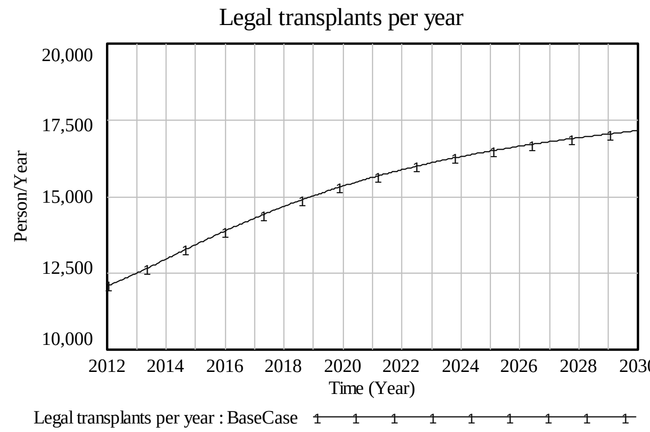
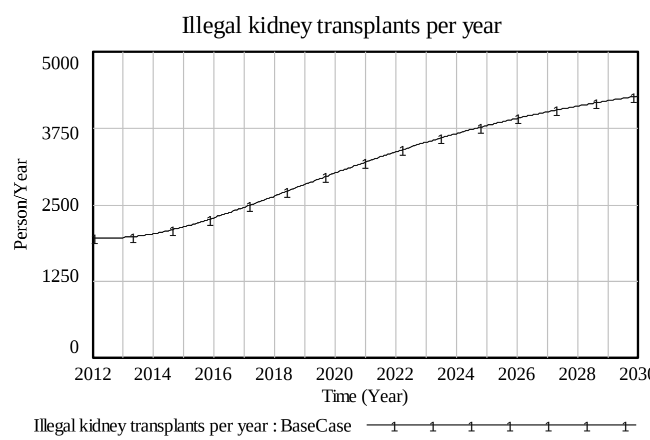


Fig. 8 shows the base case behavior of the legal transplants performed per year. A comparison of both Fig. 6 and Fig. 8 clearly shows the gap between the demand for kidney transplants and the supply. As expected, illegal kidney transplants increase in line with the waiting list, see Fig. 9. More specific, the length of the waiting list is the main driver for the illegal transplants sub-system, as this is the only link with the rest of the model. Initial interpretation showed that any effective policy against illegal kidney trafficking should come from the demand side, rather than the supply side.

Fig. 9: Base case simulation result for illegal transplants



VI. Policy Exploration

The main purpose of the model is to identify which interventions by policy makers are likely to be the most effective, taking into account the deep uncertainty of many parameters, functions and model structure. The status quo simulation showed that the available donated kidneys limit the transplants performed. Consequently, increasing transplant program capacity is only secondary relevant.

Policies are derived from those currently debated or ones that already have been implemented in other countries. For better comparability, it is assumed that all policies are implemented in 2015. The first two to be discussed policies aim to increase the deceased kidney donation, the third policy encompasses lowering of kidney quality criteria and the last two policies describe measures to increase kidney donations from unrelated living donors (Becker & Elias, 2007).

Some systems feedback loops form resistance to change and impede policy making. First, since the social pressure is related to the waiting list, there is a balancing effect: if the waiting list is reduced, less people are willing to become a donor. Second, the kidney transplant capacity limits the possibilities of implementing any policy immediately stimulating more transplants. Therefore, the effectiveness of the policies are for now only tested under the assumption that the transplant capacity is unlimited, assuming that adapting this capacity to the changed conditions, is not the core challenge.

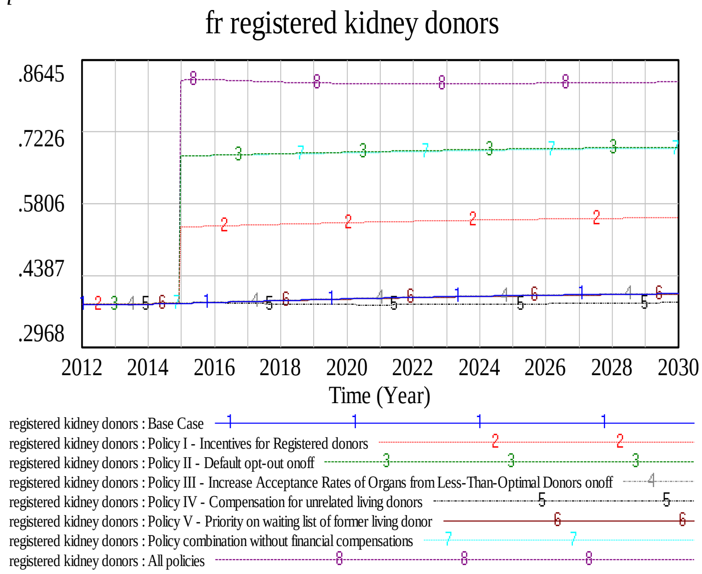
A. Policy I: Incentives for Registered donors

As the first country in the world, Israel passed a legislation in 2008 to reward cadaveric donation with financial compensation such as reimbursement of funeral costs, to encourage people to register as deceased donors. For the purpose of this model, it is assumed that this policy increases the percentage of registered kidney donors from 38% to more than 50% (Fig. 10). However the effect on the waiting list is very small, as the red lines in simulation results presented show (Fig. 12-13).

B. Policy II: Default opt-out

Implementing this policy means that every citizen will be by default registered as a donor and has to explicitly recall his/her registration. In Belgium, where this policy was implemented, the fraction of registered kidney donors doubled (Erasmus School of Economics, 2014). This percentage has been also assumed for the model. In Fig. 10, 12, and 13 the turquoise and green lines, represent the effect after the policy was activated. However, despite raising the number of registered donors, the waiting list does not shrink significantly; the effect is only slightly bigger than for the first policy. Extreme boundary assessment tests show that even under assumption that everyone becomes a deceased donor, the supply of proper kidneys is insufficient. Suggesting policy makers to explore the potential of living donation.

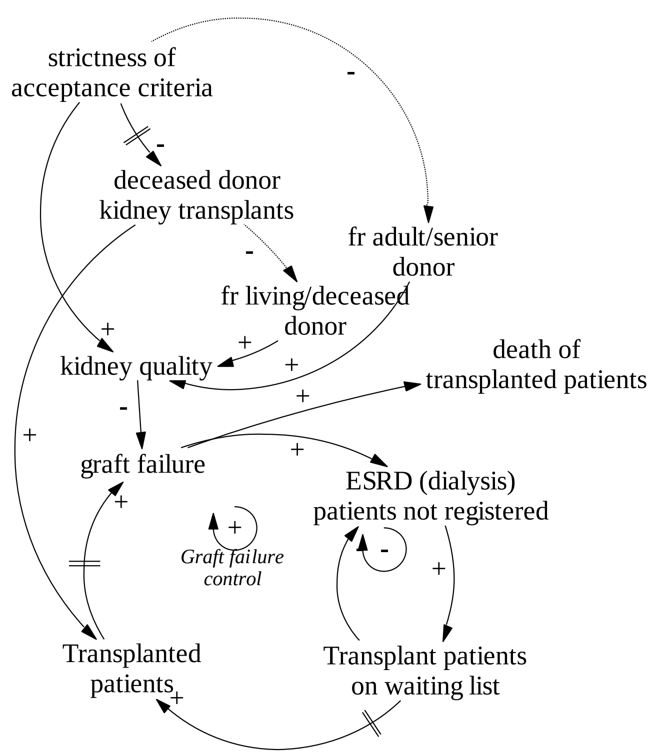
Fig. 10: Percentage of registered donors after implementation of policies



C. Policy III: Increase Acceptance Rates of Organs from Less-Than-Optimal Donors

Another often discussed policy to tackle the challenge of kidney shortage is to accept kidneys from less-than-optimal donors by lowering quality standards. Fig. 11 provides an overview of the impacts such a policy may have.

Fig. 11: Causal loop Diagram kidney quality



The quality of organ transplanted is influenced by three drivers. The first driver is the ratio of adult to senior donors, since with ageing the quality of the kidney generally deteriorates. Second, the ratio between living donors and deceased donors, as living donors provide generally kidney with higher medical quality. Lastly, the policy parameter, strictness of acceptance criteria, which in addition may influence the two first mentioned factors.

The quality of the kidney transplanted determines the probability for graft failure. The lower the quality, the more recipients will either decease as a consequence of the transplantation or will return to the ESRD patients stock.

The effectiveness of this policy is limited, though the number of transplanted kidneys raises slightly, but has a major drawback. As Fig. 14 shows, the graft failures increase after policy activation, when compared to the base case and other policies.

On the contrary, policies that enhance the number of living donors, do not only rise the number of transplants per year, but also result in a decline of graft failure, due to the earlier described dynamics.

D. Policy IV: Compensation for unrelated living donors

About half of all kidney transplants in the US come from living donors. The advantage of policies stimulating living donation, is that the additional kidney supply is not marginalized by insufficient kidney condition. Furthermore, living donor transplants have a lower probability for graft failure than those obtained from deceased donors.

Compensation for unrelated living donors may take very different forms, and does not necessarily has to be of monetary value. Experiences from other countries show the effectiveness of those policies. For example, in France, transplant centers reimburse living donor travel and lodging costs. In some Canadian provinces lost wages while recovering from the surgery are reimbursed (Laurentine & Bramstedt, 2010). The compensation for unrelated living donors may only be the correction of disincentive, so should the government protect donors from insurance companies that charge higher premiums for living donors. Some say donors should be guaranteed government-paid health insurance to cover the risk of obtaining the kidney and later complications.

Though, the effect of such granting citizens a compensation can only be estimated, the model shows that there is a lot of potential in increasing living kidney donation. In the model it is assumed that due to the incentive of US$ 15.000 the living donors tenfold, see Figure 12 and 13. Thereby it is the only policy which is found to be effective to reduce the waiting list to a lower level, and which would significantly reduce the average waiting time.

E. Policy V: Priority on waiting list of former living donor

The risk of a living donor is hardly significantly higher to develop ESRD than a person with two kidneys (Muzaale, et al.). Nevertheless it would be a powerful incentive to become an unrelated living donor if former donors can jump to the top of the transplant list once they develop ESRD in their remaining kidney and need a transplant. Though in the model it is assumed that this measure would almost double the motivation to become living donor, the effect on the waiting list is however small (Fig.12).

F. Combined policies without financial compensation

Many people have ethical concerns about financial compensations for donation (Kelly, 2013). Therefore, additionally a set of policies was created combining all policies that do not include financial compensation and thus are less controversial. Though the effect of the individual polices add up, the joint impact is still relatively small Fig. 12 and 13.

G. All Policies

Last, the effect of all policies combined are examined. If all policies are active the desired effect is greatest. Nevertheless, as Fig. 12 shows, the trend can only be reversed until 2021, from which on the growing number of ESRD patients drive the waiting list up again.

Fig. 12: Graft failures after implementation of policies

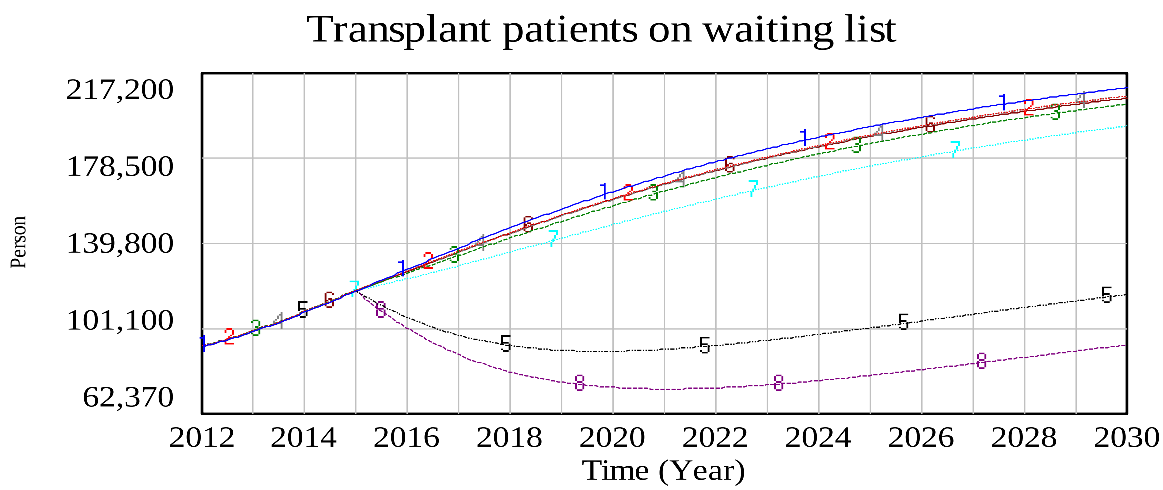


Fig. *13: Legal transplants after implementation of policies*

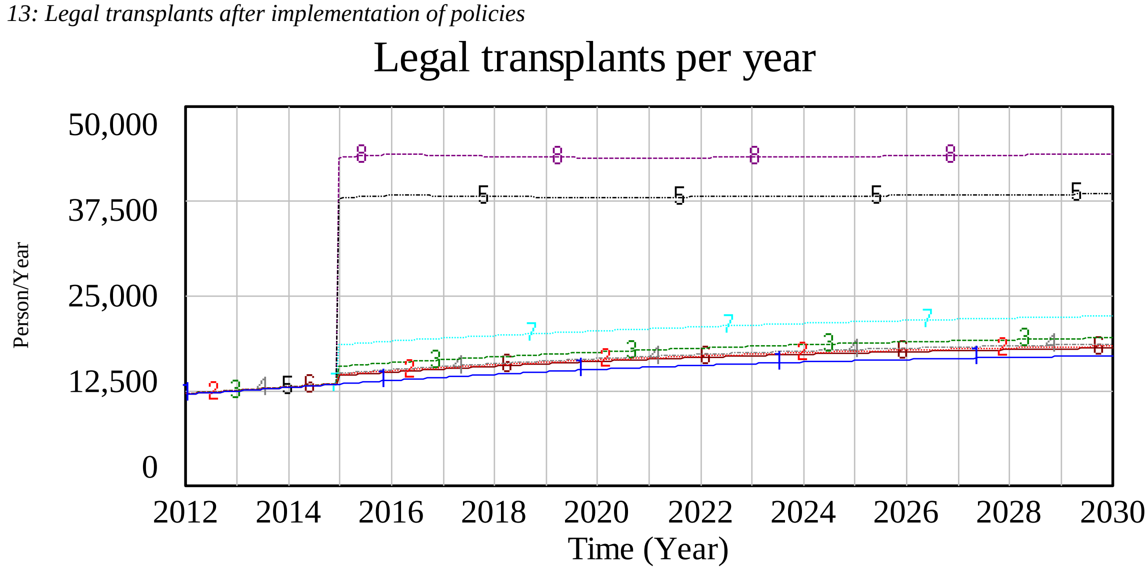
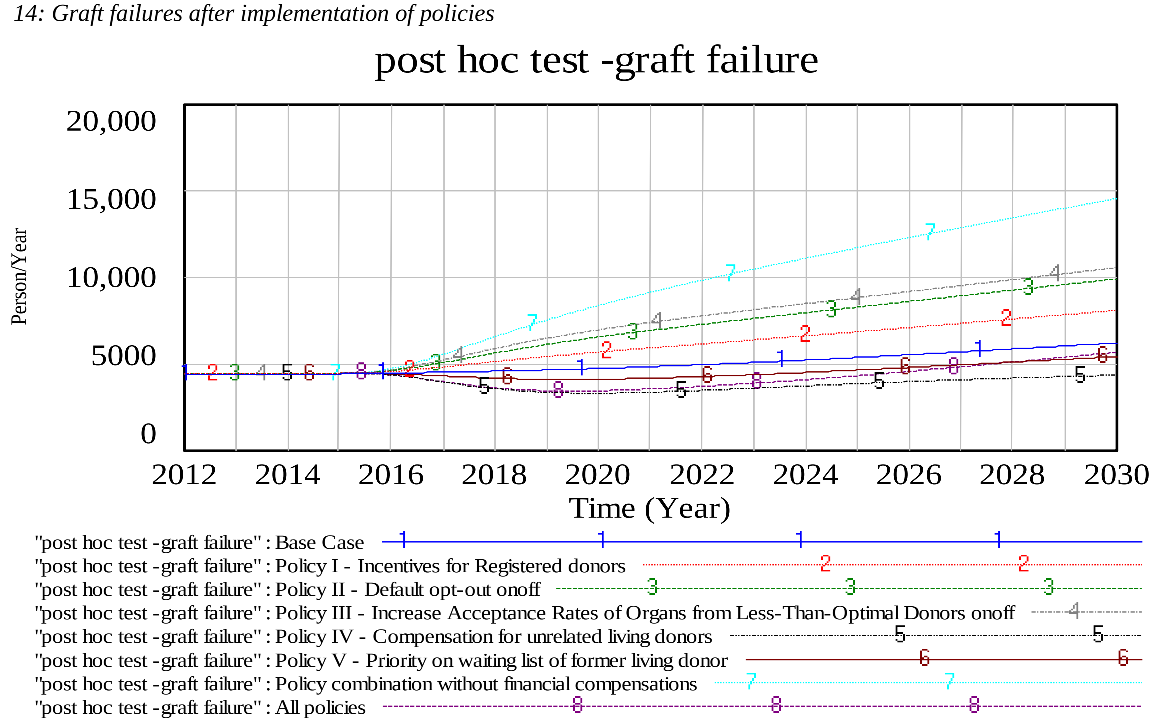


Fig. 14: Graft failures after implementation of policies



VII. Testing policies under uncertainty

The kidney transplant model described until now, incorporates numerous socio-economic factors whose values, and feedback loops, and strenght can only be estimated and not derived from solid sources of data. Furthermore, many parameters and fractions possibly change in the future, which may completely reverese trends. For the purpose of this study most relevant are dynamics, which change the effectiveness of policies.

(Bankes, 1993) was among the first suggesting to explore with models possible scenarios and dynamics related to uncertainty, rather than predicting future outcomes.

In this study, the approach of (Kwakkel & Pruyt, 2013; Pruyt, Auping, & Kwakkel, 2015) was followed, who built on this and presented several cases to demonstrate the application of policy exploration with System Dynamics.

In the following paragraph, the results taking into account both structural and parameter uncertainty and their effect on the policies are discussed. For the parameters used in the uncertainty analysis, the uncertainty ranges as well as delay order uncertainty are presented in the table in the Appendix.

For each policy 500 simulations runs where performed respectively with a different set of the possible input values selected from their uncertainty ranges with latin hypercube sampling. In addition, in order to test Policy V: "Priority on waiting list for former living donors", an extended model was used to incorporate the additional stock flow structures and dynamics.

The outcomes of the uncertainty analysis is illustrated with visual ensemble inspection (left) and kernel density estimation (right). Kernel density estimates are the continuous variant of histogram representing the distribution of data probabilities.

The figures 15 to 17 present a comparative policy analysis for the model with no priority waiting list for former living donors. Because of the uncertainty ranges, the registered donors (Fig. 16) are spread out, however repeat the base run behavior.

On the contrary, Fig. 16 indicates that the waiting list is behaviorrally sensitive. In the worst scenario 400,000 people will be awaiting a kidney tranplant in 2030. In another extreme scenario in which all policies are implemented and other conditions are optimal, the waiting list will approach zero already in 2020.

The kernel density estimation shows that there is a very clear difference between all policies in which financial compensations are povided to living donors, which confirms the initial conclusions.

Finally, Fig. 17 provides an overview of the legal transplants performed per year, with no surprising insights.

When the patients that have been living donors are prioritized, the effect on the waiting list is marginal, which can be seen from Fig. 18, comparing both models.

Fig. 15: Envelopes and kernel density estimates of registered donors

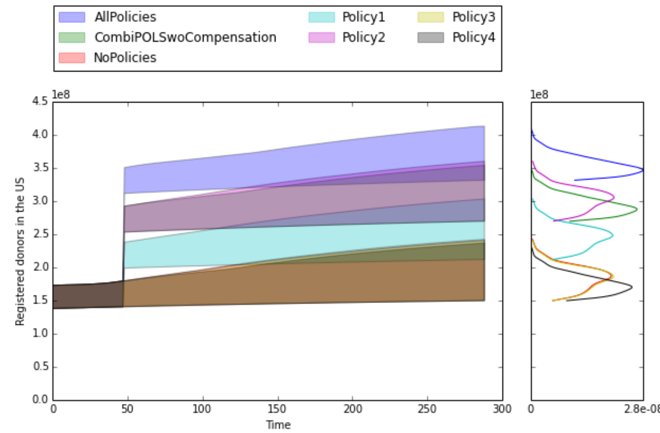


Fig. 16: Envelopes and kernel density estimates of waiting list

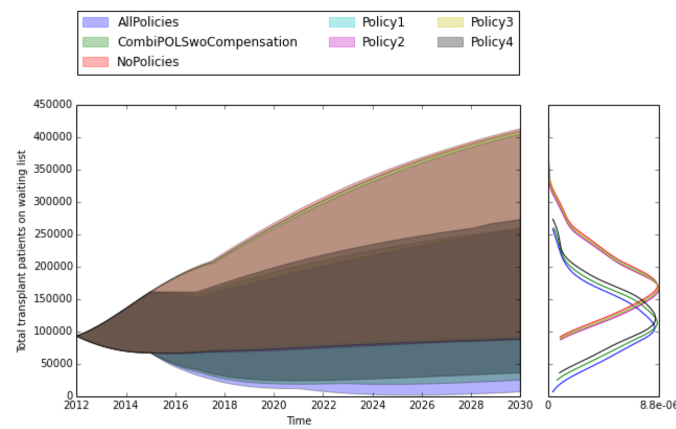


Fig. 17: Envelopes and kernel density estimates of legal transplants

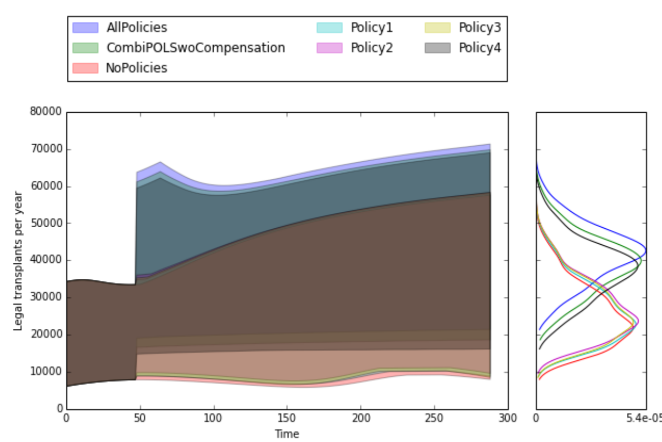
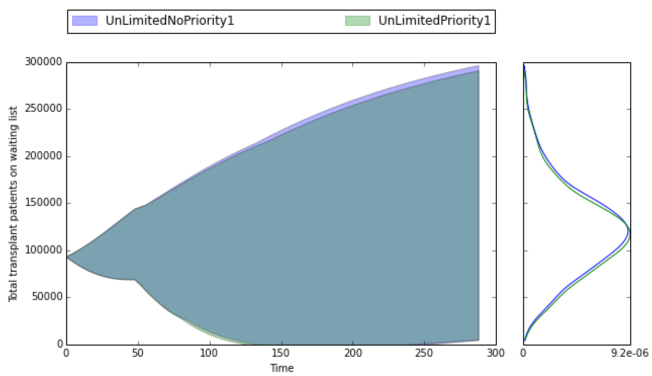


Fig. 18: Envelopes and kernel density estimates of priority policy



VIII. Conclusion & Recommendations

This study shows, traditional measures are not effective to limit the up going trend of the kidney transplant waiting list in the US. Providing financial compensations for unrelated donation was found to be the only policy that has the potential to reverse the trend and reduce the waiting list to a significantly lower level. Nevertheless, for policy makers the crux is whether it is moralistically justified to use market incentives to increase living donation to save ESRD patients' lives.

The persistent and increasing gap between kidney supply and demand, leads to the conclusion that policies have to be developed encouraging more donation. Simulation shows that the waiting list will have doubled by 2030, if no actions are taken.

Implementation imposes further hidden challenges, such as the transplant center capacity, that only adapts slowly, and thus limits the transplants that can be performed. Consequently, any initiated policy has to be coordinated with transplant center capacity. The waiting list length is the root cause for illegal trafficking; any other policy regarding illegal trading should tackle the demand rather than the supply side.

Efforts should be made on the prevention of end-stage renal failure. Furthermore, socio-economic, legal and cultural disincentives for organ donation should be eliminated, in order to endeavor effective organ transplant procurement.

Future research may enrich the picture by incorporating the root causes of kidney failure and its dynamics, along with further socioeconomic and behavioral factors. Finally, a participatory approach with stakeholders would provide the opportunity to reflect upon the models underlying assumptions and discuss the insights of the model.

References

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). (2015). *http://kidney.niddk.nih.gov/KUDiseases/pubs/kustats/*

Azar, A. T., McDonnell, G., & White, J. C. (2013). Modelling and Control of Dialysis Systems. *Springer*, 1275-1320.

Bankes S. 1993. Exploratory Modeling for Policy Analysis. Operations Research 41 (3):435-449.

Becker, G. S., & Elias, J. J. (2007). Introducing Incentives in the market for Live and Cadaveric Organ Donations. *Journal of Economic Perspectives*, *21*(3), 3 - 24.

Centers for Disease Control and Prevention. (2015). *Data base*.

Columbia University Deparment of Surgery . (2015). Retrieved from http://columbiasurgery.org/conditions-and-treatments/compatible-living-donor-kidney-transplant.

Davis, A., Mehrotra, S., & John Friedewald, D. L. (2013). Characteristcs of simulation model of the national kidney transplantation system. *Proceedings of the 2013 Winter Simulation Conference* (pp. 2320 - 2329). R. Pasupathy, S.-H. Kim, A. Tolk, R. Hill, and M. E. Kuhl, eds.

Erasmus School of Economics. (2014, December 30). *Orgaandonatie: Opt-in of Opt-out? Geen van beide!* Retrieved from http://www.eur.nl/ese/nieuws/economieopinie/artikelen/detail/article/26097/

Fernandez, L. e. (2014). A System Dynamics approach to optimizing resource allocation in kideny dialysis versus transplantation. *SMDM Society for Medical Decision Making*, 18 - 22.

Forrester, J. (1961). *Industrial dynamics.* Cambridge, MA: The M.I.T. Press.

Glazer, S. (2011). *Organ trafficking can the smuggling of human organs be stopped?* CQ Global Researcher.

Hirsch, G. B., McCleary, K. J., Saeed, K., & Myer, K. A. (2012). Deceased Donor Potential for Organ Transplantation: A System Dynamics Framework. *Annual conference of the International System Dynamics Society.* St. Gallen Switzerland.

Kelly, E. (2013). International Organ Trafficking Crisis: Solutions Addressing the Heart of the Matter. *Boston College Law Review*, 1317 - 1349.

Laurentine, K. A., & Bramstedt, K. A. (2010). Too poor for transplant: finance and insurance issues in transplant ethics. *Progress in Transplantation, 20*(2), 178 - 185.

Muzaale, A. D., Massie, A. B., Mei-ChengWang, Montgomery, R. A., McBride, M. A., Wainright, J. L., & Segev, D. L. (n.d.). Risk of End-StageRenal Disease Following Live Kidney Donation.

National Kidney Foundation. (2015). Retrieved from https://www.kidney.org/transplantation/beadonor.

OPTN. (2012). *Annual report 2012.*

Prasanna Devi, S., Suryaprakasa Rao, K., Krishnaswamy, S., & Wang, S. (2010). System dynamics model for simulation of the dynamics. *Springer*, 284-292.

Pruyt, E. (2013). *Small System Dynamics Models - Triple Jump towards Real-World Dynamic Complexity.* Delft: TU Delft Library.

Pruyt, E., Auping, W. L., & Kwakkel, J. H. (2015). Ebola in West Africa: Model-BasedExploration of Social PsychologicalEffects and Interventions. *Systems Research and Behavioral Science, 32*(1), 2 - 14.

Shimazono, Y. (2007, December). The state of the international organ trade: a provisional picture based on integration of available information. *Bulletin of the World Health Organization, 85*(12), pp. 901 - 980.

Sterman, J. (2000). *Business Dyamics: Systems Thinking and Modeling for a Compled World.* New York, NY: Irwin/McGraw-Hill.

U.S. Department of Health & Human Services . (2015, March 11). Retrieved from http://www.organdonor.gov/about/data.html.

United States Census Bureau. (2009). *United States Census Bureau 2009*. Retrieved from http://www.census.gov/population/projections/files/analytical-document09.pdf

United States Renal Data System. (2012). *2012 Atlas of CKD & ESRD*. Retrieved from 2012 Annual Data Report: http://www.usrds.org/atlas12.aspx

WHO. (2004). *Resolution on human organ and tissue transplantation.* Geneva: (WHA 57.18). Retrieved from http://www.who.int/transplantation/en/A57_R18-en.pdf

World Health Organization. (2015). Retrieved from http://www.who.int/bulletin/volumes/82/9/feature0904/en/.

APPENDIX

Fig. 19: Parameters and calibration intervals used for Uncertainty Analysis

Parameter	Units	Value	Interval	Sources/remarks
Normal graft failure rate	[1/Year]	0.289	(0.289,0.504)	(OPTN, 2012)
Average response time to illegal kidney demand	[Year]	1	(0.3,4)	Assumed
Impact of waiting list on social pressure	[Dmnl]	0.0005	(0.0001, 0.001)	Assumed
Magnitude of priority waiting list advantage	[Dmnl]	5e-005	(1e-006, 1e-005)	Assumed
Fraction of patients removed without transplants from waiting list	[1/Year]	0.04	(0.01,0.1)	(OPTN, 2012)
Effectiveness of financial compensation	[1/Dollar]	3e-009	(1e-009, 7e-009)	Assumed
Ratio that related donors organ match	[Dmnl]	0.12	(0.1,0.2)	(Columbia University Deparment of Surgery , 2015)
Mortality rate of diagnosed ESRD patient	[1/Year]	0.2	(0.15, 0.25)	(National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), 2015)
Magnitude of influence of waiting time on health status	[1/person]	3e-007	(3e-008, 3e-006)	Assumed
Magnitude of waiting list influence on registration	[1/person]	7e-007	(3e-007,1e-006)	Assumed
Initial transplanted patients	[Person]	172553	(172553, 185000)	(National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), 2015)
Impact of kidney quality on graft failure	[Dmnl]	0.05	(0,0.2)	Assumed
Impact of social pressure on living donors	[Dmnl]	0.0005	(0.0001, 0.001)	Assumed
Fraction of donor kidneys transplanted before taint	[Dmnl]	0.008	(0.006,0.01)	(OPTN, 2012)
Rate of new adult ESRD	1/Year	0.0004	(0.0002, 0.0006)	(United States Renal Data System, 2012)
Rate of new senior ESRD	1/Year	0.0016	(0.0014, 0.0018)	(United States Renal Data System, 2012)
OrderSocialPressure	[Dmnl]	3	(1,3,20)	Assumed
OrderAveragePrice	[Dmnl]	3	(1,3,20)	Assumed
OrderGraftFailure	[Dmnl]	3	(1,3,20)	Assumed