Health Council of the Netherlands

A fair compensation

Considerations for a proposal to give living kidney donors priority for transplantation

Gezondheidsraad
Health Council of the Netherlands

To the Minister of Health, Welfare and Sport

Subject : presentation of advisory report *A fair compensation. Considerations for a proposal to give living kidney donors priority for transplantation*
Your reference : GMT/IB 2959307/09
Our reference : I-6512/HvdK/tvdk/858/C1
Enclosure(s) : 1
Date : May 10, 2011

Dear Minister

It is my privilege to present to you the advisory report *A fair compensation. Considerations for a proposal to give living kidney donors priority for transplantation.*

The key issue of your request for an advisory report was whether article 18, section 3 of the Organ Donation Law – which sets out the allocation of postmortem donor organs – allows sufficient leeway for awarding extra points to the former kidney donor who requires renal replacement therapy. The Health Council has given a positive answer to this question. According to the Council, awarding these points is in agreement with the spirit of the law and medical-legal principles. International laws also do not form any impediment. The Health Council deems that a change in the Organ Donation Law is not essential for such a modification of the allocation system.

As per your request, the Health Council has also looked at the moral and medical-ethical aspects associated with awarding extra points to the former kidney donor. The Council deems that a morally and medical-ethically valid argumentation for allowing this bonus can be based on a compensation argument, supplemented by a fairness argument. Although having only one kidney does not negatively affect the normal functioning of the donor, the loss of reserve capacity makes the donor more vulnerable. If the functioning of the remaining kidney is unexpectedly endangered, for example due to the development of a renal tumour or *de novo* renal disease, the former donor will require dialysis sooner than kidney patients with two kidneys. It is fair to compensate the live kidney donor with end stage renal failure for this health disadvantage. Failing to do so would mean that precisely those people who helped drastically to reduce the average time that kidney patients have to

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wait for a postmortem kidney, are confronted more starkly with the harsh reality of the shortage of donor organs.

The Health Council wants to emphasise that only a few donors each year will be eligible for extra points as a result of this renal failure. For the other patients on the waiting list for a postmortem donor kidney, this is likely to result in their total waiting time of three to four years being extended by a few days. Because the group of patients on the waiting list collectively benefits from the sacrifice made by living kidney donors (living donors as a group ensure that the waiting times are reduced by half), the Health Council thinks that it is fair that the burden of compensation by this group is borne in the form of a slightly longer waiting time.

The Advisory Report was reviewed by the Standing Committees on Ethics & Health Law and on the Medicine. I support the conclusions and recommendations of the advisory report.

Yours sincerely
(signed)
Prof. L.J. Gunning-Schepers,
President

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No. 2011/06E, The Hague, May 10, 2011

The Health Council of the Netherlands, established in 1902, is an independent scientific advisory body. Its remit is “to advise the government and Parliament on the current level of knowledge with respect to public health issues and health (services) research...” (Section 22, Health Act).

The Health Council receives most requests for advice from the Ministers of Health, Welfare & Sport, Infrastructure & the Environment, Social Affairs & Employment, Economic Affairs, Agriculture & Innovation, and Education, Culture & Science. The Council can publish advisory reports on its own initiative. It usually does this in order to ask attention for developments or trends that are thought to be relevant to government policy.

Most Health Council reports are prepared by multidisciplinary committees of Dutch or, sometimes, foreign experts, appointed in a personal capacity. The reports are available to the public.

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This report can be downloaded from www.healthcouncil.nl.

Preferred citation:
Health Council of the Netherlands. A fair compensation. Considerations for a proposal to give living kidney donors priority for transplantation. The Hague: Health Council of the Netherlands, 2011; publication no. 2011/06E.

ISBN: 978-90-5549-871-0

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Executive summary

Patients in the Netherlands requiring a donor kidney spend three to four years on average on the transplant waiting list for a kidney from a deceased donor. Postmortem donor kidneys are in short supply. Consequently, over the past 15 years, it has increasingly been the case that living persons have donated a kidney. More than 58 percent of kidney donations in 2010 came from live donors. This development begs the question as to whether these donors ought to be given priority on the donor kidney waiting list in the event of subsequently suffering from severe renal insufficiency. This has been proposed by Eurotransplant, a collaborative organisation for the international exchange of donor organs, with which the Netherlands is affiliated. This led the Minister of Health, Welfare and Sport to request an advisory report from the Health Council of the Netherlands at the end of 2009. When allocating donor kidneys, are there any medically or morally valid reasons for taking into account that a person earlier in his life has donated a kidney? And is it legally possible to award these donors extra points on the waiting list?

Likelihood of live donors subsequently suffering renal insufficiency

The Committee has considered the effects and risks of kidney donation in the case of live donors. What is the probability of complications and death as a result of the surgery? What is the effect on the donor's life expectancy? And, left with

only one kidney, what is the risk of the donor developing severe renal insufficiency, and possibly needing renal replacement therapy?

Research among living donors indicates a low risk of complications and death as a result of the operation, in comparison with other frequently performed surgical interventions. Likewise, the loss of a kidney does not appear to make the donor more susceptible to disease or early death. However, in comparison with the present donor population, the donors in these studies were more stringently selected on the basis of their health and physical condition and screened for any disorders. Potential donors are currently more often accepted with what were previously deemed to be contraindications (higher age, mild hypertension, moderately overweight). This appears not to affect the outcome of these transplants. However, it means that some of the present live kidney donors may face a higher health risk in the future and have a lower life expectancy than the populations in the cited studies.

Another conclusion which can be drawn from research is that removing a kidney from selected donors does not, as a matter of course, increase the likelihood of progressive or accelerated loss of renal function in the long term. In fact, the residual capacity of the remaining kidney continues to provide sufficient renal function for the rest of the donor's life. The likelihood of a prior live donor nevertheless developing renal failure is extremely small (between 0.1 and 1.1%). Complications can be prevented or treated in good time by offering the kidney donor lifelong checkups.

Although having only one kidney does not in itself adversely affect normal functioning, it does make the donor more vulnerable if the remaining kidney's functioning is jeopardised, by a tumour in the kidney or *de novo* renal disease, for example. In that case, the donor may suffer accelerated or even acute loss of renal function because there is no reserve capacity. As an indirect consequence of donation, the donor would have to resort to dialysis earlier, and therefore experience the disadvantages of dialysis sooner than patients with the same disorder and two kidneys. The patient's reduction in life expectancy would consequently be more substantial.

On average, there are currently one or two prior live kidney donors a year who themselves are in need of a new kidney. One should make allowances for an increase in this number to four a year on account of relaxing the acceptance criteria for living donors.

Eurotransplant proposal

In practice, Eurotransplant's proposal means that people who donated a kidney earlier in life and later on need a transplant owing to renal failure should be awarded 500 points on the waiting list for a postmortem donor kidney. This means that they could qualify for a transplant without having to undergo prior dialysis (pre-emptive transplant). In the present situation, a patient with end-stage renal failure spends his waiting time while on dialysis treatment, which, although a life-saving therapy, is burdensome and in the long run harmful.

Awarding 500 points would mean that live donors are to be placed on the waiting list immediately below patients in one of the special priority groups, namely people classified as medically highly urgent or those with very little chance of receiving a suitable donor kidney. These patients would have priority over former donors because they would be at greater risk or more disadvantaged if left out when the offer of a suitable donor occurred. Nevertheless, the likelihood of a former donor being offered a kidney within six weeks would still be high.

If one former live donor a year would be given priority on the waiting list, this would increase other patients' waiting time by approximately one and a half days, against a total waiting period of three to four years. That waiting period would increase by three days in the case of two patients receiving a donor kidney before them. If this number were to rise to four per year, the waiting period would increase by around six days. Therefore, the adverse consequences for the remaining individual waitlisted patients of awarding 500 points to prior donors would turn out to be very limited.

Moral arguments

The Committee has listed and assessed the moral arguments in favour of awarding 500 points to former donors. One of the arguments is the potential to promote donations by living donors. This is not a sufficiently convincing argument in the eyes of the Committee, as the likelihood of the former donor developing renal failure is so small. The extra points are therefore unlikely to play a determining role in the decision to donate a kidney. The reward argument (i.e. rewarding living donors) is likewise invalid in the Committee's opinion. Rewarding living donors would be in breach of the principle of formal justice. It would mean granting people a higher place on the waiting list because they have a special negotiating position which enables them to 'buy' a more favourable position, rather than because they possess some relevant characteristic that may

be determining for their priority on the waiting list, such as medical need or the waiting period.

The Committee takes the view that reasoning on the grounds of compensation, supplemented by the argument of fairness, does provide a morally valid argument for awarding 500 points to former donors. The grounds for such reasoning are that it would be no more than fair to compensate a former donor with end-stage renal failure for having lost his reserve capacity as a result of the donation, which will turn against him when renal insufficiency develops. This donor will need dialysis sooner than patients with the same disorder and two kidneys, on account of the donor no longer having any reserve capacity. Because of this, the disadvantages of dialysis will affect the former donor at an earlier stage and his life expectancy will be reduced more substantially. This is particularly difficult to accept and also unfair since, by donating a kidney, the former donor has contributed to drastically reduce the average time kidney patients had to wait for a postmortem donor kidney. After all, every time a waitlisted patient succeeds in finding a willing live donor, the other people move one place up the waiting list. Without the contribution made by living donors, the waiting period in the Netherlands would be twice as long, making it six to eight years. As patients on the waiting list benefit jointly from the sacrifice made by living donors, the Committee is of the opinion that it is also fair for these patients to bear the burden of compensation in the form of a slightly longer waiting period.

What should the extent of compensation be? At first sight, awarding 500 points might appear to be overcompensation. However, ultimately, one is faced with accepting that prior live donors will be worse off than other kidney patients because they have to start dialysis treatment sooner, or accepting that they should be moved up in a better position. This is therefore a choice between ‘undercompensation’ and ‘overcompensation’. On the grounds of fairness, the Committee favours the latter choice. It would be unfair to allow the existing organ scarcity to affect people who have made a considerable contribution to reducing the scarcity and consequently face additional problems.

According to the Committee, awarding extra points to former kidney donors would not set an undesirable precedent. The Committee has not been able to find any examples which are completely analogous with the situation of live kidney donors who have developed renal failure.

Legal aspects

To what extent does current law provide scope for awarding extra points to former kidney donors? This mainly concerns the extent to which the proposal is reconcilable with section 18, subsection 3, of the Dutch Organ Donation Act, and article 3 of the Additional Protocol on Transplantation of Organs and Tissues of Human Origin (relating to the European Convention on Human Rights and Biomedicine).

No unambiguous answer to this question is possible in the Committee's opinion. Interpretation of the Dutch Organ Donation Act may follow either strict principles or a more liberal reading. Those who support strict principles will adhere more to the letter than the spirit of the law. They may conclude that the wording of section 18, subsection 3, provides no scope for Eurotransplant's proposal. However, the Committee presents arguments for a more liberal interpretation of this section. The Committee concludes that the proposal is indeed reconcilable with the principles of medical law and the spirit of this section and is therefore of the opinion that the Dutch Organ Donation Act need not be amended for the proposal to be accepted.

Likewise, the Committee does not believe that awarding extra points would be in breach of article 3 of the Protocol, which states that organs must be allocated on the basis of medical criteria. After all, allocation is based on the donor's medical needs and also takes into account the medical needs of other waiting patients.

Conclusions and recommendations

The Committee concludes that there are sound medical-ethical and legal arguments for accepting Eurotransplant's proposal to award 500 points to live donors with end-stage renal failure. Adopting this approach means that donors would qualify for a pre-emptive transplant of a postmortem donor kidney. The Committee is of the opinion that the proposal is reconcilable with national and international legal rules and the principles on which they are based. Consequently, the Dutch Organ Donation Act need not be amended in order to adopt the Eurotransplant proposal.

The Committee recommends incorporating Eurotransplant's proposal into the current system for allocating postmortem donor kidneys. Upon implementing the extra points scheme, the need for lifelong medical monitoring should once again be brought to the attention of all parties involved in health care provision, especially donors/prospective donors. The Committee also takes the view that

further medical follow-up studies of live kidney donors are of crucial importance if the criteria for live kidney donorship continue to be extended, in order to guarantee that living donors retain an equally good life expectancy rate as people who have not donated a kidney.

Chapter 1

Introduction

In early 2009, the Dutch Transplant Foundation (NTS) received a proposal from the Eurotransplant organisation (which serves also the population of the Netherlands) for amendment of the rules for allocation of (postmortem) donor kidneys. Eurotransplant recommended that persons who have donated a kidney during life and who themselves require a kidney transplant at a later stage due to renal failure, be given extra points – 500 to be exact – from now on. This would advance their position on the waiting list for a postmortem donor kidney in such a way that they would become eligible for a pre-emptive kidney transplant, i.e. a transplant without prior dialysis. This proposal actually originated in the Netherlands as an initiative by the National Consultation on Renal Transplantation (LONT), a working group of the Dutch Transplantation Association. In order to make the idea feasible and internationally applicable, it was then introduced to the renal transplantation committee of Eurotransplant (Eurotransplant Kidney Advisory Committee – ETKAC). The ETKAC in turn submitted it to the affiliated national organisations – including the NTS – in the form of a proposal for modification of the allocation rules.

The NTS assumed that the Dutch Organ Donation Law (WOD) did not offer enough leeway for such a proposal, so it submitted a request to the Ministry of Health, Welfare and Sport (VWS) in early February 2009, requesting the Ministry to take a stance on the proposal and to answer the question whether the proposal is sustained by the existing allocation rules and Dutch legislation.

1.1 Request for advisory report

On 12 October 2009, the Minister for Health, Welfare and Sport asked the Dutch Health Council to advise on the question whether or not art. 18, section 3 of the Organ Donation Law (WOD) – the law that sets out the allocation of (postmortem) donor organs – offers sufficient leeway for such a proposal. If such leeway is lacking, the Minister asked the Health Council to provide suggestions for amending the WOD in such a way that such leeway is created. The Minister also asked the Health Council to examine the national and international legal aspects of the issue and the medical-ethical aspects and health aspects associated with such a change in the law.

Please refer to Annex A for an integral representation of the request for advisory report.

1.2 Committee and testing

In order to answer the request for an advisory report, the President of the Health Council appointed a committee of experts in the field of nephrology, (medical) ethics and health law on 25 February 2010. The Committee was chaired by Prof. I.D. de Beaufort, professor of medical ethics at Erasmus University Rotterdam. The composition of the Committee can be found in Annex B.

As is standard procedure for the Health Council, several of its Standing Committees of experts were also consulted as a form of *peer review.* As part of this review, the advisory report was reviewed by the Standing Committees for Ethics & Health Law and for Medicine.

1.3 Set-up of the advisory report

Chapter 2 provides background information on the proposal to award former kidney donors extra points: the scarcity of (postmortem) donor kidneys, the waiting times for transplantation, the development of living kidney donation and the effect thereof on waiting times. The Chapter also contains a short description of the international allocation system for postmortem organs from Eurotransplant, the collaboration between countries to which the Netherlands is affiliated. This Chapter indicates which countries already grant preference to living donors with renal failure.

Chapter 3 describes what is known from the scientific literature about the medical consequences of being a living kidney donor. What are the medical

risks? Do kidney donors have a higher risk of renal dysfunction than people who have two kidneys? How frequent do former kidney donors suffer a loss of renal function to the extent that they will ultimately require dialysis or transplantation? What can be said about the development of their number with the current trend in expansion of the indication for living kidney donation?

In Chapter 4 the Committee weighs and evaluates the moral arguments for and against the awarding of extra points to kidney donors who require dialysis.

Chapter 5 examines the extent to which national and international legislation offer leeway for awarding extra points to donors when it comes to the allocation of postmortem donor kidneys.

Finally, Chapter 6 contains the Committee's conclusions and recommendations.

The Committee conforms to the custom of writing in the masculine form. Where he and him are used, this can also mean she or her.

Chapter 2

Background

This Chapter briefly outlines the history of kidney transplantation and in particular transplantation making use of a living donor. Next, the current situation with respect to the supply of donor kidneys for transplantation in the Netherlands will be discussed. This Chapter will also discuss the measures taken to reduce the shortage of donor kidneys (introduction of non-heart beating donation, expansion of living kidney donation and setup of a Donor Register) and the effect of these developments on the number of transplantations performed and on the waiting list. Finally, the allocation model for postmortem donor kidneys (ETKAS) will be described, as used in Eurotransplant.

2.1 Development of kidney transplantation

The history of kidney transplantation using living donors is almost as old as the beginning of organ transplantation itself: in the early 1950s, a series of kidney transplants were performed in France whereby a kidney from a living person was implanted in a blood relative. In 1952, Hamburger transplanted a kidney from a mother to her son, who had been born with only one kidney. His single kidney was damaged in an accident and this resulted in acute renal failure.[1] The transplanted kidney initially functioned normally, but was rejected after 21 days resulting in the son's death. The current practice for kidney transplantation begins when Joseph Murray performs a kidney transplant in Boston (USA) in December 1954, in which a 23-year-old man donates a kidney to his identical

twin brother.[1] This transplantation is considered the first truly successful kidney transplant. The recipient, Richard Herrick, lived for eight more years after his transplant. (The donor, Ronald Herrick, died recently in December 2010 at the age of 79 years). This transplant was made possible partly by Willem Kolff, the Dutch physician and engineer who in early 1950 brought the technology for chronic dialysis treatment to Boston, which meant that patients with end stage renal failure could survive. The choice for a transplant between identical twins was based on the finding that no rejection occurred in that case (immuno-suppressive medication for the treatment of rejection only became available in 1959). As a result, only transplants with the aid of a living genetically-related donor were feasible at the time. Following this milestone, a series of transplants were performed during the pioneering phase between both twins and other blood relatives. The first successful kidney transplants using deceased donors were only performed around 1962. In the Netherlands, the first kidney transplant using an organ from a living donor (mother to son) took place in Leiden in 1966.

2.2 Emergence of living donation

Much has changed in the field of transplantation since the first successful kidney transplant: the development of effective medication to suppress rejection meant that it was no longer essential to use a close blood relative as a living donor.[1] Donation after death (postmortem donation) resulted in a surge in the number of kidney transplants, which meant that the need for living donors decreased dramatically in many countries. In addition, a living donation by definition poses an ethical dilemma for the doctor: assuming the Hippocratic principle *primum non nocere* (first do no harm), a doctor will in general be very cautious about performing a procedure on a healthy person who will gain no (medical) benefit, but is exposed to very real risks.

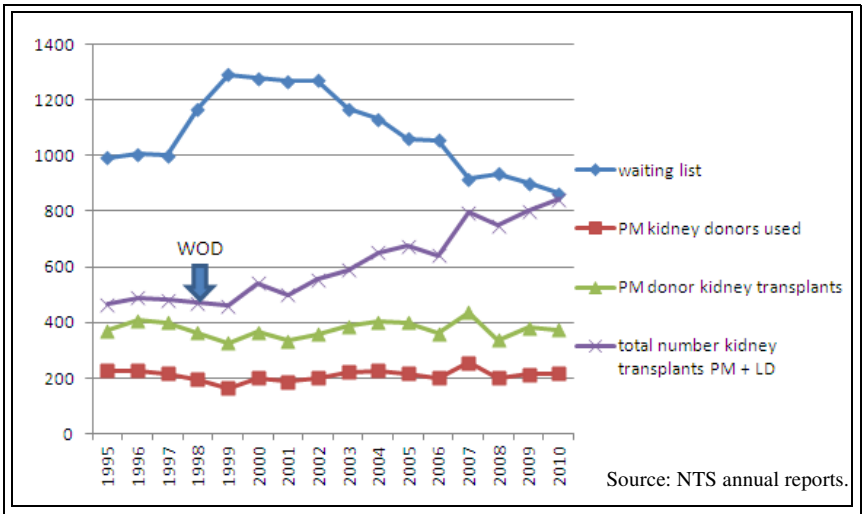
However, donation by a living person has gained an increasingly prominent role among the options for kidney transplantation. There are a number of reasons for this:

- kidney transplantation has become the preferred treatment for the end stage of chronic renal failure (CKD). Although dialysis treatment ensures the temporary survival of the patient, this treatment does not provide a cure for the underlying disease. In addition, survival and the quality of life after transplantation are significantly more favourable than for dialysis (mortality of patients on dialysis is over 50% higher than for transplanted patients)[2-5]

- the preference for transplantation means that there has been a significant increase in patients on the waiting list, with the average waiting time also increasing significantly (up to 4.5 years in the Netherlands in 2009). The need for kidney donors is also increasing, because there are more conditions in the general population (diabetes, hypertension, obesity, ageing) that eventually necessitate renal replacement therapy
- the acute shortage of postmortem donor organs means that currently one in five kidney patients on dialysis dies whilst waiting for a transplant[6]
- studies have shown that transplantation using a kidney from a living donor provides a more favourable outcome for the recipient in almost all cases when compared to transplantation using a postmortem kidney (a better transplant and patient survival)[5]
- studies have shown that the benefit of kidney transplantation using a living donor also applies when donor and recipient are not genetically matched (no blood relatives): the results of transplantation using both related and unrelated donors are almost identical and significantly better than when a postmortem donor kidney is used[7]
- apart from shortening the waiting list and avoiding long waiting times, transplantation using a living donor also offers another benefit that should not be underestimated: if a living donor is available, the transplantation can take place even before the patient needs to start dialysis treatment. Such a pre-emptive transplant significantly improves the lifespan of the transplanted organ (approx. 10% better graft survival)[8-10]
- the introduction of kidney removal (nephrectomy) via a laparoscopic procedure (minimally invasive procedure) in the 1990s, which significantly reduced the risks and discomfort for the donor compared to the usual 'open' surgery (less pain, faster recovery, shorter hospital stay, quicker return to work), further reduced the threshold for living donation for many people.[11,12]

2.3 Current scarcity of donor kidneys

Since the mid 1980s until 2000, the waiting list for kidney transplantation increased significantly in the Netherlands (and elsewhere); this is due partly to the success of organ transplantation and the availability of effective anti-rejection medication. The number of kidney transplants using an organ from a deceased donor increased initially as a result, but has remained virtually stable at approx. 400 per year since 1990. Since 1990, a donor kidney has been available for only one out of every three waiting kidney patients each year, resulting in the waiting time increasing to an average of four years. The introduction of *non-heart*



Waiting list: number of kidney patients waiting for a transplant as counted on 31/12 of each year.
PM postmortem kidney donors used: reported donors from whom at least one kidney was removed.
PM kidney transplants: kidney transplants with postmortem donor (excluding kidney in combination with other organ).
LD kidney transplants: kidney transplants with a living donor.
Total number of kidney transplants: with both postmortem and living donor.
WOD: year that organ donor law was introduced.

Figure 1 Supply of postmortem organ donors in the Netherlands (1990-2010), waiting list of kidney patients and number of postmortem kidney transplants.

beating donation (NHBD)* around 1995 initially resulted in an increase in the donor pool, but this growth also stagnated due to the gradual decrease in the number of *heart-beating* donors (HBD)**. Again, the introduction of the Organ Donation Law in 1998 did not produce a permanent increase in the number of postmortem donors. It is mainly the growth in the number of kidney donations from a living donor that has caused the total number of kidney transplants in the Netherlands to increase since 2000 and as a result caused the waiting list to decrease. Figure 1 provides a general view of these developments.

Since 1995, the waiting list for kidney patients has increased to a peak of nearly 1,300 in 1999, after which a downward trend started, which has become more apparent since 2002. This is closely related to the increase in the number of

* *Non-heart beating donation* (NHBD): organ donation after death caused by irreversible circulatory and respiratory arrest. Also indicated as: donation after circulatory death (DCD).

** *Heart-beating donation* (HBD):organ donation after death caused by total and irreversible loss of function of the brain (brain death).

kidney transplants using a living donor (further explanation in 2.6). In 2010 there were 864 kidney patients on the waiting list (per 31 December), compared to a total outflow of 843 kidney patients due to transplantation in that year.

2.4 Waiting list and waiting time

Since 2003, there has been a steady and substantial decrease of the waiting list for kidney transplantation (in contrast to the waiting list for liver, pancreas, heart and lung transplants, which remained stable or increased further). Table 1 provides the average waiting time for a transplant of a kidney from a postmortem donor.

Table 1 Waiting time for kidney transplantation with postmortem donor in 2009.

Waiting time	Days
Average dialysis duration	1,440
Median dialysis duration	1,357
Average registration duration	1,140
Median registration duration	986

Source: NTS annual report 2009.

The waiting time in the Netherlands is calculated from the start of dialysis (but this does not always correspond to the time at which the patient was actually registered on the transplant waiting list). The median dialysis duration to kidney transplantation (with a postmortem kidney donor) was approx. 3.7 years in 2009 and has shown a slight decreasing trend over the last few years (was previously 3.8 years). Approximately 24% of the kidney patients awaiting transplant undergo dialysis for more than five years. There has also been a slight decrease in this figure over the last few years (was 30%).

2.5 Effect of introduction of non-heart beating donation

Around 1995, *non-heart beating* donation was (re)introduced in a number of Dutch transplant centres. These are people who have died as a result of an (irreversible) circulatory arrest, after which organs were removed for transplantation. Figure 2 shows the development of the number of HB and NHB donations.

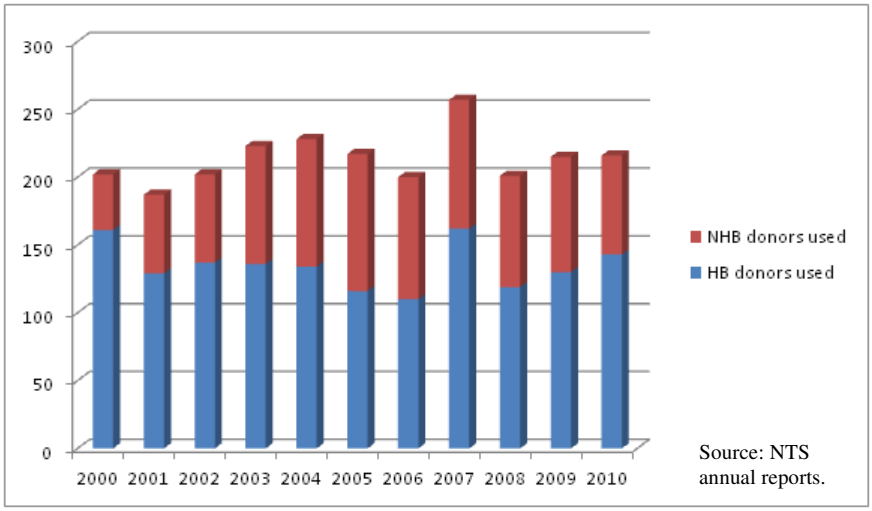


Figure 2 Development of total number of postmortem kidney donors (HB + NHB), 1995-2010.

The introduction of *non-heart beating* donation initially resulted in an increase in the total number of kidneys transplants. However, this development did not persist; since 2000 there has been a steady decrease in the number of *heart beating* (HB) donors, with a temporary recovery in 2007 and a further decrease in the years thereafter. The number of *non-heart beating* (NHB) donations stabilised after 2000 at around 90 procedures per year. On balance, the total number of effected postmortem kidney donations has remained stable since 2000 at approx. 200 per year, which has not resulted in a significant decrease of the waiting list – as was hoped.

2.6 Development of living kidney donation

The previously explained development of living kidney donation has had a great influence on the increase in the number of kidney transplants. Figure 3 shows the development of the number of kidney donations with both (genetically) related and unrelated living donors.

Before 1995, for medical reasons, living donations were almost exclusively performed on recipients who were blood relatives of the donor (so-called family transplants). However, studies have shown that persons not related to the recipient can also act as a donor, with equally good results.[7,13] The introduction of the Dutch Organ Donation Law has also made the legal acceptance of these

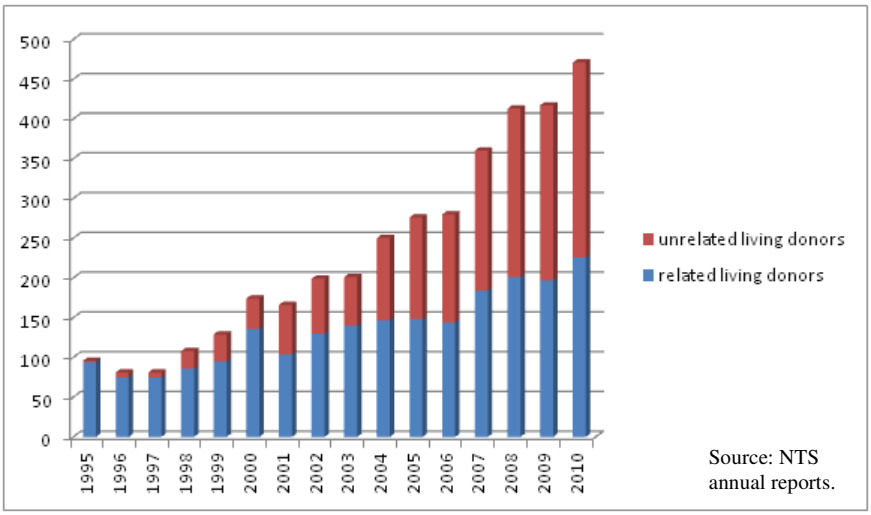


Figure 3 Development of number of living kidney donations (1995-2010).

unrelated donors easier by creating room for donation by spouses/partners, in-laws, friends and even anonymous altruistic donors. In 2010, over 58% of all kidney transplants in the Netherlands were performed with the aid of a living donor and over 52% of all kidney transplants with a living donor are now performed using an unrelated donor. For the related donors, 41% of cases involve donation by a brother or sister (sibling) and 38% involve a donation by one of the parents. For the unrelated donors, the donor is the person's own spouse in 57% of cases. In the Netherlands, men and women act as donors in almost equal numbers. women.

2.7 Effect of living donation on the waiting list for kidney transplantation

As described above, the number of donations and kidney transplants has increased significantly over the last few years thanks to living donors. Figure 4 shows this development and the effect on the waiting list.

In 2008, the number of living donor (LD) kidney transplants exceeded the number of transplants with a postmortem donor for the first time. This trend continued in 2010 (470 LD transplantations in 2010). The favourable effect on the waiting list is clearly visible since 2006. One can say that – if this increase in the number of LD transplantations had not taken place – the waiting time for a

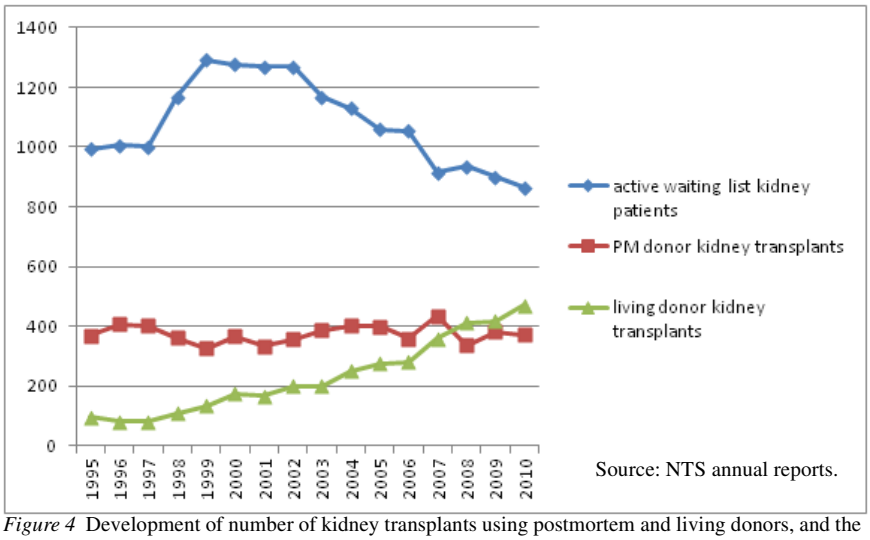


Figure 4 Development of number of kidney transplants using postmortem and living donors, and the effect on the waiting list (1995-2010).

transplant with a postmortem donor in 2010 would have been more than double at eight or nine years.

2.8 Recording of living will in the Donor Register

With the introduction of the Organ Donation Law in 1998, Dutch citizens are asked to record their wishes concerning organ donation in the central Donor Register. Table 2 shows the number of living wills recorded in the Donor Register on 31 December 2009.

In 2009, the Donor Register was consulted a total of 8,138 times; in 3,387 cases a living will was found (hit-chance 42%). This involved consent in 54% of cases,

Table 2 Number of consultable registrations in the Donor Register on 31 December 2009.

Living wills	Number	% of registered individuals
Consent	2,566,450	47.3%
Consent with limitations	553,877	10.2%
No consent	1,615,275	29.8%
Next of kin decide	589,338	10.9%
Designated person decides	100,353	1.8%
Total	5,425,293	100%

Source: NTS annual report 2009.

refusal in 38% of cases and the decision left to next of kin in 8% of cases. In 4,751 out of these 8138 cases being checked (57%), there was no registration whatsoever. In 2009, the number of registrations increased by 1.8% compared to 2008 and the number of registered consent decisions increased by 2.6%.

2.9 Family refusals

In 2009, a Medical Record Screening was performed at the Intensive Care Units of 84 Dutch hospitals. This revealed that – whenever a potential donor was not registered in the Donor Register or left the decision to his next of kin – these next of kin refused consent for donation in 68% of cases. Even when valid consent was found in the Donor Register, objections from next of kin resulted in the donation not being performed in 4% of cases. In total, the percentage of family refusals was an average of 53% of all potential donations. Seen in an international context, this percentage is very high and refusal by next of kin is an important stumbling block in our Dutch donation system.

2.10 Current allocation system for postmortem donor kidneys (ETKAS)

This section briefly describes the rules in the Netherlands for the allocation of donor kidneys and where these rules have been set out. These allocation rules are described in more detail in Annex C of this advisory report.

Documentation of allocation rules

The Dutch Organ Donation Law (WOD) sets out in general terms how the allocation of postmortem donor organs (i.e. from deceased donors) should take place in the Netherlands (also refer to paragraph 5.1 of this advisory report). Art. 18, section 3 of the Organ Donation Law (WOD) states:

> During allocation, no factors other than the blood and tissue compatibility of the donor and recipient of the organ, the medical urgency of the recipient and other circumstances related to the condition of the organ will be taken into consideration and if these factors do not provide a decisive answer, the waiting time of the recipient is taken into consideration. Further rules can be set out as an Order in Council.

According to the law, the national organ centre (i.e. Dutch Transplant Foundation – NTS) is responsible for the execution of this allocation. However, in practice, the Netherlands does not have its own allocation rules for organs, but follows the

international allocation system of Eurotransplant, of which the Netherlands is a member: for kidneys, this is the Eurotransplant Kidney Allocation System (ETKAS). This ETKAS was implemented in 1996 and has since been continuously modified and refined, with the following goals:

- establishing a favourable tissue match (HLA match) between recipient and donor
- optimising the chance of success for transplantations
- reducing the average and maximum waiting times for patients
- taking into consideration 'hard-to-treat' patients (with rare or homozygous HLA phenotypes)
- facilitating organ exchange between countries whilst maintaining a reasonable balance between importation and exportation for each country.

General starting points of ETKAS

The general starting points of ETKAS are:

- objectivity: all patients on the waiting list are treated equally (but are not all equal)
- transparency: the allocation system is clear and is followed in the same manner by all affiliated centres
- priority based on medical urgency: all patients who urgently need an organ based on set medical criteria will be given preference
- compatibility: the allocation system uses set parameters for good HLA compatibility between donor and recipient, as a result of which an organ will be allocated to a specific patient
- country balance: the determination of and correction for import/export imbalance is essential to ensure that countries with a high organ yield are not disadvantaged by the exchange of organs.

Priorities schedule for allocation

The ETKAS system is set out in such a way that – for allocation of available postmortem donor kidneys – patients with a high urgency (HU status) or those in a particular category (highly immunised or older than 65 years) will be the first to become eligible. Next, the order of the other patients on the waiting list is determined based on the blood group match (ABO compatibility), tissue match (HLA compatibility) and waiting time (calculated from the start of dialysis treatment) in particular. (See Annex C).

2.11 Current allocation for living donor with renal failure

The ETKAS system for kidney allocation does not apply to living donation. After all, virtually all living donations involve a prior selected specific recipient, which does not involve competition between waiting patients. However, if a person who previously acted as a living donor experiences renal failure at a later stage and requires dialysis or transplantation, then there are currently two options: 1) the person looks for a living donor himself and preferably undergoes a pre-emptive transplant; or 2) the person starts dialysis, is admitted to the waiting list and starts accumulating points from that moment on for waiting time; the patient now falls under the ETKAS allocation rules for a postmortem kidney. The status of 'former donor' is currently not included in the allocation. As a result, one has to be prepared for a considerable waiting time on dialysis and a pre-emptive transplant is not possible.

2.12 State of affairs in other countries

Are there countries that already grant priority to former living donors? The situation in the United States, the (other) Eurotransplant countries, the United Kingdom, the Scandinavian countries and Israel are discussed below.

United States of America

As far as we are aware, the United States is the only country now that has a formal arrangement. Policy Section 12.9.3 (*Priority on the waitlist for prior living donors*) of the most recent version (June 2009) of the OPTN/UNOS* recommendations states the following:

- a candidate is assigned 4 points if he or she has donated for transplantation a vital organ or a segment thereof (in the USA). Candidates assigned 4 points for donation status shall be given first priority for kidneys that are not shared mandatorily for 0-HLA mismatching, or for allocation based on high urgency
- if there are multiple candidates with 4 points, who are eligible for a priority kidney offer under this policy recommendation, then the organ shall be allocated according to the duration of the time waiting.

* OPTN: Organ Procurement and Transplantation Network; UNOS: United States Network for Organ Sharing.

Countries affiliated to Eurotransplant

Within Eurotransplant, the recommendation to give a former living donor who develops renal failure priority for transplantation has been accepted by Belgium/ Luxemburg, Austria, Slovenia and Croatia (without this having resulted in a formal amendment of the laws or regulations in these countries). Germany has rejected this proposal for the time being, referring to the legislation that stipulates that only medical criteria may play a role. The Committee does not know whether the Croatian and Slovenian decisions to accept priority for prior living donors have been reviewed with respect to the Convention on Human Rights and Biomedicine and the Additional Protocol on Transplantation of Organs and Tissues of Human Origin.*

United Kingdom

In the United Kingdom, some individual transplant centres also have a policy to grant priority for transplantation.to cases where a former living donor experiences renal failure.

Scandinavian countries

Current policy in Sweden is that former living donors are given the highest priority for a transplant if they become dependent on dialysis themselves. Firstly, a search is done for a living donor (related/unrelated) in order to achieve a pre-emptive transplantation. If a living donor cannot be found, this patient is placed on the waiting list with priority status. However, this is not reflected in a points system. A similar policy is in effect in Norway. Denmark has no experience as yet with living donors who require dialysis at a later stage. The number of living donors in Finland is very small and this problem has not occurred to date.

Israel

Since January 2010, Israel has new legislation concerning organ donation, which includes a priority arrangement for donors. [17] This regulation stipulates that priority in the allocation of postmortem donor organs be awarded to: 1) individuals who have registered a living will stipulating consent for donation after death AND their first degree relatives; 2) the first degree relatives of a person who actually donated organs after his death; and 3) individuals who donated an organ whilst alive to an unknown (*non-directed*) recipient AND the

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* Such review would seem obvious, because both Croatia and Slovenia have signed and ratified the Convention and Protocol. Please refer to paragraphs 5.2.1 and 5.2.2 for the contents of the Convention and Protocol.

first degree relatives of these individuals. In this country, the reciprocity principle is applied to both individuals who recorded their willingness to donate organs and those who actually donated organs (living or after death), with their direct relatives also benefiting. However, it is remarkable that priority is not awarded to persons who previously donated an organ (or part thereof) whilst still alive to a (blood-related or emotionally related) recipient of their choice.

Chapter 3

Risk screening and chance of later kidney function disorders in living donors

This Chapter briefly describes the selection and screening of people who choose to donate a kidney during life, and then focuses on the short and long-term risks and effects of kidney donation in the donor. It is described how the remaining kidney adapts to the reduction in kidney mass and how this affects its functioning (in the long term). Finally, this Chapter lists the causes (risk factors) that can be responsible for the occurrence of renal failure in the donor and what the consequences are for him.

3.1 Selection and screening of living kidney donors

A number of factors play a crucial role in the selection and screening of persons who intend to donate a kidney during life:

1 general (legal) conditions for donation:
   - age of majority and mental competency
   - voluntary and non-profit nature of donation
   - permission based on *informed consent* (sufficient knowledge about possible consequences and risks)
2 suitability requirements:
   - the relationship between donor and recipient: this initially involved mostly a genetically related blood relative; later also a non-blood relative (such as a spouse/partner). Recently, unrelated donors[7] (such as a friend or

colleague) and altruistic (so-called Samaritan) donors (anonymous or known) have also become eligible
    - selection based on psychosocial suitability (screening for factors such as motivation, stability and supportive social network)
3 medical criteria:
    - ABO compatibility (however, it is now also possible to transplant through the ABO blood group barrier using conditioning regimes)
    - negative cross match (recipient does not develop antibodies against the donor)
    - evaluation of absolute and relative contra-indications: diabetes, (severe) hypertension, hereditary renal disease in family, obesity.

3.2 Medical risks of living kidney donation: safety of the donor

The above-mentioned medical screening of potential living donors significantly reduces the chance of unexpected complications occurring. In the past decades, the surgical removal of a kidney in a living donor (nephrectomy) has also become significantly safer and less of a burden due to the development of laparoscopic surgical techniques.[12] However, the risks of unilateral nephrectomy should not be underestimated and precautions should be taken to reduce potential complications and mortality as far as possible.

3.2.1 What risks are there for the donor?

The risks for a living donor can be divided into two categories: 1) the short-term risk of complications and death as a result of the surgical procedure itself (peri-operative morbidity and mortality); and 2) the long-term risk of living with only one kidney.[18] For the latter, this involves both the loss of renal function and a decrease in life expectancy. These risks are discussed separately below.

Peri-operative risk

In a number of countries the data on kidney removal (nephrectomy) from living donors have been systematically collected and recorded in a database for many years. Studies of these registries have shown that approximately one in ten donors (10%) experience complications as a direct result of the surgical procedure.[19-21] In addition to wound pain and discomfort, these complications include – among others – pneumothorax, wound infections, pneumonia, urinary

tract infections, bleeding, hernia, pulmonary embolism and damage to the renal vessels.[22-25]

These studies also show that the mortality as a result of the surgery (peri-operative death) is very low: the average figure was 3 in 10,000 (0.03%) over the past decades. (In comparison: there are 18 deaths per 10,000 patients with the frequently performed laparoscopic gall bladder removal and 260 deaths per 10,000 patients for nephrectomy in a non-donor).[26] Analysis of the data in the registry of the Norwegian living donor programme show that the introduction of laparoscopic nephrectomy has resulted in further reduction of the morbidity and mortality: not a single death was reported for 1,800 donor surgeries and there was also a decrease in complications.[22] Recently, the results of an American study were published on the morbidity and mortality in a population of over 80,000 living donors, as described in the UNOS/OPTN database 1994-2009.[27] The risk of peri-operative mortality (within 90 days after surgery) was 3.1 per 10,000 for the entire group; the risk of death for men was significantly higher than for women, namely 5.1 compared to 1.7 per 10,000 donors. This mortality risk did not change during the entire study period of fifteen years, despite the fact that the mean age of living donors increased (marked increase in number of donors over 50 years of age) and the average body weight also increased significantly (in 2009, more than 20% of the donors had a BMI of 30 or more). Remarkable in this analysis is that the introduction of laparoscopic nephrectomy initially resulted in a (small) increase in mortality (during 1998-2005 period), but this was followed later on by a significant decrease in mortality (learning curve effect). If one looks at the mortality in the most recent study period (2006-2009), then the rate using the laparoscopic procedure is approximately 2 per 10,000 donors (0.02%).

Friedman recently performed a retrospective analysis of a randomised sample of patients in the USA discharged from hospital in the period 1999-2005. This revealed a total of 6,320 living donors: with 0% mortality and 18.4% morbidity (in hospital/peri-operatively).[28]

To summarise: the risk of peri-operative morbidity and mortality (compared to other frequently performed procedures) is limited and should not form an impediment to live donation for either the doctor or the donor.

Long-term risk

When determining the long-term risk of living kidney donation, two aspects play an important role: 1) Does the loss/donation of one kidney affect the life

expectancy of the donor? (normal or abnormal life expectancy); and 2) Does having a single kidney possibly lead to the (accelerated) development of late renal disease and the need for renal replacement therapy (transplantation or dialysis)?

Life expectancy of the donor

The data on long-term survival following unilateral nephrectomy were initially obtained mostly by indirect methods: by looking at patients who have had a single kidney from birth (congenital agenesis)[29], or patients who lost a kidney due to severe injury (including veterans from World War II).[30] The life expectancy in both groups did not differ significantly from that of a 'healthy' person with two kidneys. A more relevant analysis was performed by Fehrman-Ekholm, who compared the observed survival of a group of 430 living kidney donors in Sweden to the life expectancy of the general (healthy) population, corrected for age and gender.[31] Twenty years after donation, the observed mortality in the group of donors was 25% less than the expected mortality in the general population (control group). In another study, the total group of living donors in Norway (over 1,600) were monitored over a period of 32 years, which again revealed that the mortality risk of donors is smaller than in the 'normal' population (relative risk of dying for donors: 0.7 for women and 0.5 for men).[22,32,33] These investigators concluded from their study that donation of a kidney has no negative effect on the (normal) life expectancy. They did note that living donors were positively selected for health and physical fitness and screened for any possible conditions, so that they cannot really be compared accurately to the general population. Nevertheless, the analysis does show that – in the case of living donors – there are no reasons for assuming that the loss of one kidney would make the donor more susceptible to disease or early death when compared to the general population.

The outcome of this study should be viewed with some caution when drawing conclusions about the current and future life expectancy and safety of donors, as today's donor population differs fundamentally from the historic population in the cited studies.[34,35] Due to the current donor shortage and the success of living kidney donation, the demand for living donors has increased significantly and the selection criteria for living donation have also been expanded in recent years in order to meet this demand. This means that doctors now more often accept potential donors with what would previously have been considered contra-indications, obviously within certain limits. Donors who are older, or with mild

hypertension or moderate excess weight can now also be eligible. This development could possibly result in a slightly greater future health risk for the current donors and a less favourable life expectancy compared to historic populations.[26]

Loss of renal function after donation

Loss of renal function over time in patients with kidney disease has been studied extensively: the mechanisms of the loss of function and the risk factors for future loss of function are well documented. However, this knowledge cannot be applied directly to healthy individuals who have had one kidney removed for donation. The markers commonly used to make a prognosis about the course and the changes in renal function, such as proteinuria (presence of an excessive concentration of protein in the urine), are absent in a healthy donor. The question is therefore whether similar processes occur in the donor's remaining kidney that negatively influence the function and vulnerability (sensitivity to damage) of the organ, and whether it is possible to screen the donor for this in advance. In order to establish such a risk profile, it is important to understand how the remaining (contra-lateral) kidney responds to the loss of renal capacity in the donor.

The removal of a kidney, as is the case with a living donor, halves the person's renal function in the short term, but this does not have to be a problem due to the existing overcapacity of the kidneys.[20] Furthermore, an adaptive response takes place in the remaining kidney, which ensures that the donor's renal function is compensated in due course to approximately three quarters of the initial value. This compensatory increase is greater – on average – the younger the donor is. In the long term, compensatory growth (renal hypertrophy) also takes place in the remaining kidney.[36,37] This adaptive response results in the donor's renal function improving from approximately 50% immediately after the donation to roughly 70-80% in the long term.

The essential question now is whether there are mechanisms active in the kidney donor that could threaten the proper functioning of the remaining kidney. It is known that increasing age has an effect on renal function: everyone experiences a decrease in renal function with ageing. The same also applies to a healthy kidney donor. However, the loss is usually not significant enough for the kidney function to require support or replacement at any time. The possible occurrence of hyperfiltration plays an important role in the occurrence of loss of renal function: this causes higher than normal pressure in the kidney. The relationship between the quantity of blood flowing through the kidney and the quantity that is effectively filtered by the kidney, shifts in favour of the quantity

that is filtered in that case. This hyperfiltration can threaten the healthy functioning of the kidney. Research has shown that the loss of a significant portion of the kidney mass (as in the case of one kidney being removed) can result in compensatory hyperfiltration.[38,39] Such hyperfiltration can also occur in the case of obesity.[40]

Animal experimental studies demonstrate a link between the presence of hyperfiltration and the occurrence of high blood pressure (hypertension), proteinuria (protein in the urine) and glomerulosclerosis (damage to the kidney filters – glomeruli), which indicates loss of renal function.[41,42,43] However, it is not clear yet whether this process also occurs in the same manner in healthy kidney donors.

3.3 Possible link between donation and late complications

Data about the long-term consequences of a single nephrectomy were initially obtained primarily from studies with non-donors: patients with congenital agenesis of one kidney or loss of a kidney due to trauma (as already mentioned above). Studies on the consequences of progressive loss of renal function – as is sometimes the case in people with diabetes[44] or with congenital polycystic kidneys[45] – also provide indirect information about the risk of late kidney damage and loss of function in a living donor.[40]

A number of studies have been performed more recently, in which living donors were followed for over twenty years after donation and in which the course of their kidney function was measured (presence of proteinuria, hypertension and the creatinine values).[46,47] These studies provided no indications of an increased incidence of kidney damage or an accelerated loss of renal function in kidney donors. These donors did exhibit a gradual increase in blood pressure (2-3 mmHg per ten years)[48,49] and an increase in proteinuria (75mg/day per ten years)[50], but this does not differ significantly from the usual renal function development in non-donors and is also not accompanied by the occurrence of renal insufficiency.[51-53,54] A study in which the course of the renal function of kidney donors was compared directly to their non-donor brothers and sisters, showed no differences in creatinine values, the extent of proteinuria and the presence of high blood pressure over a period of twenty to thirty years.[19]

In 2006, the Canadian Council for Donation and Transplantation published the results of a systematic review of the medical risks for living donors.[55] From a total of 249 studies, 49 relevant studies were selected (from 28 countries, in the period 1973-2004, with a total of 4614 donors), in which the donors were

compared to healthy control individuals. The renal function (glomerular filtration rate – GFR), the systolic blood pressure and the occurrence of proteinuria/micro-albuminuria in donors and their matched controls were compared. The investigators drew the following conclusions from these results:

- following donation, the donor's blood pressure rises to an average of 5 mmHg above the increase already caused by natural ageing processes
- the renal function (GFR) decreases immediately after donation by 15-17 ml/min, and a further loss of function follows the expected loss due to normal ageing. Follow-up shows that an average of 13% of donors have a GFR of 30-59 ml/min (indicating moderate kidney damage – CKD 3). Approximately 0.4% of donors have a GFR of less than 30 ml/min (indicating severe kidney damage – CKD 4)
- kidney donation results in a small increase of the albumin level in the urine (average increase of 66 mg/day urine protein); during follow-up, the average protein level in de urine of donors was 147 mg/day and for the healthy control individuals was 83 mg/day
- none of the studies showed that kidney donation by healthy, selected donors results in a long-term risk of premature death or cardiovascular disease.

The above-mentioned shows that, although living donors experience changes in blood pressure, renal function and the amount of protein in the urine (proteinuria), the crucial question is whether this has any predictive value for the occurrence of (accelerated) loss of renal function in the long term. Studies in the general population have shown that every 10 mmHg increase in systolic blood pressure, and every 5 mmHg increase in diastolic blood pressure is associated with an increase by a factor 1.5 in death from ischaemic heart disease and stroke. Decreased renal function and proteinuria in the general population are also associated with systematic atherosclerosis and premature death, as well as cardiovascular disease. However, the possible decreased renal function and the (low-grade) proteinuria in kidney donors are the result of entirely different mechanisms and the prognostic significance of these events on later renal failure remain as yet unclear. The same applies to increased blood pressure, particularly if this hypertension is managed with medication.

To summarise: the above-mentioned facts mean that – in healthy, selected donors – unilateral nephrectomy does not automatically result in a higher risk of progressive or accelerated loss of renal function in the long term.[56] Although the chance of this does not appear raised in comparison to the normal population, there may be other risk factors for living kidney donors, which could result in

them being confronted with premature renal failure.[57] These risk factors are discussed below.

3.4 Additional risk factors for living donation

It has been demonstrated that hypertension and diabetes, particularly in combination with obesity, are the most common causes of renal damage due to hyperfiltration at an older age. Particularly in younger potential donors, significant excess weight (BMI over 30: obesity), diabetes or an abnormal glucose tolerance are absolute contra-indications. The Dutch guidelines for living donation exclude these individuals. On the other hand, the existing criteria for acceptance of living kidney donors have become less strict, partly due to the shortage of donors. As a result, potential donors who are older, have moderate excess weight or have moderately high blood pressure that is controlled with medication can now also be accepted as donors (so-called *expanded criteria donors*). This makes it essential to estimate during screening what their residual kidney function will be after donation and what the course of this function will be long-term. Studies have shown that a combination of values – namely: the kidney function before donation, the residual capacity of the kidney, the age and BMI status of the donor – provide the best prediction of the remaining renal function after donation.[58,59]

Obesity appears to be an important independent risk factor for a deterioration in renal function, particularly in combination with high blood pressure (which can also be a result of obesity).[60] Obesity is associated with a high filtration pressure and the occurrence of hyperfiltration. In the normal population, obesity (defined as a BMI of 25-30 kg/m^2) can double the risk of severe kidney damage and end-stage renal insufficiency, whilst morbid obesity (defined as a BMI over 30 kg/m$^{2)}$ more than triples this risk.[61] In addition to kidney damage, obesity in combination with hypertension also creates a risk of cardiovascular disease. It has been shown that – in kidney donors who are overweight – this can induce the occurrence of proteinuria and glomerulosclerosis, resulting in progressive kidney damage.[46,62] A Dutch study examined whether a decrease in body weight could have a favourable effect on the degree of hyperfiltration.[54] The filtration factor (FF) was measured in this study in which donors were monitored for 6 years. For donors who lost weight or maintained a stable weight, the FF remained the same or decreased, but in donors who gained weight the pressure in the kidney increased, which could indicate an extra burden on the kidney. In the case of severe obesity, this could result in the residual capacity of the remaining kidney not being used entirely and ultimately leading to renal failure. The conclusion

must be that planned weight loss prior to donation and/or the prevention of weight gain after donation should be pursued in order to favourably influence the haemodynamics of the kidney. This policy would have to form part of a long-term follow-up study of donors.

According to some authors, the increase in and acceptance of living donors with moderate to severe morbidity, such as obesity, kidney stones and high blood pressure (so-called *high risk* or *complex donors*) requires a separate medical, ethical and legal approach that focuses specifically on protecting these donors. This includes: maximum information, independent donor evaluation, a strict *informed consent procedure* and extended follow-up to evaluate the residual capacity.[63,64]

Loss of reserve capacity

As has already been mentioned above, the general conclusion is that unilateral kidney removal in a selected donor does not automatically result in an increased chance of progressive or accelerated loss of kidney function in the long term. The residual capacity of this remaining kidney ensures that sufficient renal function is maintained for the rest of the donor's life. This partly justifies this form of donation and transplantation. However, it is important to acknowledge that the living donor is potentially vulnerable for the rest of his life.

Even if having only one kidney in itself does not negatively influence normal function, it does make the donor more vulnerable when this function is endangered due to unforeseen circumstances. For example, as a result of an accident or trauma, a tumour in the kidney or the occurrence of a new (*de novo*) kidney disease.[18] In that case, the absence of reserve capacity in the donor can result in accelerated or even acute loss of renal function, making the need for renal replacement therapy (dialysis/transplantation) an unavoidable reality. The following should be taken into consideration: although dialysis treatment is a short-term life-saving treatment, in the long term it is also a burdensome and harmful therapy. The dialysis patient therefore has a strongly reduced life expectancy compared to a healthy person. Also in comparison to kidney transplantation, the mortality risk and thereby the life expectancy of the patient undergoing dialysis treatment is significantly less favourable than that of a patient after transplantation (life expectancy of dialysis population 40-44 years approx. 8 years after start of dialysis, and approx. 4.5 years for population 60-64 years. The risk of dying also increases by an average of 6% for every subsequent year on dialysis).[10]

The conclusion should therefore be that the – in itself – very small risk that the living donor has of developing renal failure can have very significant consequences for himself: as an additional consequence of the donation (namely: 'trading in' reserve capacity by donating one kidney) this person would require dialysis sooner and therefore be at significant risk of an early death. The loss of life expectancy suffered by the donor in that case would be greater than the loss of life expectancy of renal patients on dialysis with the same condition but in possession of two kidneys, because the donor would require dialysis sooner than they would. This disadvantage can only be averted by offering an urgent transplantation as a safety net (see Chapter 4).

3.5 How many living donors eventually develop renal failure?

Analysis of the international databases of living kidney donors has shown that the actual occurrence of end stage renal failure – in which dialysis or transplantation becomes essential – is no more than sporadic. In Norway, seven cases of end-stage renal insufficiency were found for a total of 1,800 living donors (0.4%). The majority of these cases were caused by primary renal disease and were not the result of glomerulosclerosis due to hypertension or hyperfiltration following the donation.[22,33] A retrospective study of more than 1,100 living donors in Sweden (donation between 1965 and 2005) found six cases in which the donor had developed end stage renal failure (0.5% of all donors), an average of twenty years after donation. Five of them were men, the average age was around 70 years.[65]

An analysis of the data from the American Organ Procurement and Transplantation Network (OPTN) until 2000 revealed how many patients on the active waiting list for kidney transplantation were former living donors.[66] Of the many thousands on the waiting list, a total of 56 people could be identified as former kidney donors. Of these, 43 actually underwent transplantation. This number could be an underestimate of the true number of kidney donors with renal failure, as only the patients who were actually on the waiting list for transplantation were counted; those who were rejected for transplantation (due to illness or old age) or had already died were not included. In a recent update of the study based on the OPTN data registration, it was revealed that of all kidney patients registered on the waiting list between 1996 and 2008, 172 had in the past donated a kidney (approx. 0.3%); the period between donation and placement on the waiting list was an average of 19 years.[67]

In 2002, Ramcharan and Matas studied the long-term follow-up data for 773 living donors who had donated a kidney in the period 1963-1979 and were monitored for 20-37 years in the University Medical Centre of Minnesota.[53] Information could be obtained on 464 former donors (60%): 84 of them had since died and 380 were still alive. Of the 84 donors who had died, three had end stage renal failure; of the 380 surviving donors, three had developed renal failure and two of them had undergone transplantation. All the others had normal renal function for their age and gender.

In a recent publication, Ibrahim and colleagues analysed the results of a new study on the incidence of end-stage renal insufficiency in living donors in the transplantation centre in Minnesota (USA).[68] In a group of 3,689 donors who donated a kidney during their life in the period 1963-2007, a total of eleven people developed end-stage renal insufficiency (average 22.5 years after donation). This translates to 0.3% of all living donors. Seven of them were women and four were men (61% of the entire group of donors studied was female). Of all the living donors, 14.5% had a GFR of less than 60ml/min (moderate kidney disease), 32.1% had high blood pressure and 12.7% had protein in their urine (albuminuria). The average follow-up time was 12.2 years. Of the eleven patients with renal failure, three had the same kidney condition as their (related) recipient, which points to an underlying congenital kidney disease in the family.

Gibney performed an analysis of all living kidney donations performed in the USA between 1993 and 2006 (a total of 62,327 donations).[69] In total, 126 patients with end stage renal failure (0.2%) were placed on the waiting list for transplantation. A remarkable finding was that 40% of them were *African Americans*, whilst this group comprised only 12% of the total number of living donors. The conclusion drawn from this was that *African Americans* may be more susceptible to develop renal failure after donation.[70]

From the studies described above it can be concluded that the incidence of renal failure in kidney donors barely exceeds the incidence of renal failure in the normal population. The risk of end stage renal failure for living donors is between 0.1 and 1.1%.[26] It should be noted that most of these studies were performed retrospectively – primarily on Caucasian population groups – and that there are indications that the outcome could be different – for example – for a non-Caucasian population group (such as African Americans or the Caribbean population).

3.6 Prognosis

Based on existing Dutch and international data, it can be stated that the number of living donors in the Netherlands who will develop renal failure in the long term – thus necessitating renal replacement therapy – will be extremely limited: this number is currently only one or two per year. However, several factors could influence this number in future, such as a possible expansion of the acceptance criteria for living donation, resulting in persons with a higher risk profile being eligible to donate; and the consequences of the increase in obesity and a higher incidence of diabetes in the (ageing) population, including living donors. However, by offering lifelong follow-up monitoring of living donors, it is possible to prevent complications and/or treat them in a timely manner, thereby limiting the deterioration in renal function. We may need to assume a total of two to four donors with renal failure per year in the future.

3.7 Conclusion

The preceding analysis has shown that donation of a kidney during life can generally be considered safe, although not entirely without risks or consequences. Both the life expectancy and the course of the donor's renal function do not differ from that of the general population. The residual capacity of the remaining kidney provides an adequate renal function. However, one should realise that the donor – by donating one kidney – has also 'traded in' his reserve capacity, thereby increasing his vulnerability. In sporadic cases, partly due to other risk factors, such as high blood pressure and obesity, this results in accelerated loss of renal function and finally renal failure. Dialysis or – even better – kidney transplantation, is then the only remaining option. The Committee anticipates a total of two to four cases per year in the Netherlands.

Chapter 4

Moral arguments for and against priority for living donors

Before the moral arguments for and against the Eurotransplant proposal can be defined and valued, the contents of the proposal itself must be clearly explained. Firstly, we will discuss what the proposal entails and what the consequences of the proposed action would be for the donor and for others. Next, the moral arguments for and against the proposal will be discussed and any precedents will also be discussed. Finally, the Committee will come to a conclusion.

4.1 What priority entails and what its intended purpose is

A number of European countries cooperate in the (cross-border) allocation of kidneys from postmortem donors to people who need such a kidney. Within the Eurotransplant, organisation, the Netherlands cooperates with Germany, Austria, Croatia, Slovenia, Belgium and Luxemburg. The allocation system for postmortem donor kidneys in the Eurotransplant region is the Eurotransplant Kidney Allocation System (ETKAS, see paragraph 2.10). Eurotransplant has recently suggested to the affiliated countries – including the Netherlands – that a person who donated a kidney during his lifetime and who now requires dialysis due to end stage renal failure, should be awarded the required number of bonus points, so that he can undergo an early (preferably pre-emptive) transplantation with a (postmortem) donor kidney. A pre-emptive transplantation is a transplantation performed prior to the moment at which dialysis would have to be started. Such transplantation is extremely favourable for the graft survival of

the transplanted organ (see also paragraph 2.2). Pre-emptive transplantations are currently only performed if a living donor is available.

Working within the ETKAS system, if people who were donors in the past were to be awarded sufficient extra points, so that they could avoid dialysis – or only require dialysis for a short period – they would have to be awarded at least 400 to 500 points immediately after being placed on the waiting list. The key element of the Eurotransplant proposal is therefore to award the former donor on the waiting list 500 points. This would bring this donor more or less level with the high urgency (HU) kidney patient or the patient with a full tissue match (zero HLA mismatch).

Eurotransplant proposes that HU patients, as well as patients on the Acceptable Mismatch (AM) list (low *match probability* and long-waiting, for whom the usual points allocation system does not apply) and patients with a *full house match* be given priority over the former donor with end stage renal failure. After all, these groups are at greater risk of being disadvantaged if they were passed over when a suitable donor becomes available.

Therefore, the proposal would mean that the former live donor would move to the top of the ranking order of all waiting patients that do not belong to one of these special priority groups. As this does not grant the donor absolute 'priority' (this is dependent on the donor supply), the term 'priority' will be used as little as possible in the discussion below. The Committee will refer to the allocation of extra points from now on.

4.2 Consequences of awarding 500 points to the donor

For the former donor, this policy means that he will almost certainly be offered a kidney within six weeks of being placed on the list, so that he will in all likelihood undergo pre-emptive kidney transplantation. This estimate takes into consideration the possible priority for a HU patient (there were seven in 2009), for a patient in the AM programme, and the mandatory exchange required when there is a recipient with a full tissue match in a country affiliated with Eurotransplant.

For the other patients on the waiting list – those that do not belong to a particular priority group – granting priority to one former live donor per year will result in an extension of their waiting time of approximately one and a half days, with the median waiting time being 1,357 days in 2009. If two former donors are given priority each year, this will result in an extension of the waiting time of the others of approximately three days. Should this number increase to four per year, then this extension will be about six days. The negative consequences for each of

the other patients on the wait list of awarding 500 points to the former donor are therefore limited.

4.3 Moral arguments for and against

The Eurotransplant allocation system aims to allocate postmortem organs based on generally applicable, transparent, impartial and relevant criteria. The basic principle is one of formal fairness. This means that equal cases will be treated equally, but unequal cases will be treated differently. The key question that the Committee must answer is therefore: in what way does the case of someone who donated a kidney in the past and now needs a donor kidney himself, differ from the case of someone who did not donate a kidney and is now also in need of a kidney? Why should a different treatment be justified in the case of the former donor compared to the treatment received by others on the waiting list?

The Committee has discussed and evaluated the arguments for special treatment of the former donor on a case-by-case basis. These arguments are discussed below.

Promotion of living donation

'Strategic' arguments for awarding extra points to the donor – such as preventing that potential live donors will drop out or stimulating potential donors to make a positive decision – are not convincing in the eyes of the Committee. This awarding of extra points is an inadequate tool for the general promotion of living kidney donation: the chance of someone who donated a kidney during his lifetime being confronted with renal failure at a later stage is far too small for this to be effective. The existence of a 'safety net' in the form of extra points may reassure people, but this is very unlikely to be a deciding factor in the decision about living donation. Compared to all the motives for live donation, this is likely to play a minor role. This can also be deduced from the fact that many people are currently prepared to donate an organ during life, even though they cannot count on extra points.

Reward

Secondly, the Committee queried whether the fact that someone has given a kidney to another person during life and by this act contributed to reducing the shortage of donor kidneys, is a satisfactory argument for rewarding such a person in the form of extra points. There is an ongoing societal discussion about the

permissibility and desirability of introducing reward elements in healthcare.[71] Even if one has no objection to this in principle, a higher place on the waiting list cannot be considered an appropriate form of reward. The Committee thinks that a reward in which the burden is carried by society as a whole would be a better option. With a reward in the form of extra points, it is the collective kidney patients on the waiting list for a kidney transplant who bear the burden of the reward, even though this burden is limited as previously stated. An important counter-argument is that rewarding living kidney donors would contradict the principle of formal justice.[72] People are given a higher place on the waiting list, not because they themselves have a relevant characteristic that can determine their place on the waiting list – such as medical need or waiting time – but because they have a unique bargaining position that allows them to 'buy' a higher place.

Compensation for medical reasons

Thirdly, the Committee investigated whether there are medical arguments for viewing the case of the former live donor as special. As indicated in Chapter 3, with the current stringent selection of donors, a donor does not have a significantly greater chance of developing renal failure in the future than someone of the same age with two healthy kidneys: living kidney donation as such does not result in a greater chance of developing later problems with the remaining kidney.

However, a realistic fact is that – should an unexpected problem with his renal function occur – the donor has only one kidney (and thus a lack of reserve capacity) to deal with that problem. In other words, if the (former) donor should experience an unexpected deterioration in renal function, then the loss will be accelerated and he will require dialysis sooner than a person with the same condition who has two kidneys, with a greater loss of life expectancy as a result. This is referred to from now on as loss of reserve capacity or 'sacrificing one's bargaining power'. This can be considered a medical reason for compensation of the former donor.

However, should the same argument not apply to people who were born with only one kidney (if one can talk about 'compensation of damage suffered' for such a natural variation), or to people who have had a kidney removed due to a tumour or trauma (this would definitely be a case of compensating for damages suffered)? What would be the reasons for giving the former donor special treatment, a treatment that we do *not* give to other people with only one kidney?

The justification for this proposal can be found in the fact that the affected individual has – as a result of his donation – made a sacrifice that should be greatly appreciated in times of such dire shortage of donor kidneys. It would be unfair for the donor to suffer additional disadvantage (requiring dialysis sooner than other kidney patients with the same condition, resulting in a greater loss of life expectancy) precisely *as a result of his sacrifice*. The very person who has made an effort to reduce the shortage of donor kidneys would then be confronted more starkly with the bitter fruits of that shortage. It is a question of fairness that the former donor should at least be compensated for the extra disadvantage as a result of the loss of reserve capacity. For the same reason, it is socially accepted that donors are compensated for other disadvantages resulting from their donation decision, such as loss of income or travel costs.

This does not answer the question of how far the compensation for the extra disadvantage suffered should reach. The following comment can be made about this. The only way to prevent that donors with renal failure will be worse off than the average kidney patient on the waiting list (because they require dialysis at an earlier stage), is by placing them in a better position, namely by ensuring that they can undergo a pre-emptive transplantation. The best way to achieve this is to award 500 points.

This should not create the impression that awarding 500 points results in complete compensation in the sense that the former donor will be as healthy after a pre-emptive transplantation as he was before he donated a kidney. That is certainly not the case. Even when someone undergoes transplantation without first receiving dialysis, he still remains a kidney patient: he still meets the diagnostic criteria for kidney disease, which continues to form a reason for life-long use of medication and life-long, regular medical follow-up. Moral objections could arise if this form of compensation were to involve the allocation of benefits of such magnitude that they would stimulate one to make an investment, since that tends to rewarding. However, compensation for loss of reserve capacity does not constitute the awarding of benefits or rewards. Therefore, one does not need to fear such ‘investments’.

A point that should be discussed separately is the fairness of compensation for the donor in relation to other patients on the waiting list for a kidney transplant. After all, it is these patients who pay the (modest) price of this compensation, in the form of a (slight) increase in their waiting time. However, this disadvantage pales into insignificance beside the great advantage that the group of waiting kidney patients experiences collectively from the fact that some people are prepared to donate a kidney during their life time. After all, every person on the waiting list for a postmortem kidney benefits from this deed.

Living donors collectively ensure that the waiting time on the wait list for a postmortem kidney is halved: every time that a person during his life donates a kidney to someone else, that recipient can be removed from the waiting list for a postmortem kidney and all the other people on the waiting list move up by one position. If there were no live donations at all, the waiting time for a postmortem kidney in the Netherlands would probably double from the current four to five years to an estimated eight to ten years.

As the patients on the waiting list for a postmortem donor kidney benefit greatly as a group from the sacrifice made collectively by living donors (halving of the waiting times), the Committee thinks that it is fair that they in turn share the burden of the compensation. In the eyes of the Committee it is understandable and justified that an exception will be made for patients on the waiting list with a high medical urgency (they maintain priority over the former donor with end stage renal failure).

Notion of fairness

A fourth argument for awarding extra points to living donors with renal failure that requires serious discussion, is the notion of fairness. This argument, which was already mentioned in relation to the compensation approach, stands apart from the question whether the donor has suffered a disadvantage by donating a kidney that calls for compensation. The question here is whether the fairness argument can *independently* carry the proposal to award the former donor extra points. Opinions differ on the answer to this question.

That the present supply of postmortem organs cannot meet the demand for kidneys for transplantation results from the fact that – in the Netherlands – more than half of the available and transplantable postmortem organs are actually lost by the absence of consent or by refusal by the individual or his next-of-kin (please refer to paragraphs 2.8 and 2.9 for the figures). The historic overview in Chapter 2 also reveals that the significant increase in living donation in recent years is partly a consequence of this shortage. It is true that some living donors would still have decided to donate, partly due to the better chance of survival, even if a postmortem organ had been available for the recipient at the same time. Even in that case, the donor is still alleviating a need that has occurred due to the choices made by others, and is still making a considerable offer even if a generous compensation were in place. If he should go on to develop renal failure and be placed on the waiting list with normal urgency, he would experience detrimental consequences as a result of this shortage. This would be harsh and unfair.

A counter-argument to the positive response to the question whether the fairness argument alone can carry the proposal to award the donor extra points, is that this would contradict the distribution principle that forms the foundation of our entire healthcare system: everyone based on his need.[73-75] Only the patient's state of health at that moment should count; his behaviour in the past should be irrelevant.

There is an ongoing social discussion about whether the patients' own responsibility for the consequences of the choices that they make regarding their lifestyle should play a role in the allocation of care. However, this discussion does not relate to this situation. Even if this own responsibility is rejected and the principle of distribution according to need is strictly adhered to, this takes place within a framework that ensures the fair distribution of the burden of the care. The starting point of the Dutch system is to distribute care according to need, because everyone pays a compulsory premium for his health insurance. This principle however does not apply to care that does not belong to the basic package, which is financed in this way. Outside of organ donation, the only health facility that distributes the burden based on voluntary contributions and the benefits according to need is the blood bank. The blood bank is only able to do so because there is no real shortage of blood.

In his advisory report 'Swapping on the waiting list', the Dutch Health Council has rejected the proposal to start a *Living Donor List Exchange* programme based on the argument that this would grant priority to individuals who performed a deed that is irrelevant to their placement on the waiting list (namely bringing along a willing donor), which makes it in contradiction to the principle of formal fairness.[72 76] This argument is also used against the proposal to use the place on the waiting list as a reward for living donation, but not against the fairness argument. That argument entails that the disadvantage resulting from the existing shortage, should not affect those who made a significant sacrifice in order to alleviate that same shortage. This last point cannot be viewed as an irrelevant characteristic.

However, opinions vary on whether this reasoning can be used to conclude that the fairness argument *on its own* is strong enough to carry the proposal. This touches on a subject on which the social discussion has barely even started. The Committee will leave this question unanswered.

4.4 Precedent effect

A point of attention for the Committee was the possible undesirable precedent action that could result from the allocation of extra points. For the moral

substantiation of the proposal, the Committee has decided not to use the argument of rewarding a special deed. Therefore, the precedent action means that anyone who does something good for healthcare or another person's health would not be able to demand a reward in the form of earlier and/or better care if this argumentation is accepted. The Committee emphasises that if a situation were to occur that is actually comparable to that of the former kidney donor with renal failure – if the precedent is 'correct' – priority could also be justified in that situation.

However, the Committee has been unable to find an example that completely matches the analogy of the kidney donor with renal failure. On closer inspection, this can be explained. For the allocation of transplantable (postmortem) organs, the allocation system is based on the principle of distribution according to need, without this being linked to someone's contribution to the system and his claim. In any context other than the allocation of transplantable organs, contribution and claim are always linked, either by making the contribution of every eligible person compulsory (compulsory contribution for healthcare insurance, taxes), or by making the claim dependent on the contribution (additional healthcare insurance). With the exception of blood donation (where there is currently no problem of shortage) and postmortem donation, a system of voluntary contributions and distribution according to need does not exist. As a rule, there is either a compulsory distribution of the burden (taxes, healthcare insurance premium) or a link between contribution and claim. It is very unusual that a system in which the distribution of the desired object takes place according to need is dependent on voluntary contributions; such a system usually only works well in the case of abundance. For this reason, the Committee deems it unlikely that an extra points ruling will have a substantial precedent effect.

A question that remains is the extent to which the arguments of compensation and fairness also apply to the allocation of organs other than kidneys. However, the fact is that there is no need for a special arrangement for living donors in that context. It is true that segments of the liver or lungs can be donated for transplantation, but transplantations of lung lobes from living donors are not performed in the Netherlands due to the great risk involved for the donor. Transplantations using segments of the liver from a living donor are performed in the Netherlands, but the situation of these liver donors is entirely different to those of living kidney donors. Liver donors whose own liver would acutely stop functioning properly as a result of the donor operation are automatically given the HU (high urgency) status on the waiting list for a donor liver today, because they would not have any chance of survival without a transplant. The practical situation in the Eurotransplant countries, including the Netherlands, is that all

liver patients with an HU status receive a liver transplant within a relatively short time, so that there is no need for a special priority arrangement for liver donors. In addition, donor livers are not matched specifically for tissue compatibility, which means that other people on the waiting list experience less of a disadvantage than for kidney transplantation due to a low *match probability.* A liver donor will also regenerate his own liver, so that in due course – usually within six to twelve months – the liver function will be practically the same as prior to donation. In this case there is no loss of reserve capacity. Egg donation, blood donation and bone marrow donation also cannot be compared to the donation of a kidney, because the medical consequences for the donor in the long term are of a different magnitude, due to regeneration of the tissue or a plentiful supply.

4.5 Conclusion

Having taken all the arguments for and against into consideration and weighing these arguments against each other, the Committee concludes that the compensation argument – supplemented by the fairness argument – is a morally valid argument for the allocation of 500 points. The allocation of these points may initially appear to be a form of over-compensation. However, closer inspection reveals that there is no middle ground: a choice has to be made between accepting that the former living donor is worse off than other kidney patients (because they have to start dialysis sooner than the others) OR accepting that the donor is placed in a better position than the other patients. Faced with the choice between 'under-compensation' and 'over-compensation', the Committee chooses the latter based on considerations of fairness. It would be unfair to allow people who made a significant contribution to limiting the existing shortage to become the victims of that same shortage and to experience extra problems as a direct result.

The Committee has decided to leave an open answer to the question whether considerations of fairness alone would be sufficient reason for giving living donors with renal failure priority. The proposal to award these donors 500 points on the waiting list differs in more respects than one from the proposal to award registered postmortem donors extra points. Firstly, the sacrifice made by living donors is of an entirely different order of magnitude. Secondly, living donors – when compared to other patients – suffer an extra disadvantage precisely as a result of that sacrifice. The Committee thinks that the lack of compensation for this sacrifice is unfair.

The Committee is of the opinion that one should not fear a substantial precedent effect by the allocation of extra points.

Chapter 5

Legal aspects of priority

In this Chapter we will examine whether the current legislation offers room for the allocation of extra points to people who donated a kidney during life and have gone on to suffer from renal failure to such an extent that they require dialysis. Both the national and the international legal framework will be discussed. The Chapter will end with a conclusion.

5.1 National legal framework: Organ Donation Law (WOD)

The Dutch national law that applies is the Organ Donation Law (WOD). Chapter 1 of this law contains general provisions about organ donation. Article 2 of this Chapter states the following:

> Consent for the removal of an organ, granted with a view to receiving compensation higher than the costs – including loss of income – that are a direct consequence of the removal of the organ, is invalid.

This provision aims to counteract the commercialisation of organ donation. It is a result of the fundamental principle of selfless* donation on which the WOD is

* Selfless means without profit motive. The principle of selflessness does not mean that the donor may not have an interest in the donation. The donation can also be in the interests of the donor, for example if it is a donation to a child or partner. The recipient of a donor kidney will no longer have to undergo dialysis, which could significantly alleviate the burden of care for the donor.

based. The stipulation allows for the reasonable compensation of costs associated with the removal of an organ. As it is not realistic to assume that people will give consent for the removal of an organ with the specific aim of gaining extra points on the waiting list for a kidney transplant ("with the intent of receiving compensation for the act"), the stipulation – interpreted in both the letter and the spirit – does not form a block to the allocation of extra points. In other words: the proposed allocation of extra points does not provide benefits or rewards that could entice investment. Therefore, the current proposal does not harm the principle of selfless donation in any way.

Chapter 2 of the WOD discusses the living donation of organs. The only article from this Chapter that is relevant to the current matter is article 7. This article relates to compensation of costs associated with organ donation and refers to the stipulation in article 2:

> Only the costs, as defined in article 2, may be reimbursed to the donor and those who are required to provide consent for the removal of an organ as set out in this Chapter.

The ban on (financial) compensation is set out in article 7 and article 2 of the WOD. However, the legislator has deemed it fair that the donor receives compensation for the costs, including loss of income, which are a direct result of the removal of the organ. It appears that the legislator was thinking about compensation for material disadvantages (travel costs, loss of income, costs of surgery/recovery) and not about compensation of any health disadvantage (pain, discomfort) suffered. One has to wonder, however, whether any compensation should not also be offered for this health disadvantage.

Other health laws however do stipulate that damage suffered to health must be compensated, for example in the Research Involving Human Subjects Act (WMO). International and national standards demand optimum protection of those wishing to serve future patients and society as a whole by (voluntarily) participating in medical scientific research. If a study subject's health is damaged as a result of participation in a scientific study, he or she must receive compensation. For example, the sponsor of the research is obliged to take out an insurance policy that covers damage caused by the study due to death or injury of the study subject (art. 7 section 1 and art. 8 section 1 and art. 1 section 1 under f. WMO). As an analogy to this regulation, one could view an extra points arrangement for living donors as a type of 'insurance': a safety net for people who have performed a great service to others and have suffered a health

disadvantage in the process when they are confronted with renal failure at a later stage (accelerated need for dialysis).

Article 18 of the WOD in Chapter 3 (Donation of organs after death) sets out the reporting and allocation of available organs. Section 3 of this article contains a (limitative) summary of the factors that may be taken into consideration when allocating an organ that has become available. It reads as follows:

> Factors other than the blood and tissue match between the donor and recipient of the organ, the medical urgency of the recipient and other conditions relating to the condition of the organ – and if these factors do not prove decisive – the waiting time of the donor, may not be taken into consideration during the allocation process. Further rules can be set out as an Order in Counsel.

The factors listed in article 18 section 3 can be divided into two categories:
- medical factors
- the waiting time.

Medical factors include:
1 the blood and tissue match between the donor and recipient of the organ
2 the medical urgency of the recipient
3 other factors related to the condition of the organ.

The waiting time may only form a deciding factor if these three factors do not provide a definitive answer.

Article 18 section 3 WOD makes no mention of the fact that someone has donated an organ during his lifetime. Due to the limitative formulation of this summary of factors ("Factors other than… may not be taken into consideration..."), one could conclude that this factor may not be taken into consideration during the allocation of organs according to the (letter of the) WOD. This conclusion is referred to below as the 'strict interpretation'.

However, there are also arguments for a more liberal interpretation of the legal text: a 'lenient interpretation'. The allocation rules currently used in practice appear not to be based exclusively on the criteria mentioned in article 18 section 3.[72] For example, the so-called country balance between Eurotransplant member states (see Paragraph 2.10) contradicts the letter of article 18 section 3. Yet this balance is not disputed: it prevents the support for the cross-border exchange of organs from waning in one country due to the 'export' of large numbers of organs from that country to other countries. Apparently, this

modification of the allocation system was not deemed a contradiction of the legal recommendations: no initiative was taken to amend article 18 section 3.

Points of support for a lenient interpretation can also be found in the report on the third evaluation of the WOD.[77] This evaluation focused – among other things – on the distribution of organs. In this context, the allocation system as it is practised was compared to the law. The conclusion of the third evaluation report was not that the allocation practice contradicts the criteria listed in article 18 section 3 of the WOD and that this forms a reason for amendment of both. The conclusion was that the WOD itself does not contain a detailed allocation system, but rather only a framework and starting points for such a system. The report characterises this framework as follows on page 122: "This framework is, in theory, medical in nature, but also lenient, because all kinds of circumstances can apparently play a role based on the three medical criteria listed. Within this broad framework, it is the need of the recipient that is seen as the central factor, provided that implantation in the affected individual is feasible and appropriate. The legislator has not opted for a purely utilitarian approach (which allocation of the organ will achieve the greatest health gain) and is more in agreement with the traditional medical ethos (first help the patient with the greatest need)".[77] Therefore, this is a legal framework "that lends itself to different interpretations and that is mainly characterised by the fact that medical circumstances (in a broad sense) should be foremost (..)".[77]

The Committee has wondered whether the allocation of extra points to donors with end stage renal failure based on the compensation approach would fit in well with this broad legal system based on medical criteria. The compensation approach entails that the donor should not experience any benefit from the donation, but also should not be disadvantaged. On the one hand, the donor should not be rewarded with a higher place on the waiting list when the situation arises that he needs an organ, because this would detract from the selfless character of donation, a principle on which the WOD is based. On the other hand, it would not be fair if the donor – when he develops renal failure himself – were to end up in a more unfavourable position than other people with renal failure. The donor should be able to receive compensation (in the form of extra points on the waiting list) for the extent to which he is placed in a more unfavourable position as a result of his donation than without donation.

As we saw in Chapter 3, there are no indications that living donors in general will suffer a substantial health disadvantage due to increased risk of end stage renal failure. However, this disadvantage does exist in the sense of the loss of reserve capacity ('having sacrificed one's bargaining power'). The essential question is whether this disadvantage is caused by the donation and to what

extent the need for a donor kidney has increased as a result. The causal link between donation and disadvantage suffered due to loss of reserve capacity is crystal clear. The second question (to what extent the need for a donor kidney is increased as a result) is answered in paragraph 3.4. The former kidney donor will develop end stage renal failure sooner than other kidney patients, because he has already exhausted his reserve capacity. As a result, he will require dialysis sooner than others and his loss of life expectancy is greater.

The allocation of extra points to donors with renal failure does introduce a new element into a system that – as a rule – allocates organs on the basis of medical criteria, but the introduction of this element does not change the essence of the distribution principle, because

- it meets the medical needs of the donor, who thereby receives compensation for extra disadvantages suffered as a result of loss of reserve capacity
- HU patients, patients who fit the Acceptable Mismatch (AM) category and *full house matches* continue to hold priority over living donors due to their medical needs
- the waiting times of the other patients do not increase substantially as a result.

Because the idea of compensation for extra disadvantages suffered is based on the medical needs of the donor, without negative effect on the needs of other patients on the waiting list, and because this idea also corresponds to a principle that is already set out in the legal stipulations as far as cost reimbursement is concerned, it is easy to justify that the legal stipulations offer scope for the intended amendment of the allocation system.

Furthermore, it is unlikely that the legislator intended to exclude this allocation of extra points to donors in article 18 section 3. It is more likely that the legislator simply did not think about this, or rather: *could* not have foreseen this, because this matter was not relevant yet at the time that this law was passed (mid 1990s). As demonstrated by the explanatory memorandum of the law*, the legislator aimed to achieve a fair distribution of organs and in particular he wanted to rule out that factors such as someone's social position or importance should be taken into consideration. The proposed compensation is compatible with the aim of a fair distribution of organs, because it involves compensation for

* "(..) As We have taken into consideration that – partly in relation to article 11 of the Constitution – with a view to the legal security of those involved, for the promotion of the supply and the fair distribution of suitable organs and for the prevention of trade in organs, it is desirable to stipulate by law the rules concerning the allocation of organs, particularly for the medical treatment of others; (..)"

a health disadvantage that is the result of a deed that made a substantial contribution to there being organs to distribute at all.

5.2 International legal framework

5.2.1 Convention on Human Rights and Biomedicine

The Convention on Human Rights and Biomedicine of the Council of Europe offers a (mandatory) minimum level of protection, which must be moulded into the national law by treaty members. The framework provided by the convention has been further realised and worked out by means of protocols on a number of sections. For transplantation of organs and tissues, this was done in the Additional Protocol on Transplantation of Organs and Tissues of Human Origin.

Countries that have ratified the Convention are obliged to provide adequate legal protection to prevent or terminate any illegal infringement of the rights and principles contained in the Convention. As a member of the Council of Europe, the Netherlands has signed the treaty, but not (yet) ratified it due to the contradiction of the proposed repeal of the ban on creating embryos for research purposes with article of 18 section 2 of the Convention. The Netherlands has also signed, but not ratified, the Additional Protocol.

Of the countries also affiliated to Eurotransplant, as mentioned in Paragraph 2.10, Croatia and Slovenia have signed and ratified the Convention and the Protocol, Luxemburg has only signed both, and Austria, Belgium and Germany have neither signed nor ratified either document.

The treaty itself does not contain any articles relevant to the allocation of donor organs, except for perhaps article 21, which states that:

> The human body and its parts shall not, as such, give rise to financial gain.

Applied to organ donation, this means that donation, as a rule, should be a selfless act.

5.2.2 Additional Protocol on Transplantation of Organs and Tissues of Human Origin

The Additional Protocol on Transplantation of Organs and Tissues of Human Origin (hereafter referred to as the Protocol) contains several articles that could be relevant to the subject of compensation. Chapter II of the Protocol is entitled

'General provisions'. Article 3 in this Chapter lists rules for the system of transplantation and states, insofar as is relevant here, that:

> Parties shall guarantee that a system exists to provide equitable access to transplantation services for patients.
>
> Subject to the provisions of Chapter III, organs and, where appropriate, tissues shall be allocated only among patients on an official waiting list, in conformity with transparent, objective and duly justified rules according to medical criteria. The persons or bodies responsible for the allocation decision shall be designated within this framework.
>
> In case of international organ exchange arrangements, the procedures must also ensure justified, effective distribution across the participating countries in a manner that takes into account the solidarity principle within each country.

It is clear that article 18 section 3 of the WOD concurs with article 3 of the Protocol, which refers to allocation of organs exclusively to people on a waiting list based on medical criteria. In contrast to the WOD, article 3 *does* offer a basis for the so-called country balance. Apparently, such a basis was deemed necessary for the legality of a country balance. The passage in article 3 about the country balance must be read as a stipulation that makes an exception to the rule that organs are allocated to the waiting patients based on medical criteria only. The question that the Committee must answer is therefore whether the proposed compensation scheme can be made compatible with the stipulation in the Protocol that the allocation of organs should take place based on medical criteria. The Committee gives a positive answer to this question, referring to the arguments brought forward in the context of the 'lenient interpretation' when answering the question whether this idea can be made compatible with article 18 section 3 of the WOD, in particular with the stipulation that allocation should be based on medical grounds.

Chapter III of the Protocol regulates the removal of organs from persons during their lifetime. According to article 9, this may only be performed 'for the good of' the recipient and it must remain a last resort. Article 10 states the following:

> Organ removal from a living donor may be carried out for the benefit of a recipient with whom the donor has a close personal relationship as defined by law, or, in the absence of such relationship, only under the conditions defined by law and with the approval of an appropriate independent body.

The practice in the Netherlands surrounding non-directed (altruistic or Samaritan) donation to an unrelated recipient contradicts this article to a certain

extent. In practice, an *independent body* is not involved in non-related donations: the hospital where the operations will be planned and performed cannot be viewed as such. This means that the Netherlands will either have to make an exception in the case of possible ratification of the Protocol, or will have to amend its legislation and practical situation to fit the Protocol. It should be noted here that various countries have been critical of the Protocol and in particular the regulation on living donation. This regulation was set out at a time when this type of donation (unrelated alruistic/Samaritan) was not yet very common and is lagging behind.

Article 21 section 1, part of Chapter VI (ban on financial gain) states the following:

The human body and its parts shall not, as such, give rise to financial gain or comparable advantage. The aforementioned provision shall not prevent payments which do not constitute a financial gain or a comparable advantage, in particular;

a compensation of living donors for loss of earnings and other justifiable expenses caused by the removal or by the related medical examinations;

b payment of a justifiable fee for legitimate medical or related technical services

c compensation in case of undue damage resulting from the removal of organs and tissues from living persons.

In this article, compensation is permitted "*in case of undue damage resulting from the removal of organs*". For the question at hand, it is important to determine how this concept of *undue damage* should be interpreted. Could this include the loss of reserve capacity that could affect the former donor with renal failure? The Explanatory Report accompanying article 21 of the Protocol states the following about the receipt of compensation for *undue damage*:

By undue damage is meant any harm whose occurrence is not a normal consequence of a transplant procedure. *

This is not a matter of compensation for damage that is inherent to the transplantation procedure.** But it could, for example, include damage compensation for problems that occurred as a result of the anaesthetic used

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* Explanatory Report to the Additional Protocol to the Convention on Human Rights and Biomedicine concerning Transplantation of Organs and Tissues of Human Origin, article 2, nr.116.

** Also refer to the Explanatory Report, article 25, nr. 128

during the removal of the organ. There is no reason why this argumentation cannot also be extended to problems caused in the long term following the removal of an organ, such as the loss of reserve capacity as a result of the donation. The disadvantage resulting from this is not inherent to the normal removal of a kidney, because the healthy kidney that remains after removal largely takes over the work of the kidney that was removed. The disadvantage only occurs when the remaining kidney starts to malfunction for whatever reason.

Article 25 of the Protocol pertains to the compensation for *undue damage*. The article states the following:

> The person who has suffered undue damage resulting from the transplantation procedures is entitled to fair compensation according to the conditions and procedures prescribed by law.

This refers to the compensation systems (under civil law) that exist in the affiliated countries. These systems vary significantly.* The damage compensation to which a person is entitled can therefore also differ significantly per country. The Committee cannot imagine that the allocation of extra points to the former donor would not fit within a system that intends to provide an all-encompassing legal framework for countries with a wide variation in rules for what is fair compensation. Article 21 of the Protocol does state a clear limit: "*any payments constituting a financial gain or a comparable advantage*" are excluded.** This limit is not exceeded by the proposal: it has already been argued that the allocation of extra points to the former donor who is waiting for a kidney is not a form of financial gain or a comparable advantage that would elicit an investment.

5.2.3 *WHO Guiding principles on human cell, tissue and organ transplantation*

The WHO Guiding principles on human cell, tissue and organ transplantation are not formally binding for the WHO member states, but these states – including the Netherlands – accept that these types of guidelines do form the basis for national policy and legislation.

Principle 9 of the WHO Guiding principles on human cell, tissue and organ transplantation states the following:

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* Explanatory Report, article 25, nr. 130.
** Explanatory Report, article 25, nr. 132.

The allocation of organs, cells and tissues should be guided by clinical criteria and ethical norms, not financial or other considerations. Allocation rules, defined by appropriately constituted committees, should be equitable, justified, and transparent.

In addition to clinical criteria, the ethical standards for allocation are also referred to here. A further description of these standards is not provided, though these standards must be fair, just and transparent. As we saw in Chapter 4, there are good ethical arguments for the allocation of extra points to the former donor.

5.3 Conclusion

The Committee has come to the conclusion that there is no possible unequivocal answer to the question whether the current national and international laws allow for the allocation of extra points to the former kidney donor when it comes to the allocation of donor kidneys. This is not surprising, as this question did not yet play a role when the national and international legislation was being drafted. Living donation has only really taken off in some countries – including the Netherlands – in the past decade.

The Committee differentiates between a strict interpretation and a lenient interpretation of the relevant rules in the Organ Donation Law. Supporters of the strict interpretation follow the letter and the spirit of the law more closely. They could come to the conclusion that the letter of article 18 section 3 of the WOD does not offer any scope for the allocation of extra points. If they want to give living donors priority on the waiting list, they must debate the question whether (and if so, how) the stipulations of the WOD can be amended such that the law will offer the required scope. The question whether a change in the law is proportional to the expected effect of priority must also be discussed. In view of the small number of people who will actually be awarded extra points, this concerns more a symbolic ‘gesture’ towards living donors than a significantly greater yield of organs.

However, the Committee has provided arguments for a more lenient interpretation of article 18 section 3 of the WOD (‘lenient approach’): in the Committee’s opinion, this article does not block the allocation of extra points in the case of such a lenient interpretation. The allocation of extra points can even be substantiated using the compensation argument. The compensation concept is also found in the WOD, although this only relates to material disadvantages suffered. Elsewhere in health law, for example the Law on Research Involving Humans Subjects, there are regulations for compensation of a health disadvantage suffered by people who made a voluntary sacrifice for others and/

or in the public interest. This tends to support the lenient rather than the stringent interpretation of article 18 section 3 of the WOD.

According to the Committee, the proposed allocation of extra points in a more lenient interpretation also does not contradict article 3 of the Additional Protocol on Transplantation of Organs and Tissues of Human Origin (allocation based on medical criteria). After all, this allocation is related to the medical needs of the donor and takes into consideration the medical needs of the other patients on the waiting list. In addition, it concurs with the idea of compensation for undue damage as set out in the Protocol and the Explanatory Report.

There is no need for a change in the current law in the case of a lenient interpretation of the relevant article in the WOD.

Chapter 6

Conclusions and recommendations

In this last Chapter, the Committee draws its conclusions and makes several recommendations.

6.1 Conclusions concerning ethics and law

The Committee concludes that there are medical-ethical and legally valid arguments for the proposal by Eurotransplant to award 500 points to the living kidney donor with end stage renal failure, in order to make this person eligible for a pre-emptive transplantation of a (postmortem) donor kidney. In the Committee's opinion, article 18 section 3 of the Dutch WOD, article 3 of the Additional Protocol on Transplantation of Organs and Tissues of Human Origin (with Convention on Human Rights and Biomedicine) and the principles for the allocation of organs that form the foundations of these articles, offer sufficient scope for this. The allocation of extra points is related to the medical needs of the donor and does not disadvantage the medical needs of other patients on the waiting list. The Committee therefore thinks that amendment of the Organ Donor Law is not essential for acceptance of the proposal.

The Committee wishes to remind one that this reasoning applies not only to living kidney donation and the allocation of postmortem kidneys, but also to the living donation and allocation of organs in general. However, in practice, there is no need for the allocation of extra points to living donors for the allocation of organs other than kidneys.

Finally, the Committee wishes to point out that modification of the allocation system in this sense does not imply that extra points will also have to be awarded to people who have registered themselves as (postmortem) donor on the donor register, as occurred in recent Israeli legislation. The discussion about awarding this group extra points too is still ongoing in the Netherlands. In the context of this advisory report, it is not necessary for the Committee to take a stance on this matter. Registering as a potential postmortem donor does not result in the actual a loss of reserve capacity, as is the case for the living kidney donor. In addition, the contribution that people make to solving the scarcity problem by registering as a postmortem donor, however important, is of a different order of magnitude than the large contribution made by living donors.

6.2 Recommendations

The Committee recommends that the proposal by Eurotransplant be incorporated into the allocation system for postmortem donor kidneys in such a way that people who donated a kidney during their lifetime and who go on to develop end stage renal failure be awarded 500 points from now on. As a result, if the need for renal replacement therapy arises, they will be eligible for transplantation of a postmortem donor kidney without first being put on dialysis.

With a progressive expansion of the criteria for becoming a living donor, one must take into consideration the possibility that more former donors will develop end stage renal failure. The justification for living kidney donation rests in the fact that kidney donors have a life expectancy that is comparable to similar individuals who have not donated a kidney. Medical-scientific follow-up research on living donors is essential in order to guarantee this in the future with expansion of the criteria for becoming a donor. In the Netherlands, the conditions for such research are present, because the data on all living donors has already been recorded in a central register, the Netherlands Organ Transplantation Registration (NOTR), maintained by the Dutch Transplant Foundation (NTS). A follow-up register of living donors is made compulsory in art. 15 section 3 of a Proposal for a Directive from the European Parliament and the Council concerning quality and safety standards for human organs destined for transplantation (now approved as Directive 2010/45/2010 on July 7, 2010). With a view to the safety of living donation in the future, the Committee recommends that such a follow-up study be taken seriously.

In conjunction with the implementation of an extra points regulation, the Committee advises that those involved in providing care, particularly to (potential) donors, be made aware once more of the need for life-long medical

monitoring, both in the form of individual counseling and in the form of information material. In the meantime, the Decree on Dutch health insurance has been amended since 1 January 2011 in such a way that the annual follow-up of the living donor by the nephrologist (in the hospital) be exempt from the compulsory excess, so that former donors will no longer lose their *no claim* status if they adhere to the request to return to their specialist for periodic monitoring.

Finally, the Committee recommends that the general knowledge and transparency of the allocation system in general be increased. The reasons for the above-mentioned amendment to the allocation rules and the consequences of these changes for patients should be explained in a concise manner, so that there can be no misunderstanding about the matter. It would be useful if the NTS could provide a clear explanation of the (amended) rules, so that patients and (potential) donors can read up on this. For example, the NTS could describe the extra points regulation on its website and explain how this fits into the allocation system. The information material provided to (potential) living donors should also be amended.

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Annexes

Annex **A**

Request for advice

On 12 October 2009 the President of the Health Council of the Netherlands received the request for an advisory report shown below from the Dutch Minister of Health, Welfare and Sport about granting priority on the waiting list to living donors:

Living donation is a form of organ donation that has increased significantly over the past few years. In its stance on the Master Plan on Organ Donation, the Cabinet has indicated that it wholeheartedly supports the proposals by the Coordination Group for Organ Donation concerning both thorough decision-making and the removal of unnecessary barriers.

One of the possible barriers to living donation of a kidney or a part of the liver could be the fear of becoming a kidney or liver patient in the future. I received a letter with respect to this some time ago from the Dutch Transplant Foundation (NTS).

The NTS wonders to what extent the Organ Donation Law (WOD) allows for kidney patients who previously donated a kidney to be given priority on the waiting list. More specifically, the proposal would be to give these kidney patients 500 bonus points, so that they would become eligible for a so-called pre-emptive transplantation.

I am asking the Council to provide me with an advisory report on the extent to which the living donation of a kidney can – or if it is not yet the case – should be seen as a factor in the sense of article 18, section 3 of the Organ Donation Law, both from a medical and a medical-ethics point of view. Following this law, this issue must be taken into consideration when allocating transplantatble organs

to recipients. For example, this matter is relevant when someone who donated a kidney during life is confronted with decreased functioning of his remaining kidney.

Please include in your advisory report any suggestions for amendment of the relevant stipulation(s) of the WOD so that they offer the desired leeway on this point.

In the advisory report, please give the necessary attention to the national and international legal aspects, as well as the various medical-ethical and health aspects that could be associated with such an amendment of the law.

As this involves a question from a third party that I would like to give an answer to in the near future, and in view of the possibility that the situation described above could occur at any moment, please expedite this request for advisory report.

Yours sincerely,
the Minister of Health, Welfare and Sport,
signed
Dr. A. Klink

Dutch Transplant Foundation

Ministry of Health, Welfare and Sport
Department Pharmaceuticals/Medical Technology
Mrs. M.J.F. Elenbaas, MA, LLM
Senior Policy Officer
PO Box 20350
2500 EJ The Hague

Our ref.: 14625_bhj
Leiden, 2 February 2009

Dear Mrs Elenbaas

Recently, the NTS received a proposal for amendment of the allocation rules, which was submitted to us for approval. It concerns the following proposal: 'Recipients suffering from end stage renal disease after having donated one of their own kidneys, are eligible for pre-emptive listing on the kidney waiting list. The recipient will be granted an allocation bonus of 500 points upon listing'.

The WOD states the following in article 18 section 3 with respect to the allocation of organs:

> 'For allocation, no other factors are taken into consideration other than the blood and tissue match of the donor and recipient of the organ, the medical urgency of the recipient and other circumstances related to the condition of the organ and – if these factors do not prove decisive – the waiting time of the recipient. Further rules can be set as a general policy measure'.

The recommendation entails that those who donated a kidney and now require an organ will be awarded 500 bonus points. In our opinion, this takes into consideration a factor other than mentioned in article 18 section 3 of the WOD, namely the fact that someone has donated a kidney in the past. The website www.wetten.overheid.nl was searched for general policy measures using the following search terms: decision, organs, direction, allocation and no general policy measure was found that relates to this.

We think that the law does not offer enough leeway here. On the other hand, it could entail a practical contribution.

We would like to hear your point of view on the above-mentioned proposal and an answer to the question whether it may be implemented in accordance with Dutch law.

Yours sincerely
signed
B.J.J.M. Haase-Kromwijk, MA
Director NTS

Annex **B**

The Committee

- Prof. I.D. de Beaufort, *chair*
  Professor of Health Ethics, Erasmus University Rotterdam
- Dr. F.J. Bemelman
  Nephrologist, Academic Medical Centre, Amsterdam
- Dr. J.C.J. Dute
  Senior Lecturer in Health Law, University of Amsterdam
- Prof. J.W. de Fijter
  Professor of Internal Medicine and Nephrology, Leiden University Medical Centre
- Prof. G.A. den Hartogh
  Emeritus Professor of Ethics, University of Amsterdam
- M.A. Bos, *advisor*
  Health Council, The Hague
- Dr. C.J. van de Klippe, *scientific secretary*
  Health Council, The Hague

The Health Council and interests

Members of Health Council Committees are appointed in a personal capacity because of their special expertise in the matters to be addressed. Nonetheless, it is precisely because of this expertise that they may also have interests. This in itself does not necessarily present an obstacle for membership of a Health

Council Committee. Transparency regarding possible conflicts of interest is nonetheless important, both for the chair and members of a Committee and for the President of the Health Council. On being invited to join a Committee, members are asked to submit a form detailing the functions they hold and any other material and immaterial interests which could be relevant for the Committee's work. It is the responsibility of the President of the Health Council to assess whether the interests indicated constitute grounds for non-appointment. An advisorship will then sometimes make it possible to exploit the expertise of the specialist involved. During the inaugural meeting the declarations issued are discussed, so that all members of the Committee are aware of each other's possible interests.

Annex **C**

Current allocation system for postmortem donor kidneys in Eurotransplant (ETKAS)

ETKAS Allocation system

All donor kidneys (including kidneys from non-heart beating donors – except in Germany) that become available in the Eurotransplant region are allocated to recipients on the waiting list via the central office in Leiden according to set distribution rules. In contrast to the distribution systems in many other countries, the ETKAS is 'patient-oriented' and not 'centre-oriented' (in other words: the available donor organ is allocated directly to a specific recipient and not to a transplant centre that chooses a recipient from their waiting list).

Specific factors in allocation

For the execution of the allocation, particular emphasis is placed on a number of patient-related factors.

1 Urgency codes
Transplant candidates are assigned a place on the waiting list based on their degree of urgency. These urgency codes reflect: 1) the status: transplantable (T) or non-transplantable (NT); 2) the medical urgency: normal or high urgency (HU); 3) the level of allosensitisation: < 6% panel reactive antibodies (PRA) against the donor = transplantable (T); ≥ 6% but < 85% PRA = immunised (I); and > 85% PRA = highly immunised (HI).

In order to be accepted by Eurotransplant (ET) as a HU kidney patient, a number of other special inclusion criteria need to be met: no or poor access to haemodialysis or peritoneal dialysis, poor toleration of dialysis, severe neuropathy, or – for example – a risk of suicide if a patient becomes severely depressed**.**

2 Special programmes
Transplant candidates can be included in one of several special transplantation programmes:
- The Acceptable Mismatch (AM) programme is intended for patients with a proven high degree of immunisation (> 85% PRA at two consecutive three-monthly screenings). This computer-directed programme identifies HLA-A, HLA-B, and HLA-DR mismatches that will not result in a positive cross-match in the recipient (via selection of those antigens from the donor, against which the recipient has not produced antibodies).
- The Eurotransplant Senior Programme (ESP) allocates kidneys from deceased donors ≥ 65 years of age to patients ≥ 65 years old. In order to keep the cold ischaemia time (CIT) as short as possible, no HLA typing/ matching is performed and these organs are allocated and transplanted – as far as possible – at a local (Austria, Belgium/Luxemburg, Slovenia), regional (Germany) or national (Netherlands) level.

3 Blood group rules
As a rule, ABO-compatible donor-recipient combinations (A to A and AB, B to B and AB, AB to AB, O to O, A, B and AB) are followed. ABO incompatible combinations are generally excluded (unless they are used in special conditioning programmes that transplant through the blood group barrier).

4 Size of organ and body weight
For some patients (children, small adults, very large adults) the size-matching between donor and recipient concerning the size of the organ and body weight is crucially important (particularly for heart and lungs). Size and weight are evaluated as special medical characteristics for allocation, but do not result in extra points or priority.

ETKAS points system and priority schedule

The ETKAS system awards points to waiting patients, which are used to determine the first eligible person for an available organ. The characteristics of both the recipient and of the donor organ are important. However, the ranking order of patients is primarily determined by a priority schedule:

- The recipient with HU status has priority over *all* other waiting patients
- Next, patients in the AM programme have priority over the other categories of patients
- If a suitable recipient is not found in the AM programme, then the search continues for recipients with a complete HLA match (full-house match). If there is more than one suitable recipient, then the ranking order for these patients is determined by the points system (as for all other patients when no 000 mismatch is found)
- Kidneys from older donors (≥ 65 years) are only allocated within the ESP programme (Eurotransplant Senior Programme)
- Kidneys from donors < 65 years old are allocated according to the points system: the patient with the highest score goes to the top and will be the first to be allocated the organ. If this offer is rejected, then the organ is offered in descending order to subsequent candidates.
- Combined transplants of a kidney with another organ are given priority over all other transplants involving only a kidney.

Points calculation (algorithm)

The number of points allocated to a waiting recipient depends on a number of variables: HLA match grade (degree of tissue match), mismatch probability (the chance of a subsequent compatible organ offer), duration of dialysis, distance from donor hospital to recipient centre, and the national organ balance. Candidates with HU status are always allocated 500 points, which places them at the top of the list; children (< 16 years at registration) are allocated points that vary with age (< 6 years = 100 points, ≥ 6-11 years 33.3 points and ≥ 11 years but < 16 year 66.6 points). In addition, the points for HLA match are doubled for all children.

As far as the HLA match is concerned, 66.67 points are allocated for each shared HLA-A, HLA-B and HLA-DR antigen; so if there is no match at all between donor and recipient (0/6) the allocation is 0 points and 400 points are allocated for a complete match (6/6).

The mismatch probability is calculated based on the chance of receiving a kidney offer with 0 or 1 HLA-A, HLA-B or HLA-DR mismatch per 1,000 kidneys offered.

Waiting time is calculated from the day of the first dialysis or resumption of dialysis after failure of a previous transplant. If a patient's transplanted kidney fails within three months, he will return to the waiting list in his original position. A patient receives 33.3 points per year (0.091 per day) on the waiting list (and on dialysis). Patients who are eligible for a pre-emptive transplant (with a living donor) are also registered on the postmortem waiting list, but do not receive points for waiting time as long as they are not receiving dialysis treatment.

Distance can be an important factor in the allocation of donor kidneys: patients on the waiting list receive extra points when a donor kidney becomes available in their own country and in particular when the donor is located in the same region (or the same hospital). In the Netherlands, local recipients receive 300 points (the points allocation in other ET countries varies for local, regional and national donors, but on balance all recipients within the ET region have equal chances).

The application of the country balance is as follows: every working day, the difference between the number of acquired and exchanged kidneys within and between each country is calculated for the immediately preceding period of 365 days. A negative balance means that a country (or centre) has received and transplanted more kidneys than it has exchanged elsewhere (import surplus), and a positive balance means that the opposite applies (export surplus). National balance points are then calculated per country to compensate for an import or export surplus.