

Toolbox Living Kidney Donation



Document developed by the Working Group on Living Donation under the European Union “Action Plan on organ donation and transplantation (2009-2015): Strengthened Cooperation between Member States”

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Special thanks go to the representatives from United Kingdom (Triona Norman) and Spain (Beatriz Domínguez-Gil) and the Netherlands (Bernadette Haase-Kromwijk), for not only contributing to the toolbox, but also reviewing the entire document, making the final adjustments and improvements and hereby concluding this ambitious work on the toolbox.

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TABLE OF CONTENT

MISSION STATEMENT..... 6

EXECUTIVE SUMMARY 7

Benefits of living kidney transplantation 8

Risks for the living donor..... 9

Protection of the living organ donor 10

Expanding the living kidney donor pool: the non-genetically related donor and non-directed living donation..... 12

Living kidney donation and organ trafficking..... 12

1. INTRODUCTION 14

Setting the scene..... 14

Classification of living donation 16

Example of practice: Netherlands 18

Supporting living donation..... 18

2. LEGAL AND ETHICAL ASPECTS OF LIVING DONATION 20

Introduction 20

Authorisation of procurement and transplant centres 22

Consent..... 22

Example of practice: Spain 22

Organ trafficking, transplant tourism & commercialism, including incentives..... 25

3. DONOR EVALUATION, SELECTION AND PROTECTION..... 26

Introduction 26

Donor evaluation and assessment 27

Example of practice: UK..... 27

Roles and responsibilities in donor selection and follow-up..... 28

Medical assessment..... 29

Example of practice: UK..... 31

Post-donation follow-up..... 32

Example of practice: EULID project findings 32

4. DONOR REGISTRY 34

Context 34

Duration and frequency of follow-up..... 35

Example of practice: Netherlands 35

5. PSYCHOSOCIAL ASPECTS.....	37
Context	37
Current situation regarding psychosocial practices in Europe	37
Living donor psychosocial assessment/follow-up: definition of criteria and common terms, and suggested data to be screening	38
Recommendations for centres with living donor programmes	39
Best practice: ELIPSY project findings	40
The post-donation medical outcome of recipients and its relationship with the psychosocial outcome of donors was assessed in both follow-ups.....	40
6. FINANCIAL/ECONOMIC ASPECTS OF LIVING DONATION PROGRAMMES	41
Introduction	41
Example of practice: UK.....	42
The costs of living donor kidney transplantation	44
Best practice example: The Netherlands	47
The cost-effectiveness of living donor kidney transplantation	48
Conclusion.....	49
7. WHAT IS AN EFFECTIVE LIVING DONOR KIDNEY TRANSPLANT PROGRAMME?.....	51
Appendix.....	53
1. Directive 2010/53/EU of the European parliament and of the Council of 7 July 2010 on standards of quality and safety of human organs intended for transplantation	53
2. Council of Europe Convention on Human Rights and Biomedicine and the Additional Protocol to the Convention on Human Rights and Biomedicine, on Transplantation of Organs and Tissues of Human Origin.....	53
3. Recommendations and Resolutions of the Council of Europe	55
4. Conference and Recommendations (professional initiatives).....	55
5. Relevant European projects funded by the European Union	55
6. WHO Guiding Principles on Human Cell Tissue and Organ Transplantation	57

MISSION STATEMENT

This document is intended to provide a Reference Toolkit for all Member States concerning living organ donation for the purpose of transplantation. It sets out, and describes, the Core Principles for the establishment, organisation and oversight of living donor transplantation, gives examples of good practice, and contains an extensive list of references to other relevant documents. This toolbox on living kidney donation and transplantation thus intends to help Member States to establish or optimise their living donor programmes, by reviewing the key aspects of living kidney donation and transplantation. Whilst the toolbox focuses on kidney donation, the principles apply to the living donation of other organs, although it is acknowledged that the detail may vary due to organ specific factors and considerations.

EXECUTIVE SUMMARY

More than 40% of the documented 79,325 kidney transplants performed worldwide in 2013 were from a living donor.¹ The number of kidney transplants in the European Union (EU) has increased over the last few years, this increase being mostly driven by transplants performed from living donors (**Figure 1**). However, the annual rate of living kidney transplants in 2014 varied from 0 to 31.8 per million population (pmp). Fourteen EU countries were under 5 pmp; 9 countries between 5-15 pmp and 5 countries over 15 pmp, including 1 over 30 pmp.² This variation suggests that, by optimising the use of living kidney donation, kidney transplantation rates can substantially increase in many European countries. This would improve access to transplantation for patients in need with the potential for significant savings in dialysis costs.

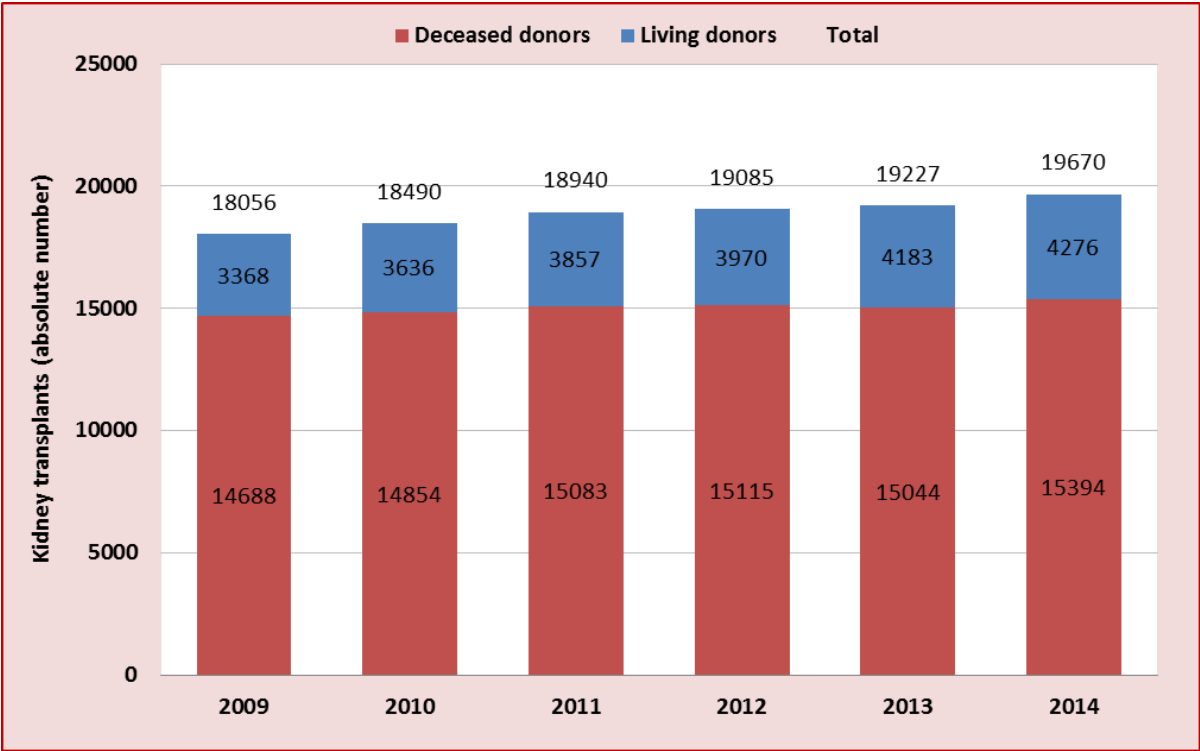


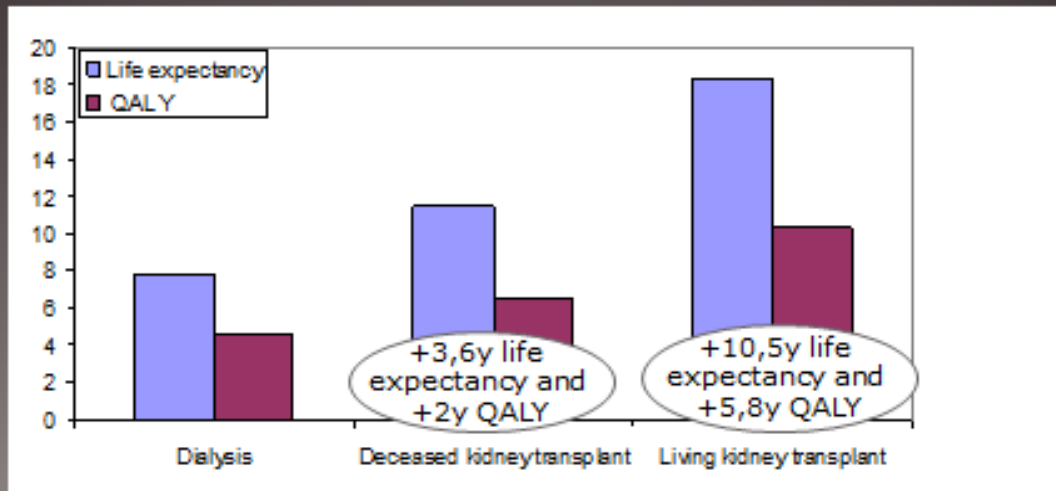
Figure 1: Absolute number of kidney transplant procedures from living and deceased donors in the European Union in 2009 and 2014. Source: Newsletter Transplant.

¹ Global Observatory on Donation and Transplantation. Available at: <http://www.transplant-observatory.org/Pages/Home.aspx>. Last access: March 2016.

² International figures on donation and transplantation 2014. Newsletter Transplant 2015; 20 (1).

Kidney transplants health outcome

Life expectancy for type1 diabetic patients with renal failure



Deceased kidney transplant adds 3,6y life expectancy and 2,0y QALY

Living kidney transplant adds 10,5y life expectancy and 5,8y QALY

Source: Knoll and Nichol, Mathematic modelling of 1000 articles, J. AM. Soc. Nephrol 2003

QALY: Quality adjusted life year, a year of life adjusted for its quality or its value. A year in perfect health is considered equal to 1.0 QALY

Benefits of living kidney transplantation

The results of transplantation with kidneys from living donors are better than those obtained with organs from deceased donors, both with regards to patient and graft survival.³ With genetically related donors, the half-life of a transplanted organ may be over 15 years, which means that for many patients the kidney transplant is a treatment for life. Organs from non-genetically related donors have as good graft survival as the best matched organs from deceased donors.

There are several reasons for the better overall results obtained with kidneys from living organ donors. Living donors are usually younger and selected on the basis of their overall good health, with less co-morbidity than that observed in deceased donors.⁴ The superior physiological state of the transplanted organ also plays a role, because the adverse consequences of hours/days of intensive care before organ donation are not present, as in the

³ Organ procurement and Transplantation network website. Available at: <http://optn.transplant.hrsa.gov/>: Last access: March 2016. Collaborative transplant study website. Available at: <http://www.ctstransplant.org>. Last access: March 2016.

⁴ Øien CM, Reisaeter AV, Leivestad T, Dekker FW, Line PD, Os I. Living donor kidney transplantation: the effects of donor age and gender on short- and long-term outcomes. *Transplantation* 2007; 83(5):600-606; Øien CM, Reisaeter AV, Leivestad T, Pfeffer P, Fauchald P, Os I. Gender imbalance among donors in living kidney transplantation: the Norwegian experience. *Nephrology Dialysis. Transplantation* 2005; 20(4):783-789.

case of deceased donation, and the events linked to brain death are avoided. Living organ donation can often mean a much shorter ischaemic time, with the time from donation to the re-perfusion of the kidney in the recipient being less than from a deceased donor. The practice of living kidney donation also makes it easier to perform pre-emptive transplantation (before the start of dialysis). The duration of dialysis therapy is an important determinant of patient and graft survival after transplantation.⁵ Pre-emptive transplantation also gives patients more choice when to have the transplant and decreases the burden and cost on society for dialysis. In some centres with a high number of living kidney donor transplants, every 4th or 5th kidney transplant is performed pre-emptively.

Risks for the living donor

Living organ donation carries, in the same way as for all surgical procedures, a certain risk.⁶ The mortality rate for the living kidney donors has been estimated at around 1/3,000.⁷ The mortality risk for living liver donation is much higher, estimated to be in the region of 1/200 for right liver lobe donation and 1/500 for left lateral segment.⁸

In a large published series of donor nephrectomies, morbidity related to the donation procedure has been reported as major in 3% and as minor in 18% of patients, with variations depending on the surgical procedure used for the donor nephrectomy.⁹ With modern laparoscopic techniques, both major and minor complication rates might be further reduced, along with a more rapid medical and social recovery and work rehabilitation.^{10 11}

⁵ Meier-Kriesche HU, Port FK, Ojo AO, Rudich SM, Hanson JA, Cibrik DM, et al. Effect of waiting time on renal transplant outcome. *Kidney Int* 2000;58(3):1311-1317.

⁶ Mjøen G, Øyen O, Holdaas H, Midtvedt K, Line PD. Morbidity and mortality in 1022 consecutive living donor nephrectomies. Benefits of kidney transplant living donor registries. *Transplantation* 2009; 88(11):1273-1279; Jakobsen A, Holdaas H, Leivestad T. Ethics and safety of living kidney donation. *Transplant Proc* 2003; 35(3):1177-1178.

⁷ Delmonico F; Council of the Transplantation Society. A Report of the Amsterdam Forum On the Care of the Live Kidney Donor: Data and Medical Guidelines. *Transplantation* 2005; 79 (6 Suppl): S53-66; Segev DL, Muzaale AD, Caffo BS, Mehta SH, Singer AL, Taranto SE, et al. Perioperative mortality and long-term survival following live kidney donation. *JAMA* 2010;303(10):959-966.

⁸ Yee LC, Simpson MA, Pomposelli JJ, Pomfret EA. Incidence of death and potentially life-threatening near miss events in living donor hepatic lobectomy: a world-wide survey. *Liver Transpl* 2013;19: 499-506.

⁹ Delmonico F; Council of the Transplantation Society. A Report of the Amsterdam Forum On the Care of the Live Kidney Donor: Data and Medical Guidelines. *Transplantation* 2005; 79 (6 Suppl): S53-66; Mjøen G, Holdaas H, Pfeffer P, Line P-D, Øyen O. Minimally invasive living donor nephrectomy – introduction of hand-assistance. *Transpl Int* 2010; 23(10):1008-1014.

¹⁰ Greco F, Hoda MR, Alcaraz A, Bachmann A, Hakenberg OW, Fornara P. Laparoscopic Living-Donor Nephrectomy: Analysis of the Existing Literature, *Eur Urol* 2010; 58(4):498-509

¹¹ Hadjinasstasiou VG, Johnson RJ, Rudge CJ, Mamode N. 2509 living donor nephrectomies, morbidity and mortality, including the UK introduction of laparoscopic donor surgery. *AM J Transplant* 2007; 7: 2532-2537

However, emerging evidence suggests that, with a longer follow-up, there might be a greater risk for some living kidney donors.^{12 13} Two recent pieces of research about the safety and long-term outcome of living kidney donors suggest that certain groups (black donors, younger donors, genetically related donors, donors to patients with immunological causes of renal failure and overweight donors) have a higher risk of developing end-stage renal disease following donation. These two publications have been summarised in a specific statement on the long-term safety of living kidney donation from the Committee of Transplantation of the Council of Europe (endorsed by the European Society for Organ Transplantation, the International Society of Nephrology and The Transplantation Society).¹⁴ Some countries have also amended their existing guidelines on Living Kidney Donation, for example the Addendum to the United Kingdom Guidelines for Living Kidney Transplantation.¹⁵ This is discussed in greater detail in Chapter 3.

Other research showed that the survival of living kidney donors was similar to that of controls matched for age, gender, race or ethnicity or that the survival and the risk of end-stage renal disease in carefully screened kidney donors was similar to the general public.^{16 17} It is therefore important to put this increased risk in context. The overall risk of developing end-stage renal disease after kidney donation remains very low, occurring in less than one in 200 (0.5%) donors, and it remains much less than that of the general (unscreened) population. Compared to the general public, kidney donors have equivalent (or better) survival, excellent quality of life, and no increase in end-stage renal disease. It is however vital that all living donors are appropriately informed of the potential risks and adequately followed-up.

Protection of the living organ donor

Living organ donors are a unique group of patients. They have voluntarily undergone surgery and the loss of a perfectly healthy kidney in order to help another person. Therefore the

¹¹ Mjoen G, Hallan S, Hartmann A, Foss A, Midtvedt K, Øyen O, et al. Long-term risks for kidney donors *Kidney Int* 2014; 86: 162-167

¹³ Muzaale AD, Massie A, Wang MC, Montgomery RA, McBride MA, Wainright JL, Segev DL. Risk of end-stage renal disease following live kidney donation. *JAMA* 2014; 311: 579-586.

¹⁴ Cozzi E, Biancone L, López-Fraga M, Nanni-Costa A. Long-term outcome of living kidney donation. Position paper of the European Committee on Organ Transplantation, Council of Europe. *Transplantation* 2016; 100(2): 270-271..

¹⁵ Guidelines for Living Kidney Transplantation. Available at: <http://www.bts.org.uk/Documents/Guidelines>. Last access: March 2016.

¹⁶ Ibrahim HN, Foley R, Tan L, Rogers T, Bailey RF, Guo H, et al. Long term consequences of kidney donation. *N Engl J Med* 2009; 360: 459-469.

¹⁷ Najarian JS, Chavers BM, McHugh LE, Matas AJ. 20 years or more of follow-up of living kidney donors. *Lancet* 1992; 340: 807-810.

evaluation and selection of the donor must be based on appropriate standards. These include an appropriate specific and informed consent process by which the donor should be made aware of the risks of the procedure and of the alternative therapies for the prospective recipient. Transplant centres performing living donor nephrectomies have also a particular obligation to instigate life-long supervision of the general health of those individuals, wherever possible. The transplant community, particularly through the *Amsterdam Forum*, has laid down guidelines for the evaluation, selection and care of the living kidney donor.¹⁸

These general principles are also consistently reflected in international legal standards, such as the *Additional Protocol to the Convention on Human Rights and Biomedicine on Transplantation of Organs and Tissues of Human Origin*,¹⁹ the *World Health Organization Guiding Principles on Human Cell, Tissue and Organ Transplantation*,²⁰ and *Directive 2010/53/EU of the European Parliament and of the Council on quality and safety standards of human organs intended for transplantation*, that had to be transposed by the 28 EU Member States by 27 August 2012.²¹ Countries engaged in living kidney transplantation procedures should record the information related to the outcome of the living organ donor, including complications related to donation in the short, mid and long-term. These tools are essential for transparency and to inform the consent process. Many countries have developed national registries to facilitate and improve the follow-up of living kidney donors,²² with some of these dating back to the early 1990s. Under *Directive 2010/53/EU*, Member States are obliged to have such registers.

¹⁸ Delmonico F; Council of the Transplantation Society. A Report of the Amsterdam Forum On the Care of the Live Kidney Donor: Data and Medical Guidelines. *Transplantation* 2005; 79 (6 Suppl): S53-66; Ethics Committee of the Transplantation Society. *Transplantation* 2004;78(4):491-492.

¹⁹ Additional Protocol to the Convention on Human Rights and Biomedicine, on Transplantation of Organs and Tissues of Human Origin, Council of Europe website. Available at:

<http://conventions.coe.int/Treaty/en/Treaties/Html/186.htm>. Last access: March 2016.

²⁰ WHO Guiding Principles on Human Cell, Tissue and Organ Transplantation. Global Observatory on Donation and Transplantation website. Available at:

<http://www.transplant-observatory.org/SiteCollectionDocuments/wholegethgp.pdf>. Last access: March 2016.

²¹ Directive of the European Parliament and of the Council on standards of quality and safety of human organs intended for transplantation. European Union website. Available at: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2008:0818:FIN:EN:HTML>. Last access: March 2016.

²² Jakobsen A, Holdaas H, Leivestad T. Ethics and safety of living kidney donation. *Transplant Proc* 2003; 35(3):1177-1178; Westlie L, Leivestad T, Holdaas H, Lien B, Meyer K, Fauchald P. Report from the Norwegian National Hospitals Living Donor Registry: one-year data. *Transplant Proc* 2003; 35: 777-778.

Expanding the living kidney donor pool: the non-genetically related donor and non-directed living donation

Up to the mid-1980s nearly all living kidney donor transplants were performed with an organ from a genetically related donor (siblings, parents and grandparents). Most transplant centres nowadays accept donors that are not genetically related to the recipient such as spouses, in-laws and friends, with equivalent outcomes. All such transplants are referred to as ‘directed donations’ (the donor knows the recipient). Some countries accept altruistic donors where the donor does not know the identity of the recipient, so-called ‘non-directed donation’. Other countries allow ‘directed altruistic’ where there is no genetic or emotional link and the recipient and donor become acquainted through, for example, a website. Some countries have developed a system of paired exchange of kidneys (or cross over donation), i.e. when there is a blood group mismatch or possible HLA mismatch between donor and recipient in couple A, and an opposite mismatch in couple B. It may be possible for the donor in couple A to donate to the recipient of couple B, and vice versa. In this way patients who would otherwise have to go on the waiting list for an organ from a deceased donor, are being transplanted. Over the years, kidney paired exchange programmes have been developed at a regional or a national scale in many European countries such as the Netherlands, Spain and the United Kingdom, and are planned in other Member States.²³

Kidney paired exchange programmes have advantages and disadvantages when compared to the application of specific protocols to allow direct transplantation through an ABO incompatibility or a positive HLA cross-match. These programmes are cheaper, but logistically more complex and involve the partial loss of the emotional component associated with direct kidney donation.

Living kidney donation and organ trafficking

The fact that living kidney transplantation can successfully be performed with a kidney from a non-genetically related donor, added to the shortage of organs and the unequal distribution of

²³ Roodnat JI, Zuidema W, van de Wetering J, de Klerk M, Erdman RA, Massey EK, et al. Altruistic donor triggered domino-paired kidney donation for unsuccessful couples from the kidney-exchange program. *Am J Transplant* 2010;10(4):821-827; Hanto RL, Reitsma W, Delmonico FL The development of a successful multiregional kidney paired donation program. *Transplantation* 2008;86(12):1744-1748; Higgins R, Hathaway M, Lowe D, Zehnder D, Krishnan N, Hamer R, Briggs D. New choices for patients needing kidney transplantation across antibody barriers. *J Ren Care* 2008;34(2):85-93; Lima BA, Dias L, Henriques AC, Alves H. The Portuguese match algorithm in the kidney paired donation program. *Organs, tissues and cells* 2010; 13: 25-32.

wealth in the world, has opened the door to transplantation outside the ethical framework consistently established by the transplant community and many international organisations. These practices include transplant commercialism, trafficking in organs and trafficking in persons for the purpose of organ removal, which are forbidden by law in most countries, but still occur in certain parts of the world.²⁴

Trafficking related to transplantation usually occurs in the context of transplant tourism, mainly consisting of wealthy potential recipients travelling to countries that lack the appropriate legal and ethical framework protecting the living donor, or the necessary control mechanisms.²⁵ Trafficking can also occur within well-established transplant programmes and special caution should be paid to non-resident living donors and/or recipients. The most vulnerable groups are then subject to exploitation, and thus especially exposed to the development of medical, psychological and social complications.²⁶ The quality and safety of the process of donation and transplantation in this setting cannot be guaranteed. In fact, recipients transplanted under these circumstances have reportedly developed frequent complications and donor-derived diseases.²⁷ It is imperative therefore that countries with living donor programmes have the necessary legislative and regulatory infrastructure in place to ensure that their living donor programme conforms to international standards, and that it can offer the donor and the recipient the assurance of safe and high quality clinical and ethical practice.

The following chapters give further information.

²⁴ Shimazono Y. The state of the international organ trade: a provisional picture based on integration of available information. *Bulletin of the World Health Organization* 2007; 85: 955-962.

²⁵ Steering Committee of the Istanbul Summit. Organ trafficking and transplant tourism and commercialism: the Declaration of Istanbul. *Lancet* 2008; 372(9632):5-6.

²⁶ Goyal M, Mehta RL, Schneiderman LJ, Sehgal AR. Economic and health consequences of selling a kidney in India. *JAMA* 2002;288(13):1589-1593. Nejatiasafa AA, Mortaz-Hedjri S, Malakoutian T, Arbabi M, Hakemi MS, Haghighi AN, et al. Quality of life and life events of living unrelated kidney donors in Iran: a multicenter study. *Transplantation* 2008;86(7):937-940; Moazam F, Zaman RM, Jafarey AM. Conversations with kidney vendors in Pakistan: an ethnographic study. *Hastings Cent Rep* 2009;39(3):29-44.

²⁷ Gill J, Madhira BR, Gjertson D, Lipshutz G, Cecka JM, Pham PT, et al. Transplant tourism in the United States: a single-center experience. *Clin J Am Soc Nephrol* 2008;3(6):1820-1828. Prasad GV, Shukla A, Huang M, D'A Honey RJ, Zaltzman JS. Outcomes of commercial renal transplantation: a Canadian experience. *Transplantation* 2006;82(9):1130-1155; Allam N, Al Saghier M, El Sheikh Y, Al Sofayan M, Khalaf H, Al Sebayel M, et al. Clinical Outcomes for Saudi and Egyptian Patients Receiving Deceased Donor Liver Transplantation in China. *Am J Transplant* 2010; 10(8): 1834-1841. .

1. INTRODUCTION

Setting the scene

- 1.1 Living kidney donation has become an essential part of transplantation practice. Historically, it has been attributed to the shortage of deceased donor kidneys and the growing waiting list of potential recipients. However, kidney transplantation from a living donor has become the treatment of choice for many patients and their families, offering better patient and graft survival, and also the chance to avoid long periods on the transplant waiting list. This is particularly the case in pre-emptive transplantation, when the transplant occurs before the start of dialysis. Living donation also offers patients who are more clinically complex, either immunologically or due to other co-morbidities, the opportunity to benefit from a transplant that they might otherwise not have received from the deceased donor waiting list.
- 1.2 The burden of end-stage kidney disease has increased at an estimated rate of 3-9% per year over the last 5-10 years and it will probably continue to increase as a result of an ageing population and the increased incidence and prevalence of diseases such as obesity, diabetes and arterial hypertension. Kidney transplantation is considered the best therapeutic strategy for patients with end-stage kidney disease, providing better results than renal replacement therapy with dialysis, both in terms of survival and quality of life.¹ It also has the most favourable cost-effectiveness ratio of all renal replacement therapies.²
- 1.3 However, the main problem that precludes the full development of kidney transplantation is the limited availability of kidneys to meet the transplantation needs of the patients. According to data from the Transplant Newsletter, more than 46,000

¹ Wolfe RA, Ashby VB, Milford EL, Ojo AO, Ettenger RE, Agodoa LY, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med* 1999;341:1725-1730; Heldal K, Hartmann A, Grootendorst DC, de Jager DJ, Leivestad T, Foss A, Midtvedt K. Benefit of kidney transplantation beyond 70 years of age.. *Nehrol Dial Transplantation* 2010 ;25 :1680-1687; Martín Navarro J, Ortega M, Gutiérrez MJ, García Martín F, Alcázar JM, Morales JM, et al. Survival of patients older than 60 years with kidneys transplanted from Spanish expanded criteria donors versus patients continued on hemodialysis. *Transpl Proc* 2009;41:2376-2378.

² Wong G, Howard K, Chapman JR, Chadban S, Cross N, Tong A, et al. Comparative survival and economic benefits of deceased donor kidney transplantation and dialysis in people with varying ages and co-morbidities. *PLoS ONE* 2012; 7(1) :e29591.doi :10.1371/journal.pone.0029591.

patients were waiting for a kidney in the European Union (EU) at the end of 2014, but only 19,670 kidney transplants were performed during that entire year.³

- 1.4 Because of this shortage of donor organs, many patients will never be included on the waiting list, particularly those with poor survival expectancy. Many patients on the waiting list may deteriorate or die while waiting to be transplanted. Desperate patients might look for alternative solutions outside the ethical and legal European framework. This could include unacceptable practices such as trafficking in organs, sometimes involving trafficking in persons for the purpose of the removal of organs, and patients going to other countries to buy donor organs – so called ‘transplant tourism’.⁴
- 1.5 As outlined in the Madrid Resolution, *‘Every country, in light of its own level of economic and health system development, should progress toward the global goal of meeting patients’ needs based on the resources obtained within the country, for that country’s population, and through regulated and ethical regional or international cooperation when needed. In order to pursue the global aim of self-sufficiency in transplantation, donation and transplantation from the deceased donor should be developed to its maximum potential’.*⁵ However, transplantation of kidneys from living donors is considered today as a necessary adjunct to meeting the transplantation needs of a given population and complementing the deceased donor programme. Therefore, each country should examine their capacity for living kidney donation, although never to the exclusion of deceased organ donation. *Resolution 57.18 of the 2004 World Health Assembly* urges Member States *‘to extend the use of living kidney donations when possible, in addition to donations from deceased donors’.*⁶
- 1.6 In the European setting, the position of the international institutions towards living kidney donation has been evolving over the years consistent with the previously mentioned standards. The *Additional Protocol to the Convention on Human Rights and Biomedicine, on Transplantation of Organs and Tissues of Human Origin*, states that

³ International figures on organ donation and transplantation 2014. *Newsletter Transplant* 2015; 20 (1).

⁴ Joint Council of Europe / United Nations Study on trafficking in organs, tissues and cells and trafficking in human beings for the purpose of the removal of organs. Council of Europe website. Available at: http://www.coe.int/t/dghl/monitoring/trafficking/default_en.asp. Last access: March 2016.

⁵ The Madrid Resolution on Organ Donation and Transplantation. National responsibilities in meeting the needs of patients, guided by the WHO principles. *Transplantation* 2011; 91 (11S): S29- S31.

⁶ World Health Assembly Resolution 57.18. Global Observatory on Organ Donation and Transplantation website. Available at: <http://www.transplant-observatory.org/SiteCollectionDocuments/wha57resen.pdf>. Last access: March 2016.

'Removal of organs or tissue from a living person may be carried out solely for the therapeutic benefit of the recipient and where there is no suitable organ or tissue available from a deceased person and no other alternative therapeutic method of comparable effectiveness'.⁷ Subsequently, an explanatory report to this Convention was produced where the benefits provided by living kidney transplantation in terms of recipient outcomes made it the preferred option for patients with advanced renal disease. Moreover, the Committee of Ministers of the Council of Europe recently adopted a Resolution, where the position in respect of living kidney donation in terms of a necessary component for self-sufficiency is clarified, as long as donor protection is ensured and efforts in maximizing deceased donation are maintained.⁸

- 1.7 Therefore, in line with international standards, the European Commission, in cooperation with the Competent Authorities of the EU, aims to support Member States to optimise kidney transplantation from the living donor, as an adjunct in the pursuit of self-sufficiency in transplantation.

Classification of living donation

- 1.8 There are a number of different types of living donation for kidney transplantation, but not all may be permissible within the domestic law of a Member State.⁹

Directed donation

Where a healthy person donates an organ (usually a kidney) to a specific recipient:

- (i) genetically-related donation: where the donation is offered to a specific person who is a blood relative of the potential recipient;
- (ii) emotionally-related donation: where the potential donor has a relationship with the potential recipient; for example, spouse, partner, or close friend;

⁷ Additional Protocol to the Convention on Human Rights and Biomedicine concerning Transplantation of Organs and Tissues of Human Origin. Council of Europe website. Available at: <http://conventions.coe.int/Treaty/en/Treaties/Html/186.htm>. Last access: March 2016.

⁸ Resolution CM/Res(2013)56 on the development and optimization of live kidney donation programmes. Available at: <https://www.edqm.eu/en/organ-transplantation-recommendations-resolutions-74.html>. Last access: March 2016.

⁹ Information about Living Donor Transplants, Human Tissue Authority. Available at: <https://www.hta.gov.uk>. Last access: March 2016.

(iii) paired-donation: where a relative, friend or partner is fit and able to donate an organ but is incompatible with the potential recipient and they are matched with another donor and recipient in a similar situation, so that both people in need of a transplant receive a compatible organ;

(iv) pooled donation: a form of paired donation whereby the pair is matched with other donors and recipients from a pool of pairs in similar situations, and more than two donors and two recipients are involved in the swap, and more than two people in need of a transplant receive a compatible organ.

(v) directed altruistic donation: where there is no genetic or pre-existing emotional relationship between the donor and recipient. These cases often arise through the intervention of a third party e.g. a social networking site or newspaper campaign, bringing the donor and recipient together for the purpose of transplantation.

Non-directed altruistic donation

(i) where a kidney is donated by a healthy person into a paired or pooled scheme or to a recipient on the transplant waiting list. The donor does not have a relationship with the recipient and their details are not given. The organ may be allocated through the same procedures as a deceased donor organ.

1.9 ELPAT has proposed a new classification of the living donation according to the relationships between the donor and the recipient. These are set out in **Table 1** below.¹⁰

Table 1 ELPAT Classification for Living Organ Donation	
Specified Donation	
Direct Donation	Where a person donates directly to his or her intended recipient <ul style="list-style-type: none"> ▪ Donation to a genetically and emotionally related recipient (e.g. child, parent, sibling) ▪ Donation to a genetically unrelated but emotionally related recipient (e.g. spouse, friend or acquaintance) ▪ Donation to a genetically related but emotionally unrelated recipient (e.g. estranged child, parent, sibling)

¹⁰ Dor FJ, Massey EK, Frunza M, Johnson R, Lennerling A, Lovén C, et al. New classification of ELPAT for living organ donation. *Transplantation* 2011 ; 91 : 935-938.

	<ul style="list-style-type: none"> ▪ Donation to a genetically and emotionally unrelated recipient, but the recipient (or the group to which he/she belongs) is specified (e.g. people younger than 18, or a person identified by the media)
Indirect donation	<p>When a person donates indirectly to his/her intended recipient</p> <p>Donation to a specified person through an exchange programme</p>
Unspecified Donation	<p>Donation to an anonymous and unspecified recipient (e.g. donation to the transplant waiting list or to the recipient of an exchange couple in the case of domino paired exchange)</p>

Example of practice: Netherlands

In the last few years over 50 percent of all kidney transplants in the Netherlands are performed with a kidney from a living donor (26.3 p.m.p.). To achieve such a successful living donor programme several measurements had to be taken. First, the living donor pool was expanded by accepting, apart from genetically-related couples, also genetically unrelated couples. These couples are only accepted when a firm relationship exists between donor and recipient (e.g. spouses, very close friends, neighbours). The second addition to the Netherlands living donor programme was the implementation of a living donor kidney exchange programme, also called paired exchange or cross-over.

Living donor kidney exchange has proven to be an efficient solution for recipients with a blood type or cross match incompatible donor. In the Netherlands, this programme was started in 2004 and clinical and administrative hurdles had to be overcome before the programme could really start. Important was the development of a computer match procedure, through which it was possible to match combinations of two or more pairs. Another important prerequisite for a successful national living donor kidney exchange programme is that allocation and cross match procedures are centralized. The programme has become particularly effective since altruistic donors were also included in the chains. During 2004-2012, 216 transplantations have been performed with this programme in the Netherlands.

Supporting living donation

Key components

1.11 Optimising living kidney transplantation relies on five main components:

a) Establishment of an appropriate medical, psychological, social, legal and ethical framework of donor care – to ensure high quality and safe clinical care in line with international standards and the necessary regulatory systems to combat the potential for organ or human trafficking.

b) Information – the option, risks and benefits of living kidney transplantation should be discussed with patients with advanced kidney disease and their relatives and friends where appropriate, ideally pre-emptively i.e. before dialysis therapy becomes necessary, together with information on other renal replacement therapies.

c) Removal of technical barriers to living kidney transplantation – clinical and surgical expertise should be developed, together with the establishment of specific programmes such as paired or pooled schemes to help overcome incompatibilities between prospective donors and recipients.

d) Financial infrastructure in place – to meet the clinical costs of the living donor programme and reimburse the out-of-pocket expenses and loss of earnings of the living donor.¹¹

e) Capacity and Capability – a sufficient and appropriately trained workforce to support a living donor programme

1.12 The following could help support living donation within Member States.¹²

National leadership

Because of the clinical benefits of living kidney transplantation, Member States could consider establishing or expanding their living donor programmes to increase the potential for transplantation considerably. Living donor kidney transplant rates vary enormously between countries with 14 countries having rates under 5 pmp. However, the clinical benefits and cost savings are significant.

1.13 Programme expansion could be helped by each Member State appointing a lead clinician to provide clinical leadership nationally and to raise the profile of living donation both publicly and with transplant clinicians. This role could be supported by the establishment of a steering group drawn from the clinical transplant community to develop a living donor kidney transplant strategy. This Group would identify the potential for living donor kidney transplantation in the Member State and help

¹¹ Wolfe RA, Roys EC, Merion RM. Trends in organ donation and transplantation in the United States, 1999-2008. *Am J Transplant* 2010; 10: 961-972; Donovan K, Ford D, van Schalkwyk D, Ansell D. UK Renal Registry 12th annual report (December 2009): Chapter 16, international comparison with the UK RRT programme. *Nephron Clin Pract* 2010;115 (Suppl 1): 309-320.

¹² Living Kidney Donor Transplantation 2020: a UK Strategy. NHS Blood and Transplant. Available at: www.nhsbt.nhs.uk. Last access: March 2016.

coordinate the necessary action to implement the recommendations within the strategy document.

Funding

1.14 As well as the clinical benefits, living donor kidney transplantation is also recognised as a cost-effective treatment for end-stage kidney disease in comparison with dialysis, offering significant financial savings to the health economy. The savings are greater if pre-emptive transplantation is provided, not only offering improved health outcomes associated with the transplantation before the need for dialysis, but the number of transplanted years versus years on dialysis. Member States will therefore need to be assured of sustainable funding through state or privately funded insurance arrangements to support their living donor programmes and meet the costs identified in Chapter 7 of this document.

Living donor coordinators

1.15 The appointment of living donor coordinators working in nephrology and transplant units has proved an effective way to encourage living kidney donation. Living donor coordinators are dedicated people available to discuss donation with the potential recipient and the potential recipient's family and friends as potential donors and able to support them through testing, work-up, transplantation and follow-up.

1.16 This document therefore provides information on the core elements necessary to establish, develop and expand living donor programmes in Member States. Although the document focuses on living kidney donation, the core principles will apply equally to the development of other living donor programmes such as live liver donation.

2. LEGAL AND ETHICAL ASPECTS OF LIVING DONATION

Introduction

2.1 The *World Health Organisation Guiding Principles on Human Cell Tissue and Organ Transplantation* (EB123/5) states that *'Donation from deceased persons should be developed to its maximum therapeutic potential but adult living persons may donate*

*organs as permitted by domestic regulations.*¹³ A legal framework surrounding the activity of living kidney donation is the first step against any unacceptable practices such as organ trafficking or commercialisation. It gives complete legitimacy to efforts to develop this activity in response to the transplantation needs of the population. It represents a guarantee of transparency, providing confidence in the programme for both the public and the health-care community. The Competent Authorities will supervise compliance with the legal framework in place in each member state.

2.2 The essential objective of a legal framework in living kidney donation concerns the protection of the donor. The benefit of living kidney donation for the potential recipient is well known. For each donor, the sole aspects to be considered are the risks of donation. Thus, when the risk-benefit has to be discussed, the analysis should focus on these risks (as direct benefits to the donor are marginal) compared to the potential benefits for the patient to be transplanted.

2.3 Article 13 of *Directive 2010/53/EU* lays out the following principles governing organ donation:¹⁴

'1. Member States shall ensure that donations of organs from deceased and living donors are voluntary and unpaid.

2. The principle of non-payment shall not prevent living donors from receiving compensation, provided it is strictly limited to making good the expenses and loss of income related to the donation. Member States shall define the conditions under which such compensation may be granted, while avoiding there being any financial incentives or benefit for a potential donor.

3. Member States shall prohibit advertising the need for, or availability of, organs where such advertising is with a view to offering or seeking financial gain or comparable advantage.

4. Member States shall ensure that the procurement of organs is carried out on a non-profit basis'.

2.4 World Health Organisation Guiding Principle 5 states that *'The sale of cells, tissues and organs for transplantation by living persons, or by next of kin, should be banned.*

¹³ WHO Guiding Principles on Human Cell, Tissue and Organ Transplantation. Global Observatory on Donation and Transplantation website. Available at: <http://www.transplant-observatory.org/SiteCollectionDocuments/wholegethgp.pdf>. Last access: March 2016.

¹⁴ Directive of the European Parliament and of the Council on standards of quality and safety of human organs intended for transplantation. European Union website. Available at: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2008:0818:FIN:EN:HTML>. Last access: March 2016.

National laws should therefore ensure that any gifts or rewards do not become a disguised form of payment for donation'.¹³

Authorisation of procurement and transplant centres

2.5 *Directive 2010/53/EU* provides rules on a framework for quality and safety covering all stages of the chain from donation to transplantation or disposal.¹⁴ Procurement and transplantation activity must be licensed or authorised by the Competent Authority in line with the requirements set out in the Directive. Article 17 also requires the Competent Authorities of the Member States to *'grant, suspend, or withdraw, as appropriate, the authorisations of procurement organisations or transplantation centres or prohibit procurement organisations or transplantation centres from carrying out their activities where control measures demonstrate that such organisations or centres are not complying with the requirements of this Directive...'*¹⁴

Consent

2.6 Consent to living donation must only be taken after clear, comprehensible and honest information has been given to the potential donor by the teams. The content should cover the main risks, serious or not, frequent or not, and the potential consequences whatever they are: medical, psychological, social, professional, financial, quality of life for both the donor and for the recipient. The principle of an independent committee (or a donor advocate) to assess the donor's motivation, to assess his or her understanding of the procedure and to confirm lack of coercion or commercial activity (even if difficult) is highly recommended. The freedom of the donor to withdraw at any time from the donation process should be clearly written and explained. Article 14 of *Directive 2010/53/EU* in this respect provides that the *'procurement of organs shall be carried out only after all requirements relating to consent, authorisation or absence of any objection in force in the Member State concerned have been met'*.¹⁴

Example of practice: Spain

Royal Decree 1723/2012 sets down provisions regulating living organ donation in article 8¹⁵. Provisions related to the consent and authorization for living organ donation are summarized below:

- Living organ donors should not be minors (minority is defined as <18 years of age) and should not have any mental incapacity or conditions that preclude consent to be provided in the indicated manner set down below.
- Living organ donors must receive appropriate information on: i) the consequences of their decision; ii) the risks for their own (medical, psychological and social); iii) the risks for the recipients; iv) the possible contraindications; v) the way the transplantation centre will proceed in the event that, once recovered, the organ is not able to be transplanted in the intended recipient. This information should be provided by a doctor independent from the team(s) in charge of organ procurement and transplantation. The information provided to the potential living organ donor, along with the motivations freely expressed by him/her and any suspicion of coercion, must be accredited by such doctor, who is also in charge of evaluating and accrediting the health status of the donor.
- Consent to living organ donation should be explicitly expressed, in a free, conscious and disinterested manner.
- The information provided to the living organ donor and the means for the expression of consent should be in adequate formats, so that it is accessible and understandable for persons with any form of incapacity.
- The living organ donation procedure should not proceed if there is any suspicion that consent has not been freely provided or if any economic, social, psychological or any other type of pressure is considered to exist.
- It is mandatory to count on the evaluation of the living donation procedure by an Ethics Committee.
- To proceed with living organ donation, the donor should express consent to organ donation before the Judge. In the appearance before the Judge, the expressed consent should follow the explanations from the doctor in charge of the recovery, provided in presence of the doctor in charge of informing and accrediting the health status of the donor, the doctor in charge of the transplantation and the person in charge of authorizing the donation procedure, as specified in the authorization of the centre for living organ donation.
- The Judge will issue a document where the consent of the donor is reflected and that will be signed by the donor him/herself, the doctor in charge of the recovery and the rest of participants in the appearance. If any of these doubt the consent having been provided in an explicit manner, freely, consciously and disinterestedly, he/she will be able to effectively oppose to the donation.
- The minimum time between the signature of the document of consent to organ donation specified above and the recovery will be 24 hours.
- The donor will be able to revoke consent at any time before the recovery of the organ, with no need for a specific formal procedure.

2.7 According to the *Additional Protocol to the Convention on Human Rights and Biomedicine on Transplantation of Organs and Tissues of Human Origin*, no organ or tissue removal may be carried out on a person who does not have the capacity to

¹⁵ Real Decreto 1723/2012 of 28 December (in Spanish). Available at: <http://www.boe.es/boe/dias/2012/12/29/pdfs/BOE-A-2012-15715.pdf>. Last access: March 2016.

consent.¹⁶ The *Amsterdam Forum* stated that minors less than 18 years old should not be used as living organ donors.¹⁷ However, some Member States, in line with well-regulated practice, may, in exceptional circumstances, enable parents or the courts to give consent to donation - for example in domino transplantation, or where the donor is under 18; a young parent wishing to donate to his or her child or adults that lack capacity.

2.8 There is a particular need to consider the donor where living donation is required in an emergency, for example where the evaluation of the donor must be undertaken within a 48 hour period. The *Vancouver Forum on the care of the living organ donor* has considered such circumstances as acceptable in relevant centres able to undertake the evaluation in the time frame.¹⁸ However, there are significant ethical issues in these situations. The potential donor may feel coerced into donating and it may not be possible to obtain a genuine consent to donation. In these circumstances for patients requiring emergency liver transplantation, Member States may wish to consider placing the patient on a priority list for a deceased donation.

2.9 There are also ethical concerns around gender imbalance in living donation. International data provided to the *Amsterdam Forum on the care of the living donor* revealed that 65% of living donors have been women and approximately 65% of recipients have been men.¹⁷ Therefore the potential for gender inequities in living donation should be looked at carefully and addressed by promoting targeted strategies and by optimising deceased donation.

¹⁶ Additional Protocol to the Convention on Human Rights and Biomedicine, on Transplantation of Organs and Tissues of Human Origin, Council of Europe website. Available at:

<http://conventions.coe.int/Treaty/en/Treaties/Html/186.htm>. Last access: March 2016.

¹⁷ Delmonico F; Council of the Transplantation Society. A Report of the Amsterdam Forum On the Care of the Live Kidney Donor: Data and Medical Guidelines. *Transplantation* 2005; 79 (6 Suppl): S53-66; Ethics Committee of the Transplantation Society. *Transplantation* 2004;78(4):491-492.

¹⁸ Delmonico FL Vancouver forum on the live lung, liver, pancreas, and intestine donor. *Transplantation* 2006; 82(9):1245. Pruett TL, Tibell A, Alabdulkareem A, Bhandari M, Cronin DC, Dew MA, et al. The ethics statement of the Vancouver Forum on the live lung, liver, pancreas, and intestine donor. *Transplantation* 2006; 81(10):1386-1387. Barr ML, Belghiti J, Villamil FG, Pomfret EA, Sutherland DS, Gruessner RW, et al. A report of the Vancouver Forum on the care of the live organ donor: lung, liver, pancreas, and intestine data and medical guidelines. *Transplantation* 2006; 81(10):1373-1385.

Organ trafficking, transplant tourism & commercialism, including incentives

- 2.10 In line with *Directive 2010/53/EU*, each Member State should state within their legislation, the penalties for infringement of the national provisions and ensure that these penalties are enforced.¹⁴ To build a better picture across the EU, access to information by Member States would be helpful.
- 2.11 To avoid transplant tourism (or commercialism), the management of a non-resident donor, or non-resident recipient (or more rarely both) should be based on bilateral agreements between the Member States involved. This will help ensure the financial provision for the entire process (donation and/or transplantation) is in line with the requirements of *Directive 2010/53/EU*, including the guarantee of donor follow-up where possible.¹⁴

3. DONOR EVALUATION, SELECTION AND PROTECTION

Introduction

3.1 It is essential that all the pre-donation aspects of the care of a potential living donor are carried out in accordance with the highest possible standards. These include the initial evaluation of the donor, the selection and assessment process, and protection of the interests of the donor. In addition to national guidelines, the following basic documents are of importance: *The Consensus Statement of the Amsterdam Forum on the Care of the Living Kidney Donor* (2004), *Human organ and tissue transplantation, Report by the Secretariat, WHO* (2008) and *The Declaration of Istanbul on Organ Trafficking and Transplant Tourism* (2008).^{1 2}

3.2 Article 15 of *Directive 2010/53/EU* provides the following general rules on the quality and safety aspects of living donation:³

'1. Member States shall take all necessary measures to ensure the highest possible protection of living donors in order to fully guarantee the quality and safety of organs for transplantation.

2. Member States shall ensure that living donors are selected on the basis of their health and medical history, by suitably qualified or trained and competent professionals. Such assessments may provide for the exclusion of persons whose donation could present unacceptable health risks.

3. Member States shall ensure that a register or record of the living donors is kept, in accordance with Union and national provisions on the protection of the personal data and statistical confidentiality.

4. Member States shall endeavour to carry out the follow-up of living donors and shall have a system in place in accordance with national provisions, in order to identify, report and manage any event potentially relating to the quality and safety of the donated organ, and hence of the safety of the recipient, as well as any serious adverse reaction in the living donor that may result from the donation'.

¹ Delmonico F; Council of the Transplantation Society. A Report of the Amsterdam Forum On the Care of the Live Kidney Donor: Data and Medical Guidelines. *Transplantation* 2005; 79 (6 Suppl): S53-66; Ethics Committee of the Transplantation Society. *Transplantation* 2004;78(4):491-492.

² Steering Committee of the Istanbul Summit. Organ trafficking and transplant tourism and commercialism: the Declaration of Istanbul. *Lancet* 2008; 372(9632):5-6.

³ Directive of the European Parliament and of the Council on standards of quality and safety of human organs intended for transplantation. European Union website. Available at: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2008:0818:FIN:EN:HTML> Last access: March 2016.

Donor evaluation and assessment

- 3.3 The living donor should be legally competent and have the mental capacity to understand the information. No minor or person not able to fully understand the information given should be accepted as a living donor other than narrow exceptions allowed under national law.
- 3.4 The primary group of potential donors is the first-degree relatives, spouses or partners. Verbal and written information should be offered about donation including the alternative treatment options for the potential recipient. It is important that the offer of information should not imply any pressure to donate. Other relatives, close friends and potential non-directed altruistic donors should also receive the same type of information if they present themselves as potential donors. The information can be disseminated by health-care professionals or social workers from the transplant hospital by inviting family and friends of the patient to a general information meeting, or by visiting and informing the social network of the patient.
- 3.5 In respect of living liver and lung donation and the higher risk for these donors compared with kidney donors, health professionals must be certain that the potential donor fully understands the implications of the donation.
- 3.6 There is often the assumption for living donation that the intended recipient will accept the procedure. The recipient should also have the option to refuse donation from one or more of the potential donors.

Example of practice: UK

The UK aims to maximise the number of potential transplants that proceed, and more than one in three of all kidney transplants that take place come from a living donor. Clinicians in the UK are encouraged to discuss living donation options with patients at an early stage of treatment.

Significant work has taken place during the last 5-10 years to optimise the benefits of the UK living donor kidney sharing schemes. The national sharing schemes mean that incompatible donor-recipient pairs can exchange kidneys so that recipients can receive alternative compatible living donor organs. Exchanges are identified between two or three incompatible pairs.

The UK also has a comprehensive non-directed altruistic donor scheme, which is an increasing trend. In January 2012, the UK introduced non-directed altruistic donor chains where a non-directed altruistic donor donates their organ into the paired / pooled scheme. By matching two or more donors and recipients, a chain of operations can be carried out. The remaining organ at the end of the chain is then donated to the best matched recipient on the national waiting list, ensuring that the number of transplants is maximised as a result of one non-directed altruistic donor.

Careful coordination is required between transplant centres to ensure that logistical difficulties can be overcome in these complex cases e.g. transportation of kidneys over long distances, theatre booking etc.

Transplants between non-genetically related donors and recipients are very common in the UK, with excellent outcomes.

Further information can be found in the British Transplantation Society's UK Guidelines for Living Donor Transplantation:

<http://www.bts.org.uk/Documents/Guidelines/Active/UK%20Guidelines%20for%20Living%20Donor%20Kidney%20July%202011.pdf>

Roles and responsibilities in donor selection and follow-up

- 3.7 The potential living kidney donor must be given written information provided by the transplant centre and verbal information given by qualified members of the transplant team, such as a physician or transplant surgeon. The transplant physician should not be the nephrologist taking care of the recipient. A list of subjects about which the potential donor should be informed can be taken from *The Consensus Statement of the Amsterdam Forum*.¹
- 3.8 It is the responsibility of the physician giving information to ensure that the donor is capable of understanding the information, and has done so. Member States may wish to consider the involvement of an independent assessor or donor advocate at this stage. The information must be given in private consultations with the possibility of "a cooling off period" and an assessment of donor retention of information is required. Written documentation of the evaluation should be provided. Any doubt concerning the mental capacity of the potential donor requires either formal psychological evaluation or refusal of donation.
- 3.9 The procedures for giving information must ensure that the potential donor can make a voluntary decision free from adverse pressure to donate and that the donation is not motivated by monetary or other reward. The donor must be informed that the decision can be withdrawn at any time in the process and also that medical and individual reasons for not proceeding with donation will be kept confidential
- 3.10 The medical and psychosocial donor evaluation should not start before the potential donor has reached an initial decision that they wish to be a donor. The medical evaluation (including a psychosocial assessment by a mental health professional where necessary) is essential and donation cannot proceed until a full medical assessment has taken place and the donor has given written consent to surgery.

Medical assessment

- 3.11 It is important to manage the expectations of the donor. For example, a donor may not be able to donate on the grounds of having a single kidney or complex renal vessels or the assessment may reveal previously undiagnosed disease. Potential donors must be warned of this possibility. In addition, the existence of a previously unrecognised condition may prejudice future attempts to obtain life insurance or specialist employment. Conversely, screening may benefit the potential donor in that early detection of a health problem can occur, which might otherwise have gone undiagnosed.
- 3.12 Importantly, all female potential donors of childbearing age must be counselled about the need to take contraceptive precautions when considering organ donation, and the possible implications of kidney donation upon future pregnancy. Where several potential living donors are available, it may be preferable to consider an alternative donor before assessing a woman who may still wish to bear children or who has young dependents; although neither are an absolute contraindication to donation.
- 3.13 A thorough clinical examination must be performed, taking particular account of the cardiovascular and respiratory systems. In most units, donor assessment will be arranged by a specialist transplant nurse, supported by a clinician. The clinician should undertake the medical examination of the potential donor and should not be exposed to a potential conflict of interest by also having direct care of the transplant recipient.
- 3.14 The EULID project has made the following recommendations: Before the surgical procedure, a donor evaluation process is needed to ensure that the potential donor is physically and mentally fit for the procedure, that no contraindications to surgery exist and to rule out any coercion, unethical or financial practices between donor and recipient. All potential donors must be appropriately motivated, properly informed and aware of the inherent risk of a living donor transplantation procedure. With kidney donation specifically, the focus of the donor evaluation process is to detect general and kidney specific factors that can constitute a risk to the donor. Some donors are more clinically complex and this needs to be taken into account and their assessment tailored appropriately.
- 3.15 Two recent pieces of research have generated discussion about the relative safety of living kidney donation. Muzaale et al reported the long-term follow up of 96,217 living kidney donors in the US between 1994 and 2011, and compared outcomes to a control

group of 20,024 participants. Median follow up was 7.6 years for kidney donors and 15 years for matched healthy non-donors. Ninety nine living kidney donors developed end-stage renal disease at a mean 8.6 years after donation, compared to 36 non-donors. The estimated risk of developing end-stage renal disease was 30.8 *per* 10,000 living donors at 15 years after donation, and 3.9 *per* 10,000 non-donors in the control group ($p < 0.001$). The estimated risk was higher in black donors (74.7 *vs* 22.7, $p < 0.001$). The estimated lifetime risk was 90 *per* 10,000 donors *vs* 326 *per* 10,000 general population *vs* 14 *per* 10,000 healthy non-donors.

- 3.16 Mjøen et al reported long-term renal function and cardiovascular and all-cause mortality in 1,901 living kidney donors in Norway between 1963 and 2007, and compared the outcomes to 32,621 non-donors who would have been considered for donation over this period. Median follow up was 15.1 and 24.9 years respectively. The hazard ratio for all cause death was 1.3 for donors compared to controls, with a hazard ratio 1.4 for cardiovascular death and 11.38 for end-stage renal disease. The median time to end-stage renal disease among donors was 18.7 years. The crude incidence of end-stage renal disease in kidney donors was 302 *per* million person-years, compared to 100 in the general population. Importantly, among donors, 80% were first degree relatives of the kidney recipient, and only 15% were genetically unrelated. Of the 9 donors who developed end-stage renal disease, 7 developed end-stage renal disease secondary to immunological causes, and 2 due to diabetes/nephrosclerosis.
- 3.17 Other analyses with large numbers and long-term follow up have shown no increased risk of end-stage renal disease or death compared to the general population. It appears therefore that for individuals at low baseline risk, donating a kidney increases their risk of later developing end-stage renal disease.
- 3.18 An addendum to the *UK Guidelines for Living Donor Kidney Transplantation* suggests the following
- Donor selection – to be aware that certain groups appear to be at an increased risk of long-term complications following kidney donation and these data have implications for donor selection.
 - Donor Consent – all potential donors must be informed of the small long-term risks of living donation but these should be placed into the context of the much higher baseline risk of end-stage renal disease in the unselected general population.

- Donor follow-up – the data highlight the need for effective follow-up, particularly when potential donors are non-resident and follow-up in their own countries may be difficult.

This is supported by the position paper of the European Committee on Organ Transplantation (CD-P-TO) *Long-term outcome of living kidney donation*⁴ who recommend the need for life-long follow-up of donors so that risk factors for end-stage renal disease that accumulate over a lifetime can be properly assessed. Health professionals and authorities should make all efforts to increase the available evidence on the risks of donating a kidney during one's lifetime to provide potential donors with the necessary data for properly informed consent.

Potential conflicts and Donor Advocacy

- 3.19 The main concern is the potential conflict of interest between the care of the potential donor and the interests of the recipient; thus the physician taking care of the recipient should not evaluate the donor. The potential donor should have an independent medical qualified advocate, for example, the donor's general practitioner or an independent assessor appointed by the hospital or regulator. The donor should also discuss donation with friends, religious leaders or any other independent person in whom the donor has confidence. The need for a legal advocate is dependent on national law and regulations and may be especially important in the case of non-directed altruistic donation.
- 3.20 The question of donation can be a frequent subject of conflict within the families of the recipient and donor. Repeated consultations during the information process and knowledge of the family and social situation are the best way of reducing the risk of such problems. Psychosocial evaluation during the medical donor evaluation is of importance in this respect.

Example of practice: UK

In the UK, any potential donation of a (or part of a) solid organ for transplantation must be assessed by an independent person, called an Independent Assessor, who is trained and accredited by the national Regulator.

Independent Assessors act as a representative of both the donor and the Regulator in order to help the Regulator ensure the requirements of the national legislation have been met. They do

⁴ Cozzi E, Biancone L, López-Fraga M, Nanni-Costa A. Long-term outcome of living kidney donation. Position paper of the CD-P-TO Council of Europe. *Transplantation* 2016; 100(2):270-271.

this by interviewing the potential donor and the recipient to ensure there is no evidence of duress, coercion or reward and the donor fully understands the risks involved in the surgery.

The Independent Assessor submits a report and the Regulator makes the decision whether or not to approve the proposed donation based on the information contained in the Independent Assessor's report. Clinicians responsible for the care of the donor or recipient are not therefore involved in whether a proposed donation can legally go ahead.

Post-donation follow-up

- 3.21 Following discharge from the transplant surgery department, a depressive or apathetic reaction is not uncommon and active contact with all donors is recommended, either by living donor coordinators or, if appropriate, by health staff at the local medical unit responsible for the pre-donation evaluation. A medical consultation should be offered, including if necessary, a psychosocial evaluation. It is vital that the donor has easy and free of charge access to support and that the donor at discharge from the hospital has received written information including whom and where to contact if needed.
- 3.22 Arrangements for follow-up may vary between Member States, but transplant centres accepting a living organ donor have the responsibility for co-ordinating medical follow-up after surgery. If adequate follow-up, free of charge, cannot be provided the donor should not be accepted. The follow-up must include both a medical and psychosocial assessment. Any out-of-pocket expenses and loss of earnings related to the donation should also be reimbursed. The follow-up programme must be performed according to an agreed plan and the transplant centre has the responsibility to ensure that adequate short- and long-term follow-up is carried out where possible. Data from donor follow-up should be collected by the transplant centre and reported to the national and if appropriate supra-national donor register. It is important that the medical, psychosocial and if necessary economic follow-up is coordinated; that responsibility is clearly defined and the donor fully understands the arrangements.

Example of practice: EULID project findings

INFORMATION

Making the decision to become a living donor should be conscious, based on complete written and independent information supported by an impartial competent authority (donor representative) that is able to answer all the questions.

Comments:

1. A living donor candidate has the right to complete, written and independent information about all aspects connected with living donation process. A standard of such information should be prepared.

2. Besides written information, the living donor candidate and his family have the right to talk with impartial authority (donor representative) – medical doctor or nurse – who is well educated and prepared for the interview and can answer all the questions. Donor representative is independent on transplant team and recipient. Living donor candidate and donor representative meetings should take place as many times as required.

3. Living donor candidate is invited to the transplant centre for the final qualification and all the doubts connected with donation are explained. Transplant team should provide reliable information about recipient's condition and alternative methods of treatment in case of candidate resignation.

EVALUATION OF RISK FOR DONOR

Every transplant team is obliged to evaluate and minimize the donor medical, social and psychological risk before making the decision about organ procurement.

Comments:

1. Medical risk for donor is well known and many studies focused on that.
2. Psychological problems such as feeling of rejection are matter of discussion as a consequences of being living donor.
3. Discrimination, problems with unemployment and economic loss are as much important and have great influence on donors quality of life.

CONSENT OF THE DONOR

Every living donor candidate has to make a conscious, independent decision before giving consent for the surgery procedure. Living donor candidate has to be informed about the possibility to resign in every moment he would feel so, without consequences.

Comments:

1. Conscious decision is necessary to obtain living donor candidate consent. He cannot decide under compulsion and he has to be of sound mind.

The EULID leaflet is available online under

<http://www.eulivingdonor.eu/eulid/diffusion-dissemination/view.php?ID=19>

4. DONOR REGISTRY

Context

- 4.1 Follow-up data is required to enable living donation to be carried out in a positive and safe way. Some EU countries already have a national living donor registry, but not all, and the follow-up data captured differs between Member States. Article 15 of Directive/2010/53/EU requires Member States to establish a National Living Donor Registry and transplant centres will need to submit data to the Registry on all donors both pre-and post-donation in order to optimise the value of the Registry Data in informing living donor practice. National follow-up guidelines for centres will need to encourage post donation follow-up for example by timing annual check-ups in line with the month of donation; offering flexible clinic times and local follow-up arrangements.
- 4.2 Registry data assists in defining good practice in donor evaluation, benchmarking and improving quality overall. Living donor registries are needed for transparency of practices and to provide evidence on the consequences of living organ donation. Moreover, it is important to register the number of living donations performed, the medical eligibility, the screening and aftercare of the donor.
- 4.3 Sharing data supra-nationally will help countries without a living donor programme. It will provide information on standards in place and expected outcomes for living donors. It will also increase the understanding of the risks of living donation, eventually making living donor programmes safer. An international living donor registry could be used for the follow-up of living donors across the EU. The supra-national donor registry would focus on the safety of the donor by collecting both pre-donation and long-term follow-up data. A common data set of living donor variables should be agreed upon between all EU member states, in order to support the establishment of living donor programmes in all member states, to maintain confidence in living donation, demonstrate quality and safety in living donor programmes across the EU and discourage organ trafficking.
- 4.4 As it is a requirement of the Directive, it is important that all Member States establish a living donor registry to make the data collection based on a minimal data set-worthwhile. The data set to be held by Registry has been determined within the ACCORD Joint Action and includes general data such as gender, age, nationality, and

relationship to the recipient, as well as a range of both essential and desirable clinical data.⁵

4.5 The overall aims are:

- **Achievements:** better possibility of evaluating the outcomes for living kidney (and living liver) donors due to a large data set.
- **Improvement:** improved insight into the long-term effect of donation on the living donor.
- **Impact:** disseminating improved knowledge on living donation within Europe leading to safer living donation programmes across the EU.

Duration and frequency of follow-up

4.6 Duration and follow-up requirements have also been determined within the ACCORD project, using the following principles:

- Life-long follow-up of the living donor is recommended.
- The follow up starts within 1-3 months of the procedure to ensure that the donor is recovering after the operation and is appropriately supported. This includes measurement of kidney function, early detection of complications such as wound infections, and the overall recovery of the donor.
- Subsequently, mid and long-term follow-up is recommended on a regular periodical basis, providing a review of general health status of the donor, any complications, kidney function, medication and/or treatment, urinalysis, blood pressure, blood status, and BMI.

Example of practice: Netherlands

The Netherlands is one of the (few) European countries with an existing follow-up database for living (kidney) donors. This national registry was founded 10 years ago and contains data about donor demographics, the pre-donation period and follow-up data (including the peri- and direct postoperative period). Currently over 3,400 living kidney donors have been included in the Dutch donor registry with a variable length of follow-up (mean number of filled in follow-up forms per donor is 4, and the number of filled in follow-up forms is 13,265).

Also the donors that have donated their kidney before the Dutch donor registry was founded, have been included in the registry (the donor with the longest period after donation donated in 1967), and

⁵ ACCORD WP 4 Living Donor Registries FINAL REPORT. Available at: <http://www.accord-ja.eu/living-donor-registries>. Last access: March 2016.

particularly these donors are important for the evaluation of risks for the donor on the long run. One of the problems encountered in the Dutch donor registry is compliance to the follow-up frequency. It is difficult to motivate healthy donors for a regular (once every three or five years) medical check. A new living donor registry should tackle this problem from the start.

5. PSYCHOSOCIAL ASPECTS

Context

- 5.1 Although follow-up of the recipient and the living donor is routinely performed, attention is usually focused on medical aspects. A more detailed investigation of the living donor outcome is also needed as they may additionally manifest psychosocial complications as a result of donation.
- 5.2 Background literature indicates that the psychosocial impact on living donors is limited. However, in some studies considering only kidney donors, negative outcomes have been reported. Mild depression and family problems have been the most extensively documented negative psychosocial issues. Most of these cases were related to graft failure or the recipients' death after transplantation.
- 5.3 Living donor psychosocial aspects is one of the interests of the European Commission, supporting projects via the European Agency for Health and Consumers (EAHC). Under this framework, EAHC supported during the years 2009-2012, the project European Living Donor Psychosocial Follow-up (ELIPSY). This was promoted and coordinated by the Hospital Clinic of Barcelona (Spain) with the collaboration of five European centres.

Current situation regarding psychosocial practices in Europe

- 5.4 Psychosocial assessment/follow-up practices are described in the literature in different centres, but a standardized methodology is still missing. Most of these studies are single-centre based and include small samples, while others describe practices limited only to their own countries. With this background, the project ELIPSY in its first phase carried out a study about the current situation of the psychosocial practices in several European centres. An ad hoc survey was used for such assessment.¹
- 5.5 The study included 10 European countries and 65 centres with living donor programmes. The survey was firstly applied in ELIPSY partners' centres and furthermore was widely applied in other centres with living donor programmes situated in partners' countries and "European Living Donation and Public Health" project

¹ Manyalich M, Menjívar A, Yucetin L, Peri JM, Torres X, Dias L, et al, Living Donor Psychosocial Assessment/Follow-Up Practices In Partner Countries Of The ELIPSY Project. *Transplant Proc* 2012; 44: 2246–2249.

(EULID) partner countries such as Poland, Romania and the UK. Both kidney and liver transplant programmes entered in the study and for each of them a specific version of the survey was designed. As it was shown, psychosocial assessment/follow-up practices were identified in 42% centres for kidney living donors and 38% centres for liver living donors. The tools applied for such psychosocial follow-up in most centres were not specified, while those centres that explained the tools gave the application of the same protocol for kidney and liver programmes. An absence of consensus in the living donor psychosocial assessment and follow-up practices in terms of methodology, professional responsibility, psychological tests or the best time to carry out an evaluation was demonstrated.

Living donor psychosocial assessment/follow-up: definition of criteria and common terms, and suggested data to be screening

5.6 *'While medical criteria have been well established, psychosocial listing criteria are less standardized.'*

The psychosocial evaluation would help to identify the patient's level of social, neuropsychiatric and cognitive functioning, assist in the development of a psychosocial treatment plan to address current social and psychiatric problems and help minimize preventable problems, mitigate risks and optimize the donor's level of functioning and quality of life post-donation.²

Furthermore, several literature reviews show that there is a relative absence of evidence-based guidelines for pre-transplant psychosocial and behavioural screening.

5.7 Currently, a standardized methodology for the psychosocial assessment/follow-up of the living donors in Europe is not available. In addition, the methodologies showed by the review of different studies are very heterogeneous, and the background literature indicates that there is limited information regarding psychosocial impact on living donors.³⁴

² Maldonado JR, Dubois HC, David EE, Sher Y, Lolak S, Dyal J, Witten D. The Stanford Integrated Psychosocial Assessment for Transplantation (SIPAT): A new tool for the Psychosocial Evaluation of Pre-Transplant Candidates. *Psychosomatics* 2012;53:123-132.

³ van Hardeveld E, Tong A. Psychosocial care of living kidney donors. *Nephrology* 2010; 15: S80-S87.

⁴ Clemens KK, Thiessen-Philbrook H, Parikh CR, Yang RC, Karley ML, Boudville N, et al. Psychosocial Health of Living Kidney Donors: A Systematic Review. *Am J Transplant* 2006; 6: 2965-2977.

- 5.8 Having a common protocol for the assessment/follow-up of living donors in the psychosocial context for all European centres with living donor transplantation activity would help to improve the quality of living donation procedures, and would provide a deeper knowledge of donors' outcomes, thus contributing to assure their health and safety.
- 5.9 The ELIPSY project selected, by a literature review and expert consensus, several psychometric tools for the assessment of those variables relevant for the psychosocial follow-up and the assessment of potential risks and protective factors:
- Quality of life
 - Mental health / Psychological well-being
 - Satisfaction with the donation process
 - Expectations and motivation for donation
 - Information received about the donation process
 - Socioeconomic status
 - Social support
 - Employment status

Recommendations for centres with living donor programmes

- 5.10 It is recommended that each centre includes a psychosocial assessment before and after donation into their protocol/guideline. This methodology might be different depending on the characteristics and resources of each centre. A multidisciplinary team might need to be involved in such activity. The centres need to provide access to psychological treatment for those donors showing adverse psychosocial outcomes.
- 5.11 The follow-up strategy will consider aspects such as evaluation timing, profile of the evaluators, donor contact pathway, minimum criteria and excellence criteria. As well this strategy will aim to evaluate the impact of the recipients' outcome on the donor.

Best practice: ELIPSY project findings

The ELIPSY Project designed and applied two types of follow-up studies in six different transplant centres situated in six different countries (France, Germany, Portugal, Spain, Sweden and Turkey):

- Short follow-up: prospective design with the aim of assessing the one-year post-donation mental health, psychological wellbeing and satisfaction of kidney living donors, and the relationship of these outcomes with their psychological profile before donation.
- Long follow-up: retrospective design to identify the long-term impact of living donation in terms of mental health, psychological wellbeing and quality of life.

The post-donation medical outcome of recipients and its relationship with the psychosocial outcome of donors was assessed in both follow-ups.

The main findings were:

- Living donors' outcome, as a group, is favourable both at short and long-term follow-up. Both studies showed non-significant differences between the psychosocial status of the kidney living donors after donation and the relative psychosocial scores of the general population.
- A small number of donors showed a worse than expected psychosocial outcome which may be, however, considered as clinically non-significant.
- In the short-term, these mild adverse outcomes were mainly related to the physical aspects of quality of life. At longer follow-up, main adverse outcomes were related to mental health.
- Donor characteristics, but not variables related to the medical status of the recipient, differentiated those donors who showed a favourable from those who showed an unfavourable outcome.

6. FINANCIAL/ECONOMIC ASPECTS OF LIVING DONATION PROGRAMMES

Introduction

- 6.1 Living donor kidney transplantation represents a unique opportunity to expand the practice of transplantation and reduce the costs for society associated with end-stage kidney disease. Economic aspects, however, are a matter of paramount importance that need to be thoroughly analysed and suitably addressed if successful living donor programmes are to be implemented and maintained in Europe.
- 6.2 In this context, the many economic variables that need to be taken into account will encompass both donor and recipient-related costs. Indeed, economics will have to be dealt with carefully, to both support the living donation process on the one hand without offering an involuntary incentive to commercial and ethically unacceptable practices on the other.
- 6.3 This chapter will review the financial burden associated with end-stage kidney disease and the possible role living donor kidney transplantation may play to alleviate the social costs related to the care of this significant group of patients. Both obvious and non-obvious costs will be considered. Thus living donation will be discussed in the wider context of existing treatment alternatives, especially with regards to haemodialysis, with the objective of illustrating its tangible financial and social benefits, and set the scene for future steps to enable the broader application of living donor kidney transplantation across Europe.
- 6.4 The aim is that the financial impact on the living donor is cost neutral. *Directive 2010/53/EU* enables donors to receive reimbursement of expenses related to the donation, such as travel costs, additional costs (support in house etc.) and coverage (or support to meet) of loss of income, which is a direct result from the donation procedure.
- 6.5 Financial support for any complications related to donation must also be included, whatever the insurance system (national health care insurance, private recipient insurance). Private insurance organisations should be aware of the principle of non-discrimination that should be applied to the living donor in the case of mortgage applications.

6.6 Recommendation No S1 of 15 March 2012 of the Administrative Commission for the Coordination of Social Security Systems concerning financial aspects of cross-border living organ donations¹ recommends the following:

‘1. The competent authorities of an organ recipient, when they prepare or authorise the living organ donation with an organ coming from a living donor insured in another Member State, should consider the access of the living donor to the health care system for problems related to the procedure of donation.

2. The competent authorities of an organ recipient shall find a humanitarian solution and reimburse the benefits in kind necessitated by cross-border living donation for the donor, if the legislation covering the donor does not provide entitlement to sickness benefits in kind for the donor.

3. The competent authority of the donor shall provide sickness cash benefits in accordance with the legislation it applies, regardless of which Member State the organ donation took place in or of who was the organ recipient. Possible loss of income by the donor linked to the donation should be treated like any other incapacity for work by the donor's applicable legislation as there is no reason to treat the incapacity for work related to the organ donation differently from other incapacities based on medical grounds’.

Example of practice: UK

The aim in the UK is to ensure as far as possible that the financial impact on the living kidney donor is cost neutral. Reimbursement of expenses must be proportionate and fair for the individual and administered in a consistent and timely manner. Best practice must be in line with the national legislation.

In the UK, it is possible for claims to be made for reimbursement for overseas donors for expenses such as flight costs, loss of earnings and reasonable accommodation costs incurred during their stay in the UK as this helps facilitate donations.

Further information can be found in NHS England Policy for reimbursement of expenses for living kidney donors.

http://www.odt.nhs.uk/pdf/reimbursement_policy_living_kidney_donors.pdf

¹ Recommendation No S1 of 15 March 2012 concerning financial aspects of cross-border living organ donations. Available at: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2012:240:0003:0004:EN:PDF>. Last access: March 2016.

The burden of End Stage Kidney Disease and the role of transplantation

- 6.7 As discussed elsewhere in this document, end-stage renal disease is a frequent and increasing health problem that affects over 2 million of the world-wide population² as a consequence of the increased size and age of the population and the risks associated with an increased prevalence of diabetes.³ As a consequence, end-stage renal disease represents one of the most expensive disease categories and a great economic burden that needs to be addressed aggressively and efficiently by health care systems.⁴
- 6.8 Indeed, money spent for end-stage renal disease has increased by 3-12% annually in the last few years⁵ and it is estimated that 6.4% of the current health Medicare budget in the US is allocated to end-stage renal disease patients who represent, however, only 1% of the beneficiaries of healthcare.⁶

At this stage, three possible treatment alternatives can be offered to patients with end-stage renal disease. These are represented by haemo- and peritoneal dialysis and transplantation. However, due to increased survival, improved quality of life and reduced costs, transplantation using a living or deceased donor is by far the preferred and preferable treatment option for patients with kidney failure, for healthcare providers but also for society at large.⁷

² Eggers PW. Has the incidence of end-stage renal disease in the USA and other countries stabilized? *Curr Opin Nephrol Hypertens* 2011; 20(3):241-245; Bommer J. Prevalence and socio-economic aspects of chronic kidney disease. *Nephrol Dial Transplant* 2002; 17 (Suppl 11):8-12.

³ Lee H, Manns B, Taub K, Ghali WA, Dean S, Johnson D, Donaldson C. Cost analysis of ongoing care of patients with end-stage renal disease: the impact of dialysis modality and dialysis access. *Am J Kidney Dis* 2002; 40(3):611-622.

⁴ U.S. Renal Data Systems. USRDS 2008 annual data report: atlas of chronic kidney disease and end-stage renal disease in the United States. Bethesda: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2008.

⁵ Klarenbach S, Barnieh L, Gill J. Is living kidney donation the answer to the economic problem of end-stage renal disease? *Semin Nephrol* 2009; 29(5):533-538.

⁶ Klarenbach S, Barnieh L, Gill J. Is living kidney donation the answer to the economic problem of end-stage renal disease? *Semin Nephrol* 2009; 29(5):533-538; Smith CR, Woodward RS, Cohen DS, Singer GG, Brennan DC, Lowell JA, et al. Cadaveric versus living donor kidney transplantation: a Medicare payment analysis. *Transplantation* 2000; 69(2):311-314.

⁷ Klarenbach S, Barnieh L, Gill J. Is living kidney donation the answer to the economic problem of end-stage renal disease? *Semin Nephrol* 2009; 29(5):533-8; Smith CR, Woodward RS, Cohen DS, Singer GG, Brennan DC, Lowell JA, et al. Cadaveric versus living donor kidney transplantation: a Medicare payment analysis. *Transplantation* 2000; 69(2):311-314; McFarlane PA. Should patients remain on intensive hemodialysis rather than choosing to receive a kidney transplant? *Semin Dial* 2010; 23(5):516-519.

- 6.9 The vast majority of expenditure related to living donor transplantation relates to pre-transplant assessments, and to medical and surgical procedures associated with transplantation that, in most cases, are fairly predictable.⁸ Accordingly, these costs will almost automatically be covered or reimbursed by state health programmes or insurance schemes. The living donation is almost inevitably associated with out-of-pocket expenses incurred by the donor and these are additional to the clinical costs.⁹ Unless met, the donor may suffer financial loss and this may possibly act as a disincentive to living donation.
- 6.10 Extensive research has been conducted by various groups to capture the various costs related to living donor kidney transplantation. This has resulted in the identification of a fairly standard list of expenditures.¹⁰ However, considerable differences or even contradictions with regard to cost of living donor kidney transplantation are evident between the various studies and several reasons may account for these discrepancies. First, existing studies have taken place in different countries where considerable differences in purchasing power and professional fees are known to exist. Second, these studies are not all contemporary but have been conducted over a period of two decades. Third, in the majority of cases only direct health-care related costs are considered and the list of these is often not exhaustive. In many of these reports the costs of donor (and/or recipient) work-up have not been included. Fourth, the clinical settings and treatments offered often differ considerably between programmes. Finally, in most cases non-medical costs sustained by donors and recipients (such as travel costs or time off work) are often overlooked and are not taken into account in the global cost-analysis of living donor transplantation.

⁸ Laupacis A, Keown P, Pus N, Krueger H, Ferguson B, Wong C, Muirhead N. A study of the quality of life and cost-utility of renal transplantation. *Kidney Int* 1996; 50(1):235-242; Barnieh L, Manns BJ, Klarenbach S, McLaughlin K, Yilmaz S, Hemmelgarn BR. A description of the costs of living and standard criteria deceased donor kidney transplantation. *Am J Transplant* 2011; 11(3):478-488.

⁹ Levy AR, Sobolev B, James D, Barrable W, Clarke-Richardson P, Sullivan SD, et al. The costs of change: direct medical costs of solid organ transplantation in British Columbia, Canada, 1995-2003. *Value Health* 2009; 12(2):282-292.

¹⁰ Smith CR, Woodward RS, Cohen DS, Singer GG, Brennan DC, Lowell JA, et al. Cadaveric versus living donor kidney transplantation: a Medicare payment analysis. *Transplantation* 2000; 69(2): 311-314; Barnieh L, Manns BJ, Klarenbach S, McLaughlin K, Yilmaz S, Hemmelgarn BR. A description of the costs of living and standard criteria deceased donor kidney transplantation. *Am J Transplant* 2011; 11(3):478-88; Levy AR, Sobolev B, James D, Barrable W, Clarke-Richardson P, Sullivan SD, et al. The costs of change: direct medical costs of solid organ transplantation in British Columbia, Canada, 1995-2003. *Value Health* 2009; 12(2):282-292.

The direct costs of living donor kidney transplantation

- 6.11 Broadly, the direct costs related to living donor kidney transplantation can be grossly divided into three major categories, according to their timing of occurrence (**Tables 2-4**).

Table 2: Direct costs incurred <u>before</u> donation/transplantation: these will include		
	Donor	Recipient
Laboratory tests	Y	Y
Diagnostic imaging	Y	Y
Outpatient services	Y	Y
Physician fees	Y	Y
Dialysis costs	NO	Y
Medications	Y	Y

Table 3: Direct costs incurred <u>at the time</u> of donation/transplantation		
	Donor	Recipient
Laboratory tests	Y	Y
Diagnostic imaging	Y	Y
Donor/Transplant surgery	Y	Y
Inpatient stay	Y	Y
Physician fees	Y	Y
Dialysis costs	NO	Y
Medications	Y	Y

Table 4: Direct costs incurred <u>after</u> donation/transplantation		
	Donor	Recipient
Laboratory tests	Y	Y
Diagnostic imaging	Y	Y
Outpatient services	Y	Y

Physician fees	Y	Y
Medications	Y	Y

6.12 There are a limited number of comprehensive and well-written reports that assess the economic impact of direct costs related to living donor kidney transplantation. The recent report by Barnieh and colleagues provides a thorough comparison of costs between living and deceased donor kidney transplantation.¹¹

6.13 Furthermore, the study demonstrates that in a high profile westernized medical reality such as that of Canada, the cost of living donor kidney transplantation is cheaper than dialysis. It shows that in the first year (that includes the transplant-related costs), living donor kidney transplantation is more expensive than transplantation with a deceased donor kidney. It also illustrates that in the second year the cost of transplantation is less than a quarter of that of dialysis, with no difference between living or deceased donors. Interestingly, other studies have likewise reported that transplantation with living donors is cheaper than with deceased donors.¹² Medication appears as the single most expensive resource utilised both in the first and in the subsequent post-transplant years but, more importantly, the studies show that living donor kidney transplantation is a very cost-effective procedure that must be supported by health-care systems to use limited financial resources available most effectively.

The direct and indirect economic costs sustained by living donors

6.14 Living donation is not without financial burdens for living donors. These expenditures can be divided into direct or indirect costs.¹³

Direct costs are those incurred because of actual financial outlay by the donor. These include:

¹¹ Barnieh L, Manns BJ, Klarenbach S, McLaughlin K, Yilmaz S, Hemmelgarn BR. A description of the costs of living and standard criteria deceased donor kidney transplantation. *Am J Transplant* 2011; 11(3):478-488.

¹² Smith CR, Woodward RS, Cohen DS, Singer GG, Brennan DC, Lowell JA, et al. Cadaveric versus living donor kidney transplantation: a Medicare payment analysis. *Transplantation* 2000; 69(2):311-314; 12; Mullins CD, Thomas SK, Pradel FG, Bartlett ST. The economic impact of laparoscopic living-donor nephrectomy on kidney transplantation. *Transplantation* 2003; 75(9):1505-1512.

¹³ Clarke KS, Klarenbach S, Vlaicu S, Yang RC, Garg AX. Donor Nephrectomy Outcomes Research (DONOR) Network. The direct and indirect economic costs incurred by living kidney donors—a systematic review. *Nephrol Dial Transplant* 2006; 21(7):1952-1960.

- Travel (including flight, rail, bus and taxi fares; passport, visa, travel insurance; mileage and parking fees for private or rented cars)
- Accommodation and meal costs
- Long-distance phone calls
- Medical incidents not covered by insurance

Indirect costs are those incurred because of lost productivity, for example:

- Lost income
- Dependent care (including caregiver costs, children and elder care)
- Housework
- Other costs (including costs for personal care, shopping and other services hired for help)

6.15 Different initiatives have been put in place in various countries to protect the donor from financial loss. These include paid leave or reimbursement of lost income, social assistance and insurance and reimbursement of donation related expenses. However, existing data demonstrate that current policies are insufficiently effective to protect living donors and that current living donation is rather frequently associated with the donor suffering some direct or indirect financial loss that may lead to unemployment in some cases.

6.17 It is therefore critical that at the time of consenting, candidate living donors are adequately informed on the medical issues involved in the living donation process but are also suitably made aware of the potential financial implications associated with their generous act.¹⁴

Best practice example: The Netherlands

In the Netherlands donor expenses – additional to all medical donor screening and recovery procedure costs, which are covered by the health insurance company of the recipient – are reimbursed by the Ministry of Health and executed by the Dutch Transplant Foundation. The aim is to reimburse the (extra) expenses the living donor has due to the donation. This includes a fixed reimbursement to pay additional hospital costs and/or extra costs at home, travel expenses, the cost of additional medical care and loss in income. All in line with the national legislation.

¹⁴ Clarke KS, Klarenbach S, Vlaicu S, Yang RC, Garg AX. Donor Nephrectomy Outcomes Research (DONOR) Network. The direct and indirect economic costs incurred by living kidney donors—a systematic review. *Nephrol Dial Transplant* 2006; 21(7):1952-1960.

It is possible for claims to be made for reimbursement for foreign donors for expenses such as travel costs, loss of income and a fixed reimbursement for accommodation costs incurred during their stay in the Netherlands.

Further information can be found in the subsidy for reimbursement of living donors.

<http://wetten.overheid.nl/BWBR0025870>

The cost-effectiveness of living donor kidney transplantation

- 6.18 Whilst the economics of living donor kidney transplantation include a close analysis of (direct or indirect) costs involved in the transplantation process, it must be remembered that a comprehensive evaluation of any proposed medical procedure or strategy must also ascertain whether this is associated with tangible benefits to individuals and society at large.
- 6.19 In this context, cost-effectiveness studies have been conducted to compare the relative costs and outcomes (effects) of the actions taken. In the field of health services the most commonly used outcome measure is quality-adjusted life years (QALY).¹⁵ Indeed, QALY takes into account both quantity and quality of life and is widely utilised by healthcare planners in allocating healthcare resources.
- 6.20 With regards to transplantation, it has been calculated that kidney transplantation results in a net QALY gain of 2 to 3.5 years over dialysis.¹⁶ In this light, as financial analysts estimate that for medical procedures a QALY is worth between \$50,000 and \$100,000,¹⁷ in addition to the costs saved from haemodialysis (estimated to be between \$33,000 and \$80,000 per year in the US¹⁸ and €40,000 in the EU¹⁹) living organ transplantation could save to society up to \$300,000 per additional transplant performed.

¹⁵ Assessing cost-effectiveness NICE. Available at: <http://www.nice.org.uk/newsroom/features/measuringeffectivenessandcosteffectivenessstheqaly.jsp>. Last access: March 2016.

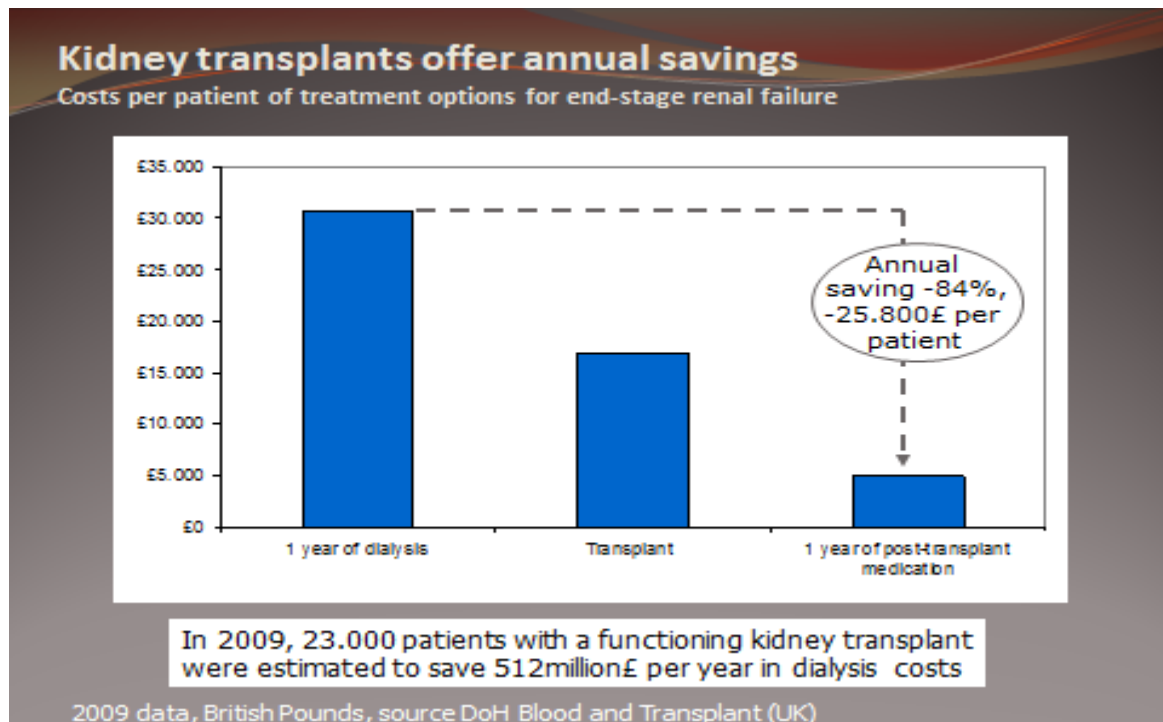
¹⁶ Matas AJ, Schnitzler M, Daar AS. Payment for living kidney donors (vendors) is not an abstract ethical discussion occurring in a vacuum. *Am J Transplant* 2004; 4(8):1380-1381.

¹⁷ Ubel PA, Hirth RA, Chernew ME, Fendrick AM. What is the price of life and why doesn't it increase at the rate of inflation? *Arch Intern Med* 2003; 163(14):1637-1641.

¹⁸ Lee H, Manns B, Taub K, Ghali WA, Dean S, Johnson D, Donaldson C. Cost analysis of ongoing care of patients with end-stage renal disease: the impact of dialysis modality and dialysis access. *Am J Kidney Dis* 2002; 40(3):611-22; Winkelmayer WC, Weinstein MC, Mittleman MA, Glynn RJ, Pliskin JS. Health economic evaluations: the special case of end-stage renal disease treatment. *Med Decis Making* 2002; 22(5):417-430.

¹⁹ Watson R. Stakeholders appeal for more kidney donations in Europe. *BMJ* 2012; 344:e1797.

6.21 An estimation in the UK found an annual saving of £25,800 per year following transplantation, compared to dialysis. For the year 2009, the transplanted patients were estimated to have saved more than half a billion pounds to the healthcare system.



Conclusion

6.22 In the face of the indisputable advantages of kidney transplantation, the number of patients on the kidney waiting lists continues to rise inexorably in the various EU nations, with increased costs to healthcare systems. Self-sufficiency in transplantation, by promoting both deceased and living donation, is a new concept that is being promoted worldwide²⁰ and, in an effort to bridge the gap between demand and organ availability, considerable efforts have been put in place by Competent Authorities from some but not all EU countries. This has ultimately resulted in different living donation rates in the EU.²¹ Therefore, based on existing transplantation figures and QALY estimates,²² it is estimated that if living donor kidney transplantation were to be

²⁰ The Madrid resolution on organ donation and transplantation: national responsibility in meeting the needs of patients, guided by the WHO principles. *Transplantation* 2011; 91 (Suppl 1):S29-31.

²¹ International figures on donation and transplantation 2014. Newsletter Transplant 2015; 20 (1).; 17:34-36; Spasovski G, Busic M, Pipero P, Sarajlić L, Popović AS, Dzhalova T, et al. Current status of transplantation and organ donation in the Balkans--could it be improved through the South-eastern Europe Health Network (SEEHN) initiative? *Nephrol Dial Transplant* 2012; 27(4):1319-1323.

²² Assessing cost-effectiveness NICE. Available at: <http://www.nice.org.uk/newsroom/features/measuringeffectivenessandcosteffectivenessandtheqaly.jsp>. Last

promoted and performed evenly throughout Europe reaching an average of 30% living donors in the programmes in each EU Members States (assuming 40 transplants p.m.p. per year), the global EU economic gain over a ten-year time-frame would exceed 4.5 billion €.

6.23 In summary, living donor kidney transplantation extends survival and increases the quality of life of many EU citizens, whilst saving at the same time a considerable portion of the restricted EU healthcare budgets. It is hoped that this toolkit will encourage discussions within Health Authorities in the various EU countries with the ultimate goal of establishing or optimising living kidney donation programmes, enabling a better healthcare resource allocation and, eventually, providing a better health care to all EU citizens.

access: March 2016.; Ubel PA, Hirth RA, Chernew ME, Fendrick AM. What is the price of life and why doesn't it increase at the rate of inflation? *Arch Intern Med.* 2003; 163(14):1637-1641.

7. WHAT IS AN EFFECTIVE LIVING DONOR KIDNEY TRANSPLANT PROGRAMME?

7.1 An effective living donor kidney transplant programme provides the following:

- A complementary programme to run alongside a deceased donor programme offering the potential to significantly increase transplant rates for adult and paediatric recipients.
- The opportunity to optimise pre-emptive living donor kidney transplantation and minimise waiting times on dialysis for suitable transplant recipients.
- A way to maximise the opportunities for donors and recipients to participate in kidney sharing schemes such as paired/pooled donation, non-directed altruistic donation and altruistic donor chains.
- Potential for significant savings in dialysis costs.

7.2 In all cases of living donation the welfare of the donor remains paramount, and vigilance in donor care and management is essential to ensure that appropriate safeguards are in place to protect individuals and to inspire public confidence.

7.3 The EULID project has concluded that the main protection systems for the living donor, regardless of organ type are:

- Careful donor evaluation and selection
- Use of independent donor advocacy
- Limiting living donor transplantation to high volume centres
- Database systems for registration of all donation-related morbidity and mortality
- Perioperative, short-term and long-term donor follow-up regimens in centres performing this kind of transplantations.

7.4 All living donor programmes must have the necessary regulatory infrastructure in place in line with European legislation and should consider other safeguards to demonstrate the integrity of the programme such as an independent assessment prior to transplant, to:

- be satisfied that no reward has been offered or given to bring about the donation;
- that consent has been given freely for the donation; and
- that the donor has not been coerced into giving consent

7.5 An effective well-regulated living donor programme offers significant clinical benefits to potential recipients by giving them the opportunity to benefit from an early planned transplant with better graft and patient survival rates. Member States will benefit from the significant savings in dialysis costs and possible wider economic benefits of a patient being able to return to work.

Appendix

1. Directive 2010/53/EU of the European parliament and of the Council of 7 July 2010 on standards of quality and safety of human organs intended for transplantation

Article 15 is dedicated to living donation:

Article 15 - Quality and safety aspects of living donation

1. Member States shall take all necessary measures to ensure the highest possible protection of living donors in order to fully guarantee the quality and safety of organs for transplantation.

2. Member States shall ensure that living donors are selected on the basis of their health and medical history, by suitably qualified or trained and competent professionals. Such assessments may provide for the exclusion of persons whose donation could present unacceptable health risks.

3. Member States shall ensure that a register or record of the living donors is kept, in accordance with Union and national provisions on the protection of the personal data and statistical confidentiality.

4. Member States shall endeavour to carry out the follow-up of living donors and shall have a system in place in accordance with national provisions, in order to identify, report and manage any event potentially relating to the quality and safety of the donated organ, and hence of the safety of the recipient, as well as any serious adverse reaction in the living donor that may result from the donation.

2. Council of Europe Convention on Human Rights and Biomedicine and the Additional Protocol to the Convention on Human Rights and Biomedicine, on Transplantation of Organs and Tissues of Human Origin

Articles 9 to 14 are dedicated to the organ removal from living persons:

Article 9 – General rule

Removal of organs or tissue from a living person may be carried out solely for the therapeutic benefit of the recipient and where there is no suitable organ or tissue available from a deceased person and no other alternative therapeutic method of comparable effectiveness.

Article 10 – Potential organ donors

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.

Article 11 – Evaluation of risks for the donor

Before organ or tissue removal, appropriate medical investigations and interventions shall be carried out to evaluate and reduce physical and psychological risks to the health of the donor.

The removal may not be carried out if there is a serious risk to the life or health of the donor.

Article 12 – Information for the donor

The donor and, where appropriate, the person or body providing authorisation according to Article 14, paragraph 2, of this Protocol, shall beforehand be given appropriate information as to the purpose and nature of the removal as well as on its consequences and risks.

They shall also be informed of the rights and the safeguards prescribed by law for the protection of the donor. In particular, they shall be informed of the right to have access to independent advice about such risks by a health professional having appropriate experience and who is not involved in the organ or tissue removal or subsequent transplantation procedures.

Article 13 – Consent of the living donor

Subject to Articles 14 and 15 of this Protocol, an organ or tissue may be removed from a living donor only after the person concerned has given free, informed and specific consent to it either in written form or before an official body.

The person concerned may freely withdraw consent at any time.

Article 14 – Protection of persons not able to consent to organ or tissue removal

No organ or tissue removal may be carried out on a person who does not have the capacity to consent under Article 13 of this Protocol.

Exceptionally, and under the protective conditions prescribed by law, the removal of regenerative tissue from a person who does not have the capacity to consent may be authorised provided the following conditions are met:

- there is no compatible donor available who has the capacity to consent;
- the recipient is a brother or sister of the donor;
- the donation has the potential to be life-saving for the recipient;
- the authorisation of his or her representative or an authority or a person or body provided for by law has been given specifically and in writing and with the approval of the competent body;
- the potential donor concerned does not object.

3. Recommendations and Resolutions of the Council of Europe

- Resolution CM/Res(2015)11 on establishing harmonised national living donor registries with a view to facilitating international data sharing Resolution CM/Res(2013)56 on the development and optimisation of live kidney donation programmes .Resolution CM/Res(2013)55 on establishing procedures for the collection and dissemination of data on transplantation activities outside a domestic transplantation system.
- Resolution CM/RES(2008)6 of the Committee of Ministers to member States on transplantation of kidneys from living donors who are not genetically related to the recipient.
- Recommendation Rec(2004)7 of the Committee of Ministers to member states on organ trafficking.

4. Conference and Recommendations (professional initiatives)

- A Report of the Amsterdam Forum on the Care of the Live Kidney Donor: Data and Medical Guidelines Kidney transplant physicians and surgeons met in Amsterdam, The Netherlands, from April 1–4, 2004 (Transplantation 2005; 79: S53–S66)
- The Consensus Statement of the Amsterdam Forum on the Care of the Live Kidney Donor, The Ethics Committee of the Transplantation Society (Transplantation 2005; 79: 491-492).
- The Declaration of Istanbul on Organ Trafficking and Transplant Tourism. The Transplantation Society and International Society of Nephrology in Istanbul, Turkey, April 30–May 2, 2008 (www.thelancet.com Vol 37:2 July 5, 2008).

5. Relevant European projects funded by the European Union

- **European Living Donation and Public Health – EULID** is a project co-funded by the European Union (2007-2009). Its main objective is to contribute to create a consensus on European common standards regarding legal, ethical, protection and registration practices related to living organ donation, in order to set standards and recommendations that guarantee the living donor health and safety.
- **European Living Donor psychosocial follow-up – ELIPSY** is a project co-funded by the European Union (2009-2012). Its main objective is to contribute to guarantee a high quality of living organ donation programs by creating a follow-up model for the

living donors 'psychological well-being and quality of life. The impact of the recipients' outcome on the donor and the donors 'perception of the donation process has been evaluated.

- **Living Donor Observatory – LIDOBS**, is a group of international experts on living donation with the worry and interest to join efforts to improve the quality of the procedure as well as to establish international consensus in order to protect living donors' health and safety through research activities. This expert's community was created during EULID project, expanded moreover during ELIPSY project and actively working nowadays.
- **EULOD**, Living Organ Donation in EUrope is a Framework Programme funded by the European Commission (FP7/2010-2012) in collaboration of the ELPAT Working Group on Living Organ Donation. ELPAT, a subsection of the European Society for Organ Transplantation (ESOT), is the European platform on Ethical, Legal and Psychosocial Aspects of organ Transplantation.
- **COORENOR** is an EU project (2009-2012) co-funded by the Public Health Programme of the European Commission and the project Associated Partner. 'This project aims to establish a Coordinated Network between national programs existing in the field of organ transplantation, taking into account some major issues such as cadaveric donation (WP5), living donation (WP6) and organ exchange (WP7).'
- The European Framework for Evaluation of Organ Transplants (**EFRETOS**) is a project (2009-2011) 'to develop a framework for realizing a pan-European Registry on post-transplant outcome data. The aim of the EFRETOS project was to describe the optimal content of a European Transplant Registry, based on the existing registries in Europe and current expertise including patients transplanted from deceased and living donors. '
- **ACCORD** is a joint action 'to strength full potential of MS in the field of organ donation and transplantation, to improve cooperation among MS and to contribute to the effective implementation of Directive 2010/53/EU and the Action Plan on Organ Donation and Transplantation (2009-2015): Strengthened Cooperation between MS'. The Joint Action is focused on three specific areas, namely, living donor registries, cooperation between intensive care professionals and donor transplant coordinators, and twinning projects. Precisely, the aim of the action on living kidney donors is to support Member States in the development of living donor registries and other

recognized legal and professional international standards, and to foster international data sharing on living organ donation across the EU.

6. WHO Guiding Principles on Human Cell Tissue and Organ Transplantation

The Guiding Principles provide an orderly, ethical framework for the procurement and transplantation of human organs, tissue and cells for therapeutic purposes. The 11 Recommendations cover consent, conflict of interest, the need for voluntary and unpaid or unrewarded donation; equitable allocation of donated organs; safe and high quality clinical care.