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How to increase kidney transplant activity throughout Europe—an advocacy review by the European Kidney Health Alliance

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ABSTRACT

Kidney transplantation offers better outcomes and quality of life at lower societal costs compared with other options of renal replacement therapy. In this review of the European Kidney Health Alliance, the current status of kidney transplantation throughout Europe and suggestions for improvement of transplantation rates are reported. Although the European Union (EU) has made considerable efforts in the previous decade to stimulate transplantation activity, the discrepancies among European countries suggest that there is still room for improvement. The EU efforts have partially been neutralized by external factors such as economic crises or legal issues, especially the illicit manipulation of waiting lists. Hence, growth in the application of transplantation throughout Europe virtually remained unchanged over the last few years. Continued efforts are warranted to further stimulate transplantation rates, along with the current registration and data analysis efforts supported by the EU in the Effect of Differing Kidney Disease Treatment Modalities and Organ Donation and Transplantation Practices on Health Expenditure and Patient Outcomes project. Future actions should concentrate on organization, harmonization and improvement of the legal consent framework, population education and financial stimuli.

Keywords: chronic renal failure, European policy, kidney transplantation, quality of life, renal replacement therapy

INTRODUCTION

Of the three options for renal replacement therapy (RRT)—haemodialysis, peritoneal dialysis and transplantation—kidney transplantation offers the best survival outcomes [1–3] and quality of life [1, 4]. This review was written by the European Kidney Health Alliance (EKHA), a non-governmental organization that proposes solutions for the challenges of chronic kidney disease (CKD) at the level of the European Union (EU) [5]. The review describes the current status of kidney transplantation in Europe and defines future potential actions for improvement. This text also includes a patient perspective based on personal experience, providing added value to the usually more theoretical medical thinking.

Each year the EKHA organizes a kidney forum in the European Parliament, intended to encourage a pan-European policy to improve quality of life and outcomes of patients with CKD and to make kidney care more harmonized and sustainable. This publication is the result of the discussions during this forum.

CURRENT STATUS OF CKD AND KIDNEY TRANSPLANTATION IN EUROPE

In high-income countries, including most EU member states, death due to CKD rises yearly, accounting for 2.5% of deaths in 2016 with an annual increase of ∼2%, making CKD one of the most rapidly increasing causes of death [6]. Since several frequent causes of death in CKD, including ischaemic and non-ischaemic cardiovascular diseases, are classified separately, the proportion of deaths due to CKD might even be underestimated.

Patients personally experience daily how harmful CKD is and the depth of its physical and emotional impact, with a heavy burden of fluid restriction and invaliding side effects like itching, poor mobility, exhaustion, fatigue, cognitive dysfunction and depression. The ability to work is lost or seriously affected. The number of drugs to be taken is impressive. Much time is spent undergoing treatment and, in the case of in-centre dialysis, on transport to and from the therapeutic unit. Patients on dialysis often feel awful, constantly thirsty and aching. The situation is almost as difficult for the family.

Although the chance to obtain a graft offers hope and kidney transplantation is the gold standard in RRT, a large fraction of dialysis patients is not listed for transplantation. Even in the

UK, a country with a high transplantation rate, of the 29 000 patients on dialysis, only 5000 are listed for transplant. One waitlisted person dies every day expecting a call that never comes. For most of the other European countries, the picture may be even more dismal, as in most of these countries proportionally more RRT patients are on dialysis than in the UK [7].

For all these reasons, it is obvious why patients request that the nephrology community and policymakers increase the opportunities for kidney transplantation as much as possible and insist that measures on the European and national level (see below) be enforced without further delay.

In addition, the health economic burden, which is already high in earlier stages of CKD, grows dramatically from the moment RRT is needed. Although the RRT population represents only 0.1–0.2% of the general population, it consumes at least 2% of health expenditures, with more recent estimates of 5–6% [8]. The prevalence of RRT continues to rise throughout Europe [9].

Hence there are good reasons to prioritize therapeutic options that, besides offering the best outcomes, generate the lowest societal cost [8]. Kidney transplantation is by far the most cost-effective RRT option, particularly after the first year of surgery, owing to the combination of prolonged survival, improved quality of life and reduced net expenses for therapy *per se* [2, 10–12].

Yet kidney transplantation remains underused throughout Europe. First, among incident RRT patients, only 4% received a pre-emptive transplantation [7]. Of course, a portion of the patients starting dialysis are transplanted after a variable period on dialysis, but this is counterproductive, as the waiting time on dialysis largely impacts mortality after kidney transplantation [13, 14]. Even among prevalent RRT patients, the percentage of patients living with a functioning transplant in Europe as a whole is only 37% [7]. Second, the percentage of transplanted RRT patients is highly discrepant among European countries. Only in very few EU countries does the percentage of prevalent RRT patients living with a functioning transplant exceed 50%, and numbers are as low as 9% for some EU countries (Table 1). Even if this ratio, which is defined both by kidney transplantation rate and by the number of patients treated by dialysis, may be confounded by varying efficacies of prevention or financial limitations to start dialysis, the differences are that important that underutilization of transplantation in many countries is likely. Also, the ratio of kidney transplantation from living or deceased donors diverges substantially, again suggesting underuse (Table 1).

Next to increasing the number of kidney transplantations, the number of people living with an active transplant also depends on short- and long-term kidney and patient survival. The current remaining lifetime of transplanted patients is ∼60% of their peers in the general population [7]. Although survival and grafted kidney outcomes improve year by year, the most important advances are observed early after kidney transplantation [15], leaving much room for improving later outcomes.

THE CONTRIBUTION OF THE EU TO EUROPEAN TRANSPLANTATION

The role of the EU extends over a much broader area than kidney transplantation alone and also covers liver, heart, lungs and pancreas, as well as other substances of human origin (blood, bone marrow, gametes and replacement tissues like corneas). Among these, kidney transplantation is the most frequent solid organ intervention (62% of all solid organ transplantations in the EU).

Article 168 of the Lisbon Treaty on the Functioning of the EU (TFEU) stipulates that health care remains a competence of the member states, which limits the role of the EU to complementing national policies and fostering cooperation between the member states and third parties [16]. However, Article 168 paragraph 4(a) also states that the EU should set high standards of safety and quality of substances of human origin.

While this mandate is relatively narrow, EU member states under rotating European presidencies [especially Spain (2010), Cyprus (2011) and Poland (2012)] have highlighted the importance of EU-level cooperation in the field of transplantation. This was also supported by several members of the European Parliament.

This political support has allowed the EU to help member states roll out the transplantation process as a whole and to mediate vis-à-vis medical professionals and national authorities in all steps from organ donation and procurement to the application of transplantation *per se* and follow-up of the grafted patient.

In 2008, the EU launched its Action Plan on Organ Donation and Transplantation (2009–15), with key aims of increasing organ availability, enhancing efficiency and accessibility of transplant systems and improving the quality and safety of transplantation [17]. The action plan contained 10 priority actions (Table 2). One of the major European weaknesses in this area (i.e. the staggering disparity among countries) was turned into an opportunity, allowing member states to improve their track record by learning from countries doing well in specific aspects. With this purpose in mind, >20 different EU-funded actions were organized (Table 3). Another program [Effect of Differing Kidney Disease Treatment Modalities and Organ Donation and Transplantation Practices on Health Expenditure and Patient Outcomes (EDITH); http://edith-project.eu] was started after 2015 and is currently studying renal replacement practices throughout Europe and the potential reasons for differences in application (see below).

The assessment of the impact of these activities is hampered by the scanty EU data spanning a long enough time period. Analysis of the overall transplantation rate (all organs) over the period of the action plan demonstrates an increase of 17% in all aggregated EU countries from 2008 through 2015, suggesting a positive effect [18]. The most important percentage increase was for lung transplantation (by 41%), while the increase for kidney and liver of ∼16% corresponds to the overall average and is almost entirely attributable to growth of living and non-heart-beating donation. In terms of absolute numbers, however, kidney and liver transplantations are by far superior.

To consistently underpin an increase in the transplantation rate over time, an increase in the slope of yearly transplantation rates should be observed. Unfortunately, we could retrieve only one report covering the entire EU before and during the action plan, starting in 2004 (5 years before the action plan) and ending in 2013 (2 years before its closure) [19]. In this analysis, the

Table 1. Kidney transplantation rate for different European countries

Country	No. of Tx pmp 2011	No. of Tx pmp 2016	% Tx of RRT 2011	% Tx of RRT 2016	% LTx 2011	% LTx 2016
Albania	3.9	5.9	26.1	17.3	**100.0**	**88.2**
Austria[a]	44.6	46.7	50.0	52.0	12.3	15.1
Belarus	18.2*	29.4	–	39.0	3.4*	4.2
Belgium[b]	41.8	39.5	41.6	42.6	7.8	10.0
Bosnia and Herzegovina	6.3	6.8	6.6	11.6	72.7	54.2
Bulgaria	2.3*	5.2	-	13.5	52.9*	29.7
Croatia	**53.7**	48.5	34.3	43.5	13.9	3.8
Cyprus	28.2*	22.2	-	-	61.3*	78.9
Czech Republic	31.9	44.6	-	40.2	12.0	10.0
Denmark	41.4	45.3	46.9	51.5	38.2	40.8
Estonia	32.8	31.9	**56.7**	56.7	6.8	9.5
Finland	32.7	47.5	**59.0**	**60.5**	7.4	8.4
France	46.3	**54.1**	44.3	44.9	10.1	15.9
Georgia	4.0*	7.0	–	9.3	**100.0***	**100.0**
Germany	34.7*	26.0*	-	-	27.9*	28.5*
Greece	17.8	13.1	20.0	18.5	25.9	37.6
Hungary	25.1*	34.9*	-	-	18.7*	9.9*
Iceland	34.5	14.9	**61.8**	**70.1**	**100.0**	**100.0**
Ireland	42.7*	36.6*	-	-	14.1*	29.1*
Italy	28.8*	34.7*	-	-	12.1*	13.5*
Latvia	36.1	34.0	53.3	53.6	4.8	17.0
Lithuania	22.7*	37.7	-	37.9	4.0*	5.5
Luxembourg	-	-	-	-	-	-
Macedonia, former Yugoslav Republic	3.0	3.5	9.3	12.4	**100.0**	**100.0**
Malta	45.0*	**50.0***	–	–	33.3*	25.0*
Moldova, Republic of	0.3*	5.4*	–	–	**100.0***	36.4*
Montenegro	3.2	3.3*	46.5	–	0.0	**100.0***
Norway	**61.0**	45.8	**71.9**	**70.3**	24.2	19.6
Poland	27.0	26.8	34.0	35.3	3.8	4.9
Portugal	**50.2**	**49.5**	36.7	36.4	8.9	12.7
Romania[c,d]	8.1	9.6	7.5	8.7	37.0	14.9
Russian Federation	6.8	7.5	21.2	19.2	18.4	21.4
Serbia[e,f]	15.6	7.4	14.0	9.5	38.9	36.5
Slovakia[g]	23.9	26.3	-	-	10.1	13.3
Slovenia	22.4	21.9*	30.0	-	0.0	4.3*
Spain[h]	**52.9**	**64.4**	49.9	52.4	12.5	11.4
Sweden	45.2	42.6	55.9	**58.2**	43.1	31.7
Switzerland[i,j]	36.6*	35.6	–	51.0	35.8*	39.3
The Netherlands	**51.6**	**58.8**	**60.0**	**63.1**	51.8	56.9
Turkey[k]	47.5	42.8	11.0	19.2	82.4	77.2
Ukraine[l]	1.4	3.1	13.1	14.6	58.1	74.0
UK[b,m,n,o]	43.7	45.3	48.9	54.0	37.5	28.7
All EU member states[p]	36.8	38.1	43.5	44.4	20.7	19.8
All non-EU member states	17.3	17.8	17.5	21.9	57.5	58.1

Data are from the ERA-EDTA Registry annual reports for 2011 and 2016. Data marked by an asterisk (*) are from the Global Observatory on Donation and Transplantation (GODT); '-' indicates no data available. Total numbers may not add up due to transplantations with unknown donor type or rounding off. Bold values indicate the five highest-scoring countries. Italics indicates current EU member states.

[a] Data based on residents and non-residents (2011 and 2016).

[b] Patients <20 years of age are not reported (2016).

[c] The overall prevalence of RRT is underestimated by ∼3% due to an estimated 30% underreporting of patients living on a functioning graft (2011 and 2016).

[d] The transplantation activity reflects 70% of the total transplantation activity in the country, because there is an underreporting of pre-emptive transplantations (2011 and 2016).

[e] The prevalence is underestimated by ∼29% due to centres not submitting complete data for 2016.

[f] The transplant activity is underestimated by ∼29% for deceased donor transplants and by ∼39% for living donor transplants due to centres not submitting complete data for 2016.

[g] Data from the Slovak Centre of Organ Transplantation (2011 and 2016).

[h] Data from the Organización Nacional de Trasplantes (2011 and 2016) from the total Spanish population.

[i] The transplant activity reflects 94% of the total transplant activity in the country (2016).

[j] The prevalence is underestimated by ∼6% due to an estimated 11% underreporting of patients living on a functioning graft (2016).

[k] Data from the Turkish Ministry of Health (2011).

[l] Data do not include Kiev city (2011).

[m] Data from NHS Blood and Transplant (2011).

[n] The prevalence is underestimated by ∼1% due to a small number of centres not submitting complete data for 2016.

[o] The transplant activity is underestimated by ∼7% due to one centre not submitting complete data for 2016.

[p] Croatia became a member of the EU in 2013 and is therefore not included in the 2011 European numbers. Iceland, Luxembourg and Malta essentially have their kidney transplants done in other countries.

Tx, kidney transplantation; LTx, living donor kidney transplantation.

slope of growth in the transplantation rate remained constant during the entire time window. The statistics from Eurotransplant, covering eight EU member states representative of ∼25% of the EU population but only referring to deceased donation, also show a stagnation in growth for kidney transplants from 1990 onwards, in contrast to a constant increase for liver and lung over the same period [20]. These figures suggest that changes over the last decades might be attributed, at least in part, to an increased use of certain organs rather than to an intrinsic increase in deceased donor organ availability.

However, these data should be regarded with care. First, there is an inevitable lag time between starting an action plan and obtaining results, and this may easily take several years. Another undeniable bias relates to external factors, like the evolution in Germany that followed a fraud allegation in 2012 after the disclosure of liver candidate data modification by transplant units to advance ranking on the waiting list [21]. A sudden decline in the German transplantation rate that essentially affected kidney and liver was observed after that incident (for kidney, the decline of >35% is a highly significant figure considering that 15% of all EU citizens are German). In addition, along with Germany, a few other countries showed a decline in transplant activity, mainly in countries severely affected by financial crises, such as Greece and Cyprus [18]. There were probably other financial priorities for these governments, but such a decline has a counterproductive effect by increasing national expenses (kidney transplantation remains the cheapest, most cost-effective RRT) in a period of financial crisis.

Table 2. EU transplantation action plan (2008–15)

Objectives	Ten priority actions
Increase organ availability	1. Transplant coordinators
	2. Quality improvement programmes
	3. Living donation programmes
	4. Communication skills of professionals
	5. Information on citizen rights
Enhance efficiency and accessibility of transplantation systems	6. Enhance organizational models
	7. EU-wide agreements (research, trafficking, mobility)
	8. Interchange of organs
Quality and safety	9. Evaluation of post-transplantation results
	10. Common accreditation systems

The ERA-EDTA Registry data show a more positive trend than what is mentioned above. Covering all EU member states and based on both living and deceased donation (Table 1), data comparison between 2011 and 2016 shows a modest increase in the total number of performed kidney transplantations per million people (pmp) by 1.3 and in the percentage of patients on RRT living with a functioning kidney transplant by 0.9%. Of note, in this analysis the German data are included.

When considering individual countries, several of them show a more positive evolution, with an increase in the transplantation rate >5 pmp (e.g. France, Lithuania, and especially Spain and The Netherlands). In most of these countries the percentage of patients on RRT living with a functional kidney transplant showed a substantial increase.

Nevertheless, taking all data together, it is suggested that further action is warranted to generate an additional boost to transplantation throughout Europe (see below).

THE EDITH PROJECT

The EDITH project, funded by the EU, was started early in 2017 [22]. This project was approved, thanks to the efforts of the EKHA at the EU level. EDITH aims to examine the effect of the substantial practice variation in the management of end-

Table 3. EU-supported programs to stimulate transplantation

Program	Main purpose or focus
Alliance – O	Coordination of national research on transplantation
DOPKI	Improving the knowledge and practices in organ donation
ETPOD	European training program on organ donation
EULID	European living donation and public health
EDD	European donation day
ELPAT	Ethical, legal and psychosocial aspects of transplantation
EFRETOS	European framework for evaluation of organ transplantation
ELIPSY	Euro living donor psychosocial follow-up
COORENOR	Coordinating a European initiative among national organizations for organ transplantation
EULOD	European living organ donation
ODEQUS	Organ donation European quality system
Train the Trainers	European training program on organ donation
MODE	Exchange best practices in organ donation and transplantation
ACCORD	Achieving comprehensive coordination in organ donation throughout the EU
FOEDUS	Facilitate exchange of organs donated in EU member states
EUDONORGAN	Increase organ donation rate in Europe
HOTT	Combating organ trafficking
LIDOBS	Living donor observatory
ONE study	A unified approach to evaluating cellular immunotherapy in solid organ transplantation
Bio-DrIM	Biomarker-driven personalized immunosuppression
COPE	Improving preservation and reconditioning strategies for kidney and liver organs procured for transplantation
STELLAR	Stem cell research in kidney disease

stage kidney disease (ESKD) and in the access to dialysis and kidney transplantation within Europe [23] on patient outcomes and costs. The EDITH consortium, led by the Deutsche Stiftung Organ Transplantation (DSO), consists of 9 European partners together with collaborating stakeholders including the EKHA, the European Renal Association–European Dialysis and Transplant Association (ERA-EDTA), the European Kidney Patients Federation (EKPF), the French Agence de la Biomédecine and a number of renal registries and national kidney foundations. The ERA-EDTA Registry participates in a work package addressing the epidemiology and costs of different treatment modalities for ESKD. The epidemiological analyses are performed by the ERA-EDTA Registry, whereas health care budgets are analysed by the Italian National Transplant Center. Other work packages aim at establishing a European Living Donor Registry and a European Kidney Transplant Registry for the follow-up of living donors and transplant recipients.

To understand the reasons for the intra-European differences, EDITH aims to examine factors that influence the choice of treatment modality and the decisions made by patients and their treating nephrologists. To this end, kidney patient surveys in all European languages as well as surveys among nephrologists have been distributed across almost all EU member states and associated countries (e.g. Switzerland, Serbia, Norway, etc.).

Research on barriers to kidney transplantation may help to identify modifiable factors that can be translated into effective interventions to increase transplant rates. Table 4, based on the current literature, shows the barriers for patients to kidney transplantation. These include fear of kidney rejection or graft failure, fear of surgery or medication, previous negative experiences after receiving a graft by themselves or others, distrust of health care professionals, doing well on dialysis, religious reasons opposing transplantation and costs [24–28, 30–40]. For living donor transplantation, additional barriers were fear for the donor's health and reluctance to ask candidate donors [26–30, 39, 41–43]. However, those barriers are expected to differ across European countries. Hence a significant part of the EDITH kidney patient survey focuses not only on the barriers and facilitators of living or deceased donor transplantation, but also on barriers and facilitators for particular modalities of dialysis or conservative care, as a substantial group of patients on RRT may not be suitable for a kidney transplant. Moreover, studies have shown that patients with CKD may not receive adequate information on treatment options [44–46], and the degree of shared decision making may influence the treatment choice [47, 48]. Therefore other parts of the survey involve the type of and satisfaction with the information provided on each treatment modality and the extent to which patients were involved in the decision-making process among the different RRT options, as well as the economic resources spent to propagate certain modalities like transplantation.

Table 4. Barriers to kidney transplantation experienced by patients with ESKD

Barriers	References
Fear of kidney rejection or graft failure	[24–28, 30]
Fear of surgery	[24–26, 31–34, 36]
Fear of medication (side effects, fear of infection)	[24–26]
Negative experiences (self or others)	[24–26, 35]
Distrust of health care professionals	[30, 33]
Doing well on dialysis	[25, 26, 30, 34, 36, 37]
Religious reasons opposing kidney transplantation	[25, 36]
Costs	[25, 28, 33, 34, 36–40]
Only for living donors	
Fear for donor's health	[26–30, 39, 41–43]
Reluctance to ask potential living donors	[28, 29, 43]

It is hoped that the EDITH project will impact treatment choices by patients and their doctors and health care policies, improving access not only to kidney transplantation, but also to dialysis throughout EU countries.

THE FUTURE—WHAT TO DO?

Whatever interventions are undertaken to improve the kidney transplantation rate, they will also affect transplantation of other organs, thus expanding their impact on a wide array of non-communicable diseases.

Even if Europe is one of the leading continents in transplantation [8], well-conceived planning and policy action are needed to further increase the numbers. Accounting for the European disparities (Table 1), a substantial number of patients with a potentially good outcome are probably denied kidney transplantation, as has also been reported in the USA [49]. The ultimate target is not only an increase in donations and transplantations, but also an increase in the percentage of patients with RRT living with a functioning kidney graft. The optimal approach would be to set well-defined ambitious aims, e.g. an increase of the number of transplantations and of transplanted patients with RRT in the EU by 10% in 10 years or an increase of donors per annum and pmp by a preset percentage per country, defined by the previous activity. This would then need to be followed by calls to action at the national level and internal and external auditing.

Rather than developing plans and targets for the EU as a whole, countries with specific characteristics might be clustered, depending on their baseline transplantation rate, with equal attention to countries with a low transplantation rate as those with a medium or high rate, but with different strategies for each group. Germany, with a medium but declining transplantation rate in spite of a sophisticated health care system, may need a country-specific approach.

Some countries are strong in living donation and others in deceased donation, but few European countries are strong in both. Action plans might be different, depending on which options need most improvement.

Several EU countries still apply an opting-in strategy in acquiring donors, which necessitates the explicit permission of the potential donor or his/her family for organ removal, a possible factor hampering the transplant rate. In contrast, other countries apply opting out (presumed consent to organ donation, which is based on assumed solidarity, allowing organ retrieval if appropriate unless the candidate donor had his/her refusal officially registered).

On average, opting out results in higher transplantation rates [50, 51], as experienced in countries like Spain, Belgium, Austria and Croatia, even if most European opting-out countries apply an 'attenuated procedure' (still asking the families for permission but supported by greater moral and legal leverage). Thus EU member states might all strive for a global opting-out system. Also, implementation, stimulation and simplification of affirmative donor registration are options to be considered [49, 52]. When in late 2015 the rules in Wales were changed from opting in to opting out, this resulted in increased consent from 44 to 72%, much higher than the 63% average in the rest of the UK.

Several EU countries do not collaborate with one of the three programs (Eurotransplant, Scandiatransplant and the South Transplant Alliance) for deceased donor organ exchange and do not have an efficient internal system, so gradual incorporation in one of the existing programs likely will boost their activity [53]. It is impossible to exactly define the impact of such exchange programs on the transplantation rate, but in countries newly adhering to such systems they may generate a boost in transplant activity, as experienced in Croatia [53] at the beginning of this century or more recently in Hungary (Table 1).

EU member states have shown great interest in participating in an information technology platform connecting allocation offices to make available surplus organs that cannot be matched within the system, which might be especially beneficial for transplantation of children and adolescents [18].

A further stimulus to increase deceased donation is the relaxation of donor and acceptor evidence-based selection criteria. These include expanded and non-heart-beating donation, which are underutilized in many European countries [18] in spite of similar outcomes compared with heart-beating deceased donation in several studies [54, 55]. Also, reimbursement incentives for families of deceased donors may be of interest, if ethically sound.

A matter of specific concern is Brexit [56]. Under EU regulations, organs that are donated in one country can be moved under harmonized public health rules to another country so that the donation and chance for life is preserved, but maintaining this provision may require the development of new exchange agreements between EU and non-EU countries, in this case the UK. Disease does not care about borders and UK kidney patients very much want their medical community to continue working with the EU to improve health care. They hope for consideration and support from UK as well as non-UK policymakers.

Although almost all European countries practice some living donation, the frequency is often low, especially in countries where the overall kidney transplantation rate is low, but also in countries with higher rates, like Belgium and Austria (Table 1). To stimulate living donation, expansion of the donor and acceptor criteria, reduction of costs for the donor (e.g. for the loss of income or need for follow-up and donation-related medications), activating spouse and unrelated donation and application of uniform procedures for donor information and recruitment could be useful [57, 58]. All these bring along organizational and ethical questions that necessitate careful consideration and debate. The European Commission and national agencies have developed a reference toolkit to this end [59].

Also, deficient patient information limits the expansion of kidney transplantation [60]. In the context of an analysis of the patient choice possibilities throughout Europe, the EKHA distributed in 2017 a questionnaire among patients of six different European countries (Table 5) asking patients for their satisfaction with information on different types of RRT. Depending on the country, patient dissatisfaction regarding information about kidney transplantation ranged from 11 to 45% (Table 5). The differences underscore that there is room for improvement in patient education almost everywhere. In addition, not all patients received information about both living and deceased donation. These data confirm a previous analysis published in 2014 [46], based on a questionnaire in 2010–11, and suggest little change over time while underscoring the utility of a streamlined European educational approach about RRT, including kidney transplantation, and of an ad hoc verification system subsequently checking patient satisfaction.

Organizing and optimizing transplant coordination deserves specific attention, with possible options being installing coordinators in each hospital (if necessary on a part-time basis), training to stimulate early and proactive donor detection and selection and internal and external auditing of hospitals for the efficacy of donor retrieval [61].

Transplantation awareness is also insufficient in the general population, which includes policymakers and regulators. This necessitates continuous public education, including adequate information offered in the regular educational system to the very young. Involvement of mass media (written press, television) and an active partnership with journalists can be a major asset [61]. Additional barriers may be present in socially deprived, less-educated communities and ethnic minorities, and it seems essential that these populations should be specifically addressed to understand their attitudes and possibly offering help to modify them [61]. The recent EKHA 'Gift of Life' campaign [62] has made a toolbox available allowing individuals and societies to promote kidney transplantation at the national policy level in an equitable way throughout Europe.

Education of involved medical professionals is also essential, with specific focus on those involved at the early stages of donor retrieval, such as emergency and intensive care unit physicians and transplant coordinators [61].

Table 5. Results of patient questionnaire on kidney transplantation education and information in seven EU countries

Question	FR	GR	LI	NL	SL	SP
Found received information insufficient (%)	21	45	17	11	22	32
Received information about both living and deceased donation (%)	80	77	85	77	30	70
Received information only about living donation (%)	1	10	6	19	0	1
Received information only about deceased donation (%)	19	13	9	4	70	29

The table shows preliminary results; data still await final analysis.
FR, France; GR, Greece; LI, Lithuania; NL, The Netherlands; SL, Slovenia; SP, Spain.

Finally, it is important that national policies in Europe focus on financial disparities, including costs to hospitals, for donor organ retrieval [60] and reimbursement differences between dialysis and kidney transplantation, as in most countries dialysis is financially more interesting to care providers. This might include financial incentives as a function of the proportion of transplant patients among the population on RRT. In addition, benchmarking of hospitals, regions and countries might be helpful. It is also essential that expansion of transplantation numbers is supported by adequate infrastructural capacity—surgeons and operating theatres—so that an increase in interventions can be accommodated.

Countries that could improve their track record should learn from countries performing well, such as Spain, France and The Netherlands. In Spain for example, coordinated actions included earlier referral of potential donors, benchmarking and training of professionals, as well as educational activities with supportive participation of the media [61, 63], and this induced an increase in the transplantation rate of >10% between 2011 and 2016 (Table 1).

CONCLUSION

In spite of a good European track record in the field of kidney transplantation compared with other continents, the substantial disparities among EU countries suggest ample room for improvement. The EU launched an action plan to increase transplant activities between 2009 and 2015, but especially with regards to kidney transplantation, further action would be helpful to boost activity. The main focus points suggested in this review are registration of data and analysis of reasons for discrepancies among countries, correction of those factors, coordination of transplantation promoting projects, clustering of countries with similar characteristics, provision of appropriate legal consent and financial frameworks favouring organ donation and education of patients, professionals and the general population. Only prolonged and coordinated action will result in a sustained effort to improve conditions for patients and society.

Apart from overarching European action, the responsibility of individual countries should be emphasized as well.

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The EKHA (http://ekha.eu) is a common effort by all European key stakeholders in kidney care to propose solutions for the challenges of CKD in Europe through effective prevention and a more efficient care pathway intended to facilitate the provision of appropriate and affordable treatment to all Europeans equally while promoting the highest quality of care. The EKHA works on the principle that the issue of kidney health and disease must be considered at the European level and that both the European Commission and European Parliament have vital roles to play in assisting national governments with these challenges. The EKHA is self-supporting but organizes an event each year related to kidney disease and care in the European Parliament with the support of industry (unrestricted grant). This year's event on kidney transplantation was supported by Amgen, Baxter Healthcare, BBraun, CSL Behring, Novartis.

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CONFLICT OF INTEREST STATEMENT

None declared. The content of this publication represents the views of the authors only and is their sole responsibility. It does not reflect the views of the European Commission or any other body of the EU. The European Commission does not accept any responsibility for use that may be made of the information this article contains.

REFERENCES

1. Tonelli M, Wiebe N, Knoll G *et al*. Systematic review: kidney transplantation compared with dialysis in clinically relevant outcomes. *Am J Transplant* 2011; 11: 2093–2109
2. Wong G, Howard K, Chapman JR *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: e29591
3. Meier-Kriesche HU, Ojo AO, Port FK *et al*. Survival improvement among patients with end-stage renal disease: trends over time for transplant recipients and wait-listed patients. *J Am Soc Nephrol* 2001; 12: 1293–1296
4. Liem YS, Bosch JL, Hunink MG. Preference-based quality of life of patients on renal replacement therapy: a systematic review and meta-analysis. *Value Health* 2008; 11: 733–741
5. European Kidney Health Alliance. http://ekha.eu/ (10 October 2018, date last accessed)
6. Insitute for Health Metrics and Evaluation. https://vizhub.healthdata.org/gbd-compare (10 October 2018, date last accessed)
7. ERA-EDTA Registry. ERA-EDTA Registry Annual Report 2016. Amsterdam: Department of Medical Informatics, Amsterdam Unversity Medical Center, 2018. https://www.era-edta-reg.org/files/annualreports/pdf/AnnRep2016.pdf (10 October 2018, date last accessed)
8. Vanholder R, Annemans L, Brown E *et al*. Reducing the costs of chronic kidney disease while delivering quality health care: a call to action. *Nat Rev Nephrol* 2017; 13: 393–409
9. Pippias M, Jager KJ, Kramer A *et al*. The changing trends and outcomes in renal replacement therapy: data from the ERA-EDTA Registry. *Nephrol Dial Transplant* 2016; 31: 831–841
10. Klarenbach S, Manns B. Economic evaluation of dialysis therapies. *Semin Nephrol* 2009; 29: 524–532
11. Haller M, Gutjahr G, Kramar R *et al*. Cost-effectiveness analysis of renal replacement therapy in Austria. *Nephrol Dial Transplant* 2011; 26: 2988–2995
12. Laupacis A, Keown P, Pus N *et al*. A study of the quality of life and cost-utility of renal transplantation. *Kidney Int* 1996; 50: 235–242
13. Meier-Kriesche HU, Kaplan B. Waiting time on dialysis as the strongest modifiable risk factor for renal transplant outcomes: a paired donor kidney analysis. *Transplantation* 2002; 74: 1377–1381
14. Haller MC, Kainz A, Baer H *et al*. Dialysis vintage and outcomes after kidney transplantation: a retrospective cohort study. *Clin J Am Soc Nephrol* 2017; 12: 122–130
15. Wekerle T, Segev D, Lechler R *et al*. Strategies for long-term preservation of kidney graft function. *Lancet* 2017; 389: 2152–2162
16. Foundation for EU Democracy. The Lisbon Treaty. http://en.euabc.com/upload/books/lisbon-treaty-3edition.pdf (10 October 2018, date last accessed)
17. European Commission. https://ec.europa.eu/health/ph_threats/human_substance/oc_organs/docs/organs_action_en.pdf (10 October 2018, date last accessed)
18. European Commission. https://ec.europa.eu/health/sites/health/files/blood_tissues_organs/docs/2017_euactionplan_2009-2015_impact_exe_en.pdf (10 October 2018, date last accessed)
19. European Commission. https://ec.europa.eu/health/sites/health/files/blood_tissues_organs/docs/ev_20141126_factsfigures_en.pdf (10 October 2018, date last accessed)

20. Eurotransplant. Statistics Report Library. http://statistics.eurotransplant.org/index.php? search_type=transplants&search_period=by+year+chart (10 October 2018, date last accessed)
21. Spiegel Online. Organ transplant scandal shocks Germany. http://www.spiegel.de/international/germany/organ-transplant-scandal-shocks-germany-a-848016.html (10 October 2018, date last accessed)
22. Jager KJ, Stel VS, Branger P *et al.* The effect of differing kidney disease treatment modalities and organ donation and transplantation practices on health expenditure and patient outcomes. *Nephrol Dial Transplant* 2018; 33: 560–562
23. Kramer A, Pippias M, Noordzij M *et al.* The European Renal Association-European Dialysis and Transplant Association (ERA-EDTA) Registry Annual Report 2015: a summary. *Clin Kidney J* 2018; 11: 108–122
24. Morton RL, Devitt J, Howard K *et al.* Patient views about treatment of stage 5 CKD: a qualitative analysis of semistructured interviews. *Am J Kidney Dis* 2010; 55: 431–440
25. Gordon EJ. Patients' decisions for treatment of end-stage renal disease and their implications for access to transplantation. *Soc Sci Med* 2001; 53: 971–987
26. Salter ML, Kumar K, Law AH *et al.* Perceptions about hemodialysis and transplantation among African American adults with end-stage renal disease: inferences from focus groups. *BMC Nephrol* 2015; 16: 49
27. Tong A, Sainsbury P, Chadban S *et al.* Patients' experiences and perspectives of living with CKD. *Am J Kidney Dis* 2009; 53: 689–700
28. Waterman AD, Stanley SL, Covelli T *et al.* Living donation decision making: recipients' concerns and educational needs. *Prog Transplant* 2006; 16: 17–23
29. Gordon EJ. They don't have to suffer for me: why dialysis patients refuse offers of living donor kidneys. *Med Anthropol Q* 2001; 15: 245–267
30. Wachterman MW, McCarthy EP, Marcantonio ER *et al.* Mistrust, misperceptions, and miscommunication: a qualitative study of preferences about kidney transplantation among African Americans. *Transplant Proc* 2015; 47: 240–246
31. Landreneau K, Ward-Smith P. Perceptions of adult patients on hemodialysis concerning choice among renal replacement therapies. *Nephrol Nurs J* 2007; 34: 513–519, 525
32. Schell JO, Patel UD, Steinhauser KE *et al.* Discussions of the kidney disease trajectory by elderly patients and nephrologists: a qualitative study. *Am J Kidney Dis* 2012; 59: 495–503
33. Ilori TO, Enofe N, Oommen A *et al.* Factors affecting willingness to receive a kidney transplant among minority patients at an urban safety-net hospital: a cross-sectional survey. *BMC Nephrol* 2015; 16: 191
34. Qiao B, Liu L, Liu J *et al.* A study on the attitude toward kidney transplantation and factors among hemodialysis patients in China. *Transplant Proc* 2016; 48: 2601–2607
35. Holley JL, McCauley C, Doherty B *et al.* Patients' views in the choice of renal transplant. *Kidney Int* 1996; 49: 494–498
36. Kabbali N, Mikou S, El Bardai G *et al.* Attitude of hemodialysis patients toward renal transplantation: a Moroccan interregional survey. *Transplant Proc* 2014; 46: 1328–1331
37. Kazley AS, Simpson KN, Chavin KD *et al.* Barriers facing patients referred for kidney transplant cause loss to follow-up. *Kidney Int* 2012; 82: 1018–1023
38. Jennette C, Derebail V, Baldwin J *et al.* Renal replacement therapy and barriers to choice: using a mixed methods approach to explore the patient's perspective. *J Nephrol Soc Work* 2009; 32: 15–26
39. Ghahramani N, Wang C, Sanati-Mehrizy A *et al.* Perception about transplant of rural and urban patients with chronic kidney disease; a qualitative study. *Nephrourol Mon* 2014; 6: e15726
40. Bailey PK, Ben-Shlomo Y, Tomson CR *et al.* Socioeconomic deprivation and barriers to live-donor kidney transplantation: a qualitative study of deceased-donor kidney transplant recipients. *BMJ Open* 2016; 6: e010605
41. Hanson CS, Chadban SJ, Chapman JR *et al.* The expectations and attitudes of patients with chronic kidney disease toward living kidney donor transplantation: a thematic synthesis of qualitative studies. *Transplantation* 2015; 99: 540–554
42. Kranenburg LW, Zuidema WC, Weimar W *et al.* Psychological barriers for living kidney donation: how to inform the potential donors?. *Transplantation* 2007; 84: 965–971
43. Pradel FG, Limcangco MR, Mullins CD *et al.* Patients' attitudes about living donor transplantation and living donor nephrectomy. *Am J Kidney Dis* 2003; 41: 849–858
44. Fadem SZ, Walker DR, Abbott G *et al.* Satisfaction with renal replacement therapy and education: the American Association of Kidney Patients survey. *Clin J Am Soc Nephrol* 2011; 6: 605–612
45. Ludlow MJ, Lauder LA, Mathew TH *et al.* Australian consumer perspectives on dialysis: first national census. *Nephrology (Carlton)* 2012; 17: 703–709
46. Van Biesen W, van der Veer SN, Murphey M *et al.* Patients' perceptions of information and education for renal replacement therapy: an independent survey by the European Kidney Patients' Federation on information and support on renal replacement therapy. *PLoS One* 2014; 9: e103914
47. Morton RL, Tong A, Howard K *et al.* The views of patients and carers in treatment decision making for chronic kidney disease: systematic review and thematic synthesis of qualitative studies. *BMJ* 2010; 340: c112
48. Murray MA, Brunier G, Chung JO *et al.* A systematic review of factors influencing decision-making in adults living with chronic kidney disease. *Patient Educ Couns* 2009; 76: 149–158
49. Schold JD, Srinivas TR, Kayler LK *et al.* The overlapping risk profile between dialysis patients listed and not listed for renal transplantation. *Am J Transplant* 2008; 8: 58–68
50. Shepherd L, O'Carroll RE, Ferguson E. An international comparison of deceased and living organ donation/transplant rates in opt-in and opt-out systems: a panel study. *BMC Med* 2014; 12: 131
51. Abadie A, Gay S. The impact of presumed consent legislation on cadaveric organ donation: a cross-country study. *J Health Econ* 2006; 25: 599–620
52. Howard K, Jan S, Rose JM *et al.* Preferences for policy options for deceased organ donation for transplantation: a discrete choice experiment. *Transplantation* 2016; 100: 1136–1148
53. Zivcic-Cosic S, Busic M, Zupan Z *et al.* Development of the Croatian model of organ donation and transplantation. *Croat Med J* 2013; 54: 65–70
54. Summers DM, Johnson RJ, Allen J *et al.* Analysis of factors that affect outcome after transplantation of kidneys donated after cardiac death in the UK: a cohort study. *Lancet* 2010; 376: 1303–1311
55. Yarlagadda SG, Coca SG, Formica RN, Jr *et al.* Association between delayed graft function and allograft and patient survival: a systematic review and meta-analysis. *Nephrol Dial Transplant* 2008; 24: 1039–1047
56. Shapey IM, Summers AM, Simkin IJ *et al.* When politics meets science: What impact might Brexit have on organ donation and transplantation in the United Kingdom? *Clin Transplant* 2018; 32: e13299
57. Mandelbrot DA, Pavlakis M. Living donor practices in the United States. *Adv Chronic Kidney Dis* 2012; 19: 212–219
58. Friedman AL, Friedman EA. A step toward solving the long-term care dilemma for living kidney donors. *Transplantation* 2012; 94: 988–989
59. European Commission. https://ec.europa.eu/health/sites/health/files/blood_tissues_organs/docs/eutoolbox_living_kidney_donation_en.pdf (10 October 2018, date last accessed)
60. Garg AX. Helping more patients receive a living donor kidney transplant. *Clin J Am Soc Nephrol* 2018; 13: 1918–1923
61. Matesanz R, Dominguez-Gil B, Coll E *et al.* Spanish experience as a leading country: what kind of measures were taken? *Transpl Int* 2011; 24: 333–343
62. European Kidney Health Alliance. Gift of Life. http://ekha.eu/gift-of-life/ (10 October 2018, date last accessed)
63. Matesanz R, Marazuela R, Coll E *et al.* About the opt-out system, liver transplantation, and information to the public on organ donation in Spain . . . Y ole! *Am J Transplant* 2017; 17: 1695–1696

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