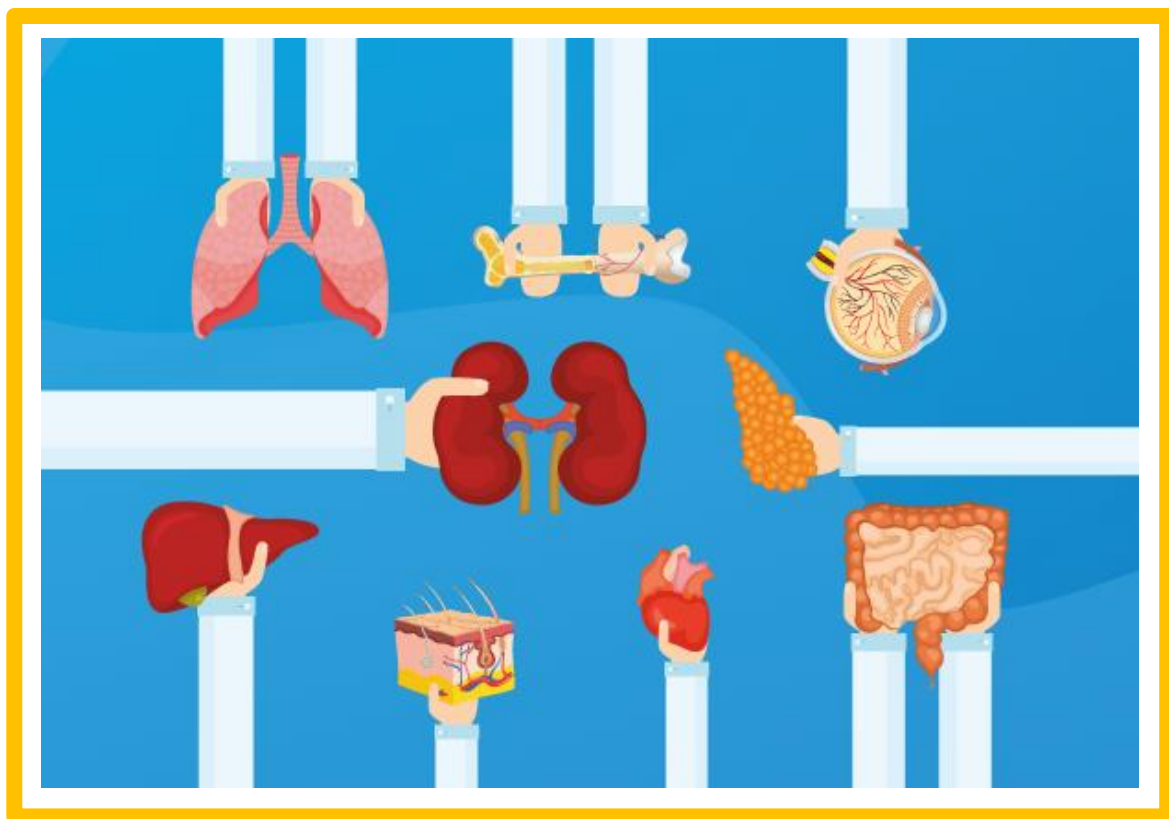


# JOINT STATEMENT

## Thematic Network on Improving Organ Donation and Transplantation in the EU 2019

### A Shared Vision for Improving Organ Donation and Transplantation in the EU



*“The crux of the matter is people, beyond funding, regulations, strategies, and data. The desired outcome from a patient’s point of view would always be to have a transplanted organ that lasts a long and healthy lifetime...”*

***Robert van der Wolk, transplant patient***

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# Organ Donation and Transplantation in the EU

Transplantation saves, extends and improves lives



Transplantation is highly cost-effective\*

\*Where an alternative is available, e.g. for kidney transplantation versus dialysis, transplantation is cost-saving for the health system.



## Over the period of the EU Action Plan on Organ Donation and Transplantation (2009-2015)

The total number of transplants increased by

**+17%**

The total number of organ donors significantly improved

Living organ donors increased by

**+29.5%**

Deceased organ donors increased by

**+12%**



**21,102**  
Kidney



**7,984**  
Liver



**2,169**  
Heart



**2,013**  
Lung

+ other organs

**33,385** in 2016



**= 34,024** in 2017

Since the end of the EU Action Plan, the total number of organ transplants in the EU has continued to increase, albeit gradually.



**Spain** is a global leader in organ donation and transplantation. With **2,183 donors**, and **5,261 organs transplanted** in 2017, it accounted for

**19.2%** of all organ donations in the EU.



In 2017, the rate of deceased organ donors per million population (pmp) in Spain was the highest in the EU (47 donors pmp), followed by Portugal (34.1 donors pmp) and Croatia (33.3 donors pmp).



On the other hand, transplantation rates have been stagnant or even decreasing in some EU countries



In Europe, some **18 patients die every day** waiting for a transplant.

Over

**143,000**



patients were registered on waiting lists in 2015 (+5% compared to 2014)

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# Joint Statement: Calls and Recommendations

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# CONSIDERATIONS

Chronic or non-communicable diseases (NCDs) are among the most important health issues in Europe, imposing a substantial and rising burden on healthcare systems and having a crucial impact on economies, quality of life, employment status and social activities.

Over the period of the EU Action Plan on Organ Donation and Transplantation (2009-2015), the number of transplants in the EU increased by 17%. Despite this significant progress, in Europe, some 18 patients die every day waiting for the organs they need and more than 143,000 patients were on waiting lists for transplantation in 2015<sup>1</sup>.

Transplantation is one of the highest value treatments in medicine as it

- is often the only **life-saving** option for patients with end-stage organ failure.
- improves **quality of life** by restoring organ function.
- **eliminates debilitating symptoms** of chronic organ failure such as poor mobility, depression or infertility, and in children, growth and development deficiencies.
- is highly **cost-saving** both for patients and healthcare systems.
- **facilitates social re-integration** as it enhances mobility, as well as employment and education possibilities.

In spite of these overwhelming advantages, transplantation remains largely underutilised in Europe and there is considerable room for improvement.

Challenges to be addressed encompass:

- **Significant variation in both living and deceased organ donation rates** across the EU.
- **Significant variation in annual organ transplantation** across the EU, with over tenfold difference between countries with the highest and lowest annual rates.
- Marked **inequities in access** to transplantation for specific subgroups in society.
- **Persistent shortage of available organs**, as illustrated by the ever-growing waiting lists and people deteriorating or dying while awaiting transplantation.
- **Considerable variation in the outcomes** of transplantation, due to reasons such as organ rejection, cancer, vascular disease or infections.

There is thus a need for renewed political momentum to further optimise organ donation and transplantation activity throughout Europe. Below, calls and recommendations are outlined as part of a shared vision of several stakeholders in the European organ donation and transplantation community to stimulate action. Given the EU's limited mandate in healthcare, national efforts to enhance organ donation and transplantation remain vital, which can be supported and complemented by the EU and the European Commission.

<sup>1</sup> <https://www.coe.int/en/web/pristina/-/european-day-for-organ-donation-and-transplantation-2017>



# CALLS AND RECOMMENDATIONS

## CALL 1: MOBILISE POLITICAL WILL TO MAKE ORGAN DONATION AND TRANSPLANTATION A PRIORITY

Over the last two decades Europe has been one of the leading continents in transplantation. However, **a renewed political momentum is imperative** for future efforts to improve organ donation and transplantation rates, quality, and safety within countries. **The realisation of a follow-up EU Action Plan that will build upon the success of the EU Action Plan on Organ Donation and Transplantation (2009-2015) could help place organ donation and transplantation high on the political agenda once again**, by providing forward-looking and actionable guidance at national level, while continuing to promote strong cooperation between Member States.

### RECOMMENDATIONS:

#### Member States

- Take the **lead in improving organ donation and transplantation** by placing related issues high on the national political agenda and showing readiness to commit necessary resources to implement actions
- **Determine realistic organ donation and transplantation targets** according to domestic needs and capabilities, and monitor their attainment.
- **Future Presidencies of the Council of the EU**, such as the upcoming Croatian and German Presidencies: Advocate for organ donation and transplantation both at the EU level and within the Member States, and **interlink the Council presidency priorities in the health field with the Commission priorities in the Substances of Human Origin (SoHO) field**, i.e. the Evaluation of the EU legislation on Blood, Tissues and Cells (BTC) and the possible revision of the BTC legislative framework<sup>2</sup>.
- **Develop, implement or refine National Action Plans** that are aligned with the follow-up EU Action Plan, if and when it's realised.

#### European Commission

- Place organ donation and transplantation high on the political agenda via the realisation of **a follow-up EU Action Plan with a focus on fostering implementation at the national level**.
- Ensure that following the **BTC evaluation** and in the course of the possible **revision of the BTC legislation**, the synergies across the fields of BTC and organs are explored, particularly with respect to the protection of donors and recipients, vigilance systems and inspections.
- **Propose and monitor the implementation of ambitious and clearly defined short-, medium-, and long-term goals for the EU as a whole, and call on the Member States to set their own targets**, as part of an integrated EU vision.
- **Promote and monitor Member States' development and implementation of up-to-date national Action Plans**, aligned with the objectives of the follow-up EU Action Plan and tailored according to domestic needs and capabilities.

<sup>2</sup> [https://ec.europa.eu/health/blood\\_tissues\\_organs/policy/evaluation\\_en](https://ec.europa.eu/health/blood_tissues_organs/policy/evaluation_en)



- Ensure that the next **DG Health and Food Safety (SANTE) Strategic Plan** beyond 2020 contains objectives and actions on organ donation and transplantation.
- **Facilitate dialogue with and provide guidance to non-EU countries** willing to exchange knowledge and best practices on promoting organ donation and transplantation.

### Stakeholders

- **Put pressure from below** by working collectively to sustain political momentum on organ donation and transplantation and **strengthen the patients' voice** at policy level.
- **Engage actively in policy conversations and initiatives** to ensure that the frameworks and national plans best serve the patients and communities they are designed for.
- **Provide support in the determination of national targets** and closely monitor their attainment.
- **Actively shape the follow-up EU Action Plan as well as the national Action Plans inspired by it**, by sharing knowledge and expertise, and lobbying to voice the evolving needs and concerns of the stakeholders.

## CALL 2: IMPROVE LEGAL AND INSTITUTIONAL FRAMEWORKS

Removing legal and institutional barriers is fundamental to enhance organ donation and transplantation activities in the Member States. While the discussion is often centred on the choice between 'opt-in' vs. 'opt-out' legislations (i.e. necessitating a potential donor's or their family's explicit consent vs. presuming consent to organ donation), there should be greater focus on other measures to achieve this goal.

These include: 1) **promoting 'expanded criteria donation'**, which allows for the donation of organs from living or deceased donors that are not considered ideal or standard but are still of sufficient quality for transplantation and, as such, can significantly shorten the waiting time to receive a transplantation. However, transplantation of organs from expanded criteria donors is still underdeveloped or even non-existent in most Member States; 2) **improving living donation**, particularly via currently underexploited options such as **kidney sharing schemes** (exchange of organs among donor/recipient pairs who cannot exchange organs with their own partner); 3) **facilitating international organ exchange**, 4) **regulating and guiding transplantation from donation after circulatory death (DCD)**—as opposed to the usual approach of accepting donors after brain death (DBD) when the heart is still functioning—, and 5) **applying an appropriate allocation strategy** to optimise post-transplant outcomes.

### RECOMMENDATIONS:

#### Member States

- **Build legal and institutional frameworks conducive to increasing and facilitating organ donation and transplantation** in light of EU guidance, with focus on aligning organ and tissue donation, expanded criteria donation, living donation, kidney-sharing schemes, international organ exchange, DCD, and allocation strategies.
- **To optimise living donation**, set up frameworks ensuring that organ donation does not entail financial loss for the donor, activating spouse and unrelated altruistic donation, and applying uniform procedures for donor/recipient information and recruitment. Suggested approaches include: informing patients, removing barriers (e.g. by promoting cross-over donation, whereby patients who cannot be given their own partner's organ are given an organ from the partner of another patient, in exchange for an organ from their own partner), and protecting the living organ donor against material or physical damage due to donation.





- Refer to the “**Toolbox Living Kidney Donation**” in developing an ethical framework for unrelated living donation<sup>3</sup>.

### **European Commission**

- Provide **recommendations to guide Member States’ efforts to improve their legal and institutional frameworks** with a view to boosting organ donation and transplantation, such as on criteria for acceptance of patients on the waiting list, acceptance of DCD, adequate post-transplant follow-up, and standards for transplantation centres. To stimulate expanded criteria donation, provide recommendations on which organs from which donors are valid.
- **Launch and support kidney sharing schemes and international organ exchange initiatives.**

### **Stakeholders:**

- **Be proactive in promoting the appropriate legal and institutional frameworks**, through sharing knowledge and expertise, and lobbying to reflect the needs and concerns of the organ donation and transplantation community.

## **CALL 3: STREAMLINE ORGANISATION AND INVEST IN LEADERSHIP AT ALL LEVELS**

Differences in the organisation of organ donation and transplantation services may explain the variation in transplantation rates among countries.

**The optimisation of the processes at each step from donor identification to transplantation is critical**, to ensure organs from deceased donors reach the recipient as quickly as possible. Special attention should be paid to Intensive Care Units (ICUs) since many steps leading to efficient deceased donor selection take place within them.

Further, an organised network of suitably trained and empowered donor coordinators has been key to the success of some countries such as Spain and Croatia in optimising the donation process.

### **RECOMMENDATIONS:**

#### **Member States**

- **Establish a well-organised donor coordinator network** at national, regional and hospital level.
- **Empower donor coordinators** by maximising and clearly defining their roles and investing in their leadership and communication skills.
- **Participate in meetings** organised by the European Commission and become involved in peer networks of National Competent Authorities.
- **Optimise the role and competency of ICUs** by making organ donation an integral part of end-of-life care.

<sup>3</sup>[https://ec.europa.eu/health/sites/health/files/blood\\_tissues\\_organs/docs/eutoolbox\\_living\\_kidney\\_donation\\_en.pdf](https://ec.europa.eu/health/sites/health/files/blood_tissues_organs/docs/eutoolbox_living_kidney_donation_en.pdf)



- **Support the establishment and organisation of transplant- or NCD-related foundations and patient organisations** to promote well-organised transplantation frameworks.

### European Commission

- **Cluster countries with similar issues and contexts**, and facilitate peer-to-peer exchange of best practices to help all Member States to benefit from the experiences of countries performing particularly well.

### Stakeholders

- **Provide support to regulators and policymakers** in setting up well-functioning organ donation and transplantation programmes.
- **Involve patient organisations** in the development of a network of suitably trained and empowered donor coordinators.
- Participate in the **activities of transplant- or NCD-related foundations and patient organisations**.

## **CALL 4: ALLOCATE APPROPRIATE FUNDS FOR ORGAN DONATION AND TRANSPLANTATION PROGRAMMES**

Robust funding is indispensable to achieve sustainable outcomes in organ donation and transplantation.

The EU's repeated calls for improving cost-effectiveness and equal access in healthcare are particularly relevant in the field, since transplantation is a highly cost-saving treatment that has the potential to contribute significantly to alleviating the mounting burden on healthcare and social protection systems across Europe.

### **RECOMMENDATIONS:**

#### Member States

- **Seize EU funding and technical support opportunities** by applying to programmes dedicated to developing and reforming infrastructure, education and training, digitalisation, and research in healthcare.
- **Devise policies to ensure appropriate reimbursement of costs to hospitals** for deceased donation.
- **Allocate funding to enhance the capacity to carry out more transplantations** (e.g. increase the number of transplantation units, surgical theatres, surgeons, nursing staff, ICU capacity and personnel).

#### European Commission

- **Engage and leverage support from the EU Structural Reform Support Service (SRSS)**, particularly to provide expert advice and plan for reorganisations and investment.
- **Foster greater investment in national transplant programmes** via the **European Semester** and **InvestEU** programme.
- **Increase funding opportunities under the new European Social Fund Plus (ESF+)**.
- Support Member State efforts to implement national action plans on organ donation via **European Structural Investment Funds (ESIF)** and its most relevant elements for health investments, **European Regional Development Fund (ERDF)** and **European Structural Fund (ESF)**.



## Stakeholders

- **Closely follow EU and national funding opportunities in the field** to ensure more funding is channelled towards the needs of the organ donation and transplantation community. **This could be realised collectively and facilitated via a partnership, such as an extension of this Thematic Network.**

## **CALL 5: PROMOTE EDUCATION AND TRAINING AMONG ALL STAKEHOLDERS**

Continuous education is a vital aspect of improving organ donation and transplantation, not only for informing patients and their families or training medical professionals, but also for raising awareness among the general public and policymakers. Accordingly, mass media information campaigns via all possible channels, including the press and visual and social media, remain important vehicles for diffusing information, educating, and raising awareness.

On the other hand, refusal of requests for solid organ donation by next of kin is a major barrier to increasing the supply of transplantable organs. **As such, honing communication skills is especially important for donor coordination in ICU or end-of-life settings.**

### **RECOMMENDATIONS:**

#### Member States

- **Promote public education** via the integration of organ donation and transplantation into the school curricula.
- Implement programmes to **increase access to information on organ donation and transplantation among the socially deprived, less educated communities and ethnic minorities.**
- **Ensure that the mandatory education of clinical staff** involved in organ donation and transplantation includes developing communication skills to better inform and support patients and their families.
- **Educate all healthcare professionals and medical students** on the importance of organ donation and transplantation.
- **Establish liaison with the mass media** to launch and support awareness-raising campaigns.

#### European Commission

- Support **the provision of education and training programmes** to facilitate the exchange of best practices between EU countries and health experts,
- Via DG Education, Youth, Sport and Culture (EAC), **implement initiatives under Erasmus+ to support the training and education** of healthcare professionals; such as educational symposia, online knowledge sharing platforms, exchange programmes and study tours to **stimulate practical learning**.
- **Continue to fund educational initiatives**, such as the ones under the EU Action Plan 2009-2015, namely the European Training Program on Organ Donation (ETPOD) providing formal training programs for healthcare professionals and the EUDONORGAN programme, which focused on training and raising social awareness via events.
- **Focus on exploring the factors at play in countries with low transplant rates.**



### Stakeholders

- **Advocate for and contribute to the continuous training of healthcare professionals** involved in organ donation and transplantation.
- **Organise campaigns** to empower patients and families, and inform the public, with the involvement of patient organisations.
- **Engage the political establishment** to further influence transplantation policies.
- **Create educational toolboxes** on organ donation and transplantation, such as the recent EKHA “Gift of Life” campaign<sup>4</sup>.

## **CALL 6: ERADICATE INEQUITIES IN ORGAN DONATION AND TRANSPLANTATION**

Equity in donation is a major principle of the **Guide to the Quality and Safety of Organs for Transplantation** developed by the European Directorate for the Quality of Medicines & HealthCare of the Council of Europe 2017. There is an urgent need to address persistent disparities which are pervasive in the demand for, access to, and waiting times for organ transplantation services due to ethnicity, education, socio-economic status, health illiteracy, language barriers and possibly gender.

The recent migratory waves may result in barriers in access to healthcare, including transplant services, **for immigrants and refugees in the EU.**

**Children** (due to difficulties to find donor organs of matching size) and **highly sensitised individuals** (due to enhanced rejection risk necessitating exclusion of potential donors) also have more difficult access to transplantation.

On the other hand, **transplant recipients may face significant difficulties upon entering or returning to the job market** following transplantation.

### **RECOMMENDATIONS:**

#### Member States

- **Develop national strategies and actions to address inequities** in organ donation and transplantation.
- Develop and facilitate implementation of programmes to **reintegrate transplanted patients into employment.**

#### European Commission

- **Develop strategies to address inequities in organ donation and transplantation and give greater visibility to issues of inequity**, by fostering the exchange of good practices among Member States and including the topic in National Competent Authority Meetings.
- Support specific programmes to **improve access for children and highly sensitised individuals.**
- DG Employment, Social Affairs and Inclusion (EMPL) and DG SANTE:
  - Promote initiatives to **enhance employment and rehabilitation opportunities** of transplant recipients.
  - Provide guidance on **measures to prevent living donors’ financial or employment loss due to donation.**

<sup>4</sup> <http://ekha.eu/gift-of-life/>



### Stakeholders

- Patient organisations: **Give visibility to the stories of those who have been impacted by inequities in access to transplantation** to ensure that their voice is heard by the broader public and political establishment.

## **CALL 7: BOOST BENCHMARKING**

Benchmarking is vital to help compare performances, evaluate and improve practices and results, monitor and improve equity in access, and better inform patients. **In the EU, there is an urgent need for reliable registry data assessing not only the number of transplants but also the long-term medical and social outcomes among recipients and living donors.** Access to such data could help shape clinical practice and future research.

Additionally, within countries, ensuring continuous assessment of results with external audits and comparison of hospitals' performance are key to assure quality and safety.

### **RECOMMENDATIONS:**

#### Member States

- Ensure that **all transplantation outcomes are well registered, analysed and acted upon**, in collaboration with national transplantation or organ-specific societies.
- **Demand and support the development of EU-wide registries and benchmarking platforms.**
- **Follow diligently EU guidelines and standards on data collection, provision and governance** to facilitate the work of registries and improve benchmarking.
- Have external audits and compare hospitals' performance.

#### European Commission

- Call on the Member States to **have all transplantation outcomes well registered, analysed and acted upon.**
- DG Communications Networks, Content and Technology (CNECT) and DG SANTE:
  - o Develop **common guidelines aimed at standardising data collection as well as the evaluation, auditing and benchmarking** of hospital performance.
  - o **Facilitate the establishment of EU-wide registries and the EU-wide collection and exchange of data.**
  - o Set up a **common EU-level vigilance and benchmarking platform for organ donation and transplantation.**
- DG CNECT, DG SANTE and DG Research and Innovation (RTD): **Address the development and use of digital technologies as well as means of data collection in organ donation and transplantation**, particularly through **Digital Europe** programme initiatives on eHealth and EU data.

#### Stakeholders

- Pay closer attention to EU initiatives on the digitalisation of the health sector and better communicate the prospects of enhancing the use of digital technologies in the field of organ donation and transplantation to policymakers.
- Call for the establishment of EU registries, **while promoting mutual trust and cooperation among healthcare professionals** to foster their willingness to share and learn from each other's data.



## CALL 8: LEVERAGE RESEARCH

Thanks to research efforts, organ transplantation outcomes have steadily improved over the past decades. However, there is still substantial room for further improvements in a number of areas, including but not limited to: the improvement of transplantation outcomes, donor optimisation, organ quality and preservation, alternative sources of organs, new technologies, health-economic aspects, patient-oriented outcomes, social integration, and ways to improve health literacy in organ donation and transplantation.

To enhance research, it is important that common priorities are set as part of a strategic research agenda and that research funding opportunities are fully exploited.

### RECOMMENDATIONS:

#### Member States

- **Provide public funding** for research on organ donation and transplantation **and seize funding opportunities at the EU level.**

#### European Commission

- **Provide specific funding opportunities for research and innovation in organ donation and transplantation under the next EU research and innovation programme, Horizon Europe**, as the topic closely pertains to the Cancer mission (since transplant recipients have a high cancer risk) and spans all three pillars of the programme (open science, global challenges and industrial competitiveness, and open innovation).
- **DG RTD and DG SANTE: Bring together stakeholders to outline the common priorities of the organ donation and transplantation research agenda, and reinvigorate ALLIANCE-O**, a 2004-2007 EU-funded initiative to harmonise respective national research programmes.

#### Stakeholders

- Be proactive in building a **strategic agenda for transplant research under Horizon Europe** and **submit proposals on organ donation and transplantation for future Horizon Europe calls.**



# Joint Statement: Rationale

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# INTRODUCTION

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Organ transplantation, as a therapeutic option for organ failure, has a major impact on patient survival, quality of life and societal cost. Although the European continent is considered to play a leading role in this field, transplantation rates remain markedly different among countries, suggesting ample room for improvement.

Over more than two decades, the European Union (EU) has played an active and leading role in stimulating transplantation in its Member States. Nevertheless, there remain many options for further improvement that could help to increase access to transplantation. The aim of this joint statement, prepared by several leading experts and relevant stakeholders in the transplantation community at EU level, is to describe practical possibilities and provide recommendations to positively influence organ donation and transplantation rates, and prevalence of patients living with a functioning transplant throughout Europe. Of note, these recommendations cover both adult and pediatric transplantation, although this text only contains specific references to children when the situation or their condition diverge from those of adults. This text will essentially focus on transplantation of solid organs and to a certain extent tissues (e.g. cornea, tendons), obtained from living or deceased donors.





# CURRENT STATUS

## 1.1. THE PLACE OF TRANSPLANTATION AMONG THERAPEUTIC OPTIONS

### 1.1.1. Severe organ failure

In Europe, non-communicable (chronic) diseases (NCDs) have become a major health issue over the last decades. They impose a substantial burden on health-care systems and have a crucial impact on economy, quality of life, employment status and social activities. About one in four Europeans suffers from one or more chronic diseases. NCDs cause 86% of European deaths and are responsible for 77% of the disease burden<sup>1</sup>.

Although all chronic diseases initially can be treated conservatively by lifestyle measures and/or drugs, a substantial number of affected people evolve to a status of severe organ failure. Functional failure then becomes so severe that a life-threatening condition ensues.

Due to a rise of comorbidities at the origin of NCDs and therapeutic improvements increasing the longevity of those affected, a further increase in their prevalence can be expected in the coming years. To keep these numbers under control, countries are recommended to become self-sufficient, first by preventing NCDs and their progression and, once those NCDs have progressed to end stage-organ failure, by providing sufficient transplants within their respective legal frameworks<sup>2,3</sup>.

Acute organ failure is less frequent, but often results in serious complications or a life threatening condition, whereby the risk of death for many patients is immediate and virtually irrevocable.

### 1.1.2. Therapeutic options for end stage organ failure

For end-stage organ failure there are only two therapeutic alternatives to a conservative (palliative) approach: artificial organ replacement therapy or human organ transplantation. Long-term, large scale artificial organ replacement therapy is well developed only for kidney disease. Hence, transplantation of human organs - obtained by deceased or living donation - is for many patients the only therapeutic solution to restore failing solid organ function.

### 1.1.3. Transplantation with various types of donation

Organs can be transplanted within the same person (autotransplantation) or from one human being to another human being (allogeneic transplantation). In this joint statement only



allotransplantation will be discussed. This implies the active retrieval of one or more organs from a donor to be transplanted into another human being – the recipient.

#### 1.1.4. Solid organ transplantation

Virtually every solid organ can be transplanted, although there are differences in incidence, largely depending on different technical possibilities and the availability of donor organs. Throughout the EU, the main solid organs that can be transplanted, in order of frequency, are: kidney (approximately 60%), liver ( $\pm 20\%$ ), heart ( $\pm 6\%$ ), and lung ( $\pm 5\%$ ) (fig.1)<sup>4,5</sup>. All other solid organ transplants (e.g. small bowel and pancreas) represent only a small fraction. Those transplantations are mostly life-saving and, at the same time, improve quality of life (see below). A disadvantage is the life-long need for immunosuppressive therapy to prevent rejection, which by itself causes complications (e.g. cancer, cardio-vascular disease, opportunistic infections, kidney failure) which, in turn, also affect health and survival outcomes.

In some cases of combined organ failure, more than one graft is transplanted (e.g. kidney-pancreas, kidney-liver).

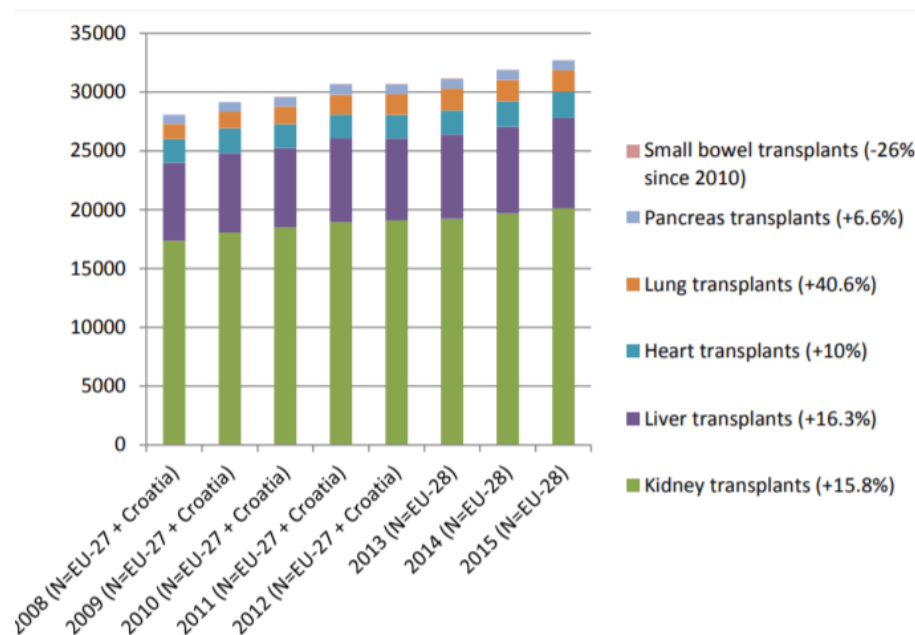


Figure 1: Organ Transplants in the EU in 2008-2015<sup>4,5</sup>

#### 1.1.5. Non-solid organ transplantation and tissue transplantation

Beside solid organs, certain types of severe functional problems can also be corrected by the implantation of tissues of human origin, such as cornea, heart valves, pancreatic islets,



tendons, cartilage, bone, skin, vessels (arteries or veins), among others. These therapies may have a life-saving impact, or in general, help to improve quality of life.

### 1.1.6. Living vs. deceased organ donation

Most organs for allotransplantation are obtained from deceased persons. Deceased donation occurs via two different clinical pathways; donations from persons declared dead by neurological criteria (donation after brain death - DBD) or death declared by circulatory criteria (donation after circulatory death - DCD). DBD is the most common deceased donation pathway. However there is a great difference in representation of deceased donation pathways among the EU countries<sup>4</sup>.

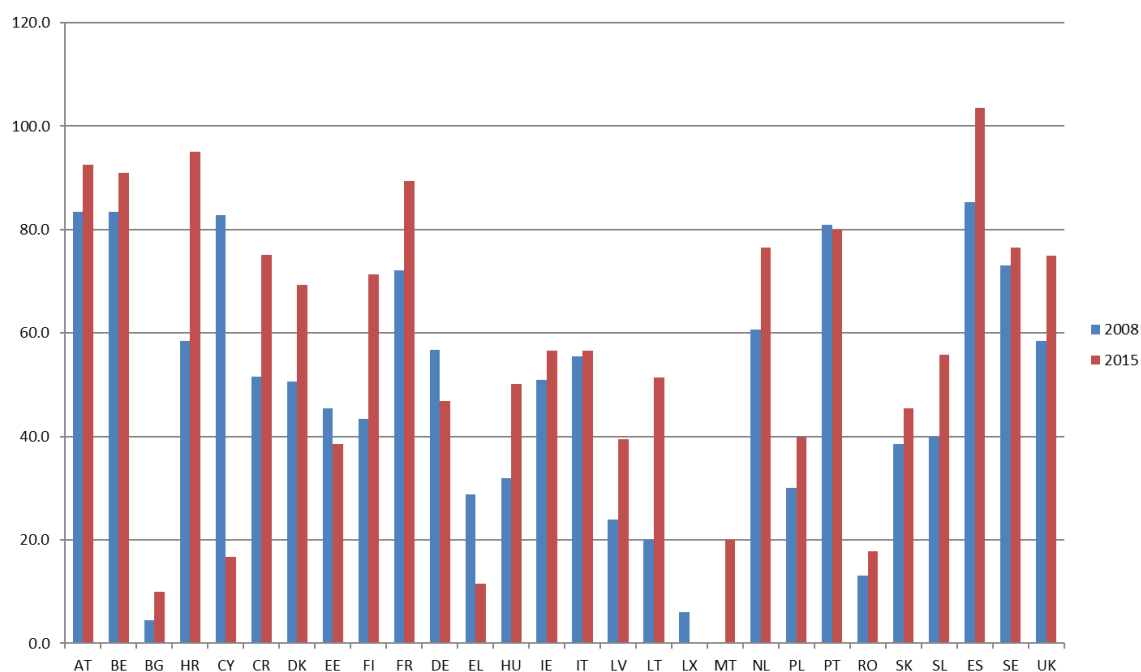
In some cases, a living person offers an organ to another person. The living donor provides one organ (in case of two organs per human being such as the kidneys), or a part of an organ (in case of liver, lung or pancreas), to the recipient. Living donation implies a meticulous evaluation, selection, pre-operative care and life-long follow-up of the donor to minimize the risks of jeopardizing his or her survival or quality of life as a result of donation<sup>6,7</sup>.

## 1.2. ACCESS TO TRANSPLANTATION THROUGHOUT EUROPE

### 1.2.1. Transplantation rates per country

The average incidence of all organ transplantation rate for the EU as a whole is 65 per million population (pmp). However, when taking into account individual EU countries, dramatic differences appear<sup>4,5</sup>, with figures ranging from less than 10 to more than 100 transplants pmp (fig. 2). Similar extreme differences among countries can as well be observed if we consider the transplantation rate for each individual organ<sup>5</sup>. Such variations cannot only be explained by population characteristics, epidemiologic factors and efficacy of prevention and pre-transplant therapy. Presumably, substantially more important are the differences in the way donation and transplantation activities are organized and implemented in each country, which also depends on local healthcare organization and the level of technical, organizational and infrastructural development.





**Figure 2: Total Number of Transplants pmp (all organs, all donor programmes)<sup>8,9</sup>**

Specifically, for kidney transplantation (where dialysis is frequently offered as an alternative option), non-medical, mainly economic factors are recognized to be fundamental in explaining inter-country differences in the provision of health interventions like dialysis<sup>10</sup>. Data on the factors influencing the choice between different kidney replacement therapy options (dialysis vs. transplantation) remain scarce. The first such comprehensive analysis of differences in prevalence of kidney replacement therapy modalities among countries will be delivered by the EU-funded project Effect of Differing Kidney Disease Treatment Modalities and Organ Donation and Transplantation Practices on Health Expenditure and Patient Outcomes (EDITH)<sup>11</sup>. The project is aimed at addressing the most challenging differences and providing recommendations for improvement.

Furthermore, the ratio between kidney transplantation from living or deceased donors varies substantially and, in many EU countries, remains below 15%, again suggesting underuse. In addition, among incident kidney replacement therapy patients included in the European Renal Association – European Dialysis and Transplant Association (ERA-EDTA) Registry, only 4% receive a pre-emptive kidney transplantation<sup>12</sup>. Of course, a number of patients starting dialysis are transplanted after a variable period on dialysis, but this is counterproductive, as the waiting time on dialysis negatively impacts survival after transplantation<sup>13,14</sup>.

### 1.2.2. Transplantation rates over time

Between 2008 and 2015 (the time period of the EU Action Plan on Organ Donation and



Transplantation – see below), an increase was observed in the incidence of transplantation for almost every solid organ, with an average rise of about 16%, and the most prominent increase for lungs (41%), followed by liver and kidneys (16%), heart (10%), and pancreas (7%). Small bowel was the only organ showing a decline in transplant rate (- 26%) (fig. 1)<sup>5</sup>.

Considering data per country, in most EU member states between 2008 and 2015 there was an increasing trend in all organ transplantation rates. Remarkably, in spite of all efforts by the EU, some countries displayed a decrease. Regarding deceased donation, again the majority of countries show an increasing trend. However, similarly to transplantation at large, some countries showed a decreasing trend (fig. 2)<sup>4</sup>.

Country evolutions for specific organs may deviate from these general trends, especially for heart or lungs which are less frequently transplanted. However, this is also the case for kidneys, although it is by far the most frequently transplanted solid organ<sup>15</sup>. The accessibility of transplantation varies among special patient groups, i.e. children, elderly or immunised candidates; marked differences among countries can be observed with regard to almost every key aspect of transplantation (i.e. the number of transplants per year, their evolution over time, and the percentage of living donation transplants). This suggests there is room for improvement in many EU countries to ensure an optimized access to transplantation in all valid candidates.

### 1.3. BENEFITS OF TRANSPLANTATION

#### 1.3.1. Life-saving capacity

For most failing vital organs (liver, heart, lungs), large scale and/or long-term rescue with artificial organs is not possible. In that case, transplantation is a relative or absolute emergency and, thus, a question of life or death. In contrast, in the case of End-Stage Kidney Disease (ESKD), which in high income countries is one of the most rapidly rising causes of death<sup>16</sup>, kidney replacement therapy with dialysis is common practice. However, in ESKD, kidney transplantation offers far better survival chances than dialysis<sup>17-19</sup>. In patients with imminent loss of vascular access for dialysis, transplantation represents a life-saving procedure.

Some 18 patients die every day in Europe while waiting for a transplant<sup>20</sup>, which corresponds to thousands of Europeans waitlisted for transplantation who die every year while still expecting a call for transplantation that never came<sup>4</sup>. Over 143,000 European patients were registered on a waiting list in 2015 (+5% compared to 2014). Five new patients are added to waiting lists every hour. In 2015 alone, 6,702 patients died while waiting for a transplant, which was an increase of 7 % vs. 2014. From this evolution, it can be expected that year-by-year,



more patients will be added to the waiting list, and an even greater proportion of patients will die on the waiting list, unless measures are taken to correct this deleterious trend.

While patients who are valid transplantation candidates also die without having received a graft in countries who perform well on the transplantation rate scale, such as Spain, Belgium and France, it can be surmised that in many other EU countries the picture will be more dismal, as in some of these countries the chances of valid candidates receiving a transplant are markedly lower<sup>4,12</sup>.

### 1.3.2. Health economic impact

Next to an impact on the economy at large, chronic diseases also specifically affect health economy, due to a high need for consultations, medication, surgery, imaging, technological intervention, and hospitalization. Also, in severe acute organ failure, societal cost may be enormous, due to a need for highly sophisticated intensive care therapy.

It is difficult to fathom the health economic impact of organ transplantation if no large scale alternative long-term therapy (i.e. artificial organ therapy) is available, which would mean comparing survival at an unavoidably high additional cost vs. imminent death restricting surplus expenses. However, in case of kidney transplantation, the most frequently applied option, dialysis is such alternative. Although the kidney replacement therapy population represents only 0.1-0.2 % of the general population, it consumes at least 2% of health expenditures, with more recent estimates referring to 5-6%<sup>21</sup>. Societal costs will further increase as the prevalence of kidney replacement therapy continues to rise throughout Europe<sup>22,23</sup>. Kidney transplantation is by far the most cost-effective kidney replacement therapy option, particularly after the first year of surgery, owing to a combination of prolonged survival, improved quality of life, and reduced net expenses for therapy per se, and reducing cost by at least 60%<sup>18,24-27</sup>. The economic impact of different kidney replacement therapy options will also be addressed by the EDITH project<sup>11</sup>.

### 1.3.3. Social re-integration

The ability to work is lost or seriously affected in the chronically ill population. The risk of unemployment increases with the combined number of chronic diseases<sup>28</sup>, which is a matter of concern as most of these conditions are intertwined and impact each other<sup>21</sup>. Reasons are frequent hospitalizations and interruptions for consultation or treatment next to loss of functional capabilities. The result has a major negative impact on economy with increased stress on social security combined with less productivity and buying power. Transplantation offers a possibility to break this vicious circle, although pro-active mechanisms are needed to



promote (re)activation<sup>29-31</sup>. Joint efforts are needed to develop and facilitate implementation of rehabilitation programs and encourage harmonization among EU countries with regards to employment.

### 1.3.4. Quality of life

While previously the main clinical focus points were survival and hard outcome events, recently attention is also paid to patient centered outcomes and quality of life. Both elements are in turn related to physical fitness, mental status and social deployment. Patients experience every day how harmful severe organ failure is, with a heavy burden on diet and invalidating side-effects such as shortness of breath, itching, poor mobility, exhaustion, fatigue, depression, sexual dysfunction and infertility. Most patients are prescribed a large number of drugs. Much time is spent in hospital, for consultation, undergoing ambulatory treatment or being hospitalized for complications, and on transport to and from the therapeutic unit. The situation is almost as difficult for the family. By restoring organ function to almost normal, transplantation offers an opportunity to restore quality of life, even in the case of kidney failure where, in contrast to other transplanted solid organs, large scale long-term artificial organ treatment (dialysis) is available<sup>17,25,32</sup>.

Specifically with regards to children, severe (chronic) disease impacts greatly on quality of life, also including development, growth, education and mental health, which are equally corrected by transplantation<sup>33,34</sup>.

The EDITH project (see above) is expected to provide further information on quality of life after transplantation<sup>11</sup>.

## 1.4. EU ACTION PLAN ON ORGAN DONATION AND TRANSPLANTATION

### 1.4.1. Role of EU in the health care field

Article 168 of the Lisbon Treaty on the functioning of the EU 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<sup>35</sup>. However, article 168 4 (a) also states that the EU should set high standards of safety and quality for 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 European Parliament. The upcoming Croatian Presidency (1 January 2020 to 30 June 2020) will allegedly also highlight transplantation as one of its priorities.

This political support allows the EU to help Member States in rolling out the transplantation process as a whole, fostering cooperation and ensuring standards across EU to enable all EU citizens to have access to comparable quality healthcare.

## **1.4.2. The EU Action Plan on Organ Donation and Transplantation**

### **1.4.2.1. Aims and scope**

The key aims of the EU Action Plan on Organ Donation and Transplantation (2009-2015) were (1) to increase organ availability, (2) to enhance efficiency and accessibility of transplant procedures and (3) to improve quality and safety of transplantation<sup>36</sup>. The action plan contained 10 priority actions (table 1)<sup>15</sup>. 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 for specific aspects. With this purpose in mind, more than 20 different EU-funded actions were organized (table 2)<sup>15</sup>. Another important EU initiative, the EDITH project (see above), was launched after finalization of the Action Plan<sup>11</sup>. An important part of this project (see above) is to roll-out a self-sustaining European Living Donor Registry (ELDR) for living donors.

### **1.4.2.2. Outcomes of the Action Plan**

The assessment of the Action Plan has been carried out using the data collected in Newsletter Transplant<sup>4</sup>. Although there is information for a large number of countries, a longer time period is needed to allow for a reliable comparison of the situation before, during and after this initiative. The 17% increase of overall transplantation rate (all organs) over the period of the Action Plan in all aggregated EU countries suggests a positive effect<sup>5</sup>. The most important percentage increase was for lung transplantation by 41%, while the rise for kidney and liver of around 16% corresponds to the overall average, and is almost entirely attributable to growth of living donation and donors after death declared by circulatory criteria.

To consistently underpin a rise in transplantation rate over time, an increase in the slope of yearly transplantation rates should be observed. A number of data sources allow to compare the periods for the whole of the EU before and during the Action Plan<sup>4,37</sup>. In these analyses, the slope of growth in transplantation rate did not change significantly during the entire time window. The statistics from Eurotransplant, covering 8 EU Member States representative of about 25% of the EU population but only referring to deceased donation, also exhibit a





stagnation in growth for kidney transplants from 1990 onwards, in contrast to a constant rise for liver and lung over the same period<sup>38</sup>. These figures suggest that changes over the last decades might at least in part be attributed to an increased use of certain organs rather than to an intrinsic rise in deceased donor organ availability.

However, these data should be considered 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<sup>39</sup>. A sudden decline in German transplantation rate as a result of this incident was observed. A similar decline in Greece and Cyprus<sup>5</sup>, two countries severely affected by financial crisis, is noteworthy. It is likely that the Greek and Cypriot governments had other priorities, but such decline has a counterproductive effect, by increasing rather than decreasing national health expenditure in a period of financial problems. It would be useful if specific measures are discussed by the European transplant community with representatives of these countries to support these countries in remedying their problems.

Specifically for kidney transplantation, 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, data comparison between 2011 and 2016 shows a rise in the total number of performed kidney transplantations per million people by 1.3 and in the percentage of patients on kidney replacement therapy living with a functioning kidney transplant by 0.9%<sup>15</sup>.

## 1.5. CONCLUSION

In spite of a good European track record in the field of transplantation compared to 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 further action would be helpful to generate a supplementary boost in activity. Only prolonged and coordinated actions will result in a sustained effort to improve conditions for patients and society by providing an additional increase in the prevalence of transplanted patients throughout Europe.



# TOPICS FOR ACTION

## 2.1. INTRODUCTION

Even if Europe is one of the leading continents in transplantation<sup>21</sup>, well-conceived planning and policy action are needed to further increase the numbers. Accounting for the European disparities as summarized in the previous section, a substantial number of patients with a potentially good outcome are probably denied kidney transplantation, as has also been reported outside Europe<sup>40</sup>. The ultimate target is not only an increase of donations and transplantations but also a rise in the percentage of patients living with a well-functioning graft. The optimal approach would be to set well defined ambitious aims, e.g. an increase of the number of transplantations 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 the realization of well-defined plans about which elements in which countries need support for development and in which areas gains should be accomplished, to be followed by calls to action at the national level and internal and external auditing.

Countries that could improve their track record could learn from countries performing well such as Spain, Belgium and France. In Spain for example, coordinated actions included the establishment of a donor coordination network, the engagement of critical care professionals, the continuous training of professionals, as well as educational activities with supportive participation of the media<sup>41,42</sup>, the evaluation of performance in deceased donation to identify areas for improvement and the reimbursement of hospitals for their participation in donation and transplantation activities. Innovation has entailed efforts to ensure the systematic referral of possible organ donors in intensive care units but also in in-patient units such as neurology and emergency units<sup>43</sup>, the use of organs from expanded criteria donors or imposing non-standard risk. As a result, the Spanish transplantation rate which was already high at the beginning of this century, has increased substantially over the last few years, e.g. for kidneys by more than 10% between 2011 and 2016<sup>42</sup>.

Many of the aspects discussed in detail below are intended to lead to an increased number of donations, and may automatically lead to a higher number of transplanted patients. They should be directed at overcoming current barriers to transplantation, which, apart from being medical, are essentially psychological and practical in nature, and may be avoided by appropriate measures, such as education or regulation<sup>15</sup> (table 3). Such barriers have up until now only rarely been studied<sup>44,45</sup>.



Nevertheless, next to this crucial aspect, society and medical community should also do their utmost to increase the longevity of each transplanted organ. When patients who already had received a kidney graft were asked about their priorities, the Standardized Outcomes in Nephrology (SONG) initiative found that, maintaining graft health appeared to be their main priority<sup>46</sup>.

Of note, the Council of Europe has in the past formulated several recommendations and resolutions concerning the items discussed below<sup>47</sup>.

## **2.2. MAXIMIZING THE ROLE OF DONOR COORDINATORS**

While in the USA organization of deceased donation has been based on the set-up of the so-called organ procurement organizations, successful European models are based on the figure of in-hospital donor coordinators who are key persons for the donation process. Organizing and optimizing the process of donation after death has proven to be possible by designating donor coordinators at each hospital with a potential for deceased donation. If necessary, donor coordinators can work on a part-time basis and combine several hospitals. Training of donor coordinators is essential to stimulate early and pro-active donor detection and appropriate donor selection, with special attention to techniques to communicate in critical situations. Internal and external auditing of donor hospitals to identify areas for improvement in the process of deceased donation is also required<sup>41</sup>.

Optimally the process of donor selection and identification should be coordinated by a different person from the one dealing with the recipient. Hospital donor and transplant coordinators should be part of an organized network at national and (if required) regional level. The process of their development and organization would profit from involving patient organizations, that could provide information on patient needs and perceptions.

## **2.3. OPTIMIZING THE ROLE OF THE INTENSIVE CARE UNITS (ICUs)**

Many steps leading to an efficient identification of possible deceased donors take place at the ICU. Hence, special attention should be paid to the processes taking place at the ICU<sup>48,49</sup>. Several of these seminal steps are summarized in table 4. Some of them will be discussed more extensively in other paragraphs of this section.

## **2.4. OPTIMIZING THE PROCEDURE FROM DONOR IDENTIFICATION TO TRANSPLANTATION**

Especially for deceased donation, where organs are allocated based on specific medical criteria, program organization and careful consideration of each step involved may allow



decreasing the time lapse between organ recovery and transplantation. In the case of kidney transplants, a short interval is important as the length of cold ischemia time (the period an organ is not perfused by blood so that no oxygen is delivered to it) is associated with the risk of delayed graft function<sup>50</sup>, graft failure and mortality<sup>51</sup>. It is desirable that planning in this area includes consideration of new developments in organ preservation and machine perfusion technologies.

Several measures can be taken to avoid loss of useful donors, such as combating: non-identification or non-referral of possible deceased donors; inappropriate decisions taken by non-qualified persons to classify a possible donor as medically unsuitable; inadequate clinical support to preserve optimal organ function in a potential donor; refusals for organ donation; and, objections by legal officials (coroners or judges) against recovery of organs and tissues from potential donors<sup>52</sup>.

## 2.5. EDUCATION

### 2.5.1. Improving communication skills of health-care professionals

Education of involved health-care professionals is essential, with specific focus on those implicated in the early stages of the process of deceased donation, such as emergency and intensive care physicians and donor coordinators<sup>41,53</sup>. Communication skills in relation to donation procedures are essential and should be part of regular medical education. This also includes the organization of training courses and the formulation of recommendations<sup>41</sup> and spans the entire spectrum of medical teaching, from student education to professional and specialist training and postgraduate learning. Professionals should be instructed on proposing systematically the option of organ donation when a patient dies or is about to die in conditions consistent with organ donation. In addition, also the quality of the information offered by physicians and nurses to the patient who is a potential candidate for transplantation should be optimized. This is especially important for kidney transplantation where alternatives like dialysis are available and in a number of cases the patient may be insufficiently informed about all treatment options, including the options of deceased or living donation<sup>15,54</sup>. Specific designation within a treatment team of health-care professionals who are trained for patient education might be extremely helpful. Educational processes should pay attention to the fact that procedures and information given might differ in the context of living vs. deceased donation, and information always should cover both.

### 2.5.2. Education of the public

Awareness on the need to contribute to donation and transplantation is also insufficient among the public, which includes policy makers and regulators. This necessitates continuous public



education, including adequate information offered in the regular educational system already to the very young. Involvement of the mass media (written press, television) and active partnership with journalists can be a major asset<sup>41</sup>.

Additional barriers are present in the socially deprived, less educated communities, and refugees, immigrants and ethnic minorities; these barriers should be specifically addressed via a better understanding of attitudes towards organ donation and transplantation in these populations, to further support with the development of targeted strategies, advice and with modifying possible beliefs and mindsets<sup>41</sup>. It could be extremely useful for the development of these education programs to involve patients and patient organizations.

The recent EKHA “Gift of life” campaign has made a toolbox available allowing individuals and societies to promote kidney transplantation at the national policy level in an equitable way throughout Europe<sup>55</sup>.

### **2.5.3. Patient education/information**

Full information is to be offered about all kidney replacement therapy options to all patients approaching ESKD. Likewise, full information on all therapeutic options should be provided to all patients in advanced stages of failure of other transplantable organs. Patient files at that stage should contain an explicit statement why a given patient is suitable for transplantation or not, and the views by the patient and his/her next of kin on this. Education should not be limited to the choice of treatment modality but should also include lifestyle (diet, maintenance of healthy body weight and blood pressure, exercise), because these may have an impact on outcomes post-transplantation.

Deficient health literacy and patient information also limit the expansion of kidney transplantation<sup>56</sup>. In the context of an analysis of the patient choice possibilities throughout Europe, EKHA distributed in 2017 a questionnaire among patients of 6 different European countries (table 5) asking patients for their satisfaction with information on different types of kidney replacement therapy<sup>15</sup>. Depending on the country, patient dissatisfaction regarding information about kidney transplantation ranged from 11-45% (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<sup>57</sup> published in 2014 based on a questionnaire in 2010-2011, and suggest little change over time, while underscoring the utility of a streamlined European educational approach about kidney replacement therapy including kidney transplantation but also transplantation at large. A centralized check by regulators on how the patient experiences



the quality of information delivery is to be considered as an approach to verify patient satisfaction in this regard.

### CASE STUDIES

In **Croatia**, several **elective courses** on organ donation and transplantation are provided for medical students in the Faculty of Medicine of University of Rijeka. In addition, an awareness-raising campaign by the Croatian Donor Network provides **flyers that include answers to Frequently Asked Questions about kidney transplantation, living donation and waiting lists**.

In **Finland**, the **web portal Health village/Kidney house (“Terveyskylä/Munuaistalo”)** educates **patients and the general public** on kidney diseases and their treatment, with special emphasis on donation and transplantation.

In **the Netherlands**, an information and awareness-raising campaign is undertaken as candidates for renal transplantation are offered **home visits** by a nurse and social worker. The family, friends, neighbours and colleagues of the patients are also welcome to these meetings, whereby information on end-stage kidney disease, renal replacement therapies as well as living donation is provided.

## 2.6. CLUSTERING OF COUNTRIES

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 to those with a medium or high rate, but for each group probably different strategies. This clustered approach does not exclude country-specific measures for problems occurring in one particular country. Such policy will probably necessitate in depth discussion of the local transplant community and authorities with representatives of other countries and the EU, taking into account the local circumstances and sensibilities to develop country-specific measures.

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 option(s) need(s) most improvement.

In addition, countries may be strong in transplanting some organs, but may be weak for others. Also these discrepancies are worthwhile to be addressed.

## 2.7. OPTING IN/OUT

Several EU countries still apply an opting-in strategy as deceased donor acquisition system, which necessitates the explicit permission of the potential donor or his/her family for organ removal, a possible factor for hampering 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). An alternative (or additional) approach to be considered is the implementation,



stimulation and simplification of affirmative donor registration<sup>40,58</sup>.

It has been suggested that opting-out results in higher transplantation rates as most explicitly experienced in Belgium, and some studies confirm this assumption<sup>59,60</sup>, 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). A recent analysis, however, found no difference in incidence of transplantation for all considered solid organs between opt-in and opt-out countries<sup>61</sup>. In addition, opting-out seemed to have a negative impact on living donation<sup>61</sup>. Of note, irrespective of the results, this type of studies may be prone to confounding and depends on the definitions used. Nevertheless, as results are contradictory, opting out alone cannot be viewed as a panacea to increase deceased donation rate. If taken into consideration, it should be accompanied by a series of other measures<sup>62</sup>, such as all those depicted in the other parts of this text.

#### CASE STUDY

**Country:** Italy

**Responsible organisation:** The Italian Ministry of Health

**Type of practice:** Tool/Instrument/Guideline, Information campaign

**Target population:** National residents over 18 years of age

**Start date of the practice:** 2012

**Background and objectives:** With the “Una Scelta in Comune” initiative implemented through a cooperation between the Italian National Transplant Network (CNT and regional transplant centres) and the Home Affairs Ministry as well as the information systems of town councils, registry offices of local town councils are allowed to get declarations of will on organ and tissue donation and transplantation when ID documentations of individuals are released for the first time or renewed. Such statements on donation are then directly transferred to the Italian National Transplant system, together with those collected at local health units and by the national donor association (AIDO). This new opportunity to express willingness about donation is regulated by a national law issued on February 10, 2010 and subsequent decrees. In addition to allowing to gather the declaration of the whole adult population within a set period (10 years, which is the period of ID paper validity), the tool gives the population an additional/institutional opportunity to be informed about organ donation and transplantation. From 2012 to date, more than 4 million Italian citizens/residents have expressed their will, out of which 70,8% consented to donation.

## 2.8. PROMOTION OF EXPANDED CRITERIA DONATION

A stimulus to increase deceased donation is the expansion of donor selection criteria. These include the selection of organs based on expanded criteria donors (such as those > 60 years old, or those > 50 years old with a least two of the following: history of hypertension, serum creatinine > 1.5 mg/dL or death from cerebrovascular accident) and donors after death declared by circulatory criteria (DCD). The latter are underutilized in many European countries<sup>4,63,64</sup>, although outcomes are adequate and almost comparable to the results obtained with organs transplanted from donors after death declared by neurological criteria (DBD)<sup>65,66</sup>.



There is a need for recommendations about which organs from which donors are valid options for expanded donation, so that the medical community has clear cut rules on how to approach this problem. For example, the proportion of older than 60-year-old donors per country ranges from 26 to 1 pmp<sup>4</sup>, and again, this gives the impression that also this donor pool is underused in many countries. In addition, there is a need for appropriate information including risks and benefits to the potential acceptor of an organ from an expanded donor.

The implementation of this approach might also necessitate the installment of specific legal and professional frameworks and adapted organ perfusion protocols to preserve organ quality and to prevent unnecessary discarding of valid organs<sup>67,68</sup>. In the Netherlands, all kidneys and expanded livers and lungs are put on preservation machines, and expanded livers and lungs are tested for quality, helping to determine whether they can be used or not. There is, however, a need for more evidence on whether machine perfusion has added value above the standard procedure.

#### CASE STUDY

**Country:** Croatia

**Responsible organisation:** Department of Urology, University Hospital of Rijeka

**Type of practice:** Service delivery approach/method, Training

**Target population:** Transplant patients

**Start date of the practice:** 2016

**Background and objectives:** The persistence of donor organ shortage requires an expansion of the criteria for acceptability of deceased-donor organs, thereby increasing the number of “marginal” donors. This programme aims to address this issue through the use of “en-bloc” and “horseshoe” kidneys. In addition to increasing the number of transplantations, knowledge and experience on these special cases is also disseminated throughout Croatia via congresses and seminars.

## 2.9. OPTIMISING LIVING DONATION

Living donor organ transplantation is used in almost every European country but the extreme differences in the percentage share this takes in the overall transplantation landscape underscores that in many countries there is room for improvement.

Although almost all European countries practice some living donation, frequency is often low, especially in countries where overall kidney transplantation rate is low, but also in countries with higher transplantation rates like Belgium and Austria.

To optimize living donation, expansion of the donor and recipient criteria, ensuring that donation is financially neutral (e.g. compensating the donors for loss of income or need for follow-up and donation-related complications), activating spouse and unrelated altruistic donation and application of uniform procedures for donor/recipient information and recruitment, all could be useful<sup>69</sup>. All measures in this respect should however be undertaken





with a guarantee for donor protection. Another currently underexploited option is kidney sharing schemes (exchange of organs among donor/recipient pairs who cannot exchange organs with their own partner). Such programs have been rolled out in a number of EU countries but remain non-existing or very limited in others<sup>4,70</sup>. Of note, a number of European and cross-border initiatives have recently been launched to cope with this situation. The European Network for Collaboration on Kidney Exchange Programmes (ENCKEP), an EU-supported European Cooperation in Science and Technology (COST) action, is intended to share current practices on kidney exchange and to identify risks and opportunities<sup>71,72</sup>. There are also a number of specific cross-border initiatives (Italy, Portugal and Spain; and Czech Republic and Austria)<sup>73,74</sup>.

All this also brings 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<sup>75</sup>. Ethical frameworks should be developed for unrelated living donation, taking heed of the potential negative aspects (health risks for the donor and whether the donation is truly voluntary), and balancing them against the positive aspects (benefits to the recipient, psychological benefits of the altruistic act of donation to the donor and reduced societal cost).<sup>76</sup>

## 2.10. REDUCING FINANCIAL BARRIERS

It is important that national policies in Europe also focus on inadequate reimbursement of costs to hospitals for deceased donation and organ retrieval<sup>56</sup> and reimbursement differences between dialysis and kidney transplantation, as in most countries dialysis is financially more rewarding to care providers. Any clinical activity emanating directly or indirectly in transplantation should be subject to a fair remuneration. This might also include higher reimbursement for dialysis units/nephrology sections with higher percentages of patients living with a functional graft among their kidney replacement therapy population or other measures to decrease the reimbursement gap between the different kidney replacement modalities.

It is furthermore essential that expansion of transplantation numbers is supported by adequate infrastructural capacity – surgeons, operating theatres, intensive care units with sufficient capacity to maintain hemodynamic status of a potential donor until organ removal, but also appropriate hospitalization and outpatient follow-up capacity and well trained nursing and medical staff - so that an increase in donor selection and transplant interventions can be accommodated. It would be useful that the transplant community provides recommendations



about an optimal infrastructure and staffing of transplant units, and in as far as transplant donor candidate management is concerned, of intensive care units.

#### CASE STUDY

**Country:** Belgium

**Responsible organisation:** Belgian Federal Government, Federal Public Health Service

**Type of practice:** Tool/Instrument

**Target population:** All patients with end-stage kidney disease who are valid candidates for transplantation

**Start date of the practice:** 2003

**Background and objectives:** This initiative decreases the gap in reimbursement benefit between different renal replacement strategies in case of a pay-for-service system (as is applicable for dialysis in Belgium). The relatively favourable reimbursement of hospital hemodialysis may stimulate hospitals or providers to prefer the latter strategy as it is financially more rewarding than transplantation. This reimbursement initiative is partially (but far from entirely) compensating for the financial disparity between in-hospital hemodialysis and transplantation.

### 2.11. INTERNATIONAL ORGAN EXCHANGE

Several EU countries do not collaborate with one of the three programs for deceased donor organ exchange (Eurotransplant, Scandiatransplant and the South Alliance for Transplantation) and do not have an efficient internal system so that gradual incorporation in one of the existing programs likely would boost their activity<sup>77</sup>. It is impossible to exactly define the impact of such exchange programs on transplantation rates, but in countries newly adhering to such systems they may generate a boost in activity as experienced in Croatia at the beginning of this century or more recently in Hungary.

EU member states have shown great interest in participating in an IT-platform that connects allocation offices to make surplus organs, that cannot be matched within the system, available outside (FOEDUS-EOEO), which might be especially beneficial for transplantation of children and adolescents<sup>5</sup>.

Not only for children, but also for other vulnerable patient groups (i.e. highly sensitized patients, candidates for cross-over transplantations), broader international collaboration should be established and encouraged to provide better access to transplantation.

### 2.12. EQUITY

Women are more often living donors than living recipients<sup>4,78</sup>. On the other hand, recipients of organs (irrespective of living or deceased donation) are mainly males, but that is probably also reflecting a gender bias in the incidence of transplant necessitating pathologies, as males seem to be more prone to developing some forms of chronic organ failure like end-stage kidney disease<sup>79</sup>.



In addition, other subgroups such as children and immunologically highly sensitized people (e.g. people with a history of multiple transfusions, previous transplants or pregnancies) have more difficult access to transplantation for technical reasons. For these populations, the development of dedicated programs is needed (e.g. identifying donor organs of appropriate size for children, or detecting appropriate donors by specific cross-matching methods for the highly sensitized)<sup>80</sup>.

Furthermore, other inequalities have been reported to exist in certain population cohorts, which may make it more difficult for these patients to access transplantation care. These inequalities have been associated with ethnicity, education, socio-economic status, religion, health illiteracy or language barriers<sup>81</sup>, deserving specific attention. Educational programs to increase outreach to these populations and overcoming cultural or linguistic barriers are of critical importance in this process.

In the UK, people of Asian or African-Caribbean descent are three to four times more likely than white people to develop end-stage renal failure and need a kidney transplant. However, UK Transplant data shows that Asian and African-Caribbean make up 23% of the kidney waiting list, whilst representing only 8% of the general population<sup>82,83</sup>.<sup>84</sup>

In Sweden, socioeconomic status-related inequalities exist with regard to placement on the waiting list and receipt of a transplant once waitlisted<sup>84</sup>.

African-American adults in the US are less likely to receive organ transplants compared with white adults<sup>85</sup>. Also for Hispanics and Asians, the proportion of waitlisted patients largely exceeds the number of available donors from the same ethnic background<sup>85</sup>. This was attributed to a multitude of reasons, encompassing lower awareness of transplantation, religious or cultural distrust of the medical community and fear of racism. Likewise, people of African-American descent are less likely to donate their organs compared to white adults<sup>85</sup>. Given that ethnicity is an important determinant of a strong match between donor and recipients, and closer matches can be expected for individuals in the same ethnic groups, this may create a smaller donor pool among the non-Caucasian community, which makes it difficult to find sufficient donors for this group.



The recent migratory waves in European countries may result in barriers for immigrants and refugees in access to healthcare, including transplant services,. Immigrants may face issues with access to healthcare as a result of linguistic obstacles, unawareness of service availability, limited resources, and lack of perception of chronic and mainly asymptomatic illnesses, such as renal insufficiency. All these factors may lead to delayed treatment and non-familiarity with the medical model of the hosting countries<sup>86</sup>. Despite existing legal frameworks, practical access to care before, during and after transplantation may prove to be extremely complicated for immigrants and particularly those without documents, who are subject to a vast burden of disparities, compared to documented immigrants and citizens.

#### CASE STUDY

**Country:** Croatia

**Responsible organisation:** Department of Urology, University Hospital Rijeka, Rijeka, Croatia

**Type of practice:** Service delivery approach/method, Training

**Target population:** Organ donors and transplantation candidates who are Jehovah's witnesses

**Start date of the practice:** 2016

**Background and objectives:** As Jehovah's Witnesses do not accept blood transfusions for religious reasons, it is often assumed that they are against organ donation and transplantation. However, it is possible to perform transplants without involving blood transfusions, meaning the procedure would not be rejected on religious grounds. This requires medical professionals to agree to performing the surgery without the use of donated blood, and requires a close teamwork between anaesthesiologists, transplant surgeons, and other healthcare professionals involved in the process. The practice increases the Jehovah's Witnesses community's access to organ transplantation, by implementing the necessary procedures routinely and aims to disseminate the knowledge thereof through Croatia, via congresses, seminars, and the Croatian Transplantation School.

### 2.13. LONG-TERM PRESERVATION OF GRAFT ORGAN FUNCTION

Although it is important to increase the number of donations and transplantations which automatically will increase the number of transplanted patients, the other side of the coin, i.e. preserving the function of the grafted organ as long as possible once it has been transplanted, is an as important target. Keeping a well-functioning organ as long as possible is the most precious outcome for patients<sup>46</sup>. This entails avoidance of damage to the grafted organ by rejection, medication, complications or comorbidities, avoidance of damage to other organs (e.g. kidney damage in heart or liver transplants due to immunosuppressive medication) as well as specific attention to fatal outcomes or complications jeopardizing future transplantation (e.g. opportunistic infections or malignancy)<sup>87</sup>. Especially for kidney transplantation, delayed graft function has been related to accelerated graft failure on the long term<sup>88</sup>. In patients with definitive graft loss, all possible measures should be taken to allow a smooth transition phase towards a novel transplantation, including timely and uncomplicated move of patients with failing kidney grafts to dialysis.



In line with this aspect, there is an urgent need for reliable registry data not only assessing number of transplants but also their long-term outcomes, which could help shaping clinical practice and future research to better preserve graft function and improve survival.

## 2.14. BENCHMARKING

Successful optimization of donation and transplantation programs necessitates continuous assessment of the results with external audits and comparison of hospitals with regards to their results and efficiency<sup>89</sup>. A quality control system for organ donation that is universally applied throughout Europe is necessary. Selecting the best performers and studying their approaches will lead to identification of a number of critical factors for success, which then can be implemented elsewhere to improve overall efficacy of country programs<sup>90</sup>. To allow adequate procedures necessitates a reliable and uniform pan-European registration system.

Specific frameworks promoting and guiding appropriate evidence-based decision making in the context of transplantation should be facilitated and supported. Such recommendations might include but should not be limited to: criteria for acceptance of patients on the waiting list; adequate follow-up post-transplant; criteria for DCD transplantations (see above); and standards for transplantation centers.

If European recommendations will be made to offer guidance to countries on ways to improve their transplantation rates, it would be useful that subsequent check-ups are performed on how and in how far these advices were implemented at a national level.

Likewise, under the impulse of Council of Europe committee on organ transplantation, initiatives to compare organ donation frequency and transplantation outcomes of different countries can be of help stimulating countries seeking out best practices<sup>91</sup>.

Also this type of vigilance system should be based on a common pan-European platform, which does not exclude specific accents for individual countries. European countries should preferably be stimulated to share best practices so that countries performing not so well can learn from countries with better results.



## 2.15. RESEARCH

Several seminal questions in the field of transplantation remain partially or totally unsolved, comprising basic patho-physiologic, immunologic, molecular biologic as well as clinical, societal, psychological and quality of life aspects.

In addition, there is room for improvement of technical and organizational approaches, and the definition of appropriate endpoints. As the EU has a strong portfolio of research programs, transplantation deserves specific attention for funding and support. It would be of interest to patients, the medical professional community as well as society, that this research would be streamlined in the following priority areas: 1) improving organ quality and assessment, and increasing organ availability; 2) socio-economic and societal impact of transplantation; 3) extending the life of a transplant and reducing graft loss; 4) benchmarking, professionalism and governance; and 5) what matters to patients. Table 6 provides a non-exhaustive list of a number of topics which are of prime interest to the medical and patient community, with the intent to help to better shape future research priorities in the field.

### CASE STUDY

**Country:** Germany

**Responsible organisation:** A consortium of nephrologists, transplant surgeons and nephrologists in collaboration with Eurotransplant.

**Type of practice:** Research project

**Target population:** All Eurotransplant-associated countries (except Luxembourg)

**Start date of the practice:** 2018

**Background and objectives:** The objective of this project is to accurately predict the risk of delayed graft function and transplant loss during the first year via an investigator-led trial to develop a two-stage clinicopathological algorithm for the quality assessment of deceased donor kidneys. Based on retrospective evaluation of clinicopathological data and prospective validation, the clinical data and reproducible histopathological criteria to be incorporated into a two-step algorithm will be identified. This score will help risk assessment in order to maximise exploitation of the scarce pool of deceased donor kidneys without risking adverse outcomes, particularly for frail recipients. This is neither intended to dictate acceptance or discard of a deceased donor kidney nor is it intended to improve the already good rate of one-year transplant survival for the currently transplanted deceased donor kidneys. The working hypothesis of this project is that for some donor/recipient matches clinical data alone and for the rest clinical plus histopathological data at the time of transplantation are sufficient to accurately predict the risk of delayed graft function and transplant loss within the first year.



## CONCLUSION

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In spite of a good European track record in the field of transplantation compared to other continents, the substantial disparities among EU countries suggest room for improvement. The EU launched an Action Plan to increase organ donation and transplant activities between 2009 and 2015, but further action would be helpful to boost activity. One of the main focus points suggested in this review is that, considering that substantial differences persist among countries, there is a need for further in-depth analysis of these discrepancies to inform the realization of strategies to deliver across the board improvements. There is also a need for educating patients, professionals and general population alike, as well as for the provision of appropriate legal consent and financial frameworks favoring organ donation and transplantation. Only prolonged and coordinated action will result in a sustained effort to improve conditions for patients and society.

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# ANNEX

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**Table 1: EU transplantation action plan (2008-2015) – ten priority actions**

<b>OBJECTIVES</b>	<b>10 PRIORITY ACTIONS</b>
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 transplant 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



**Table 2: EU supported programs to stimulate transplantation**

<b>PROGRAM</b>	<b>MAIN Purpose or Focus</b>
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 European Union
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	<b>A unified approach to evaluating cellular immunotherapy in solid organ transplantation</b>
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



**Table 3: Non-medical barriers to transplantation**

Stakeholder level	Type of Barriers Encountered
Barriers on the patient level	<ul style="list-style-type: none"> <li>- Problems with attitude, role perception, motivation</li> <li>- Distrust of health care professionals</li> <li>- Lack of knowledge</li> <li>- Fears and concerns               <ul style="list-style-type: none"> <li>o Fear of rejection or graft failure</li> <li>o Fear of surgery</li> <li>o Fear of medication, side effects</li> <li>o Negative experiences (self or others)</li> <li>o Fear for living donor's health</li> </ul> </li> <li>- Sociocultural background</li> <li>- Religious reasons opposing against transplantation</li> <li>- Unsuitable living circumstances</li> <li>- Costs</li> <li>- Shortcomings in patient efforts or investments</li> <li>- Reluctance to ask potential living donors</li> <li>- Lack of social support</li> <li>- Lack of adherence or hygiene</li> </ul>
Barriers at the level of the health care professional	<ul style="list-style-type: none"> <li>- Problems with attitude, role perception, motivation</li> <li>- Lack of knowledge and expertise</li> <li>- Fears and concerns</li> <li>- Working style</li> <li>- Difficulty in selecting patients</li> <li>- Lack of communication skills</li> </ul>
Barriers at the level of the health care system	<ul style="list-style-type: none"> <li>- Financial barriers</li> <li>- Lack of supporting staff</li> <li>- Competition with other treatment modalities</li> <li>- Doing well on other treatment modalities</li> </ul>

Modified based of refs<sup>15,44,45</sup>



**Table 4: Steps optimizing the processes taking place at the ICU**

- Routine referral of potential donors to DTCs or OPOs
- Definition of simple clinical triggers for starting donor identification
- Donor suitability assessment by DTCs or OPOs and not by treating physicians
- Systematic brain death testing
- Optimization of clinical condition of candidate donor until donation
- Appropriate family approach to discuss potential donation
- Education and training of involved professionals
- Audits and performance assessment
- Identification of one clinician per ICU unit to specifically stimulate donation
- Considering donation as a definite part of end-of-life care

ICU: Intensive care unit; DTC: donor transplant coordinators; OPO: organ procurement organization.

Data modified from ref<sup>48</sup>.



**Table 5: Results of patient questionnaire on satisfaction about kidney transplant education and information in 6 EU countries**

Question	FR	GR	LI	NL	SL	SP
Found 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

FR: France; GR: Greece; LI: Lithuania; NL: the Netherlands; SL: Slovenia; SP: Spain

Data modified from ref<sup>15</sup>





**Table 6: Suggested research topics**

<p><b>Improving organ quality and assessment, and increasing organ availability</b></p> <ul style="list-style-type: none"> <li>• <i>Studies on novel preservation methods and new technology for testing organ quality</i></li> <li>• <i>Establishing pan-European follow-up data collection and use (i.e. registries)</i></li> <li>• <i>Exploring alternative sources of organs (hybrids, xenotransplantation)</i></li> <li>• <i>Study of factors affecting outcomes of expanded criteria donation and donation after circulatory death</i></li> <li>• <i>Comparison of strategies for Increasing donor availability</i></li> <li>• <i>Identification and prevention of factors leading to delayed graft function</i></li> <li>• <i>Studies on non-HLA incompatibility</i></li> <li>• <i>Development of strategies combating acute and chronic rejection</i></li> <li>• <i>Development and assessment of methods to improve transplant rates in children, elderly and highly sensitized patients</i></li> <li>• <i>Study of barriers against transplantation and measures to correct those; comparison among countries</i></li> </ul>
<p><b>Socio-economic and societal impact of transplantation</b></p> <ul style="list-style-type: none"> <li>• <i>Health-economic comparison of transplantation programs in different EU countries</i></li> <li>• <i>How to decrease societal cost of transplantation</i></li> <li>• <i>Studies of the ecologic footprint of kidney transplantation vs. dialysis</i></li> <li>• <i>Studies of factors refraining reemployment after transplantation</i></li> </ul>
<p><b>Extending the life of a transplant and reducing graft loss</b></p> <ul style="list-style-type: none"> <li>• <i>Defining surrogate endpoints for post-transplant outcomes</i></li> <li>• <i>Identification of biomarkers for acute and chronic rejection, graft failure and negative outcomes at large</i></li> <li>• <i>Detection of mechanisms causing graft dysfunction via development of fibrosis and ways to prevent this evolution</i></li> <li>• <i>Prevention of post-transplantation malignancy and cardio-vascular disease</i></li> <li>• <i>Prevention and adequate treatment of post-transplant infections</i></li> <li>• <i>Strategies to improve outcomes at transition of patients with a failing kidney transplant to dialysis</i></li> </ul>
<p><b>Benchmarking, professionalism and governance</b></p> <ul style="list-style-type: none"> <li>• <i>Certification of skills of professionals and professional regulation</i></li> <li>• <i>Transplant outcome benchmarking (based on registry data)</i></li> <li>• <i>Study of barriers to transplantation in different countries</i></li> </ul>
<p><b>What matters to patients</b></p> <ul style="list-style-type: none"> <li>• <i>Studies on patient-reported outcomes</i></li> <li>• <i>Study of mechanisms ruling treatment choice (transplantation vs. alternatives such as dialysis) and suggestions on how to channel valid patients to transplantation</i></li> <li>• <i>Comparison of educational programs (general population, patients, students, professionals) and development of best practices</i></li> </ul>

