Proceedings of the Workshop
"The Role of Science in the Development of International Standards of Organ Donation and Transplantation"

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A Workshop organized by the Pontifical Academy of Sciences

and co-sponsored by the World Health Organization

Editorial group:

Nancy L. Ascher, Professor and Past Chair, Department of Surgery, University of California, San Francisco, United States. Past President, The Transplantation Society (TTS)

Beatriz Dominguez-Gil, Director General, Organización Nacional de Trasplantes, Madrid, Spain

Efstratios Chatzixiros, Adviser, Transplantation and Products of Human Origin, Department of Health Products Policy and Standards, WHO, Geneva, Switzerland

Francis L. Delmonico, Professor of Surgery, Harvard Medical School at the Massachusetts General Hospital, and Chief Medical Officer, New England Donor Services, Boston, United States.
Councilor of the Pontifical Academy of Sciences (PAS) and Chair, WHO Task Force Donation and Transplantation of Organs and Tissues.

Disclaimer: The perspectives expressed during the presentations of this Workshop were given with absolute academic freedom. Although published by the Pontifical Academy of Sciences (PAS), the Proceedings represent only the points of view of the participants and not those of the PAS nor those of the World Health Organization.

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EXECUTIVE SUMMARY

Transplantation is the best if not the unique treatment for patients with end-stage organ failure. However, thousands of patients die or endure a poor quality of life (QoL) while waiting for a transplantable organ. The shortage of available organs is also the root cause of organ trafficking and transplant tourism, practices that pose a severe risk to individual and public health and to the notion of national self-sufficiency. Organ trafficking and transplant tourism violate fundamental human rights, as protected in the WHO Guiding Principles on Human Cells, Tissue and Organ Transplantation.

Pope Francis has urged the international community of transplant professionals to address organ trafficking as a crime against humanity. Because combatting organ trafficking requires addressing its root cause, which is the inability of countries to provide for the transplantation needs of patients, **the Pontifical Academy of Sciences (PAS) convened in June 2021, a Workshop for promoting *the Role of Science in the Development of International Standards of Organ Donation and Transplantation*.** The Workshop addressed the following health-care issues:

- Evaluation of the burden of disease that results in organ failure and necessitating organ transplantation for treatment and the need to include transplantation in the treatment continuum as part of universal health-care;
- A compelling case for prioritizing organ transplantation in the treatment of organ failure;
- Technical considerations for developing and optimizing organ transplantation as a health-care treatment option for patients with organ failure; and
- Strengthening the regulatory capacity for oversight of practice.

The Workshop was co-sponsored by the World Health Organization (WHO) and was attended by more than 200 health officials and transplant professionals from 63 countries throughout the world. A panel of renowned international experts comprehensively presented the latest scientific evidence and best practices, analysed the various factors that are relevant in the development of a national transplantation system and suggested common standards.

The Burden of Disease

The burden of disease that results in organ failure is increasing in relation to underlying risk factors. There is insufficient progress to reverse trends in the burden of these diseases that have a profound social and economic impact on communities and on individuals. The justification for action is strong. Data need to be examined to implement preventive measures, but also to utilize the most cost-effective treatment for patients who are suffering with organ failure and to have access to care through organ transplantation. **Transplantation should be considered in the continuum of care for patients with chronic organ disease, in keeping with pursuit of Sustainable Development Goals 3.4. (premature mortality from non-communicable diseases) and 3.8 (Universal Health-Care).**

A compelling case for prioritizing organ transplantation in the treatment of organ failure: benefits of Kidney and Liver Transplantation

There is a disproportionate worldwide use of dialysis as kidney replacement therapy when compared to kidney transplantation, that cannot be explained when governments consider the survival, QoL and cost-effectiveness advantage of kidney transplantation. Worldwide in 2019, 100,094 kidney transplants were performed, compared to more than 5 million patients undergoing dialysis annually. People with chronic kidney disease experience reduced QoL because of high symptom and treatment burden. Once an individual reaches end-stage renal disease, the treatment modalities are limited to transplantation, hemodialysis and peritoneal dialysis. In all WHO regions, with the possible exception of Africa, hemodialysis is more costly than maintaining a kidney transplant, and this cost difference is widest in high-income countries. **The scientific analysis of cost and outcome data suggests that kidney transplantation should be considered the optimal treatment for renal failure. The current reality that this is not the case in so many countries is unacceptable.**

There is substantial evidence that liver disease is increasing in incidence and is a major source of death and disability in the world. Liver disease affects patients of all ages compromising their life expectancy, QoL and productivity. Liver transplantation is an effective treatment for chronic liver disease, fulminant hepatic failure and hepatocellular carcinoma with excellent short and long-term survival. The alternative to transplantation is death in patients with both acute and chronic liver failure. **Many countries do not have active liver transplant programs** and those newly developed in countries without robust governmental support, generally initiate the programs utilizing living donors. This approach requires extensive surgical expertise and substantial hospital resource and relies on protection of living donors from exploitation. The extensive hospital support often limits activity to private for-profit institutions.

Technical Considerations for Developing and Optimizing Organ Transplantation

The decision to embrace and support transplant activity must be assessed on the background of the community's (country's) burden of disease, loss to the community of productive members and other health obligations. It may be that the community must start with the greatest potential for benefit (e.g. living donor kidney transplant in place of dialysis therapy or living donor liver transplant for liver cancer). Once the infrastructure is in place and the work force has been developed, transplantation services may be expanded to include deceased donor transplants and the indications widened. **Requirements for the development of a transplant program are: 1) Legislation, credentialing and regulatory oversight; 2) Financing of all aspects from donation to the long-term care of living donors and recipients; 3) Workforce; 4) Interventions and procedures; 5) Laboratory; 6) Medication; and 7) Protocols.** (See Table 1 of the Proceedings pages 20 -21)

The Legislative Framework

Consistent with WHO Guiding Principles, legislation pertaining to donation and transplantation should be adopted to establish a **National Transplant Agency** that provides oversight and coordination of donation and transplantation activities, and the establishment of **registries and a**

system of traceability and vigilance to ensure safety (both for donors and recipients), efficacy and quality of organs. Legislation should provide the **legal basis for organ removal from deceased donors**, with the ultimate goal to maximize donations from the deceased. Legal and logistical steps are needed to establish deceased donor programs where these do not exist, and to make existing programs as effective and efficient as possible. Organs should not be removed from the body of a deceased person unless that person has been certified dead in accordance with the law and unless the consent or authorization required by law has been obtained. **A schematic of the minimum health requirements for performing deceased organ transplantation is provided from these Proceedings.** Intensive care professionals should be actively engaged in the development of deceased organ donation programs and the criteria for the determination of death.

The Council of Europe has been actively involved in the elaboration and promotion of legal instruments that aim at harmonizing international legal frameworks to provide concerted and effective efforts to prevent and address **illicit transplantation practices** at international level. The Council of Europe Convention against Trafficking in Human Organs is built around the notion of the "illicit removal of human organs". This is defined as organ removal: 1) without the free, informed and specific consent from living donors or without valid consent or authorization for deceased donation; or 2) in exchange for financial gain or comparable advantage. Any subsequent action involving illicitly removed organs is also considered to be organ trafficking. By ratifying this Convention, parties show their commitment to preventing and combating these crimes.

Deceased Organ Donation

Well-established deceased organ donation programs are essential components of each transplant system and a prerequisite for achieving self-sufficiency. Life-saving transplant treatments (such as heart transplantation) cannot be developed unless deceased organ donation is established. Lung and liver (kidney as well) transplant programs should rely on deceased donation to avoid the burden and minimize the risk for living donors. Therefore, national competent authorities should target this goal as a priority when building up transplant programs or optimizing access to transplantation treatment.

Living Organ Donation

Living kidney and liver donation has proven to be safe when performed under an appropriate framework of donor care even though an inevitable small mortality risk is well documented. Transplantation of kidneys from living donors is considered a necessary adjunct today to achieving national self-sufficiency. However, **the national program of organ transplantation should not exclusively rely on living donation.** Governments should not enable rich patients to travel to foreign destinations and undergo kidney transplantation from living donors that are unknown to the recipients. **Registries of living donor transplants** should focus upon the safety and well-being of the living donor. Complications that require re-hospitalization of the living donor should be recorded and so should donor deaths associated with the procedure of organ removal. Thus, registries provide important data to base the donor´s consent on the assessment of known risks (at the specific center, national and international level).

Strengthening the Regulatory Capacity for Oversight of Practice

There is no standard of data collection by responsible national agencies to assess performance of transplant centers and improve patient care for transplant recipients and the living organ donors. Ideally, data should be collected at three levels: internationally (exemplified by the Global Observatory on Donation and Transplantation), nationally and at a center level. National waiting list, donor, recipient and follow-up registries are essential **to achieve and continuously monitor quality, expertise, safety and transparency of all steps of the organ donation and transplantation process.**

Models of evolving and established systems of donor and transplantation practices are provided in these proceedings.

Conclusions

- Organ failure, particularly kidney and liver failure, caused by non-communicable and transmitted infectious diseases are exponentially increasing throughout the world;
- The cost of caring for these patients exceeds many other disease entities;
- Organ transplantation as a treatment provides the best survival and QoL with a cost efficiency. The “cost efficiency” issue may not be the case in the poorest countries, but can only be determined with the acquisition of accurate burden of disease data;
- The cost of inaction is substantial given the impact of organ failure upon individuals, and the social and economic impact of diseases leading to organ failure on communities;
- Governments must address national self-sufficiency by developing systems that provide organs for their patient population via living and deceased organ donation;
- National self-sufficiency requires a legislative framework that includes oversight of a national agency;
- The Workshop provided operational guidance of ethically sound living and feasible deceased donor transplantation including a mandated collection of data pertaining to safety of the living donor and outcome measurements for the recipients;
- International cooperation (financial, exchange of best practices, and provision of technical expertise) is required to support countries in progressing towards self-sufficiency in transplantation, particularly to low resource countries;
- The development of effective transplant systems is the fundamental means to prevent organ trafficking and protect the vulnerable from exploitation.

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Pope Francis has urged the international community of transplant professionals to address organ trafficking as a crime against humanity. Because combatting organ trafficking requires addressing its root cause, which is the inability of countries to provide for the transplantation needs of patients, **the Pontifical Academy of Sciences (PAS) convened in June 2021, a Workshop for *Promoting the Role of Science in the Development of International Standards of Organ Donation and Transplantation***. The Workshop aimed at addressing the following health-care issues:

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OPENING REMARKS

Bishop Marcelo Sánchez-Sorondo, Chancellor of the Pontifical Academy of Sciences

The PAS in thankful to the organizing committee of this Workshop and to the WHO for co-sponsoring this initiative.

There is an epidemic of non-communicable diseases (NCD) that the WHO seeks to address in its mission of providing universal health coverage. Millions of patients are suffering and dying as a result of organ failure. A multicultural organizing committee, with representatives from the different WHO regions, has been committed to the presentation of our agenda to governmental stakeholders and ministers of health in order to contribute to solve this tragic situation. The so-called miracle of organ transplantation has had an unwanted effect, which is organ trafficking. On

the direction of Pope Francis, the PAS has addressed this crime against humanity seeking to offer solutions, which is the goal of the Workshop.

In this line, governments should restore the dignity of victims of organ trafficking, by organizing a transparent donation and transplantation system, and by providing independent monitoring of activities to combat this crime. Governments should be aware of the importance of organ transplantation to restore the dignity of patients with organ failure and address the opportunity of optimizing transplantation as a cost-effective treatment that improves survival and quality of life (QoL). We hope this Workshop will be influential in achieving this goal.

Mariângela Simão, Assistant Director General, Access to Medicines and Health Products, World Health Organization

The WHO is thankful to the PAS for hosting this Workshop and to all the experts for their valuable contributions.

Transplantation of organs, tissues or cells is an established form of treatment that is acknowledged as the best and very often the only life-saving therapy for several serious and life-threatening diseases or conditions. Most recent data from the Global Observatory on Donation and Transplantation (GODT) indicate that more than 150,000 solid organ transplants are performed worldwide annually, but it is estimated that this number represents less than 10% of the global need (**Figure 1**).[1] Furthermore, this activity is reported by only 82 countries (42% of Member States) meaning that either many countries do not have such services or that there might be a lack of appropriate monitoring and registration by the national authorities. The situation of acute organ shortage may lead people to obtain a transplant through illegal and unethical pathways, usually from the poor and vulnerable, that are trafficked as sources for organs.

WHO is also concerned about the increasing prevalence of non-communicable diseases (NCD) such as diabetes as well as various social determinants (e.g. alcoholism) that may lead to acute and chronic organ failure. **Strategies and policies for prevention have been developed, although it is necessary to also address the management and treatment options.**

WHO Guiding Principles on donation and transplantation of organs, tissues and cells were issued in 2010 and have been endorsed by many Member States (Resolution WHA63.22).[2] Furthermore, through the engagement of non-state actors such as The Transplantation Society (TTS) and the International Society of Nephrology (ISN), these Guiding Principles are diffused to the entire body of transplant professionals. As a result, the global practices in donation and transplantation have significantly improved. There still remains however, a huge gap and great inequalities in the availability of and access to transplantation programs in many countries.

[1] Global Observatory on Donation and Transplantation. Available at: http://www.transplant-observatory.org/. Accessed: July 2021.
[2] WHA Resolution 63.22 on Human Organ and Tissue Transplantation. Available at: https://apps.who.int/gb/ebwha/pdf_files/WHA63/A63_R22-en.pdf. Accessed: July 2021.

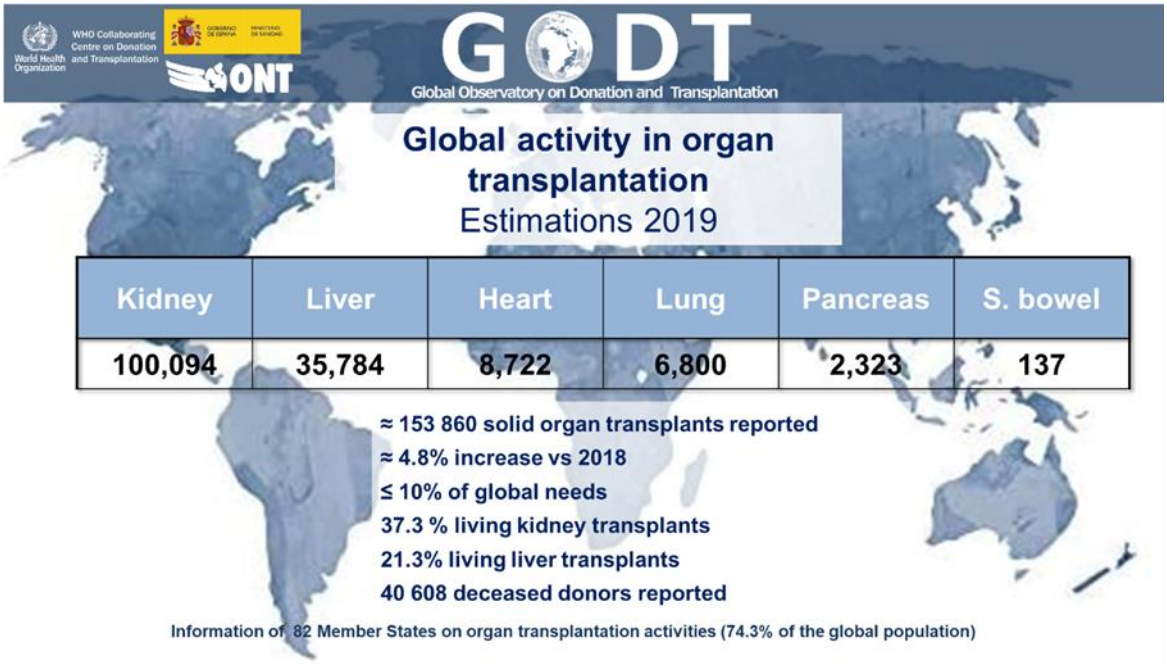


Figure 1: Global data on solid organ donation and transplantation in 2019. Source: Global Observatory on Donation and Transplantation (http://www.transplant-observatory.org)

WHO will soon be launching a comprehensive Global Action Framework on Transplantation (GAFT) for organs and tissues, that will seek to address the challenges and provide solutions for strengthening national transplantation systems (e.g. regulatory oversight, good practices in transplantation centers, donor and patient management, surveillance) with the overall objective of achieving national self-sufficiency in donation and transplantation.

Improving access to essential transplantation services will contribute to reaching WHO goals and strategic priority of "*One billion more people benefiting from universal health coverage" and "One billion more people enjoying better health and well-being".*

The WHO is very much looking forward to the outcome of this Workshop and expects that the information to be presented during these two days will greatly assist its work. This event is an excellent opportunity to exchange experiences and best practices, to agree on priority activities to be implemented at international and country level.

The WHO express its gratitude to the Government of Spain that has supported technically and financially WHO transplantation program for many years. Other countries are invited to also collaborate with WHO in making this plan effective.

Carmen de la Peña Corcuera, Ambassador of Spain to the Holy See

Spain is thankful to the PAS and the WHO for this initiative and for inviting the Embassy of Spain to the Holy See to participate in this event. Spain has one of the most successful models in donation and transplantation within the framework of a public and universal health-care system, that has

been followed by many countries throughout the world. Since 2005, the Government of Spain has been supporting the WHO transplant program and has been collaborating with many countries through multi and bilateral agreements in its commitment to facilitate the development of solid transplantation programs worldwide. These programs are essential to avoid premature deaths and improve the QoL of patients suffering from diseases treatable with transplantation, which burden keeps increasing.

SETTING OF THE AGENDA

Efstratios Chatzixiros,

Adviser, Transplantation and Products of Human Origin, Department of Health Products Policy and Standards, WHO, Geneva, Switzerland

This Workshop has been designed with the objective of presenting data that will be useful for Member States, responsible authorities and transplant professionals, to strengthen their systems and, where not available, to develop their transplant systems. The WHO is working in developing and Action Framework on the occasion of the 11 years of Resolution 63.22 and of the adoption of the WHO Guiding Principles on Transplantation of Human cells, tissues and organs. The framework has been developed with the contribution of members of the WHO Task Force. WHO will be soon engaging in consultations with Member States and will have the opportunity to listen to the needs and the challenges faced by the different WHO regions. This Workshop will provide information that will guide us in this very first step and provide the opportunity for interaction between Member States and the WHO to further cooperate in the near future.

Francis L. Delmonico,

Professor of Surgery, Harvard Medical School at the Massachusetts General Hospital, Boston, United States. Chief Medical Officer, New England Donor Services. Chair, WHO Task Force Donation and Transplantation of Organs and Tissues

The objective of this Workshop is to influence practices around the world. This is in light of the worldwide epidemic of NCD that the WHO seeks to address its mission of providing universal health coverage. The Workshop agenda was sent to 100 Member States with transplantation services across the world. A multicultural organizing committee from all six WHO regions has been committed to the presentation of the agenda to governmental stakeholders and ministries of health, because millions of patients are suffering and dying with organ failure.

The shortage of deceased and living donors has resulted in organ trafficking that the PAS, under the direction of Pope Francis, has asked global attention. Pope Francis has urged governments and transplant professionals to address organ trafficking as a crime against humanity. Governments should address the opportunity of optimizing organ transplantation, with a disproportionate number of patients with renal failure under dialysis treatment, while kidney transplantation is a more cost-effective treatment and provides better survival and quality of life. Governments should also provide independent monitoring of donation and transplantation activities because of the widespread organ trafficking that exists throughout the world.

The objective of this Workshop is to bring science and a remedy of the worldwide epidemic of organ failure.

1. THE BURDEN OF DISEASE AS IT RELATES TO THE NEED FOR TRANSPLANTATION IN THE WHO GOAL OF UNIVERSAL HEALTH-CARE

André Ilbawi,

Technical Officer, NCD Management-Screening, Diagnosis and Treatment, Department for Non-Communicable Diseases (NCD), WHO, Geneva, Switzerland.

MODERATORS:

Nancy L. Ascher,
Professor and Past Chair: Department of Surgery, University of California, San Francisco, USA.
Past President, The Transplantation Society (TTS)

Philip J. O'Connell,
Executive Director, The Westmead Institute for Medical Research, Director Centre for Transplant and Renal Research, Professor, Faculty of Medicine and Health, The University of Sydney, Australia

The evaluation of the disease burden and trends is essential for health-care planning. For a condition such as e.g. chronic kidney disease (CKD), a decision needs to be made on the interventions (including transplantation) that a community should prioritize, taking into account the social and economic impact of such interventions that justify investment in them and a framework for action.

For transplantation as an intervention, it is critical to understand the burden of diseases relevant for transplantation and what the trends are therein, as well as the social and underlying risk factors that impact upon the burden of such diseases. This evaluation must be made within a broader health-care system context that frames how we respond to these diseases.

The burden of CKD has increased over the past decades in nearly all countries throughout the world, not being exclusively a disease or condition of the eldest populations, since the increase in the burden of CKD has been observed across different age groups.[3] The drivers of these trends have been an increase in diabetes and arterial hypertension (particularly in low and middle income countries[LMIC]). **The same is true for end-stage liver disease or cirrhosis, with an increasing burden despite some areas of progress, because of conditions such as Non-Alcoholic Steato Hepatitis (NASH)**.[4] In the past two decades, there have been an increased burden of obesity, which is a major public health-care priority. Consequently, the number of patients needing a liver

[3] GBD Chronic Kidney Disease Collaboration. Global, regional, and national burden of chronic kidney disease, 1990-2017: a systematic analysis for GBD Study 2017. Lancet 2020;395(10225):709-733.
[4] GBD 2017 Cirrhosis Collaborators. The global, regional, and national burden of cirrhosis by cause in 195 countries and territories, 1990-2017: a systematic analysis for GBD Study 2017. Lancet Gastroenterol Hepatol 2020; 5(3):245-266.

transplant from NASH has progressively increased and is expected to keep increasing in the foreseeable future.

Diseases that affect the need for transplantation not only impact upon individuals, but do so upon an entire community.[5] [6] The social and economic impact of these diseases (e.g. major losses in productivity, people leaving the workforce, spouses leaving the workforce to care for those who are ill, divorces, drop-out from education) provide reasons for immediate action. There is a need to care for the increasing number of patients diagnosed with these diseases, and for the communities at large.

The disease burden is increasing related to underlying risk factors (+/ viral hepatitis), with insufficient progress to reverse trends and a profound social and economic impact. So the justification for action is strong.

To best contextualize transplantation, it is useful to resort to references that already exist and to commitments that can leverage transplantation as an important tool in the broader public health response. All countries have committed to the Sustainable Development Goals (SDG) to address overall health and development towards 2030, where transplantation fits as a tool to address the SDG related to NCD. There are two important entry points: 1) the burden of NCD and how scaling the transplantation capacity can reverse the trends; 2) a change in the narrative that transplantation is a luxury treatment for high income countries, where transplantation is seen as part of a broader health system response to ensure health is optimized for every individual around the world. We need to look to the means for implementation (access to medicines, health financing and workload) as *per* the SDG agenda.

Addressing CKD (and liver disease) through transplantation can support attainment of SDG target 3.4 (premature mortality from NCD)[7] and 3.8 (universal health-care). While prevention is a critical public health intervention, something else must be done in the immediate future, since it will take years for preventive measures to have an impact. The number of organ transplants barely covers 10% of the transplantation needs of patients worldwide. To justify the priority of transplantation within the context of other public health responses (*versus* prevention, dialysis, medical and surgical interventions), financial considerations and current capacity must be taken into account. Transplantation *versus* dialysis is justified by cost-effectiveness, acceptability, fairness and feasibility. Transplantation and prevention are interventions with different time horizons and hence value for achieving SDG.

[5] Afroz A, Hird TR, Zomer E, et al. The impact of diabetes on the productivity and economy of Bangladesh. BMJ Glob Health 2020 Jun;5(6):e002420.

[6] Bajaj JS, Wade JB, Gibson DP, et al. The multi-dimensional burden of cirrhosis and hepatic encephalopathy on patients and caregivers. Am J Gastroenterol 2011; 106: 1646-1653.

[7] Martinez R, Lloyd-Sherlock P, Soliz P, et al. Trends in premature avertable mortality from non-communicable diseases for 195 countries and territories, 1990-2017: a population-based study. Lancet Glob Health 2020; 8(4): e511-e523.

What should be a feasible benefit package that governments include as part of universal health coverage for transplantation? Transplantation can cost as much as $ 1,500 *per* capita, while many LMIC have a total health expenditure of $ 500-1,000 *per* capita. Decision-making for governments of both high and LMIC should consider: 1) packages of services and indications (e.g. kidney versus all types of organs); 2) costs that can be mitigated (be feasible for LMIC); 3) scale-up scenarios. Investment in dialysis has increased importantly in the last 5-10 years in high and LMIC. However, there has been limited increase in investment in transplantation **The key message should be that transplantation is not a too costly, unfeasible and hence a low priority intervention.**

In conclusion:

- Success breeds success:
    - set clear priorities and achievable goals;
    - generate stronger investment cases for internal and external stakeholders.
- Consider entry points:
    - leverage existing governmental, partner commitment, and global initiatives (eg. WHO Global Diabetes Compact), and expand stakeholder network;
    - strengthen dialogue with governments, development partners.
- Invest in people- trained, enabled workforce, necessary for access and universal health-care

2. A COMPELLING CASE FOR PRIORITIZING ORGAN TRANSPLANTATION IN THE TREATMENT OF ORGAN FAILURE

MODERATORS:

Curie Ahn,
Professor, Division of Nephrology at National Medical Center, Seoul, South-Korea. Secretary-General, Asian Society of Transplantation

Elmi Muller,
Professor of Surgery, University of Cape Town, and Head, Transplant Services, Groote Schuur Hospital, Cape Town, South Africa. President-(elect) of The Transplantation Society (TTS)

2.1. Benefits of kidney transplantation: survival, quality of life and cost-effectiveness

David Harris,
Professor of Medicine, University of Sydney at Westmead Hospital, Australia. Past President of the International Society of Nephrology (ISN)

Despite recognition by the nephrology community of the importance of preventing development and progression of CKD, and recent advances in therapies that effectively slow progression, many patients develop kidney failure and require dialysis or transplantation to remain alive.

There is a disproportionate worldwide use of dialysis as kidney replacement therapy (KRT) when compared to kidney transplantation, that cannot be defended when governments consider the survival, QoL and cost-effectiveness advantage of kidney transplantation.

Worldwide in 2019, 100,094 kidney transplants were performed, compared to more than 5 million patients undergoing dialysis annually.[8] [9] Information on the prevalence of kidney transplantation is available in only 34% (n=75) of countries worldwide.[10] No low income countries have data available; lack of data is a major obstacle in the analysis of the potential value of transplantation. Globally, the average number of people who have received kidney transplants is 255 per million population (pmp), ranging from 3.1 pmp in the Bahamas to 693 pmp in Portugal. On average, high income countries have a much higher prevalence of kidney transplantation (363 pmp) than upper-middle (80 pmp) or lower-middle (27 pmp) income countries. The prevalence of kidney transplantation is below the global average in Africa, Latin America, North America, North and East Asia, OSEA, and NIS and Russia, and above the global average in Eastern and Central Europe, the Middle East, and Western Europe. Only 12 countries worldwide utilize kidney transplantation as the majority treatment for kidney failure.[11]

Kidney transplantation is associated with lower mortality and improved quality of life when compared with chronic dialysis treatment

A large systematic review of 110 cohort studies comparing adult chronic dialysis patients with kidney transplantation recipients, with a total of 1,922,300 participants has summarised the benefits of kidney transplantation across a range of parameters.[12] Most studies found significantly lower mortality and risk of cardiovascular events, and substantially better QoL among transplant recipients. Despite increases in the age and comorbidity of contemporary transplant recipients, the relative benefits of transplantation seem to be increasing over time.

People with CKD experience reduced QoL because of high symptom and treatment burden. In a recent multinational study involving 1,700 patients, the following characteristics were associated with lower QoL across all stages of CKD: treatment by dialysis, female gender, presence of multiple

[8] Global Observatory on Donation and Transplantation. Available at: http://www.transplant-observatory.org/. Accessed: July 2021.

[9] Global Burden of Disease 2019. Available at: http://www.healthdata.org/gbd/gbd-2019-resources. Accessed: July 2021.

[10] 2019 Global Kidney Health Atlas. Available at: https://www.theisn.org/initiatives/global-kidney-health-atlas/. Accessed: July 2021.

[11] United States Renal Data System (USRDS): Available at: https://www.usrds.org/. Accessed: July 2021.

[12] Tonelli M, Wiebe N, Knoll G, et al. Systematic review: kidney transplantation compared with dialysis in clinically relevant outcomes. Am J Transplant 2011; 11(10):2093-2109. doi: 10.1111/j.1600-6143.2011.03686.x.

comorbidities, lack of a partner, and lower educational attainment.[13] These findings strongly support increasing the number of people worldwide that benefit from kidney transplantation.

In all WHO regions, hemodialysis is more costly than maintaining a kidney transplant.

A large systematic review of 147 studies has shown that in all WHO regions, with the possible exception of Africa, hemodialysis is more costly than maintaining a kidney transplant, and this cost difference is widest in high-income countries.[14] Marginal costs of maintenance dialysis *versus* kidney transplantation may be smaller in LMIC for several reasons: the major drivers of the high cost of dialysis in high-income countries (buildings and staff salaries) contribute much less to costs in LMIC, practices such as dialyser reuse minimize the cost of dialysis consumables, and the cost of transplantation is kept relatively high in developing countries by the price of immunosuppression. Immunosuppression and post-transplant events are the most significant drivers of health-care costs post-transplant.

For developing countries with undeveloped transplant programs, the costs of donor procurement are high and difficult to quantify, especially where this involves illegal and unreported costs. The uncertainties surrounding illegal commercial transplantation need to be considered in terms of the overall cost-effectiveness picture from a societal perspective, but there are no available data to allow for this analysis.

Policy makers should take into account the potential economic savings when considering investment in transplantation infrastructure, training and programs to promote organ donation. For the economic benefits of transplantation to be realised, governments need to remove non-financial constraints on the development of transplantation services (legislative, system barriers, workforce, drug availability) and negotiate reliable and affordable supply of immunosuppressants.

A central goal of this Workshop is to raise the following question: Why is kidney transplantation the main treatment for kidney failure in so few countries worldwide?

2.2. Benefits of liver transplantation: survival, quality of life and cost-effectiveness

Marina Berenguer,

Professor of Medicine, University of Valencia and Chief, Hepatology and Liver Transplant Unit Research, CIBERehd and Instituto de Investigación Sanitaria, La Fe University Hospital, Valencia, Spain. President (Elect) of the International Society of Liver Transplantation (ILTS)

There is substantial evidence that liver disease is increasing in incidence and is a major source of death and disability in the world. **Liver disease affects patients of all ages compromising their life expectancy, QoL and productivity.** Hepatitis B can be eradicated with active neonatal vaccination programs and the infection is currently decreasing globally. New cases of Hepatitis C are decreasing

[13] Krishnan A, Teixeira-Pinto A, Lim WH, et al. Health-Related Quality of Life in People Across the Spectrum of CKD. Kidney Int Rep 2020; 5(12):2264-2274. doi: 10.1016/j.ekir.2020.09.028.
[14] White SL, May 2021, unpublished

due to lower blood borne transmission and decreased intravenous drug abuse. Hepatitis C can now be treated with direct acting antiviral agents. These treatments are expensive, though there are active programs developing less expensive generic agents for widespread use. Despite global WHO efforts to curb alcohol use and to develop healthy eating habits and regular exercise, alcoholic liver disease and NASH are major sources of liver death and disability. Primary liver cancer, which can occur on the background of cirrhosis from any of the aforementioned diseases. is a major cause of cancer deaths. **Liver cancer is the 6th leading cancer in frequency and the 3rd largest cause of cancer death.** The African continent is a huge reservoir of primary liver cancer with many cases in young patients. Early diagnosis improves outcome with the possibility of resection or liver transplantation.

Liver transplantation with both deceased and living donors is an effective treatment for chronic liver disease, fulminant hepatic failure and hepatocellular carcinoma with excellent short and long term survival. The alternative to transplantation is death in patients with both acute and chronic liver failure. Cost effective analysis has not been done, since the alternative is death.

Many countries do not have active transplant programs and newly initiated transplant programs in countries without robust governmental support, generally begin the liver transplant program utilizing live donors. This approach requires surgical expertise and relies on protection of living donors from exploitation.

2.3. Requirements for a transplant program (financing, workforce, infrastructure-equipment, medication) to progress towards self-sufficiency)

Vivekanand Jha,

Executive Director, George Institute for Global Health, India, and Faculty of Medicine, Imperial College, London, UK. Immediate Past President of the International Society of Nephrology [ISN].

Decision-making regarding prioritization of treatment reflects the cost of treatment and the number of patients who could benefit. Simple treatments that delay or prevent mild renal disease progression affect a large number of patients and therefore should be prioritized (**Figure 2**). Once an individual reaches end-stage kidney disease (ESKD), the treatment modalities are limited to transplantation, hemodialysis and peritoneal dialysis.

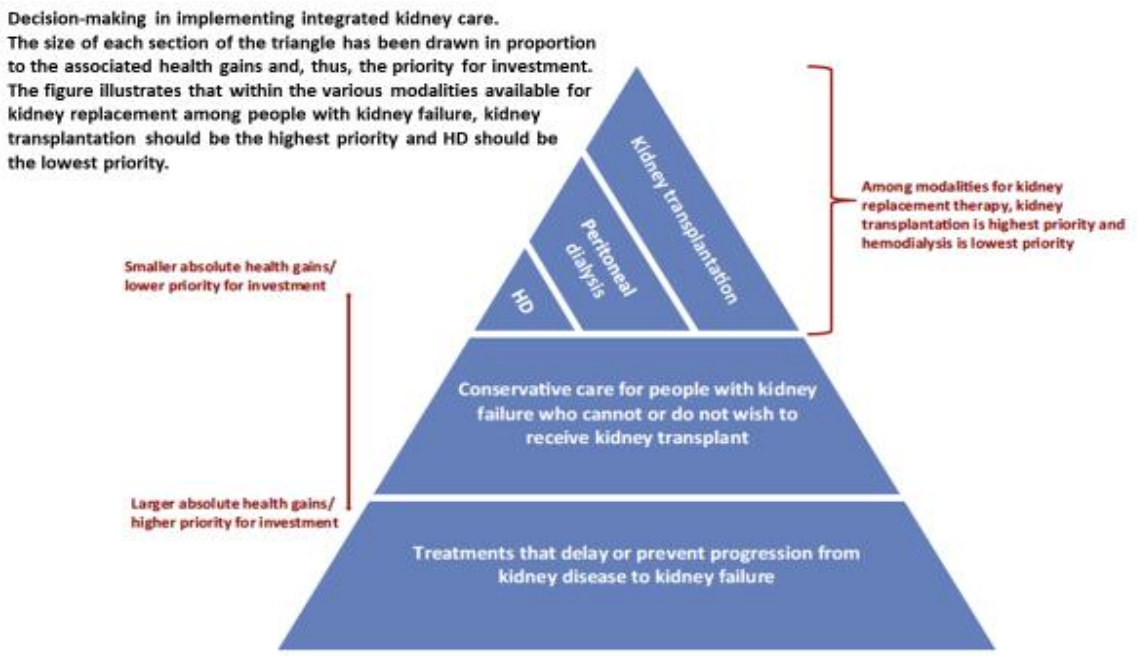
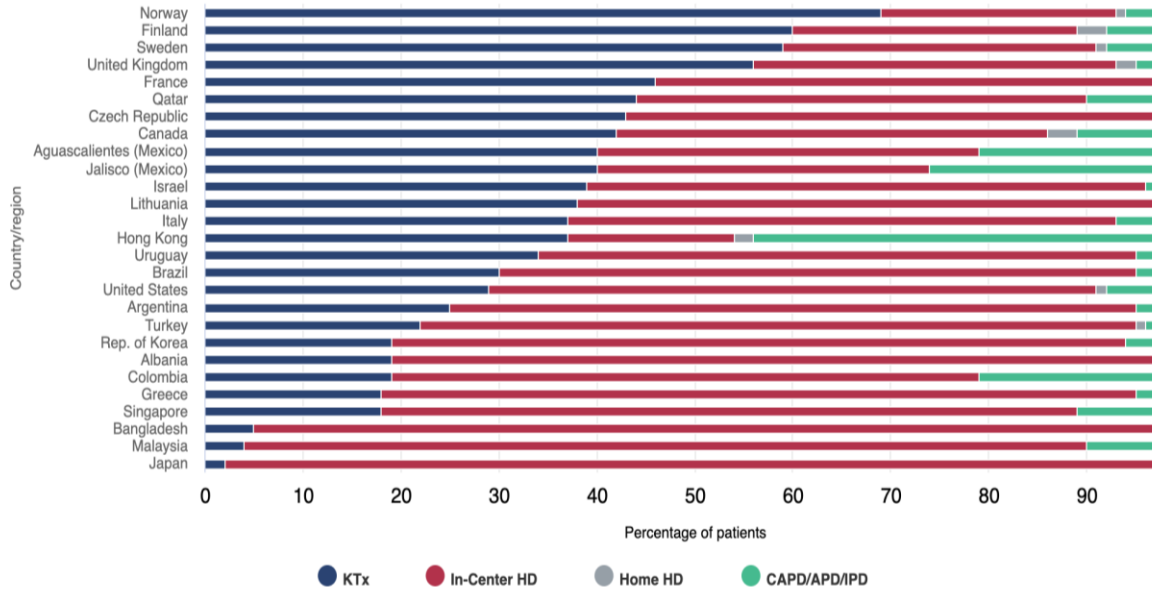


Figure 2: Decision-making in implementing integrated kidney care.

The transplantation activity around the world, as reflected by the global prevalence of kidney transplantation, is highly variable (**Figure 3**), and is likely inequitable, because it does not correspond to the areas of greatest need, but rather to the availability of funding and other resources.

A



B

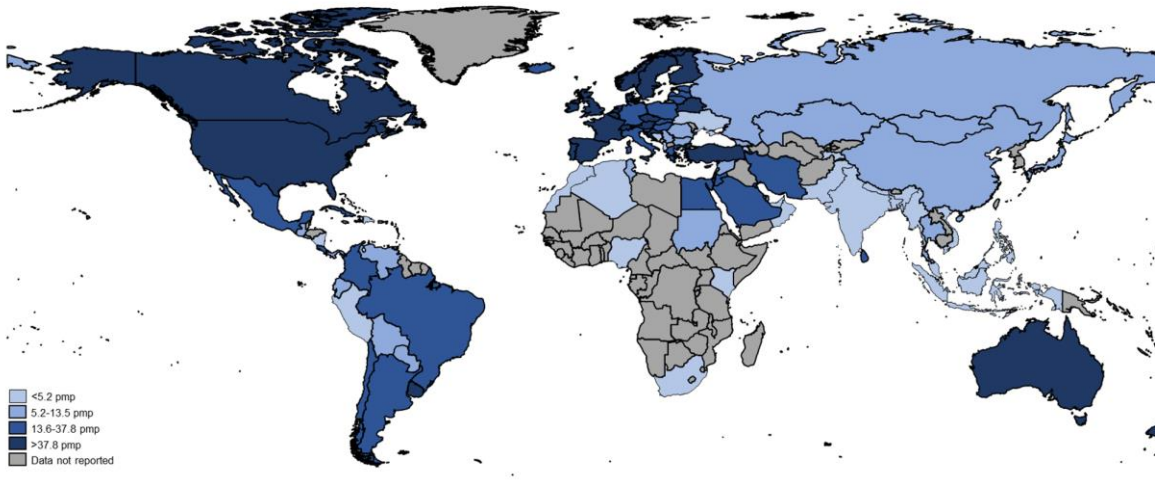


Figure 3: A. Percentage distribution of treatment modality for end-stage kidney failure (arranged in decreasing order of prevalence of transplantation in different countries). (Data source: US Renal Data System) B. Current global prevalence of kidney transplantation. (Data source: ISN Global Kidney Health Atlas)

A health-care system reflects the integration of the workforce, service delivery, health information systems, medication, financing and leadership (**Figure 4**). The current availability of multidisciplinary transplant teams, organ procurement frameworks and immunosuppression in different parts of the world according to the Global Kidney Health Atlas **(Figure 5).** The decision to embrace and support transplant activity must be assessed on the background of the community's(country's) burden of disease, loss to the community of productive members and other health obligations. The community must start with the greatest potential for benefit (e.g. living donor kidney transplant in place of dialysis therapy or living donor liver transplant for liver cancer). Once the infrastructure is in place and the work force has been developed, transplantation services may be expanded to include deceased donor transplants and the indications widened. All of these need to be underpinned by the principles of solidarity, social justice, access and community participation consistent with local values and preferences.

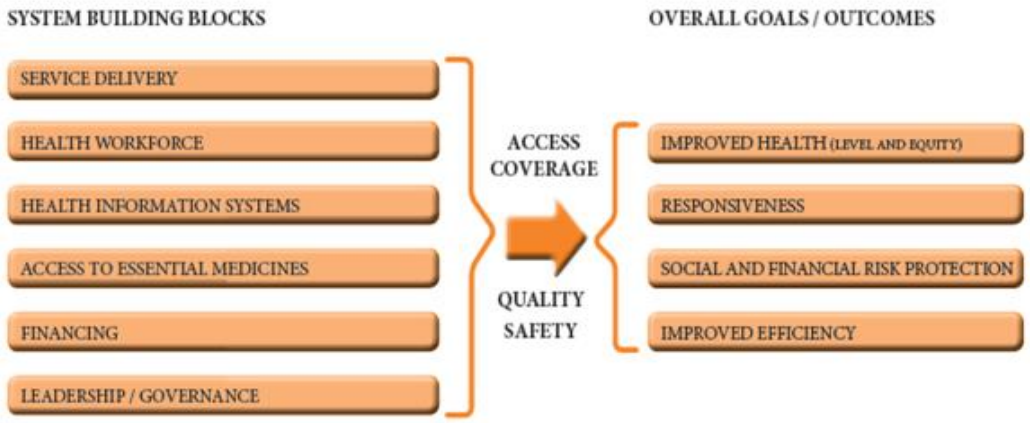


Figure 4: The six bulding block of a health system: aims and desirable attributes

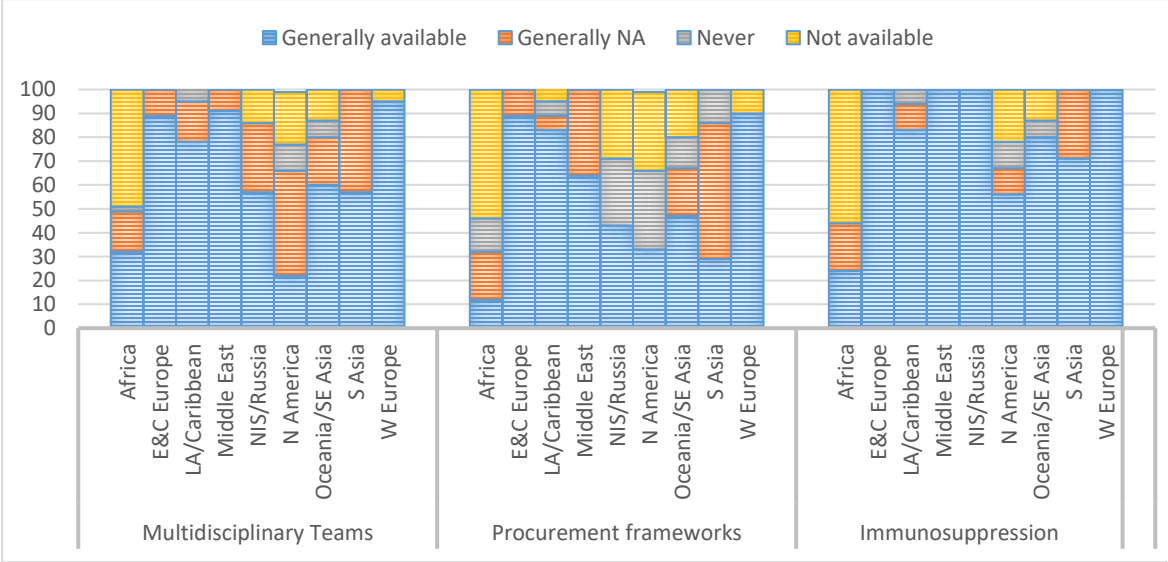


Figure 5: Availability of multidisciplinary transplant teams, organ procurement frameworks and immunosuppression in different parts of the world (Source: ISN Global Kidney Health Atlas).

The ISN has identified a number of essential requirements for a transplant program, as elaborated in **Table 1.**

Table 1: Requirements for a transplant program
Legislation, Credentialing and Regulatory Oversight

- A legal framework to prohibit and criminalize organ trafficking and commercialization.
- Ethical standards, including consent for living and deceased organ donation, and identification, care, and follow-up with the living donor. These should be consistent with the WHO Guiding Principles and Declaration of Istanbul.
- A legislative framework to protect the rights and well-being of organ donors, their families, recipients, and transplant personnel.
- Regulatory oversight to ensure equity and evidence-based schema of organ allocation, safety, and adherence to legislation.
- Credentialing of centers to ensure appropriate standards.
- Regular outcome reporting and audits of transplant units.

Financing

- A national funding mechanism covering all aspects of transplantation, from donation to long-term care of donors and recipients, including affordable medication that is consistently accessible.
- Reliance on external funding, donors and charities is not sustainable.

Workforce

- Physician/nephrologist/hepatologist with expertise in all aspects of transplantation (including patient selection.
- Surgeon skilled in organ procurement, implantation, and management of surgical complications.
- Histopathologist skilled in the interpretation of transplant pathology.
- Access to ancillary services for management of medical problems.
- Specialized nursing and support staff.

Interventions and procedures

- Access to dialysis.
- Transplant biopsy and histopathological examination.
- Interventional radiology.

Laboratory

- Standard laboratory assessment of blood and urine for biochemistry, blood count.
- Access to microbiology and virology services, including the ability to screen for diseases that may be transmitted by the donor to the recipient.
- Laboratory assessment of drug levels of immunosuppressants.
- Access to histopathology for assessment of transplant biopsies.
- Access to a laboratory for immunological work up, including human. leucocyte antigen (HLA) typing, crossmatch and detection of donor specific antibodies.

Medications

- Standard immunosuppressive agents for induction and maintenance.
- Infection prophylaxis.
- Other basic medications

Protocols

- Living donor selection and evaluation including adequate donor protections and ethical oversight.
- Suitability/eligibility of potential recipients including waiting-list management and the criteria for temporarily removing patients from the active waiting-list for medical and other reasons
- Suitability/eligibility of potential recipients including waiting-list management and criteria for placing active patients on and off hold for medical and other reasons.
- Immunosuppression regimens depending on patient risk of rejection.
- Retrieval, perfusion and storage of organs.
- Immediate post-operative management, fluid management.
- Long-term follow-up of the recipient including the treatment of rejection and other complications such as technical events.
- Long-term follow-up with the donor.
- Deceased donor organ consent and procurement.
- Management of the deceased donor pre-donation.

The Global Kidney Health Atlas, a project of the ISN, has identified significant variations in kidney transplant activity and availability of services around the world.[15] Lower income countries lack the pre-requisite of transplant facilities, waitlists, workforce, political will, and publicly funded health-care systems to facilitate increased access to transplantation, especially deceased donor and pre-emptive kidney transplantation. Health-care financing, including universal health coverage, health-care infrastructure, and system design are significant barriers to improving access to quality care, and improving access to transplantation is contingent on a multitude of financial, governmental, and societal factors. High income countries have challenges too and must address them - especially low public awareness and education and lack of access among geographically remote populations to ensure equitable access to quality kidney transplant care. Understanding how different challenges are faced by countries in different income strata and cultural attitudes will inform efforts to increase awareness and the adoption of practices that will ensure high quality transplant care is provided around the world. Hierarchical levels of capacity of organ donation and transplantation services are described in **Table 2**.[16]

Table 2: Hierarchical levels of capacity of organ donation and transplantation services
Level 1 No local transplantation activity – either reported to the Global Observatory on Donation and Transplantation or detected by additional investigation.

[15] 2019 Global Kidney Health Atlas. Available at: https://www.theisn.org/initiatives/global-kidney-health-atlas/. Accessed: July 2021.

[16] White SL, Hirth R, Mahíllo B, et al. The global diffusion of organ transplantation: trends, drivers and policy implications. Bull World Health Organ 2014; 92(11):826-835. doi: 10.2471/BLT.14.137653.

Level 2 At least one kidney transplant center – with the capacity to perform living donor nephrectomy, kidney transplantation and post-transplant management of recipients – within the country's borders. No deceased donor activity reported to the Global Observatory on Donation and Transplantation.
Level 3 Countries that have commenced deceased donor kidney transplantation within their own borders. Sufficient local capacity – including local medical expertise – exists to perform kidney recovery surgery from deceased and living donors, kidney transplantation and recipient management. Activities may also include liver transplantation and isolated cases of heart and lung transplantation.
Level 4 Deceased donor kidney and liver transplantation have been performed for at least five years. Heart and lung transplantation also available, either locally or via formal international cooperative organ-sharing agreements such as Eurotransplant and Scandiatransplant. Legislation permits and regulates organ donation and transplantation.
Level 5 An established multi-organ deceased donor transplant program exists that is capable of providing kidney, liver, heart, lung and pancreas transplantation either locally or via formal international cooperative organ-sharing agreements. The transplant program has been providing multi-organ deceased donor transplants consistently for at least five years, with an overall rate of transplantation above 30 solid organ transplants per million population. The country has a government-recognized authority that is responsible for oversight of organ donation and transplantation activities.

2.4. Developing integrated kidney replacement therapy in low-resource settings

Elmi Muller,
Professor of Surgery, University of Cape Town, and Head, Transplant Services, Groote Schuur Hospital, Cape Town, South Africa. President-(elect) of The Transplantation Society [TTS])

The availability of KRT is lower in underdeveloped countries as clearly shown in Africa when compared to other region of the world, and the true scale of the unmet need for treatment of ESKD is unknown. In many other parts of the developing world, the situation is the same –there is a struggle to estimate the underlying burden of ESKD and its risk factors in many developing world countries. Ideally, population-based studies, death registration data and dialysis and transplant registries would enable quantitative estimation of the problem. Still, a significant limitation is the lack of data and reporting mechanisms present in these countries.

Africa is made up of 5 WHO sub-regions with the countries at varying levels of economic development. However, many belong to the low- and middle-income economies. In high-income economy countries, health insurance schemes or social welfare schemes help alleviate the economic

burden of expensive treatments. Unfortunately, in most African countries, especially Sub Saharan African countries, there is none or poorly structured insurance or social welfare programs, hence the individual or immediate family members bear the burden of the disease.

Transplantation in all its ramifications (pretransplant, transplant surgery and post-op-care) is very expensive. This dictates a structure or framework be put into place that helps with this cost burden. There is a need to have the human resources and the minimum required facilities.

Because of a lack of regulatory oversight and coordinating authorities, transplantation professionals often rely on a locally elected or independent ethics team to help with professional monitoring and patient selection. Tools for LMIC must be flexible enough to apply to many different ethical and medical realities across the globe.

- Legislation on brain death;
- Development of infrastructure, personnel and capacity for coordination required to support deceased donation;
- Tissue typing and cross-matching facilities, an organ procurement program, an on-call surgical team, capacity to fund this infrastructure;
- Public perception of deceased donation.

Therefore, in advocating for deceased donor transplantation, the requirements in terms of resources, infrastructure, track-record, and capacity for coordination need to be realistically acknowledged. It remains a possibility that transplantation may not be a viable alternative to other methods of KRT in the poorest countries in Africa until a work force and generic immunosuppression are available.

It is important to note that a deceased donor program requires a legislative framework for transplantation and organ donation. **Figure 6** shows an example of information that can be considered by each country.

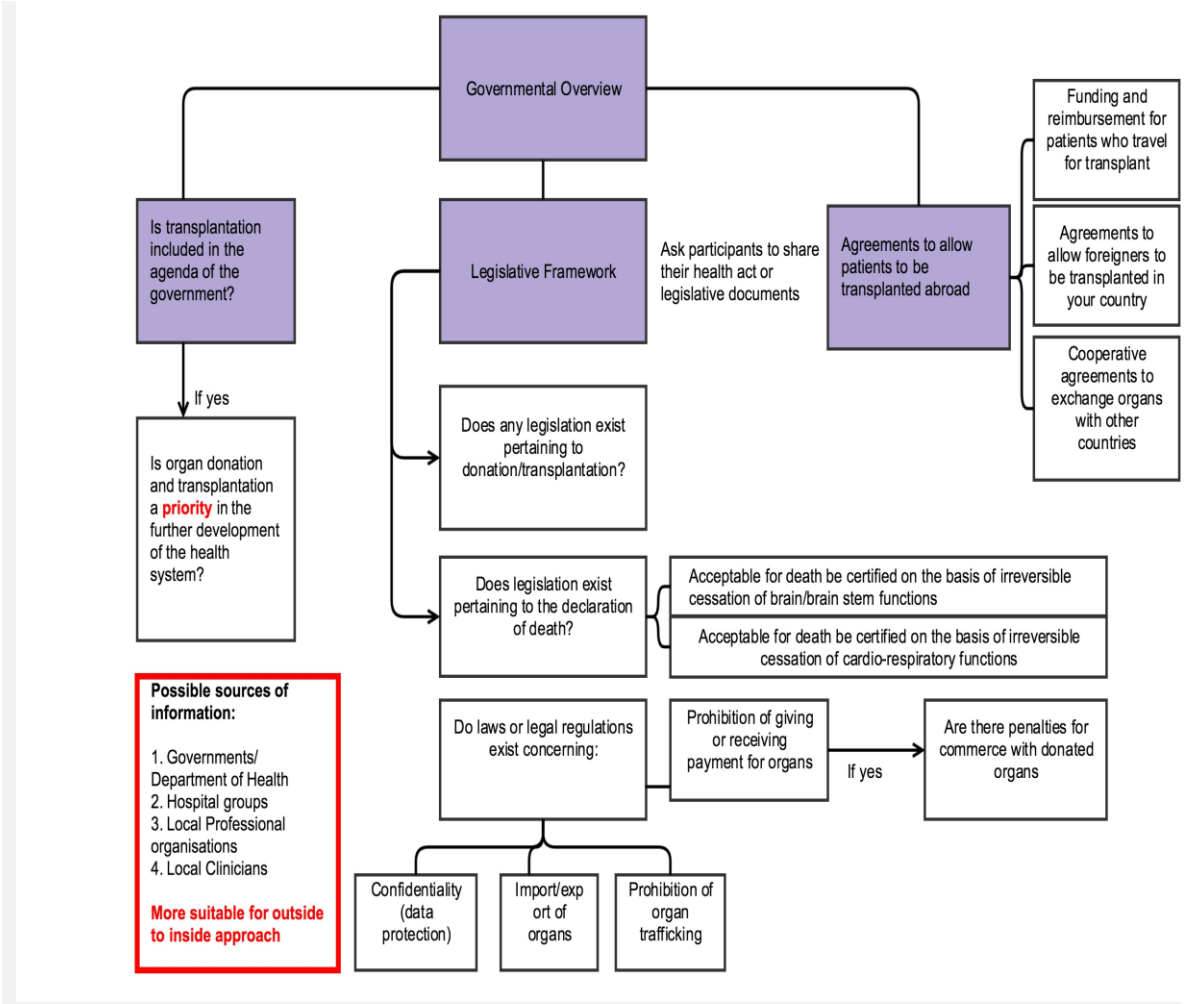


Figure 6: Elements to consider in developing legislation in donation and transplantation.

High cost of transplantation and follow-up care become an obstacle, and in particular the cost of maintenance immunosuppression. For example, in Cameroon the government pays for patients to travel abroad to receive transplantation, but when patients return, they must contend with the very high cost of immunosuppression themselves. The cost of maintaining a functioning graft *versus* dialysis (as dialysis is often supported by the government, but transplant is not) needs an assessment relevant to the geographic area.

Successful transplant programs require some positive government involvement. This positive environment results in funding, support, and a willingness from the Ministry of Health to work on a legislative framework.

It is otherwise difficult for professionals to drive transplantation (multidisciplinary and costly) as an individual or as an individual institution. Issues around training and expertise remain an important concern, avoiding the wide dispersion of expertise by allowing many centers in one country to develop simultaneously. Another important issue is how to address the brain drain of professionals.

Many physicians and scientists who leave their home country to pursue some training elsewhere never return.

Transplant tourism and official arrangements in which governments send donor-recipient pairs abroad to undergo transplantation are relatively common. Destination countries for patients travelling abroad to receive transplants include Tunisia, Pakistan and India. Often local programs fail to thrive because of these practices and a lack of confidence from local patients and physicians in their local surgical team. Financial incentives from Indian hospital groups to individual nephrologists who send patients there.

An approach to address some of the issues experienced by LMIC is to first understand the current reality of each geographical area. This includes the level of surgical expertise, critical care availability and experience and an assessment of radiological and laboratory clinical services. Some of these services can be shared digitally (for instance, pathology slides), but the clinicians on the ground still need to be able to perform the biopsy and blood tests in their local facility. A gap analysis assessing current needs and identification of areas with future needs should be performed. Furthermore, there are many stakeholders that need to be considered in planning a transplant program, which includes hospital managers, departments of health, medical practitioners and patients. These stakeholders should be trained and informed to understand the future needs and long-term maintenance of the program. In terms of these activities, there are several partners and key resources available internationally that can participate in this endeavor.

3. TECHNICAL CONSIDERATIONS FOR DEVELOPING AND OPTIMIZING ORGAN TRANSPLANTATION AS A HEALTH-CARE TREATMENT OPTION FOR PATIENTS WITH ORGAN FAILURE

MODERATORS:

Beatriz Domínguez-Gil,
Director General, Organización Nacional de Trasplantes, Madrid, Spain

Gabriel E. Gondolesi,
Professor of Surgery, and Chief, Liver, Pancreas and Intestinal Transplant, Fundación Favaloro Hospital Universitario, Buenos Aires, Argentina

3.1. The Legislative Framework

General aspects of legislation

Kristof Van Asche,
Research Professor in Health law, University of Antwerp, Belgium

Legislation should be adopted to establish a national transplantation system. This includes the establishment of a National Transplant Agency that provides oversight, organization and

coordination of donation and transplantation activities, and the establishment of registries and a system of traceability and vigilance to ensure safety, efficacy and quality of organs.[17]

Legislation should provide the legal basis for organ removal from deceased donors, with the ultimate goal to maximize donations from deceased donors. Legislation needs to include the following elements:

- The principle that organs should not be removed from the body of a deceased person unless that person has been certified dead in accordance with national law.
- Requirements for the determination and declaration of death.
- The principle that physicians determining the death of potential donors should not be involved in the removal or transplantation of their organs.
- The principle that organs should not be removed from the body of a deceased person unless consent or authorization required by national law has been obtained.
- Rules regarding the system of consent or authorization, specifying the process of obtaining and recording consent or authorization for organ donation after death. No removal shall be carried out if the deceased person had objected to it.
- **Legislation should provide the legal basis for living organ donation**, as a complement to deceased organ donation. Legislation needs to include the following elements:
    - The requirement that living donors are selected on the basis of their health and medical history. Persons whose donation could present unacceptable health risks should be excluded.
    - Rules regarding the nature of the relationship that would allow a person to donate to the intended recipient. Where living donation is allowed in the absence of a close personal relationship, the law should define procedural safeguards against coercion and commercialism.
    - The requirement that living donors should be legally competent. No organs should be removed from legally incompetent donors, unless narrow exceptions are defined and specific protective measures are in place.
    - Rules regarding the information to be provided, which should include the nature and purpose of the surgical procedure, and the probable risks, benefits and consequences of donation.
    - The principle that an organ should only be removed from a living person when that person's free, informed and specific consent is obtained. Donor motivation should be evaluated by an appropriately qualified, independent party so as to ensure that

[17] WHO Guiding Principles on Human Cell, Tissue and Organ Transplantation. Available at: https://www.who.int/transplantation/Guiding_PrinciplesTransplantation_WHA63.22en.pdf. Accessed: July 2021.

they act willingly and free of coercion and any undue influence such as commercialism.

  - The requirement that consent should be either in written form or before an official body. The person concerned may freely withdraw consent.

- **Legislation should also ensure equity and privacy in donation and transplantation**. This includes:
  - The principle that the allocation of organs should be guided by clinical criteria and ethical norms, not financial or other considerations. Allocation rules should be equitable, externally justified, and transparent.
  - Rules to ensure adequate follow-up of living donors and recipients.
  - Measures to protect the privacy and anonymity of donors and recipients.
- Finally, **legislation should ensure altruism and non-commercialization** in donation and transplantation. This requires including the following provisions:
  - The principle that organs should be donated freely, without any financial gain or comparable advantage.
  - The prohibition of advertising the need for or the availability of organs with a view to offering or seeking financial gain or comparable advantage.
  - The principle that professional fees for medical or technical services rendered in connection with transplantation should be justified.
  - The principle that health-care professionals and institutions should not engage in transplantation if organs have been obtained through exploitation, coercion or payment.

Criminalization of illicit transplant-related activities

Marta López-Fraga,
Scientific Officer, European Directorate for the Quality of Medicines & Health-Care, and Secretary, European Committee on Organ Transplantation [CD-P-TO], Council of Europe, Strasbourg, France)

Despite worldwide initiatives to enlarge the donor pool, organ shortage remains the main obstacle in transplant medicine and no country is yet able to meet the transplantation needs of their patients. Under these circumstances, desperate patients may seek organs outside legal transplantation networks, and unscrupulous medical professionals and an array of intermediaries may take advantage of a highly profitable, unethical and vulnerable market. Trafficking in human beings for the purpose of organ removal and trafficking in human organs are real and growing problems all over the world. According to the WHO, 5–10% of all transplants performed worldwide are conducted illegally.

In order to address these crimes, the Council of Europe has been actively involved in the elaboration and promotion of legal instruments that aim at harmonizing international legal frameworks to provide concerted and effective efforts to prevent and address illicit transplantation practices at international level.

The Convention against Trafficking in Human Organs is built around the notion of the "illicit removal of human organs".[18] This is defined as organ removal: 1) without the free, informed and specific consent from living donors or without valid consent or authorization for deceased donation; or 2) in exchange for financial gain or comparable advantage. Any subsequent action involving illicitly removed organs is also considered to be organ trafficking. By ratifying this Convention, parties show their commitment to preventing and combating these crimes.

This Convention is a seminal international legal instrument that for the first time reaches illicit transplant practices that may currently escape prosecution and has broad international scope: it is open to all countries and is not restricted to Council of Europe Member States. By complementing the provisions included in other international instruments criminalizing different but related crimes (in particular those covered under the criminal law framework of human trafficking for the purpose of organ removal), these instruments provide a comprehensive legal framework to prevent and combat transplant activities that violate basic human rights.

As a result, the following activities that are considered as **organ trafficking** need to be criminalized:

- The illicit removal of an organ, which includes the following activities:
    - the removal of an organ from a living donor without that person's free, informed, and specific consent
    - the removal of an organ from a deceased donor without the removal being authorized under its domestic law; and
    - the removal of an organ where in exchange the donor or a third party has been offered or has received a financial gain or comparable advantage
- The preparation, preservation, storage, transportation, transfer, receipt, import, and export of an illicitly removed organ;
- The implantation or other use of an illicitly removed organ;
- Soliciting or recruiting donors or recipients, where carried out for financial gain or comparable advantage;
- Offering and requesting of undue advantages to/by health professionals or public officials to facilitate or perform illicit removal or use; and
- Attempting to commit, or aiding or abetting the commission of, any of these acts.

[18] Council of Europe Convention against Trafficking in Human Organs. Available at: https://rm.coe.int/16806dca3a. Accessed: July 2021.

In addition, the following activities that are considered as **human trafficking for the purpose of organ removal** need also to be criminalized: the recruitment, transportation, transfer, harboring, or receipt of persons, by means of the threat or use of force or other forms of coercion, of abduction, of fraud, of deception, of the abuse of power or of a position of vulnerability, or of the giving or receiving of payments or benefits to achieve the consent of a person having control over another person, for the purpose of the removal of organs.[19] Finally, the criminalization should be considered of the following activities:

- Removal of an organ outside of the domestic transplantation system or in breach of essential principles of national transplantation law.
- Implantation of an organ outside of the domestic transplantation system or in breach of essential principles of national transplantation law.
- Selling or buying of organs (organ trade), which would make donors and recipients criminally liable, when deemed appropriate under domestic law.

For these criminal offences effective, proportionate, and dissuasive sanctions should be introduced that correspond to the seriousness of the offence. Applying **extraterritorial jurisdiction** should be considered in an attempt to strengthen the enforcement of existing laws governing transplant-related crimes across national boundaries.

3.2. The Role of Professional Societies to Propose Standards of Suitability for Organ Transplantation

Marcelo Cantarovich,
Professor of Medicine, and Associate Director Multi-Organ Transplant Program, McGill University Health Center, Montreal, Quebec, Canada. President of The Transplantation Society [TTS])

Considering the technical requirements for developing and optimizing organ transplantation as a health-care treatment option for patients with organ failure, TTS takes note of the absence of, and advocates for, **international standards addressing the criteria for an individual to undergo organ transplantation.**

TTS represents a group of transplant champions advocating for the development and refinement of ethical transplant practices and supports standard medical criteria for deceased and living donors. As a non-governmental organization in official relationships with the WHO, TTS requests these issues to be addressed in a WHO Global Consultation:

- foster standards of practices optimizing organ transplantation as a treatment for patients with organ failure;

[19] Protocol to Prevent, Suppress and Punish Trafficking in Persons Especially Women and Children, supplementing the United Nations Convention against Transnational Organized Crime. Available at: https://www.unodc.org/unodc/en/organized-crime/intro/UNTOC.html. Accessed: July 2021.

- ensure that access to organs transplanted from deceased donors should be based upon medical criteria and not advantaged by gender, ethnicity or social status;
- data available through the GODT be used to develop “report cards” for countries involved in transplantation, allowing Member States to view their own progress and facilitate ongoing transplantation activities.

TTS takes on the mandate (and has the audience) to promote the objectives of this Workshop, which will define the need and place of transplant in the health-care continuum of Universal Health-Care. TTS will develop and promote the criteria used for recipient selection in the case of deceased donor transplant and both the recipient and donor criteria for living donor transplantation.

3.3. Deceased Donor Transplantation

Mirela Bušić,
National Transplant Coordinator, Ministry of Health, Croatia

Legal and logistical steps are needed to establish deceased donor programs where these do not exist, and of making existing programs as effective and efficient as possible. The ultimate goal is to maximize donation from deceased donors and to guarantee equitable access to transplantation. Figure 7 presents the fundamental elements of this program.

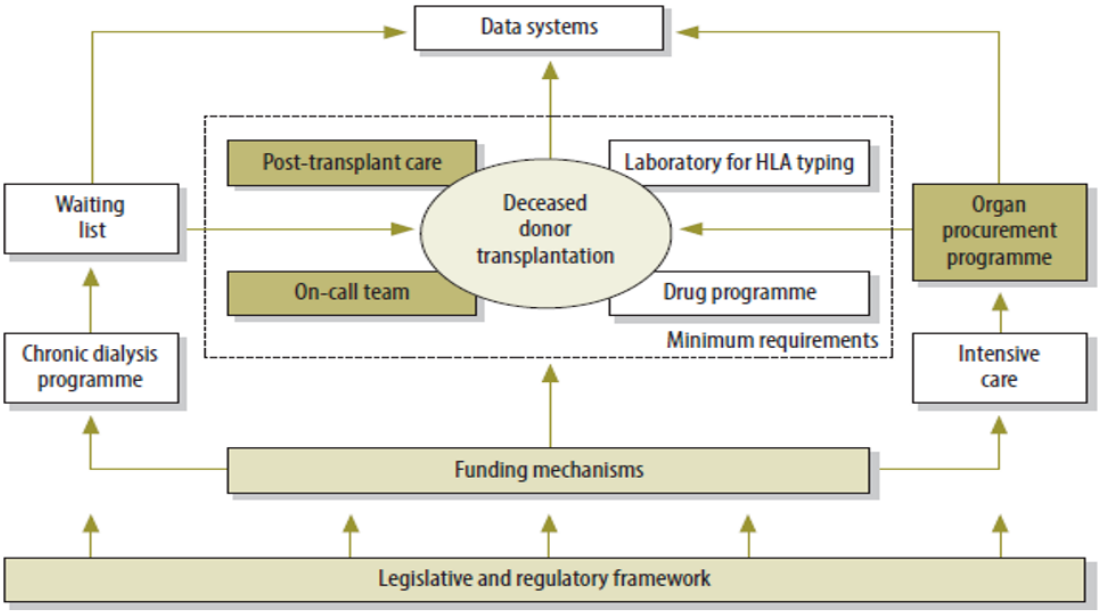


Figure 7: Minimum health system requirements for deceased donor organ transplantation.

Legislation should provide a legal basis for organ recovery from deceased donors. Organs should not be removed from the body of a deceased person unless that person has been certified dead in accordance with the law and unless consent or authorization required by law has been obtained. Legislation would need to include the following elements:

- Requirements for the determination and declaration of death. The principle that the physicians who certify the death of potential donors: 1) should not participate directly in the removal of their organs; 2) should not participate directly in the subsequent transplantation procedures; and 3) should not have any responsibilities for the care of potential recipients. This principle is designed to avoid a possible conflict of interests, which would undermine public trust.

- Rules regarding the system of consent or authorization in place, specifying the process of obtaining and recording consent or authorization for organ donation after death. No removal shall be carried out if the deceased person had objected to it. Appropriate measures should also be taken to inform the public about the system of consent or authorization.

Government through its Ministry of Health should establish a **National Organization** with the authority to implement a program for deceased organ donation. This organization should authorize, certify and coordinate programs for the recovery of organs from deceased donors. The Ministry of Health should also exercise its responsibility to develop the framework to allocate organs to a valid waiting list of candidates equitably receiving organs irrespective of gender, ethnicity or social status. If waitlisted patients are prioritized by social status and thus restricted from receiving organs, the motivation to donate organs will be jeopardized. The National Organization should also collect data, provide annual reports on donation activities, and develop strategies for improvement. In that regard, a critical pathway has now been developed by the WHO that categorizes the procedural steps to enable a transition from a possible deceased donor to an actual organ donor ---and then to a utilized donor by the recovery and transplantation of at least one organ.[20] Unawareness of the medical suitability of dying patients to be organ donors is a major reason for the failure of physicians to identify them appropriately. The National Organization should conduct death audits with the evaluation and recording of potential deceased donors for a retrospective assessment of performance and for the prospective improvement in achieving deceased donation.

The formal appointment of an **organ donation coordinator/ physician** in the intensive care units (ICUs) of each hospital is widely recognized as a most effective approach to successful organ donation. The National Organization should also be accountable to the Ministry of Health with the following functions prescribed:

- the medical assessment and management of the deceased organ donor;
- the consent process;
- the implementation of the critical pathway;
- the care of the family of the deceased;
- the traceability of organs and tissues derived from the donor through a national registry and the monitoring of outcomes for transplant recipients and living donors.

[20] Domínguez-Gil B, Delmonico FL, Shaheen FA, et al. The critical pathway for deceased donation: reportable uniformity in the approach to deceased donation. Transpl Int 2011; 24(4):373-378. doi: 10.1111/j.1432-2277.2011.01243.x.

These activities require **funding for a sustainable infrastructure and activity**. The human development index strongly correlates with programs of deceased donation, suggesting that a minimum level of development is required to establish and maintain a national program of deceased donation. However, the epidemic of ESKD is confronting all countries. Emerging and developing countries are establishing programs of dialysis-- for example, in West Africa. These countries should not omit a portion of the appropriated resources to kidney transplantation which is less costly and provides better QoL and survival.

The National Organization should undertake the following tasks in implementing the deceased organ donation process in each country:

- the identification of suitable potential organ donors utilizing the WHO critical pathway;
- conducting death audits to assure appropriate referral of possible organ donors;
- the management of deceased organ donors prior to organ (surgical) recovery;
- the recovery of deceased donor organs by authorized transplant centers;
- the allocation of recovered organs to a wait list of candidates medically suitable for transplantation based upon transparent criteria;
- the collection of data in a central registry which provides for an annual report of deceased organ donation and also detailing the distribution of organs;
- professional training and education of physicians within intensive care units and donor hospitals and transplant coordinators;
- public education and involvement of the media in the support of deceased organ donation;
- collaboration with regional/international organizations for potential sharing of organs;
- funding accountability in a review of annual budget;
- establishment of a donation committee within each hospital;
- identify responsible ICU professionals within each hospital for the conduct of organ donation whose responsibility in end-of-life care includes the identity and referral of organ donors;
- participation in the organ donation committee.

These efforts require governments to appropriate funds to no longer make this a voluntary effort left to professionals.

Well-established deceased organ donation programs are essential components of each transplant program and a prerequisite for achieving self-sufficiency. Life-saving transplant treatments (such as heart transplantation) cannot be developed unless deceased organ donation is established. Lung and liver (kidney as well) transplant programs should rely on deceased donation to avoid the burden and minimize the risk for living donors. Therefore, national competent authorities should target this

goal as a priority when building up transplant programs or optimizing access to transplantation treatment.

Professional societies of neurology and intensive care medicine should provide national guidelines for a valid and accurate diagnosing protocol(s) for the determination of death, aligned with internationally accepted criteria.

National credentials system and **continuous medical education** in brain death determination and optimal donor management should be developed in collaboration with professional societies (neurology/neurosurgery and intensive care medicine).

Awareness (quality improvement) organ donation programs should be developed and implemented in all ICUs under the leadership and guidance of intensive care professional societies and competent authorities. Th organ donor program should at least provide tools and national guidelines for a:

- rapid alert/response system for close monitoring and reporting of persons with imminent death (possible/potential donors);
- end-of life care and optimal donor management;
- psychosocial support and step-wise approach to donor families;
- determination of death by neurological and circulatory criteria (medical, legal and ethical code of practice).

Proper legal framework for determination of death by neurological criteria should be promoted globally as a binding legal requirement regardless of organ donation to guarantee the equal approach and valid medical standards in determination of (brain) death, and to help in overcoming mistrust and barriers in those countries where the concept of brain death is not well implemented or embraced by the professionals.

Further collaborative effort in achieving global consensus on the standards and protocols for the determination of death by neurological or circulatory criteria that allows for organ donation pathway should be enhanced and promoted under guidance of the WHO and the relevant international societies.

3.4. Living Donor Transplantation

Hiroto Egawa,
Chairman, Department of Surgery, Tokyo Women's Medical University, Tokyo, Japan)

The disparity between the need for solid organ transplant (chronic or acute organ failure not amenable to other therapies) and the organ availability is profound and growing in most countries. Much interest and activity has centered around increasing organ availability (deceased and living donation), but another approach to addressing the gap between the need for solid organ transplantation and the availability of organs is to decrease demand. **Japan is an important example of a country which has decreased the need for liver replacement by aggressively approaching Hepatitis B, Hepatitis C, and primary liver cancer**. Several national policies have been put in place

to decrease the incidence of Hepatitis B, aggressively treat and prevent the progression of Hepatitis C to cirrhosis and to achieve early detection and treatment of hepatocellular carcinoma. In instituting these measures, Japan has seen a decrease in deaths from hepatocellular carcinoma over the past few years and in doing so has decreased the overall demand for liver transplantation.

Japan is also an example of a country that has well developed living donor liver and kidney transplantation, but a limited deceased donor program. The underdeveloped deceased donor program inhibits the ability to meet the needs of patients with ESKD and end-stage liver disease.

Japan has also led in the context of short and long term follow-up of both liver and kidney recipients as well as their living donors. Short and long-term morbidity and mortality has been captured; the limitations of these registries reflect the voluntary nature of patient follow-up.

Living kidney donation has proven to be safe when performed under an appropriate framework of donor care even though an inevitable small mortality risk is well documented. Transplantation of kidneys from living donors is considered a necessary adjunct today to achieving a national self-sufficiency. However, the World Health Assembly has urged Member States to promote deceased donation and not to make a national program totally rely on living donation. Furthermore, the Declaration of Istanbul on Organ trafficking and Transplant Tourism calls upon governments to ensure the protection and safety of living donors, recognizing their heroic act while combating transplant tourism, organ trafficking and transplant commercialism.[21] **Governments should not enable patients to travel to foreign destinations and undergo kidney transplantation from living donors that are unknown to the recipients**. Israel has set an important precedent to prohibit the authorization of insurance benefits to cover the costs of performing a transplant in a foreign country that does not conform to the provisions of the Israeli 2008 Organ Transplant Act that condemns organ trade.

Registries of living donor transplants should focus upon the safety and well-being of the living donor. Complications that require re-hospitalization of the living donor should be recorded and of course, donor deaths associated with the procedure of organ removal. Thus registries provide important data to base the donor´s consent on the assessment of known risks (at the specific center, national and international level).

National authorities, together with civil society organizations, should take measures to increase public awareness and understanding of the benefits of organ transplantation and of the shortage of organs for transplantation, and to overcome possible cultural resistance and lack of education that negatively affects their populations' willingness to donate. These measures should be aimed at fostering a positive attitude on the part of society regarding donation, including posthumous donation, as a gesture of altruism, solidarity and community participation. This normative change, to a perception of responsibility across all levels of society, necessitates unambiguous legislation, committed support, and ongoing education and public information campaigns. Education of the public should begin in school, emphasizing individual and community ethical values such as solidarity and reciprocity, and promoting organ donation as a civic responsibility.

[21] The Declaration of Istanbul on Organ Trafficking and Transplant Tourism. Available at: https://www.declarationofistanbul.org/. Accessed: July 2021.

4. STRENGTHENING THE REGULATORY CAPACITY FOR OVERSIGHT OF PRACTICE

MODERATORS:

Benita Padilla,
Head, Human Organ Preservation Effort National Kidney and Transplant Institute, Manila, Philippines

Riadh A. S. Fadhil,
Professor of Urology and Transplant Surgery and Director of Qatar Organ Donation Center, Hamad Medical Corporation, and Associate Professor of Clinical Urology, Weill Cornell College of Medicine-Qatar, Doha, Qatar

4.1. Role of Ministerial Agency in Oversight of Practices

Sergio Andrés Madera,
Coordinator, International Relations Department, INCUCAI, Buenos Aires, Argentina

A national donation and transplantation agency should contribute to **developing a legal framework** to regulate this governance activity. Such framework must follow the WHO Guiding Principles, including the following components:

- develop criteria to authorize centers to perform transplants and to certify transplant professionals;
- oversee the maintenance of a waiting list available for patients to undergo organ transplant from deceased donors;
- develop the process of actively monitoring the wait list and transplant activities of the transplant center.

Secondly, the agency should **address the availability of organs and tissues through voluntary non-remunerated donation and with a focus on donation from deceased individuals**. To do so, the promotion of organ donation in the communities is an important strategy. However, more importantly the agency should organize and consolidate an efficient donation and transplantation services network. This effort is essential to ensuring access for all the population to such treatment.

An efficient services network requires several features, among them:

- Trained human resources;
- Laboratory infrastructure;
- Logistics (organ transport);
- Medications, especially immunosuppressants.

Thirdly, the agency should have a **robust informational technology (IT) system** for all donation and transplantation processes to be registered accurately with comprehensive monitoring. This gives credibility to the system as it becomes the most important tool against organ trafficking and transplant tourism.

Therefore, the agency must oversee the maintenance of registries as considered in the Regulatory presentation at this Workshop (see details in Sections 4.2 and 4.3. below) inclusive of:

- organ donors, both living and deceased;
- the demographics of the donor/recipient relationship and their country of residence;
- patients listed for organ transplants;
- outcome (patient and graft survival) of the recipients of organ transplants;
- the transmission of donor infection or malignancy.

Having a specialized agency can provide more powerful advocacy within the government in general, as well as within the health sector. This advocacy can result in more resources for the activity, financial and otherwise. However, an agency nested inside the ministerial structure is not a condition sine qua non for the development the of donation and transplantation activity. This activity may be managed within the ministry of health (as part of a department, program, etc.)

4.2. Requirements for National Transplant Registries and Reporting to the Global Observatory on Donation and Transplantation

Axel Rahmel,
CEO and Medical Director, DSO–Deutsche Stiftung Organtransplantation [German Organ Procurement Organisation], Frankfurt am Main, Germany

There is no standard of data collection by responsible national agencies to assess performance of transplant centers and improve patient care for transplant recipients and living organ donors. Ideally, data should be collected at three levels; internationally (exemplified by the GODT), nationally and at a center level.

National waiting list, donor, recipient and follow-up registries are essential to achieve and continuously monitor Quality, Expertise, Safety and Transparency of all steps of the organ donation and transplantation process, based on the QuEST-principles:

- **Qu** ality: continuous improvement of the quality of the deceased and living donor organ donation and transplantation process:
    - Donor detection / donor management;
    - Organ allocation;
    - Transplantation and short and long transplant outcome;
    - Living donor short and long outcome.

- **E** xpertise: analysis of all aspects of the organ donation and transplantation process to enhance scientific knowledge and by developing innovative strategies to improve quality of outcome for transplant recipients and living donors.
- **S** afety: continuous monitoring and improvement of safety for recipients and living donors:
    - Recipient: preventing donor-transmitted diseases (e.g. tumor, infection, genetic disease);
    - Careful recipient evaluation: indication / contraindication for transplantation, establishment of standardized criteria for selection, monitoring of severe adverse events and reactions;
    - Donor (living donor): general health, long-term organ function, complications.
- **T** ransparency: guaranteeing transparency of all steps of the organ donation and transplantation process including:
    - Access to the waiting list;
    - Medical criteria, socioeconomic factors, nationality/residency;
    - Organ donation activity: donor detection and reporting – involvement/activity of donor hospitals, donor evaluation including determination of death (deceased donation);
    - Transplant activity: access to transplantation, adherence to allocation rules (deceased donation);
    - Transplant follow-up: organ transplant recipient graft failure and patient mortality.

The QuEST-principles constitute the basis for the development and refinement of key policies for organ donation and transplantation both by the Scientific Community and National Authorities.

A well-defined core data set should be established to cover all elements of the organ donation and transplantation chain, covering:

- the transplant by each organ;
- the transplant by donor source: living or deceased;
- the identity of the living donor by nationality and relationship to the recipient;
- the occurrence of a complication in the living donor; death (including cause) or rehospitalization;
- the recipient graft survival at 1, 3, 6, 12 months, 3 years and 5 years, and causes of graft loss;
- the recipient patient survival at the same time intervals, and causes of death;
- a recording of the immunosuppression;
- recipient rehospitalization: infection, cancer, graft function.

International data integration gives faster and more comprehensive insights, including identification of best practices. Internationally harmonized data field definitions are strongly recommended to facilitate data merging.

Organ donation and transplantation registries can help to enhance organ donation and transplantation by promoting public trust.

National authorities should facilitate the establishment / strengthening of a national organ donation and transplant registry including mandatory reporting to the GODT by linking the authorization of transplant centers to the continuous and reliable delivery of the relevant data to the respective national agencies.

4.3. Comprehensive Data Collections at Center Level to Ensure the Quality and Safety of Organ Transplantation

Ryutaro Hirose,
Professor and Vice Chair, Clinical Operations, Department of Surgery, University of California, San Francisco. Surgical Director, Scientific Registry of Transplant Recipients, USA)

NSQIP Transplant (Transplant Quality Improvement Project) is a nascent Clinical Quality Registry which represents a collaborative effort between the American College of Surgeons (ACS) and TTS that is designed to collect, abstract and analyze clinical data elements and outcomes, the acquisition of which is triggered by a transplant event. **The program which was developed and beta tested by transplant centers in the United States can be used to effect outcome analysis and quality improvement efforts at a center level.** An individual center has the capability to compare their own results with other regional, national and international centers-the center receives its own data; the results from other centers are made available to all participating centers, but are center de-identified. At the present time, the program has identified the data sets to be collected for kidney and liver transplantation, but could be expanded to other organs. The data elements to be collected globally are under consideration by an international panel of clinicians.

The center data provides a contemporaneous registry of transplant data which in turn could be submitted to the GODT individually or on a regional or national basis. Additionally, this data set could be the foundation of clinical trials which in turn can facilitate access of transplant patients to novel drugs and procedures. The ACS and TTS hope to offer this program to transplant centers globally as a means to achieve best practices, facilitate registry development and encourage clinical trial activity.

5. PANEL DISCUSSION: COUNTRY MODELS

MODERATORS:

Mehmet Haberal,

Professor of Surgery and Founder President, Başkent University, Ankara, Turkey. Editor-in-Chief, Experimental and Clinical Transplantation, and Immediate Past-President, The Transplantation Society (TTS)

Faissal A.M. Shaheen,

Head, Nephrology, King Fahad Hospital, and Former Director-General, Saudi Center for Organ Transplantation, Riyadh, Saudi Arabia. Co-Chair, WHO Task Force Donation and Transplantation of Organs and Tissues

5.1. China: the Burden of Organ Failure of NCD and the Demand for Efficient National Deceased Organ Donation System

Haibo Wang,

Director, China Organ Transplant Response System, Beijing, China

Organ failure, particularly kidney and liver failure of NCD, are exponentially increasing throughout the world. For example, ESKD is a leading cause of morbidity and mortality worldwide. It was estimated that 2.62 million people were receiving KRT in 2010, and at least 2.28 million people with ESKD had died prematurely because KRT was inaccessible. Globally, diabetes is the leading cause of ESKD, accounting for one-third of incident ESKD patients. It is estimated that diabetic kidney disease will account for 30% of the 1.1 trillion US dollars in medical costs for dialysis worldwide during this decade.

The prevalence of diabetes has increased dramatically during the last few decades in developing countries. It is reported that 77% of people with diabetes live in LMIC in 2014, concurrent with the lifestyle and societal changes accompanied with economic development and globalization. For example, the prevalence of diabetes in China rose from less than 1.0% in 1980, to 11.6% in 2010. It is estimated that there were 113.9 million Chinese with diabetes in 2010, and 66.8 million Indians with diabetes in 2014, accounting for 47.7% of patients with diabetes worldwide. It is reported by Hong Kong Diabetes Registry that the incidence of ESKD among Chinese patients with diabetes was 8.69 (95% CI 7.78-9.60) per 1,000 person years. Thus, the estimated annual incidence of patients with diabetes related ESKD is around 0.99 million in China, in contrast to 0.10 million patients receiving dialysis in China in 2008. The annual incident number of 0.99 million patients with ESKD translates into additional 59.4 billion Renminbi direct cost every year, creating a huge demand for kidney transplantation with a better QoL and cost-efficiency.

The annual death rate of 2019 in China was 7.14% (9.98 million, 714 pmp). Although the medical suitability of patients dying within the hospital (number of potential deceased donors) is under study, the current deceased organ donation rate (4.07 pmp) indicates a large potential improvement for the efficiency of national organ donation system in China.

5.2. Spain: a focus on developing deceased donation to its maximum therapeutic potential

Beatriz Domínguez-Gil,
Director General, Organización Nacional de Trasplantes, Spain

The Spanish Organización Nacional de Trasplantes (ONT) was created in 1989 as an agency dependent upon the Ministry of Health with the role of organizing, coordinating and overseeing donation and transplantation activities of organs, tissues and cells in Spain. The creation of ONT placed transplantation in the political health-care agenda. The Transplantation Law had been enacted in 1979. The country had the capacity to perform transplants and worked within the framework of a public and universal health-care system – but organizing the development of the complex process of posthumous donation was soon identified as the priority to develop deceased donation to its maximum therapeutic potential. A model of coordination was agreed upon with the Regional Authorities and implemented in the country, that evolved from registering 14 donors pmp to more than 30 in less than a decade. After a period of apparent stabilization of the activity, a set of innovative strategies were put in place that allowed to further increase deceased donation rates, reaching 49 deceased donors pmp in 2019, the highest deceased donation activity ever described for a large country.

The principles of the Spanish Model have been well described in the literature.[22] The donor transplant coordination system is structured at three different but inter-related levels: national, regional and hospital. The national level is represented by ONT and the Regional level by the regional coordinators, who are designated by and report to the regional authorities. The hospital level is composed of a network of hospitals specifically authorized for organ recovery. For a hospital to be authorized for organ recovery, a specific requirement is to have a donor coordination unit, that is led by a physician, usually a specialist in intensive care. This system has relied upon intensive care physicians to orchestrate the deceased donation process and has fostered the ownership of the process of deceased donation within the intensive care community in the country. ONT and the regional coordination units act in support of the process of deceased donation, by designating donor coordinators, providing them with standards of practice, ensuring continuous professional training and evaluating performance to identify areas for improvement. Training of all professionals who directly or indirectly participate in the process of deceased donation is an important element of the system that is covered every year with governmental (ONT) funds. A potential donor audit that continuously assesses the potential of donation and identifies reasons for potential donor losses is managed by ONT to run the system with a focus upon improving performance.

Innovative strategies to further increase organ availability include the transplantation of organs from expanded and standard criteria donors, the practice named “intensive care to facilitate organ

[22] Matesanz R, Domínguez-Gil B, Coll E, de la Rosa G, Marazuela R. Spanish experience as a leading country: what kind of measures were taken? Transpl Int 2011; 24(4):333-343. doi: 10.1111/j.1432-2277.2010.01204.x.

donation" and donation after the circulatory determination of death, among others.[23] These lines of action are built on the need to increase organ availability, but also on the concept that donation should be systematically presented as an option in end-of-life care to give patients the opportunity of posthumous donation if this is consistent with their individual principles and values.

5.3. Iran

Katayoun Najafizadeh,
Pulmonologist and Associate Professor, Shaheed Beheshti University of Medical Sciences, Tehran, Islamic Republic of Iran. CEO of Iranian Society of Organ Donation

Iran is a country with 82 million inhabitants, 99.4% of which are Muslim (90% Shia and 10% Sunni). The first living donor kidney transplant from a relative in Iran was performed in 1968. In 1974, the Ministry of Health of Iran established the first dialysis center. Since then, different modalities of KRT are free of charge and accessible for all.

Throughout the next 12 years after the first renal transplant in Shiraz (the period prior to Islamic revolution), 112 renal transplantations were performed from related living-donors. In 1980, 2 years after the Islamic Revolution, all transplant activities were stopped because of the Iran-Iraq war and the focus of all resources and human power on this disaster. Many ESKD patients died because of the shortage of dialysis and transplant facilities.

The Ministry of Health developed a project named the Iranian kidney transplant model in 1982 in which money was given by the government to non-relatives to provide kidneys. Transplantation of deceased donors was started in 1986 and the first heart and first liver transplants happened 4 years later. In 2000, the Parliament accepted the law of deceased donation and the first network for transplant was developed and the rate of renal transplant went up rapidly with both deceased and living kidney donation.

In 2010, organ donation model of Iran was revised and adjusted according to what had been learned from the successful countries of the world in terms of organ donation (Spain and US) and adjusting it with Iran's culture and conditions. This raised the organ donation rates in the country. In 2017, a NGO named the Iranian Society of Organ Donation (ISOD) was established by dedicated organ donation and transplantation experts of Iran and the Ministry of Health outsourced most of the organ donation related activities such as educating donor teams, establishing the national organ donation and transplant registry, designing the organ transfer program, social awareness activities, and donor family support to this NGO.

Iran is first ranking of organ donation in Asia in 2019 (14.3 donors pmp), the first rank of annual number of liver transplants in one center (Avicenna hospital in Shiraz with 587 liver transplant in 2019), and has the ability to perform multiple organ and tissue donation and transplantations: 2,101 kidney (64% from deceased), 961 liver (92% from deceased), 126 heart, 7 lung, 29 pancreas and 9

[23] Matesanz R, Domínguez-Gil B, Coll E, Mahíllo B, Marazuela R. How Spain Reached 40 Deceased Organ Donors per Million Population. Am J Transplant 2017; 17(6):1447-1454. doi: 10.1111/ajt.14104.

intestine transplants, as well as 5,744 skin, 246 heart valve and 19,041 musculoskeletal tissue implants in 2019.

The Ministry of Health is now accepting living kidney donors by HLA matching with recipients, curtailing unrelated living donors.

Despite the considerable improvements in organ donation in Iran, because only one third of suitable brain dead cases are used and there are still 32,000 ESKD patients receiving dialysis and 7-10 patients die every day on different organ transplant waiting lists in hope of receiving a suitable organ. The Ministry of Health, ISOD and Iranian organ donation and transplantation teams are all still working on improving the availability of organs for Iranian patients in need.

5.4. Kenya: Kidney Transplantation

Ahmed Twahir,
Consultant Physician/Nephrologist, Aga Khan University Hospital, and Clinical Director, Parklands Kidney Centre, Nairobi, Kenya

Out of the approximately 50 million people, it is estimated that there are 5 million with some form of kidney disease ranging from stages 1-5. Of these, Kenya has 5,000 patients who are on hemodialysis. The reimbursement program introduced by the National Hospital Insurance Fund (NHIF) has greatly assisted the country increase accessibility to KRT. However, kidney transplant is the ideal form of KRT for those who qualify. There are only 6 transplant centers in the country with a capacity of about **160 transplants in a year**. This is clearly well below the needs of the country and urgent measures must be put in place to address this situation.

The Human Tissue Act of 1967 addressed the recovery of organs from deceased persons for therapeutic purposes and for medical education and research. The Kenya National Patients' Rights Charter of 2013 provides for every individual to donate their organs after death.

In 2010, Kenya introduced a new constitution which provided for the right to the highest attainable standards of health to every Kenyan citizen. It is now the responsibility of the government to ensure that every citizen who needs transplantation receives a transplant. Following the enactment of the Health-Act in July 2017, the Ministry of Health created the Blood Transfusion and Organ Transplantation Technical Working Group (TWG) in October 2017. The main task of this TWG was to "examine the Health Act, with specific focus on the establishment of Blood Transfusion and Organ Transplantation".

There are many challenges facing transplantation in Kenya. These include an inadequate legal and regulatory framework. There is no definition of death which greatly limits deceased donor transplantation. There is no oversight authority to monitor donation, transplantation, and patient outcomes. There are not sufficient trained personnel and centers to meet the demands. The cost of the transplant work-up, the transplant costs and costs of medication is beyond the reach of many. There is also lack of public awareness on organ donation and benefits of transplantation.

Possible solutions for these challenges include:

- formation of the Kenya National Blood Transfusion and Transplant Services that will help oversee the transplant services in the country;
- amend the law to define criteria to declare death by neurologic criteria, clarify government oversight and include matters relating to ethical living organ transplantation;
- training transplant personnel to cope with the increasing demand;
- lobby for reimbursement of transplant evaluation;
- lobby to increase transplant reimbursement and post-transplant medications by the NHIF;
- WHO to provide template for transplant laws and regulations that can be adapted to individualized countries;
- support to set up Tissue/Immunology laboratory;
- promote organ and tissue donation in the community through continued public education and public awareness to increase their availability and ensure timely access.

5.5. Global situation

Efstratios Chatzixiros,
Adviser, Transplantation and Products of Human Origin, Department of Health Products Policy and Standards, WHO, Geneva, Switzerland

From a global review of country models, a variety of organizational approaches and best practices can be identified. There are some common key elements however, especially when it comes to the oversight responsibility and the coordination functions. Furthermore, these models depend on the availability of deceased donation, which requires more complex structures.

The WHO Guiding Principles on donation and transplantation emphasize on the importance of taking the necessary legal and logistical steps for developing deceased donation to its maximum therapeutic potential. From a WHO analysis of data that has been collected through the GODT, it is noted that less than 40% of Member States report on the existence of a functioning deceased donation programme and almost half of the countries have a governmental recognized authority that is responsible for overseeing the activities at national level. There are major differences between the 6 WHO Regions, with the European area having achieved the most. This is relevant to the existence of the European Union frameworks and strategic action plans. Less resourced regions, such as the sub-Saharan area, show the lowest organizational capacity and availability of transplantation systems.

In meeting the needs of the population, it is suggested to establish cooperation frameworks and agreements to allow patients to be transplanted abroad. The analysis however shows that less than 20% of member states have achieved such cooperation with the significant majority being again in the European Region. The limitations in access to transplantation services can also been seen in the number of centers/programs that are available in the Regions. Especially when it comes to deceased donor transplants (i.e. heart or lungs), there is a huge gap that ranges from 1 center *per* 285 or 570 million inhabitants, respectively, in the African region *versus* 1 center *per* 3.5 and 9 million inhabitants in the Americas.

For the establishment of national self-sufficiency, every country, in light of its own level of economic and health system development, should progress toward the global goal of meeting patients' needs based on the resources obtained within the country, for that country's population, and through regulated and ethical regional or international cooperation when needed.

The Madrid Resolution on organ donation and transplantation (WHO Global Consultation 2010) suggested the following steps:

1. Action should begin locally (not precluding international cooperation);
2. Strategies should be targeted to decrease transplantation needs of a population and increasing organ availability;
3. Strategies must be based on solid ethical principles: solidarity, voluntary donation, and non-commercialization;
4. Strategies should be tailored to the local realities.

In conclusion, it is the responsibility of governments to setup and sustain national donation and transplantation systems based upon the assessment of needs (burden of disease) and the existing resources (**Figure 8**). Components that exist in international models must be adapted to the existing national health system and capacities. The requirements for supporting a successful programme are summarized:

- Enact legislation to define death that enables recovery of organs
- Establish a National Agency that oversees the practice of donation and transplantation
- Certify transplant centers, training programs and transplant personnel
- Certify organ and tissue procurement agencies and personnel
- Certify histocompatibility laboratories
- Develop registries for donors, potential recipients and transplant patients
- Review outcome data
- Review burden of disease that necessitates organ transplantation

- CKD = chronic kidney disease;
- CVD = cardiovascular disease;
- COPD = chronic obstructive pulmonary disease.

Figure 8: Schematic representation of the concept of national accountability in meeting the donation and transplantation needs of the population.

Annex 1 provides information on the models in Argentina and South Korea, that were not presented during the Workshop, although references were made by the respective experts that acted as session moderators.

Conclusions:

- Organ failure, particularly kidney and liver failure, caused by non-communicable and transmitted infectious diseases are exponentially increasing throughout the world;
- The cost of caring for these patients exceeds many other disease entities;
- Organ transplantation as a treatment provides the best survival and QoL with a cost efficiency. The "cost efficiency" issue may not be the case in the poorest countries, but can only be determined with the acquisition of accurate burden of disease data;
- The cost of inaction is substantial given the impact of organ failure upon individuals, and the social and economic impact of diseases leading to organ failure on communities;
- Governments must address national self-sufficiency by developing systems that provide organs for their patient population via living and deceased organ donation;
- National self-sufficiency requires a legislative framework that includes oversight of a national agency;
- The Workshop provided operational guidance of ethically sound living and feasible deceased donor transplantation including a mandated collection of data pertaining to safety of the living donor and outcome measurements for the recipients;
- International cooperation (financial, exchange of best practices, and provision of technical expertise) is required to support countries in progressing towards self-sufficiency in transplantation, particularly to low resource countries;
- The development of effective transplant systems is the fundamental means to prevent organ trafficking and protect the vulnerable from exploitation.

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ANNEX 1: OTHER DONATION AND TRANSPLANTATION COUNTRY MODELS

Argentina:

Gabriel E. Gondolesi,
Professor of Surgery, and Chief, Liver, Pancreas and Intestinal Transplant, Fundación Favaloro Hospital Universitario, Buenos Aires, Argentina

Organ transplantation started in South America in 1957 with the first kidney transplant in Buenos Aires (Argentina). In 1979, Argentina developed a National Organization to centralize procurement and transplant services, currently called Instituto Nacional Central Unico Coordinador de Ablación e Implante (INCUCAI). INCUCAI is part of the National Ministry of Health and one of the first organizations of its kind in South America. INCUCAI functions as a central organization, coordinating and legalizing all donation and transplant activities and processes. Since 2001, all insurance companies, physicians, patients have free access to regulations at all steps of transplantation (www.incucai.gov.ar/SINTRA), providing an entirely transparent process.

In order to increase kidney donation, INCUCAI created the "Old for Old" program in 2010, prioritizing the placement of older kidneys into older recipients. In 2015, INCUCAI approved paired exchange programs. These measures have improved the deceased donor rate to 15 p.m.p. In 2019, INCUCAI established binational agreements for lung and small bowel transplantation with Uruguay. Argentinian transplant activities cover all organs and exits in both the private and public health systems. In 2020, a COVID-29 registry for dialysis, waitlisted and transplanted patients was established.

Argentina is working on: a) development of new programs for utilizing donors after circulatory determination of death; b) utilization of ex situ perfusion devices; c) expansion of vascular composite grafts (VCA), including uterine transplantation and d) the ongoing engagement of ICU physicians with emphasis on pediatric intensivists to enhance development of deceased organ donation and the dissemination of the criteria for the determination of death. The goal is for authorities of the different health administration systems and physicians to understand the medical and the clinical advantages of organ transplantation as the treatment of choice for end-stage organ failure. Increasing the current low organ donation rates is essential to achieve self-sufficiency.

South Korea

Curie Ahn,
Professor, Division of Nephrology at National Medical Center, Seoul, South-Korea. Secretary-General, Asian Society of Transplantation

The organ transplantation program was initiated in Korea in 1969, with the first living donor kidney transplant being followed by the first deceased donor kidney transplant10 years later. Korea developed two action plans to enhance kidney and liver transplantation and to address national self-sufficiency: the establishment of a legislative and regulatory framework and the establishment of the national organ transplantation organization, the Korean Network for Organ Sharing (KONOS).

Early success with live donor transplant evolved to the appreciation of the need for developing deceased donor transplantation as a way to address the concern of Korean patients traveling to foreign destinations for transplant when living donor transplantation was not possible in the country. The first iteration of this process was the development of hospital-based procurement activity (Hospital based Organ Procurement organizations [HOPO]), but this has expanded to the development of a national independent organ procurement organization, the Korean Organ and Tissue Donation Agency (KODA), established in 2009 to facilitate retrieval from every hospital in Korea. KODA can optimize the use of donated organs, disseminate standardized processes, and cooperate with tissue and eye donation. KODA mandates information on potential donors to be communicated from both hospital Emergency Departments and Intensive Care Units to allow for assessment of potential versus realized donors.

The Vitallink, an NGO established by the Korean Society of Transplantation (KST) has launched important educational activities for high school and medical school students. It has also proposed a first-person authorization program, which is legally binding, and currently in legislative process in Congress.

In 2012, Korea has established a National Transplantation Database (KOTRY) to serve as an objective registry, to provide biobanking services and promote transplantation research. Further effort is needed to increase the number of organ donor cardholders and family consent through meaningful programs of targeted education and the creation of a memorial park to build a national culture that honors and thanks donors and their families in Korea.