



Review article

Organ donation in the US and Europe: The supply vs demand imbalance

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ABSTRACT

Organ donation and transplantation remain the best and most cost-effective clinical solution for end-stage organ failure. Several agencies across the US and Europe provide legislative, regulatory, and humanitarian services to generate smoother applications in all transplantation processes and donor-recipient relationships. US and European statistics present nine types of grafts, with kidneys being the most transplanted organ worldwide. However, organ shortage, religion, underrepresented minority groups, difficulties in obtaining consent, lack of understanding, and general ethical concerns present challenging barriers to organ donation, reflecting the complexity of graft procurement and allocation. Breaking down these barriers to reduce the organ-supply imbalance requires an appropriate multifaceted approach. Some of the key areas include increasing the potential donor pool and consent rates, apt organ allocation, and improving organ health. Additionally, suitable policies and standardized guidelines for both donors and recipients, alongside educational initiatives, are needed to ensure patient safety and global awareness. Looking forward, novel and effective research plans and initiatives are needed if we are to avoid a colossal supply-demand gap.

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Contents

1.	Introduction	2
2.	Organ donation in the US and Europe	2
2.1.	US overview	2
2.2.	Europe overview	4
3.	Barriers to organ donation	4
3.1.	Consent	4
3.2.	Ethics	5
3.3.	Lack of understanding	5
3.4.	Religion	6
3.5.	Race	6
4.	Breaking down the barriers	6
4.1.	Early identification and expanded donor eligibility	6
4.2.	Compensation and incentives	6
4.3.	Education and communication	6
4.4.	Efficiency of organ allocation	7
4.5.	Awareness and prevention of disease	8
5.	Alternative solutions to organ donation	8
6.	Concluding remarks	8
	In memoriam	8
	Declaration of Competing Interest	8
	Acknowledgements	8
	References	8

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1. Introduction

Practicing clinical transplantation has proven to be lifesaving [1]. Data from the Global Observatory of Donation and Transplantation in 2018 disclosed 140,964 organ transplants worldwide [2]. In 2017, kidney and liver were the most frequently transplanted organs, whilst small bowel transplants were the least frequent [3].

Specified and unspecified donation form two significant classification types for the donor-recipient relationship [4]. A specified donation entails an intended/known recipient to whom the graft donor may be genetically and/or emotionally related (e.g., a spouse giving her kidney to her husband represents a *specified direct* donation, whilst a donation to a known recipient through an exchange program is a *specified indirect* donation) [4]. An unspecified donation represents an undefined graft recipient (completely anonymous) who is placed in a fixed donation waiting list [4,5]. Contraindications to organ donation (i.e., infections, general conditions, reimbursement policies, etc.) and long waiting lists (e.g., 3–5 year waitlist for kidney transplants in Europe) are challenging processes both for the donor and the recipient [6–8], with organ shortage being one of the utmost threats in organ transplantation. Statistics confirm this gap, with 74.63% of candidates failing to receive a transplant in the US in 2015, and 19.89% in the UK in 2018 [9,10].

Living Organ Donation (LOD) is a promising solution for preventing this gap from widening [6,11]. LOD is an upcoming, and in some countries, already established procedure, that is possible due to several medical advances [6]. The most common LOD transplants in Europe and the US are kidney and liver [6,12] and include preemptive and early transplants. [13] Individuals suffering from kidney disease can receive transplants prior to their dialysis therapy (preemptive transplants) or shortly after their kidney failure (early transplants) [13]. The benefits of preemptive/early transplants include reduced transplant rejection, improved life quality and avoidance of dialysis therapy [13]. Nevertheless, the physical, psychological, and social risks of LOD, combined with discrepancies in donor screening and donor-recipient relationships in different countries, create a blurry environment for the protection of both graft donors and recipients [6]. The World Health Organization provides information on acceptable practices for LOD to help obtain safer and smoother applications worldwide [6].

Donation after brain death (DBD) remains one of the primary sources for organ transplants [1]. Irreversible coma from a known cause, brainstem areflexia, and apnoea are the essential criteria for brain death determination [8]. Preparation for organ procurement following brain death involves prognosis, a series of haematologic testing, and checking of the general pathophysiologic changes of the deceased individual to determine the viability of potential donation [8,14]. Debating whether DBD is an ethical act has generated philosophical, medico-legal, and religious arguments. One of the main controversies describes the connection of brain death to death, and whether these concepts are equal [8]. Such arguments use various misconceptions of body movements after brain death or cases where heart-beating is still possible following brain death [8,11].

Organ donation also occurs after circulatory death (DCD); defined as the permanent loss of consciousness capacity and brainstem functioning [1,11,15]. Compared to DBD, DCD donors are younger and healthier [7], with a recent increase in white male DCD donors who suffered a stroke [7,15]. Notwithstanding, DCD is among the riskiest transplantations and is associated with frequent graft failure [7,11]. Overcoming DCD graft failure requires donor-recipient risk factors, such as DCD status, donor/recipient age, cause of death, and body mass index, to be consistently examined [7].

Paediatric DCD (pDCD) practices should also be incorporated into deceased organ donation acts and guidelines [15]. Weiss et al., argue on the importance of minimum standards and good practice statements for pDCD [15]. Furthermore, the discussion of the withdrawal

of life-sustaining therapies (WLST) in pDCD raises ethical concerns and is the main reason why pDCD remains controversial [15]. A recently presented guideline on WLST applications states the need to show compliance with hospital practices, alongside the administration of psychosocial support to any donation decision-makers [15]. Emphasis needs to be given to the psychological support of family members and healthcare professionals, especially when neonatal DCD takes place [15].

2. Organ donation in the US and Europe

2.1. US overview

In the US in 1968, the Uniform Anatomical Gift Act (UAGA) initiated a regulatory framework for organ donations for individuals over 18 [8,16]. This led to the administration of the Organ Procurement and Transplantation Network (OPTN) in the US [8,17]. Each Organ Procurement Organization (OPO) is an accountable liaison for hospitals and United Network Organ Sharing (UNO) associations for procuring, preserving, and allocating organs and tissues [8]. Since 1968, various federal notices and legislation policies have expanded, clarified, and improved safety on organ donation procedures nationally [16]. For example, the Organ Donation and Recovery Improvement Act (PL 108–216) in 2004 expanded the authorities of the National Organ Transplant Act and provided reimbursement of travel and subsistence expenses for living organ donors and administered various states with grants [13]. In addition to OPOs and UNOs, the internet is also a source for organ donation. For instance, “since 2004, [MatchingDonors.com](https://www.matchingdonors.com) has facilitated over 600 transplants and currently has over 15,000 registered altruistic living donors, with waitlist times significantly less than the US government waitlist” [18]. However, the use of such an innovative platform is still not broadly adopted due to unfamiliarity and doubt towards internet/cyberspace processes [14].

The US OPTN reports eight standard types of organ transplants in the US: kidney, pancreas, liver, intestine, heart, lung, kidney/pancreas, and heart/lung [10]. New York is among the states which perform the most transplants across the US (see Fig. 1) [19]. In 2014, the first vascularized composite allografts (VCAs) occurred and continue to be included in OPTN strategies for graft allocation [10].

In 2018, the annual number of transplants in the US was 36,528, with an average of 80 people receiving a transplant each day (see Fig. 2) [16]. Statistics from 2016 reported an average of 3.54 and 3.06 organs recovered and transplanted respectively per donor, with a total of 4859 (13.8%) organs recovered for transplant and later discarded due to poor organ function, infections, anatomical abnormalities, etc. [16]. The majority of donors were male (59.7%), white (66.7%), and aged between 18 and 34 years (31.1%) [20]. However, patients' economic status, age, and/or illness stage are a determinant aspect of acceptance in the US transplant waiting list, resulting in an additional 253 patient deaths daily [21].

The need for transplants far outstrips supply, with 113,000 patients in the US in need of a transplant in 2019, and more than half (67,000) being of ethnic minority [16]. Furthermore, approximately only 58% of the US population is registered as a potential donor (145.5 million actual donors), making organ shortage an ongoing issue [16,22,23]. Waiting varies from 213 to 370 days, depending on the organ [19,22], with 4925 deaths in 2019 occurring whilst waiting for a transplant [13]. Waitlist numbers and deaths in the US (and Europe) have remained relatively stable over the past nine years (see Table 1).

Some of the most common primary diagnoses for single organ/tissue transplants include multiple myeloma (i.e., autologous bone marrow organ transplants), cardiomyopathy, and lung disease, whereas diabetes mellitus usually results in multiple organ transplants [19,24]. The process of organ transplantation (both prior and post transplantation)

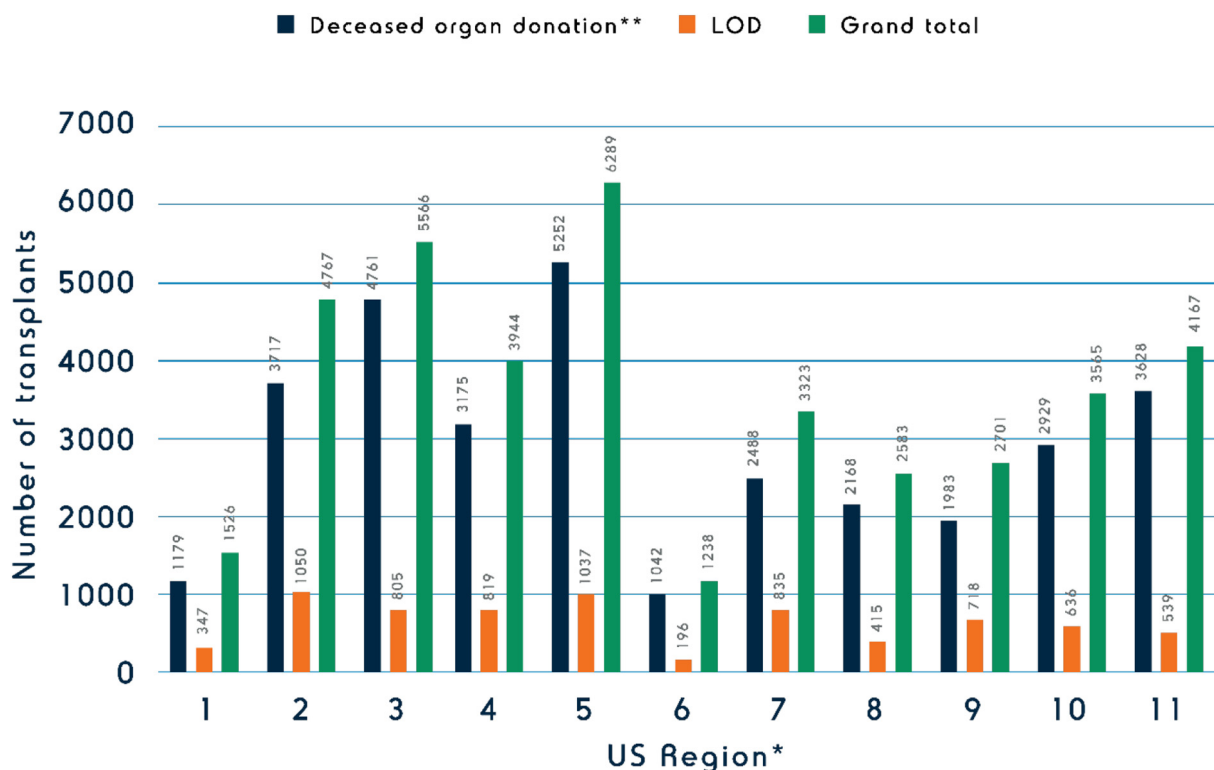


Fig. 1. Total number of transplants in 2019 for all US regions. *US Regions: Region 1: Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Region 2: D.C., Delaware, Maryland, New Jersey, Pennsylvania, West Virginia. Region 3: Alabama, Arkansas, Florida, Georgia, Louisiana, Mississippi, Puerto Rico. Region 4: Oklahoma, Texas. Region 5: Arizona, California, Nevada, New Mexico, Utah. Region 6: Alaska, Hawaii, Idaho, Montana, Oregon, Washington. Region 7: Illinois, Minnesota, North Dakota, South Dakota, Wisconsin. Region 8: Colorado, Iowa, Kansas, Missouri, Nebraska, Wyoming. Region 9: New York, Vermont. Region 10: Indiana, Michigan, Ohio. Region 11: Kentucky, North Carolina, South Carolina, Tennessee, Virginia. **Deceased Donors include: DCD and DBD donors. Source: <https://optn.transplant.hrsa.gov/data/view-data-reports/regional-data/>.

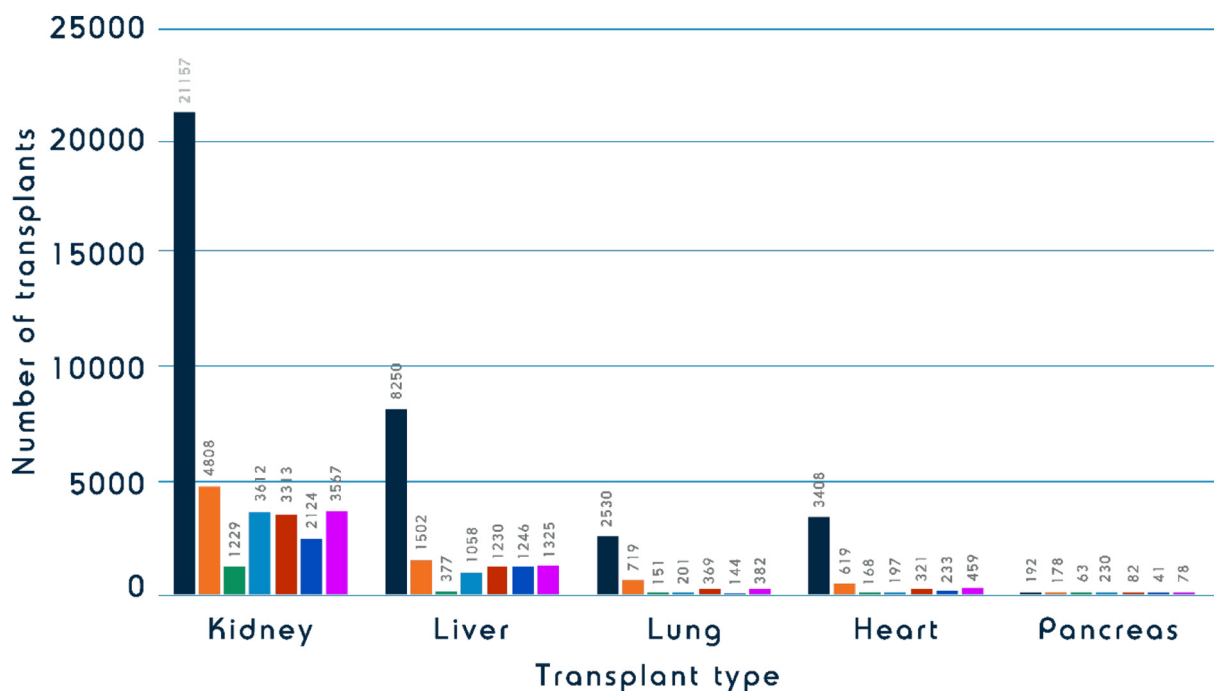


Fig. 2. Total number of transplants in the US and Europe for kidney, liver, lung, heart, and pancreas in 2018. *Eurotransplant is an international collaboration between the following countries: Austria, Belgium, Croatia, Germany, Hungary, Luxembourg, the Netherlands, and Slovenia. **Scandiarttransplant is an international collaboration between the following countries: Denmark, Finland, Iceland, Norway, Sweden, and Estonia. Sources: <https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/>; <https://statistics.eurotransplant.org/>; <https://www.odt.nhs.uk/statistics-and-reports/annual-activity-report/>; <http://www.scandiarttransplant.org/data/>; <http://www.transplant-observatory.org/>.

Table 1

Total waitlist count by year and region. Deaths that occurred whilst on the waitlist are shown in parentheses.

Year	Region			
	US	EuroTransplant ^a	Scandiatransplant ^b	UK
2018	113,759 (5565)	14,129 (1289)	2660 (129)	6077 (400)
2017	115,759 (5850)	14,773 (1386)	2629 (111)	6044 (411)
2016	119,362 (6199)	14,533 (1370)	2487 (100)	6388 (457)
2015	122,071 (6688)	14,560 (1437)	2402 (105)	6476 (466)
2014	123,851 (6727)	14,928 (1387)	2280 (99)	6943 (429)
2013	121,272 (6488)	15,292 (1392)	2211 (122)	7026 (456)
2012	117,040 (6585)	15,027 (1543)	2116 (112)	7332 (466)
2011	112,816 (6786)	15,499 (1552)	2093 (118)	7636 (508)
2010	110,375 (6624)	15,591 (1561)	2117 (102)	7800 (511)

Sources: <https://www.organdonor.gov/statistics-stories/statistics/data.html>; <https://statistics.eurotransplant.org/>; <https://www.odt.nhs.uk/statistics-and-reports/annual-activity-report/>; <http://www.scandiatransplant.org/data>; <https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/#>.

^a EuroTransplant is an international collaboration between the following countries: Austria, Belgium, Croatia, Germany, Hungary, Luxembourg, the Netherlands and Slovenia.

^b ScandiaTransplant is an international collaboration between the following countries: Denmark, Finland, Iceland, Norway, Sweden and Estonia.

is costly. The approximate annual cost for all transplant recipients in the US in 2020 will be 332.7 million dollars (276.6 million for the US population <65 years of age and 56.1 million for >65) [19].¹

2.2. Europe overview

The European transplantation strategies [25] (formed of the Organ Exchange Organizations (OEOs), transplant coordinators, and professional training programs) ensure organ donation and transplantation processes are legitimate. European OEOs act as non-profit bodies that aid donor hospitals and transplant units by representing all members, ensuring appropriate organ allocation and satisfying all requested needs [25]. Transplant coordinators help develop links between intensive care units and transplant centres, donation protocols, and organ donation communication tactics [25]. Training programs help initiate awareness, procurement policies, and an understanding of the intricacies of organ donation [25]. European Organs Directive (EOD 2010/53), Commission Directives (i.e., 2012/25/EU), and guidelines and action plans (2009–2015) complete all European organ transplantation legislative practices [26].

Regarding access to transplantation services, the EU commission helps enable access by providing and allocating funds to organ donation and transplantation programmes. Member states devise policies to ensure appropriate reimbursement of costs to hospitals for deceased donation, to stakeholders following EU funding opportunities, and to EU commission obtaining European structural investment funds [27]. However, inequity of access can be an issue for some EU countries, for example figures from 2005 indicate that liver transplants in southern Italy were almost four times lower than the north and centre of Italy, with similar differences occurring between regions in France and Spain [28].

The most common transplants in Europe include kidney, liver, heart, and lung (see Fig. 2). Other graft operations in Europe in 2018 included: intestine, small bowel, hand, and face [26]. 10-year statistics for deceased and LOD donors in Europe (and the US) can be seen in Table 2. The Spanish transplantation system performed an average of 100 transplants per million population (pmp) in 2015, of which 60–70 pmp were deceased donors [29]. However, approximately 4000 kidney candidates remain on waiting lists in Spain, with 6–8% of all organ candidates dying

¹ The abovementioned approximate costs are the sum of costs per member per month (PMPM) for individuals who receive organ and tissue (i.e., bone, cornea, etc.) transplants. More specifically, PMPM average costs are up to \$11.22 for individuals who are under the age of 65 and up to \$16.48 for the elderly. These charges cover costs for the 30 days before transplantation, organ procurement, hospital transplant admission, physician services, etc.

or being removed from the waitlist each year [29]. France performs islet cell, pDCD, and VCA grafts (in addition to the common transplants in Europe), with a total of 5746 transplantations in 2015 [30]. Additionally, data from 2015 indicate 1769 DBD donors, 76.9% liver organ recoveries, and 73.6% liver transplants [30]. Survival rates are increasing steadily, with 88.9% and 67.8% for 5-year kidney and heart graft survival, respectively [30].

Shortage of available organs in Europe persists [31], with an average of 15–30% of patients dying annually on waitlists; a fact that does not go unnoticed by organ trafficking organizations [25,32]. Since several barriers occur prior to successful transplantation, there is pressure for indigent individuals to sell their organs [25,26,32]. Although transplant demand is rising due to the increase of diseases (i.e., diabetes, liver disease, etc.), an unlimited organ supply does not seem to be the solution, due to general healthcare budget issues [33,34].

3. Barriers to organ donation

3.1. Consent

Two main systems exist for organ donation after death; the opt-in system (explicit consent) and the opt-out system (presumed/deemed consent). The former requires potential organ donors to actively give consent to the procurement of their organs after death, whereas the latter entails consent as the default option. The two systems have become a highly discussed political matter, with numerous countries recently switching from opt-in to opt-out, such as Wales, the Netherlands, England and Scotland,² with on-going debate in (but not limited to) Denmark [35] and the US [36].

There is some evidence to suggest that switching to an opt-out system may increase organ donation rates [37,38], for example, switching organ donation to the default option enables the conversion of intention to donate to actual donation [39,40]. Changing the default option to opt-out also enables a 're-branding' of donation as the standard and recommended choice, as opposed to a decision that goes against the status quo [37,39,40]. Likewise, the default option is the easier choice, as it requires less physical effort (i.e., filling out forms) and, in the case of organ donation, requires less cognitive and emotional effort by removing the need to make an active choice on a complex topic [37].

Spain is cited as an example of how the opt-out system can increase donation rates. For the last 26 years it has consistently held the highest number of organ donors per pmp, with a pmp of 47 in 2017, compared to 31.7 in the U.S. [41]. However, Spain's success is not merely a result of a change in legislation to an opt-out system, but rather due to an overhaul of the organ donation model. Improvements were made regarding the early identification/referral of organ donors, broadening of eligibility criteria of usable organs, the process of DCD, and training in communication with family members of potential organ donors [29,42]. Moreover, the evidence to suggest that the opt-out system alone leads to increased donation rates is not entirely clear [39,43,44], with some showing that deceased donor rates are higher in opt-out countries, but that living donor rates are lower [45]. Additionally, as the opt-out system varies in terms of 'soft' and 'hard' legislation, with the 'soft' version requiring that relatives are allowed to reject organ donation of a relative, results are likely influenced by these differing versions [44–46].

One major concern with the opt-out system is the ethical issues it raises. For instance, presumed consent for organ donation reached its peak in the US in 1990 but was later rejected in 2006 by the UAGA, partly due to concerns about professionals abusing the authority that presumed consent entailed [47]. Furthermore, there is concern as to whether presumed consent accurately reflects the patient's wishes,

² Wales: Human Transplantation (Wales) Act, 2013.

Netherlands: Active Donor Registration Law. In force from Summer 2020.

England: Organ Donation (Deemed Consent) Act 2019. In force from May 2020.

Scotland: Human Tissue (Authorisation) (Scotland) Act 2019. In force from Autumn 2020.

Table 2
Total donor type count by year and region.

Year	Donor Type ^a	Region						
		US	EuroTransplant ^d	ScandiaTransplant ^e	UK	France	Italy	Spain
2019	Deceased ^b	11,870	6277	1430	1600	1924	1495	2302
	LOD ^c	7383	1299	339	1039	529	364	356
2018	Deceased	10,721	6709	1266	1574	1881	1466	2241
	LOD	6850	1438	340	1051	555	318	316
2017	Deceased	10,286	6002	1336	1413	1933	1714	2183
	LOD	6183	1406	334	1043	629	328	349
2016	Deceased	9971	6329	1294	1364	1859	1478	2019
	LOD	5975	1460	320	1075	581	287	371
2015	Deceased	9079	6498	1263	1282	1809	1369	1851
	LOD	5991	1415	340	1092	562	326	418
2014	Deceased	8596	6523	1236	1320	1675	1384	1682
	LOD	5820	1460	358	1146	526	267	444
2013	Deceased	8269	6236	1107	1212	1673	1323	1655
	LOD	5989	1536	352	1101	414	238	405
2012	Deceased	8143	6668	1128	1088	1642	1337	1643
	LOD	5867	1507	337	1055	366	208	389
2011	Deceased	8126	6847	1124	1010	1630	1325	1667
	LOD	6023	1474	385	1045	316	226	340
2010	Deceased	7943	6980	1968	959	1538	1298	1502
	LOD	6562	1406	377	1061	300	194	260

Sources: <https://www.organdonor.gov/statistics-stories/statistics/data.html>; <https://statistics.eurotransplant.org/>; <https://www.odt.nhs.uk/statistics-and-reports/annual-activity-report/>; <http://www.scandiatransplant.org/data>; <https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/#>.

^a Deceased Donor Type Organs for EuroTransplant include: Heart, Kidney, Lung, Liver (plus split liver), Pancreas (plus pancreatic islets), Living Donor Type Organs for Eurotransplant include: Heart, Kidney, Lung, Liver (plus split liver). For ScandiaTransplant only kidney and liver deceased and living donor data are included. US and UK data include: Kidney, Heart, Lung, Liver, and Pancreas both for deceased and living donors.

^b Deceased Donors include: DCD and DBD donors.

^c Living Organ Donors (LOD) for France, Italy, and Spain include kidney and liver transplants only.

^d EuroTransplant is an international collaboration between the following countries: Austria, Belgium, Croatia, Germany, Hungary, Luxembourg, the Netherlands, and Slovenia.

^e ScandiaTransplant is an international collaboration between the following countries: Denmark, Finland, Iceland, Norway, Sweden, and Estonia.

with the potential to violate a donor's autonomy if they did not want to donate but failed to register to opt-out [48]. Indeed, "the moral wrong involved in interfering with a dead person's body against his (un)stated wish may be seen as worse than the moral wrong involved in non-interference with the body against his (un)stated wish" [49 p. 94].

An alternative option to both the opt-in and opt-out systems is mandated consent, which requires that competent adults register their intent to donate or not donate [49,50]. It allows individuals to choose which organs they want to donate and to give permission to relatives to have the final say. However, if relatives are not granted this permission, then the wishes of the deceased are final and cannot be superseded [48,50]. Mandated consent removes the ethical concerns regarding the intentions of those who fail to register a choice. However, it poses other ethical implications, such as forcing individuals to make a choice [48,50]. A fourth option is organ conscription, in which all usable organs are available for transplantation regardless of consent; however, there has been little discussion of this approach [51,52].

3.2. Ethics

As previously mentioned, there are ethical issues that hinder the procurement of organs, such as potential violation of autonomy. Beyond consensual matters, there are problems related to the definition of a deceased patient, due to a lack of standardization of determining brain death worldwide [53–55] and difficulty in public understanding and acceptance of brain death [56–58].

A more recent consideration that raises ethical concerns is organ donation after assisted death [59]. Although organ donation after assisted death removes the difficulties around consent (as first-person consent is given), there is a risk of the two processes becoming intertwined, with eligibility of assisted dying being influenced by the potential to procure organs. There may also be added pressure on the potential donor, leading them to choose assisted dying earlier than they may have otherwise [see 60 for a discussion]. In Canada there is discussion

as to whether organs should be removed from consenting euthanasia patients while they are still alive, allowing for organs to be retrieved at optimal condition (with blood and oxygen flowing through them up until the point of removal). Death of the patient would then be brought about by the removal of the heart ("euthanasia by organ donation"), rather than by lethal injection [61,62].

Ethical concerns also surround the procurement of organs from living donors. In particular, pressure to donate from the recipient or relatives (whether explicit or subtle) can be an issue, as well as more direct concerns, such as the risk of harm to the donor [63]. [MatchingDonors.com](https://www.matchingdonors.com) has made it possible to find living kidney organ donors online. In 2012 it was also brought to the UK, yet controversy surrounds the issue despite reassurances that all transplants facilitated through the platform will require consent and no form of reward will be given. [64,65]

3.3. Lack of understanding

Understanding what organ donation entails has been linked to the acceptance of organ donation [66,67]. Unfortunately, understanding of the process of organ donation and transplantation is not always evident, with studies reporting that not enough information is provided on the topic [68–70]. Stemming from this, a common barrier to becoming an organ donor is a mistrust in the system, with the belief that professionals have control over the process, and because of a conflict of interest to help those in need of transplants, professionals may procure organs unethically [68,71]. Education and knowledge of the process would likely alleviate these concerns, as ultimately the choice of organ donation is with the donor or donor's relative and not the professionals (except for organ conscription).

Public perception of organ donation also influences those in need of a transplant. A lack of understanding about kidney transplantation means that many patients remain on dialysis; "you'd be surprised at how many people, patients, and even providers, think of (transplantation) as a

method of last resort... (transplantation) is, no question, a better option for the patient." [72].

3.4. Religion

Religious views on organ donation are diverse and often subject to interpretation [73,74]. A systematic review found that some people regard religion as supportive of organ donation, due to it being consistent with altruistic teachings. However, others were concerned about effectively 'playing God' and interfering with one's natural course towards their end of life, or worried that their body would not be accepted into the afterlife if it was not whole [68]. This later concern also applied to non-religious individuals, who worried about the effect this would have on family members [68]. As organ donation did not exist when many religious texts were written, a potential way to address the issues with religious interpretation on organ donation is for religious leaders and institutions to actively engage with the issue and provide a clear stance [75,76].

3.5. Race

Minorities have a greater need for transplants due to certain diseases occurring more frequently than the general population. For example, in the US in 2016, kidney failure was highest among minority groups, with incident rates 9.5 times higher in Native Hawaiians and Pacific Islanders than whites, yet the majority of organ transplants occurred in whites [77]. Recent changes to the organ allocation system in the US (2002) helped address this balance somewhat. The previous allocation system allocated organs to waitlist patients by location rather than need; a system that was deemed unfair and inefficient [78]. However, the system was partly justified, as the duration of graft ischemia (hot and cold), and the time needed for the organ to be procured until it is reperfused, has an impact on the recipient's quality of life post transplantation. If donor and recipient were close in proximity, results seemed better [79]. For patients with liver failure, a model for end-stage liver disease (MELD) is used, which indicates disease severity and prioritizes those with the highest severity for transplantation [80]. Given that minorities are often top of the list in terms of severity, this system has helped minorities in need of a liver transplant. [77].

The imbalance between whites and minority groups is also evident in organ donor numbers. Donation rates tend to be lower in minorities, with low consent rates in blacks, Hispanics, and Asians, which may be a result of language barriers in cases where English is not their first language [81]. However, an effort has begun to reduce this disparity. For example, funding for a grass-roots initiative that emphasised education and empowerment, resulted in the percentage of African American donors quadrupling between 1990 and 2008 in Washington D.C. [82].

4. Breaking down the barriers

Addressing the supply-demand problem requires a multifaceted approach. Fig. 3 illustrates four target³ areas that are needed to address this supply-demand imbalance adequately.

4.1. Early identification and expanded donor eligibility

Early identification of donors has many benefits, including reducing the risk of injuries to organs after brain death [83], identification and resolution on potential Coronial/Procurator Fiscal problems, early tissue typing and virology screening, and the planning of approaching the issue of consent with relatives [9]. Obstacles to early detection include lack of specific training and communication between professionals [84] and lack of familiarity and understanding of the need to identify

brain dead patients as soon as possible [83]. In the UK, the NHS Blood and Transplant published a strategy guide in 2012 to aid with identifying and referring all potential donors as soon as possible. The statistics from 2018 show that the DBD and DCD referral rate was 99% and 93% respectively, and has been steadily improving since 2014, suggesting the success of the strategy on early identification and referral [85].

Converting referrals to actual donors is vital to improve the donor pool. In the US in 2017, the number of organ donors was higher in the majority of OPOs compared to 2016. This increase occurred alongside a higher proportion of donors with drug intoxication as a mechanism of death and an increased risk of blood-borne disease, suggesting that (safely) expanding the eligibility criteria accounted for some of the donor number increase [86]. Other evidence supports this trend of increased donations from expanded criteria donors (ECD) [31] defined as kidney donors over 60 without comorbidities, or over 50 with two of the following comorbidities: blood hypertension, death by cerebrovascular accident or terminal serum creatinine levels >1.5mg/dl [87]. In the UK, ECD is not used, but rather a donor risk index, which accounts for donor age, weight, history of hypertension, days in hospital and adrenaline [88]. Figures from 2017/2018 show that the number of transplants performed using kidneys from high risk donors in the UK rose to 40% from 29% in 2008/2009, indicating the potential for higher risk donors [88]. Expanding the criteria for living donors could also be an option. For example, Ahmadi et al. suggest that living kidney donors should not be automatically excluded if they are elderly (up to age 70), obese, have vascular abnormalities or are women of childbearing age, as they found no evidence for increased risk or poorer outcomes in these populations. [89] Moreover, in South Africa, kidney transplants from HIV-positive donors to HIV-positive recipients has been possible since 2010, and the first transplant of a HIV-positive living donor was achieved in 2017 (2019 in the USA) [90]. HIV-positive donors to HIV-negative recipients has also recently become possible in South Africa, opening up the possibility for other countries to follow [90].

4.2. Compensation and incentives

Donation can be costly, particularly in the case of LOD. In most countries donation is limited to "altruistic" donors, meaning that no monetary or material value can be given in exchange for an organ [91]. Expenses are reimbursed, however in the US they do not cover loss of wages or child care [92], whereas the UK covers costs to the extent that there is no financial incentive or disincentive to becoming a donor [93].

Compensating above and beyond the expenses of donating opens up many ethical concerns, such as the potential for unregulated organ markets [91]. As such, the purchase or sale of organs is illegal worldwide, with Iran being the exception [94]. However, there is discussion of financial and other incentives, such as tax breaks, allocation priority for registered donors, funeral expenses, and payments [91,92,95–98].

4.3. Education and communication

One way to increase donor consent rates is to provide the public with sufficient information on the organ donation process, allowing them to make an informed decision and alleviate any mistrust in the system [68,71]. Some initiatives have already shown success; organ registration rates in the US dramatically increased following a Facebook initiative that provided educational information to unregistered donors [99]. In the case of kidney transplants, an initiative named Explore Transplant aims to ensure that US transplant patients can make informed choices about their treatment options, specific to their stage of kidney failure [100]. The initiative also aims to provide education to those outside transplant centres and in minority groups, due to inconsistent and inadequate information in these groups [101].

Education is also needed when it comes to understanding brain death [102]. Findings suggest that understanding and accepting brain

³ This is not an exhaustive list.

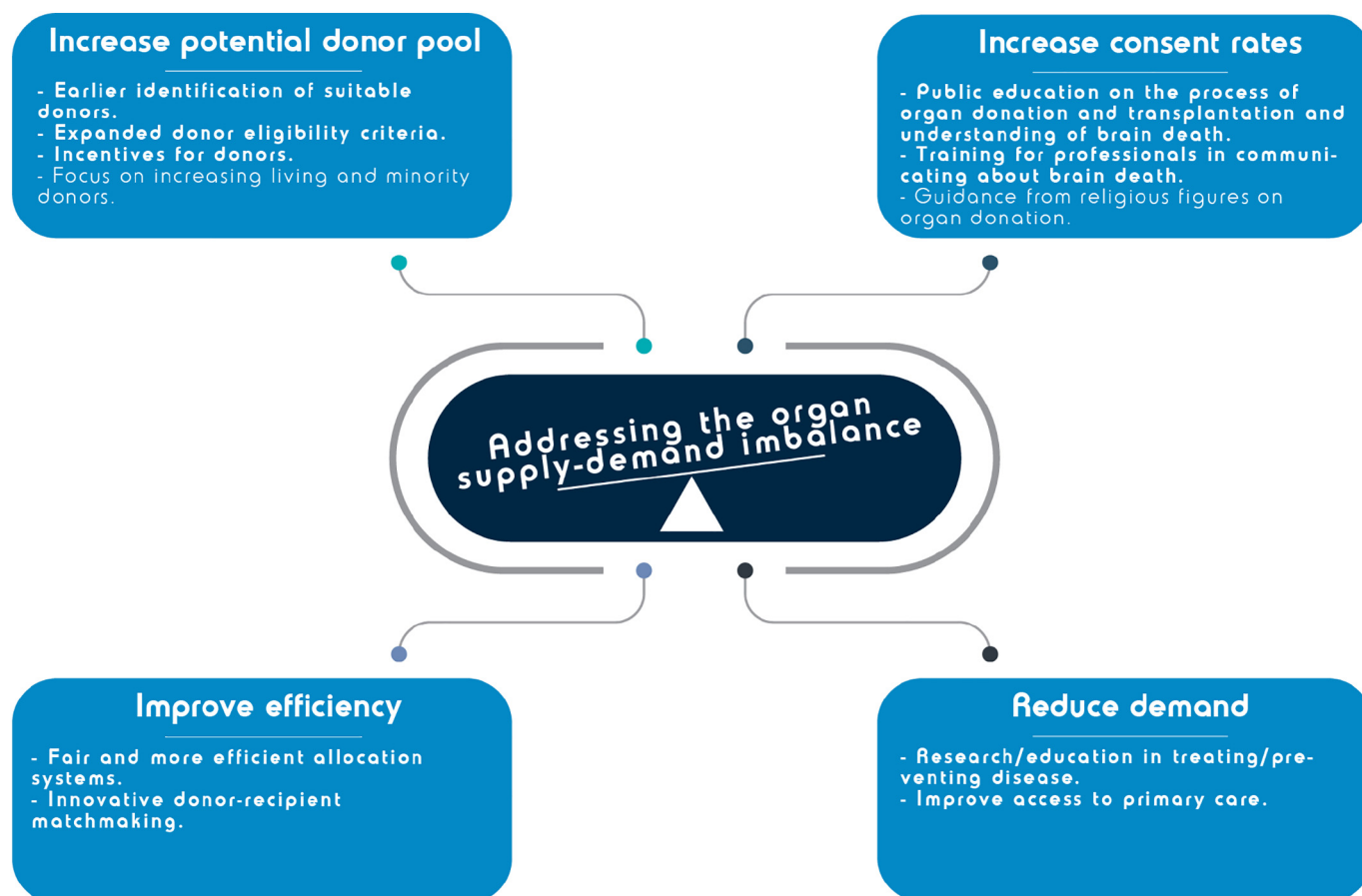


Fig. 3. Key areas to address the organ shortage. Points in bold are discussed in Section 4 of this article.

death is associated with a positive effect on the organ donation process [103], with a lack of understanding showing the converse [57], yet knowledge and acceptance of brain death appears to be low [56–58]. As such, communicating the process of DBD to deceased patient's relatives is of great importance. Family meetings are also crucial during DBD practices, allowing family members to deal with the treatment plan and the concept of brain death [8]. Lack of knowledge of brain death has also been found to be lacking in medical students [104]. However, training initiatives can improve awareness among medical students and increase their comfort in diagnosing and communicating about brain death [104]. As such, educating both the general public and healthcare professions in all areas of organ donation is vital.

4.4. Efficiency of organ allocation

Allocating organs efficiently is crucial to maximize the number of successful transplants. The difficulties faced with optimally matching donor and recipient vary per organ. Medical urgency is one of the most important matching criteria for heart and liver allografts; the patient with the highest risk of death gets the allograft. Regarding liver allografts, the US now uses the points-based system MELD to ensure that those with the highest need/severity are prioritised. However, an equally important consideration for allocating organs is the patient's outcome after transplantation. Consideration of risk factors, independent from MELD score, can potentially improve the use of available allografts [105]. For example, patients with alcoholic liver disease have to prove at least 6 months of abstinence from alcohol to become candidates for liver transplantation,

even though there is no overall survival impact [106]. Likewise, those with chronic infections and substance addictions cannot receive lung transplants [107]. Candidates are also required to have a reliable social support system and the absence of untreatable psychological or psychiatric conditions that influence the ability to cooperate or comply with medical therapy [107]. In the case of MELD, the outcome of the patient is part of the model; however, it only applies to conditions for which data exists to generate valid models. This means that MELD scores don't apply to those with rare conditions, even though they may be excellent candidates for liver transplants [108]. Additionally, MELD score, as well as modifications of MELD score (e.g. UKELD) do not include any of the donor's factors [109]. As such, updating models and conducting new research and development is vital to the continual improvement of organ allocation [108].

Efficiency of organ allocation may also be improved through novel initiatives for donor-recipient matchmaking; "MatchingDonors.com" currently has the world's largest database of living altruistic donors for incompatible kidney exchange and can receive between 3 and 26 new organ donor registrations each day" [110]. The exchange works by assisting donor/patient pairs who have incompatible blood types to find another donor/patient pair who they are compatible with to exchange kidneys [110]. A Kidney Paired Donation Pilot Program already exists in the US, however, it has not yet been implemented in every state [111]. Paired kidney schemes also exist in the UK, Spain, and the Netherlands, with many other European countries beginning to implement programs [112]. Future collaboration between these schemes could lead to sharing of best practices and cross-border exchanges, improving access to the most effective treatment [112].

4.5. Awareness and prevention of disease

Efforts to reduce the need for organ transplants should be of key consideration. For instance, novel research into appropriate clinical care and pathology of kidney disease could help identify alternative therapies for kidney disease, relieving the burden on kidney transplants [113–115]. Moreover, improvements in healthcare literacy and education in disease prevention could reduce the number of individuals developing chronic kidney disease [116,117]. Improving access /education to primary care could also reduce organ failure and, ultimately, the demand for organ transplants. For instance, some countries lack necessary primary care facilities, meaning that the ability to contain or slow disease progression is limited [118].

5. Alternative solutions to organ donation

Due to the continued organ supply-demand imbalance, alternative options such as artificial organs and xenotransplantation are being investigated [119–124]. Artificial extracorporeal liver support devices have been developed that perform haemodialysis, therapeutic plasma exchange (TPE) and albumin dialysis. Clinical trials show that the devices are well tolerated, with TPE demonstrating survival benefits for patients with acute liver failure [123]. For those awaiting a donor heart, the total artificial heart (TAH), a mechanical circulatory support that restores total pulmonary and systemic flow, is an alternative option [121]. In the US, only the Syncardia TAH is available for clinical use, however, other TAHs are being developed (e.g., BiVACOR, RealHeart, Reinhart, Carmat) [124]. Likewise, clinical trials on wearable artificial kidneys are ongoing globally, however, major progress has been difficult due to insufficient funding [122]. Nevertheless, attempts to raise funding to develop external haemodialysis devices and implantable artificial kidneys are being made [122].

Xenotransplantation (pig-to-human transplantation) has been brought a step closer to reality, due to the recent development of genome editing approaches that allow the breeding of pigs free of xenoantigens and porcine endogenous retroviruses [120]. Xenotransplantation can be achieved via genetically modified pigs or human-animal chimeras (stem-cell technology).

Although these alternative approaches are promising, they raise concerns regarding organ source, animal rights, human dignity, potential cancer risk of stem-cell technology, and fear of misusing genetic editing approaches [119,120,125]. Additionally, the re-evaluation of guidelines/regulations on xenotransplantation is needed before clinical trials can begin [120].

6. Concluding remarks

The organ donation agenda resides on more than medical necessity grounds. Ethical considerations, together with a lack of understanding/awareness and mistrust in the system, pose difficulties for reducing the organ supply-demand imbalance. Reducing the imbalance will involve a multifaceted approach, including increasing the donor pool, educating professionals and the public, and a focus on alternative options to human transplantation. There is also a continuous need to standardize guidelines towards medical and psychosocial evaluations to ensure the safety of all donors and recipients.

In memoriam

In loving memory of Dimitrios Kazis. To inform and educate the public of the benefits and need for active organ donors.

Declaration of Competing Interest

The authors declare that there are no declarations of interest.

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Glossary

D:
 Donation After Brain Death: DBD
 Donation After Circulatory Death: DCD
 E:
 European Organs Directive: EOD
 European Union: EU
 L:
 Living Organ Donation: LOD
 M:
 Model for End-Stage Liver Disease: MELD
 N:
 National Health Service: NHS
 O:
 Organ Exchange Organization: OEO
 Organ Procurement Organization: OPO
 Organ Procurement and Transplantation Network: OPTN
 P:
 Paediatric Donation After Circulatory Death: pDCD
 Per Member per Month: PMPM
 Per Million Population: pmp
 T:
 Total Artificial Heart: TAH
 Therapeutic plasma exchange: TPE
 U:
 Uniform Anatomical Gift Act: UAGA
 United Network Organ Sharing: UNOS
 United Kingdom Model for End-stage Liver Disease: UKELD
 V:
 Vascularized Composite Allograft: VCA
 W:
 Withdrawal of Life Sustaining Therapies: WLST