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## Introduction

The pioneering and subsequent development of organ transplantation was one of the greatest advances in medicine of the late twentieth century. A glance at the World Health Organization's Global Observatory on Donation and Transplant's homepage readily demonstrates the worldwide reach of transplantation medicine. Their statistics for 2019 showed that globally, 153,863 organs were transplanted that year, marking a 4.8% increase compared with the previous year [1]. There was an average of 17.5 organs an hour transplanted in 2019.

The story of organ donation is however far more than just statistics. It results in people's lives being saved and transformed. Such uplifting and inspiring human elements of transplantation are clearly evident in the moving 2007 memoir, *The Power of Two* [2]. This and the subsequent film based on it, tell the remarkable story of Japanese twin-sisters, Anabel Stenzel and Isabel Stenzel Byrnes, born with cystic fibrosis. Their "survival through miraculous double lung transplants, and improbable emergence as authors, athletes and global advocates for organ donation" [3] is a radiant testament to the life-transforming benefits of organ transplantation. There is however a correspondingly sobering side to this personal human story in terms of the potential and actual costs to those donating organs in the case of living donation, and to donors' relatives in deceased donation. Maylis de Kerangal's novel *Mend The Living* [4], graphically illustrates the bewilderment and emotional trauma of parents approached about giving consent for organ donation from their son, who has been determined to be brain dead following a road crash. There is pain too when transplants fail or recipients die from complications of the surgery and aftercare. Furthermore, the transplant recipient remains under medical follow up indefinitely and so in one sense, still remains a patient even following successful surgery.

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The statistics at the start of this chapter also tell a troubling story when placed in their wider context. Despite so many thousands of transplants carried out, they only meet a fraction of the need, even in countries with advanced healthcare systems let alone those with no coordinated system of organ allocation. The threat of death from organ failure also drives a heinous trade in trafficked organs which generally exploits and harms the ‘donor’ and undermines trust in transplantation medicine generally. It is estimated that 1 in 10 kidney transplants worldwide is of a trafficked organ [5].

The latest global statistics are even more disturbing. They show 129,681 transplants (15 per hour) were carried out, representing a 17.6% decrease in numbers of organs transplanted in 2020 compared with 2019 [6]. This is because of the global effects of the COVID-19 pandemic crippling health care systems, making hospital admission unsafe for healthy live donors, and making deceased donation more difficult because of the pressures on operating theatres and critical care units. The numbers on the waiting list for transplants also fell in many countries though, because many on the list also died during the pandemic. In the United Kingdom (UK) for example the waiting list decreased from 6138 to 4256 yet there were fewer transplants for 2020–2021 than the previous year. Though overall global transplant activity fell by around a third, there were considerable global disparities in how badly individual nations were affected. A paper comparing 22 different countries showed for example, that while transplant activity in Argentina during the pandemic fell by almost 61%, in Austria the decrease was only just over 10% [7].

All of this illustrates why there is a continuing pressure to increase the availability of organs for allotransplantation and to invest in finding possible alternatives such as bioprinting of organs or xenotransplantation. This chapter however will give a broad overview of some the ways in which allotransplantation is either being currently expanded or may be in the near future.

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## Living Donations

Donations of non-vital organs from voluntary donors are essential to any transplant program. Living donations have significant advantages for recipients as, unlike deceased donation, there is no risk of deterioration of the organ if there are delays between the death of the donor and implantation into the recipient. In developed healthcare systems there is little risk to the donor either. The risk of death with 3 months after kidney donation (which is by the far the commonest solid organ transplanted) is less than 1 in 3,000 for example [8]. There is of course a slightly greater risk of end-stage renal diseases eventually developing in the donor as a result of having only one kidney but this remains low at 1 in 100 over a lifetime [9]. With liver lobe donations, the operative risk of death at 1 in 588 operations is higher than that for kidneys, but there are fewer long-term adverse consequences [10]. However, taking into account the total number of years lost as a result of each donation, live kidney donation accounts for more than liver donation [11].

In the early days of kidney transplantation, hopes ran high that improvements in organ preservation, immunosuppression and tissue typing would eventually make the results from transplants of deceased organs as good as those from living donors [12]. However living donation overall still leads to better outcomes than deceased donation and therefore remains an essential element of transplant services worldwide with increasing effort being put into increasing the numbers of such donations. In the United States (US) in 2019, living donors comprised 37.7% of all kidney donors [13], and a new record of the total number of living donors was also set at 3797 [14]. In the UK, up to 2019–2020, living donors accounted for 40% of all donors before the COVID-19 pandemic hit [15]. Global figures for living kidney donors in 2019 are comparable at 37.3% of all kidney donors [16].

The COVID-19 pandemic hit transplantation rates badly. A large part of the problem was that living donation became very unsafe for potential donors because of the high risk of acquiring the virus in hospital. In the UK, living donations in 2020–2021 fell to just 444 from 1058 the previous year. Living donations in the US fell by 27% as of August 11th 2020, compared to the same point in 2019 [17]. Ninety percent of all US transplant programs reported at least a halving of the number of living donor evaluations during the pandemic [18]. Since 2021 developed health care systems have restored their transplantation rates back to pre-pandemic levels and various schemes to increase the number of living donors that have been re-implemented.

## Methods of Increasing Living Donation

In 1954 the first successful kidney transplant was carried out in the US between male twins who were immunologically compatible [19]. For many years thereafter the only transplants carried out were from living donors who were close relatives of the recipient. As understanding of the mechanisms of immune rejection of transplanted organs increased, immunosuppression became increasingly safe and effective thus enabling expansion of both living and deceased donations. There have been three principal ways in which increasing the number of living donations has been achieved—relaxation of the safety criteria to enable more living donors, the introduction of donor incentives, and broadening the range of potential recipients from living donors.

## Relaxation of Criteria to Become a Living Donor

With the increasing importance from the 1980s onwards of respecting patient autonomy within medical practice [20], the priority of wherever possible, respecting the request to be a living donor has received increasing attention. During the 2000s previous restrictions arising from such factors as age, weight, adverse family history, smoking, obesity, diabetes, hypertension and heart disease have been relaxed to permit more donors without compromising safety [21]. With regard to age for

example, the UK has no upper age limit for living donations and Canada's oldest living donor to date was 92 years old at the time of donation [22]. Most US programs have no upper age limit for eligibility though there are still strict criteria on donations from young children. Attitudes have changed to allow patients to donate who for example had progressive debilitating diseases such as multiple sclerosis or chronic respiratory problems or even specific types of cancer such as some brain tumours, which were not considered to be transmissible to organ recipients [23].

## Incentivizing Donors

Though the risk to living donors is small, the inconvenience and costs involved, especially in travel and time off work, may be considerable. It is not surprising therefore that many countries offer some form of reimbursement of costs to living donors. Even in 2009, a survey of 40 countries showed that reimbursement of living donors occurred in 21 countries and was legally specified in 16 of them [24]. The UK [25, 26], New Zealand [27] and Canada [28] for example all offer some reimbursement of costs to living donors. A recent study of reimbursement of expenses for living donors covering 109 countries showed an overall positive effect and concluded such programmes “may be an effective approach to alleviate the kidney shortage worldwide” [29]. Although introducing such initiatives was more effective in relatively less developed economies and countrywide introduction was recommended as in the US, no significant improvement on donor rates had been found at individual state level [30].

A few countries, notably Iran [31], and Saudi Arabia [32] have offered financial incentives to become living donors rather than just paying compensation for expenses and lost income. However, there is considerable doubt about the effects of introducing financial incentives rather than reimbursed expenses in countries with different political systems from these countries [33]. Other countries such as Israel [34] and Singapore [35] have introduced medical incentives such as awarding points to prioritize living donors for a transplant should they require one themselves. The introduction of incentivized systems however risks decreasing the number of altruistic unpaid donors on whom the system depends. Once the public perceives their altruism is no longer valued by a state, the number of living donations may decrease.

## Broadening the Range of Potential Donors

With the exponential rise of digital communications and use of social media, it is now very easy to broaden outreach by and to potential recipients in ways not previously possible. Use of the internet to find a donor is legal in many countries and has been widely taken up in the US, despite concerns of a “transplant beauty contest” where the eventual recipient is not the one most in need but the one with the best online publicity profile [36]. In 2004, [MatchingDonors.com](#) was one of the first websites launched to match donor and recipients and it generally has over 15,000 potential donors registered on it at any one time [37].

The Human Tissue Authority, the UK's regulating agency for transplantation, issues guidance for people interested in becoming live donors [38], which includes the fact that it is illegal to seek financial reward for donating an organ and that potential donors should not use sites which charge a fee for potential recipients to register. Both Facebook [39] and Twitter [40] are also increasingly used to locate living donors.

Though there are obviously complex ethical issues linked with the use of social media, they are here to stay and rather than seeking to dissociate from them, transplant authorities should seek to cooperate with them and indeed utilize them, too, to the benefit of donors and recipients alike [41].

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## Deceased Donations

Though living donations form a large minority of total donations, the global transplantation system relies on deceased donations which form the majority source of organs overall. Deceased donations have a number of advantages over living donations. Vital organs, most commonly the heart, cannot come from living donors,<sup>1</sup> and whereas usually only one organ is removed from a living donor, multiple organs, including both kidneys rather than just one, are removed from deceased donors, who can therefore save more than one life through donation. In the UK, though deceased donors comprised 60% of all donors in 2019 [42], during the pandemic this percentage rose to nearly 73% for 2020, because of the disproportionate decline in living donations. In the US, 2019 was a record year for deceased donation with a total of 11,870 (62% of total donations) [14]. In contrast to the UK, the number of deceased donations rose in the US by 6% to over 12,500 donations [43]. Globally, the figures for 2020 show the total number of kidney transplants was 80,912, of which 62.7% were from deceased donors [44].

## Types of Deceased Donation

Unlike living donations, deceased donations are classified into two different categories: donation after circulatory death<sup>2</sup> and donation after brain death.<sup>3</sup> The proportion of donations from each category varies from one nation to another. Part of the reason for this is that there are still ongoing medical and philosophical debates about the diagnosis and nature of brain death (see for example: [45]), even decades after the concept was first formulated. Some countries for religious and cultural reasons do not accept brain death as being an acceptable criterion for organ removal. In Singapore for example, deceased organ donors remain low at 7–9 per million

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<sup>1</sup>Except in the rare circumstances of 'domino donations'.

<sup>2</sup>Previously referred to as donation after cardiac death or 'non-heart-beating' donors.

<sup>3</sup>Previously referred to as 'beating-heart' donors.

population annually compared to many other developed countries, mostly because of concerns about brain death [46].

Though some ethicists take the view that morally “Dead bodies don’t matter” [47], they clearly do matter to the loved ones of the deceased and it is essential to ensure that people are actually dead rather than just being ‘as good as dead’ in the eyes of some, before organs are removed. Though there are a large number of ethical issues raised by deceased donation, the primary areas targeted to increase deceased donations are making it easier to obtain consent and extending the scope of those who are considered dead.

## Increasing Consent Rates for Deceased Donation

It is generally agreed that the wishes of the deceased regarding donation should be respected but in order to be respected, they should ideally be expressed in a verifiable form [48]. In countries which operate an opt-in system, where individuals must expressly indicate their wish to donate, efforts to increase deceased donation focus on encouraging donors to sign up and increasing ways to do so. The over 50% increase in transplants in the UK, a decade after implementation of the recommendations of the 2008 Donation Task Force [49], shows how effective such strategies can be. However, the UK along with many other countries, most notably Spain with record levels of donors per million population [50], now operate on an opt-out basis [51]. Here, unless individuals actively take steps to indicate unwillingness to donate, it is assumed they are willing, though in most countries the consent of relatives is sought and rarely over-ruled. However, some ethicists recommend relatives’ wishes should never be allowed to prevent donation [52].

## Expanding Categories of the Dead

The ‘dead donor’ rule (DDR), the ethical principle which stipulates that “(vital) organs be only removed from dead patients” [53], has been increasingly questioned as the demand for organs worldwide has increased. Various suggestions have been put forward to modify the criteria for both donation after circulatory death [54] and donation after brain death [55] so that increasing numbers in both groups could fulfil the DDR, whilst others have suggested that the DDR be abandoned altogether [56] in order to maximise organ retrieval from those for example with persistent disorders of consciousness (PDOC). The claim is made that causing the death of such patients is not morally wrong. “What matters is not when a patient dies but whether their death constitutes some further harm” [57]. Whilst indeed it may not matter to the patient, it certainly may matter to their relatives and to the general public whose trust in transplantation could be undermined [58, 59].

## Conclusions

To date no country in the world, with exception of Iran, has managed to completely meet the demand within its population for organs. In a post-pandemic world, the situation for most countries has already been substantially worsened in the short term. In the long term, adverse health consequences of the pandemic continue to take their toll, especially in terms of renal and respiratory damage, which in turn could increase the need for organs. Even if trust in the transplantation system is not undermined by future ill-considered moves to expand the pool of both living and deceased donors, possible sources of organ replacement other than allotransplants will need to be explored. Alongside bioprinted organs, implantable biorobotic organs, and organs grown in vitro or in chimeras, xenotransplantation has an important place in research for such alternatives.

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