Currently, liver transplantation remains the only effective treatment for end-stage liver disease [1], and living and deceased donor graft (the organ) survival rates are nearly equivalent (82.5 percent and 82.0 percent at 1 year post-transplant; 72.2 percent and 71.9 percent at 3 years after transplant; 65.9 percent and 65.1 percent at 5 years after transplant) [2]. According to the Organ Procurement and Transplantation Network, there have been at least 15,000 patients awaiting liver transplant at the start of each year since 2011 [2-5]. The size of the waitlist fluctuates during the year as patients are added or removed (because they received transplants or died), but when patients are listed at more than one hospital, the patient is counted only once [3]. In the United States, between 2006 and 2012, approximately 6,391 liver transplants occurred each year, indicating a consistent shortfall of organs [3]. Living liver donation is a risky elective surgical procedure [6]; thus the ethically optimal way forward is not increasing the number of living donations to facilitate more transplants but increasing the number of deceased donor livers available for transplantation.

Attempts to increase the deceased donor pool encounter the intersecting clinical problems of an aging donor population with ever-increasing rates of diabetes and steatosis (fatty liver) [7] that contribute to high discard rates (i.e., grafts rejected by transplant teams because of poor quality). Specifically, in 2010, the utilization rate of deceased donor livers in the United States was 78 percent; however, this rate is expected to decline to 44 percent by 2030 [7]. The best approaches to increasing the deceased donor liver pool will likely entail a combination of technology and policy strategies (see table 1 and table 2).

**Technological Strategies**

As shown in table 1, the technological approaches to expanding the deceased donor liver pool comprise three categories: surgical techniques, medical devices, and organ procurement and selection methods.

<table>
<thead>
<tr>
<th>Technology Type</th>
<th>Examples</th>
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<tr>
<td>Surgical technique</td>
<td>Split liver transplantation</td>
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Split liver transplantation (SLT). In the US, it has been estimated that 20 percent of donor livers are suitable for SLT [8], and thus wider use of this technique could significantly impact the rate of liver transplantation. SLT involves dividing a deceased donor liver into two portions for transplantation. Most commonly, a child is the recipient of the left lateral segment (Couinaud segments II and III), while an adult receives a right extended graft (Couinaud segments I, IV-VIII). Less commonly, the donor liver is divided for two adult recipients (right graft, Couinaud segments V-VIII; left graft, Couinaud segments I-IV). In both scenarios, SLT is technically challenging due to complex biliary anatomy, and high-quality livers are generally selected for optimized outcomes [9]. (Importantly, SLT remains the key source of transplants for children [10]; thus skilled teams are an ethical necessity.) According to Lauterio et al. [9], the outcomes of SLT that involve the left lateral segment graft and right extended graft are “equivalent” to those of whole liver transplant when these surgeries are performed by experienced teams. When the liver is split for two adult recipients, one- and five-year graft and patient survival rates are roughly 20 percent lower than for whole liver transplants [9]. SLT has been in clinical use since 1988 [11], but, due to the challenging nature of the procedure and need for high-quality grafts at baseline, SLT is rare, representing only about 6 percent of all liver transplants in Europe and Oceania [9] and 1 percent of US liver transplants [8].

Reuse of auxiliary livers. It is estimated that 10 percent of liver transplants are due to acute hepatic failure [9]. Auxiliary liver grafts (from both living and deceased donors) are liver segments implanted adjacent to the native liver as a form of in vivo bridging therapy while the native liver recovers from acute failure. Leiden University Medical Centre (Netherlands) has been successful at reusing auxiliary liver grafts after they have regenerated in their original recipient and are no longer needed due to recovery of native hepatic function [9]. If widespread reuse of these grafts were feasible, it could impact the number of recipients who could be helped. Feasibility for reuse will depend on matters such as the observed success of in vivo graft regeneration, the structural integrity of the graft following removal, and the absence of chronic rejection, which would cause deterioration in the graft.

Liver regeneration with three-way sharing. A technology that has the potential to vastly expand the pool of deceased donor livers is ex vivo liver regeneration with graft sharing.
Specifically, researchers at the Wyss Translational Center Zurich are developing a method of splitting a whole donor liver into three segments, followed by ex vivo regeneration of each segment into full liver grafts for transplant into three patients [13]. The Wyss group also proposes to use this same technology for liver disease patients to grow their own grafts for transplant by way of resection of a healthy portion of the patient’s liver, followed by ex-vivo regeneration of that segment into a graft suitable for transplant back into the patient (at which time the remaining diseased native liver would be removed). As this work is in the early stages, there are many unknowns, such as what criteria define a pristine liver for three-way splitting or optimal ex-vivo regrowth [14]. Furthermore, while potentially promising, this technology raises ethical concerns when the donor graft originates from a living person with end-stage liver disease: the live donor will be exposed to more risks, because this technique requires two surgical procedures (explant and replantation) rather than the customary primary transplant, and it is unknown whether the technology will be affordable, which may raise questions about justice and access [14].

**Ex vivo perfusion (EVP).** EVP could enable the use of organs that would otherwise be discarded or be of elevated risk due to “marginal quality” (i.e., grafts from older donors, fatty livers, DCD livers). It is a leap beyond routine cold, static liver storage before transplant. In general, EVP involves perfusion of donor livers with either normothermic or subnormothermic solution after procurement (prior to transplantation) with the aim of nourishing the liver while also flushing out toxins and cytokines. The technology is still relatively new, and teams are using various temperatures and perfusion solutions to determine which have the best protective effects [15]. Guarrera et al. [16] report fewer biliary complications and significantly shorter hospitalizations for patients receiving EVP extended criteria livers than for patients receiving static cold storage extended criteria (see discussion below) livers. Machine and solution costs are potentially challenging, but EVP could result in overall savings if it led to fewer livers being discarded and improvements in patient and graft outcomes with marginal grafts. If EVP becomes standard practice, all organ procurement organizations could incorporate the technology by transferring the associated costs into the organ acquisition fee. Transplant teams should specifically discuss EVP in their consent process, just as they do extended criteria organs.

**HIV-positive livers for HIV-positive recipients.** It is estimated that the US could provide approximately 250 HIV-positive donor livers annually for HIV-positive patients [17], thus increasing the number of organs available overall. Three-year patient and graft survival for HIV-positive recipients of HIV-positive livers is roughly the same as that for HIV-negative recipients receiving HIV-negative livers [18]. A problem, however, is that many HIV-positive liver grafts are also positive for hepatitis C antibodies and thus only suitable for patients who are also infected with hepatitis C. This latter group of patients has worse outcomes after transplant than those not co-infected with hepatitis C [18],
making decisions about burdens and benefits complex for hepatology teams. As the opportunities for treating HIV and hepatitis C co-infection improve, the transplant opportunities for this population should be further enhanced [19].

**DCD livers.** Livers procured after controlled circulatory death (donation after circulatory death—DCD) have evidenced poor outcomes due to problems with nonanastomotic biliary strictures, bile leaks, hepatic artery stenosis, and graft failure [20–22]. Contributing factors include advanced donor age and lengthy cold ischemic time. But these livers could be successfully used if evidence for EVP’s effectiveness is compiled [15] or if antemortem interventions are used. The latter are ethical as long as they provide clinical benefit (improved organ viability), have a low chance of patient harm, and are consented to by the patient or family.

**Extended criteria livers.** The term “extended criteria liver” is a broad category for livers that are not “pristine.” In general, these are livers from older donors (age 55 or older); grafts with increased ischemic exposure, hepatitis C virus, and hepatitis B core antibodies; and steatotic grafts. Because there is no standard definition for the “extended criteria liver,” the conceptualization can creep wider to include variables such as length of hospitalization of the donor and donor weight. With knowledge of the rising rate of discarded organs [7], it is critical to develop an understanding of how “extended criteria” variables impact graft and patient outcomes in order to create options for donation that are clinically and ethically sound. By using “extended criteria,” the discard rate can potentially fall and the rate of transplantation rise.

**Policy Options**

As shown in table 2, the policy options for expanding the deceased donor liver pool can be categorized into three areas: referrals, consent, and incentives. Referrals are hospital-driven activities; consent is focused on individuals or families, depending on the procedure; and incentives involve both financial and nonfinancial rewards for donation.

<table>
<thead>
<tr>
<th>Policy type</th>
<th>Examples</th>
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<tbody>
<tr>
<td>Referral policies</td>
<td>Routine referral legislation</td>
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<td>Consent policies</td>
<td>First-person authorization</td>
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<td>Presumed consent</td>
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<td>Incentives</td>
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<td>Noncurrency incentives</td>
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<td>Currency incentives</td>
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**Routine referral legislation (RRL).** RRL is fundamental to organ donation practice in the US [23]. With RRL, hospitals are required to notify their regional organ procurement
agencies of all deaths and impending deaths, regardless of cause of death or patient age (as examples) so that trained procurement personnel, rather than hospitalist physicians, make the clinical judgments regarding the suitability of potential donor organs. Clinician fatigue or personal biases are ethically inappropriate reasons for failing to make donor referrals [24]. If these practices were implemented worldwide, it would result in the elimination of missed opportunities for potential donation.

Various policy models governing donors’ consent to donate have also been used to try to increase the deceased donor pool.

First-person authorization (FPA). The US uses FPA policy as a method of increasing the number of deceased donors. FPA means that those who register to be organ donors via a registry or advance directive/living will are voicing their voluntary, autonomous wish to donate, and therefore no additional consents or permissions are needed from the next of kin [25]. Furthermore, family members are not permitted to veto or cancel their relative’s donation registration [25, 26]. Not only does FPA save time in a time-sensitive specialty such as transplant, but families are not burdened with donation decision making when they are emotionally stressed by the death or impending death of their loved one [26]. However, many countries, including Australia and the UK [26], do not use FPA because they believe family should be the ultimate decision makers regarding organ donation even when adults have formally registered their wish to donate [21]. From an ethics perspective, it is important to honor the values and wishes of those registered as donors. Families who are upset by the donation decision of their loved ones can receive counseling and emotional support from specially trained staff within organ procurement organizations and hospital pastoral care programs.

Presumed consent (PC). PC is used in some countries, particularly in Europe, to increase the number of available organs. PC means that adults are assumed to have consented to organ donation when they die, unless, while alive, they register themselves as opting out of organ donation. In the “hard” PC model (practiced in Austria, for example [27]), there is no further approach to next of kin regarding people’s preferences in the matter and donation proceeds for those who have died and have not opted out. The “soft” PC model (practiced in Spain, for example [27]) requires next-of-kin consent for all donations, even for those patients who did not opt out. We express ethical concern about the “hard” PC model’s not accounting for those who might not want to be donors but have not yet opted out or have not been able to due to lack of computer or transport access. It would seem that home visits could be made to facilitate opt-out registration in these situations, although this service could be expensive to support if there was a large volume of home visit requests.

Mandated choice (MC). The MC model forces adults to make and register a choice about organ donation at the same time they are engaging other civil processes (e.g., seeking a
vehicle driver’s license, registering to vote, filing a tax return). It has been argued by the American Medical Association that MC would be ethical only if the choice was made with informed consent and the consent documentation verified [28]. In our view, this is not ethically necessary, as FPA does not require informed consent [25, 26] yet has been the gold standard in the US for many years [25].

Other potential ways to increase the pool of donors are to reward those who donate and to remove financial barriers that impede donation. The following sections discuss these concepts.

Reciprocal altruism (RA). Altruism is generally accepted as a fundamental source of motivation for organ donors that can be used to frame policy. The foundational principle of RA is higher priority on transplant waiting lists for those who have previously donated or registered to be an organ donor in the future [29]. Israel [30, 31] has an RA donation policy, and there is a nongovernmental RA donation organization in the US [32]. Legally and ethically, RA programs are not considered a form of remuneration but rather motivators to encourage people to register as donors [29]. Whether the registrant or family member receives priority for transplantation, it is the prioritization that is the reward for registration. Overall, RA is an ethically permissible approach that embraces the willingness to both give and receive an organ, rather than to be a free rider. Also, organ donor registration is an altruistic activity.

Government-sanctioned noncurrency incentives (NCI). NCIs focus on conveying gratitude without any exchange of money (real or virtual, such as tax credits). According to Section 23 of Israeli transplant law [31], living donors receive a certificate of recognition and an exemption from entrance charges to national parks and nature reserves. In the US, living organ donors and family members of deceased donors can receive a bronze Stephanie Tubbs-Jones Congressional Gift of Life Medal [33]. Because NCIs honor the altruism of organ donation they are ethically permissible, but the motivators described are not likely to be strong enough to trigger future organ donations, partly because they are not widely promoted as being available.

Currency incentives. Currency-based incentives can take various forms. Payments for organs are illegal in the US [34]. Additionally, we view such incentives as ethically problematic, because the direct involvement of money (other than reimbursement of donor costs, below) commodifies the human body and creates vulnerability to exploitation. Iran provides a stipend to living kidney donors (approximately $400) and one year of free medical insurance [35]. Controversially, the Iranian government permits the exchange of money between organ recipients and their donor candidates (even providing a “private space” where these negotiations can take place) [36]. There is no limit to the fees proposed by the donor candidate, but if the rate rises too high for the recipient’s budget, the Iranian Patients’ Kidney Foundation [36] will provide new...
potential donors for consideration. Israel pays the cost of transport and burial (inside or outside of Israel) for those who are organ donors [31]. Because it is a reimbursement of costs related to donor death, not a payment for organ donation, this incentive can be viewed as ethically permissible.

Furthermore, we argue that removing financial barriers (disincentives) to donation is important and should be ethically encouraged. When such barriers are in place, living donation can be financially burdensome, which is ethically unacceptable in the setting of a lifesaving altruistic gift [37]. In the US, several states provide tax deductions up to $10,000 for travel, lodging, and lost wages related to the living donation process [38]. Also, the US Health Resources and Services Administration provides grants up to $6,000 for reimbursement of travel, accommodation, meals, and incidental expenses incurred by the donor and a support person during the donor candidate assessment, hospitalization, and clinical follow-up [37].

**Conclusion**

The ethically optimal way to achieve more transplants is to implement a combination of technological and policy strategies. FPA and RRL policies are ethically and legally proven and should be implemented worldwide. Continuing efforts to prove the efficacy of *ex vivo* perfusion and liver regeneration with three-way sharing should continue, as these approaches have great potential to expand the deceased donor liver pool. Additionally, technologies that optimize donor registration (i.e., accessible, user-friendly, informative, streamlined processes) and donor referrals [39], as well as continued community education efforts to *raise organ donation awareness*, should be encouraged.

**References**


13. Wyss Zurich Translational Center. Regeneration of the human liver outside of the body.


29. Bramstedt KA. Is it ethical to prioritize patients for organ allocation according to their values about organ donation? *Prog Transplant.* 2006;16(2):170-174.


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