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OPINION AND HYPOTHESIS SECTION

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Global experience and perspective on anonymous nondirected live donation in living donor liver transplantation

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Abstract

Anonymous nondirected living liver donation (ANLLD), sometimes referred to as "altruistic" donation, occurs when a biologically unrelated person comes forward to donate a portion of his/her liver to a transplant candidate who is unknown to the donor. Here, we explore the current status of ANLLD with special consideration of published reports; US experience; impact on donor psychosocial outcomes; barriers to donation; and current global trends with respect to ethical considerations. Between 1998 and 2019, 105 anonymous nondirected living liver donor (ND-LLD) transplants have been documented in the US Scientific Registry of Transplant Recipients. Sixteen donors (15%) were reported to experience a postoperative complication. Currently, 89 donors remain alive (85%), 16 (15%) have unknown status, and none are confirmed deceased. Although there are only a handful of case series, these data suggest that ANLLD is a feasible option. While there are no liver-specific data, studies involving anonymous nondirected kidney donors suggest that anonymous donation does not adversely impact psychosocial outcomes in donors or recipients. There are substantial financial burdens and ethical considerations related to ANLLD. Further studies are required to assess donor demographics, psychosocial motivations, long-term health-related quality of life, and financial impact of ANLLD.

KEYWORDS

altruistic, anonymous; living liver donation, living donor liver transplantation, nondirected

1 | BACKGROUND

Liver transplantation is the definitive treatment for patients with end-stage liver disease and refractory liver failure.[1] Excellent outcomes can be achieved using deceased donor livers, but growth on the liver transplant waiting list continues to outpace the limited supply of organ donors.[2] After the first successful adult living donor liver transplant (LDLT) was reported in 1989 in Australia, LDLT was quickly adopted by several centers in the United States to address the problem of organ shortage.[3] In the early era of LDLT, technical challenges and complications were encountered in both donors and recipients.[4,5] As centers gained more experience, the number of procedures performed in the United States peaked in 2001 at approximately 10% of total adult liver transplants but has since remained 5% (Figure 1, Panel A). A highly publicized live liver donor mortality in 2001 and adoption of the MELD-based organ allocation in 2002 are factors which may have contributed to the decline in LDLT since the early 2000s in the United States.[5-10]

Although many of the early technical challenges of LDLT have been overcome, donor risk continues to be a major concern. Data from the Adult-to-Adult Living Donor Liver Transplantation Cohort Study (A2ALL) demonstrated that 38% of living donors experience a variety of postoperative complications, the majority occurring within the first year post-donation.[5] Although the possibility of catastrophic donor outcomes cannot be ignored, a recent study has estimated the risk of early death among live liver donors to be 1.7 per 1000, statistically similar to the risk of early death for both live kidney donors and healthy participants.[9] Furthermore, in recent years, US liver transplant data suggest that, similar to what is observed in kidney transplantation, living donor allografts may offer the same, if not superior, graft longevity for both pediatric and adult liver transplant recipients.[4,11,12] Thus, as the gap widens between availability of deceased donor organs and the ever-expanding waiting list, greater use of living donor liver grafts provides an opportunity to increase organ supply without compromising post-transplant outcomes.

Anonymous nondirected living liver donation (ANLLD) has emerged as a novel yet critically important subset within LDLT given its potential to increase the donor pool. There is considerable variation in terminology present in the literature referring to biologically unrelated individuals who come forward to donate a portion of their liver without knowing the identity of the recipient, herein referred to as "anonymous nondirected living liver donors." Anonymous donors are biologically unrelated individuals unknown to the recipient at time of evaluation, while "directed donors" are individuals donating an organ to a specified recipient and can still be referred to as "anonymous" if they are biologically unrelated and their identity is unknown to the transplant recipient. More commonly, however, directed organ donors are simply specified as "related" or "unrelated" to the recipient.[1] Meanwhile, anonymous nondirected living liver donors (ND-LLDs) are individuals who come forward to donate without specifying an intended recipient, who is ultimately selected by the transplant center. While these donors are often referred to as "altruistic donors," most transplant centers would consider all living donors, whether related or anonymous, to be altruistic.

The published literature related to nondirected living liver donation thus far has been largely anecdotal, and many programs struggle to balance concerns about the motivation, judgment, and risk appreciation on the part of the anonymous donor candidate with the liability, risk, and ethical considerations for the transplant center.

2 | OBJECTIVES

1. Part I: Discuss the current experience with ANLLD on a global level and utilize the Scientific Registry of Transplant Recipients (SRTR) to examine the US experience.
2. Part II: Review the anonymous nondirected renal transplant literature to extrapolate psychosocial considerations and views on anonymity in ND-LLD counterparts. Thereafter, report our single-center experience with long-term health-related quality of life (HRQOL) in ND-LLDs, as there is no published literature on this topic for these patients.
3. Part III: Broadly examine financial barriers and public policy which impact the utilization of ND-LLDs among high-volume LDLT countries.

Taken together, this article provides the first comprehensive review of anonymous living liver donation and highlights areas for future research and policy development to facilitate the utilization of this unique donor group.

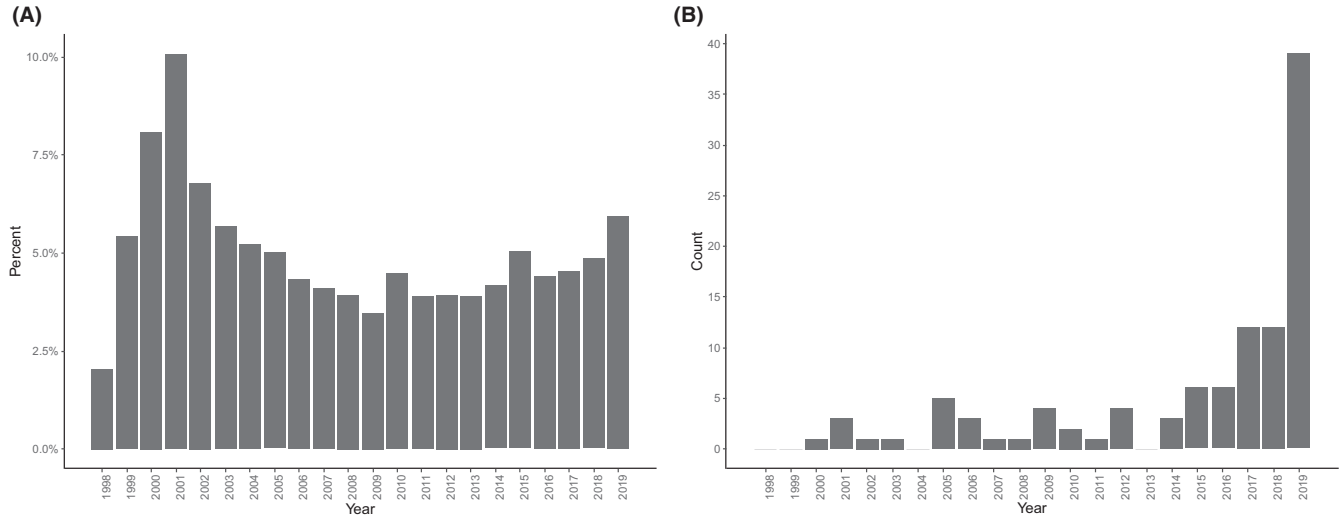

FIGURE 1 Trends in LDLT and anonymous nondirected living liver donation in the United States, 1998-2019. Panel A depicts trends in LDLT as percentage of total adult liver transplants performed per year. Panel B depicts total number of anonymous nondirected living liver donor transplants performed per year. Data obtained from SRTR

3 | PART I: DATA SURROUNDING THE UTILIZATION OF ANONYMOUS NONDIRECTED LIVING LIVER DONORS

3.1 | Analysis of the scientific registry of transplant recipients

In order to review the US experience of anonymous nondirected living liver donation, this study examined data from the SRTR. The SRTR data system includes data on all donors, wait-listed candidates, and transplant recipients in the United States, submitted by the members of the Organ Procurement and Transplantation Network (OPTN). The Health Resources and Services Administration (HRSA), US Department of Health and Human Services, provides oversight to the activities of the OPTN and SRTR contractors. Data were collected for anonymous nondirected living liver donors who donated between January 1, 1998, and December 31, 2019. Domino liver donors were excluded.

An upward trend in the number of ND-LLD transplants performed on a year-by-year basis since 1998 has been observed, particularly in 2018-2019 (Figure 1, Panel B). Demographic characteristics of individuals undergoing ANLLD are summarized in Table 1. A total of 105 such donors have been reported in the SRTR, and the mean age at donation was 39.2 ± 10.3 years. In donors for whom the following variables are documented, a vast majority were Caucasian (93%), obtained some form of postsecondary education (79%), and were employed full-time (89%) at time of donation. There are insufficient data to accurately describe donors' insurance profile from the SRTR database. Of note, 16 (15%) experienced some form of postoperative complication or had to be readmitted following surgery. While there is only follow-up to date for 85% of the donors, all of these are confirmed alive and there are no reported deaths. In our center's experience, many individuals come forward as an ND-LLD following a positive past experience as a directed living kidney donor. SRTR data indicate that 30 ND-LLDs (29%) have also donated a kidney, including 29 donors who did so prior to ANLLD and one afterward. Nearly one third of the ND-LLDs in the United States donated a left lateral segment, suggesting that these organs have been preferentially allocated to pediatric recipients. However, there are no data to determine how individual programs have chosen to allocate ND-LLD livers.

3.2 | Published reports of anonymous nondirected living liver donors

When compared to nondirected kidney donation, the literature related to nondirected liver donation is sparse (summarized in Table 2). In 2007, the Toronto group published a case report of a 46-year-old man who offered to donate a liver lobe anonymously with a good outcome.[13] The donor was close to someone who had successfully undergone renal transplantation and was impressed by its positive

TABLE 1 Characteristics of all ND-LLDs in the United States, 1998-2018. Data obtained from SRTR and given in n (%)

Variable	N = 105 total patients, N (%)
Age (mean ± SD), years	39.2 ± 10.3
Gender, male	51 (49)
Ethnicity	
Caucasian	98 (93)
Black	1 (1)
Asian	4 (4)
Multiracial	2 (2)
BMI (mean ± SD), kg/m^2	25.2 ± 3.5
Type of donation	
Left lateral segment	33 (31)
Left lobe	19 (18)
Right lobe	46 (44)
Not reported	7 (7)
Transfusion	1 (1)
Education	
High school	13 (12)
Attended college/technical school	20 (19)
Associate/bachelor's degree	43 (41)
Graduate degree	20 (19)
Not reported	9 (9)
Employment status	
Full time	79 (89)
Part time	7 (8)
Not reported	3 (3)
Insurance status	
Medicaid	1 (1)
Medicare	2 (2)
Public-CHIP (Children's Health Insurance Program)	3 (3)
Unknown	99 (94)
Current donor status	
Alive	89 (85)
Deceased	0
Unknown	16 (15)
Marital status	
Married	54 (55)
Single	34 (34)
Divorced/separated/widowed	10 (10)
Not reported	1 (1)
Donor-experienced complications	
Biliary	3 (3)
Other complications	10 (10)
Readmission	6 (6)
Not reported	7 (7)

TABLE 2 Published experience of anonymous nondirected living liver donation

First author and year of publication	Country	Center	Year	N	Age range	Surgery (N)
M. Jendrisak, 2006[22]	United States	Washington University, Washington University Medical Center	[a]	1	35	LLS
L. Wright, 2007[13]	Canada	University of Toronto, Toronto General Hospital	[a]	1	46	LLS
J-B. Otte, 2009[14]	Belgium	Université Catholique de Louvain, Cliniques Saint-Luc	2004	1	50	LLS
TW Reichman, 2010[15]	Canada	University of Toronto, Toronto General Hospital	2005-2009	12	20-54	RTH (7), LLS (5)
N. Goldaracena, 2019[16]	Canada	University of Toronto, Toronto General Hospital	2005-2017	50	20-59	RTH (21), LLS (24), LL (5)

Abbreviations: LL, left hepatectomy; LLS, left lateral segmentectomy; RTH, right hepatectomy.
[a]Not provided.

impact on recipient quality of life. Emerging from this case report was eligibility criteria employed by the institution before accepting the individual's request to undergo anonymous donation (Table 3). A second case report of an ND-LLD was published in 2009, from a center in Belgium.[14] A 50-year-old gentleman, motivated by the death of a close relative on the bone marrow transplant waiting list, volunteered a part of his liver to a recipient in need. This case was approved by the hospital ethics committee which imposed the following restrictions: free-of-charge life insurance contracted by University Hospital for the benefit of live donors, and as specified by Belgian law, coverage of all medical costs by the recipient. The recipient was a 12-year-old boy weighing 12 kg, suffering from Alagille syndrome, who was on the waiting list for over two years. The donor was discharged on postoperative day 6 with liver function tests returning to normal in addition to full physical recovery and resumption of professional work within 2 months. The recipient's postoperative course was described as uneventful with a return to normal liver function tests at one year post-transplant.

In 2010, the University of Toronto published their experience with nondirected liver donation as a case series.[15] They analyzed 29 consecutive potential donors, of which 17 potential donors were rejected and 12 donors were ultimately accepted. The overall complication rate for the cohort was 40%. There was no difference in complications between the right hepatectomy donors and the left lateral segment donors, and four complications (33%) were Clavien-Dindo Grade II or above. These included *Clostridium difficile* infection treated with metronidazole, urinary tract infection treated with oral antibiotics, pulmonary embolus treated with low molecular weight heparin followed by warfarin for six months, and intraoperative rupture of a hemangioma in the liver leading to graft loss secondary to bleeding but no further donor complication. All but one donor returned to his/her previous occupation without limitations by a mean time of 8 weeks (range: 2-12 weeks). At postoperative visits, none of the donors expressed any regret about their decision. Of note, all were motivated by a desire and strong sense of responsibility to help others.

TABLE 3 Toronto criteria for accepting anonymous nondirected liver donation. Adapted from Wright et al[13]

1. History of altruistic behavior
2. High level of motivation to donate
3. Logical rationale for donation
4. Altruistic motivation
5. No expectation of secondary benefit
6. Provision of voluntary informed consent
7. No evidence of increased risk of negative psychiatric or psychosocial outcomes
8. Willingness to maintain confidentiality
9. Family support of donor's decision to donate anonymously
10. Donor's understanding and acceptance of standard organ allocation criteria

In 2019, the University of Toronto published their experience with 50 anonymous living liver donations.[16] Of these donors, 35 patients were nondirected and 15 were directed (donating to a specified recipient without the recipient's knowledge). The majority of donors first learned about the possibility of organ donation through local, national, or social media and had a history prior to donation significant for altruistic acts. Donor surgical outcomes were described as similar to outcomes reported for directed donation. Thirteen donors experienced postoperative complications, of which only one experienced a complication of Clavien-Dindo Grade III. Demographically, the majority of anonymous living liver donors in the cohort were described as Caucasian, well-educated, and living a secure lifestyle void of financial difficulties which ultimately helped facilitate their decision to donate. A perceived moral duty and giving back "in acknowledgement of a privileged life" were listed as prevalent motivations to donate.

Surprisingly, despite anecdotal evidence that several North American centers have experience with ANLLD including the University of Southern California,[17] University of Colorado,[18] Cleveland Clinic,[19] University of Alberta,[20] University of Pittsburgh,[21] and Washington University,[22] no further reports of experience using this category of donor have been published in recent

years. It is important to note that there are no data surrounding the best practice for allocating nondirected living liver donor organs to the transplant waiting list.

4 | PART II: PSYCHOSOCIAL CONSIDERATIONS AND HEALTH-RELATED QUALITY OF LIFE

4.1 | Psychosocial considerations

The motivation and mental health of individuals who step forward to donate anonymously are subjects of much debate. Psychosocial assessment criteria in ND-LLDs are not well-established; however, there are reasonable data in this regard from the nondirected renal transplant literature. While differences in procedural complexity and associated risks may impact one's ability to extrapolate postsurgical outcomes for ND-LLDs from nondirected kidney donor studies, there are enough pretransplant parallels between the two procedures and patient populations to merit further review.[23]

Washington University published their experience with "altruistic" living donors interested in nondirected kidney or liver segment donation prior to transplant center referral.[22] Nineteen candidates completed psychological evaluation, and seven underwent donation to include six kidneys and one liver segment. All candidates were found to be free of psychopathology, highly cooperative, and self-directed. Most patients were free of any past or current psychiatric disorders, while three had a remote history of anxiety/panic disorder and/or depression. None exhibited attention seeking behavior or religious motivations. Of the seven who ultimately underwent kidney or liver segment donation, all donors and recipients were noted to do well postoperatively.

A study from the United Kingdom surveyed deceased donor kidney transplant recipients regarding their views on "altruistic" donation and concluded that the anonymity of the donor to the recipient appears to be a benefit of anonymous nondirected ("altruistic") live donor kidney transplants.[24] Overall, anonymity was perceived by donors to protect from pressure or coercion to donate, while releasing the recipient from feeling controlled or manipulated by the donor. Clarke *et al* published the experience of 14 nondirected ("unknown") kidney donors, concluding that these patients reported satisfaction with no lasting psychosocial concerns.[25] Going through the process of live donation was noted to improve resilience and self-confidence in donors. Nonetheless, donors encountered psychosocial hurdles involving a justification of their decision "perceived as renegotiating their sanity" with friends and family.[25] Embarrassment from perceptions of stupidity or attempts to "elicit praise through bravado" had to be balanced with a deep-felt obligation to share the good fortune of their health with others.[25] Some nondirected kidney donors met resistance from their employers, which presented a major challenge both financially and emotionally in relation to social support.

4.2 | Health-related quality of life after anonymous nondirected living liver donation

Our center is involved in an ongoing study of long-term HRQOL in living liver donors, including ND-LLDs. Herein, we report preliminary physical and mental health outcomes assessed in these donors using the Short Form 36 Health Survey (SF-36).[26] This standardized tool has been validated and published in greater than 18,000 studies, including multiple studies related to LDLT.[27-35] Consisting of 36 questions across eight categories, the survey allows comparison of long-term health outcomes in a study sample to the general US population using correlated physical (PCS_c) and mental (MCS_c) component summary scores.[27,36,37] Out of 11 total ND-LLDs at our center, eight (73%) donors have responded to the SF-36 (results summarized in Figure 2). Two donors were lost to follow-up >2 years post-donation, and a third has not yet been approached due to recent surgery. Median age at donation was 51.0 [IQR: 41.7-52.8] years, and the majority of respondents were female (n = 5, 63%). Median follow-up time was 3.3 [IQR: 0.5-4.8] years. Preliminary analysis indicates that ND-LLDs at our center experience comparable long-term HRQOL outcomes to the general US population using the latest available normative data from 1998.[27] Study participants exhibit SF-36 scale scores similar to the general US population across all eight categories in addition to PCS_c and MCS_c. Further collaborative, multicenter studies are required to accurately assess long-term HRQOL and compare health outcomes in this unique donor group.

5 | PART III: FINANCIAL BARRIERS AND PUBLIC POLICY RELATED TO ANONYMOUS LIVING LIVER DONATION

5.1 | Financial barriers

Ethical financial support of potential living organ donors continues to be controversial, particularly in the context of nondirected organ donation where donor motivations may already be difficult to define. Overall, opponents of financial incentives point out that there may be decreased emotional gain for the donor family, decreased respect for life, and a possible loss of the personal link that currently exists in the donation process.[38] On the other hand, one of the reasons cited for the decline of living donation in the United States has been the lack of adequate financial coverage for the donors. While the living donor evaluation and surgery is typically covered by the recipient's insurance in the United States, the extent of this coverage, amount of co-pay, and consideration for post-donation complications vary widely. A survey of donors and recipients of directed living kidney donation between 2001 and 2009 concluded that reimbursements for the costs of participation (ie, eliminating travel), but not cash payments, may increase participation of compatible donors and recipients in kidney paired donation.[39] Some have speculated that with the relative absence of other motivators, unrelated individuals may require large financial incentives to pursue nondirected organ

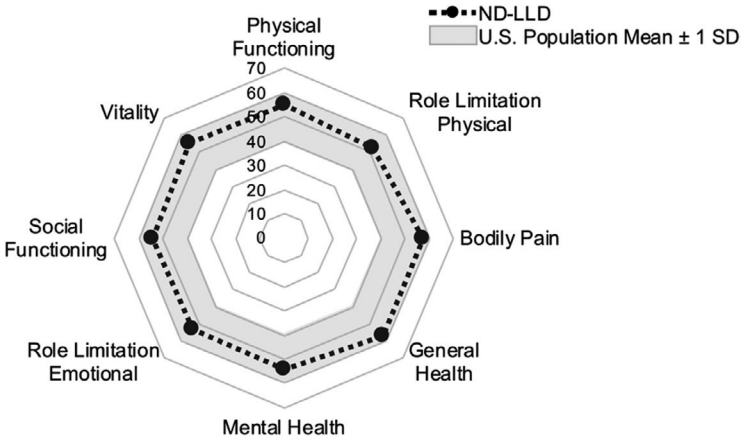

FIGURE 2 Single-center experience of SF-36 measured long-term HRQOL in ND-LLDs

Short Form-36 Health Survey	**ND-LLD** (n = 8) Mean (SD)	**U.S. Population** Mean (SD)
Physical functioning	55.2 (2.2)	50.0 (10.0)
Role limitation-physical	51.9 (9.3)	50.0 (10.0)
Bodily pain	57.2 (5.8)	50.0 (10.0)
General health	57.4 (5.8)	50.0 (10.0)
Mental health	54.0 (5.2)	50.0 (10.0)
Role limitation-emotional	53.1 (4.2)	50.0 (10.0)
Social functioning	54.6 (4.0)	50.0 (10.0)
Vitality	55.3 (7.9)	50.0 (10.0)
Physical Component Summary	55.9 (5.0)	50.0 (10.0)
Mental Component Summary	55.2 (4.5)	50.0 (10.0)

donation, which continues to be illegal in most countries, including the United States secondary to the National Organ Transplantation Act.[39,40]

Long-term financial outcomes in ND-LLDs have not been studied, but data can be inferred from the experience reported for directed liver donors. Data from the A2ALL Study demonstrated that the majority of 271 living liver donors interviewed reported cumulative out-of-pocket medical and nonmedical expenses.[41] Forty-four percent of donors judged these expenses as burdensome. Although greater than 92% of donors reported having health insurance after donation, 37% reported to have incurred out-of-pocket donation-related medical bills and medication costs not covered by insurance. Seventy-five percent of donors reported out-of-pocket nonmedical expenses such as lost wages, transportation, housing, food expenses, and child or family care costs. Another study reviewing the A2ALL cohort found that up to 60% of living liver donors expressed socioeconomic concerns related to financial expenditures and insurance difficulties post-donation.[7] To our knowledge, the latest study quantifying out-of-pocket donation-related expenses incurred by living liver donors was conducted more than a decade ago, reporting the average cost to be greater than that for nondirected kidney donors at $540 per month for patients at a single center.[42] It is reasonable to assume that these out-of-pocket costs would also be incurred by ND-LLDs, thus limiting the donor pool to those whose altruism can be further supported by a pillar of financial security. These data suggest a pressing need to address concerns related to donor financial well-being if ANLLD is to be equitably advanced in the United States.

In addition to burdensome financial costs, challenges associated with accessing financial resources when the donor is nondirected, as opposed to having an identified recipient, adds yet another unique financial hurdle to nondirected living liver donation. For example, in 2008, the US Department of Health and Human Services established the National Living Donor Assistance Center (NLDAC) to reimburse donors' travel-related expenses if the intended recipients' family income fell below a threshold value.[43] According to a recent report, the program was associated with increasing the number of living donor kidney transplants by nearly 14% at participating centers.[43] Although nondirected donors are eligible for financial assistance, there is a requirement that a recipient be identified before the nondirected donor can apply for assistance, eliminating the possibility of travel-related expense reimbursement for preliminary evaluation trips to the transplant center.[44] Not only do these financial challenges potentially limit nondirected living liver donors from coming forward, but they also serve injustice to the otherwise eligible but economically vulnerable transplant candidates who are denied the chance of receiving an organ by way of policy.

R Hays *et al* have proposed the concept of "financial neutrality," which offers inclusion of coverage of all medical, travel, and lodging expenses, along with lost wages related to the act of donating an organ, guidance for consideration of medical care coverage, and other expense reimbursements.[40] Financial neutrality in living donation can be achieved with the following considerations: issuance of a national guidance document by the Federal Government clarifying permissible coverage by individual transplant centers without violation of the National Organ Transplantation Act, contracting guidelines for private insurance coverage, advancing policy initiatives to offer living donors civil protections, and allocating resources to develop systems for long-term wage reimbursement and medical coverage. It is likely that implementing such steps will encourage more living donors to come forward (both nondirected and

directed), particularly those with limited financial means. These policy proposals bear even more weight in the context of nondirected organ donation where significant financial disincentives for donors may undermine any perceived moral duty to alleviate suffering in unknown transplant candidates.

5.2 | Global practice and ethical perceptions

Living donor liver transplant has been rapidly adopted by Asian countries, particularly in Japan, where sociocultural norms pertaining to brain death and organ transplantation historically stymied public acceptance of transplantation using deceased donor organs.[45-47] Hence, since the early era of LDLT, Western and Asian populations have addressed the problem of donor organ shortage in markedly different ways. LDLT was slow to be adopted in countries such as the United States and the UK, where deceased donor liver transplantation (DDLT) predominates, largely due to concerns related to donor well-being.[46] In contrast, Asian countries such as Japan, South Korea, and Taiwan have been successful in shaping public perception in favor of living donation due to a critical shortage of deceased donor organs.[46,48] This has resulted in greater than 90% of liver transplants using living donors in the region, with a similar result in the Middle East.[48,49]

As LDLT has become an accepted practice across the globe, international opinion on the use of anonymous donors in high-volume LDLT countries remains mixed at best, largely due to ethical concerns (summarized in Table 4). In 2006, the Ethics Committee of The Transplantation Society published a statement endorsing the use of anonymous living donors as ethical insofar as the aggregate benefits to the donor-recipient pair would outweigh the risks.[50] However, concerns related to organ trafficking via donor coercion and financial inducements targeting vulnerable populations have persisted. The concept of transplant tourism has threatened to malign global transplant activity since the 1980s, in which potential recipients travel to clinics around the world to receive an organ from impoverished and poorly paid "donors," particularly in India, Pakistan, Egypt, the Philippines, and Eastern Europe.[51] Transplant commercialism, defined by the Declaration of Istanbul on Organ Trafficking and Transplant Tourism of 2008 as "a policy or practice in which an organ is treated as a commodity, including being bought or sold or used for material gain," has also emerged as a key ethical issue.[52] The legal practice of organ procurement from death-row prisoners in China further confounds the ethics of organ resourcing and allocation, particularly with regard to living organ donation.[53]

In most countries, due to ethical concerns, living organ donation remains limited to the recipient's close relatives or spouse.[54] Within Europe, anonymous nondirected living organ donation is lawful in Sweden, Italy, Belgium, Denmark, England, Latvia, the Netherlands, Portugal, Scotland, Spain, and Switzerland.[55] Countries such as Bulgaria, the Czech Republic, Estonia, Finland, France, Germany, Hungary, and Lithuania expressly prohibit anonymous nondirected living donation.[55] In Japan, nondirected living organ donation is virtually unheard of, but guidelines have been developed to allow for such donation if authorized by an institutional ethics committee and reviewed by the Japan Society for Transplantation.[56,57] In South Korea and Hong Kong, centers have instituted programs containing elements of nondirected living donation through paired liver and kidney exchange.[58,59] Taiwanese law limits organ donors to the recipients' spouse or relatives within a fifth degree of consanguinity.[54] Turkey also prohibits nondirected organ donation, but legislation was proposed in 2016 to allow for "extrafamilial" organ donation if approved by a dedicated provincial ethics committee.[60] Organ donation by unrelated individuals in India is still subject to stringent regulatory oversight following an amendment in 2011 to the Transplantation of Human Organ Act of 1994, which originally permitted organ donation only from a spouse or first-degree relative.[61] Many high-volume centers employ detailed human leukocyte antigen testing to confirm biological relationships for living donors, and they also require marital relationships to have been established at least one year prior to donation (personal communication). In Egypt, where transplantation using deceased donor organs has only recently been legalized, organ donation is limited to relatives within a fourth degree of consanguinity owing to concerns related to historical exploitation of individuals through transplant tourism and organ commercialism.[62]

Globally, there is consensus among the transplant community that although financial inducements encouraging organ donation remain unethical, costs incurred by the donor along all aspects of the donation journey should be reimbursed.[63] In 2009, Sickand *et al* analyzed 40 countries with live organ donation programs and found that legislation explicitly allowed financial reimbursements in 16 countries, was unclear in 18 countries, and prohibited in one.[63] Permanent reimbursement programs existed in 20 countries. A majority of programs reimbursed travel expenses (19 countries), lost income (17 countries), accommodation (17 countries), meals (14 countries), and childcare costs (12 countries). However, the authors concluded that most living organ donors across the globe do not have access to organized programs to help defray the costs related to donation. Given the reality that only a small minority of living donors globally are nondirected, it would be prudent for policymakers to address gaps in organ shortage not only through legislation making anonymous nondirected organ donation a legal option, but also instituting ethically sound reimbursement programs to encourage motivated individuals to come forward.

6 | FUTURE DIRECTIONS

In summary, anonymous nondirected living liver donation will increasingly become an option as the practice of LDLT expands and demonstrates equivalent, if not superior, outcomes when compared to DDLT. Literature highlighting the use of ND-LLDs is sparse, but our review of the SRTR indicates that US programs are increasingly willing to accept anonymous nondirected liver donors. There are presently no established criteria for selection of potential

TABLE 4 Approach to anonymous nondirected living liver donation in high-volume LDLT countries

Country	Reporting year	Population (millions)	Deceased donor liver transplants	Living donor liver transplants	Approach to nondirected donation
India	2015	1311.10	Unknown	1200	Legal but not currently being used due to challenges in determining motivation; special authorization committee permission required.[61]
Turkey	2016	79.6	392	1004	Illegal; legislation allowing for "extra-familial" organ transplants after approval from provincial ethics committee pending.[60]
South Korea	2015	50.3	456	942	Illegal; live organ donation restricted to family members of the fourth degree.[64]
Egypt	2015	91.5	0	450	Illegal; live organ donation restricted to family members of the fourth degree.[62]
China	2016	1382.0	3,264	408	Illegal; living donor and recipient have to be genetically or maritally related and every case must be approved by a provincial health ministry.[65]
Japan	2016	126.3	57	381	Unclear; living donors should be limited to relatives within the sixth degree or third degree by marriage. Living donation from other than aforementioned individuals should be individually approved by an institutional ethics committee and reviewed by the Japan Society for Transplantation.[56]
United States	2017	324.5	7715	359	Legal.[66]
Brazil	2017	209.3	1921	186	Unclear; living organ donation is allowed by a spouse or blood relatives within the fourth degree, or any other person by judicial authorization according to law. As of 2008, a separate ordinance has been passed stating that anonymous ("living unrelated") donors will only be accepted for recipients whose time on the waiting list has been more than 1,350 days.[67]
Pakistan	2016	192.8	0	177	Legal; Transplantation of Human Organs and Tissues Act of 2010 allows for organ donation by someone other than a "close blood relative" if approved by an Evaluation Committee.[68]
Jordan	2016	7.7	4	174	Unclear; The Jordanian Act of Organ Donation defines a donor who is genetically related to the index patient or emotionally related (ie, spouse) but involves no mention of anonymous, nondirected, or unrelated organ donors.[69,70]
Saudi Arabia	2017	32.9	79	147	Legal; anonymous ("unrelated") living donation is allowed pending an ethics committee approval, a psychiatric evaluation of the donor, and the donor's written consent.[71,72]

Note: Data obtained from WHO-ONT Global Observatory on Donation and Transplantation website.[72]

anonymous nondirected liver donors nor criteria for waitlist allocation. The published experience of anonymous nondirected living kidney donors suggests that long-term psychosocial well-being in these individuals is well-preserved. Long-term health-related quality of life in ND-LLDs remains the subject of future research. Given that existing anonymous nondirected organ donors report persistent, substantial financial barriers to donation, elimination of financial disincentives to donation should be of paramount importance. Simultaneously, we must encourage conversation where ethical concerns related to organ trafficking and donor vulnerability have led

to legislation limiting the ability of ND-LLDs to come forward. As a global transplant community, we must continue to develop policies that balance concerns pertaining to donor well-being with those of transplant candidates.

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CONFLICT OF INTEREST

The authors of this manuscript have no conflicts of interest to disclose as described by *Clinical Transplantation*.

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