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Assessing the value and cost of Organ Donation and Transplantation (ODT)

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Assessing the value and cost of Organ Donation and Transplantation (ODT)

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Editorial: Assessing the value and cost of Organ Donation and Transplantation (ODT)

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Editorial on the Research Topic
Assessing the value and cost of Organ Donation and Transplantation (ODT)

Healthcare financing has been defined by the World Health Organization as a "core function of health systems" (1); such a pertinent statement underscores the importance of better understanding the value and costs of Organ Donation and Transplantation (ODT). Although the clinical value of transplantation remains undisputed, the financial value and real costs of the whole process of offering life-saving or life-prolonging treatment to thousands of patients worldwide each year have only rarely been analyzed in-depth and even more rarely contextualized as a unique, multidisciplinary, and interdependent healthcare entity (Leonardis et al.). In particular, the value of the complex activities consisting of several phases, supporting organ donation and retrieval and culminating in the actual transplantation procedure, should also be analyzed against the social and treatment costs of managing patients with End-Stage Organ Failure. Equally important, the economic benefits together with the efficiency of the procedures and their value are not only evident for the patients and their families, but for the whole community; therefore, the definition of the actual "value" should not be limited to a favorable cost-benefit analysis, but should extend to the social aspects of care, which may be very difficult to capture and fully appreciate.

The many steps and procedures involved in the transplant of organs that are immediately life-saving are generally perceived and accounted for as highly expensive for any healthcare service. This is undoubtedly true; however, the actual financial savings produced by the "gold standard" of treatment for eligible patients with End-Stage Kidney Disease (ESKD), that is Kidney Transplantation (KT), can comfortably offset the costs of Organ Donation (OD) services. Therefore, a "Keynesian perspective" of the health economics of KT where savings represent the actual financial resources, may benefit the whole ODT service to the extent that financial self-sufficiency can be achieved (Leonardis et al.).

There are several aspects of ODT practice that will contribute to improving the understanding of the value of the service. It was indicated by Kim et al. that KT is the

preferred Renal Replacement Therapy (RRT) for suitable patients, adding that Living Donor Kidneys should be preferred over Deceased Donor kidneys because of their superior quality, which results in improved patient and graft survival. Such considerations extend to the issue of supply and demand in the "economics of transplants." Boadu et al. outlined in their analysis carried out on different population subgroups in England, that there is an emerging consensus supporting the concept that an increase in living donation could contribute even more than deceased donation to reducing inequalities in organ donation. The machine learning (ML) approach used in the study identified important factors that influence intentions to become a living kidney donor. Support for organ donation, awareness of public campaigns, and younger age were all positively associated with the predicted propensity to become a living donor (Boadu et al.). Zhang et al. also highlighted that organ donation is a prosocial behavior as it is aimed at prolonging the life of the recipient. However, the authors report that the supply-demand ratio of organs in China is highly unbalanced and it should be investigated what hampers organ donation in their country, which is characterized by diverse social representations and perceived barriers to organ donation (Zhang et al.). In this context, the media may be a highly relevant channel for improving organ donation knowledge; in this sense, Gong et al. explored the influence of media use on willingness to donate organs and the factors influencing willingness to donate organs in people with different levels of media use. Their results outlined how high-frequency media users are positively correlated with their willingness to consider organ donation. Hence, it is necessary to formulate personalized and targeted dissemination strategies for health information on organ donation for different media users (Gong et al.). Confirmation of the global need for adequate education also comes from the contribution of Jazienicka-Kiełb et al., who assessed the knowledge of CKD among primary care physicians (PCPs) in Poland. They reported that despite a fairly high level of knowledge among PCPs regarding the causes, risk factors, and progression of CKD, there is still a need for further education and an increase in factual information among this professional group (Jazienicka-Kiełb et al.). The importance of knowledge and education about ODT is also highlighted in the study by Wang et al., which focused on target populations who have undergone solid organ transplant (SOT) to bolster preventative practices in these patients during the Coronavirus Disease 2019 (COVID-19) pandemic. They report that while sufficient levels of knowledge are generally correlated with a higher likelihood of adequate levels of practice, they found that positive attitudes toward transplantation were not correlated with adequate levels of practice in the United states (Wang et al.).

The financial insecurity caused by global instability and the ongoing COVID-19 pandemic caused by SARS-CoV-2 have exposed several weaknesses of the entire healthcare system, with hard-to-estimate, but predictably significant repercussions on the healthcare services routinely offered to worldwide users (Leonardis et al.). Hence, a reliable estimate of the financial value of ODT paired with an optimization strategy is of critical relevance, for both developing and developed countries. Indeed, the substantial savings generated by KT benefit the entire healthcare service. The work of Leonardis et al. on the evaluation of the actual financial benefits generated by KT, offers a novel perspective on the health economics of KT and SOT in general, and developed a specific methodology for the definition of a novel coefficient; the Kidney Transplant Coefficient of Value (KTCoV) which contributes to a reliable estimation of the savings generated by KT activity. It is also maintained that an adequate optimization of the funding process can lead to the financial self-sufficiency of the ODT service.

A more in-depth benchmark analysis of three different ODT programs produced by Cacciola et al. compared the financial resources obtained in the Italian regions of Sicily and Lazio with those obtained in Scotland identifying multiple and interdependent, factors influencing the different levels of KT activity with an estimate of the associated "foregone savings." Organ donation rates, access to the transplant waiting list, and KT from living donors appear to be the most prominent determinants of the observed different levels of activity. In this light, the Authors suggest replicating the international experience with a comprehensive strategy to be implemented by a "task force" that would successfully address the critical areas of the service to reverse the observed trend and promote the growth of the service (Cacciola et al.).

A constructive governance process is critical to the achievement of positive outcomes for both patients and healthcare commissioners (2); therefore psychosocial aspects of care undoubtedly represent a highly relevant aspect of ODT. In their contribution, Zerbinati et al. investigated the psychosocial factors that frequently occur in kidney transplant recipients and that lead to behavioral changes and reduced therapeutic adherence. Their study showed that somatization and mood disorders may predict costs for hospital admissions and emergency department use and may be risk factors for poor outcomes, including death, in KT (Zerbinati et al.).

In conclusion, the value of ODT extends from the highly successful clinical practice of saving or prolonging the lives of patients with end-stage organ disease, to the positive impact on their families and wider society. Uniquely, the clinical and social benefits are also associated with conspicuous savings that should attract the attention of healthcare commissioners. The traditional fee-for-service funding methodology, in which providers are paid based on the number of healthcare services they deliver does not reflect the needs and value of the whole ODT. Consequently, it can be argued that ODT, because of its complexity and the highly successful practice of SOT, consisting of patient and graft survival rates, would benefit from being funded as an in-hospital service with a comprehensive fee-for-value rather than a compartmentalized fee-for-service funding method [Leonardis et al.; (3)].

Author contributions

LG: Conceptualization, Project administration, Supervision, Writing – original draft, Writing – review & editing. EF: Data curation, Methodology, Validation, Writing – review & editing. EG: Data curation, Formal analysis, Investigation, Validation, Writing – review & editing. RC: Writing – original draft, Writing – review & editing.

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A cross-sectional study of knowledge, attitude, and practice toward COVID-19 in solid organ transplant recipients at a transplant center in the United States

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Objectives: Knowledge, attitude, and practices (KAP) have been widely used during times of pandemic to quantify and locate gaps of care during pandemics. Using this tool, we can identify and target populations who underwent solid organ transplant (SOT) to bolster preventative practices in these patients during COVID-19.

Materials and methods: An institution-based cross-sectional study was conducted between June 1, 2020 and June 30, 2021 on patients who underwent a liver and/or kidney transplant at Methodist Dallas Medical Center in Dallas, Texas, USA. A KAP questionnaire of 26 questions about COVID-19 was designed based on the clinical and community management guidelines published by the WHO. The participant's overall KAP was categorized using Bloom's cut-off point. A KAP domain was considered sufficient if the score was between 60 and 100% and insufficient if the score was <60%. The strength of association was assessed by using odds ratio (OR); only significant independent factors in each tested area were assessed.

Results: Respondents with children in the household were less likely to have sufficient practices than those who did not [OR = 0.2491, 95% Confidence Interval (0.0893–0.6120), $p = 0.001$]. We also found that sufficient levels of knowledge correlated with higher likelihood of sufficient levels of practices [OR = 4.94, 95% CI (1.646–14.2159), $p < 0.005$]. Interestingly, we found that sufficient levels of attitude did not correlate with sufficient levels of practice ($p = 0.201$).

Conclusion: Our study found that knowledge and having children in the household correlated with higher levels of practice.

KEYWORDS

knowledge, attitude, practices, COVID-19, immunosuppression, liver transplant, kidney transplant, health disparities

Introduction

COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was declared to be a global pandemic by the World Health Organization (1, 2). During this time, several at risk populations were identified to have an increased risk of mortality and morbidity from COVID-19, including patients with metabolic liver disease and decompensated cirrhosis (3–6). These findings are even more pronounced in solid organ transplant (SOT) recipients (SOTRs) who are on chronic long-term immunosuppression and are vulnerable to infection. Interestingly, this data deviates from prior epidemics which haves shown that outcomes in SOTRs are comparable to the general population (7–9). While we wait for new data to accumulate for this population, the medical field can still take large strides in improving COVID-19 related outcomes in SOTRs by determining gaps of care and enforcing guidelines applicable to the general population.

Knowledge, attitudes, and practices (KAP) studies have been widely used during pandemics to quantify and locate gaps in the healthcare system (10, 11). During the initial phase of the COVID-19 pandemic, various prevention and control measures were adopted globally, including shelter-in-place policies, social distancing and telehealth (12–14). In accordance with the KAP theory, adherence to these measures is affected by the population's KAP toward the disease (15). Despite widespread concern about the impact of COVID-19 on SOTRs, COVID-19 KAP studies in the United States thus far do not include data specific to SOTRs. In this study, we report the KAP toward COVID-19 among a SOTR cohort in Dallas, Texas during the first year of the pandemic (early 2020 to mid-2021) to determine key demographics of SOTRs to target and improve areas of outreach and education.

Materials and methods

Study design and patient recruitment

An institution-based cross-sectional study was conducted between June 1, 2020 and June 30, 2021 on all patients who underwent a liver and/or kidney transplant at Methodist Dallas Medical Center in Dallas, Texas, USA. The sample size of this study was based on the number of transplants performed at the center during the allotted time frame. The authors factored in a 30% non-response rate. All organs were donated voluntarily with written informed consent, and this was conducted in accordance with the Declaration of Istanbul. Of note, this study was conducted at a time when the COVID-19 vaccine was not available to the general public, therefore, all participants were unvaccinated. Participants provided verbal or electronic written informed consent before completion of the KAP questionnaire. Only questionnaires returned by June 30, 2021 were considered for analysis. The study was approved by the Methodist Health System institutional review board (Protocol ID: 032.HEP.2020.D).

Questionnaire design

A KAP questionnaire of 26 questions about COVID-19 was designed (Supplementary Document 1). The questionnaire was developed based on the clinical and community management guidelines that were published by the WHO at the time (15). The questionnaire was also piloted on 20 healthcare professionals and modified accordingly. Results from the pilot study were excluded from the final analysis. The questionnaire was administered to the patients *via* e-mail or paper during in-office visits. The first part of the questionnaire collected demographic data (e.g., age, sex, marital status, education level, number of children, zip code of residence, type of SOT, type of immunosuppressive therapy after SOT, if the patient ever tested positive for COVID-19, and if they had difficulties accessing masks). The second part of the questionnaire focused on KAP toward COVID-19. The KAP consisted of 17 questions about COVID-19. Those who answered affirmatively that they had contracted COVID-19 were asked further questions regarding their COVID-19-related symptoms and hospitalizations. The participants were also surveyed regarding immunosuppression use during the pandemic and their attitudes toward COVID-19 vaccinations.

To assess the knowledge score, seven items on the questionnaire were measured. Each correct answer was scored one point and incorrect questions were scored zero points. To assess the attitude score, six items were analyzed. Each item had three answer choices: to continue to receive optimum medical care, to reflect an indecisive attitude, or to neglect their healthcare needs. One point was assigned to those who chose to continue receiving optimal medical care and zero points were awarded for "indecisive attitude" or "neglect their healthcare needs." To assess positive changes in practice, four items were analyzed. After the scores from all the sections were compiled, the percentage of "correct" answers out of the total was determined.

Statistical analysis

All statistical analyses were performed using Stata 16 (StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC). The data were analyzed using appropriate descriptive statistics and summarized by frequency and percentage. Independent variables were gender, age, marital status, number of children in household, education level, type of organ transplant, difficulty accessing a mask, tested positive for COVID-19 and triple immunosuppressant use.

The percentage of correct responses was calculated by dividing the total number of correct answers by the total number of questions and multiplying that result by 100 in each tested area (i.e., knowledge, attitude, and practice). The participant's overall KAP was categorized using Bloom's cut-off point (16). For our study we only categorized into two categories: sufficient and insufficient. A KAP domain was considered sufficient if the score was between 60 and 100% and insufficient if the score was <60%. Although previous studies used Bloom's cut-off point as 80–100% being good scores, 60–79% being moderate scores, and <60% and below for poor scores; our team decided to create 2 subdivisions instead of 3. Here we chose to merge moderate and good as one and kept poor as <60%. This was done to better distribute the survey's scores into more distinct categories given the volume of questions for each KAP section. The strength of association was assessed by using odds ratio (OR) and confidence intervals (CI); only significant independent factors in each tested area were assessed. A $p < 0.05$ level was considered statistically significant.

Results

Demographics

Most respondents were male (58.0%), over the age of 61 (53.8%), married or in a domestic partnership (64.7%), and had children in the household (58.8%) (Table 1). In this study, 42.4% of the patients completed high school, 37.0% completed college, and 12.6% completed a post-graduate degree. In addition, most participants were liver (62.6%) or kidney transplant (34.5%) recipients. The most common reported immunosuppressants were mycophenolate (38.7%) and prednisone (49.6%). At the time of the survey 15.1% of the patients had contracted COVID-19 infection.

TABLE 1 Socio-demographic and clinical characteristics of the solid organ transplant patient study population.

Variable, n (%)	Category	Overall ($N = 238$)
Gender	Female	100 (42.0%)
	Male	138 (58.0%)
Age	<40 years	17 (7.1%)
	41–60 years	93 (39.1%)
	>61 years	128 (53.8%)
Marital status	Single	35 (14.7%)
	Married	154 (64.7%)
	Widowed	14 (5.9%)
	Divorced	35 (14.7%)
Children in household	Yes	140 (58.8%)
	No	98 (41.2%)
Education level	<High school	18 (7.6%)
	High school	101 (42.4%)
	College degree	88 (37.0%)
	Post-graduate	30 (12.6%)
Type of organ transplant	Liver	149 (62.6%)
	Kidney	82 (34.5%)
	Liver and Kidney	7 (2.9%)
Difficulty accessing a mask?	Yes	36 (15.1%)
	No	202 (84.9%)
Tested positive for COVID-19	Yes	24 (15.1%)
	No	193 (84.9%)
Immunosuppression	Steroid	118 (49.6%
	Mycophenolate	92 (38.7%)
	Tacrolimus	41 (17.2%)
	Sirolimus	14 (5.9%)
	Triple immunosuppression	76 (31.9%)

Knowledge, attitudes, and practices of COVID-19

Most of the patients were aware that COVID-19 was caused by a type of virus (90.3%) and at the time of the survey there were no effective medications or vaccines available to cure or prevent the disease (87.0%) (Table 2). Additionally, most of the patients were aware that the virus could be spread even without signs or symptoms (95.0%) and social distancing during the peak of the pandemic was important to control the spread of the virus (86.6%). The areas with the most misconception were the clinical manifestation of COVID-19 and its mode of transmission. Less than three-quarters of the respondents knew the signs and symptoms of the infection (71.0%) and lacked adequate knowledge on the various modalities for the spread of the virus (60.9%).

Almost three-fourths (73.1%) of the SOTRs had a positive attitude toward vaccination and if made available were open to receiving immunization (Table 3). Additionally, most were willing to encourage friends or family members to consider vaccination (77.3%). Half (53.8%) of the patients surveyed stated that they would have been more inclined to decline a SOT during the COVID-19 pandemic if they were still on the transplant list. Less than half (45.4%) of the respondents stated that they would avoid seeking routine health care visits, if possible, until the pandemic had resolved.

In response to practices toward COVID-19 prevention, most of the respondents reported that the COVID-19 pandemic had increased their overall awareness and knowledge of maintaining hygiene, including taking sanitary precautions in public places (83.2%) and hand washing (85.3%) (Table 4). Despite improved awareness, less than half the patients were willing to wear a mask in appropriate situations (42.9%).

TABLE 2 Knowledge responses about COVID-19 among solid organ transplant recipients ($N = 238$).

Serial no	Knowledge question	Frequency (%)	
		Correct	Incorrect
1	COVID-19 is caused by a novel coronavirus	90.3%	9.7%
2	COVID-19 virus spreads *via* the following method(s): respiratory droplets of infected individuals, contact with blood of infected individual, contaminated water, or all of the above.	60.9%	39.1%
3	The main clinical symptoms of COVID-19 are fever, dry, cough, shortness of breath and myalgia, chest pain or shortness of breath, only fever, abdominal pain, and diarrhea, or all of the above.	71.0%	29.0%
4	Although COVID-19 can affect everybody, the populations that are mostly likely to develop severe symptoms are elderly people, patients suffering from ailments such as heart disease, diabetes, blood pressure and immunocompromised (low immunity) individuals	95.0%	5.0%
5	Currently there is no available cure for COVID-19	87.0%	13.0%
6	COVID-19 can also be spread by individuals who do not have symptoms	95.0%	5.0%
7	Social distancing will help reduce and eliminate COVID-19 disease?	86.6%	13.4%

TABLE 3 Attitude responses toward COVID-19 among solid organ transplant recipients ($N = 238$).

Serial no	Attitude question	Frequency (%)	
		Correct	Incorrect
A1	If you develop fever or cough with sore throat, are you more likely to self-quarantine for 14 days and only get tested if fever or symptoms worsen, get tested for COVID-19 immediately, or continue normal routine.	45.8%	54.2%
A2	If you were to receive an organ for liver or kidney transplant during this COVID 19-9 epidemic (assuming you were still on waitlist) you would accept the organ, decline the transplant, accept only if donor was checked for COVID-19?	53.8%	47.2%
A3	In your opinion, what is the best way to seek health care during the COVID-19 pandemic?	45.4%	54.6%
A4	Do you believe that COVID-19 can be prevented by vaccination?	74.8%	25.2%
A5	If a vaccination of COVID-19 is available, would you like to be vaccinated?	73.1%	26.9%
A6	Will you advice your relatives and family to obtain immunization of COVID-19 vaccine	77.3%	22.7%

We also see that those with children in the household were less likely to have sufficient practices than those who did not (OR = 0.2491, 95% CI (0.0893–0.6120), $p = 0.001$) (Table 5). We also found that sufficient levels of knowledge correlated with higher likelihood of sufficient levels of practices [OR = 4.94, 95% CI (1.646–14.2159), $p < 0.005$]. However, there was not a significant correlation between sufficient levels of attitude and sufficient levels of practice ($p = 0.201$) (Table 5).

Discussion

To our knowledge, this was the first study to assess the KAP of SOTRs in the United States during the early stage of the pandemic in 2020. The United States imposed a stringent lockdown across the country for several months to control the spread of COVID-19. Though there has been a vaccine rollout, the spread of new variants of SARS-CoV-2 continues to be rampant in the United States and in many countries around the world. Therefore, despite vaccination there continues to be an immediate need for effective prevention at various levels of public health. Adequate prevention measures could be successful by enhancing the KAP of the population.

The COVID-19 pandemic has increased the risk of mortality and morbidity in those with chronic illnesses including those with liver disease and cirrhosis (3–6). SOTRs have been shown to have higher rates of infection and complications from COVID-19 due to use of immunosuppressive medications. They also have more comorbidities than the general population. The pandemic has increased anxiety levels among SOTRs, leading to modifications to their daily lifestyle (17, 18).

The results of our study showed participants achieved a mean score of 83.3% in the knowledge portion of the questionnaire. These results are comparable to those in studies

TABLE 4 Practice responses toward COVID-19 among solid organ transplant recipients ($N = 238$).

Serial no	Practice question	Frequency (%)	
		Correct	Incorrect
P1	As a transplant recipient, has the COVID-19 pandemic increased your awareness and knowledge of maintaining hygiene, including taking precautions in public places to avoid contracting other infections in the future?	83.2%	16.8%
P2	Has the COVID-19 pandemic increased your practice of hand sanitation?	85.3%	14.7%
P3	What do you use to wash/clean your hands?	99.6%	0.04%
P4	When are you likely to wear a mask?	42.9%	57.1%

done in both the general population and high-risk populations (19, 20). Therefore, adequate knowledge could have led to better social distancing practices and sanitary precautions leading to a lower incidence of COVID-19 among SOTR. These findings highlight the need to continue to encourage and emphasize maintaining social distancing as a means of preventing the spread of COVID-19. We also found that only a quarter of the respondents shared a negative attitude toward COVID-19 vaccination including not wanting their relatives to be vaccinated. Interestingly, the mean score in the attitude portion of the questionnaire (61.7%) was relatively lower than those in studies from other countries (21). Hesitancy rates for vaccination in our SOTR cohort were comparable to the national trend suggesting that SOTR attitudes toward vaccination were similar to the general US population (22). To achieve higher vaccination rates, it is important to implement adequate policies and use various media platforms to address the safety aspects and existing misconceptions of the COVID-19 vaccines. During the pandemic, routine office consultation visits were canceled or deferred by patients due to increased fear of contracting an infection at a health care facility when compared to staying at home. In our study, 54.6% of the SOTRs wanted to avoid or minimize regular office visits. As the duration of the pandemic progresses, it is more likely that SOTRs might postpone health care visits. One way to deliver better health care during the COVID-19 pandemic is to bolster the practice of medical care *via* telehealth. Similarly, there was an overall decline in all SOT especially among kidney and living donors during 2020 compared to 2019 (7). Almost 47.2% stated that they would decline an offer for a transplant during the pandemic. It is possible that once again the fear of contracting an infection from a healthcare setting and the increase in the availability of deceased donors from deaths related to COVID-19 could have resulted in these results. To ameliorate this concern, the United Network for Organ Sharing has made it mandatory to test all donors and recipients for COVID-19 and make this information available to patients on the waiting list.

As expected, SOTRs with sufficient knowledge scores reported to adhere to higher levels of practices compared to those with insufficient scores. This finding underlines the importance of robust communication strategies in vulnerable populations. Another factor that correlated to higher levels of practice were if patients had children living in the household at the time of survey. A similar study conducted by Alremeithi et al. also reflects this finding. A possible explanation for this is that parents would want to pursue and project a mindset for their children to emulate to prevent contracting COVID-19. Furthermore, it was interesting to see that mask accessibility did not have a significant impact on reporting good attitude or practices around COVID-19. Given the time when this survey was conducted, this could suggest that in the initial stages of the pandemic SOTRs may have faced geographic or financial obstacles keeping them from maintaining awareness and good practices regarding COVID-19.

Study limitations

Some limitations should be considered when interpreting the findings of our study. The data were from self-reported information, increasing the chance of reporter bias. The use of a small sample size and the cross-sectional nature of the study does not allow for determination of any cause-and-effect relationships. Given that all patients surveyed were from Methodist Dallas Medical Center, the results of the study may not reflect the KAPs of SOTRs worldwide. Additionally, the survey responses were received over different time points in the pandemic. Those who responded later could have had a different perspective on the pandemic compared to those who responded earlier due to better dissemination of knowledge and information.

Conclusion

To our knowledge, this was the first KAP study conducted among SOTRs in the United States. The immunosuppressed state of the cohort makes them vulnerable to infection with higher morbidity compared to the general population. We found that having sufficient knowledge about COVID-19 does correlate with maintaining higher standards of practices in preventing infection. However, in this study we also found that a significant amount of SOTRs. This

TABLE 5 Sociodemographic determinants of sufficient practice scores.

Variables [N (%)]	Practice		*p*-Value odds ratio 95% confidence interval
	Insufficient $N = 40$	Sufficient $N = 198$	
Knowledge			**<0.005**
Insufficient	9 (22.50)	11 (5.56)	**OR = 4.9355**
Sufficient	31 (77.50)	187 (94.44)	**95% CI = [1.646, 14.2159]**
Attitude			0.201
Insufficient	18 (45.00)	68 (34.34)	
Sufficient	22 (55.00)	130 (65.66)	
Gender			0.777
Male	24 (60.00)	114 (57.58)	
Female	16 (40.00)	84 (42.42)	
Age			0.083
<40	2 (5.00)	15 (7.58)	
41–60 years	22 (55.00)	71 (35.86)	
>60 years	16 (40.00)	112 (56.57)	
Marital status			0.816
Single	6 (15.00)	29 (14.65)	
Married	26 (65.00)	128 (64.65)	
Widowed	1 (2.50)	13 (6.57)	
Divorced	7 (17.50)	28 (14.14)	
Children in household			**0.001**
No	7 (17.50)	91 (45.96)	**OR = 0.2491**
Yes	33 (82.50)	107 (54.04)	**95% CI = [0.0893, 0.6120]**
Education level			0.601
< High school	1 (2.56)	17 (8.59)	
High school	17 (43.59)	84 (42.42)	
College degree	15 (38.46)	73 (36.87)	
Post-graduate	6 (15.38)	24 (12.12)	
Type of organ transplant			0.051
Liver	20 (50.00)	129 (65.15)	
Kidney	17 (42.50)	65 (32.83)	
Liver and Kidney	3 (7.50)	4 (2.02)	
Difficulty accessing a mask.			0.104
No	37 (92.5)	165 (83.33)	
Yes	3 (7.5)	33 (16.67)	
Tested positive for COVID-19			0.240
No	30 (83.33)	163 (90.06)	
Yes	6 (16.67)	18 (9.94)	
Triple immunosuppressant			0.648
No	26 (65.00)	136 (68.69)	
Yes	14 (35.00)	62 (31.31)	

Bolded values represent statistically significant comparison ($p < 0.05$).

may represent a key point in the healthcare battle against COVID-19 as it insinuates that improving education of the disease may lead to increased prevention of contraction from a mass population perspective. Overall, this study demonstrates that a more comprehensive understanding of COVID-19 correlated with an increased adherence to practices to prevent its spread. Based on these results, we strongly recommend bolstering avenues for education, particularly

amongst patient populations at most risk for worse COVID-19 outcomes. In the end, we believe that a better-informed population will lead to one that adheres to COVID-19 preventative practices.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Methodist Health System Institutional Review Board (Protocol 032.HEP.2020.D). The patients/participants provided their written informed consent to participate in this study.

Author contributions

LW: organized and participated in data gathering and primary manuscript author. MA: participated in data gathering. HO: secondary manuscript author. PA: primary statistician. MC: secondary statistician. ED: reviewer and editor. MP: Principal Investigator and editor. All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

Conflict of interest

Authors PA, MC, and AM were employed by Methodist Health System.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

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Excavating the social representations and perceived barriers of organ donation in China over the past decade: A hybrid text analysis approach

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Background: Organ donation has been claimed as a prosocial behavior to prolong the recipient's life and deliver great love. However, the supply-demand ratio of organs in China is highly unbalanced. Being entangled with multiple factors derived from individual and supra-individual levels, organ donation in China is important but sensitive. Previous scholars usually depended on obtrusive approaches to explore the facilitators and hindrances of organ donation, which is hard to discover genuine perceptions toward organ donation. Besides, relatively limited scholarly attention has been paid to what hampers organ donation in China.

Objective: We intended to excavate the diversified social representations and perceived barriers to organ donation in China over the past decade.

Method: Two kinds of text analysis methods—semantic network analysis and conventional content analysis, were applied to 120,172 posts from ordinary users on the Sina Weibo platform to address the research questions.

Results: Regarding social representations, the "hope, understanding, and acceptance" of organ donation was the most pronounced one (34% of the whole semantic network), followed by "family story" (26%), "the procedure of organ donation in NGOs" (15%), "the practical value of organ donation" (14%), and "organ donation in the medical context" (11%). Regarding perceived barriers, a four-layer framework was constructed, including (1) the individual level, mainly about the fear of death and postmortem autopsy; (2) the familial level, which refers to the opposition from family members; (3) the societal level, which alludes to distrust toward medical institutions and the general society; (4) the cultural level, which covers religious-cultural concerns about fatalism.

Conclusion: In concordance with prior works on social representations regarding organ donation, the current study also uncovered the coexistence of antithetical representations about organ donation—the longing for survival and the fear of death. This representation pair serves as the foundation of Chinese people's ambivalence. Besides, family-related narratives were dispersed over various representations, demonstrating the critical position of family support

in organ donation. Moreover, the four-layer framework concerning donation barriers affords a reference for future empirical studies. The practical implications of this work are further discussed.

KEYWORDS

organ donation, social representation, China, semantic network analysis, conventional content analysis, cultural factors, social media

Introduction

Organ donation is an important worldwide public health issue. Regrettably, many countries are facing a stagnant organ donation rate and an unbalanced organ supply-demand ratio (1), and China is no exception. According to official statistics, although the organ donation rate per million people has risen from 2.01 in 2015 to 4.16 in 2019 in China (2), the actual donation is far from meeting the demand (3). When it comes to the question of what hampers people from becoming potential organ donors, a considerable number of studies were conducted in Western contexts (4–6). While non-Western societies, like China, received scarce scholarly attention.

The current study aims to leverage social media traces to excavate how the Chinese public perceived organ donation (RQ1) and what constituted perceived barriers to organ donation (RQ2). RQ1 is analyzed in light of the social representation theory (SRT). SRT aims to disentangle people's daily meaning-making by analyzing opinions, knowledge, and beliefs around specific social objects (7). Previous researchers have drawn upon SRT to understand how people perceive organ donation (5, 8–11). For instance, Moloney et al. (9) found that organ donation-related representations include gifts of life, benefits to oneself, negative consequences, and concerns over medical care. Most of them were underpinned by two antithetical concepts—life and death. By adopting SRT, researchers can discover diverse public perceptions toward one issue and distill the essential driving factors behind the perceptions. Understanding public perceptions toward organ donation is of paramount importance in China. Different from countries applying the "opt-out" system (e.g., Chile, Spain), which means consent to posthumous organ donation is presumed unless citizens explicitly refuse (12), China implements an "opt-in" system, requiring manifested consent or authorization from organ donors or their immediate relatives (1). In this scenario, organ donation in China relies heavily on people's understanding and inner motivation. Therefore, comprehending the current perception landscape helps to find out the hidden cruxes and assists in tailored public health interventions to improve public knowledge and nurture a positive attitude about organ donation.

In terms of perceived barriers to organ donation, extant scholarship grounded in the Western context found that knowledge deficit, religious uncertainties, mistrust of medicine, hostility to new ideas, and misinformation were significant impediments to organ donation (13). By conducting a meta-synthesis of the qualitative literature regarding organ donation, Newton found that the desire to maintain an integral body and distrust in medical professionals are the most commonly identified barriers (14). Afifi et al. highlighted family resistance's adverse impact on becoming an organ donor (15). Another survey led by Stephenson et al. disclosed that the conception of bodily integrity had been a major deterrence of organ donation willingness (6). It is not hard to conjecture that barriers to organ donation are highly context-sensitive and can never be exhausted. In China, people's organ donation decisions may be intertwined with traditional spiritual beliefs (16), longstanding moral ethics (17), and other specific sociocultural factors (18). As one of the few empirical endeavors to supplement what makes the Chinese public reluctant to become organ donors, this study intends to respect the uniqueness of the Chinese context by extracting perceived barriers from voluntary disclosure more systematically.

Another point to be noted is that previous works regarding organ donation perception and perceived barriers were always situated in specific theoretical frameworks (15, 19, 20). On the one hand, established theories can shed light on comprehending organ donation succinctly and compactly; on the other hand, predefined theoretical frameworks limit motivators or impediments to specific concepts and somewhat sacrifice the richness of public opinion. The current work draws insights from emergent social media discussions (i.e., a corpus-driven approach) rather than the previously widely adopted theory-driven approach. Social media traces enable researchers to procure unobtrusive and naturalistic data from diverse audiences and help avoid social desirability bias that threatens traditional studies developed on survey data (21). We believe this exploratory research would extend the scholarship regarding Chinese people's perceptions of organ donation and contribute to pinpointing concerns when making the donation decision.

Specifically, this study adopts a hybrid text analysis approach to answer the two proposed research questions. The "hybrid" word means a combination of the quantitative and qualitative approaches in text analysis. The quantitative way emphasizes text as data, which aims to discover the underlying thematic or semantic structures of a given

text (usually a large-scale corpus) by calculating the mathematical relationships among words. In contrast, the qualitative way mainly focuses on drawing insights by manual interpretation, which is more suitable for small-size data and an in-depth understanding of the implicit meaning. The following section will introduce the details of the hybrid text analysis approach and show how they help solve the two questions.

Materials and methods

Data source

Sina Weibo (hereafter referred to as Weibo) is a social media service launched in 2009. It has been acknowledged as the Chinese equivalent of Twitter. According to Weibo's annual report, the number of monthly active users has transcended 500 million as of September 2020 (22). Continuous content contribution from considerable active users makes Weibo an ideal platform for comprehending public perceptions or attitudes toward diverse issues (3, 23). Although the user characteristics of Weibo are not entirely chimed with the actual demographic characteristics in China, it remains an important window to understanding public opinion and social mentality.

After getting approval from the ethics committee in the first author's affiliation (No. THU202211), a Python web scraping script was developed to collect relevant posts from Weibo. According to the registration form for voluntary organ donation in China, we designated our search terms as "organ donation," "donate organs," "donate the body," and combinations of the "donate" word with all types of organs listed in the form (see Supplementary material A for a bilingual inventory of search terms). Since Weibo launched its services at the end of 2009, we set our time range from January 1st, 2010 to December 31st, 2020.

We pursued a fine-grained data collecting strategy by entering each search term into Weibo's advanced search platform and traversing through all conditions under each search option (e.g., time slot, location, user type). Simply put, we aimed to retrieve all posts in every subdivision of the combinations of search options. Each record in our dataset contains the Weibo content, user name, time of posting, user type, and other social media metrics. The original number of posts is 487,522. Since our focus is the public's social representations of organ donation, we excluded posts from accounts owned by governments, media, and other certified institutions. The quantity of ordinary users' posts is 120,172. Figure 1 illustrates the distribution of the number of original and ordinary users' posts over time. The two curves share a similar changing tendency.

Methods

Following the hybrid approach, we choose appropriate methods according to the characteristics of the research questions. To address RQ1, semantic network analysis (SNA) was utilized to extract the major social representations around organ donation. Since social representations of a particular issue always reside in daily meaning-making, which manifests in diversified expressions, the considerable data volume calls for a highly efficient way to analyze the expressions automatically. SNA is a popular automated text analysis branch that demonstrates associations among concepts by discovering co-occurrence relationships (24, 25), which could further detect the most salient words and latent semantic structures from the text following a networked perspective (26). SNA has been widely adopted in social representation studies and coincides with the associative schema behind social representation's structural approach (27, 28). Compared with traditional manual coding, SNA is less affected by pre-defined theoretical rationale and opens to all possible semantically meaningful categories. These unique advantages make it an extensively used method in investigating online public opinion (29–31).

There are three requisite procedures in SNA. The first step is text preprocessing, including removing URLs, stopwords, punctuations, special characters, and search terms from the corpus. In the second step, we created the semantic matrix based on word co-occurrence. Miller suggested that people can only process an information unit with five to nine words at one time (32). Thus, we regarded two words as retaining a co-occurrence relationship if they appeared within a five-word chunk in one Weibo post (26, 31). We then calculated the co-occurrence frequency per word pair and filtered out word pairs below the average frequency (31). Lastly, Gephi, an open-source network analysis software, was leveraged for network visualization and clustering (33). We chose only the top 100 words by frequency for subsequent modularity analysis regarding our large corpus. In former studies, three essential indicators for network measurement—network density, degree centrality, and eigenvector centrality, were reported (26, 31, 34). Network density ranges from 0 to 1, referring to how intertwined the words are in a semantic network and the complexity of discussion around a particular issue. Mathematically speaking, network density equals the proportion of existing edges in all possible edges in an undirected network (35). Degree centrality represents the number of links one word has. In other words, it measures how many words are linked with the target word, which is intuitive and straightforward. Eigenvector centrality shows the centrality of one word in the network and indicates its relative influence. Generally speaking, a high eigenvector score denotes that a word is connected to many other words with high scores (36). Eigenvector centrality is based on degree centrality but is more advanced than degree centrality. Degree centrality or eigenvector centrality exhibits how pronounced a word is in a

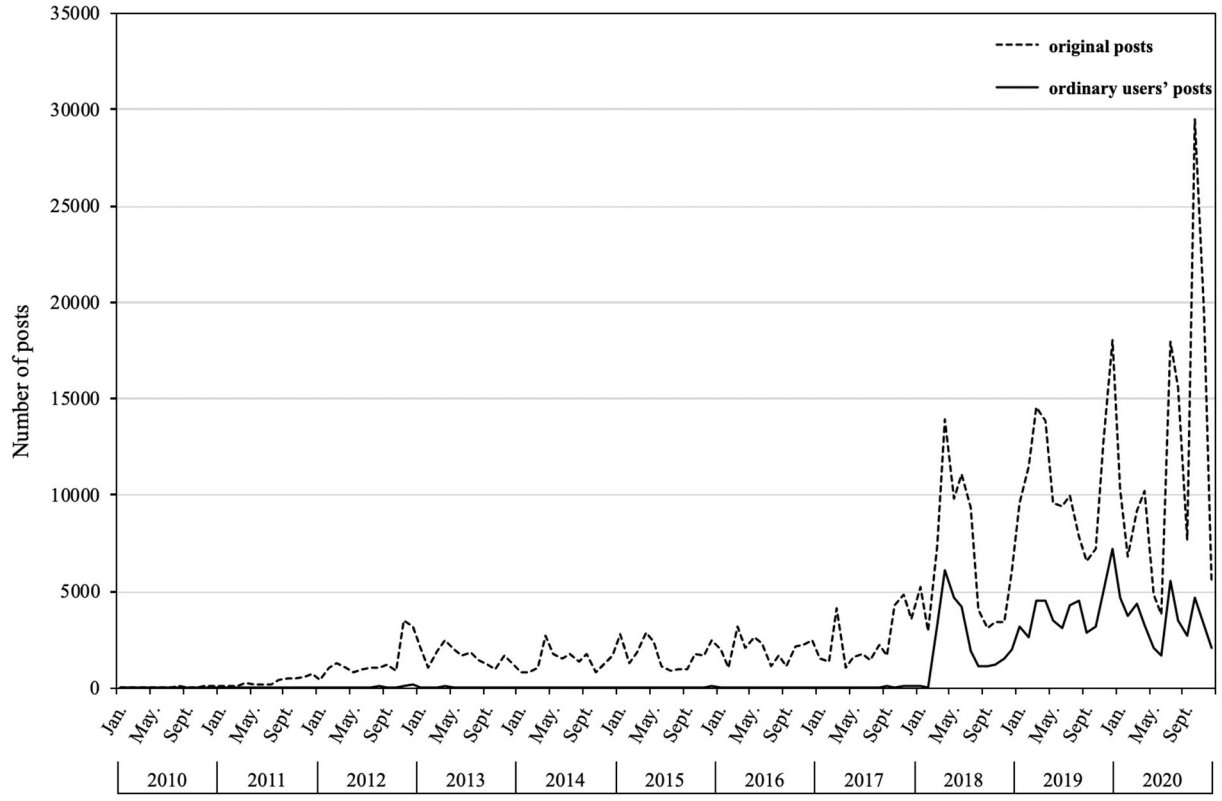

FIGURE 1
Distribution of the number of original and ordinary users' posts over time.

particular context. We also applied the LDA (Latent Dirichlet allocation) topic modeling to cross-validate the reliability of the SNA results. LDA topic modeling and SNA are widely adopted methods for identifying latent thematic structures in a given corpus (37). Different from SNA, LDA topic modeling is more algorithm-driven and relies on a three-level hierarchical Bayesian model to infer latent topics from recurring patterns of word occurrence in documents (37, 38).

Regarding RQ2, conventional content analysis, which is a typical method in the qualitative approach of text analysis, was employed. Hsieh and Shannon contended that conventional content analysis could be exploited to describe phenomena by directly extracting themes or labels from the text (39). In this way, scholars could immerse themselves in text and allow the emergence of new insights (40). Conventional content analysis is free from preconceived categories or theoretical frameworks (41). Conventional content analysis enables an in-depth comprehension of the corpus, through which researchers can build a conceptual framework based on subjective interpretation. 2,326 posts containing specific keywords were extracted from the corpus, including Chinese synonyms of the word "nonsupport" (i.e., "不理解", "不支持", "不选择", "不接受", "不同意" in Chinese) and the Chinese variations of the word "anxiety" (i.e., "担心", "恐惧", "害怕", "忧虑", "担忧", "不安", "顾忌", "顾虑", "怕" in Chinese). To ensure reliability and avoid biases that may be derived from manual interpretations, two coders first went through all selected posts and summarized several primary dimensions. Then 20% of the total posts ($n = 465$) were randomly sampled at the pilot stage for intercoder reliability assessment based on the preliminary dimensions. Cohen's Kappa was 0.93, indicating a satisfying agreement between the two coders according to previous practice (41). The remaining posts ($n = 1{,}861$) were split and coded by the two coders separately. Eventually, the coding results were merged into several meta categories.

In a nutshell, SNA was adopted on the whole corpus for extracting social representations automatically, and conventional content analysis was adopted on the selected posts about organ donation reactance or hesitance for a thorough understanding of perceived barriers. The two methods correspond to the quantitative approach and qualitative approach, respectively. However, they are complementary to each other for solving the research questions.

Reliability and validity

Sufficient reliability and validity are necessary for the robustness of one study. Regarding the reliability of SNA, LDA topic modeling was employed to cross-validate the results of SNA. Specifically, after conducting a grid search for the best combination of prior parameters (e.g., the number of topics), the result of the best topic model acted as a standard of measurement of the SNA. A detailed comparison between the two approaches was exhibited in Supplementary material D. For the reliability of the conventional content analysis, previous experience showed that high intercoder reliability is a prerequisite for a reliable content analysis study (42). The value of Cohen's Kappa in our research indicates a nearly perfect agreement between the two coders (43), confirming the reliability of the content analysis part.

With respect to validity, compared to previous works, the current study is based on social media data across 11 years, which enables a higher probability of discovering diverse and comprehensive perceptions than those built on data within a limited time span. In other words, the internal validity of this study has gotten certain assurance. Regarding external validity or the generalizability of results, scholars contend that social media data are rarely representative and face the threat of biased structures (44, 45). The data volume can be neither treated as a sign of validity nor invalidity of the findings (45). This uncertainty is nearly an intrinsic shortcoming of social media studies and is hard to overcome at the present stage; thus, we proposed the limitation at the end of our study.

Results

Semantic network analysis

After time slicing, we found no significant variations in social representations over the past 11 years. Therefore, this study did not differentiate years when constructing the semantic network (please refer to Supplementary material B for semantic network and social representations summary per year). As mentioned before, only the top 100 words by frequency were incorporated in the final network, with 4,693 edges connecting them. The average degree of the network was 93.86, and the average weighted degree was 9,366. A network density value of 0.948 indicated that the network is relatively compactly interconnected. Table 1 exhibits the 30 most central terms along with their frequency, degree, weighted degree, and eigenvector centrality. The leading central words about organ donation on Weibo include *being* (*being* in this study means conscious existence or a living thing), *society*, *China*, *hope*, and *human organ*.

The semantic network is illustrated in Figure 2. The network's layout follows the ForceAtlas2 algorithm in Gephi. This layout algorithm performs better on convergence and compactness and gives nodes with a high degree centrality a more central position in the graph (46). For clarity, only edges with a weight above the average edge weight were exhibited (31). The entire semantic network was presented in Supplementary material C. Edges represent co-occurrence relationships between words, and their thickness embodies the co-occurrence frequency. The larger the word, the higher eigenvector centrality the word has, which manifests a more salient position of the corresponding word. Next, modularity analysis was conducted for community detection, which helps uncover the semantic substructures of a given network (47). With the assistance of modularity analysis, we extracted social representations of organ donation and rendered different colors to distinguish them. Table 2 enumerates all representations with their related terms and proportions.

Five social representations were drawn out from Figure 2, which objectifies prime public perceptions of organ donation on Chinese social media. The largest category was "hope, understanding, and acceptance" (34% of the network), mainly referring to the transmission of hope by donating organs and the reconciliation between organ donation and traditional beliefs. Hope contains two-fold meanings—one is about the motivation to donate organs, such as "I hope that after talking with my parents, I can sign the organ donation form." The other is related to the expectation of new life, such as "When I leave this world in the future, at least four families can get hope again with my donated organs." The second-largest category was "family story" (26% of the network), mainly about the experience of post-mortem organ donation of a family member, such as "There is a cute little kid in my neighborhood who passed away and his parents donated his organs. The child stayed alive in another way, and his parents are brave and kind." "organ donation procedures in NGOs" (15% of the network) followed as the third-largest category, associated with specific procedures within the NGO system, such as registering as an organ donation volunteer and submitting the donation form. The fourth category revolved around "the practical value of organ donation" (14% of the network), emphasizing organ donation's merits in extending recipients' life length and improving recipients' life quality. Also, some users lauded organ donation as a manifestation of altruism and a noble deed of spreading great love. The last category discussed "organ donation in the medical context" (11% of the network), which focused on the importance of organ donation for medical experiments, research, and teaching.

Topic modeling based on the LDA algorithm was introduced to ensure our findings' robustness and reliability. Borrowing previous experience (37), we performed a grid search for the most reliable parameter combination. The semantic coherence value suggested a topic number of 5 is the most appropriate. All themes generated by the topic model are consistent with the modularity analysis

TABLE 1 Summary output of the top 30 central terms in the semantic network.

No.	Term	Frequency	Degree	Weighted degree	Eigenvector centrality
1	Being	27,007	99.00	51,545	1.00
2	Society	22,714	98.00	9,622	0.99
3	China	20,020	99.00	31,574	1.00
4	Hope	19,886	99.00	38,153	1.00
5	Human organ	17,805	99.00	31,102	1.00
6	Register	13,502	98.00	19,974	0.99
7	Passed away	12,611	99.00	28,423	1.00
8	World	12,035	99.00	18,518	1.00
9	Mom	11,768	97.00	17,233	0.98
10	Parents	9,199	98.00	20,412	0.99
11	Doctor	9,058	97.00	12,448	0.98
12	Volunteer	8,963	97.00	14,160	0.98
13	Child	8,846	99.00	14,640	1.00
14	Hospital	8,608	98.00	11,725	0.99
15	Families	7,623	99.00	15,558	1.00
16	Patient	7,467	97.00	18,343	0.98
17	Death	6,774	98.00	8,617	0.99
18	Girl	6,755	92.00	11,368	0.93
19	Continue	6,370	99.00	17,766	1.00
20	Son	6,248	98.00	14,023	0.99
21	Pass away	6,159	94.00	15,611	0.95
22	Before death	5,801	92.00	11,651	0.93
23	Living	5,729	98.00	7,644	0.99
24	Significance	5,725	98.00	10,007	0.99
25	Daughter	5,668	99.00	10,081	1.00
26	Body	5,562	97.00	8,901	0.98
27	Volunteering	5,525	94.00	8,675	0.95
28	Brain death	5,192	92.00	12,293	0.93
29	Life	5,163	98.00	6,804	0.99
30	Father	5,132	95.00	11,331	0.96

results, lending credence to our findings' reliability. Please turn to Supplementary material D for the parameters selection process and the final output of the best-performing topic model.

Conventional content analysis

We manually coded 2,326 posts containing the appointed keywords. The final classification framework was settled when the two coders found no new category emerged. In other words, we stopped adding new categories when the final framework reached saturation. The ultimate framework consists of four dimensions: individual perception, family disapproval, social mistrust, and cultural beliefs. Figure 3 depicts the four salient dimensions, with typical examples chosen from our corpus.

Individual level: The fear of death and postmortem autopsy

20.78% of the filtered posts demonstrated that hindrances to organ donation arose from individuals' dread of death, resistance to body exposure, fear of body dissociation. Those inhibitors also chime with the viewpoint of Moloney et al. that the fundamental representations of organ donation can't be separated from life and death (27). When encountering death-related topics like organ donation, individuals' survival instinct surpasses their rational judgments and fortifies the psychological discomfort of death. Sample posts are as follows.

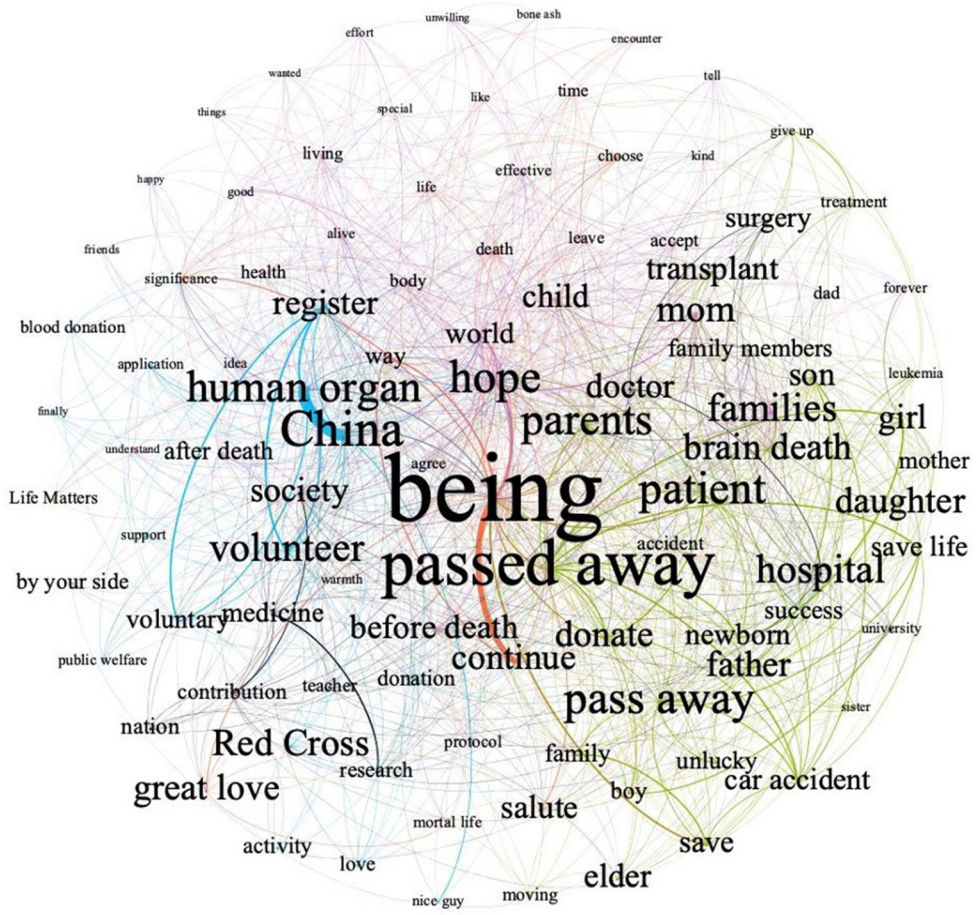

FIGURE 2
Semantic network visualization regarding organ donation on Weibo.

> *Organ donation and hospice care are callous things. It is so heavy to face death or organ donation. Everyone has a fear of death and what we should do is cherish life.*
>
> *I was even naive enough to think about signing up for a body donation. And I'm afraid that my body will become a part of someone I have no connection to.*

The preoccupation with the body also hinders the willingness to donate organs due to the individual body perception (48). There exist two aspects of body perception regarding organ donation—exposure and dissociation. For one thing, people may fear that their privatized bodies will be publicly exhibited to strangers when procuring organs. The introverted and self-restrained characteristics of the Eastern culture further consolidate this perception. For another, the mutilated and disfigured body imagery becomes a mental disturbance. In a similar vein, the previous study has identified the fear of disruption of body integrity as one principal reason for refusing organ donation (49, 50). Additionally, the traditional Chinese values, such as "maintain an intact body after death," also subconsciously keep people away from body dissociation operations.

> *Suddenly, I was so scared! I don't know why I'm so sensitive to life and death! I don't want to donate my organs, nor my body! Because I still want to keep myself intact, no matter now or later.*
>
> *Every time I look at the tomographic specimens, the thought of donating organs comes to my mind. The passion is always accompanied by intense terror. I don't know whether the fear of death or the feudal education engraved in the bone makes me scared of being sliced after death without a soul.*

Familial level: Opposition from family members

In contrast to the previous study, 58.13% of the disapproval comes from family members' opposition, which is the most significant perceived barrier in our study. Regardless of country,

TABLE 2 Summary of social representations derived from the semantic network.

No.	Social representations	Top associations	Association count	Color	Share of the network (%)
1	Hope, understanding, and acceptance	World-hope	1,853	Purple	34%
		Hope-before death	808		
		Hope-body	563		
		Agree-families	366		
		Hope-understand	363		
2	Family story	Family-save	1,600	Green	26%
		Save life-boy	1,290		
		Pass away-parents	1,237		
		Son-father	1,220		
		Son-car accident	1,129		
3	The procedure of organ donation in NGOs	China-human organ	12,359	Blue	15%
		Human organ-register	2,300		
		Volunteer-register	2,083		
		Human organ-volunteer	1,741		
		China-good guy	955		
4	The practical value of organ donation	Continue-being	6,428	Orange	14%
		Way-being	1,745		
		Significance-being	1,242		
		Great love-being	998		
		Being-salute	961		
5	Organ donation in the medical context	Medicine-research	1,724	Black	11%
		Society-contribution	1,152		
		Doctor-hospital	956		
		Medicine-contribution	676		
		Doctor-surgery	673		

a large percentage of organ donation decisions are not made by the donor per se but rather by the family members after the donor's death. In China, if a citizen does not expressly disagree during his or her lifetime, the immediate family of that citizen has a 100% right to decide on organ donation after his or her death (51). Families have an inherently influential, if not decisive, position in organ donation. We provide two examples of posts.

> *Dad said, "We are both highly educated, and we can accept this (organ donation) from a rational point of view. But we are not alone. We all have relatives. We have to consider the feelings of our family members. Let's imagine one of your family members who was breathing and alive at this moment, but in the next second, he or she passed away. A group of people removes all the available organs immediately. What do you think of it?"*
>
> *I asked my mother for her opinion on signing the donation petition, she disagreed. When I went to the Red Cross to apply, the staff told me that if your husband or your immediate family members objected, you would not be able to donate your organs. I was furious, and I said, "Shouldn't my own will take precedence?"*

The family-related discourse about the organ donation topic is particularly pronounced in China. Liu accentuated that Chinese society has a nature of consanguinity (or the so-called kinship) rather than individualism or collectivism (52), which means that family is given priority in this particular cultural context (19). As a culturally embedded persuasive force, filial piety shapes the behavioral principle in every Chinese family (53). To comply with filial piety, Chinese people are inclined to adhere to the norm that "the body and the skin are gifts from parents." Therefore, misunderstanding and opposition from family members become a salient barrier to organ donation in China.

More importantly, the opposition from family is interspersed with other social representation elements. Family concerns permeate into how the individual contemplates death. Family traditions or disciplines also echo the common

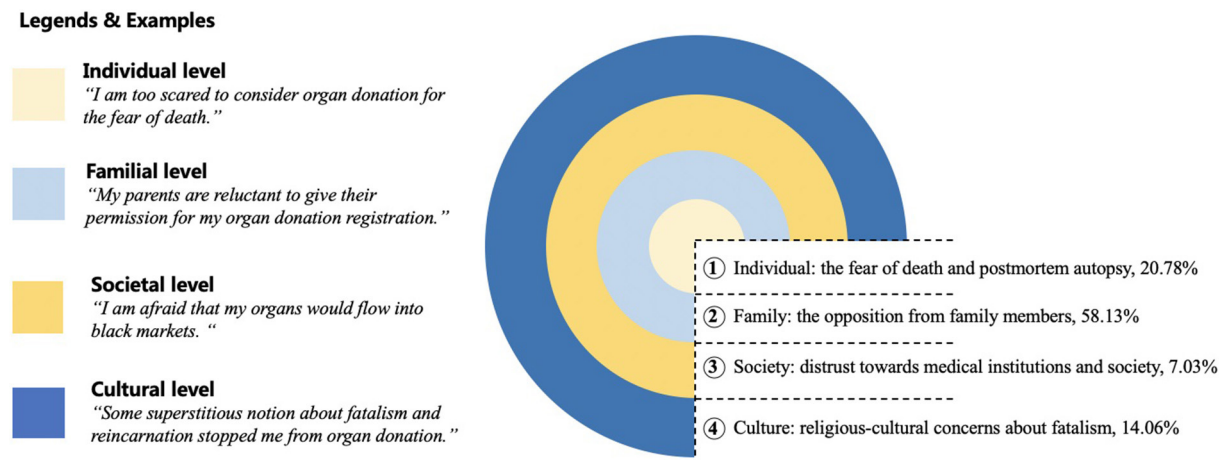

FIGURE 3
Hindrances to organ donation derived from the conventional content analysis.

cultural roots of Chinese people. Thus, the conversations about organ donation with family members are often related to spiritual beliefs. We offer some examples below.

> *I saw a blogger posting about registering for organ donation. I registered a few days ago, but I was afraid to mention it to my parents. Although they occasionally watch programs about organ donation on TV, I don't know what kind of attitude they hold toward it. I worry that they would be reluctant to talk about it because of their taboo against "death."*
>
> *I received the registration card for the organ donation volunteer. My mother saw it with a huge shock! She immediately blamed me and reminded me that it is inauspicious to consider organ donation at such a young age. "You must be crazy! That means no whole corpse!" I am so easily influenced by my mom. Now I am stuck in a dilemma.*

Societal level: Distrust toward medical institutions and society

This category occupies 7.03% of the whole filtered corpus, a relatively small percentage compared to those studies carried out in Western societies (54, 55). Consistent with previous studies, denial and rejection of brain death hindered the decision to donate organs (56), which in turn triggered worries about the early termination of medical treatment and inadequate care for donors. All of those concerns bring about mistrust toward hospitals. There also exist posts oppugning the integrity of the healthcare system, fairness of the organ allocation procedure, and transparency of the double-blind design. For instance, some people fear that their organs may be brutally removed, or their organs may be supplied to the powerful class or evil person.

> *My reason for the reluctance to donate organs is quite simple: what if the person who gets my organs is not a good guy? What if the person who survives brings misfortune to other people?*
>
> *One day in the future, if the opportunity to be a recipient is genuinely equal, with no money or power involved, I would donate without hesitation.*
>
> *I thought that I would like to register for organ donation. But I'm afraid of information leakage. Someone may kill me to get my organs.*

Cultural level: Religious-cultural concerns about fatalism

This category accounts for 14.06% of the overall obstacles in organ donation. According to Chinese tradition, the concepts of rebirth and ancestor worship challenge the implementation of organ donation (16, 57). Chinese people believe in keeping their organs and bodies intact in anticipation of being reborn as human beings in the next samsara. Otherwise, they may be abandoned in the reincarnation process (58). Despite the religious shift among the Chinese in recent years, the above spiritual, or even superstitious notions, continued to exert influences on public perceptions. We provide two typical narratives below.

> *I have been thinking about the morality and Buddhist laws of organ transplantation and donation. It is beyond doubt that donating a body after death is a noble virtue and colossal support to scientific research. But in Buddhist tenets, you cannot do it because it would lead to falling into hell.*

> *The more I grew up, the more superstitious I became . . . I am afraid of many unknown things . . . Donate or not, not because of other people's opinions, but to the reflection of the meaning of it to my life.*

Discussion

Principal findings

Organ donation has always been highlighted in the public health agenda, intriguing public and scholarly attention. To our knowledge, this study is among the few to address the organ donation issue in China by exploiting natural expressions on social media. Following a corpus-driven approach, we disentangled from predefined theoretical frameworks and allowed the emergence of perceptions and perceived barriers. Previous studies examined the antecedents of organ donation statistically (59, 60) but lacked profound inquiry into the whole opinion landscape during an extended period. To supplement, we jumped out of a specific time phase and inspected the general trend of social representation from 2010 to 2020. Firstly, it can be observed distinctly from Figure 1 that organ donation discussed by ordinary users corresponds to the trend of total posts, with an evident surge after 2018. This sudden surge has been impacted chiefly by policy guidance. The *Law of the People's Republic of China on Red Cross Society* was amended in May 2017 to legitimize organ donation, which clarified the responsible agency for organ donation. In March 2018, the Human Organ Donation Management Center launched a nationwide campaign to memorize human organ donors, stirring large-scale public discussion. In a nutshell, the national agenda successfully led the public's agenda, even for sensitive topics like organ donation.

Secondly, this work enriches the study of the social representations of organ donation in the Chinese context. In conformity with Liu as well as Moloney and Walker, we back up the coexistence of antithetical representations (5, 8, 52). The longing for survival and the fear of death were juxtaposed to create a dialectical perception prevailing in China. On the one hand, it is conspicuous that many people intended to pass hope or great love to others or even aspired to contribute to pushing forward medical research by donating their organs. On the other hand, the desire for a decent death, along with the ingrained reverence for life, counterbalance the dedication. The two forces intertwined and maintained an equilibrium. This pair of antinomic representations shape the primary psychological state of potential Chinese donors.

Thirdly, the family-related narratives are dispersed over multiple representations, including "hope, understanding, and acceptance," "family story," and "the practical value of organ donation." What's more, hindrance from the familial level predominates all the barriers. Hence, family support is of paramount importance to organ donation in China. Not only because the family unit was the cornerstone that constitutes the conventional Chinese society, but also because the family culture renders the bottom color of the Chinese culture.

Fourthly, the Chinese cultural context was examined from a unique perspective. Although the dilemma of reluctance to organ donation troubles the whole world, the Chinese esoteric attitude toward organ donation deserves further exploration. To a certain extent, impacted by cultural traditions such as Confucianism, Buddhism, and Taoism, Chinese society is not so supportive of cadaveric organ donation (61). Some scholars found that the organ donation system in China is far behind the international level (59, 62). One probable explanation can be attributed to the deeply embedded traditions about the significance of good death in Chinese society (61, 63). Dutta put forward the cultural sensitivity approach to underscore the crucial position of cultural characteristics in health interventions (64). Our concentration on the Chinese cultural context somewhat dovetails this approach and reminds latecomers of the importance of cultural traits when probing into organ donation.

Lastly, the current endeavor established a framework concerning organ donation's hindrances, casting light on future empirical studies. Prior analyses on organ donation intention were always grounded on individual-level behavioral theories and focused on limited motivating or obstructive factors (19, 65, 66). We extended the impediments to four layers, encompassing individual, familial, societal, and cultural factors. Informed by the proposed hierarchical model, as shown in Figure 3, scholars could adapt existing measures or develop new scales to cover all the essential constructs to better grasp what inhibits potential donors from performing the actual behavior. For example, beyond self-efficacy and perceived social norms, public health pundits need to allocate attention to pressures from parents and the broader cultural context. Furthermore, our framework contributes to comparative studies. Some extant studies have attempted to understand health-related behavior disparities in cross-cultural settings (67, 68). By following our systematic model, follow-up studies can distinguish what factors are more influential in affecting organ donation in other cultures. Findings from the comparative perspective would undoubtedly facilitate organ donation worldwide and inform the designing of effective persuasive messages on organ donation.

Practical implications

Based on the four levels distilled from the conventional content analysis. We propose the following strategies to promote organ donation in China for public health pundits. Firstly, at the individual level, more public health education is needed to enhance the Chinese public's knowledge level regarding organ donation. Since organ donation is a sensitive topic in China, the government and public institutions should lead the tide in desensitizing organ donation by encouraging more people

to learn the scientific principles and operation process behind organ donation. For example, in 2022, Zhejiang Province in China took the lead in incorporating organ donation knowledge into textbooks, which helped dispel the mystery of organ donation (69). Secondly, at the familial level, family-unit-based health intervention is an urgent need because family members' disapproval is one of the most significant barriers. Moreover, the family-related representations even bridge the individual and sociocultural levels and permeate the whole collection of barriers. Therefore, the government could take advantage of the family unit to persuade organ donation and allocate more attention to the interaction of family members. For example, the UK NHS (United Kingdom National Health Service) launched a campaign in 2021 to facilitate discussions among two generations regarding organ donation. Effects of the campaign proved family intervention's effectiveness in creating a supportive family atmosphere that benefits positive attitudes toward organ donation (70). China can borrow this experience. Thirdly, at the societal level, although distrust toward medical institutions and the whole society is not that significant compared to other barriers, the government can devote itself to enhancing public confidence and trust in public institutions. For instance, the China Organ Transplant Response System (COTRS)—a system that was progressively introduced in China to make the organ donation and allocation process more transparent (71), could be a promising way to quell the doubts of the public. Fourthly, at the cultural level, the transformation of religious-cultural concerns is a long process, which necessitates a joint effort from all societal sectors. The individual should absorb more evidence-based information regarding modern medical technologies like organ donation to counterbalance cultural concerns. Meanwhile, the government needs to advocate a new social ethos to limit the expansion of superstitious beliefs. A typical example is the Healthy China Initiative, which promotes medical and scientific information in ordinary communities across China to encourage evidence-based decisions and critical thinking (72). Future public health campaigns should proceed with this endeavor for a new social climate.

Furthermore, our study adopts an unobtrusive way to excavate the social media platform for social representations regarding public health issues. The findings advance our understanding of how people perceive organ donation over a relatively long period. This manner of scrutinizing digital traces outcompetes the traditional social survey or in-depth interview, for they can hardly unfold long-term public perceptions or perception fluctuation in a longitudinal sense. In concordance with preceding works on vaccination perception (31), emerging infectious diseases (73), and chronic diseases (74), the current study bolsters the idea that public health researchers should take full advantage of social media to comprehend how the public makes sense of some vital health issues. Moreover, temporal and spatial dimensions can be integrated for a fine-grained dataset, enabling scholars to answer more intricate questions, such as how significant social events disturb an established social representation toward organ donation? Did social representations about organ donation vary across provinces or states?

Limitations

Our retrospective observational study has some limitations. The Chinese public was approximately substituted by the general public user group on Weibo, which is a compromise suffering validity threats because there exist some Chinese who do not use social media or have no access to social media. Besides, scholars have cautioned that "digital footprints left behind by technology users are rarely representative" (44). Therefore, we should be keenly aware of the biased nature of the current dataset (e.g., the unbalanced distribution of age, gender, occupation, or other demographic characteristics), which implies that conclusions drawn from this work cannot be easily generalized to the entire population. It is necessary for future researchers to cross-validate our findings by conducting national surveys based on probabilistic sampling strategies. Furthermore, since the research corpus covers 11 years, some momentous events may change how people perceive organ donation. The possible changes across the years are open to further empirical testimony.

Conclusion

This study utilized a hybrid text analysis approach on social media corpus to excavate the Chinese public's social representations of organ donation and perceived barriers over the past decade. Five pivotal representations were distilled, and a four-layer hierarchical model regarding hindrances was proposed to understand public perceptions toward organ donation in China.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

ZZ and JJ: conceptualization, formal analysis, methodology, project administration, visualization, writing—original draft, and writing—review and editing. CL: conceptualization, formal analysis, methodology, writing—original draft, and writing—review and editing. AC: conceptualization, data curation, and writing—review and editing. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2022.998737/full#supplementary-material

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Media use and organ donation willingness: A latent profile analysis from Chinese residents

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Background: Previous studies have paid attention to media as an important channel for understanding organ donation knowledge and have not divided groups according to the degree of media use to study their differences in organ donation. Therefore, the purpose of this study is to explore the influence of media use on organ donation willingness and the influencing factors of organ donation willingness of people with different media use levels.

Methods: A cross-sectional study of residents from 120 cities in China was conducted by questionnaire survey. Using Mplus 8.3 software, the latent profile analysis of seven media usage related items was made, and multiple linear regression was performed to analyze the influence of varying levels of media use on organ donation willingness of different population.

Results: All the interviewees were divided into three groups, namely, "Occluded media use" (9.7%), "Ordinary media use" (67.1%) and "High-frequency media use" (23.2%). Compared with ordinary media use, high-frequency media population ($\beta = 0.06$, $P < 0.001$) were positively correlated with their willingness to accept organ donation, residents who used media occlusion ($\beta = -0.02$, $P < 0.001$) were negatively correlated with their willingness to accept organ donation. The influencing factors of residents' accept willingness to organ donation were different among the types of occluded media use, ordinary media use and high-frequency media use.

Conclusion: It is necessary to formulate personalized and targeted dissemination strategies of organ donation health information for different media users.

KEYWORDS

media use, organ donation, willingness to accept, cross-sectional study, latent profile analysis

Introduction

Organ transplantation is an effective method for the treatment of end-stage organ failure, which is widely practiced around the world (1). The organ donation rate per million population had increased from 2.01 in 2015 to 3.70 in 2020 (2). By July 15, 2022, the number of organ donation volunteers in China has reached more than 4.85 million, the number of organ donations has reached more than 40,000, and the number of donated organs has reached 120,000 (3). Even so, an ongoing challenge for organ donation and transplantation is that the demand for organs far exceeds the supply (4). In most countries, organ donation is carried out based on the prior consent of donors or his or her close relatives upon death (5). Public attitudes toward living organ donation and transplantation are very important, however, their awareness is inadequate or biased, which may hinder the development of organ donation and transplantation, such as in Belgium, Spain, China and Australia (6–9). The media plays a key role in establishing a newsworthy story agenda for the society. It has become the main information source for the public to know about organ donation by establishing the topic and publicity channels of organ donation in various ways (10, 11). The longer people use the media, the more information they get. It increases people's sensitivity to organ donation, strengthens their motivation to donate and promotes practical action. By analyzing the content of organ donation on TV, Brian L. Quick found a positive influence on the actual transplant rate during the period of 1990–2005 (12). Andrew M. Cameron used social networks for organ donor registration, and found that the number of online organ donation registrations in the United States increased by 2,200%. In some states (such as Georgia), the number of registered people increased by 12,000%, and even in the state with the lowest response rate (such as Hawaii), it increased by 800% (13). Greg Moorlock and Heather Draper found that social media can be used to arouse people's sympathy for organ donation and promote organ donation by using identifiable victim effect by exploring three methods of organ donation (14). While promoting organ donation, mass media may bring to a pretty pass due to negative or sensational reports (15, 16). For example, Polish national newspapers, tabloids and TV news programs reported a series of negative events related to transplantation in 2007, followed by the number of transplantation dropped by 56% 2.5 months after the report (17). A similar thing happened in Australia from 1989 to 2003, when the number of donors dropped from 14 to 9 (18, 19).

Although previous studies have paid attention to the relationship between media and organ donation, they have not divided groups according to the degree of media use to study the differences in organ donation. Studies have shown that when the audience gets information, they will form three groups of people. First, news avoiders who do not contact the mass media (20). Second, people who contact information through various mass media (21). Third, people who are exposed to information only through new media or traditional media (22). There is obvious group heterogeneity in the use of media, and the information of organ donation obtained by different groups is also uneven (23). Latent Profile Analysis (LPA) was used to identify information seeking attributes and patterns, and to classify people into different profiles (i.e., types) (24). In this person-centered approach, mass media usages and interpersonal communication patterns are treated as information seeking characteristics of different types of people (25). LPA can identify the media use types of different groups of people, and accurately analyze the related factors that affect the public's willingness to accept organ donation. By identifying the media usage types of different groups of people through LPA, we can accurately analyze the related factors that affect the public's willingness to accept organ donation, so as to achieve accurate communication and enhance the public's willingness to accept organ donation. Therefore, this study adopted the individual-centered latent variable method to identify the media use types of different groups of people through latent profile analysis. The purpose was to explore the relationship between media use patterns and people's willingness toward organ donation, find out the factors that affect the public's willingness and put forward valuable suggestions for improving their donation willingness.

Methods

Ethics statement

The study protocol was approved by the Institutional Review Committee of Jinan University (JNUKY-2021-018), Guangdong, China. All respondents have informed consent and voluntarily participated in the survey.

Data source and sample

Inclusion criteria for this study: (1) The nationality of the People's Republic of China; (2) Age $\geq$12 years; (3) China's permanent resident population (annual travel time $\leq$1 month); (4) Participate in the study voluntarily and fill in the informed consent form; (5) Participators can complete the network questionnaire survey by themselves or with the help of investigators; (6) Participate can understand the meaning of each item in the questionnaire.

Exclusion criteria include: (1) inconvenient movement, confusion, mental disorders; (2) Those who are participating in other similar research projects; (3) People are unwilling to cooperate.

Survey method

Multi-stage sampling was used. First, the provincial capitals and four municipalities of 23 provinces and five autonomous regions in China were directly included, and 2–6 cities, a total of 120 cities, were selected from the non-provincial-level administrative regions of each province and autonomous region by random number table method. At least one investigator or one investigation team (≤10 people) were openly recruited in these cities. Based on the results of the seventh national census, the residents of these 120 cities were sampled with quotas (the attributes of quotas are gender, age, urban and rural distribution), which basically accords with the population characteristics of China. With the help of Questionnaires Platform, the investigators distributed questionnaires to the public one-on-one, and the respondents answered by clicking the link, and the investigators entered the questionnaire number. If the respondent has thinking ability but not enough action ability to answer the questionnaire, the investigator will query and fill in the questionnaire instead of him. The survey was conducted from July 10, 2021 to September 15, 2021.

Measurement

The questionnaire included social demographic information (such as gender, age, ethnicity and education level), media use, social support, depression, anxiety, pressure and willingness to accept organ donation. Among them, media use, pressure and willingness to accept organ donation were self-designed scales, while social support, depression and anxiety were international general scales.

The research team designed the questionnaire after consulting books and literature scientifically and comprehensively. Before the questionnaire was officially used, experts consulted and discussed on June 7, June 11, June 15, June 18, July 3, and July 8, 2021. The consulted experts were all senior professional titles and regional representatives. Specialties include social medicine, health education, health statistics, health management, psychology, humanities, journalism and communication, pharmacy, nursing, sociology, philosophy, etc.

Scale of willingness to accept organ donation

Residents' willingness to accept organ donation was reported by the residents themselves (26). Use a score from 0 to 100. The higher the score, the stronger the will power.

Self-made media usage scale

The self-made media usage scale was used to measure the type and degree of media usage. Through scientific and comprehensive access to books and literature, the research team designed the questionnaire (27, 28), and experts (all with senior titles and regional representation) were consulted and discussed to ensure that the questionnaire is applicable to all media users. There were items items in the scale, which were used to know the contact frequency of respondents to seven kinds of media: newspapers, magazines, radio, television, books (non-textbooks), personal computers (including tablets) and smart phones. Each entry was set with five options: never use, occasionally use, sometimes use, often use and almost every day, which were assigned to 1–5 in turn (never use = 1, almost every day = 5). The number of days that the measured person was exposed to various media in one week was used as the scoring basis, and the total score of each option was added as the scoring result, with a total score of 35 points. A higher score indicates that the subjects' media usage was higher. The Cronbach's alpha of the scale was 0.70.

Perceived social support scale

The PSSS was used to measure social support (29). PSSS was a 12-item self-report that assessed emotional support from friends, family and significant others. There were seven options in this scale, from "extremely disagree" to "extremely agree", which were assigned 1–7 in turn (extremely disagree = 1, extremely agree = 7). The respondents scored the degree of consent of each item, and the scores of all items were added together to get a score between 12 and 84, which reflected the total degree of social support felt by the individual. The higher the score, the higher the degree of support. The Cronbach's alpha of the scale was 0.96.

9-item patient health questionnaire

The depression was measured by 9-Item Patient Health Questionnaire (30). The subjects' self-assessment based on their past two weeks' situation and the depression assessment based on the self-assessment scores have good reliability and validity in assisting the diagnosis of depression and assessing the severity of symptoms. The scale consists of 9 items. For each item, four options were set: almost nothing, a few days, more than half, and almost every day. The score was assigned to 0–3 (almost nothing = 0). The total score of each option was added as the scoring result, and the total score was 27. The higher the score, the more prone to depression. The Cronbach's alpha of the scale was 0.94.

7-item generalized anxiety disorder

The anxiety was measured by 7-item generalized anxiety disorder (GAD-7). The subjects made self-evaluation based on their own situation in the past two weeks, and evaluated anxiety disorder according to the results of self-evaluation scores. GAD-7 had good reliability, as well as criterion, construct, factorial, and procedural validity (31). There are seven items in the scale. For each item, four options were set: none at all, a few days, more than half, and almost every day. The score was assigned to 0–3 (none at all =0). The total score was 21 points. The higher the score, the more anxious you were. The Cronbach's alpha of the scale was 0.96.

Self-made pressure scale

The self-made pressure scale was used to measure the pressure (32). Self-evaluation of personal pressure by subjects. The scale was scored by six points, and the subjects scored from 1 to 6 according to their perceived level. The higher the score, the more obvious the pressure. The scoring method was mainly the addition of three self-rated scores, which was the level of personal pressure. The measurement mainly focuses on the individual's ability to deal with pressure, taking time as a unit, from 2weeks to 1 year to perceive and evaluate the pressure in life (including family and work). There were three questions in total. The Cronbach's alpha of the scale was 0.86.

Statistical analysis

Continuous variables were expressed by M±SD, Chi-square (x^2) test was used for comparison between groups, and classified variables were expressed by frequency. The potential profile of seven items used by media was analyzed by Mplus8.3 software, the smaller the values of Akaike Information Criteria (AIC) and Bayesian Information Criteria (BIC) were, the better the LPA fitting model was. The entropy value was between 0 and 1, and the closer to 1, the more accurate the classification. The significant difference between Lomendell-rubin (LMR) and Bootstrap Likelihood Ratio Test (BLRT; $P < 0.05$) indicates that K-type model was superior to K-1 model. Gradually increase the number of categories in the model from the initial model until the model with the best fitting data was found. On the basis of retaining the best category model, SPSS26.0 software was used for stepwise regression analysis. $P < 0.05$ (two-side) is statistically significant.

Results

Analysis of potential profile of media use

Selected 1–6 potential profile models to analyze the frequency of media usage. The results showed that the values of AIC, BIC, and aBIC decreased with the increase of the number of classifications. The two indexes of LMR and BLRT ($P < 0.001$) showed that the models of Class 2, Class 3, Class 4 and Class 5 fit well, and the value of Entropy was closest to 1 when it was in Class 4, followed by Class 3. Combined with the model diagrams of various categories, the classification models of three potential categories (C1, C2, and C3) were finally selected as the classification of residents' media usage frequency. The average probability of residents belonging to each category was between 95 and 98%, indicating that the results of the three models are reliable, as shown in Table 1.

There were obvious differences in the scoring probability of the three potential categories in seven media usage items, showing different characteristics. The most obvious characteristics were judged according to the dimensional differences within and between groups. The subjects in category C2 account for about 67.1% of the total subjects, and the frequency of media use (18.504 ± 2.643) was higher than that in category C1 but lower than that in category C3. Therefore, this category was named "Ordinary media use". Category C1 subjects accounted for about 9.7% of the total subjects, and the scores of each item (12.515 ± 1.788) were not high, and were significantly lower than those of C2 and C3. According to its scoring characteristics, this category was named "Occluded media use". Category C3 subjects accounted for about 23.2% of all subjects, and its score (24.571 ± 3.510) was significantly higher than that of C1 and C2. Therefore, this category was named as "High-frequency media use" (see Figure 1).

Descriptive statistics and one-way ANOVA

A total of 11,031 questionnaires were collected. Among the participants, 5,998 (54.4%) were females, 4,665 (42.3%) were younger than 30 years old, 6,360 (57.7%) were non-agricultural registered permanent residence, 8,008 (72.6%) were urban residents, and 6,487 (58.8%) had college degree or above (see Table 2).

Based on the analysis of the potential profile of media use, it was found that the number of residents aged less than 30 (55.4%) was the largest among the ordinary and high-frequency media users. Among the media- occluded people, the majority (42.5%) had primary school education or below. In the cases of no depression (49.5%), no anxiety (61.3%), and mild stress (26.2%),

TABLE 1 Potential profile model fitting indicators of media usage types.

Model	K	AIC	BIC	aBIC	Entropy	LMR	BLRT	Category probability (%)
1	14	246944.918	247047.237	247002.746				1
2	22	230380.614	230541.400	230471.487	0.919	<0.001	<0.001	0.747/0.253
3	30	221958.644	222177.898	222082.562	0.948	<0.001	<0.001	0.097/0.672/0.231
4	38	216424.795	216702.517	216581.758	0.959	<0.001	<0.001	0.089/0.115/0.668/0.128
5	46	208110.241	208446.430	208300.248	0.943	<0.001	<0.001	0.298/0.207/0.262/0.134/0.098
6	54	207582.155	207976.812	207805.207	0.985	0.994	1.000	0.449/0.080/0.080/0.239/0.055/0.098

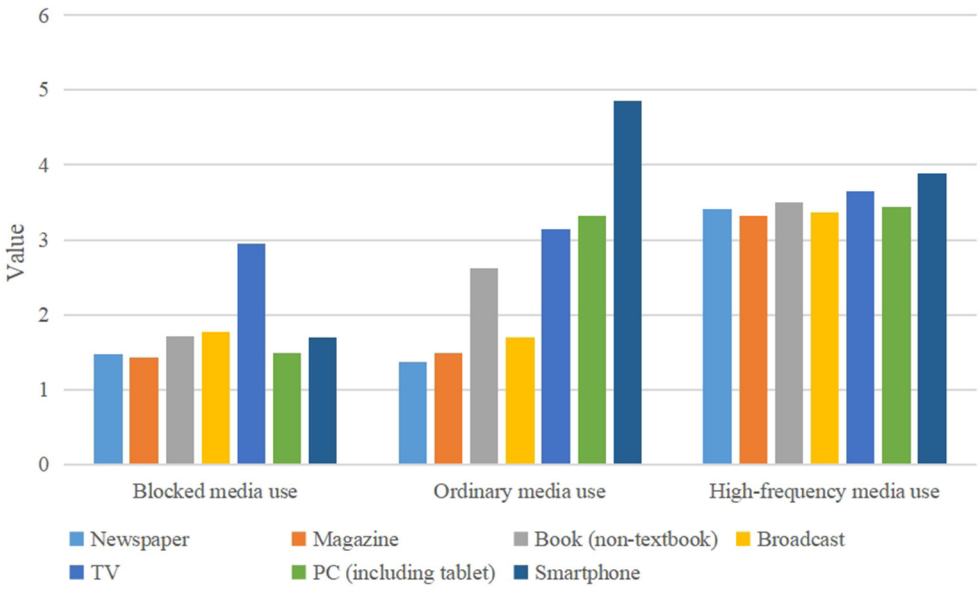

FIGURE 1
Profile of three potential categories of residents' media use of seven items.

people with ordinary contact with media accounted for more, while in the cases of severe depression (6.1%), severe anxiety (6.4%), and severe stress (11.5%), people with high frequency of media use accounted for more.

The differences of residents' willingness to accept organ donation were statistically significant ($P < 0.05$) in terms of age, permanent residence, registered permanent residence, education level, marital status, number of houses, number of children, number of brothers and sisters, debt, religious belief, anxiety, depression and stress, etc., which indicated that these factors had significant influence on residents' willingness to accept organ donation.

Scores of media use and willingness to accept organ donation

The scores of all scales of the included people were shown in Table 3: Among them, newspapers scored the lowest (1.86 ± 1.08) and smart phones scored the highest (4.33 ± 1.13). It showed that Chinese people were more inclined to smart phones in media use. The scores of the subjects' willingness to accept organ donation were moderate (56.93 ± 32.36), which indicated that Chinese residents' willingness to accept organ donation was average at present.

TABLE 2 Descriptive statistics and one-way ANOVA.

Category	All Comers ($N = 11031$, 100%)	Ordinary media use use (N1 = 1067, 9.7%)	Occluded media use (N2 = 7415, 67.1%)	High-frequency media use (N3 = 2549, 23.2%)	x^2	P
Gender					117.2	<0.001
Female	5,998 (54.4)	538 (50.4)	4,268 (57.6)	1,192 (46.8)		
Male	5,033 (45.6)	529 (49.6)	3,147 (42.4)	1,357 (53.2)		
Age					634.5	<0.001
≤18	1,065 (9.7)	109 (53.0)	772 (63.3)	184 (65.3)		
19–40	5,332 (48.3)	257 (55.2)	3,829 (60.6)	1,246 (63.1)		
41–65	3,759 (34.1)	318 (48.2)	2,570 (50.3)	871 (61.1)		
≥66	875 (7.9)	383 (39.7)	244 (42.9)	248 (52.6)		
National minorities	645 (5.8)	66 (6.2)	412 (5.6)	167 (6.5)		
Permanent residence					224.3	<0.001
Rural	3,023 (27.4)	571 (53.5)	1,857 (75.0)	670 (73.7)		
Urban	8,008 (72.6)	496 (46.5)	5,558 (25.0)	1,879 (26.3)		
Household registration permit					187.6	0.010
Agriculture	4,671 (42.3)	442 (41.4)	3,018 (59.3)	1,028 (59.7)		
Non-agriculture	6,360 (57.7)	625 (58.6)	4,397 (40.7)	1,521 (40.3)		
Education level					559.3	<0.001
Primary school and below	1,127 (10.2)	453 (42.5)	481 (6.5)	193 (7.5)		
Middle school	3,417 (31.0)	340 (31.9)	2,334 (31.5)	743 (29.2)		
College level or above	6,487 (58.8)	274 (25.7)	4,600 (62.0)	1,613 (63.3)		
Marital status					323.7	<0.001
Unmarried	4,363 (39.6)	263 (24.7)	3,115 (42.1)	985 (38.7)		
Married	6,226 (56.4)	658 (61.7)	4,089(55.1)	1,479 (58.0)		
Divorced	207 (1.9)	14 (1.3)	142 (1.9)	51 (2.0)		
Widowed	235 (2.1)	132 (12.4)	69 (0.9)	34 (1.3)		
Number of houses owned					376.3	<0.001
0	1,083 (9.8)	151 (14.2)	618 (8.3)	314 (12.3)		
1	6,598 (59.8)	713 (66.8)	4,493 (60.6)	1,392 (54.6)		
2	2,440 (22.1)	146 (13.7)	1,706 (23.0)	588 (23.1)		
≥3	910 (8.3)	57 (5.3)	598 (8.1)	255 (10.0)		
Family economic status					189.5	<0.001
≤6000	7,500 (68.0)	861 (80.7)	5,061 (68.3)	1,578 (61.9)		
6001–12000	2,769 (25.1)	162 (15.2)	1,886 (25.4)	721 (28.3)		
>12000	762 (6.9)	44 (4.1)	468 (6.3)	250 (9.8)		
Whether have children					432.7	<0.001
No	5,062 (45.9)	306 (28.7)	3,600 (48.6)	1,156 (45.4)		
Yes	5,969 (54.1)	761 (71.3)	3,815 (51.4)	1,393 (54.6)		
Whether have brothers or					206.4	<0.001
No	2564 (23.2)	178 (16.7)	1746 (23.5)	640 (25.1)		
Yes	8,467 (76.8)	889 (83.3)	5,669 (76.5)	1,909 (74.9)		
Whether have debts					125.6	0.001
No	6,780 (61.5)	791 (74.1)	4,381 (59.1)	1,608 (63.1)		
Yes	4,251 (38.5)	276 (25.9)	3,034 (40.9)	941 (36.9)		
Whether have medical insurance					115.7	<0.001
No	2,299 (20.8)	224 (21.0)	1,507 (20.3)	568 (22.3)		
Yes	8,732 (79.2)	843 (79.0)	5,908 (79.7)	1,981 (77.7)		

(Continued)

TABLE 2 (Continued)

Category	All Comers ($N = 11031$, 100%)	Ordinary media use (N1 = 1067, 9.7%)	Occluded media use (N2 = 7415, 67.1%)	High-frequency media use (N3 = 2549, 23.2%)	x^2	P
Whether have religious beliefs					142.5	<0.001
No	10,709 (97.1)	1,019 (95.9)	7,214 (97.3)	2,476 (97.1)		
Yes	321 (2.9)	48 (4.5)	201 (2.7)	73 (2.9)		
Depression					601.6	<0.001
No depression	5,031 (45.6)	496 (46.5)	3,671 (49.5)	864 (33.9)		
Mild depression	3,801 (34.5)	384 (36.0)	2,722 (36.7)	695 (27.3)		
Moderate depression	1,148 (10.4)	116 (10.9)	672 (9.1)	360 (14.1)		
Moderate to severe depression	803 (7.3)	56 (5.2)	273 (3.7)	474 (18.6)		
Severe depression	248 (2.2)	15 (1.4)	77 (1.0)	156 (6.1)		
Anxiety					457.3	<0.001
No anxiety	6,170 (55.9)	571 (53.5)	4,542 (61.3)	1,057 (41.4)		
Mild anxiety	3,364 (30.5)	358 (33.6)	2,324 (31.3)	682 (26.8)		
Moderate anxiety	1,198 (10.9)	94 (8.8)	317 (4.3)	389 (15.3)		
Severe anxiety	299 (2.7)	44 (4.1)	232 (3.1)	421 (16.5)		
Pressure					746.1	<0.001
Mild pressure	2,719 (24.6)	251 (23.5)	1,946 (26.2)	522 (20.5)		
Moderate pressure	7,653 (69.4)	704 (66)	5,217 (70.4)	1,732 (67.9)		
Severe pressure	659 (6.0)	112 (10.5)	252 (3.4)	295 (11.6)		

TABLE 3 The scores of media use and willingness to accept organ donation of the subjects.

Scales	Items	Range of scores	M ± SD
Newspaper	1	1–5	1.86 ± 1.08
Magazine	1	1–5	1.91 ± 1.05
Book (non-textbook)	1	1–5	2.73 ± 1.26
Broadcast	1	1–5	2.10 ± 1.19
TV	1	1–5	3.24 ± 1.28
PC (including tablet)	1	1–5	3.17 ± 1.44
Smartphone	1	1–5	4.33 ± 1.13
Organ donation acceptance willingness	1	0–100	56.93 ± 32.36

Summary of residents' willingness to accept organ donation scores

In the summary of residents' willingness to accept organ donation scores (Figure 2), about 51.69% residents' willingness to accept organ donation scores were ≤60, and only about 20.70% residents' willingness to accept organ donation scores were between 91 and 100.

Among the organ donation intentions of the three categories of people who use media, people with "Ordinary media use" scores between 91 and 100 are the most (1,551), people with "High-frequency media use" followed (582), and people with "occluded media use" were the least (150). However, in their respective categories, "High-frequency media users" accounted for 22.83%, followed by "Ordinary media users" accounted for 20.92%, and "occluded media users" accounted for 14.06% of the lowest.

Regression analysis of predictive variables on accept willingness of organ donation

As shown in Table 4, compared with ordinary media use, high-frequency media population ($\beta = 0.06$, $P < 0.001$) were positively correlated with their willingness to accept organ donation, residents who used media occlusion ($\beta = -0.02$, $P < 0.001$) were negatively correlated with their willingness to accept organ donation.

Residents with college level or above ($\beta = 9.93$, $P < 0.001$) and non-agricultural registered permanent residence ($\beta = 3.30$, $P < 0.001$) were more willing to accept organ donation. Male ($\beta = -2.38$, $P < 0.001$), older ($\beta = -4.20$, $P = 0.001$), residents with religious beliefs ($\beta = -5.12$, $P = 0.004$) were less willing to accept organ donation. Among individual social support, friend support ($\beta = 0.95$, $P < 0.001$) and other support ($\beta = 0.30$, $P = 0.029$) could enhance residents' willingness to

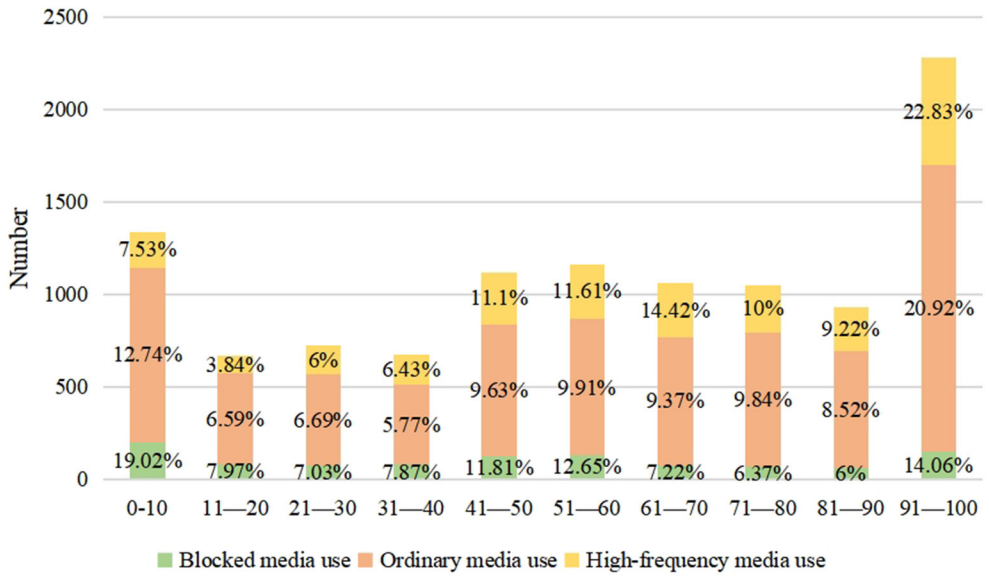

FIGURE 2
Summary of residents' willingness to donate organs.

accept organ donation. On the contrary, family support ($\beta = -0.62$, $P < 0.001$) could hinder residents' willingness to accept organ donation.

Among people with media use occlusion, residents with three or more houses ($\beta = 0.08$, $P = 0.020$), moderate anxiety ($\beta = 0.07$, $P = 0.022$), moderate stress ($\beta = 0.15$, $P < 0.001$), severe stress ($\beta = 0.33$, $P < 0.001$) and high support from friends ($\beta = 0.26$, $P = 0.007$) were more willing to accept organ donation. Other support ($\beta = -0.23$, $P = 0.005$) hindered residents' willingness to accept organ donation (see Table 5).

Among people with ordinary media use, residents with college degree or above ($\beta = 0.17$, $P < 0.001$), non-agricultural registered permanent residence ($\beta = 0.06$, $P < 0.001$), mild anxiety ($\beta = 0.04$, $P = 0.005$), moderate anxiety ($\beta = 0.05$, $P < 0.001$) and severe stress ($\beta = 0.07$, $P < 0.001$) were more willing to accept organ donation. Male ($\beta = -0.04$, $P < 0.001$), had religious beliefs ($\beta = -0.03$, $P = 0.002$) and residents with children ($\beta = -0.10$, $P < 0.001$) were less willing to accept organ donation. In social support, friends' support ($\beta = 0.12$, $P < 0.001$) and other support ($\beta = 0.07$, $P = 0.002$) increased residents' willingness to accept organ donation, family support ($\beta = -0.10$, $P < 0.001$) hindered residents' willingness to accept donations (see Table 6).

Among the high-frequency media users, the residents with college degree or above ($\beta = 0.13$, $P = 0.001$), moderate pressure ($\beta = 0.09$, $P < 0.001$) and severe pressure ($\beta = 0.27$, $P < 0.001$) were more willing to accept organ donation. Older residents ($\beta = -0.11$, $P = 0.005$) with high frequency of media exposure are less willing to accept organ donation (see Table 7).

Discussion

This study investigated and analyzed the influence of media use on Chinese residents' willingness to donate organs and other factors that may affect their willingness to accept organ donation. The study found that the degree of media use had a significant impact on residents' willingness to accept organ donation. "High-frequency media use" and "ordinary media use" had positive effects on organ donation willingness, "occluded media use" had a negative impact on organ donation willingness. In other words, the higher the degree of media use, the more willing to accept organ donation, and the lower the degree of media use, the lower the willingness to accept organ donation.

The content of media used might affect people's willingness to accept organ donation. Among the three categories of media use, the residents of "high-frequency media use" and "ordinary media use" were mainly young people, with the largest number of people using smart phones. There was an interactive platform of social media in smart phones, and social media played a certain role in increasing the effectiveness of living donation (33). For example, setting up online organ donation registration links (34), developing smart phone applications to increase living organ donation (35), implementing publicity and training programs to find living donor (36), etc. In addition, medical professionals in organ transplantation have begun to explore how to expand and educate the public through online platforms and social media (37). This made the smart phone-based "high-frequency media use" and "ordinary media use" people

TABLE 4 Regression analysis of media use on the accept willingness to organ donation.

Model		Unstandardized coefficients		Standardized coefficients	*t*	*P*	EXP(*β*) 95% confidence interval	
		β	SE	*β*			LLCI	ULCI
Independent variable	Media use (Ref: ordinary)							
	Occluded	−2.79	1.05	−0.02	−1.35	<0.001	−3.81	−0.69
	High frequency	4.69	0.71	0.06	5.60	<0.001	3.11	5.96
Control variable	Gender (Ref: Female)							
	Male	−2.38	0.60	−0.04	−4.00	<0.001	−3.46	−1.11
	Age (Ref:≤18)							
	≥66	−4.20	1.21	−0.04	−3.47	0.001	−10.44	−3.76
	Level of education (Ref: Primary school or below)							
	High school	5.96	1.13	0.09	5.26	<0.001	3.23	7.78
	College level or above	9.93	1.16	0.15	8.59	<0.001	7.52	12.31
	Household registration permit (Ref: Agriculture)							
	Non-agriculture	3.30	0.63	0.05	5.25	<0.001	2.01	4.49
	Whether have children (Ref: No)							
	Yes	−7.40	0.65	−0.11	−11.34	<0.001	−7.71	−4.32
	Whether have religious beliefs (Ref: No)							
	Yes	−5.12	1.76	−0.03	−2.91	0.004	−8.49	−1.59
	Pressure (Ref: Mild pressure)							
	Moderate pressure	3.91	0.71	0.06	5.54	<0.001	2.58	5.34
	Severe pressure	21.01	1.37	0.15	15.29	<0.001	18.50	23.90
	Social support							
	Family support	−0.62	0.11	−0.09	−5.47	<0.001	−0.84	−0.39
	Friend support	0.95	0.12	0.14	8.19	<0.001	0.69	1.15
	Other support	0.30	0.14	0.04	2.18	0.029	0.03	0.57

received more knowledge about organ donation, more objective understanding, and higher willingness to accept organ donation.

The residents with "media use occlusion" were mostly middle-aged and elderly people, and the media they were exposed to were mainly TV and radio. These media reports on organ donation issues were relatively lacking, which led to this group's little knowledge of organ donation and low willingness to accept organ donation. The findings of this study were inconsistent with a study conducted in Murcia, Spain. Television had the greatest influence on the public's awareness and attitude toward organ donation (38). Older people with lower education level were more likely to be affected by health problems depicted on TV (39). However, in China, TV, radio and other mass media seldom report on organ donation issues, and the low attention of Chinese mass media on organ donation issues had become the main restricting factor to improve the willingness to accept organ donation and the acceptance rate of organ transplantation (40).

The study also found some other factors that may affect residents' willingness to accept organ donation. Gender, age, whether have children or not, religious belief and so on all had negative influences on residents' willingness to accept organ donation. Education level, registered permanent residence nature, degree of stress, etc. all had positive influence on residents' willingness to accept organ donation. Studies showed that the younger (41) and better educated people (42) were more likely to make organ donation. Previous studies have found that men were less willing to donate and less likely to have conversations about organ donation, while women were more likely to mention their willingness to donate and their moral/altruistic/religious reasons (43). However, due to the lack of understanding of the religious aspects of organ donation and transplantation, many people rejected the concept of organ

TABLE 5 Regression model of accept willingness to organ donation among people with media occlusion.

Model	Unstandardized coefficients		Standardized coefficients	*t*	*P*	EXP(*β*) 95% confidence interval	
	β	SE	*β*			LLCI	ULCI
Number of houses owned (Ref:0)							
1	1.9	2.81	0.03	0.68	0.499	−3.57	7.46
2	6.35	3.63	0.08	1.75	0.081	−0.95	13.33
≥3	11.15	4.79	0.08	2.33	0.02	2.23	21.07
Anxiety (Ref: No anxiety)							
Mild anxiety	−0.37	2.17	−0.01	0.17	0.865	−5.92	5.33
Moderate anxiety	7.42	3.24	0.07	2.29	0.022	2.62	21.23
Severe anxiety	−0.79	6.81	−0.01	−0.12	0.907	−10.50	24.44
Pressure (Ref: Mild pressure)							
Moderate pressure	10.54	2.42	0.15	4.35	<0.001	5.8	15.37
Severe pressure	34.91	3.87	0.33	9.03	<0.001	27.63	42.85
Social support							
Family support	−0.15	0.41	0.03	−0.38	0.705	−0.98	0.62
Friend support	1.49	0.35	0.26	4.25	<0.001	0.85	2.25
Other support	−1.27	0.45	−0.23	−2.83	0.005	−2.18	−0.42

donation for religious reasons (44). The results were consistent with the data of this study.

Besides, social support was considered as a predictor of organ donation willingness (45). Social support is defined as information leading the subject to believe that he is cared for and loved, esteemed, and a member of a network of mutual obligations (46). The social support system aims to assess the views on the adequacy of social support from three specific sources: family, friends and other important sources (47). Individual attitude is not the only determinant of organ donation behavior (48). One of the major concerns about organ donation is the opposition of other people. Donors must deal with conflicts with their families in the decision-making process (49, 50), it will make the donors have ambivalence before organ donation. Social support can reduce the worries related to living donation and reduce the influence of worries on ambivalence (51), and then increase the willingness to accept organ donation. We found that the support of friends and other important people in social support had a significant positive impact on residents' willingness to accept organ donation, and the opinions or suggestions of friends and other important people could enhance people's willingness to accept organ donation. On the contrary, family support could hinder residents' willingness to accept organ donation to some extent. The reason was probably influenced by Chinese cultural environment. In the Chinese mind, everyone has a different distance from himself. The nearest others are family members, who usually have the strongest relationship with themselves, while the farthest others are unfamiliar members of society, who have the weakest relationship with themselves (52). The willingness to accept organ donation is often closely related to the closest family members. In "The Book of Filial Piety", it was mentioned: "When the body is skinned, the parents are afraid to damage it, and filial piety begins." Under the influence of Chinese traditional filial piety culture, family emotional factors will hinder people's willingness to accept organ donation to a certain extent.

In fact, the idea of "The Book of Filial Piety" was to oppose unnecessary damage to the body, but not to advocate absolute preservation of the body. Organ donation in modern society is aimed at helping others to treat patients and prolong their lives, and its loss to the body is positive, rather than meaningless (53). Since ancient times, China has emphasized "benevolence". Altruistic organ donation is a virtue that emerged only today in the development of medical science, because it can save lives and give others a chance to be reborn (54). This is a typical "benevolence". Many people only know that "the skin of the body is affected by the parents" is the absolute preservation of the body, but they don't know that it is a fearless injury against the body, which makes people not willing to accept organ donation. Therefore, the media can design some publicity contents aiming at Chinese traditional culture when conducting popular science propaganda on organ donation, so as to alleviate or dispel citizens' concerns about the traditional concept of organ donation, with a view to increasing the organ donation rate.

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TABLE 6 Regression model of accept willingness to organ donation among ordinary media users.

Model	Unstandardized coefficients		Standardized coefficients	*t*	*P*	EXP(*β*) 95% confidence interval	
	β	SE	*β*			LLCI	ULCI
Gender (Ref:Female)							
Male	−2.89	0.75	−0.04	−3.87	<0.001	−4.36	−1.43
Age (Ref:≤18)							
19–40	−3.43	1.37	−0.05	−2.51	0.012	−6.12	−0.75
41–65	−5.03	1.67	−0.07	−3.01	0.003	−8.31	−1.76
≥66	−8.68	2.56	−0.05	−3.39	0.001	−13.7	−3.66
Level of education (Ref: Primary school or below)							
High school	5.2	1.62	0.07	3.22	0.001	2.03	8.37
College level or above	11.29	1.68	0.17	6.71	<0.001	7.99	14.58
Household registration permit (Ref:Agriculture)							
Non-agriculture	3.92	0.79	0.06	4.95	<0.001	2.37	5.48
Whether have religious beliefs (Ref: No)							
Yes	−6.91	2.27	−0.03	−3.05	0.002	−11.4	−2.47
Whether have children (Ref: No)							
Yes	−6.84	1.09	−0.1	−6.25	<0.001	−8.99	−4.7
Anxiety (Ref: No anxiety)							
Mild anxiety	2.45	0.86	0.04	2.86	0.004	0.76	4.13
Moderate anxiety	6.33	1.64	0.05	3.86	<0.001	3.11	9.54
Severe anxiety	−1.21	3.08	−0.01	−0.39	0.694	−7.25	4.82
Pressure (Ref: Mild pressure)							
Moderate pressure	1.45	0.9	0.02	1.62	0.106	−0.31	3.22
Severe pressure	12.67	2.22	0.07	5.71	<0.001	8.32	17.02
Social support							
Family support	−0.75	0.13	−0.1	5.61	<0.001	−1.01	−0.49
Friend support	0.93	0.14	0.12	6.63	<0.001	0.65	1.2
Other support	0.5	0.16	0.07	3.04	0.002	0.18	0.81

TABLE 7 Regression model of accept willingness to organ donation among people high-frequency media user.

Model	Unstandardized Coefficients		Standardized Coefficients	*t*	*P*	EXP(*β*) 95% confidence interval	
	β	SE	*β*			LLCI	ULCI
Age (Ref:≤18)							
19–40	−3.27	2.34	−0.06	−1.4	0.162	−8.29	0.92
41–65	−4.17	2.35	−0.07	−1.78	0.076	−8.84	0.38
≥66	−10.9	2.82	−0.11	−3.85	<0.001	−16.1	−4.99
Level of education (Ref: Primary school or below)							
High school	7.69	2.34	0.12	3.28	0.001	3.12	12.33
College level or above	7.9	2.28	0.13	3.46	0.001	3.91	12.89
Pressure (Ref: Mild pressure)							
Moderate pressure	5.83	1.46	0.09	4	<0.001	1.93	7.62
Severe pressure	24.88	2.12	0.27	11.76	<0.001	20.24	28.55

Research highlights and limitations

This study is the first survey of residents' willingness to accept organ donation in Chinese mainland, with a large sample size and wide representation. In addition, this study takes media use as an independent variable for the first time and classifies people, so as to explore the degree of influence of different residents' media use on their willingness to accept organ donation, which is innovative.

This study also has some limitations: firstly, this study uses cross-sectional data as the data source, so it is difficult to make causal inference. Secondly, due to the limitation of sampling methods, there may be sample selection bias.

Conclusion

It is suggested that the government and relevant departments should pay more attention to the willingness of people with different media usage levels to accept organ donation, formulate personalized and targeted dissemination strategies for organ donation health information for different media usage groups, and focus on different public groups with different media usage characteristics.

Data availability statement

The original contributions presented in the study are included in the article/supplementary files, further inquiries can be directed to the corresponding authors.

Ethics statement

The studies involving human participants were reviewed and approved by the Institutional Review Committee of Jinan University (JNUKY-2021-018), Guangdong, China. The participants provided their written informed consent to participate in this study.

Author contributions

FG and YJ provided the formal analysis, writing—original draft, and writing—editing. YW and XS provided the conceptualization and methodology. FG and YW provided the validation. JZ, MC, XJ, and YW provided the writing—review. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Assessment of primary care physicians' knowledge of chronic kidney disease in Poland

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Chronic kidney disease (CKD) affects 10–15% of the adult population worldwide and is a major societal problem. A latent course of the disease and little alarming, gradually increasing symptoms usually do not cause concern in patients and diagnostic vigilance in physicians. CKD is most often diagnosed in its end-stage when treatment options are extremely limited. This study aims to assess the knowledge of CKD among primary care physicians (PCPs) in Poland. A CAWI survey was conducted based on an authors' own questionnaire that consisted of two parts. The first part concerned patients' socioeconomic data while the second part consisted of nine single- and multiple-choice questions assessing knowledge of the criterion for diagnosis, risk factors, diagnostic evaluation, and course of CKD. A total of 610 physicians took part in the survey, including 502 (82.3%) who fully completed the questionnaire. Women accounted for 83.1% of the study group. The mean age of the study group was 37.4 ± 10.1 years. Specialists or resident physicians in family medicine accounted for 79.9% of respondents and 93.8% of physicians are those who mainly work in primary care settings. In the knowledge test, the mean score obtained by physicians was 6.5 ± 1.3 out of possible 9, with only 2.4% of respondents answering all questions correctly. According to the survey, 78.4% of respondents correctly indicated the criterion for the diagnosis of CKD, while only 68.9% identified a test for increased urinary albumin loss as the one of the greatest diagnostic values in the early stages of CKD. More than half, 63.1%, of physicians selected the correct set of answers in the multiple-choice question regarding CKD risk factors. Despite a fairly high level of knowledge among family medicine physicians regarding the causes, risk factors and course of CKD, there is a need for further education and an increase in the factual information held by this professional group, especially that the vast majority of PCPs declare a desire to expand their knowledge and believe that this will help them in their daily clinical practice.

KEYWORDS

chronic kidney disease (CKD), knowledge, physicians, family medicine, general practice

Introduction

Chronic kidney disease (CKD) is a multifactorial condition, resulting from a reduced number of nephrons in response to an ongoing inflammatory process. Along with diabetes, hypertension and other cardiovascular diseases, CKD is one of the diseases of affluence in the 21st century (1). Data concerning the epidemiology of CKD in Poland are scarce and there are no up-to-date statistics on how many patients suffer from the disease. According to the 2007 PolNef study, the largest epidemiological study of CKD in Poland, the disease was diagnosed in 11.9% of patients after including albuminuria as a diagnostic criterion. With additional analysis of urine sediment and renal ultrasound changes, the criterion for the diagnosis of CKD was met by 18% of patients (1–3). The NATPOL 2011 study, a nationwide analysis of the prevalence and control of heart disease risk factors in Poland, found CKD in 5.8% of patients who participated in that study and, according to the results, estimated the prevalence of CKD to be almost 2 million in the Polish population aged 18–79 years (4). According to available global data, it is estimated that CKD may occur in up to 15% of the population (4–6).Consequently, CKD should be suspected in an even larger number of Polish people —up to 4 million.

According to official statistics provided by the Polish National Health Fund—NFZ, 210,000 Polish people have been diagnosed with CKD. It should be borne in mind, however, that reported cases usually concern the kidney failure, when patients remain under the constant care of nephrologists and are selected for renal replacement therapy (RRT) (7). In comparison with the previously cited data, this shows that the detection of CKD in Poland is underestimated.

The reason may be the lack of adequate awareness among patients and physicians regarding the causes, symptoms, risk factors, diagnostic evaluation, and treatment of CKD. This may contribute to a lack of adequate vigilance among physicians.

Many patients are only diagnosed in advanced stages of the disease, when alarming clinical signs appear and the only treatment offered is RRT. It was found that non-pharmacological management, when implemented early enough, can significantly reduce disease progression, prolong patients' lives, and improve their quality of life (1). This is why 1) diagnostic vigilance—when a patient visits the doctor's office for other chronic diseases that often coexist with CKD, 2) appropriate frequency of follow-up examinations and 3) knowledge of risk factors are of so much importance.

Given these aspects, PCPs' knowledge of CKD is crucial in the diagnostic and therapeutic process of CKD.

To the best knowledge of the authors, there are no Polish studies concerning the level of knowledge of CKD among PCPs. Moreover, there are also single references to this subject in the world literature, from countries such as the United States, Nigeria, Pakistan and Cameroon (8–11).

At the same time, in the United Kingdom (UK) where CKD is diagnosed and treated primarily in primary care settings, a tool was created in 2014—a questionnaire assessing confidence and knowledge in terms of the care of CKD patients compared to other chronic diseases. The tool was named QICKD-CCQ (Quality Improvement Interventions in Chronic Kidney Disease -The Clinician Confidence and Knowledge Questionnaire). Although the questionnaire met its expectations in a study concerning its practical use and the authors recommend this tool be added to the standard armamentarium of tools useful for PCPs, the study itself had several limitations. Such limitations included, for example, conducting the study not in practices selected at random but those indicated by researchers. Therefore, they were not representative of all family medicine physicians' practices in the UK (12).

Accordingly, the authors aimed to assess the level of knowledge of CKD among PCPs in Poland and determine the extent to which knowledge of this disease needs to be improved.

Methodology

This study is a CAWI (Computer-Assisted Web Interview) survey using an authors' own questionnaire that was made available as part of the ankieta.pchn.edu.pl domain, which was created for the "Chronic Kidney Disease" project implemented by the Polish Society of Family Medicine and the Polish Society of Nephrology. Distribution of the questionnaire took place *via* facebook.com within the doctors' group, where membership is verified by medical license number. Furthermore, the questionnaire was distributed by e-mail using the mailing database of the Polish Society of Family Medicine. The target group of the study was physicians working in primary care settings. The survey distribution period was from 22 Feb. 2022 to 16 May 2022.

Prior to participating in the survey, respondents were informed of the aims and nature of the study. Subsequently, they gave their informed consent to participate in the study. During course of the study, its participants were allowed to withdraw from it without giving any reason. Participation was fully anonymous and voluntary, and respondents received no financial consideration for completing the survey.

The used author's own questionnaire consisted of two parts. The first part included questions assessing sociodemographic status (age, gender). Subsequently, data concerning professional status were collected, including the main place of work (primary care clinic/specialist outpatient clinic/hospital), its location (rural area/town $<$ 50,000 inhabitants / city of 50,000–250,000 inhabitants / city $>$ 250,000 inhabitants), years of seniority, career stage (specialist in family medicine / resident physician

in family medicine / specialist in another specialty / resident physician in another specialty) and number of hours worked per week (≤10 h/11–24 h/ ≥25 h) in primary care settings. Using a 10-point Likert scale, respondents were asked to rate their level of knowledge regarding CKD.

The final stage of the survey concerned the level of knowledge of CKD. It consisted of both single- and multiple-choice questions. Within these questions, respondents were asked about the criterion for the diagnosis of CKD, the most common cause of CKD, diagnostic evaluation and clinical signs of CKD, and the most common cause of death in the course of CKD. Further multiple-choice questions addressed risk factors, preventive management during the early stage of CKD, and an assessment of cases when to be vigilant in terms of estimating eGFR. In each question, the maximum number of points was 1. In the case of single-answer questions, the respondent earned 1 point for each correct answer. For multiple-answer questions, 1 point was obtained for all indications of all correct answers. The maximum possible number of available points to score was 9. Final questions addressed the desire to improve knowledge of CKD. An English-language version of the survey is presented as supplementary material.

The study was conducted in accordance with the Declaration of Helsinki and approval was obtained from the Bioethics Committee at the Lower Silesian Medical Chamber; Resolution No. 1/BNR/2022.

The survey represents the first stage of a nationwide epidemiological and educational study concerning CKD. The project was designed in collaboration with the Polish Society of Family Medicine and the Polish Society of Nephrology. It is intended that the project will have three stages. The first stage will assess physicians' knowledge of CKD. The next stage involves conducting a voluntary, free, online educational course for all interested physicians. The final stage is a nationwide epidemiological study of CKD in a group at high risk of developing the disease. The project is ongoing and further publications of its results are planned for the future.

Statistical analysis

The statistical analysis was conducted using Statistica software, version 13.0, StatSoft. The variables analyzed were qualitative, quantitative and ordinal. The Shapiro-Wilk test was used for assessing the normality of the distribution. Basic descriptive statistics were used for describing the study group and assessing the level of knowledge. Basic linear models were used for assessing the relationship between mean scores and gender, place of work, career stage, number of hours worked in primary care settings. In contrast, the Pearson's correlation was used for assessing the correlation between scores and age, years of seniority, subjective assessment of the level of knowledge regarding CKD. The effect of career stage and place of work on the distribution of answers to individual questions was assessed using the Pearson's chi-square test Statistical significance level was established at $p < 0.05$ for each case.

TABLE 1 Characteristics of the study group.

Variable		*N* (%)
Gender	Male	82 (16.9)
	Female	417 (83.1)
	Age [M ±SD]	37.4 ± 10.1
Career stage	Has not begun specialist training	25 (5.0)
	Resident physician in family medicine	226 (45.0)
	Specialist in family medicine	175 (34.9)
	Resident physician in another specialty	23 (4.6)
	Specialist in another specialty	53 (10.5)
Place of work	City > 250,000 inhabitants	208 (41.4)
	City of 50,000–250,000 inhabitants	99 (19.8)
	Town < 50,000 inhabitants	115 (22.9)
	Rural areas	80 (15.9)
Years of seniority [M ± SD]		8.4 ± 8.9
Main place of work	Primary health care	471 (93.8)
	Outpatient health care (OHC)	6 (1.2)
	Hospital	25 (5.0)
Number of working hours in primary care settings [hours/week]	≥ 25	412 (82.1)
	11–24	67 (13.3)
	≤ 10	23 (4.6)
Contact with CKD at work	Yes	489 (97.4)
	No	13 (2.6)

M, mean; SD, standard deviation.

Results

Characteristics of the study group

A total of 610 physicians took part in the study, including 502 (82.6%) who completed the questionnaire. All respondents agreed to participate in the study. The vast majority of participants were women-417 (83.1%). The mean age of the study group was 37.4 ± 10.1 years (min. 24; max. 80). According to the survey, 401 (79.9%) physicians are specialists or resident physicians in family medicine and 471 (93.8%) physicians mainly work in primary care settings. The average seniority was 8.4 ± 8.9 years (min. 1, max. 51). A detailed description of the study group is shown in Table 1.

Level of knowledge regarding CKD

Based on a 10-point Likert Scale, the mean score assessing the subjective level of knowledge about CKD was 5.6 ± 1.66. In the knowledge test, the mean score obtained by physicians was 6.5 ± 1.3. Only 12 (2.4%) physicians answered all questions correctly. In contrast, the question-by-question analysis found that 394 (78.4%) physicians correctly identified the diagnostic criterion for CKD and 473 (94.2%) correctly identified the most common cause of the disease. Only 346 (68.9%) physicians correctly identified a test for urinary albumin loss as the one of greatest diagnostic value in the early stages of CKD. The most frequently indicated risk factors by physicians include diabetes (98.4%) and hypertension (96.8%); however, the correct set of risk factors was identified by only 317 (63.1%) physicians. A detailed comparison of all answers is shown in Table 2.

There was no statistically significant difference between the mean scores compared to gender, career stage, place of work or number of hours worked in primary care settings. Those who declare contact with CKD scored on average 1.02 points higher than doctors who declare no contact with CKD in daily practice ($p = 0.004$). Moreover, an inverse correlation was found between respondents' age and mean score ($r = -0.183$; $p < 0.001$) or years of seniority ($r = -0.194$; $p < 0.001$) (Figures 1, 2). There was also a positive correlation between the subjective assessment of the level of knowledge and the mean score ($r = 0.127$; $p = 0.007$) (Figure 3). A detailed comparison of mean scores is shown in Table 3.

Furthermore, the analysis of individual questions in terms of the career stage revealed that resident physicians in family medicine were most likely to indicate the correct answer regarding the test of greatest diagnostic value in the early stages of CKD. The remaining questions revealed no statistically significant differences in terms of place of work and career stage. A detailed comparison is shown in Table 4.

According to the study, 469 (93.4%) physicians agree or strongly agree after completing the survey that they intend to improve their level of knowledge regarding CKD in the near future. On the other hand, 496 (98.8%) physicians believe that this knowledge could be useful in their daily medical practice.

Discussion

The role of the family medicine physician is crucial in terms of initiating diagnostic and therapeutic management at the appropriate stage of CKD, as well as in terms of monitoring the patient's health status and assessing the effectiveness of the treatment process. Family medicine physicians have more regular interaction with a patient than physicians in other specialities. During consultations for infectious diseases, chronic diseases and even during prescription consultations, family medicine physicians have the opportunity to identify risk factors for CKD in their patient and initiate diagnostic evaluation even in the latent stage of the disease (13). The control of the treatment process and the assessment of disease progression by the PCP is also very important due to the long waiting time for consultation in specialists in nephrology. According to available data, there are 1,389 nephrology physicians who are professionally active in Poland, and this number is assessed as insufficient (14, 15). Therefore, part of the responsibility in providing care for CKD patients should belong to general practitioners. However, a high level of awareness of the disease among physicians is necessary to provide adequate care.

The results of this study revealed knowledge gaps among PCPs in Poland and areas for potential educational intervention. PCPs are aware that their knowledge of CKD is not sufficiently comprehensive—in their subjective assessment of own knowledge, they gave themselves a score of 5.6 ± 1.66 on a ten-point Likert scale. Moreover, there was a positive correlation between the respondents' subjective assessment of their knowledge level and the knowledge test score obtained by them in the survey. This indicates the physicians' self-awareness regarding sophistication of their own knowledge and their understanding of the associated limitations. Furthermore, it should be noted that 93.4% of physicians agree with the statement that they intend to increase their level of knowledge of CKD in the near future. Almost 99% of respondents identify as true the statement that this knowledge could be useful in their daily clinical practice. The above-mentioned results clearly indicate a great need for educational activities, which are likely to be of interest to physicians working in primary care settings. This is in line with further intentions of the Chronic Kidney Disease Programme to provide a free educational course for interested physicians. A US study found an online course to be effective in improving knowledge of CKD among resident physicians in internal medicine, highlighting such advantages of online education as ease of access and use (16).

Physicians who declared that they had no interaction with CKD patients scored worse than their colleagues who were actively involved in providing care for these patients. CKD is a condition which is so prevalent and with so many risk factors that every PCP can expect to identify this disease in their patients. According to the authors, in terms of a declared lack of interaction with CKD patients it is more likely that physicians are insufficiently aware of the prevalence of this disease than that they actually have no contact with it. It should be noted that CKD is estimated to affect more than one in ten adult patients in Poland, so its prevalence is high (2). Only 78.4% of respondents identified a correct diagnostic criterion for CKD. This is a relatively low percentage, given that lack of knowledge of the definition and criterion for diagnosis (in this case it is the criterion based on eGFR) prevents identification of the disease in many cases and reduces diagnostic vigilance. In a similar survey conducted in Cameroon, the correct definition of CKD was indicated by only 58.8% of physicians (10). In other developing

TABLE 2 The comparison of answers to questions assessing the level of knowledge of CKD.

Question		*N* (%)
Criterion for diagnosis of CKD	**GFR < 60 ml/min./1.73m^2 for at least 3 months**	394 (78.4)
	GFR < 90 ml/min./1.73m^2 for at least 3 months	67 (13.3)
	GFR < 60 ml/min./1.73m^2 for at least 1 month	23 (4.6)
	GFR < 90 ml/min./1.73m^2 for at least 6 months	18 (3.7)
Most common cause of CKD	**Diabetic kidney disease**	473 (94.2)
	Coronary artery disease	13 (2.6)
	Chronic dehydration	13 (2.6)
	Polycystic kidney degeneration	3 (0.6)
	Neoplastic diseases of the urinary tract	0 (0.0)
Can CKD be asymptomatic?	**Yes, it can. Clinical signs of CKD develop slowly and become a concern to patients in the late stage of the disease.**	500 (99.6)
	Yes, it can. However, clinical signs of CKD appear early and are usually severe.	0 (0.0)
	No, it cannot. Clinical signs appear almost immediately.	2 (0.4)
Which of the following tests is of the greatest diagnostic value in the early stages of CKD?	**Test for increased urinary albumin loss**	346 (68.9)
	Serum urea levels	83 (16.5)
	Abnormal urine specific gravity	61 (12.2)
	Presence of erythrocytes in urine sediment	11 (2.2)
	White blood cell (WBC) count	1 (0.2)
GFR at which RRT should be initiated	**<10 [ml/min./1.73 m^2]**	436 (86.9)
	< 30 [ml/min./1.73 m^2]	66 (13.1)
Main cause of death in the course of CKD	**Cardiovascular complications**	404 (80.5)
	Ketone coma	8 (1.6)
	Protein-calorie malnutrition	19 (3.8)
	Electrolyte imbalance	44 (8.7)
	Infections	27 (5.4)
Risk factors for the development of CKD include (multiple-choice question):	**Diabetes**	496 (98.8)
	Hypertension	486 (96.8)
	Old age	451 (89.4)
	History of cardiovascular diseases	445 (88.6)
	Obesity	359 (71.5)
	Regular physical activity	2 (0.4)
	Percentage of correct answers	317 (63.1)
Management during the early stage of CKD should include (multiple-choice answer):	**Proper treatment of underlying disease**	500 (99.6)
	Avoidance of nephrotoxic drugs	478 (95.2)
	Reduction of dietary sodium intake	403 (80.3)
	Introduction of a protein-rich diet	37 (7.4)
	Increase in dietary phosphate intake	9 (1.8)
	Admission to dialysis as soon as possible	3 (0.6)
	Percentage of correct answers	356 (70.9)
In whose patients should caution be exercised when estimating GFR?	**In patients with abnormal amounts of muscle tissue or with skeletal muscle diseases**	469 (93.4)
	In obese patients	355 (70.7)
	In patients aged > 60 years	303 (60.4)
	In smokers	71 (14.1)
	Percentage of correct answers	55 (11.0)
Number of correct answers [M ± SD]		6.5 ± 1.3

M, mean; SD, standard deviation. Correct answers are in bold.

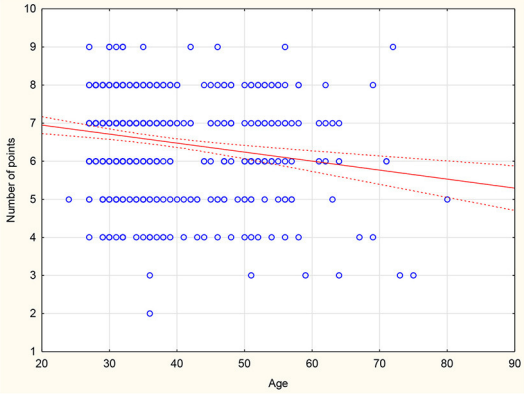

FIGURE 1
Correlation between age and scores on the CKD knowledge assessment test.

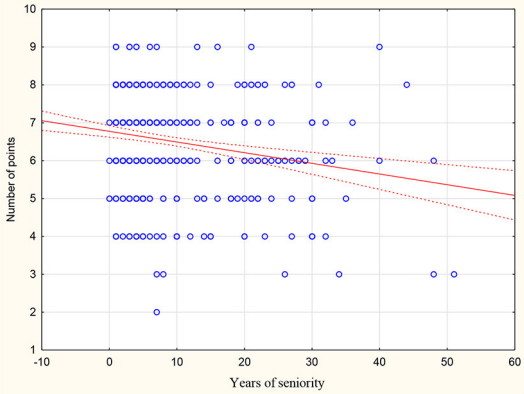

FIGURE 2
Correlation between years of seniority and scores on the CKD knowledge assessment test.

countries, results obtained from surveys assessing physicians' knowledge of the definition of CKD are even lower—only 38.8% of respondents from West Africa correctly defined CKD while only 38% of physicians from Pakistan were aware that GFR could be used for identifying CKD (8, 9). Furthermore, when asked about a laboratory test of particularly high value in the early stages of CKD, albuminuria was indicated by only 68.9% of respondents. Several reasons are possible for such low awareness of the value of this test. Albuminuria is not part of reimbursed services in primary care settings in Poland, making it much less used in daily practice. Similar results were obtained in other global studies—many physicians are unaware of the value of this test, which is one of the earliest indicators of kidney damage. Out of US resident physicians surveyed, not even half of them were aware that persistent albuminuria for 3 months allows the diagnosis of CKD. Albuminuria may be present and alert for further diagnostic evaluation when the results of other tests are within normal limits (1, 8, 9, 11, 16–18).

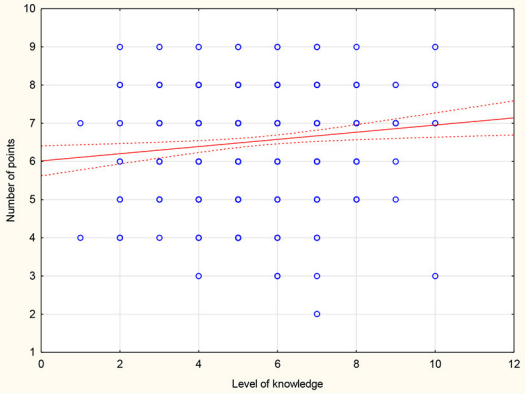

FIGURE 3
Correlation between level of knowledge and scores on the CKD knowledge assessment test.

Diabetes and hypertension were identified by the vast majority of respondents as risk factors for CKD (98.8 and 96.8%, respectively). Similar data were obtained in other previous studies concerning knowledge of CKD among PCPs and internal medicine physicians. In terms of US respondents, 99% identified diabetes and hypertension as risk factors for CKD, while the above-mentioned disease entities were identified as risk factors by more than 80% of Pakistani respondents (diabetes 88.4%, hypertension 80%) (9, 11, 17). The risk factor of old age was also identified by the vast majority of respondents (89.4%). This factor was often overlooked by physicians among the answers selected during surveys in other countries. It was identified by only 33.6% of physicians in Karachi and 71% in the United States (8, 17). The elderly are particularly predisposed to CKD due to structural changes in the renal vasculature and a decrease in the number of active glomeruli. Deterioration of renal function is associated with aging and a decline in GFR starts as early as 40 years of age (2). Relatively few respondents identified obesity as a risk factor for CKD—only 71.5%. This answer was selected less frequently than diabetes and hypertension also among US resident physicians—only 38% of the physicians identified obesity as a risk factor for CKD (11). This is particularly alarming given that there has been a pandemic of obesity over the last 50 years (19, 20). Obesity is also one of the most common risk factors for CKD in children and adolescents (21). A complete set of all risk factors for CKD in the multiple-choice question was identified by only 63.1% of the physicians participating in this survey, which indicates a significant knowledge gap in this area and calls for a quick intervention to raise awareness among physicians.

In addition to diagnostic evaluation and risk assessment, the family medicine physician's role is to implement appropriate therapeutic management. This is particularly important in the early stages of CKD, when morphological changes are small, and appropriate management can help to inhibit the disease

TABLE 3 The comparison of mean scores according to gender, career stage, place of work and past contact with CKD.

Variable		Mean	B	SD	t	p
Gender	Male	6.78	0.144	0.08	1.88	0.059
	Female	6.49	Ref.	Ref.	Ref.	Ref.
Career stage	Has not begun specialist training	6.24	−0.227	0.22	−1.05	0.295
	Resident physician in family medicine	6.72	Ref.	Ref.	Ref.	Ref.
	Specialist in family medicine	6.38	−0.084	0.11	−0.74	0.461
	Resident physician in another specialty	6.65	−0.185	0.22	−0.82	0.411
	Specialist in another specialty	6.34	−0.127	0.16	−0.79	0.430
Place of work	City > 250,000 inhabitants	6.57	0.043	0.09	0.49	0.623
	City of 50,000–250,000 inhabitants	6.48	−0.048	0.11	−0.44	0.661
	Town < 50,000 inhabitants	6.43	−0.098	0.11	−0.94	0.348
	Rural areas	6.64	Ref.	Ref.	Ref.	Ref.
Number of working hours in primary care settings [hours/week]	≥ 25	6.58	0.189	0.11	1.70	0.091
	11–24	6.37	0.017	0.14	0.12	0.902
	≤ 10	6.21	Ref.	Ref.	Ref.	Ref.
Contact with CKD at work	Yes	6.56	0.512	0.18	2.84	0.004
	No	5.54	Ref.	Ref.	Ref.	Ref.

Ref., reference; SD, standard deviation; B, coefficient value of a given variable; t, test value; p, statistical significance.

progression. In the question assessing the management during the early stage of the disease, 70.9% of respondents correctly indicated all the listed correct principles for the management during the early stage of CKD (proper treatment of underlying disease; avoidance of nephrotoxic drugs; reduction of dietary sodium intake). However, the authors are aware that these are not all the recommendations that should be followed by the CKD patient. The analysis of individual answers reveals that 99.6% of surveyed physicians indicated the need to treat underlying disease. This is crucial because, as it is well-known, CKD is most often a secondary condition of, among other things, diabetes and hypertension (1, 2). The awareness of family medicine physicians and their recommendations for behavioral intervention are of great value in terms of slowing the disease progression (13).

By analyzing the sum of correct answers obtained, an inverse correlation was found between the age of respondents and mean score obtained ($r = -0.183$; $p < 0.001$) as well as between years of seniority and mean score obtained ($r = -0.194$; $p < 0.001$). Resident physicians in family medicine scored highest on average in the knowledge test. These results are in line with those obtained in other studies, where resident physicians exhibited a higher level of knowledge regarding CKD compared to specialists (22). Simultaneously, the inverse relationship between the age of respondents and their score obtained is noteworthy. This relationship indicates the need for conducting training and educational programmes because as years of seniority increase, knowledge that is not updated can result in a decline in the quality of patient care.

In the US study, physicians (97% of respondents had been in the profession for more than 10 years) were asked about the difficulties associated with providing appropriate care to CKD patients. The most important obstacles that were pointed out by them included the lack of sufficient knowledge of CKD, the lack of clear guidelines for patient management and the difficulty in keeping up with dynamically changing recommendations. The respondents also pointed to the lack of a simple algorithm that would be useful in daily practice (23). The Australian team of Manski-Nankervis is working on such an algorithm. In 2021, the team published their proposal and the status of their work on a computer programme that is a sort of platform being tested within two family medicine physicians' practices. The programme is designed to assist in the identification of CKD, record-keeping, and continued patient management. Both family medicine physicians and specialists in nephrology—from academic and non-academic circles—are involved in building the platforms, as well as computer scientists, statisticians, lawyers and economists (24). The project of the authors of this study also uses a multidisciplinary approach that has the best chance of success in terms of increasing the rate of diagnosis and improving the quality of care for CKD. In China, attention is also being paid to the growing need for eHealth services for CKD. This need comes from both patients and physicians (25).The observations described above again support the need for education among PCPs in Poland. Specialists in family medicine who are burdened with work often do not have enough time and adequate knowledge of educational tools that are appropriate to their needs and may additionally fall into a routine in terms of their daily professional duties. Resident physicians are partly motivated to educate themselves on an ongoing basis and stay up to date with guidelines through the specialty training programme. As physicians get older, both mobility and willingness to use online educational courses often decrease due to their professional and family commitments. It

TABLE 4 The comparison of individual questions according to career stage and place of work.

	Career stage						Place of work				
	Percentage of correct answers n (%)					p	Percentage of correct answers *n* (%)				p
	Resident physician in family medicine	Specialist in family medicine	Resident physician in another specialty	Specialist in another specialty	Physician who has not begun specialist training		City > 250,000 inhabitants	City of 50,000 – 250,000 inhabitants	Town < 50,000 inhabitants	Rural areas	
Criterion for diagnosis of CKD	184 (81.4)	137 (78.3)	18 (78.3)	38 (71.7)	17 (68.0)	0.376	160 (76.9)	82 (82.8)	85 (73.9)	67 (83.8)	0.246
Most common cause of CKD	215 (95.1)	164 (93.7)	22 (95.7)	50 (94.3)	22 (88.0)	0.682	195 (93.8)	93 (93.9)	108 (93.9)	77 (96.3)	0.867
Symptoms of CKD	225 (99.6)	174 (99.4)	23 (100.0)	53 (100.0)	25 (100.0)	0.968	208 (100.0)	98 (98.9)	115 (100)	79 (98.8)	0.297
Test with the greatest diagnostic value	173 (76.6)	107 (61.1)	16 (69.6)	36 (67.9)	14 (56.0)	**0.011**	140 (67.3)	68 (68.7)	80 (69.6)	58 (72.5)	0.856
GFR criterion for RRT	198 (87.6)	155 (88.6)	21 (91.3)	42 (79.3)	20 (80.0)	0.322	184 (88.5)	87 (87.9)	94 (81.7)	71 (88.8)	0.327
Cause of death	188 (83.2)	131 (74.9)	21 (91.3)	46 (86.8)	18 (72.0)	0.067	169 (80.8)	73 (73.7)	94 (81.7)	69 (86.3)	0.196
Risk factors	147 (65.0)	106 (60.6)	16 (69.6)	29 (54.7)	19 (76.0)	0.325	136 (65.4)	63 (63.6)	72 (62.6)	46 (57.5)	0.665
Management during the early stage of CKD	166 (73.5)	124 (70.9)	14 (60.9)	35 (66.0)	14 (60.9)	0.636	151 (72.6)	66 (66.7)	80 (69.6)	59 (73.8)	0.667
Caution when estimating GFR	23 (10.2)	19 (10.9)	2 (8.7)	7 (13.2)	4 (16.0)	0.879	26 (12.5)	12 (12.1)	12 (10.4)	5 (6.3)	0.476

Significant values are in bold with the significance level set at $p < 0.05$.

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would also be advisable to create educational tools for specialists in family medicine, so that they can easily and conveniently stay up to date with current recommendations and guidelines despite their busy schedules. The creation of a management algorithm would be useful in daily clinical practice, especially that US studies indicate the difficulty in terms of determining the appropriate timing for a family medicine physician to refer a patient to a specialist in nephrology (23, 26). There is also little knowledge among US physicians regarding drug dosage in patients with a history of CKD (27). According to studies conducted in the United States and Australia, knowledge of one's own disease is also very low among patients who suffer from CKD, which poses even greater challenges for the physician who provides care for them (28–30). Such a physician should communicate to the patient, in a clear and accessible way, the principles to be followed in their everyday life with the new disease.

The authors are aware of the limitation of this study, which is undoubtedly the lack of survey methodology—authors' own questions concerning CKD were used. To the best knowledge of the authors, however, there is no current tool validated under Polish conditions that could be used. The proposal for the tool originated in the UK but has several limitations (12). The authors are aware that these 10 questions addressing CKD are not sufficient to assess knowledge of the disease. The authors, however, attempted to select questions in such a way that they addressed different stages of the diagnostic and therapeutic process and were varied as possible. The creation of the questions was consulted with the specialists in nephrology who were patrons of the authors' project. Another limitation is the selection of the study group that is not representative of PCPs in Poland due to low age of respondents and significant predominance of women. For the reasons described above, the following results should not be considered reflective of the population as a whole, and further observations are necessary.

Conclusions

In conclusion, this study reveals that the level of physicians' knowledge regarding CKD in Poland is insufficient, as a mean score for correct answers was 6.5 out of possible 9. Only three quarters of physicians know correct criteria for the diagnosis of CKD, 68.9% correctly indicate the diagnostic significance of albuminuria and 71.5% correctly select all risk factors for the disease. Moreover, 70.9% of the surveyed physicians correctly identify proper recommendations for the management during the early stage of CKD. The number of correct answers decreases with the work experience and age of the respondents. All this points to a lack of adequate awareness regarding CKD among physicians.

Therefore, there is a need to organize an appropriate educational offer, including e-learning, especially that physicians are motivated to use it. The educational offer should not only be addressed to resident physicians but also to specialists, who find it difficult to keep up with changing guidelines and recommendations in the course of their work and with their busy schedules. It should be noted that PCPs are highly motivated to educate themselves and expand their knowledge of CKD as declared in the questionnaire survey.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by the study was conducted in accordance with the Declaration of Helsinki and approval was obtained from the Bioethics Committee at the Lower Silesian Medical Chamber; Resolution No. 1/BNR/2022. The patients/participants provided their written informed consent to participate in this study.

Author contributions

Conceptualization and data curation: AJ-K, MB, and AM-M. Formal analysis: MB. Funding acquisition and project administration: AM-M. Investigation: AJ-K and MB. Methodology and writing—review and editing: AJ-K, MB, MK, AO, KK, and AM-M. Supervision and validation: MK, AO, KK, and AM-M. Visualization: AJ-K, MB, and KK. Writing—original draft: AJ-K, MB, KK, and AM-M. All authors have read and agreed to the published version of the manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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A machine-learning approach to estimating public intentions to become a living kidney donor in England: Evidence from repeated cross-sectional survey data

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Background: Living kidney organ donors offer a cost-effective alternative to deceased organ donation. They enable patients with life-threatening conditions to receive grafts that would otherwise not be available, thereby creating space for other patients waiting for organs and contributing to reducing overall waiting times for organs. There is an emerging consensus that an increase in living donation could contribute even more than deceased donation to reducing inequalities in organ donation between different population sub-groups in England. Increasing living donation is thus a priority for National Health Service Blood and Transplant (NHSBT) in the United Kingdom.

Methods: Using the random forest model, a machine learning (ML) approach, this study analyzed eight waves of repeated cross-sectional survey data collected from 2017 to 2021 (n = 14,278) as part of the organ donation attitudinal tracker survey commissioned by NHSBT in England to identify and help predict key factors that inform public intentions to become living donors.

Results: Overall, around 58.8% of the population would consider donating their kidney to a family member (50.5%), a friend (28%) or an unknown person (13.2%). The ML algorithm identified important factors that influence intentions to become a living kidney donor. They include, in reducing order of importance, support for organ donation, awareness of organ donation publicity campaigns, gender, age, occupation, religion, number of children in the household, and ethnic origin. Support for organ donation, awareness of public campaigns, and being younger were all positively associated with predicted propensity for living donation. The variable importance scores show that ethnic origin and religion were less important than the other variables in predicting living donor intention.

Conclusion: Factors influencing intentions to become a living donor are complex and highly individual in nature. Machine learning methods that allow for complex interactions between characteristics can be helpful in explaining these decisions. This work has identified important factors and subgroups that have higher propensity for living donation. Interventions should target both potential live donors and recipients. Research is needed to explore the extent to which these preferences are malleable to better understand what works and in which contexts to increase live organ donation.

KEYWORDS

public perceptions, public support, public intentions, living donor, cost-effectiveness, kidney donation, organ donation

1. Introduction

In developed countries with well-established healthcare systems living donation is common, offered as a routine part of healthcare, and proactively promoted to the public *via* media campaigns (1–4). As medical science and technology advances so does the scope of what is possible to retrieve from a living donor (5). Generally, in high income countries routine living donation will include blood (including cord blood) and plasma (1–4, 6, 7); breast milk (8); sperms and embryos (9); bone, tissue (including amniotic membrane, and the most common and more well-known liver lobe and kidneys (1–4). Globally, 31.5% of kidney transplants and 24.4% of liver transplants in 2020 were from living donors (10).

In the United Kingdom (UK) – a health service with a globally recognized live kidney donor programme (1–4)– a total of 2,567 kidney transplants occurred in 2020 and about 21.7% were from living donors (10). Generally, there are two pathways to become a living kidney donor: 1. donating to someone known to the donor e.g., a relative or friend, or 2. Altruistic (non-designated) donation. Altruistic (non-designated) donation can be directed, that is, donating to someone the donor has no prior relationship with but may be aware (normally *via* social media or a campaign from the potential recipient) of the need for a kidney donation, or non-directed, that is, a person agrees to donate a kidney but does not know, and will likely never know the recipient (1–4).

In the UK, the Living Kidney Sharing Scheme (UKLKSS) operated by National Health Service Blood and Transplant (NHSBT) ensures the best match between live donors and recipients. They do this *via* a process of paired or pooled donation (11). This means that often people who want to donate a kidney to a relative or friend but are not a (good) match will instead donate their kidney to what is called the "kidney donor pool". This system enables a much more comprehensively assessed matching process in terms of blood group or tissue type rather than just on relationship to the recipient (1–4).

Live kidney donation continues to be promoted as a better option for patients with kidney failure and is associated with better outcomes (more effective matching profiles mean kidneys function better, last longer, with less risk of rejection) (12, 13) and is cost effective (patients normally receive a transplant quicker, cost the health service less, and if well-planned, patients can often avoid costly dialysis) (14, 15).

For example, in 2022 kidney transplantation resulted in a cost-benefit of about £27,155.8 per annum compared to dialysis, thus accruing benefits to both patients and national health services (1–4). Also, Gibbons et al.'s (16) analysis of 12 months' post-transplant cross-sectional survey data suggested a better quality of life and treatment satisfaction for patients who received a kidney transplant from live donors compared to those who received deceased donor organs. Furthermore, the risks to live donors are minimal – data suggest that mortality is on par with routine surgery, which equates to about 1/3,000 for kidney donors, 1/200 for right liver lobe donors and 1/5,000 for left lateral liver donors (17–20).

In spite of such developments there remains a critical shortage of available organs for transplantation to meet the health needs of over 7,000 people on the transplant waiting lists in the UK; with about three people estimated to die every day while awaiting an organ transplant (21). There is also emerging evidence that although the number of live donors has increased over the past 20 years, more recently these numbers plateaued (around 1,000 donors per year, accounting for around 35% of overall transplant activity in 2019) (22, 23).

In addition, the world continues to be burdened with end-stage kidney disease due to increasing population size and age, as well as increasing prevalence of associated co-morbid chronic health conditions such as diabetes, cardiovascular disease and hypertension (24). Variation in health systems in addition to public awareness, and cultural and ethnic differences in support for donation, mean that uptake of live donation can vary dramatically in and between countries (25). Although increasing the number of live donations remains a global health priority, interventions designed to increase live donation are poorly understood, lack an evidence base, and do not easily translate across diverse populations, so the unmet health needs and the

economic burden of those awaiting transplant remain high (26, 27).

While research continues at pace to expand the numbers of deceased organs available for transplant including organ preservation (28), public attitudes (29), family behaviors (30, 31), professional training (32), law and policy changes (21, 33) and awareness and understanding in and between minority and faith perspectives, (21, 26, 31, 34, 35); investigations into (changing) attitudes and motivations to become a living donor have been much more limited. In 2018, NHSBT also published a warning after living donation hit an 8-year low (36). Studies which have investigated public perspectives on living donation have identified preconceived ideas, misconceptions, concerns about the risks involved, lack of trust in systems, cultural beliefs and personal values as potential barriers to live organ donation (37–39). However, these studies were conducted some time ago, are likely not reflective of what is achievable today in living donation, and did not aim at characterize who is more likely to want to become a living donor and why. The aim of this study was to better understand the factors that influence intentions to become a living kidney donor to inform current and future policy interventions designed to increase the number of live donors.

2. Article materials and methods

2.1. Questionnaire and data

This study was undertaken as part of a wider national evaluation into the evolving organ donation system in England following the introduction of a soft opt-out policy in May 2020 (40). Following ethics approval for the study from the LSHTM ethics committee (Ref: 26427) and HRA (Ref: 21/NW/0151), NHSBT's national organ donation survey data were shared with the research team which included a series of questions related to live donation. The key question asked and the response options are shown in Box 1. This question was the focus of the current analysis.

The data comprised of eleven repeated cross-sectional surveys undertaken from August 2015 to November 2021 ($n = 19{,}011$) with an average of eight months' interval in between surveys. The same questions were administered to a new sample of respondents at each of the serial surveys. The data were collected as part of the organ donation attitudinal tracker survey commissioned by NHSBT.

The participants were recruited from the online panel of the survey organization called Kantar. The online panel consists of recruited adults aged 16 years and over who have given their explicit permission to be contacted about surveys. The panelists were recruited using telephone recruitment from small area census statistics and Postcode Address File (PAF) in England. These areas are of similar population sizes formed by the combination of wards with the constraint that each point must be contained within a single Government Office Region. The total size of the panel is about 30,000. The survey participants were invited to answer the survey using a quota sampling of individuals with random locational sample selection. Each quota was set based on national census data on age, education and geographical region. Different quota was set for each round of survey so there were not duplicate responses by the same individual in the serial surveys. Panelists were invited by email to answer the survey. They were offered small financial rewards after completing the surveys. The samples were weighted to represent the adult population of England who are 16 years of age and older.

BOX 1 Key question of analysis.

In which, if any, of the following circumstances would you consider donating one of your kidneys while you were alive? Please select all that apply.

Options:

- I would consider becoming a living kidney donor for a family member
- I would consider becoming a living kidney donor for a friend
- I would consider becoming a living kidney donor for someone I don't know
- I am unlikely to consider becoming a living kidney donor.
- I would never become a living kidney donor
- Not applicable - I have been a living kidney donor/recipient
- Don't know

We excluded all responses in the first three rounds of survey because the key question of focus (see Box 2.1) was not asked during these surveys ($n = 4{,}110$). All respondents who resided in Wales ($n = 200$) during the survey, and all those who did not provide information on their age were excluded from the dataset ($n = 194$). In addition, respondents who had been a living kidney donor or recipient were excluded because their responses were not related to future intentions ($n = 229$). A total sample of 14, 278 was used for the analysis.

2.2. Statistical analysis

Statistical analysis was done using R (41). As well as undertaking an overall analysis using all those who would consider donating a kidney to a family member, a friend or an unknown person, and those not willing; sub-analysis was done focusing on those who would consider donating to a family member and those not willing; those who will consider donating to a friend and those who are unwilling; as well as those who will consider donating to an unknown person and those who would be unwilling. Frequency distributions, weighted percentages, means and standard deviations were

used to describe the characteristics of respondents. The relationships between the demographic characteristics (age, sex, ethnic origin, number of children in household, religion, occupation, awareness of organ donation publicity, and support for organ donation) of respondents and their intentions to become a living kidney donor were determined using Pearson's x^2 test.

We used random forest model, a machine learning approach, to identify important factors influencing intentions, and predicting decisions to become a living donor. Applications of the random forest model in the fields of economics (42), and health and environmental sciences (43) have increased rapidly in recent years. Studies that have compared results of random forest model to other approaches either found similar results (44) or that the random forest model algorithm perform well in predicting decisions compared to approaches such as ordinary least squares regression (45) and logistic regression (46, 47). This is because of its adaptability to both linear and non-linear distributions, allowing complex interactions between characteristics and because it requires no prior model specification. We use random forest model because in addition to prediction accuracy, the random forest model enables identification of subgroups and their decision formation patterns (decision tree), a feature that cannot be obtained from one traditional methodology.

The random forest model is an ensemble of decision-trees which involves recursively partitioning a given data into two groups based on the response distribution until a predetermined stopping condition is achieved (48). The forest repeats this process many times using random subsets of the observations and variables. Hence, random forests are less prone to overfitting than a single decision tree (44). Based on how the partitioning and stopping criteria are set, the model can be designed for both categorical outcome variables and continuous outcome variable of interest. For a categorical outcome problem, as in the current study, a commonly used splitting criterion is entropy (49). At a given internal node of the decision tree, entropy is given as:

$$E = -\sum_{i=1}^{c} p_i x \log\left(p_i\right) \tag{2.1}$$

Where c is the number of unique classes or splits and p_i is the probability of each given class or split. The value of the probability is maximized in order to gain the most information at every split of the decision tree.

Based on available data, literature and intuition, the variables included in the model, their definitions and measurements are shown in Appendix 1. Individuals were grouped according to the quintile of their predictions, and the mean characteristics were presented by quintile to allow a better understanding of the relationship between the variables and the predicted intentions to become a living donor.

3. Results

3.1. Characteristics of respondents

Of a total sample of 14, 278 included in the analysis, 58.8% (n = 8,400) would consider becoming a living kidney donor while the remaining 41.2% (n = 5,878) would not consider becoming a living kidney donor. The characteristics of respondents (age, gender, ethnic origin, number of children in household and occupation) are shown in Table 1. Apart from the number of children in respondents' household, and ethnic origin, the differences in the aforementioned characteristics were statistically significant at 5% level across the categories. For instance, the average age of all respondents was 43 years (standard deviation 17). The average age was a year less for those who would consider donating their kidney than for those not willing to become a living donor. The difference in age was statistically significant at the 1% level. About 51% (n = 7,528) of the respondents were female. The proportion of females who would consider becoming a living kidney donor was about 10% higher compared to males. The differences were statistically significant at 1% level. The majority, about 92.8% (n = 11,736) of respondents self-described as being ethnically White. The level of awareness of organ donation publicity was modest at 37.1% (n = 5,520). The level of awareness of organ donation publicity campaigns for those who would consider becoming a living donor was 40.5% (n = 3,561), this is 8% higher compared to those who would not consider becoming a living kidney donor. Support for organ donation was high among the respondents with 78.1% (n = 10,966) in overall support. Support for organ donation was 20% higher for those respondents who would consider donating their kidney to either a family member, a friend or an unknown person (86%) compared to those who were not willing to become a living kidney donor.

Of the 58.8% (n = 8,400) who would consider becoming a living donor, 50.5% (n = 7,210) would consider becoming a living kidney donor for a family member, 28% (n = 3,992) would consider donating their kidney to a friend, and 13.2% (n = 1,877) would consider donating to an unknown person (Figure 1). Also, 44.3% (n = 3,720) would only consider donating to a family member; 6.4%(n=536) would only consider donating to a friend, and 7.2% (n = 607) would only consider donating to an unknown person (Figure 1).

Table 2 show the characteristics of respondents who would consider donating to a family member, a friend or an unknown person. The results show that those who would consider donating a kidney to a family member were 3 years older, with an average age of 47 years, compared to those who would consider

TABLE 1 Characteristics of respondents.

Characteristics	Would not consider becoming a living donor [n = 5,878 (41.2%)]	Would consider becoming a living donor [n = 8,400 (58.8%)]	Total (n = 14,278)	P-value (χ^2 test)
Age, mean (SD%)	44 (17%)	43 (17%)	43 (17%)	0.000
Sex, *n* (%)				
Male	3055 (53.1%)	3683 (45.57%)	6738 (48.68%)	0.000
Female	2821 (46.9%)	4707 (54.29%)	7528 (51.22%)	
Prefer not to say	1 (0.03%)	0 (0%)	1 (0.01%)	
Other	1 (0.02%)	10 (0.14%)	11 (0.09%)	
Ethnic origin, *n* (%)				
Other	1085 (7.9%)	1457 (6.77%)	2542 (7.24%)	0.087
White	4793 (92.1%)	6943 (93.23%)	11736 (92.76%)	
Number of children in household, *n* (%)				
1	739 (10.98%)	1259 (14.03%)	1998 (12.76%)	0.242
2	602 (8.9%)	1034 (11.53%)	1636 (10.44%)	
3	170 (2.07%)	302 (3.13%)	472 (2.69%)	
4	55 (0.63%)	77 (0.84%)	132 (0.75%)	
5	19 (0.32%)	15 (0.17%)	34 (0.23%)	
More than 5	10 (0.08%)	15 (0.16%)	25 (0.13%)	
No response	4283 (77.01%)	5698 (70.15%)	9981 (73%)	
Religion, *n* (%)				
Christianity	2575 (47.17%)	3974 (50.43%)	6549 (49.07%)	0.000
Islam	475 (4.06%)	488 (2.79%)	963 (3.31%)	
Hinduism	154 (1.25%)	239 (1.35%)	393 (1.31%)	
Sikhism	54 (0.47%)	103 (0.57%)	157 (0.53%)	
Buddhism	41 (0.74%)	58 (0.73%)	99 (0.73%)	
Judaism	35 (0.7%)	53 (0.72%)	88 (0.71%)	
Other	115 (1.84%)	165 (1.99%)	280 (1.93%)	
No response	2429 (43.77%)	3320 (41.43%)	5749 (42.4%)	
Occupation, *n* (%)				
High managerial, administrative or professional	375 (5.25%)	688 (7.2%)	1063 (6.39%)	0.000
Intermediate managerial, administrative	1273 (20.66%)	2036 (22.79%)	3309 (21.91%)	
Supervisor, clerical, junior managerial	1515 (24.77%)	2156 (25.27%)	3671 (25.06%)	
Skilled manual worker – e.g., mechanic,	1072 (20.75%)	1576 (21.19%)	2648 (21.01%)	
Semi-skilled or unskilled manual worker	820 (14.9%)	1091 (13.82%)	1911 (14.27%)	
Housewife/househusband	160 (2.68%)	191 (2.48%)	351 (2.57%)	
Unemployed	453 (8.74%)	402 (5.13%)	855 (6.63%)	
Student	205 (2.22%)	246 (2.01%)	451 (2.1%)	

(Continued)

TABLE 1 (Continued)

Characteristics	Would not consider becoming a living donor [$n = 5,878$ (41.2%)]	Would consider becoming a living donor [$n = 8,400$ (58.8%)]	Total ($n = 14,278$)	P-value (χ^2 test)
Do not wish to answer	3 (0.01%)	5 (0.04%)	8 (0.03%)	
No response	2 (0.01%)	9 (0.06%)	11 (0.04%)	
Awareness of organ donation publicity, *n* (%)				
Yes	1959 (32.25%)	3561 (40.46%)	5520 (37.05%)	0.000
No	3575 (62.31%)	4503 (55.48%)	8078 (58.31%)	
Don't know	344 (5.44%)	336 (4.06%)	680 (4.63%)	
Support for organ donation, *n* (%)				
Support organ donation	3830 (67.06%)	7136 (86.11%)	10966 (78.19%)	0.000
Indifferent	1523 (24.93%)	897 (9.9%)	2420 (16.15%)	
Oppose organ donation	303 (4.63%)	297 (3.23%)	600 (3.81%)	
No response	222 (3.38%)	70 (0.76%)	292 (1.85%)	

% represents weighted percentage; SD represent standard deviation.

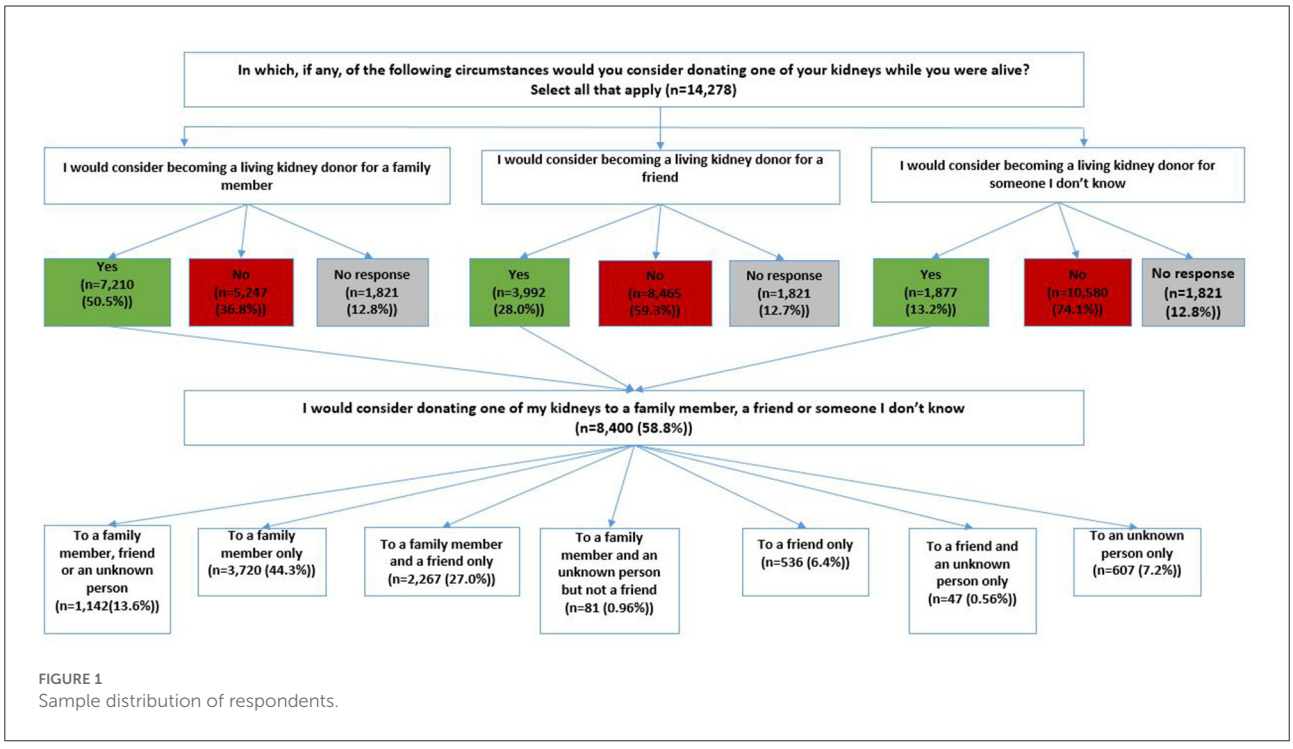

FIGURE 1
Sample distribution of respondents.

donating to a friend and an unknown person. Male respondents were more likely to consider donating a kidney to a friend (48%, $n = 1,799$) or an unknown person (48%, $n = 869$); while females were more likely to consider donating to a family member (57%, $n = 4,215$). These differences were statistically significant at 1% level. Overall, the majority of respondents who self-described as being ethnically White were more likely to donate to a family member (94%, $n = 6,119$), and to a friend (94%, $n = 3,387$), compared to an unknown person (92%, $n = 1,523$). The level of awareness of organ donation publicity was comparatively higher among respondents who would consider donating to a friend, 40%, ($n = 1,699$). Support for organ donation were generally high for all living donor intended categories, about 88% (Table 2).

TABLE 2 Characteristics of respondents who would consider donating to a family member, a friend or an unknown person.

Characteristics	I would consider donating my kidney to			*P*-value (X^2 test)
	Family [*n* = 7,210 (50.5%)]	Friend [*n* = 3,992(28.3%)]	Unknown [*n* = 1,877(13.2%)]	
Age, mean (SD)	47.38 (17.51)	43.59 (17.71)	44.39302 (17.83)	0.000
Age groups, n (%)				
16–29	1821 (18.71%)	1314 (25.73%)	595 (24.82%)	
30–49	2433 (33.45%)	1351 (34.93%)	647 (34.6%)	0.000
50–64	1908 (24.68%)	896 (21.89%)	423 (22.22%)	
65 and over	1048 (23.16%)	431 (17.45%)	212 (18.36%)	
Sex, *n* (%)				
Male	2989 (43.15%)	1799 (47.54%)	869 (48.45%)	0.000
Female	4215 (56.74%)	2186 (52.26%)	1000 (50.99%)	
Other	6 (0.11%)	7 (0.20%)	8 (0.56%)	
Ethnic origin				
Other	1091 (5.79%)	605 (5.97%)	354 (7.55%)	0.000
White	6119 (94.21%)	3387 (94.03%)	1523 (92.45%)	
Number of children in household, *n* (%)				
1	978 (12.81%)	578 (14.11%)	305 (15.3%)	
2	825 (10.78%)	434 (10.33%)	226 (11.46%)	
3	240 (2.89%)	152 (3.45%)	78 (3.99%)	0.198
4	56 (0.65%)	35 (0.83%)	16 (0.84%)	
5	9 (0.11%)	9 (0.21%)	1 (0.01%)	
More than 5	12 (0.15%)	4 (0.09%)	4 (0.22%)	
No response	5090 (72.61%)	2780 (70.98%)	1247 (68.18%)	
Religion, *n* (%)				
Christianity	3454 (50.98%)	1769 (49.45%)	868 (49.45%)	
Islam	338 (2.05%)	208 (3.28%)	114 (3.28%)	
Hinduism	176 (1.11%)	96 (1.86%)	67 (1.86%)	0.000
Sikhism	74 (0.5%)	48 (0.73%)	31 (0.73%)	
Buddhism	40 (0.56%)	31 (0.79%)	14 (0.79%)	
Judaism	47 (0.75%)	23 (0.58%)	12 (0.58%)	
Other	138 (1.95%)	96 (1.94%)	34 (1.94%)	
No response	2943 (42.1%)	1721 (41.36%)	737 (41.36%)	
Occupation, *n* (%)				
High managerial, administrative or prof	551 (6.61%)	325 (7.24%)	159 (7.43%)	
Intermediate managerial, administrative	1717 (22.52%)	990 (22.93%)	434 (21.08%)	
Supervisor, clerical, junior managerial	1909 (25.91%)	1036 (25.45%)	434 (22.35%)	0.000
Skilled manual worker - e.g., mechanic,	1367 (21.36%)	729 (20.51%)	357 (21.83%)	

(Continued)

TABLE 2 (Continued)

Characteristics	I would consider donating my kidney to			*P*-value (X^2 test)
	Family [*n* = 7,210 (50.5%)]	Friend [*n* = 3,992(28.3%)]	Unknown [*n* = 1,877(13.2%)]	
Semi-skilled or unskilled manual worker	951 (14.06%)	481 (13.4%)	246 (15.22%)	
Housewife/househusband	174 (2.61%)	85 (2.37%)	44 (2.48%)	
Unemployed	345 (5.11%)	193 (5.32%)	112 (6.47%)	
Student	182 (1.69%)	142 (2.60%)	86 (2.98%)	
Do not wish to answer	5 (0.04%)	3 (0.05%)	2 (0.09%)	
No response	9 (0.07%)	8 (0.12%)	3 (0.09%)	
Awareness of publicity, *n* (%)				
Yes	2889 (38.15%)	1699 (39.99%)	860 (44.37%)	
No	4016 (57.55%)	2107 (55.11%)	943 (51.82%)	0.000
Don't know	305 (4.30%)	186 (4.90%)	74 (3.80%)	
Support for organ donation, *n* (%)				
Support organ donation	6258 (87.84%)	3559 (89.87%)	1650 (88.34%)	
Indifferent	720 (9.25%)	299 (7.05%)	153 (7.68%)	0.000
Oppose organ donation	177 (2.18%)	112 (2.62%)	62 (3.49%)	
No response	55 (0.73%)	22 (0.46%)	12 (0.48%)	

3.2. Factors influencing intentions to become a living donor

The most important factors influencing intentions to become a living donor are shown in Figure 2. The results are presented separately for the total sample, those who would consider donating to a family member, a friend and an unknown person. The vertical axis shows the factor importance score–the figures represent the number of times a given factor/variable is used by the random forest to inform predicted intention to become a living donor. In the modeling process, the importance score represents the number of times a given variable is used to split on in the trees in the forest. The sum of all the importance scores is equal to 1 (100%). Out of the 25 factors/variables included in the model, the algorithm identified 13 important intention factors for the total sample, 14 important intention factors for the sub-sample who would consider donating their kidney to a family member, 12 important intention factors for those who would consider donating to a friend and 15 important factors for those who would consider donating to an unknown person (Figure 2).

The results from the total sample show that the most important factor that informs living donor intentions is support for organ donation. This is followed by awareness of organ donation publicity. These factors precede other important sociodemographic factors such as gender, age, occupational status, religion, number of children in household and ethnic origin, in reducing order of importance. A similar trend of factor importance was found in the subgroup analysis, however, the order of importance and the factor scores differed somewhat across the subcategories. For all the subgroups, the most important living donor intention factor is support for organ donation. While this was followed by gender in the case of those who intend to donate to a family member; age was the second most important factor taken into consideration by those who intend to donate to a friend or an unknown person (Figure 2).

The mean predicted propensity for living donation by quintile for each of the estimated models are shown in Figure 3. The results show that the mean predicted propensity for living donation in the first quintile is 35.8% (in the total sample), compared to 71.1% for those in quintile 5 (Figure 3).

Results for the propensity to donate to anyone (total sample) follows a similar pattern to the propensity to donate to a family member. There is considerable heterogeneity with the predicted propensity for living donation, which increased substantially from quintile 1 to quintile 5. The propensity to donate to a friend or unknown person is lower and displays less heterogeneity, increasing modestly from quintile 1 to quintile 5 (Figure 3).

Table 3 shows the mean estimates of covariates/factors by quintile of predicted propensity to living donation. The results show that females are positively associated with predicted propensity for living donation.

The proportion of females in the first quintile was 49%, this reduced to 16% in the second quintile but increased thereafter

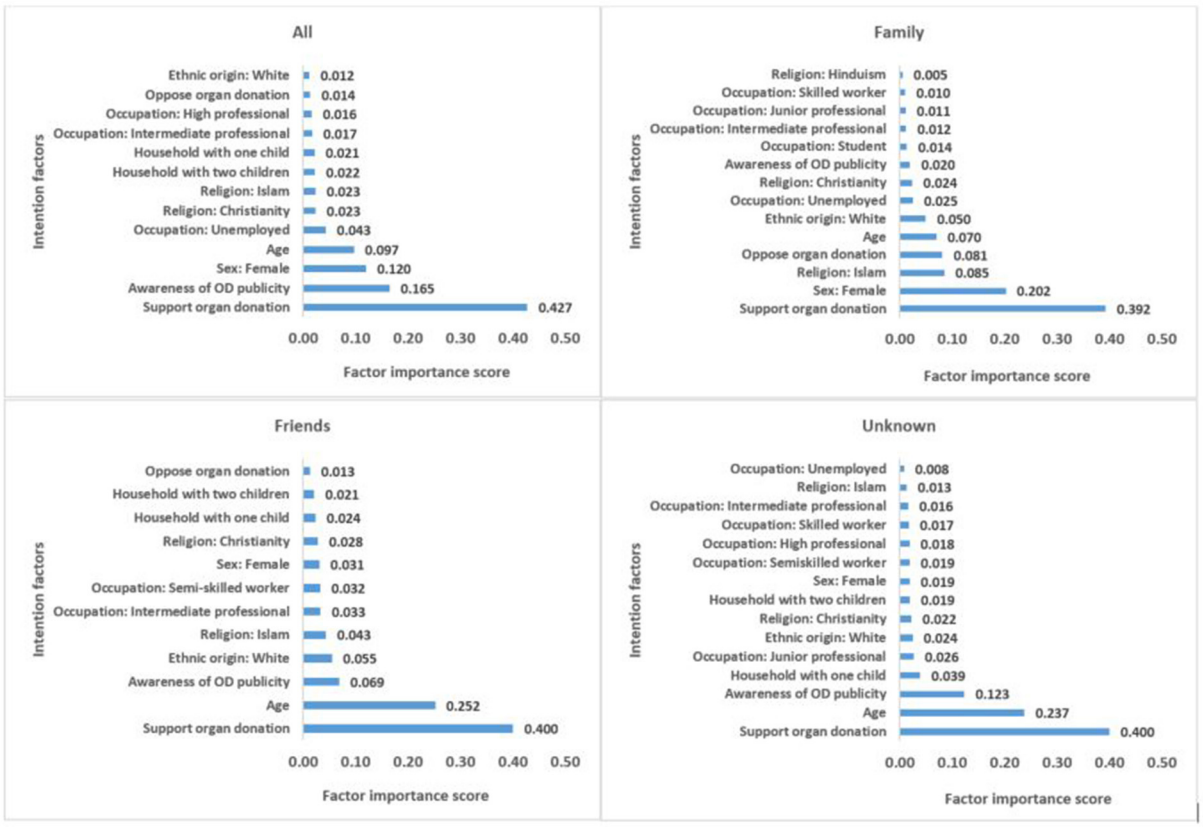

FIGURE 2
Important factors influencing intentions to become a living donor by recipient type.

to 83% in quintile 5. Age was negatively related with predicted propensity for living donation with a mean of 43 years in the first quintile, which increased to 50 years in the second quintile. The mean age then decreased continuously, reaching 33 years in quintile 5 (Table 3). Support for organ donation is positively related to predicted propensity for living donation. The proportion which had support for organ donation was 1% in the first quintile and raised to 99% in the fifth quintile. On the contrary, opposition to organ donation was negatively associated with predicted propensity for living donation. The proportion of those who oppose organ donation in the first quintile was 12% and reduced to 1% in the fifth quintile. Awareness of organ donation publicity was positively associated with predicted propensity for living donation, with 19% level of awareness in the first quintile which rises to 62% level of awareness in quintile 5 (Table 3). The results for family, friend and unknown person samples can be found in Appendix 2–4.

The random forest decision tree distribution showed a complex decision formation process that are highly individualized in nature, based on the identified factors, in informing intention to become a living kidney donor. Although we could not show all the decision trees in the forest, Figure 4 shows pruned decision trees based on the first four most important factors - that is, support for organ donation, awareness of organ donation publicity, gender and age.

The decision nodes show the number and size of subgroups as well as their predicted propensity for living donation (see violet nodes). For instance, the first four most important factors result in 19 subgroups with similar propensities for living donation. The results also show that although some people may oppose organ donation, they might consider becoming a living donor as indicated in the left hand nodes of the decision tree (Figure 4).

4. Discussion

We identified important factors that influence intentions to become a living kidney donor. They include support for organ donation, awareness of organ donation publicity, gender, age, occupation, religion, number of children in the household, and ethnic origin, in reducing order of importance. Support for organ donation, awareness of public campaigns, being younger, female and unemployed were all positively associated

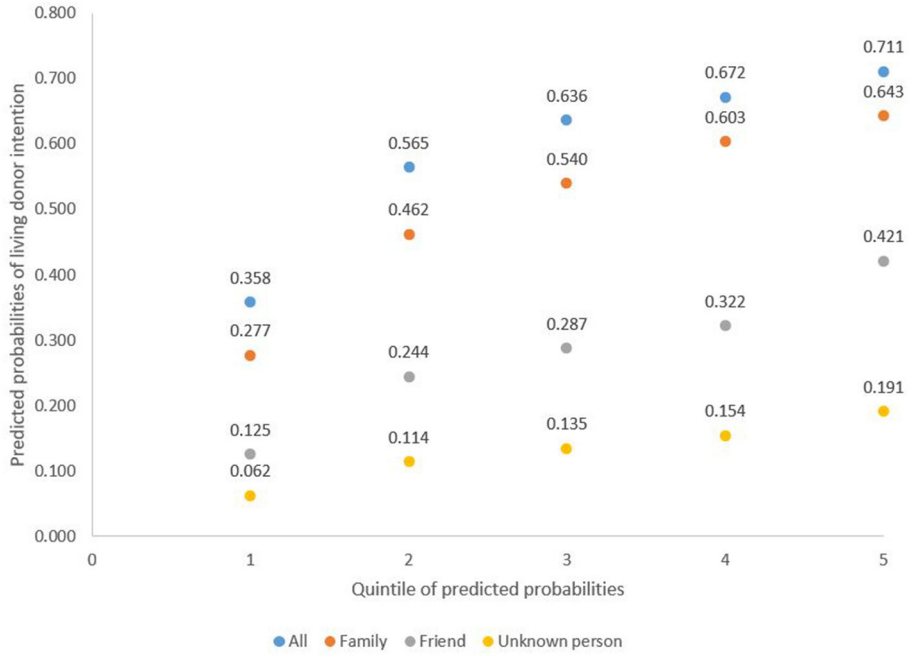

FIGURE 3
Mean prediction of likelihood of intention to become a living donor per quintile of predicted intention probabilities.

with people who reported being happy to become a living kidney donor. Our analysis also highlighted the complexity and individual nature of people's intentions to become a live kidney donor. Decision-making was highly personal and dependent on a range of factors, and likely a result of people's experiences as well as personal preferences and characteristics. For example, we noted a small number of cases where individuals do not support organ donation but nonetheless would be comfortable to donate a kidney to a relative, friend or even an unknown person. This may indicate that intentions to become a living donor are sometimes a result of individual circumstances including life events, not solely determined by demographics, and also that a person's intentions to become a live donor may change over time.

In a global context, interventions designed to increase living organ donation have varied considerably, largely due to factors such as health system capacity, health of the population, policy contexts, trust in government, and an established organ donation (including research) culture (50–53).

In the UK and countries with similar healthcare systems research has more recently focused on live donor trends in relation to deceased organ donation (54). Some evidence suggests that as the number of deceased donations has increased, the number of live donations has fallen (55). We do not yet fully understand why this is happening, but a recent multi-stakeholder call to action has highlighted the need to optimize live donation as a priority, while at the same time listing some key factors, in particular, the need to demystify the risks of live donation, and develop better education for potential donors and recipients (56).

Increasing the number of live donations is seen by health authorities as vital to help address the substantial inequalities apparent in organ donation and transplant. In the UK people from Black, Asian and minority ethnic backgrounds are overrepresented on the transplant waiting lists, overrepresented on the opt-out organ donor register, and are more likely to say no to deceased organ donation (57). Improving the uptake of live donation across these populations is widely agreed will do more to help level-up inequalities across these populations than any other single intervention (1–4).

Previous study findings have highlighted the important role played by ethnicity and religion in decisions associated with deceased organ donation (26, 35). Our findings show that ethnic origin and religion are of less importance in the case of living kidney donation. Although the proportion of ethnic minorities in the surveys was small (7.4%) and the surveys were not specifically designed to look at their perspectives, our findings are consistent with Siegel et al. (39) who employed planned behavior and a vested interest approach to explore the differences in intentions to become a living and deceased organ donor. They concluded that intention to become a living and deceased organ donor are very different and require independent examination and further study. For example, a clear difference in practice is that the living donor

TABLE 3 Mean/proportional estimate of covariates by quintile of predicted probability of living donation (Total sample).

Covariates	Quintile1		Quintile2		Quintile3		Quintile4		Quintile5	
	Mean/ Proportion	Standard error	Mean/ proportion	Standard error	Mean/ proportion	Standard error	Mean/ proportion	Standard error	Mean/ proportion	Standard error
Sex: Female	0.49	0.008	0.16	0.008	0.40	0.008	0.76	0.008	0.83	0.008
Age	43	0.304	50	0.304	48	0.304	42	0.304	33	0.304
Household with one child	0.11	0.006	0.09	0.006	0.11	0.006	0.16	0.006	0.23	0.006
Household with two children	0.08	0.006	0.09	0.006	0.10	0.006	0.14	0.006	0.16	0.006
Household with three children	0.04	0.003	0.02	0.003	0.03	0.003	0.05	0.003	0.02	0.003
Household with four children	0.01	0.002	0.01	0.002	0.01	0.002	0.01	0.002	0.01	0.002
Household with five children	0.01	0.001	0.00	0.001	0.00	0.001	0.00	0.001	0.00	0.001
Ethnic origin: White	0.74	0.007	0.88	0.007	0.85	0.007	0.84	0.007	0.81	0.007
Religion: Christianity	0.42	0.009	0.38	0.009	0.56	0.009	0.50	0.009	0.43	0.009
Religion: Islam	0.13	0.005	0.06	0.005	0.06	0.005	0.04	0.005	0.04	0.005
Religion: Hinduism	0.02	0.003	0.01	0.003	0.03	0.003	0.04	0.003	0.04	0.003
Religion: Sikhism	0.02	0.002	0.01	0.002	0.01	0.002	0.01	0.002	0.01	0.002
Religion: Buddhism	0.01	0.002	0.01	0.002	0.01	0.002	0.01	0.002	0.01	0.002
Religion: Judaism	0.01	0.001	0.01	0.001	0.01	0.001	0.01	0.001	0.00	0.001
Occupation: High professional	0.04	0.005	0.05	0.005	0.08	0.005	0.08	0.005	0.12	0.005
Occupation: Intermediate professional	0.16	0.008	0.26	0.008	0.26	0.008	0.18	0.008	0.31	0.008
Occupation: Junior professional	0.25	0.008	0.24	0.008	0.26	0.008	0.31	0.008	0.22	0.008
Occupation: Skilled worker	0.20	0.007	0.18	0.007	0.19	0.007	0.20	0.007	0.16	0.007
Occupation: Semiskilled worker	0.17	0.006	0.12	0.006	0.12	0.006	0.15	0.006	0.11	0.006
Occupation: Housewife husband	0.03	0.003	0.02	0.003	0.02	0.003	0.03	0.003	0.02	0.003
Occupation: Unemployed	0.11	0.004	0.11	0.004	0.06	0.004	0.02	0.004	0.01	0.004
Occupation: Student	0.04	0.003	0.01	0.003	0.03	0.003	0.03	0.003	0.05	0.003
Awareness of organ donation publicity	0.19	0.009	0.27	0.009	0.46	0.009	0.41	0.009	0.62	0.009
Support organ donation	0.01	0.003	0.86	0.003	0.99	0.003	1.00	0.003	0.99	0.003
Oppose organ donation	0.12	0.004	0.06	0.004	0.02	0.004	0.01	0.004	0.01	0.004

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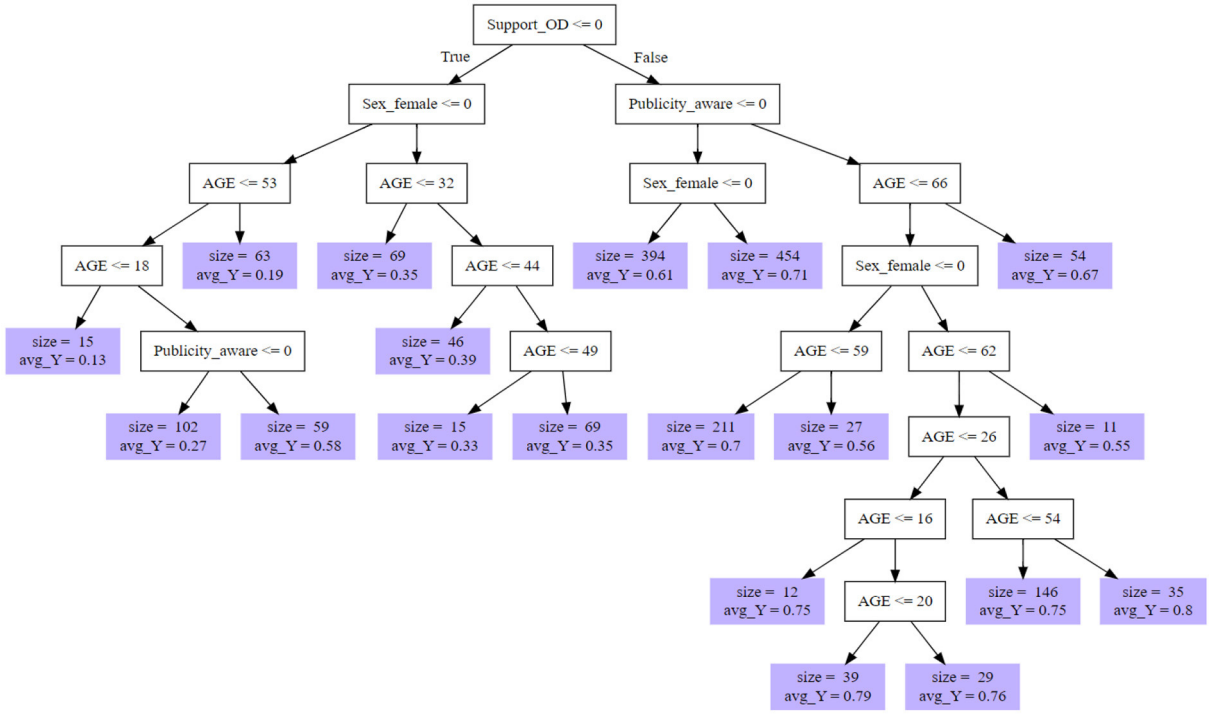

FIGURE 4
Pruned decision tree for predicted propensity for living kidney donation based on top four most important factors.

gives their own consent to the surgery which, unlike in the case of deceased organ donation, cannot be overridden by relatives.

Finally, our findings indicate that people are perhaps unsurprisingly more likely to want to donate to a relative only. This may indicate a lack of awareness and understanding of the process of live kidney donation since it is often the case that people do not donate directly to their relative but to a donor pool, and that importantly this process actually enables better matching and outcomes for recipients (39, 58).

4.1. Strengths and limitations

This study applied random forest model, a machine learning approach, to identify and predict the factors that influence intentions of becoming a living kidney donor to help inform present and future health communication programmes and interventions aimed at increasing living organ donation. The random forest approach was used because it does not require prior correct model specification, prevents overfitting of the model and produces accurate estimates of measurement errors. For some of the analysis we split the dataset into three categories based on whether respondents' intent to donate their kidney to a family member, a friend or an unknown person. Grouping the dataset this way provided a more detailed understanding of the data routinely collected by NHSBT and helped develop understanding of the factors that can inform people's intentions to become a living kidney donor either to a family member, friend or unknown person. This is important as the UK is currently a world leader in paired/pooled living kidney donation through the UK Living Kidney Sharing Scheme (UKLKSS) which enables family members to donate to a "donor pool" rather than directly to their relative (1–4). The living donor is unlikely to ever know who received their kidney but will be reassured that their relative is better matched *via* blood and tissue type and will wait less time for a kidney.

The main limitation of this study is that the authors were not involved in the questionnaire design or data collection and so were limited in their analysis to a small number of questions asked about living donation as part of a series of cross-sectional national surveys looking generally at attitudes to organ donation. This limited the number of variables that could be included in the model. Overall, our model predicted 71.1% of the factors that informs intentions to become a living kidney donor. Future studies should help to account for the remaining 28.9% of the factors not accounted for in this study. Also, the sampling might not be sufficient to capture thorough

population level distributions and may involve biases. The surveys were not longitudinal and so we were unable to look at changes over time including patterns or events which may have influenced public attitudes to live donation, e.g., changes in organ donation policy – for example, those introduced in England in May 2020.

4.2. Recommendations and future research

The study results demonstrate the need to promote health communication campaigns to increase public awareness of living organ donation as well as educating the public on existing structures and processes involved in becoming a living donor. Such interventions could target adult population who are below the age of 45 years. There remain large gaps in knowledge in relation to motivations and eventual behavior related to live donation, for example ethnic minority perspectives, the personal views and experiences of those who have become living donors, those who have requested a live donation from a relative or friend, and importantly more detailed data on why people say they do not want to become live donors, or donate to certain people, for example, those with serious drug use, convicted of serious crime or those who are perceived to have "abused" a previous organ following transplantation; why people refuse the offer of a live donation, and how perspectives and attitudes may change over time. Plus, we have very little evidence about the ethical or positive and negative psychological impacts or consequences of living donation. For example, what are the experiences of donating to a relative if the relationship breaks down or they do not look after the kidney as well as the donor would expect?

The survey could be improved by including additional questions such as educational level of respondents, motivations/demotivations to becoming a living kidney donor and their experiences with living donation, among others. Also, the survey could be implemented as panel survey instead of repeated cross-sectional survey with different sample of respondents for each survey wave. That would help to measure changes in behavior and intentions to become a living donor over time. The online survey could be complemented with paper-based survey *via* post to targeted respondents within the selected same small area census statistics and Postcode Address File (PAF) in England to reduce possible sample selection bias. Although the results show that ethnic origin is of less importance in the case of living kidney donation, future surveys could be designed to purposively increase response from ethnic minority groups in order to fully capture their perspectives. Future research needs to take a more complex system perspective including looking at what can be done to increase the donor pool and make more live donor organs available for transplant, complimented with longitudinal data investigating patients' outcomes and cost effectiveness.

5. Conclusion

Live kidney donation remains the best treatment for end-stage renal diseases as it is cost-effective, and a preferred choice for many patients compared with other forms of treatment such as dialysis. Nonetheless, despite investments, the number of people becoming live kidney donors has plateaued in recent years. Our analysis has identified some of the key factors which are likely to influence people to be potentially willing to become a living kidney donor and at the same time (re)established the complexity of decision making around this highly personal and sometimes controversial topic. There are gaps in public knowledge and awareness of live donation in general, and how it is likely to come about in practice. Addressing some of these gaps may facilitate greater uptake of live organ donation. Nonetheless, additional research is required in order to better understand motivations toward live donation and ensure those who are eligible and want to become live organ donors are able to do so in future.

Data availability statement

The data analyzed in this study are subject to licenses/restrictions. The authors do not have the permission to publish the dataset. Requests to access these datasets should be directed to https://www.nhsbt.nhs.uk.

Ethics statement

The studies involving human participants were reviewed and approved by LSHTM Ethics Committee (Ref: 26427) and HRA (Ref: 21/NW/0151). The participants provided their informed consent to participate in this study.

Author contributions

PB conceptualized the analysis, performed data analysis, drafted the first version of the manuscript, and finalized the manuscript. LM, MA-H, and JB conceptualized the analysis, supported drafting the manuscript, and provided feedback on early versions. SO'N conceptualized the analysis, supported data analysis, provided feedback on early versions, and approved the final version of the manuscript. JN and NM conceptualized the analysis, provided feedback on early versions, and approved the final version of the manuscript. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2022.1052338/full#supplementary-material

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Pre-emptive living donor kidney transplantation: A public health justification to change the default

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KEYWORDS

living donor, pre-emptive, kidney transplantation, public health, kidney replacement therapy (KRT), evidence based healthcare, dialysis, end-stage kidney disease (ESKD)

1. Introduction

Kidney transplantation (KT) is the preferred kidney replacement therapy (KRT) for suitable patients with end-stage kidney disease (ESKD) (1). Donor kidneys could be from a deceased donor (DD) or a living donor (LD). LD kidney transplantation (LDKT) is preferred over DD kidney transplantation (DDKT), because of superior quality kidneys that result in improved patient and graft survival (2), greater flexibility for transplantation across the ABO (3, 4) and HLA (5, 6) barriers, and the possibility for kidney exchange (7) including chains initiated by unspecified donors (8). Perhaps the most important advantage of LDKT is the ability to plan the transplant and hence avoid dialysis, thereby offering the most secure way to achieve pre-emptive KT (PKT). This is not entirely possible with DDKT which may occur too early or too late with respect to the onset of ESKD in an era of continuing shortage of DD organs (9).

The very first successful KT in 1954 (10) which took place 6 years before haemodialysis became available as KRT (11) was in-fact pre-emptive.

PKT has many advantages over non-pre-emptive KT (nPKT) and should be considered for all patients eligible for KT. These include longer patient and graft survival (12–15) and avoiding the risks, complications and restrictions of dialysis. Despite these evidence-based advantages of PKT, both in adult (12, 15) and paediatric (13, 14, 16) patients, the clinical reality is that pre-emptive LDKT (PLDKT) rates are disappointing, even in countries with high rates of LDKT, as it is not used as a quality indicator in most countries. This is worthy of discussion, especially if parallels are drawn to other clinical fields such as oncology, where best treatment options according to the latest evidence are strived for.

In this article, we seek to explore what the justifications may be to promote a greater proportion of our patients undergoing PLDKT, and thus advocate for drastic pathway changes to make PLDKT the default KRT that clinical teams should be delivering on.

2. Background

The barriers towards PLDKT have been widely discussed in the literature (17, 18). These include late referral, lack of cohesion, lack of education and insufficient infrastructure and financial support.

Historically, there have been several theoretical drawbacks to PKT raised. These include earlier exposure to the risks of immunosuppression and transplantation surgery (19, 20), potential earlier loss of residual native kidney function and higher risk of non-adherence to immunosuppressants due to not having experienced the morbidity of dialysis (12). The latter fear however has since been disproven (21).

The most common pathway in the United Kingdom (UK) remains DDKT after starting dialysis (22). The UK Renal Registry 24th Annual Report showed that only 17% of all KRT starters are listed or receive LDKT before starting dialysis (23). Between April 2021 and March 2022, only 40% of adult kidney only transplants were from LDs (22) and only 35% of these transplants were pre-emptive (24). In comparison, 50% of kidney transplants in the Netherlands in 2021 were from LDs and a greater proportion of these patients (44%) were pre-emptive (25).

In the UK, median waiting time from start of dialysis to DDKT was 1,044 days for adults transplanted between April 2021 and March 2022 (22). There is substantial mortality on dialysis (26), in addition to a negative impact on employment (27), societal participation (28) and quality of life (QOL) (29, 30). Dialysis also leads to considerable healthcare costs (31). Patients also face a significant risk of suspension from the waiting list (WL) with associated increased mortality and worse graft outcome (32). In comparison to DDKT waiting times, the process of working up an LD to secure PKT is considerably shorter at 90–120 days in the UK (33).

3. Guidelines

Currently, there is limited guidance with regards to PLDKT. Most guidelines recommend LDKT over DDKT but do not comment on PKT (34–37).

The position statement by the Descartes Working Group and the European Renal Best Practise Advisory Board provides strong recommendations in support of PKT and PLDKT (38).

"Guidelines for Living Donor Kidney Transplantation" published jointly by the Renal Association and British Transplantation Society from March 2018 states that "kidney transplantation from a living donor, when available, is the treatment of choice for most patients with end-stage kidney disease" and that "the goal should be pre-emptive transplantation" (39). With regards to children with ESKD, it states, "pre-emptive living related renal transplantation is the gold standard therapy."

The National Institute for Health and Clinical Excellence recommends including "living donor transplantation in the full informed discussion of options for RRT" and offering "pre-emptive living donor transplant ... or pre-emptive listing for deceased donor transplantation to people considered eligible" (40). Pre-emptive listing for DDKT however does not necessarily translate into high rates of PKT, given the nature of the allocation systems worldwide.

4. COVID

The SARS-CoV-2 pandemic had a profound impact on KT (41) and especially on LDKT with 1,023 fewer adult kidney only transplants being performed in the UK between April 2020 and March 2021 compared to the previous year (42). Only 17% of these transplants were from LDs, compared to 30% the year before, equating to 573 fewer LD kidney transplants. PKT rate was however maintained at 38% and LDKT was more likely to be pre-emptive than DDKT (43).

A similar picture was seen worldwide with KT from LDs decreasing in most countries (44, 45).

5. The public health case

5.1. Cost

The cost and sustainability of healthcare has never been as important given the increasing age of the worldwide population (46).

When directly compared, PLDKT was found to be a "cost-saving strategy compared with non-pre-emptive KT strategies" (47). Compared to maintenance dialysis, LDKT was associated with cost-savings of $94,579 over a 20-year period in one study (29) and "represented a saving of €13,102.97 per patient/year" with a payback period of <1 year in another (30). In the latter study, 89% of the transplants were pre-emptive with the authors concluding that PKT should be encouraged from a health budget perspective (30). PKT avoids the cost of dialysis, which has been estimated to be between £20,660 to £31,785 per patient per year (31), and its complications completely.

Decreasing the number of patients starting dialysis by virtue of undergoing PKT will reduce the need for dialysis capacity, allowing resources to be reallocated elsewhere. Preventing the burden of having dialysis three times a week, may enable patients to continue to work and contribute to society.

5.2. QOL and recipient outcomes

PLDKT is not just cost saving but also beneficial to the patient's QOL and clinical outcomes.

Compared to non-pre-emptive strategies, the quality-adjusted life year (QALY) "gained of PLDKT was 0.47" (47). Furthermore, LDKT when compared with maintenance dialysis added 3.5 QALYs over 20 years (29) and was associated with enhanced QOL (30).

Superior graft and patient survival are seen when comparing PKT to nPKT (12, 14–16). This was the case for both adult (12, 15) and paediatric (13, 14, 16) patients, and well as DDs and LDs (12). This is not surprising, given dialysis vintage prior to transplantation has been demonstrated to negatively impact graft survival and proposed to be the "strongest independent modifiable risk factor for renal transplant outcomes" (48, 49).

5.3. PLDKT vs. pre-emptive DDKT

There has been no direct comparison of PLDKT and pre-emptive DDKT (PDDKT) as identified in a recent systematic review and meta-analysis (50).

There is inherent difficulty in achieving PDDKT as there is no guarantee that pre-emptive listing will lead to PKT. With a DD, it is not possible to know in advance when KT will take place. Furthermore, PDDKT poses ethical dilemmas over the allocation of a scarce resource (51).

6. Donor risk

An important caveat that cannot be ignored is the risk to an LD. These include the risks of surgery (52), albeit very low complication risks if well selected (53), and the consequences of living with one kidney.

Kidney donors have an increased relative risk of ESKD; however, the magnitude of the absolute risk increase is small, and LDs still have a risk of ESKD that is much lower than the general population due to the screening and selection of healthy individuals (54). There is also an increased risk of cardiovascular and all-cause mortality however the authors concluded that they would continue to promote LDKT despite these findings (55). Finally, the ERA-EDTA DESCARTES working group concluded that "living kidney donation should be regarded as an acceptable procedure, as the long-term risks for the donor are generally low and, in many instances, offset by the overall benefit for both the donor and recipient" (56).

It is important to factor in the risk mitigation that takes place for LDs. This includes thorough workup, a focus on operative and anaesthetic safety and yearly follow up post-donation, all according to clear guidelines (39). Annual follow-up means that potential issues such as diabetes and hypertension may be detected earlier than if the individual had not donated allowing effective management. In some countries, such as the Netherlands and the UK, prioritisation on the WL is given should LDs develop ESKD (57).

LDKT, being a planned procedure enables a more thorough work up of the donor, reducing the risk of transmission of infection and/or cancer to the recipient (33). For the healthcare organisation, it permits greater control over theatre, bed and workforce availability. For those without an LD option, increasing LDKT rates will increase the availability of DD kidneys.

7. Equitable access

The UK National Health Service states that "public health contributes to reducing the causes of ill-health and improving people's health and wellbeing through … ensuring that our health services are most effective, most efficient and equally accessible" (58).

We have so far presented the case for PLDKT as the most effective and efficient form of KRT from a public health point of view. What follows is ensuring PLDKT is equally accessible.

The Getting It Right First Time programme national specialty report for renal medicine recommended reducing "unwarranted variation in deceased and living donor transplantation" (1). Inequity in access to KT (59) clearly exists. There is a 22% increase in time to being wait-listed and a 47% increase in time to LDKT for patients of low education level (60). Wide variation was seen in pre-emptive listing rates across centres (59). There is further variation according to age, ethnicity and socioeconomic status in the UK (61, 62) with older age and body mass index of >35 lowering the likelihood of pre-emptive listing (59).

Suggestions to improve PKT rates can be found in the literature. Early referral (63) is vital in ensuring there is time to sort out the logistics of PKT and LD work up. The timing of this referral should take into consideration the individual recipient's circumstances including rate of renal function decline and disease progression (39) rather than being defined by a specific level of renal function alone. Sufficient time should be allowed for patients to discuss donation within their social network to identify potential LDs.

Education to empower the patient through this process is essential (64, 65). A change in healthcare policy to reduce dialysis capacity and increase transplantation capacity have also been put forward (66).

One example of action being taken is the peer phone buddy scheme by the Gift of Living Donation organisation in the UK which seeks to "provide Black African Caribbean patients with … information about living kidney donation from people from their own community who have lived experience of living kidney donation" (67).

Another is the Kidney Team at Home intervention in the Netherlands which has been shown to be a cost-effective way of significantly increasing LDKT (68, 69). This involved group educational intervention of the patient and the patient's social network, in the patient's home.

Although the focus of these interventions is LDKT, strategies to successfully increase PKT largely rely on maximising LDKT.

8. Summary and conclusion

The drastic changes required cannot be understated. The shift from current practice, which sees DDKT after starting dialysis to PLDKT will significantly impact and challenge healthcare systems and practices.

The UK is clear that PLDKT is a major objective as set out in the "Organ donation and transplantation 2030: meeting the need" strategy (70). Another key objective is a more sustainable and reliable system. PLDKT due to its elective nature fulfils these criteria. Although PLDKT cannot fully replace DDKT, maximising its potential would reduce the need to recondition DD organs with expensive technology and infrastructure.

The evidence strongly supports PLDKT as the treatment of choice for ESKD. It is therefore our duty, not only for the individual ESKD patient, but also from a public health perspective, to urgently deliver PLDKT on a much larger scale as the default and in an equitable fashion, and for this to be used as a quality indicator.

Author contributions

IK and FD conceptualised and wrote the article. UM, SK, RR, and LP reviewed and revised the article.

All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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A Keynesian perspective on the health economics of kidney transplantation would strengthen the value of the whole organ donation and transplantation service

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Background: In this study, the Keynesian principle "savings may be used as investments in resources" is applied to Kidney Transplantation (KT), contextualizing the whole Organs Donation and Transplantation (ODT) service as a unique healthcare entity. Our aim was to define the financial resources that may be acquired in the form of savings from the KT activity.

Methods: We analyzed registry and funding data for ODT in our region, between 2015 and 2019. Our hypotheses aimed to evaluate whether the savings would offset the Organ Donation (OD) costs, define the scope for growth, and estimate what savings could be generated by higher KT activity. To facilitate the evaluation of the resources produced by KT, we defined a coefficient generated from the combination of clinical outcomes, activity, and costs.

Results: The ODT activity reached a peak in 2017, declining through 2018–2019. The savings matured in 2019 from the KT activity exceeded €15 million while the OD costs were less than €9 million. The regional KT activity was superior to the national average but inferior to international benchmarks. The estimated higher KT activity would produce savings between €16 and 20 million.

Conclusion: The financial resources produced by KT contribute to defining a comprehensive perspective of ODT finance. The optimization of the funding process may lead to the financial self-sufficiency of the ODT service. The reproducible coefficient allows a reliable estimate of savings, subsequently enabling adequate investments and budgeting. Applying such a perspective jointly with reliable estimates would establish the basis for an in-hospital fee-for-value funding methodology for ODT.

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KEYWORDS

organ donation, organ transplantation, Keynesian model, public health, health economics, funding, savings, kidney transplantation

1. Introduction

Organ Donation and Transplantation (ODT) services cover a critical and complex role in healthcare. A wealth of evidence over the years has defined with clarity the overall benefits for patients and the cost-effectiveness of Solid Organ Transplantation (SOT). Among all types of SOTs, kidney transplantation (KT) is recognized as being the best treatment for eligible patients with End-Stage Renal Disease (ESRD), but also, it achieves significant cost benefits in the form of savings when compared to the other types of renal replacement therapy (RRT). Different from ESRD, the actual financial implications of the management of patients with other organ failures, who would benefit from SOT, are not as similarly or reliably measurable.

The health economics of the three components of the ODT service, Organ Donation (OD), Organ Retrieval (OR), and SOT, are rarely contextualized as a whole, unique, and interdependent healthcare entity as most studies focus on the cost-effectiveness of specific organ transplants. Relevantly, the actual costs of OD and OR services are only occasionally included in the analysis. This is despite such costs are functional to the volume activity and success of SOT services.

The Coronavirus Disease 2019 (COVID-19) pandemic has mercilessly revealed several weaknesses in the healthcare systems. In particular, ODT services may be vulnerable, because of the organizational and funding complexity. In the context of current economic insecurity, with foreseeable financial repercussions, the Keynesian principle indicating that "savings may be used as investments in resources" would be applicable to healthcare in general, but more specifically to ODT. The application of such a principle is also sustained by post-Keynesian theories highlighting the relevance of health economics as belonging to the macroeconomic instead of the microeconomic sphere (1).

The present study aims to define the financial resources that may be acquired in the form of savings from the KT activity. The retrospective analysis of the whole ODT activity and costs in the Lazio region of Italy, between 2015 and 2019, also included the definition of a coefficient that allows to reliably estimate the potential resources that KT services may produce. In our hypotheses, we evaluate whether the savings generated by KT may offset the annual expenses for the OD services in our region. In order to define the scope for growth of KT activity, we compared the national and international benchmarks of ODT activity. Subsequently, we produced four different simulations of incremental KT activity that, following the application of the coefficient that we defined, have allowed us to estimate the hypothetical resources obtained. The suggested health economics perspective adds further strength to the established clinical value of ODT. In addition, it may facilitate the construction of a value-based model for the funding of the whole ODT. Such a perspective, potentially reproducible in any regional or national healthcare system, would be of critical relevance and pertinence in both developing and developed economies, as well as ODT programs.

2. Materials and methods

2.1. Description of the ODT services and funding in the Lazio region

In Italy, healthcare services are commissioned by the regional governments and authorities. The regional legislation is very similar across the 20 Italian regions. Although some variations may be observed, healthcare providers (HP) are funded by the Regional Commissioners of the Services (RCS) following regional legislation.

The Lazio region counts almost five million inhabitants which makes it like European countries such as Ireland, Finland, Norway, and Scotland. The five transplant centers of the Lazio region, one of which is exclusively dedicated to pediatric patients, are all located in the regional and national capital of Italy, Rome. The SOT activity is funded with a tariff system, therefore dependent on the volume activity of each transplant center. Each type of SOT is funded with a different tariff (kidney, €33,162; liver, €62,647; heart, €62,601; and lung, €72,572) (2). All Local Health Agencies (ASL) and their hospitals (HP), part of the National Health System (Sistema Sanitario Nazionale, SSN), receive funding for the OD from the RCS. There are two different types of payments. The first type of payment is allocated for the coordination of OD services in the form of a block payment. This payment is aimed to cover the costs of the providers for the personnel and the maintenance of the OD services. The second type, again in the form of a block payment, aims to reimburse the costs of the donation activity. The organs procured from any deceased-donor in Italy are allocated following established procedures agreed upon by the national and regional authorities. Therefore, any organ retrieved in any hospital of the SSN may be allocated in the same region, or to a patient in the transplant waiting list (TWL) of a different region. The management of the regional TWL, the allocation of organs, and the overall coordination of the OD and OR activities are under the responsibility of the National Centre for Transplantation (Centro Nazionale Trapianti, CNT) and the Regional Transplant Centre of Lazio (Centro Regionale Trapianti Lazio, CRTL) that is funded separately. The funding for the only regional histocompatibility laboratory (HL) is also separated. The costs related to the CRTL and the HL were €2.5 million and €280,000 per year, respectively (3). These costs were included in our analysis despite not being exclusive to SOT, as both absorb other activities concerning the donation and transplantation of bone marrow and tissues. The regional TWL for a SOT from a deceased-donor in Italy may include patients who are residents of any Italian region, as transplant centers offering KT, liver transplantation (LT), heart transplantation (HT), or lung transplantation (LuT) may not be available in the same region of residence or because of patient preference. The OR activity is not specifically financed as it is considered included in the organ transplantation tariff. Living donation does not appear to be included in the expenditures of the RCS. The service funding typology is as follows: OD coordination,

block payment; OD activity, block payment; OR, not specifically funded; and SOT, tariff payment.

2.2. Data source

The ODT activity data were obtained from the CRTL database and cross-referenced for accuracy with the annual reports of the CNT (4). The data relating to the funding and finance of the ODT service were obtained from the financial regional legislation published by the RCS in the Official Gazette (2, 5, 6).

2.3. Activity analysis of ODT

We analyzed the volume activity of the ODT services in the Lazio region of Italy for 5 consecutive years (namely, from 1 January 2015 to 31 December 2019). The years 2020 and 2021 have not been included because the COVID-19 pandemic did substantially influence ODT activity globally (7–9). The OD activity was evaluated through the number of utilized donors (UD) defined as donors from whom at least one organ was transplanted (10). Our analysis of SOT included the number of all organs transplanted in the regional transplant centers.

2.4. Cost analysis of ODT

The cost analysis was based on the officially documented expenditures for the ODT services reported in the regional legislation (2–6). The OD costs were divided into two components: activity and coordination. The SOT cost was produced by applying the regional tariff to all organs transplanted in the study period. The savings produced by KT were calculated from two established pieces of evidence. The first one is represented by the minimal savings obtained per year per functioning kidney transplant (FKT), and after the first year of transplant, is indicated €25,000 (11–14). The second one is represented by the minimum predictable efficacy of treatment (EoT) based on a minimum graft survival (GS) of 80% every year for the first consecutive 5 years (15, 16). Such established evidence allowed the definition of the Kidney Transplant Coefficient of Value (KTCoV) that was also used in our analysis.

2.5. Parameters and formulas

Estimated Functioning Kidney Transplant (eFKT) = 80% of total number of KT = (1,156/100) × 80 = 924.8;

Estimated Non-Functioning Kidney Transplant (eNFKT) = 20% of total number of KT = (1,156/100) × 20 = 231.2;

The estimated Gross Savings (eGrSav) was calculated from the difference between the savings produced by the eFKT and the cost of the eNFKT: (eFKT × 25,000) − (eNFKT × Tariff) = eGrSav = (924.8 × 25,000) − (231.2 × 33.162) = 23,120,000–7,667,054.4 = €15,452,945.6;

The Estimated Net Savings (eNSav) were obtained from the balance between eGrSav and the costs of OD, CRTL, and HL: eGrSav − (OD + CRTL + HL) = eNSav (€) = 15,452,945.6 − (5,832,590 + 2,500,000 + 280,000) = €6,840,355.6;

The KTCoV was determined by dividing the eGrSav by the total number of KT performed: eGrSav/number of KT = KTCoV = 15,452,945.6/1156 = €13367.6.

2.6. Hypotheses

> *H1*: Would the savings matured in 2019, through the KT activity of 2015–2019, offset the OD costs for 2019?

We evaluated whether the eGrSav and eNSav produced by the number of KT in the study period with minimal expected EoT may offset the annual costs of the OD services.

> *H2*: How does the Lazio region ODT activity compare nationally and internationally?

In order to define the scope for the growth of KT activity, we compared the type and rate/per million population (pmp) of UD and SOT observed in the Lazio region in 2019 (the last year of the study) with the Italian national average and other European countries comparable to Italy for the number of inhabitants and ODT activity. We used the data produced yearly by the International Registry of Organ Donation and Transplantation (IRODaT) (17).

> *H3*: What savings would generate a higher KT level of activity (LoA) in the Lazio region?

We produced four different simulations with an incremental number of KT over a 5-year period. Subsequently, we applied the KTCoV to the hypothetical number of KT.

3. Results

3.1. OD activity

The data analyzed from the official sources revealed that in the study period, the number of UD increased till 2017; thereafter, the following year remained identical, but with an inferior number of organs utilized. In 2019, both the number of UD and organs transplanted decreased. The average rate of UD/pmp ranged between 19.1 and 24.4. The average number of organs utilized per UD was constant in the 5 years, and it was 2.8 per UD. As shown in Table 1, kidneys were the most utilized among all organs retrieved in the study period (917/1590; 57.6%).

3.2. SOT activity

The number and type of transplants performed varied across the years. All deceased-donors were from donation after brain death (DBD) and the overall rate of KT from living-donor (LDKT) was 15.2% (176/1156). The number of LT was substantially superior to the number of UD and procured livers in the region. The activity of cardiothoracic transplantation shows that the HT activity, after

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TABLE 1 Activity and costs of Organ Donation and Transplantation service in Lazio region, Italy, between 2015 and 2019.

	2015	2016	2017	2018	2019	2015–2019
UD (n)	98	117	122	122	105	561
UD/pmp (n)	19.6	23.4	24.4	24.4	21	22.6 ± 2.2
KT from UD (n)	160	189	208	197	163	917
LT from UD (n)	86	99	99	90	87	461
HT from UD (n)	19	33	27	12	17	108
LuT from UD (n)	13	24	22	22	23	104
SOTs from UD (n)	278	345	356	321	290	1,590
SOTs per UD (n)	2.8	2.9	2.9	2.6	2.9	2.8 ± 0.1
Funding of activity (€)	2,820,590	2,820,590	2,820,590	2,820,590	2,820,590	14,102,950
Funding of coordination (€)	3,012,000	3,012,000	3,012,000	3,012,000	3,012,000	15,060,000
Total cost of OD (€)	5,832,590	5,832,590	5,832,590	5,832,590	5,832,590	29,162,950
Average cost per UD (€)	59,517	49,852	47,809	47,809	55,548	51,984
KT (n)	164	241	262	266	223	1,156
KT tariff cost (€)	5,438,568	7,992,042	8,688,444	8,821,092	7,395,126	38,335,272
LT (n)	141	163	145	149	155	753
LT tariff cost (€)	8,833,227	10,211,461	9,038,815	9,334,403	9,710,285	47,128,191
HT (n)	28	30	26	17	18	119
HT tariff cost (€)	1,754,116	1,878,030	1,627,626	1,064,217	1,126,818	7,450,807
LuT (n)	12	16	10	8	12	58
LuT tariff cost (€)	870,864	1,161,152	725,720	580,576	870,864	4,209,176
Total SOTs (n)	345	450	443	440	408	2086
Total SOTs tariff cost (€)	16,896,775	21,242,685	20,080,605	19,800,288	19,103,093	97,123,446

UD, utilized donor; n, number; pmp, per million population; KT, kidney transplant; LT, liver transplant; HT, heart transplant; LuT, lung transplant; SOT, solid organ transplant; OD, organ donation.

peaking in 2016, progressively reduced by 40% in 2019, while the number of LuT in 2019 was the same as in 2015 (Table 1).

3.3. Cost analysis

The OD services received a fixed payment of €5.8 million per year, for financing both coordination and activity. The SOT is financed *via* tariff payments. In our series, it ranged between €16.9 million and €19.1 million, reaching a peak in 2016 of €21.2 million. The cumulative tariff cost of the whole SOT activity in the study period was calculated at €97.1 million. The annual average was €19.4 million.

3.4. Hypothesis 1

The eGrSav calculated from the savings produced by the eFKT and the costs of the eNFKT was €15.5 million. The documented costs per year related to OD services including CRTL and HL were in total €8.6 million. Our calculations indicate that the eNSav in 2019 matured after 5 years of KT activity was €6.8 million (Table 2).

3.5. Hypothesis 2

The analysis of the OD activity as reported by IRODaT includes the rates of donation after circulatory death (DCD) and UD after DCD. The KT activity was divided between KT from deceased-donor (DDKT) and LDKT. All other SOT rates/pmp are also included.

According to the database of IRODaT, the European ODT programs with the highest LoA and with a comparable population to Italy are the United Kingdom (UK), France, and Spain. The ODT activity observed in the Lazio region and the comparison with the national averages of Italy, the UK, France, and Spain is summarized in Table 3. The overall rate of UD in Lazio was 22.5/pmp which is slightly inferior to the national average (23.2/pmp), and very close to the lower value of the international comparison range (22.8–42.8/pmp). It is noticeable that there were no DCD in Lazio. The KT rate in Lazio is 46.2/pmp, which is superior to the national average (36.1/pmp), but inferior to the lower value of the international comparison range (54.4–73.7/pmp). The high rate of LT (31/pmp) is noticeable in Lazio compared to national (22/pmp) and international (14.5–26.4/pmp) rates. In order to achieve a KT rate of 54/pmp, and be in the range of the high-performing European KT programs, it will be needed to

TABLE 2 Calculation of estimated gross savings and estimated net savings obtained in 2019.

	Savings	Costs	Balance
Estimated functioning kidney transplant (n) × Annual saving (€) (924.8 × 25,000)	23,120,000	–	–
Estimated non-functioning kidney transplant (n) × Tariff (€) (231.2 × 33,162)	–	7,667,054	–
Estimated gross saving (€)	–	–	15,452,946
Kidney transplant coefficient of value* (€)	13367.6	–	–
Cost of organ donation in 2019 (€)	–	5,832,590	–
Cost of CRTL (€)	–	2,500,000	–
Cost of histocompatibility laboratory (€)	–	280,000	–
Cumulative cost of organ donation (€)	–	–	8,612,590
Estimated net saving (€)	–	–	6,840,356

*KTCoV: Estimated Gross Saving/Total number of kidney transplants = 154,529,456/1156.
KTCoV, kidney transplant coefficient of value; OD, organ donation; CRTL, Centro Regionale Trapianti Lazio.

TABLE 3 Summary of 2019 Organ Donation and Transplantation activity (rate/pmp) in Lazio Region, Italy, UK, France, and Spain.

	Lazio	Italy	UK	France	Spain
Total UD/pmp	22.5	23.2	22.8	28.7	42.8
UD DCD type (n)	0	1.08	9.07	2.89	13.08
Total kidney transplant/pmp	46.2	36.1	54.4	55.6	73.7
Deceased-donor kidney transplant (n)	38	30.4	39.2	47.8	66.5
Living-donor kidney transplant (n)	8.2	5.7	15.2	7.8	7.2
Liver transplant (n)	31	22	14.5	20.7	26.4
Heart transplant (n)	3.6	4.14	2.8	6.63	6.47
Lung transplant (n)	2.4	2.58	2.5	6	9.03

ODT, organ donation and transplantation; UD, utilized donor; pmp, per million population; DCD, donation after circulatory death.

perform 270 KT/year. Hence, it will require an increase of 39 more KT per year (16.8% increase).

3.6. Hypothesis 3

The four simulations ranged from an average of 240 to 300 KT per year that, if maintained for 5 consecutive years, would produce between 1,200 and 1,500 KT. The calculation of the hypothetical eGrSav produced by the increased activity, achieved by multiplying the hypothetical number of KT in 5 years by the KTCoV (€13367.6), indicates that the hypothetical eGrSaV ranges between €16.1 million and €20.1 million, while the eNSav ranges between €7.4 million and €11.5 million per year (Table 4).

4. Discussion

4.1. The rationale for a Keynesian perspective

> "He must study the present in the light of the past for the purposes of the future" John M. Keynes.

The expenditures in financing the regional ODT service are clearly reported. However, some critical aspects of the actual costs of the service incurred by HP may not be fully reflected in the current combination of block and tariff payments. This represents a limitation of our study, as much as a burden in service costing and budgeting.

The current finance model of the care pathway, starting from the identification of potential donors to the ultimate number of UD, is based on block payment. This is despite a critical amount of expenses encountered by HP are dependent on the volume of activity produced. The most critical costs related to OR activity are included in the SOT tariffs. Such costs may translate into highly onerous commitments for HP. Undoubtedly, the financial implication of OR activity would benefit from a broader national strategy, rather than a regional or HP-based organization. In addition, the balance of organs exchanged between regions, with the payment of tariffs for patients transplanted outside the regional services, may be linked to relevant, but not fully accounted for, financial aspects of ODT services.

In our analysis, we have intentionally under-represented the EoT of KT basing our calculations on a GS rate of 80% from the first year after KT. We aimed to define the minimum savings that would be acceptable as a reliable estimate. Numerous scientific and governance reports confirm that stratified GS rates are substantially superior; therefore, suggesting that the actual savings produced by successful KT may be higher than that indicated by our analysis (15, 16). In addition, the savings produced by successful KT functioning for more than 5 years (in particular, those from standard criteria DBD and living-donors) have not been intentionally stratified in our analysis. The cost-effectiveness of other SOTs demonstrated by the quality-adjusted life years (QALY) is not included because the actual

savings produced are not as clearly measurable as for KT. However, growing evidence indicates that LT may produce robust savings after the initial costs linked to the surgical procedure are compensated. Furthermore, the costs related to the management of patients with liver failure who would benefit from LT, as much as the costs of death caused by liver failure complications, are substantial (17–19).

The fee-for-service remains the most used method of financing healthcare services in Italy and internationally. However, the application of such a method for financing ODT services may not fully reflect the current requirements and the future challenges that the whole service will be confronting in a global healthcare crisis such as the one we are already witnessing (20, 21). Consequently, the interdependence of the three components of ODT (OD, OR, and SOT) that extends beyond its scientific and clinical boundaries, reaching organizational aspects of the service, may be optimized with a more comprehensive and integrated perspective of the financial processes of the whole ODT. Addressing the savings produced by KT as resources for ODT components, such as OD and OR, is fully justified by the fact that KT is the major beneficiary of both services. This is also indicated in our series, where on average five UD produced eight KT, four LT, one HT, and one LuT. In addition, the demonstrable savings obtained by a globally reproducible EoT offer a unique opportunity in healthcare in defining the actual value of a multidisciplinary service through the contextualization and merging of clinical benefits and finance.

Our analysis indicates that the fixed funding for OD, allocated to regional HP through block payments, was not associated with the progressive growth of UD as observed elsewhere (22). Although the actual recession of UD might not be exclusively ascribed to unchanged funding, this observation alone may prompt the evaluation of adequate resources and workforce.

The rate of 46.2 KT/pmp observed in the Lazio region is not associated with a similarly high rate of UD. Such apparent inconsistency may be explained by an increased allocation of kidneys to satisfy the increasing demand of a large regional TWL of 900 patients at present.

According to our analysis, it appears that the estimated savings produced by KT alone in 2019 may comfortably offset the current OD services expenditures, including CRTL and HL costs, providing also almost €7 million as a resource for wider healthcare.

4.2. Hidden costs and hidden savings

> "It is better to be roughly right than precisely wrong" John M. Keynes.

The expenditures of RCS in financing the regional ODT service are clearly reported. However, some critical aspects of the actual costs of the service incurred by HP may not be fully reflected in the current combination of block and tariff payments. This represents certainly a limitation of our study, as much as a burden in service costing and budgeting.

The current finance model of the care pathway, starting from the identification of potential donors to the ultimate number of UD, is based on block payment to HP. This is despite a critical amount of expenses encountered by HP are dependent on the volume of activity produced. Arguably, the high variability of the costs may not be fully honored only with block payments, particularly so, to HP with the high-volume activity of OD. Conversely, HP with low-volume activity receives a block payment that may exceed the costs encountered. The most critical costs related to the OR activity are included in the SOT tariffs. Such costs may translate into highly onerous commitments for individual HP, even if benefitting from SOT tariffs. Undoubtedly, the financial implication of OR activity would benefit from a broader national rather than regional or

TABLE 4 Simulations of increased kidney transplantation activity with estimated gross and net savings.

	Actual (2015–2019)	Simulation 1	Simulation 2	Simulation 3	Simulation 4
	KT 46.6/pmp	KT 48/pmp	KT 52/pmp	KT 56/pmp	KT 60/pmp
Average annual number of KT required (n)	231	240	260	280	300
Annual increase rate required (%)	–	3.9%	12.5%	21.2%	29.8%
Number of KT in five years (n)	1,156	1,200	1,300	1,400	1,500
Estimated Gross Saving* (€)	15,452,946	16,051,920	17,389,580	18,714,640	20,064,900
Organ Donation Cost (€)	5,832,590	5,832,590	5,832,590	5,832,590	5,832,590
CRTL and Histocompatibility Laboratory (€)	2,780,000	2,780,000	2,780,000	2,780,000	2,780,000
Estimated Net Saving (€)	6,840,356	7,439,330	8,776,990	10,102,050	11,452,310

*Estimated gross saving: (number of kidney transplant) × (KTCoV).
KT, kidney transplant; pmp, per million population; KT, kidney transplant; CRTL, Centro Regionale Trapianti Lazio; KTCoV, kidney transplant coefficient of value (€13376.6).

HP-based strategy and, as importantly, commissioning for cost optimization. In the context of regionalized healthcare, the balance of organs exchanged between regions, as well as the payment of tariffs for patients transplanted outside the regional services, may be linked to a relevant, but not fully accounted, financial aspect of the ODT services.

In our analysis, we have intentionally under-represented the EoT of KT basing our calculations on a GS rate of 80% from the first year after KT. We aimed to facilitate the calculations for defining the minimum savings that would be accepted as a reliable estimate. Numerous scientific and governance reports identify stratified GS rates as substantially superior; therefore, suggesting that the actual savings produced by successful KT may be higher than that indicated by our analysis (15, 16). In addition, the savings produced by successful KT functioning for more than 5 years (in particular, those from standard criteria DBD and living-donors) have not been accounted for in our analysis. The cost-effectiveness of other SOTs demonstrated by the related quality-adjusted life years (QALY) is not included because the actual savings produced are not as clearly measurable as for KT. However, there is growing evidence indicating that LT may produce robust savings after the initial costs linked to the surgical procedure are compensated. Furthermore, the costs related to the management of patients with liver failure who would benefit from LT, as much as the costs of death caused by liver failure complications, are substantial (17–19).

Conciliating the actual costs encountered by HP with the funding for ODT and the savings produced by SOT would be crucial for future spending reviews. In Table 5, we highlighted aspects of the service not clearly captured by the current financing process.

TABLE 5 Costs and Savings related to Organ Donation and Transplantation not clearly reported.

Hidden costs	Hidden savings
Identification of potential donor:	Savings from Graft survival >80%
Multidisciplinary consultations	
Usage of ICU beds	
Evaluation of potential donor:	Savings from Graft survival >5 years
Laboratory	
Radiology	
Samples transportation	
Organ Retrieval:	Savings from LT/HT/LuT
Workforce	
Transportation of teams	
Transportation of organs	
Operative room	
Organs Imported from other regions	Organs exported to other regions
Tariff paid for patients resident in Lazio who were transplanted in other regions	Tariff received for patients resident in other regions who were transplanted in Lazio
Living Donation:	
Workforce	
Assessment	

ICU, intensive care unit; LT, liver transplant; HT, heart transplant; LuT, lung transplant.

4.3. Potential objectives

> "The importance of money flows from it being a link between the present and the future" John M. Keynes.

The KTCoV facilitated the calculations of hypothetical savings produced in the study years and in the four simulations. Producing a reliable estimate of the minimum savings enables the definition of clear objectives of growth and related budget. The factors used for the definition of the KTCoV may vary in time, according to the ODT program, tariff, or EoT. In addition, the estimated savings may change in time due to inflation or discount rates. Similarly, the tariff for KT may change or vary between regional or national ODT programs. Furthermore, the application of specific GS rates produced by detailed governance reports allows an even more accurate estimate, as much as a more granular evaluation of the savings produced, according to different GS rates (23). Therefore, independently of the corrections that may be required, the adaptability of the formula determining the KTCoV suggests that it may be used by the commissioners and stakeholders of any regional or national ODT program.

The critical mass of patients waiting for a KT defines "*per se*" the scope for the growth of KT services as, if not transplanted, they will remain exposed to suspension or removal from the lists, or death while waiting (4, 24).

The realistic feasibility of obtaining higher LoA of KT may be identified when contextualizing the KT/pmp of the Lazio region with international rates; in particular, when comparing it with the UK. In fact, despite the UK suffering the lowest rate of UD from DBD (13.7/pmp), the actual rate of KT is remarkably higher than Lazio and the Italian national average. Such observation proves that LDKT and DCD may substantially contribute to reaching high rates of KT and may be potentially reproducible also in other ODT programs (25). A substantial contribution to the growth of KT may be offered by a living donation. Although it may be conceptually acceptable to rely on LDKT growth in order to achieve a desired objective, it may be difficult, albeit possible.

The allocation of resources in the context of a restrained healthcare budget represents a remarkable challenge; more relevantly so during the ongoing COVID-19 pandemic associated with global economic uncertainty. In our simulations, the robust, yet hypothetical, savings achieved through an incremental number of KT ranges between €7.4 million and €11.5 million per year; undoubtedly representing a precious resource.

Applying the principle of considering the whole ODT as a unique healthcare entity that embraces interdependent services, we reproduce in Figure 1 a potential flow of resources.

4.4. A value-based approach for ODT

> "The difficulty lies not so much in developing new ideas as in escaping from old ones" John M. Keynes.

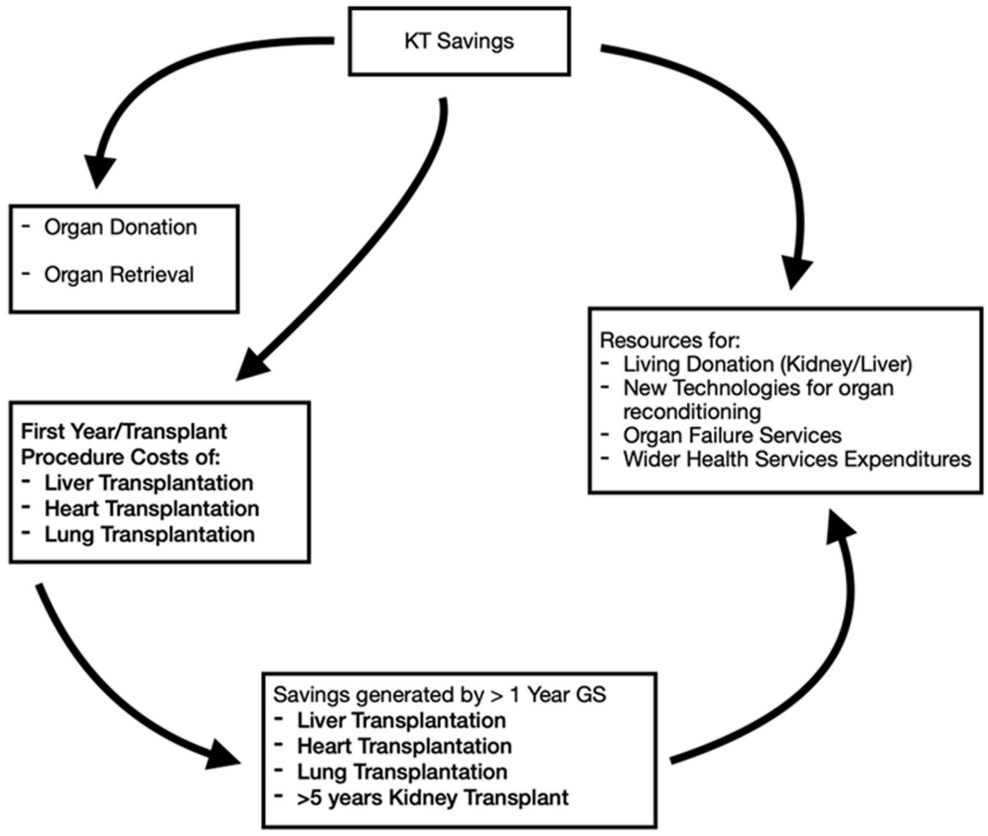

FIGURE 1
Potential flow of resources originating from the implementation of kidney transplant (KT) activity.

Value-based care differs from a fee-for-service in which providers are paid based on the number of healthcare services they deliver. In value-based healthcare, the "value" is derived from measuring health outcomes against the cost of delivering the outcomes (26). Consequently, it may be sustained that ODT, because of its complexity and the highly successful practice of SOT, consisting of high rates of survival of both patients and grafts, would benefit from being funded as an in-hospital service with a comprehensive fee-for-value rather than a compartmentalized fee-for-service funding method.

Our study has reaffirmed the rather unique attributes of KT that embrace remarkably high success rates with the production of demonstrable financial resources. Conceivably, these resources could represent the "economic engine" for the whole of ODT. In this context, the perspective of addressing the health economics of the ODT services comprehensively, instead of a fragmented structure, would contribute to defining the overall economic benefits of ODT, as well as it would lay the fundament for a fee-for-value funding methodology for the whole ODT. The cost-effectiveness of SOT demonstrated through the QALY linked to the concept of "willingness-to-pay" may represent a true limit (27). In fact, such a concept inevitably will be confronted in the future with the actual "capacity-to-pay."

The yearly eGrSav produced by KT beyond rendering OD financially independent could also contribute to offset OR activity, contributing partly or entirely to the procedure-related costs of other SOTs; therefore, further enhancing the "value" of the whole ODT that may be addressed as a financially self-sufficient healthcare entity.

The implementation of effective strategic growth is certainly possible also by expanding the same governance structure that ensured globally reproducible success rates toward those parts of the service ensuring access to transplantation, adequate infrastructures, and workforce.

Our study does not identify a new flow of money. Instead, it offers an instrument to reliably estimate the financial benefits produced by KT that, with adequate corrections, may be potentially applied to other Italian regions, nationally and internationally. In Italy, OD and SOT are included in those services recognized as essential that will cost at least €200 million per year (28, 29). Although ODT may represent a small proportion of such costs for the taxpayers, addressing ODT as a national resource and a financially self-sufficient service may realistically represent an enormous benefit for patients, wider ODT community, commissioners, and HP.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Author contributions

FL, LG, IC, and RC: rationale of the study and original draft of the manuscript. EF, AM, DS, TM, GT, and RC: final revision. FL, LG, AO, RA, and IC: data collection and interpretation. RA, TM, and RC: literature review. EF: editing. EF, AM, and RC: supervision. AO, DS,

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Psychosocial determinants of healthcare use costs in kidney transplant recipients

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Introduction: Psychosocial factors frequently occur in kidney transplant recipients (KTRs), leading to behavioral alterations and reduced therapeutic adherence. However, the burden of psychosocial disorders on costs for KTRs is unknown. The aim of the study is to identify predictors of healthcare costs due to hospital admissions and emergency department access in KTRs.

Methods: This is a longitudinal observational study conducted on KTRs aged >18 years, excluding patients with an insufficient level of autonomy and cognitive disorder. KTRs underwent psychosocial assessment via two interviews, namely the Mini-International Neuropsychiatric Interview 6.0 (MINI 6.0) and the Diagnostic Criteria for Psychosomatic Research Interview (DCPR) and via the Edmonton Symptom Assessment System Revised (ESAS-R) scale, a self-administrated questionnaire. Sociodemographic data and healthcare costs for hospital admissions and emergency department access were collected in the 2016–2021 period. Psychosocial determinants were as follows: (1) ESAS-R psychological and physical score; (2) symptomatic clusters determined by DCPR (illness behavior cluster, somatization cluster, and personological cluster); and (3) ICD diagnosis of adjustment disorder, anxiety disorder, and mood disorder. A multivariate regression model was used to test the association between psychosocial determinants and total healthcare costs.

Results: A total of 134 KTRs were enrolled, of whom 90 (67%) were men with a mean age of 56 years. A preliminary analysis of healthcare costs highlighted that higher healthcare costs are correlated with worse outcomes and death ($p < 0.001$). Somatization clusters ($p = 0.020$) and mood disorder ($p < 0.001$) were positively associated with costs due to total healthcare costs.

Conclusions: This study showed somatization and mood disorders could predict costs for hospital admissions and emergency department access and be possible risk factors for poor outcomes, including death, in KTRs.

KEYWORDS

psychiatric diagnosis, ICD, DCPR, mood, somatization, distress, hospital admission, emergency access

1. Introduction

Kidney transplantation (KT) is the most desired therapy for stage 5 chronic kidney disease as for these patients it represents the most cost-effective treatment, improving quality of life and prolonging survival (1, 2). In spite of being less costly than dialysis (3, 4), KT is however related to substantial costs (5–8), which can also derive not only from health problems such as cardiovascular disease, infections, graft rejections, and neoplastic disease (9–11) but also from the indirect effects of psychological conditions, such as depression or anxiety (12).

KT is often accompanied by high patient expectations, but it is indeed a stressful condition both physically and mentally that requires special adaptations encompassing changes in a patient's personal and financial life, meeting possibly unrealistic expectations, the possibility of rehospitalizations, infections, graft rejections, and the necessity of long-term immunosuppression therapy (13, 14). Indeed, 25 to 40% of KT recipients (KTRs) have been found to develop mood and anxiety disorders in the post-transplant period (15–21) according to the traditional Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International Classification of Diseases (ICD). Furthermore, 60% of KTRs have shown some form of psychological distress when using the Diagnostic Criteria for Psychosomatic Research (DCPR) (22), a diagnostic and conceptual framework whose aim is to capture psychological dimensions and subthreshold syndromes (23, 24). These conditions are particularly relevant as they may generate dysfunctional illness behaviors (e.g., somatization, frequent attender behavior, and illness denial) that are associated with worse outcomes (12), medical non-adherence (25, 26), decreased quality of life, and increased costs (27, 28). More importantly, psychological conditions are both identifiable and treatable (22, 29–33), thus representing additional superfluous costs for the healthcare systems.

While many studies have highlighted the detrimental effects of psychosocial conditions on KTRs, this is the first study with the intent to directly investigate the contribution of psychiatric and psychosocial diagnoses as identified by both ICD and DCPR systems on healthcare use costs in KTRs. Specifically, using linear regression models, we aimed to identify predictors of total healthcare costs due to hospital admissions and emergency department access.

2. Methods

A monocenter prospective observational longitudinal study was performed at the kidney transplant center of the Ferrara University Hospital from 2016 to 2021. The study was conducted according to the 1995 Declaration of Helsinki and its revisions (34). The Ethical Committee of the local academic hospital approved the protocol of the study (Protocol n: 151297, 2016). All participants signed written informed consent.

Inclusion criteria were age $\geq$ 18 years and being a recipient of a kidney from a cadaveric or living donor. Exclusion criteria were an insufficient level of autonomy (Karnofsky Performance Status Scale $<$ 50) and the presence of cognitive disorders (Mini-Mental State Examination $<$ 24). Two individual interviews, namely the Mini-International Neuropsychiatric Interview (MINI6.0) (35) and the Diagnostic Criteria for Psychosomatic Research Semi-Structured Interview (36) were administered by the same psychiatrist, an expert in psychosomatic research (L.Z.). A self-reporting instrument, the Edmonton Symptom Assessment System revised (ESAS-Revised) in the Italian language, was also filled in by patients. The characteristics of the above tools were extensively described elsewhere (37, 38). Briefly, the MINI6.0 is a structured diagnostic interview for assessing the major psychiatric disorders in ICD-10, which was used to make a psychiatric diagnosis. A DCPR semi-structured interview evaluates the presence of 12 syndromes divided into three different clusters: (1) abnormal illness behavior (AIB) (i.e., Disease Phobia, Health Anxiety, Illness Denial, and Thanatophobia); (2) somatization (i.e., Functional Somatic Symptoms Secondary to a Psychiatric Disorder, Persistent Somatization, Conversion Symptoms, and Anniversary Reaction); and (3) personological and psychological dimensions frequently diagnosable in KTRs (39) (i.e., Alexithymia, Type A Behavior, Irritable Mood, and Demoralization).

The ESAS-R is a pragmatic patient-centered symptom assessment tool with a visual analog scale, designed to assist in the assessment of six physical (i.e., pain, tiredness, nausea, drowsiness, lack of appetite, and shortness of breath) and four psychological (i.e., depression, anxiety, feeling of not being well, and emotional distress) symptoms. In particular, the physical symptoms are assessed objectively (i.e., pain is based on a knowledge of pain behaviors; shortness of breath as accelerated respirations causing patient distress; tiredness as lack of energy; lack of appetite, nausea, and drowsiness as the presence of eating, retching/vomiting, and sleep, respectively). The items can be summed in order to create subscales of psychological, physical, and total distress, which can be used to monitor symptoms and screen for mental and psychological disorders. It has been validated in dialysis patients (40) and kidney transplant cohorts (41). The Italian version shows an acceptable level of validity and good psychometric properties in KTRs (33, 42).

All data, including clinical characteristics and routine biochemistry, were collected from digital patients' archives.

The following variables were used as a measure of outcome: total healthcare costs due to hospital admissions in the 2016–2021 period; and total healthcare costs due to emergency department access in the 2016–2021 period. Costs, covered by Italy's National Health Service, were expressed in euros (€), the Italian currency, and were extracted from a hospital software database, searching for each patient record both the type of medical service delivered and the related amount charged across the period from 2016 to 2021.

As predictors of healthcare costs, we used the following psychosocial determinants, all measured before the outcome: ESAS, as a severity measure of physical and physiological symptoms; symptomatic clusters as measured by the DCPR; and clinical diagnosis according to MINI6.0 within the mood, anxiety, and adjustment disorder spectrum. Age (years), sex (men versus women), body mass index (BMI; kg/m^2), time under dialysis before the transplant (months), transplant vintage (months), estimated glomerular filtration rate (eGFR) (ml/min), blood creatinine (mg/dl), blood albumin (g/dl), blood hemoglobin (g/dl), blood phosphate (mg/dl), blood calcium (mmol/l), blood inactive vitamin D (ng/ml), and past psychopathology (positive history versus no history) were entered as covariates in the analysis to control for variables that can affect healthcare use or somatic outcomes of the kidney transplant.

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TABLE 1 Distribution in the sample ($n = 134$) of the variables included in the study according to sex.

Clinical and biochemical variables	Males ($n = 90$)	Females ($n = 44$)	Statistics	Effect size
Age (years)*	55.2 (11.7)	58.0 (12.6)	$t = 1.29$; $p = 0.199$	Hedges'g = 0.23
BMI (m^2/kg)*	24.5 (3.2)	24.5 (4.0)	$t = 0.0$; $p = 1.00$	Hedges'g = 0.00
Time under dialysis (months)*	30.8 (30.8)	26.6 (25.9)	$t = 0.77$; $p = 0.44$	Hedges'g = 0.14
Kidney graft vintage (months)*	116.9 (92.0)	125.7 (129.6)	$t = 0.45$; $p = 0.65$	Hedges'g = 0.08
Basal glomerular filtration rate (ml/min)*	58.6 (21.02)	76.8 (27.2)	$t = 3.90$; $p < 0.001$	Hedges'g = 0.78
Blood creatinine (mg/ml)*	1.5 (0.5)	1.2 (0.4)	$t = -3.49$; $p < 0.001$	Hedges'g = 0.64
Blood albumin (g/dl)*	58.2 (4.7)	57-9 (5.0)	$t = 0.25$; $p = 0.801$	Hedges'g = 0.04
Blood hemoglobin (g/dl)*	12.6 (1.6)	12.0 (1.3)	$t = 2.21$; $p = 0.029$	Hedges'g = 0.40
Blood phosphate (mg/dl)*	3.2 (0.6)	3.3 (0.8)	$t = 0.76$; $p = 0.448$	Hedges'g = 0.14
Blood calcium (mmol/l)*	2.5 (1.1)	2.6 (1.4)	$t = 0.49$; $p = 0.620$	Hedges'g = 0.09
Blood vitamin D (ng/ml)*	30.1 (11.6)	27.0 (10.4)	$t = 1.48$; $p = 0.141$	Hedges'g = 0.27
Past psychopathology, *n* (%)	27 (30.0)	14 (31.8)	$\chi^2 = 0.0$; df = 1; $p = 0.988$	Cramer's V = 0.02
ESAS-R				
ESAS psychological (scale score)*	10.4 (8.0)	11.4 (8.7)	$t = 0.68$; $p = 0.498$	Hedges'g = 0.12
ESAS physical (scale score)*	9.7 (7.7)	11.2 (9.7)	$t = 0.944$; $p = 0.347$	Hedges'g = 0.17
DCPR diagnosis				
Illness behavior cluster *n* (%)	23 (25)	12 (27)	$\chi^2 = 0.0$; df = 1; $p = 0.988$	Cramer's V = 0.02
Somatization cluster *n* (%)	10 (11)	9 (20)	$\chi^2 = 1.42$; df = 1; $p = 0.233$	Cramer's V = 0.13
Personological cluster *n* (%)	51 (57)	15 (34)	$\chi^2 = 5.15$; df = 1; $p = 0.023$	Cramer's V = 0.21
ICD diagnosis				
Adjustment disorder diagnosis, *n* (%)	14 (15)	7 (16)	$\chi^2 = 0.0$; df = 1; $p = 1.00$	Cramer's V = 0.005
Anxiety disorder diagnosis, *n* (%)	8 (9)	6 (13)	$\chi^2 = 0.29$;df = 1; $p = 0.587$	Cramer's V = 0.07
Mood disorder diagnosis, *n* (%)	7 (8)	4 (9)	$\chi^2 = 0.0$; df = 1; $p = 1.00$	Cramer's V = 0.02
Healthcare Costs				
Total healthcare costs due to hospital admissions and emergency department access (€)*	9077.63 (11020.19)	11448.00 (16602.49)	$t = -0.984$; $p = 0.327$	Hedges'g = 0.18

*Data are expressed as mean (standard deviation); BMI, body mass index; DCPR, Diagnostic Criteria for Psychosomatic Research; ESAS, Edmonton Symptom Assessment System; ICD, International Classification of Diseases. The effect size was reported for each comparison: Hedges' g was used for continuous variables and Cramer's V for categorical variables. The following thresholds were used: <0.20 = negligible; 0.20 to 0.50 = small; 0.50 to 0.80 = moderate; >0.80 = large for Hedges' g; <0.20 = small; 0.20 to 0.60 = moderate; >0.60 = large for Cramer's V.

TABLE 2 Outcome of kidney transplant according to health care use costs in the 2015–2021 observational period.

	Alive at 2021 $n = 106$ (79%)	Dead at 2021 $n = 28$ (21%)	Mean difference (95%CI)
Total healthcare costs due to hospital admissions and emergency department access (€)*	6780.55 € (10287.60 €)	214498.91 € (16005.13 €)	14718.36 € (19630.47 € – 9806.24 €)

*ANOVA: $F_{[1;132]} = 35.13$; $p < 0.001$.

2.1. Statistical analysis

Data were entered in Excel, then coded and analyzed using the Statistical Package for Social Sciences (SPSS) version 28. All tests were two-tailed, with alpha set at $p < 0.05$.

Descriptive statistics were reported as means with standard deviation and range, or as counts and percentages. A regression model to test the association of our predictors to the outcomes was used. A preliminary exploration of the association of each variable with the outcomes, using univariate linear regression models, was performed. Afterward, a stepwise multivariable regression model to evaluate the association of our predictors with the outcomes were tested, by taking into account the considered covariates with the significance level for removal fixed at $p < 0.10$. In the model, discrete variables were entered as continuous values while nominal variables were entered as dichotomous [absent (0) vs. present (1)] values.

The minimum required sample size for multiple regression, given a desired power of 80% at alpha = 0.05 with 21 predictors and aiming at detecting an effect size of $f^2 = 0.20$, was 124 participants. The calculation was carried out according to Soper (43). Multicollinearity was measured with the variance inflation factor (VIF), using a cut-off of 2.5 as a threshold to consider the presence of multicollinearity that could affect the regression model (44). As an effect size of the linear regression model, we used Cohen's f^2, according to the formula: $f^2 = R^2/(1–R^2)$. By convention (45), f^2 effect sizes of 0.02, 0.15, and 0.35 are considered small, medium, and large, respectively.

3. Results

Overall, 134 kidney transplant recipients, of whom only 10 were from living donors, were included in the longitudinal study, of which 90 (67%) were men and 44 (33%) were women. Nine patients declined to participate (six for work or family reasons and three because of health reasons). Men and women did not differ in demographic characteristics, biochemical values, and healthcare costs except for eGFR, blood creatinine, and personological cluster (Table 1). In fact, eGFR was on average higher in women (76.8 ± 27.2) than in men (58.6 ± 21.02): $t = 3.90$; $p < 0.001$. Conversely, blood creatinine was on average higher in men (1.5 ± 0.5) than in women (1.2 ± 0.4): $t = -3.49$; $p < 0.001$. Men [n = 51 (57%)] were more likely than women (n = 15 (34%)] to have a personological cluster ($\chi^2 = 5.15$; df = 1; $p = 0.023$). Above all, kidney transplant patients were Caucasians, coming from local districts.

At the end of the 2016–2021 observational period, the sample included 28 participants (21%) who had died. In preliminary investigations, increasing costs were related to an increased chance of a worse outcome, such as death (Table 2). Hence, healthcare use costs, either for hospital admission or emergency department access, represented an indicator of pejorative trajectories after a kidney transplant; in other words, higher costs were associated with poorer health.

The results of the univariate linear regression model are reported in Table 3. The beta can be interpreted as the increase (or decrease) in the outcome for each score point of a discrete variable or the presence of a nominal variable. For example, each year of age imports an increase of €216.61 in the total healthcare cost for hospital admissions. Hence, older people had higher healthcare use for hospital admissions, and as higher total healthcare costs for hospital admissions were related to a higher risk of death, they were also exposed to a greater risk of death. The standardized beta describes the strength of the association between the predictor and the outcome, and it is measured in units of standard deviation. The role of age was non-negligible as the change of 1 standard deviation in its value corresponded to a 19.9% of standard deviation in the dependent variable. Overall, only a minority of the predictors were related to the outcomes in a statistically significant manner. The presence of a mood disorder had the greatest impact on the outcomes and was associated with the largest increase in healthcare costs for both hospital admissions and emergency department access. It also had the largest association with the outcomes.

We then proceeded to apply the stepwise multivariable model to evaluate the independent contribution of each predictor taking into account the covariates and the impact of the other predictors.

The model, concerning total healthcare costs due to hospital admissions and emergency department visits in the 2016-2021 period, extracted four variables as predictors of the outcome according to the predefined threshold for removal, with the other variables excluded for their negligible contribution (Table 4).

In this model, the presence of a mood disorder diagnosis, the presence of the somatization cluster, transplant vintage, and blood creatinine were associated with higher healthcare costs due to hospital use [$F_{(4;128)} = 7.88$; $p < 0.001$; $R^2 = 19.6\%$; adjusted $R^2 = 17.1\%$; $f^2 = 0.244$). Effect size, according to Cohen's f^2, was estimated as medium to large. None of the variables in the model had a VIF higher than the suggested cutoff for multicollinearity.

Some diagnostic plots were used for testing the assumptions underlying the linear regression model by taking into account residual errors and fitted values. The model, which focused on total healthcare costs due to hospital use, showed a reasonable adaptation. In the residual vs. fitted plot, the residuals were spread equally around a horizontal line without distinct patterns (and the red line was approximately horizontal near zero), indicating a linear relationship. In the Q-Q plot, the majority of the residuals follow the straight dashed line. In the Scale-Location plot, there was a minor deviation from the homoscedasticity, confirmed by the Breusch–Pagan test (46): BP = 10.22, df = 4, $p = 0.037$. Just one point (case 19) was identified as influential based on Cook's distance (Supplementary Figure 1). We repeated the analysis by

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TABLE 3 Factors associated with total healthcare costs due to hospital admissions and emergency department access in kidney transplant recipients in a univariate linear regression.

	Unstandardized Beta	Unstandardized standard error	Standard beta	*t*	*p*-value	95%CI
Sex (males)	−2370.58	2401.23	−0.085	−0.984	0.327	−7138.26 to 2397.10
Age (years)	216.61	92.96	0.199	2.330	0.021*	32.73 to 400.49
BMI (m^2/kg)	−157.05	324.98	−0.042	−0.483	0.630	−799,71 to 485,60
Time under dialysis (months)	76.69	38.70	0.171	1.982	0.050*	0.14 to 153.24
Transplant vintage (months)	23.91	10.61	0.192	2.253	0.026*	2.92 to 44.89
Estimated glomerular filtration rate (ml/min)	−99.17	45.39	−0.187	−2.185	0.031*	−188.96 to −9.38
Blood creatinine (mg/ml)	5332.61	2055.03	0.220	2.595	0.011*	1267.56 to 9397.67
Blood albumin (g/dl)	−441.94	234.59	−0.162	−1.884	0.062	−905.98 to 22.10
Blood hemoglobin (g/dl)	−2026.10	719.67	−0.238	−2.815	0.006*	−3449.69 to −602.51
Blood phosphate (mg/dl)	2429.32	1727.04	0.122	1.407	0.162	−986.93 to 5845.58
Blood calcium (mmol/l)	152.92	966.00	0.014	0.158	0.874	−1757.92 to 2063.76
Blood vitamin D (ng/ml)	−61.10	101.00	−0.053	−0.605	0.546	−260.90 to 138.69
Past psychopathology (present)	3051.77	2450.89	0.108	1.245	0.215	−1796.33 to 7899.87
ESAS						
ESAS psychological (scale score)	340.93	135.25	0.214	2.521	0.013	73.40 to 608.47
ESAS physical (scale score)	298.69	133.15	0.192	2.243	0.027*	35.29 to 562.09
DCPR diagnosis						
Illness behavior cluster (present)	−475.99	2585.74	−0.016	−0.184	0.854	−5590.84 to 4638.86
Somatization cluster (present)	7149.41	3196.61	0.191	2.237	0.027*	826.20 to 13472.63
Personological cluster (present)	2343.51	2263.13	0.090	1.036	0.302	−2133.18 to 6820.21
ICD diagnosis						
Adjustment disorder diagnosis (present)	−3252.34	3112.10	−0.091	−1.045	0.298	−9408.39 to 2903.72
Anxiety disorder diagnosis (present)	575.72	3713.63	0.013	0.155	0.877	−6770.20 to 7921.64
Mood disorder diagnosis (present)	15372.52	3916.24	0.323	3.925	<0.001*	7625.80 to 23119.24

BMI, body mass index; DCPR, Diagnostic Criteria for Psychosomatic Research; ESAS, Edmonton Symptom Assessment System; ICD, International Classification of Diseases; s.e., standard error; std., standardized; VIF, variance inflation factor. *Statistically significant.

excluding this influential point (Table 5). In the new model, just the presence of a mood disorder diagnosis remained statistically related to healthcare costs due to hospital use, with a decrease in the overall effect size: $F_{(4;127)} = 3.06$; $p = 0.019$; $R^2 = 8.7\%$; adjusted $R^2 = 5.9\%$; $f^2 = 0.095$. According to the diagnostic plots, the model had a good fit, there was no influential point according to Cook's distance, and there was no more deviation from the homoscedasticity (BP = 2.53, df = 4, $p = 0.639$).

TABLE 4 Factors associated with total healthcare costs due to hospital admissions and emergency department access in kidney transplant recipients in a stepwise multivariable linear regression model.

	UB	USE	SB	*t*	*p*-value	95% CI	VIF
Mood disorder diagnosis (present)	14214.12	3795.74	0.299	3.745	<0.001*	6703.61 to 21724.63	1.014
Somatization cluster (present)	6063.72	2976.39	0.162	2.037	0.044*	174.41 to 11953.02	1.007
Blood creatinine (mg/ml)	3949.73	1939.14	0.163	2.037	0.044*	112.81 to 7786.64	1.022
Transplant vintage (months)	21.27	9.89	0.171	2.151	0.033*	1.70 to 40.83	1.008

CI, Confidence interval; SB, Standard beta; UB, Unstandardized Beta; USE, Unstandardized standard error; VIF, variance inflation factor. *Statistically significant.

TABLE 5 Factors associated with total healthcare costs due to hospital admissions and emergency department access in kidney transplant recipients in a stepwise multivariable linear regression model after the exclusion of the influential point.

	UB	USE	SB	*t*	*p*-value	95% CI	VIF
Mood disorder diagnosis (present)	9312.50	3666.12	0.216	2.540	0.012*	2058.45 to 16566.54	1.013
Somatization cluster (present)	3430.03	2810.10	0.103	1.221	0.224	−2130.22 to 8990.24	1.002
Blood creatinine (mg/ml)	3006.24	1805.77	0.141	1.665	0.098	−566.78 to 6579.27	1.008
Transplant vintage (months)	10.20	9.45	0.092	1.079	0.282	−8.50 to 28.90	1.008

CI, Confidence interval; SB, standard beta; UB, unstandardized Beta; USE, unstandardized standard error; VIF, variance inflation factor. *Statistically significant.

4. Discussion

In this study, we found that some psychosocial variables and clinical dimensions influenced total healthcare costs, hence total healthcare use, in kidney transplant recipients. In particular, a propensity to somatization and the presence of a mood disorder increased healthcare use costs for emergency department visits and hospital admissions. Furthermore, greater access to the emergency department and a higher chance of admission to the hospital were related to a greater risk of death in KTRs. These findings underline the need to assess psychosocial dimensions, such as somatization and mood disorder as predictors of healthcare use in kidney transplant recipients and possible risk factors for poor outcomes until death, using the DCPR semi-structured interview and MINI6.0 structured interview, respectively.

Mood disorders were also shown to increase total healthcare costs due to emergency department access and hospital admission. Regarding the former, this is in line with the literature, as approximately 50% of frequent emergency department users have a mental health diagnosis (47) and patients with mood disorders have been found to carry a 3-fold risk of frequent emergency department use (48). Besides a possible increase in emergency department use, higher costs might also be the result of the harmful effect of the mood disorder itself, thus raising the total healthcare costs due to hospital admission. Depression, which represents the most common type of mood disorder, specifically represents a risk factor for graft failure and post-transplant mortality (12), and it is associated with poor adherence to immunosuppressive medication (49). Non-compliance to medications can dangerously affect the outcomes of kidney transplantation (50, 51) and, together with alcohol consumption and cigarette smoking (52, 53), is a hallmark of depression (54). The detrimental effect of mood disorders on physical health might be also explained by other mechanisms, such as autonomic dysfunction (55), impaired cellular immune response (56), heightened inflammation (57), and increased platelet aggregation (58). Finally, in patients affected by mood disorders, harm could also come from treatments, as there is evidence that antidepressant medication use, which represents the most prescribed drug for mood disorders, is associated with increased mortality and all-cause graft failure in the year following transplantation (59). Even though this could just represent an association, the consumption of other medications used to treat mood disorders, such as antipsychotics or lithium, represents instead a well-established risk for poorer physical health (60, 61). In our study, the presence of mood disorders remained a significant predictor of increased healthcare costs even when excluding the influential point.

Regarding somatization, it was found to be a predictor of higher costs. Compared with the general population, this tendency to experience and communicate somatic distress in response to psychosocial stress (and to seek medical help for it) has been associated with a higher hospital length of stay, higher inpatient costs, and more specialist visits (62). Patients with these conditions often present with vague and difficult-to-identify symptoms, leading to detrimental economic effects (63). In fact, the annual medical costs for "somatizers" have indeed been found to be 2.3 times that for a "non-somatizer', with three times as many hospitalizations (62). Furthermore, KTRs affected by this cluster of syndromes might be more exposed to iatrogenic harm (64–67), leading to a further increase in hospital stays, examinations, and costs.

Furthermore, some limitations of our study should be also mentioned. First, the lack of data regarding the costs of ambulatory care and their changes on the basis of psychosocial clinically significant conditions in KTRs. However, it is complex to quantify the economic burden of this activity as it requires the systematic quantification of the additional costs, which is not always comparable, due to the multiple medical and surgical procedures. Second, the absence of a control group with chronic kidney disease in other settings. Third, some demographics, such as the socioeconomic status (68) (a combined measure of education, income, and occupation) of KTRs, biochemical (69, 70), and ultrasound (71, 72) data were not available to better characterize the population. Additionally, the therapeutic protocols to treat chronic kidney rejection, including steroid dosage, and the economic contribution of physical activity levels, both modifiable risk factors of mental health (73–75), were not evaluated. Finally, no healthcare cost before the kidney transplant was collected.

5. Conclusion

This study demonstrated that higher healthcare costs for hospital admissions and emergency department access were strongly predicted by the DCPR diagnosis of somatization cluster and the ICD diagnosis of mood disorder, respectively. In addition, these healthcare costs were associated with a higher risk of poor outcomes until death in kidney transplant recipients. Further studies of cost analysis, cost-effectiveness, cost-benefit, and cost minimization analysis should be conducted to estimate the economic advantages of early diagnosis and treatment of psychosocial syndromes in kidney transplant recipients. Indeed, the healthcare allocation strategy, a pressing question in the transplantation community, should be rethought to invest accurately the resources that are even more limited; therefore, a comprehensive systematic economic analysis of the physical, physiological, and social aspects is needed.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by the Ethical Committee AVEC. The patients/participants provided their written informed consent to participate in this study.

Author contributions

Conceptualization: YB. Investigation: LZ and YB. Formal analysis: AP. Data curation: NN and FG. Writing and editing—original draft: YB and LZ. Writing—review and editing: PE and FB. Supervision: RC and AS. Validation: LG. All authors have read and agreed to the published version of the manuscript.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1158387/full#supplementary-material

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Health economics aspects of kidney transplantation in Sicily: a benchmark analysis on activity and estimated savings

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Background: International and national registries consistently report substantial differences in kidney transplant (KT) activity despite demonstrable clinical and financial benefits. The study aims to estimate the financial resources gained by KT and produce a benchmark analysis that would inform adequate strategies for the growth of the service.

Methods: We analyzed the KT activity in our region between 2017 and 2019. The benchmark analysis was conducted with programs identified from national and international registries. The estimate of financial resources was obtained by applying the kidney transplant coefficient of value; subsequently, we compared the different activity levels and savings generated by the three KT programs.

Findings: The KT activity in the region progressively declined in the study years, producing a parallel reduction of the estimated savings. Such savings were substantially inferior when compared to those generated by benchmark programs (range €18–22 million less).

Interpretation: The factors influencing the reduced KT activity in the study period with the related "foregone savings" are multiple, as well as interdependent. Organ donation, access to the transplant waiting list, and KT from living donors appear to be the most prominent determinants of the observed different levels of activities. International experience suggests that a comprehensive strategy in the form of a "task force" may successfully address the critical areas of the service reversing the observed trend. The financial impact of a progressively reduced KT activity may be as critical as its clinical implications, jeopardizing the actual sustainability of services for patients with end-stage kidney disease.

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KEYWORDS

kidney transplantation, living donation, organ donation, clinical governance, health economics, access to transplantation, kidney transplant waiting list, benchmarking

Introduction

The clinical benefits of successful kidney transplantation (KT) have been consolidated over the course of the last decades by a wealth of evidence that has been globally reproduced. Similarly, the cost-effectiveness of any type of KT compared to other forms of renal replacement therapy (RRT) has been unequivocally demonstrated (1).

Despite the overwhelming evidence indicating the clinical advantages offered by KT for the treatment of eligible patients with end-stage kidney disease (ESKD), associated with the financial savings produced in favor of any healthcare system, the database of the International Registry of Organ Donation and Transplantation (IRODaT) reports substantial variations of the rate of KT/per million population (pmp) between different countries (2). Noticeably, similar differences may be also observed in regions and territories of countries with developed economies and successful ODT programs (3).

The *Centro Nazionale Trapianti* (CNT), the regulatory body of organ donation and transplantation (ODT) in Italy, has consistently reported substantial differences in the organ donation (OD) and KT activity between Italian regions (4).

The study aims to analyze the KT activity in Sicily and estimate the financial resources obtained; subsequently, we produce a benchmark analysis with national and international programs in comparable regions and territories.

The recently proposed methodology (5) that we used in our study for the financial analysis produces results that may constructively inform the wider transplant community, stakeholders of the KT services, as well as decision-makers on future policies and growth strategies beyond the boundaries of our regional program.

Methods

Our study is articulated in two components. In the first part, we have analyzed the OD and KT activity in Sicily between 2017 and 2019. To contextualize the performance of the service, as well as define a potential scope for growth in the region, we have identified two demographically comparable ODT programs that we used for the benchmark analysis.

In the second part of the study, we focused on the financial resources generated by KT activity in the study period.

Rationale for choosing national and international benchmarks

The healthcare system in Italy is devolved to Regional Governments; therefore, the commissioners of the ODT services are part of a healthcare structure that is similar across all 20 Italian regions. In addition, Sicily is an *Autonomous Region* allowing legislation on local matters to be promulgated independently from the National Government.

In Italy, there are no other *Autonomous Regions* with a number of residents similar to Sicily; therefore, we used as a national benchmark for OD and KT activity, the Central Italy region of Lazio that has a number of residents close to Sicily.

The search for a comparable international ODT program to be utilized as a benchmark excluded National programs as comparing a regional with a national healthcare service may be influenced by several biases. Therefore, we searched the IRODaT database for countries with similar population and OD rates to Italy from which we could extract and compare regional data.

The only country reflecting such comparable characteristics with Italy is the United Kingdom (UK) (2). In addition, in the United Kingdom, the devolution of powers to the *Home Nations* (England, Scotland, Wales, and Northern Ireland) on a number of domestic matters including healthcare offers a pertinent similarity with the *Autonomous Region* status of Sicily. In this context, Scotland with a number of residents similar to Sicily and Lazio represents a plausible international benchmark for the benefit of our study.

Data source

The OD and KT activity data of Sicily were obtained from the database of the Regional Center for Transplantation, *Centro Regionale Trapianti Sicilia* (CRTS) (6), and cross-referenced for accuracy with the official national activity reports produced by the CNT (4). The comprehensive regional database includes the ODT activity, the waiting list for a KT from a deceased donor (KTWL), the prevalence of patients with ESKD, and their modality of RRT.

The data for the benchmark comparison were extracted from the reports of the Regional Center for Transplantation Lazio, *Centro Regionale Trapianti Lazio* (CRTL), Regional Registry of Dialysis and Transplant Lazio (RRDTL), and Scottish Renal Registry (SRR) (7, 8). For accuracy, the data were cross-referenced with the reports published by the relevant national authorities, respectively, CNT and NHS Blood and Transplant (NHSBT) (4, 9, 10).

The Scottish Renal Registry data are reported by calendar year, while NHSBT reports by financial year; therefore, the OD and KT reports for Scotland refer to the period from 1 April 2017 to 31 March 2020.

Analysis of organ donation and kidney transplantation activity

The comparability of the national ODT programs in Italy and the United Kingdom was obtained through data extracted from the IRODaT database. The OD activity was evaluated through the rate/pmp of Utilized Donors (UD) defined as *"donors from whom at least one organ was transplanted"* (11). The rate of UD was subdivided into Utilized Donors from Donors after Brain Death (UDBD) and Utilized Donors from Donors after Circulatory Death (UDCD). Almost all

deceased donors in Sicily and Lazio were Donors after Brain Death (DBD), as in the study period the Donation after Circulatory Death (DCD) program was at the initial implementation stage in Sicily, while in Lazio had not yet started.

The national rate of KT/pmp was also included in our analysis, and it was divided into kidney transplant from living donor (KTLD) and kidney transplant from deceased donor (KTDD). The specific typology of KT in Sicily was compared with the respective number of kidney transplants from donors after brain death (KTDBD), KT from DCD, and KTLD in the benchmark programs.

We analyzed the OD and KT activity in Sicily, Lazio, and Scotland for 3 consecutive years, from 1 January 2017 to 31 December 2019. The years 2020 and 2021 have not been included because the ongoing SARS-CoV-2 pandemic did substantially influence ODT activity nationally and internationally (12).

The selected benchmark OD and KT activity programs of Lazio and Scotland will be referred, respectively, as National Benchmark 1 (NBench1) and International Benchmark 2 (IBench2).

Kidney transplantation vs. dialysis

The landmark study of Wolfe et al. (13) demonstrating the survival advantage of patients receiving KT from a deceased donor (DD) vs. RRT paved the way to a wealth of evidence that has been globally reproduced over the subsequent years.

The continuous expansion of KT practice has confirmed not only the survival advantages but also established the superiority in terms of quality-adjusted life years (QALY) of KT vs. any other form of RRT (1), also when considering more challenging and more diverse typology of donors, such as living donors (LD) with blood group incompatible, extended criteria donors (ECD), or donors after circulatory death (DCD).

The survival and QALY advantages of KT are also associated with demonstrable savings. Such savings translate into financial benefits for the healthcare services, naturally extending into wider benefits for the society matured through the return to normal or near normal personal and working life of patients with ESKD. Remarkably, such savings have been quantified allowing a realistic calculation of the financial benefits produced by KT. Among the several publications confirming the positive financial impact of KT, we have identified two separate reports produced by the regulatory bodies of organ donation and transplantation in Italy and in the United Kingdom (CNT and NHSBT). Both national authorities achieve almost identical conclusions regarding the costs of RRT and KT, as well as both indicate that the savings initiate after the first year of a successful KT; thereafter, the savings calculated from the second year of a successful KT are substantially similar. For the benefit of our study, we used the demonstrated saving of €25.000 per year per functioning single KT from the second year of transplantation (14, 15).

Metrics used for the financial analysis

The metrics that we used for the financial analysis are reproduced from a recently published study merging the fixed financial parameters (tariff and savings) together with the reported efficacy of treatment (rate of functioning and non-functioning KT) that are subsequently applied to the efficiency of the service (actual number of KT performed per year).

The reimbursement costs represented by the tariff paid by regional commissioners to healthcare providers (HP) together with the estimated savings produced by each functioning KT, including the tariff costs of each non-functioning KT, represent the financial parameters.

KT Tariff in € = 33.162

Savings in € per functioning kidney transplant per year after first year of KT = €25.000

The efficiency and efficacy parameters used are represented by the total number of KT performed together with the estimated rate of functioning and non-functioning KT extracted from the governance reports of the national regulatory bodies.

Estimated functioning kidney transplant (eFKT) = 80% of total number of KT

Estimated non-functioning kidney transplant (eNFKT) = 20% of total number of KT

These metrics allow a realistic estimate of the savings produced by KT. Specifically, the estimated gross savings (eGrSavs) are achieved by subtracting from the demonstrable savings (obtained by eFKT) the costs inflicted by eNFKT according to the formula:

(eFKT × 25.000) - (eNFKT × 33.162) = eGrSav

The laborious calculation may be simplified by the use of a coefficient defined as the kidney transplant coefficient of value (KTCoV). Such coefficient is produced using the same parameters used to calculate the eGrSav and dividing the result by the actual number of KT performed according to the formula:

(eFKT × 25.000) - (eNFKT × 33.162) / Total number of KT = KTCoV

Or

eGrSav/n. KT = KTCoV

The KTCoV being the product of fixed financial parameters (tariff and savings) and variables (eFKT and eNFKT) that are obtained from the actual denominator (total number of KT) is constant regardless of the number of KT retrospectively or prospectively for any year of KT activity analyzed.

The value that we obtained for the KTCoV is €13.367,6.

The simulations reported in the supplement, with the hypothetical number of 50, 100, or 150 KT per year, confirm that the KTCoV is a constant value as already reported (5); therefore, it will be used in our study for the financial analysis and estimates.

Financial analysis

The savings produced by KT initiated after 1 year of successful KT; therefore, our calculations are based on the activity observed in Sicily and in the benchmarks program in the years 2017–2019 and the savings estimated for the following years, starting from 2018.

The calculation of the estimated gross saving (eGrSav) was achieved by applying the KTCoV to the number of KT. Available evidence applicable to our study indicates that the KTCoV consists of €13.367,6 (5). The analysis aims to

1. calculate the eGrSav produced by the actual KT activity in Sicily in the study years (2017–2019) and
2. compare the eGrSav of Sicily with the Benchmark KT programs for the years 2020, 2021, and 2022.

Statistical analysis

This study is not designed to evaluate a statistically significant difference in the efficiency between the KT program in Sicily and the

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TABLE 1 Utilized donors and kidney transplants in Italy and the UK (2).

	2017		2018		2019	
	Italy	United Kingdom	Italy	United Kingdom	Italy	United Kingdom
UD/pmp (Cumulative)	27.7	21.34	22.6	23.35	22.8	23.01
- UDBD/pmp	27.2	13.18	21.82	14.79	21.7	13.86
- UDCD/pmp	0.5	8.16	0.78	8.56	1.1	9.15
KT/pmp (Cumulative)	41.3	52.95	35.14	55.14	35.3	54.9
- KTDD/pmp	36.3	37.84	30.2	39.5	29.7	39.56
- KTLD/pmp	5	15.11	4.94	15.64	5.6	15.34

benchmark programs that we have selected. However, we focused our attention on the different typologies of KT as determinants of the overall activity; therefore, we calculated, where appropriate, with Fisher's exact test whether the typology of KT may show a statistically significant difference.

The savings produced by KT have not been compared with a statistical methodology as even non-significant differences in finances may still be highly relevant for the commissioning authorities, depending on the status of healthcare service and overall expenditures.

Results

National context and comparability

The population of Italy and the United Kingdom is reported as consisting of 60.4 million and 68.5 million, respectively (16). The rate of UD confirming the comparability of both national OD activities is reported in Table 1. Noticeably, in Italy, the rate/pmp of UDBD is constantly higher than in the United Kingdom, while the KT/pmp rate is substantially higher in the United Kingdom.

Results of organ donation and kidney transplantation activity

The regional and national registries demonstrate consistency of data. The CRTS reports indicate that 71 Sicilian patients received a KT out of the region in the study period. These patients were excluded from our analysis, although such relevant cohort deserves separate considerations. The report of the RRDTL does not include information on the prevalent ESKD patient resident in the region receiving RRT in the form of a KT. However, the absence of such specific information does not affect the focus of our study.

The rate of UD in Sicily declined from 15.4/pmp in 2017 to 8/pmp in 2019. In addition, the overall number of KT progressively decreased from 160 in 2017 to 101 in 2019.

The detailed typology of UD and KT divided by year and in comparison with NBench1 and IBench2 is reported in Table 2.

The average number of patients on hemodialysis (HD) observed in Sicily is similar to the NBench1 (4,327 vs. 4,424) but substantially superior to IBench2 (4,327 vs. 1940). However, the average number of patients on the KTWL in Sicily is substantially inferior to NBench1 (550 vs. 930) and superior to IBench2 (550 vs. 417). Specifically, the KTWL in Sicily represents 12% (550/4554) of the HD and Peritoneal Dialysis (PD) population combined, while in NBench1 and IBench2 are both 19.5% (930/4770 and 417/2147).

There are in total 379 KT reported in Sicily in the study period, while the NBench1 and IBench2 reports show a substantially superior number, respectively, 748 and 830. Notably, the number of KT from DBD in Sicily is similar to IBench2, with a calculated rate/pmp actually superior (23.6 vs. 21.4). The number of KTLD in Sicily is substantially inferior to both the NBench1 and IBench2 (Table 3) with a calculated annual rate of 1.9/pmp in Sicily, 6.6/pmp for NBench1, and 16.8/pmp for IBench2. The typology of KT practice with a higher number of KTLD in both NBench1 and IBench2 programs compared to Sicily is also statistically significant, as summarized in Table 4. In addition, the substantial number of KT from DCD in IBench2 is not comparable with the activity in Sicily representing the initial experience.

Results of financial analysis

The savings produced by KT mature after the first year of transplantation. The eGrSav is calculated by applying the KTCoV (€13.367,6) to the yearly KT activity; therefore, it is directly proportionate to the number of any type of KT performed.

1. The calculated eGrSav is the product of the previous year KT activity; therefore, in 2018, only the activity observed in 2017 may be taken into consideration. Consequently, in 2019, the eGrSav is calculated from the KT activity in 2017 and 2018. Finally, the KT activity of the years 2017, 2018, and 2019 produces the eGrSav of matured in 2020 (Table 5).
2. The same eGrSav matured in 2020 is also available for the years 2021 and 2022. The savings produced by the limited activity during the pandemic years 2020 and 2021 are not included in the study.
3. In Sicily, the estimated savings between 2018 and 2022 reached the amount of €21.053.970. The detailed year-by-year eGrSav is reported in Table 5.
4. The comparison between Sicily and benchmark programs reveals that the cumulative eGrSav matured in the study period was substantially less than both NBench1 and IBench2 (€21.053.970 vs. €40.517.195,6 and €44.474.005,2). The detailed year-by-year eGrSav reported in Table 5 demonstrates the savings accrued in the study period.
5. In Sicily, the highest savings were produced in 2018 (€2,138,816) from the activity of 2017 (160 KT), while the

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TABLE 2 Yearly comparison of RRT population, UD, and KT.

	Sicily	NBench1	IBench2
2017	//	//	//
RRT prevalence	5,106	*	5,177
- HD	4,328 (84.7%)	4,340	1959 (38%)
- PD	235 (4.6%)	356	194 (4%)
- KT	543 (10.7%)	NA	3,024 (58%)
Waiting list	529	922	402
UD/pmp (DBD/DCD)	15.4	24.4	19.3 (11.3/8.0)
KT (Total number)	160	262	287
- KTDD (DBD/DCD)	151	236	203 (128/75)
- KTLD	9	26	84
2018	//	//	//
RRT prevalence	5,056	*	5,318
- HD	4,199 (83%)	4,398	1942 (37%)
- PD	224 (4.5%)	334	215 (4%)
- KT	633 (12.5%)	NA	3,161 (59%)
Waiting list	568	910	439
UD/pmp (DBD/DCD)	9	24.4	17.9 (12.5/5.4)
KT (Total Number)	118	263	263
- KTDD (DBD/DCD)	109	222	167 (113/54)
- KTLD	9	41	96
2019	//	//	//
RRT prevalence	5,126	*	5,436
- HD	4,183 (81.6%)	4,534	1919 (35%)
- PD	221 (4.3%)	348	213 (4%)
- KT	722 (14.1%)	NA	3,304 (61%)
Waiting list	551	958	409
UD/pmp (DBD/DCD)	8.2	21	18.4 (11.9/6.5)
KT (Total number)	101	223	280
- KTDD (DBD/DCD)	90	181	182 (113/69)
- KTLD	11	42	98

*RRDTL does not report the exact number of patients receiving RRT with a KT in the region (7).

TABLE 3 Cumulative comparison of RRT population, UD, and KT.

	Sicily actual	NBench1	IBench2
Average number of prevalent patients with ESRD by type of RRT 2017–2019	5,197	*	5,310
HD	4,327	4,424	1940
PD	227	346	207
KT	643	NA	3,163
Average number of patients on KT Waiting List 2017–2019	550	930	417
Average UD/pmp (DBD/DCD) 2017–2019	10.8 (10.8/0)	23.2 (23.2/0)	18.5 (11.9/6.6)
Cumulative number of KT 2017–2019	379	748	830
KT DBD	348 (91.8%)	639 (85.4%)	354 (42.7%)
KT DCD	2 (0.6%)	0	198 (23.8%)
KTLD	29 (7.6%)	109 (14.6%)	278 (33.5%)

*RRDTL does not report the exact number of patients receiving RRT with a KT in the region (7).

TABLE 4 Comparison of activity by different types of KT.

	KTDD	KTLD	*p*-value
Sicily	350	29	//
NBench1	639	109	0.0007
IBennch2	552	278	0.0001

TABLE 5 Comparison of yearly and 5-year cumulative estimated savings in €.

	Sicily	NBench1	IBench2
2017*	//	//	//
eGrSav in 2018	2.138.816	3.502.311,2	3.836.501,2
eGrSav in 2019	3.716.192,8	7.017.990	7.352.180
eGrSav in 2020	5.066.320,4	9.998.964,8	11.095.108
eGrSav in 2021**	5.066.320,4	9.998.964,8	11.095.108
eGrSav in 2022**	5.066.320,4	9.998.964,8	11.095.108
Cumulative 5-year eGrSav (2018–2022) from KT activity 2017–2019	21.053.970	40.517.195,6	44.474.005,2

*No Savings in 2017 activity as savings begin 1 year after KT. **Cumulative Savings produced only by KT activity in the study period (2017–2019).

lowest savings were €1.350.127,6, those were calculated from the activity reported in 2019 (101 KT) that represented 26.6% of the savings produced in 2020 (€5.066.320,4). The eGrSav produced by the NBench1 and IBench2 is similarly consistent over the years of the study period, as well as being both considerably superior to those generated by the Sicilian program.

Discussion

The acknowledgement that "health financing is a core function of health systems" (17) amplifies the importance of the financial savings that may be produced through improved clinical performance. As importantly, benchmarking the activity volumes and processes contributes to care quality improvement (18). However, finding the most appropriate realistically achievable benchmarks and indicators may be highly challenging, particularly so, in ODT where numerous variables may substantially affect the performance of a program.

Our efforts in finding suitable benchmarks for Sicily were inspired by identifying realistic terms of comparison that could generate achievable objectives, rather than performing an ineffectual comparison with historically highly performing ODT programs *per se* such as those in Spain, the US, or in countries with a smaller population. In this spirit, we opted to analyze exclusively categorical data omitting the production of a statistical analysis of the savings, despite the data we report in our study may be amenable to produce significant *p*-values, when comparing KT activity and savings between Sicily and ODT benchmarks programs.

The considerations on the KT activity and its financial implications in Sicily necessarily require an adequate contextualization with the OD performance and volume of the KTWL.

The observed sharp decline of 47% of UD/pmp (from 15.4/pmp in 2017 to 8.2./pmp in 2019) in Sicily has inevitably impacted on the number of organs available for transplantation in the region and nationally. Available evidence suggests that in Italy, each UD generates on average three organs available for transplantation. Accordingly, five UD may lead to eight kidney transplants (4, 5). The reduction of UD consisting in 6.4/pmp and 7.2/pmp, respectively, in 2018 and 2019 reported in Sicily would account for 66 less UD; consequently, it would translate in at least 104 less kidneys available for the patients active on the KTWL.

Several factors may influence the UD/pmp rate; in particular, it would be valuable establishing whether a progressive contraction of the number of P*otential Donors* (11) is associated with a reduction of consent to donation. Undoubtedly, the combination of such events would lead to a reduced number of UD. Although a regional strategy integrated with the national OD framework will address a consent rate of 50% in 2019 (4), the reduced identification of potential donors, if confirmed, may indicate that a review of the processes, as well as of the service infrastructures and workforce, should be considered.

While the number of organs available for transplantation is the product of the efforts produced by the regional OD network, culminating in the UD rate, another pivotal factor affecting the KT activity is represented by the number of patients active on KTWL.

In Sicily, the proportion of patients with ESKD receiving RRT in the form of HD/PD who are active on the KTWL is inferior to both NBench1 and IBench2. The analysis of the reported data shows that the average number of patients active on the KTWL in Sicily and NBench1 is substantially different (550 vs. 930). Although such observation may suggest that access to transplantation may be highly efficient in NBench1, it is noted that during the study period, an average of 38.5% of KT per year is performed on non-residents of the region (7). In this regard, it should be highlighted that in Italy, patients eligible for a KT may be activated on two regional KTWLs on their request. Implicitly, the evaluation of the regional pathways supporting ESKD patients toward access to transplantation in NBench1 may be arduous if based on this single observation; furthermore, such specific comparison with Sicily may be biased by the presence of more transplant centers (TxC) in Nbench1; five TxC in NBench1 vs. three in Sicily. The discrepancy of the KTWL population between Sicily and NBench1 may therefore be explained by the fact that a substantial number of patients active on the regional KTWL of NBench1 are actually residents of other Italian regions. In support of this explanation, we notice that despite a higher KT activity in NBench1, the number of patients on HD/PD remains very similar to Sicily. A further potentially critical similarity between Sicily and NBench1 is represented by the fact that in both regions, almost 70% of the HD centers are private (6, 7).

The average HD/PD population in IBench2 is substantially inferior to Sicily: 53% less (2,147 vs. 4,554). In addition, the KTWL in IBench2, despite consisting of an inferior number of patients (417), it still produces a higher rate of patients waiting for a KT than Sicily (19.5% vs. 12.5%).

Notwithstanding the fact that it may be arduous finding a valid explanation for the limited access to transplantation, as also reported by other developed ODT programs (19, 20), it may be relevant highlighting that the HD/PD services in IBench2 are entirely public and provided by the National Health Service, while in Sicily such service is largely delivered by private healthcare providers (6). This observation

indicates that adequate governance measures should be implemented to ensure that such prominence of private HD providers might not affect the access to the KTWL, hence limiting the option of KT that remains the gold standard of treatment for patients requiring RRT (21).

In the light of these observations, it may be sustained that the pool of patients who would be eligible for a KT in Sicily is currently underrepresented by the regional KTWL. Therefore, access to transplantation represents a critical aspect of the regional ODT services. In particular, adherence to the *Kidney Disease: Improving Global Outcome* (KDIGO) guidelines (22), concerning access to transplantation, would require the enhancement and consolidation of the interactions between the renal network and transplant centers (TxC).

The overall number of 379 patients who had a KT in Sicily produces a yearly average rate of 25.3/pmp in the study period, which is substantially below the national Italian average of 37/pmp.

The cohort of 71 patients, who were transplanted out of the region in the study period, is a further contributing factor in generating a wider gap between regional and national average of KT/pmp. In fact such difference would be reduced if the KT would have been carried out in one of the Sicilian TxC. The expected costs for this cohort, generated by a tariff of €33.162 per KT, amount to €2.354.502. However, such expected costs may be an underestimate as out of the region healthcare providers (HP) may apply different tariffs. In addition, patients may be entitled to the reimbursement of part of the travel and subsistence expenses representing a further aspect of the social costs of the phenomenon of "internal emigration" for KT that is met primarily by patients.

The difference between the calculated eGrSav of Sicily with those generated by the KT activity in NBench1 and IBench2 may be regarded as substantial *"Foregone Savings"* for the Sicilian healthcare services, strengthening, beyond the established clinical benefits, the scope for growth of the KT service (Table 5).

The contributing factors may be multiple, and some may be corrected or mitigated. The diversification of KT typology observed in IBench2 that includes high rates of KT from DCD and KTLD allows the service not to rely exclusively on DBD. The data analyzed, in fact, indicate that the rate of UDBD and average number of KT from DBD in Sicily and IBench2 are substantially identical. Consequently, the reduction of the KTWL in IBench2 reflects the fact that the majority of patients with ESRD (60%) receive RRT in the form of a KT, because of the more diversified typology of KT including DCD and KTLD.

Such consolidated practice that has been sustained in the course of the last decade in IBench2 has undoubtedly contributed to achieve substantial savings for the wider healthcare service. It may be argued that if the same KT activity was replicated in Sicily over the study period, the savings over the 3 following years may exceed €50 million as suggested by our estimate. Noticeably, the eGrSav produced in our analysis (Table 5) represents the minimal savings that can be obtained from KT activity. In fact, the reports of both CNT and NHSBT indicate a sustained GS at 5 years well above 80%; hence, indicating that the actual savings produced by a superior number of functioning kidney transplants could be more conspicuous than actually indicated in our analysis.

The benchmark activity identified for the benefit of the study may be reproducible in Sicily, provided that a comprehensive strategy recognizing ODT as a unique healthcare entity scientifically and financially interdependent may be designed by the stakeholders of the service (5). The successful implementation of adequate measures aimed to reverse the observed trend in OD and KT could be addressed comprehensively with the institution of a regional "task force" integrated with a national strategic plan of the growth of the service.

International experience in this regard supports such approach. The most clear example of a successful implementation of a comprehensive strategy may be identified in the United Kingdom; where following the institution of the OD Task Force in 2006 and the implementation of its recommendations, it was observed a remarkable countrywide increase of UD and KT in the course of the following decade (23).

A potentially successful pathway that may be followed is represented by the Spoke-and-Hub model aimed to consolidate the ODT network on the island of Sicily. Such model, already suggested and successfully implemented in other healthcare services (24) including Sicily itself (25), may address the critical aspects of the ODT services that we have presented. Undoubtedly, an effective and capillary network strongly linked with the centers of excellence operating in the Sicilian territory would allow more patients to access the better option of RRT represented by KT either from a DD or a LD, ultimately reproducing the well-recognized benefits to the patients, their families, and the finances of the regional healthcare services.

The financial impact of a progressively reducing KT activity may be as critical as the clinical implications of a large population on HD/PD, in particular taking into consideration those patients eligible for a KT who may be suspended from the KTWL (26). The incremental costs of healthcare in the context of a global crisis and financial insecurity, inevitably will jeopardize the sustainability of a number of services. It may be conceived that a progressive investment in resources, parallel to the increment of savings produced, may constitute a realistic budget aimed to guarantee the growth and, ideally, the financial self-sufficiency of the OD and KT services.

Healthcare systems funded by taxpayers may not afford to miss potential financial resources; certainly, regular evaluation of performance following extensive benchmarking processes, as well as constructive clinical governance, would be of paramount importance (27, 28).

The health economics of KT constitutes a highly challenging area of healthcare with undervalued potentials and unexplored benefits. Our study does not have the ambition to address all the issues generated by the health economics of KT; similarly, we do acknowledge the limitations of our study and the proposed model.

The recent proposal of new metrics merging demonstrable financial and clinical outcomes (savings/rate of FKT) requires a more contemporary validation. In fact, the actual costs of RRT, including KT, on which we, as most of the other authors on the topic, have based the financial analysis are now a decade old, or actually older. Furthermore, the continuously evolving practice of organ donation associated with the growing use of new and expensive technologies such as Normothermic Regional Perfusion or *ex situ* organ reconditioning (30) will require to be factored in the general costs of the ODT services affecting also the cost analysis of KT. Relevantly, the necessary expansion of the donor pool, through the implementation of DCD programs, as well as an increased utilization of extended criteria donors aimed to treat an increasingly more complex pool of patients with ESKD, is linked to heterogenous graft survival rates. Although such diversified donor and recipient pool characterizing contemporary practice in KT still produces a survival advantage of KT vs. any other forms of RRT (1) as demonstrated by the governance reports on which we based the rate of FKT for the production of the KTCoV, a more granular and visible governance processes would be required to satisfy the expectations of commissioners, wider transplant community, and patients.

The more accurate definition of a budget generated by the eGrSav produced by KT activity certainly would be gladly received; however, it may generate some repercussions on the management of the allocation of healthcare resources that, in current times, have been progressively restricting. From this perspective, it should be highlighted that our proposed model does not identify a "new" stream of funding; instead, it allows a reliable estimate of financial resources that are already available but not as visible as they could, particularly so in a regional healthcare budget. In our opinion, the funding method for the whole ODT services may benefit from accurate budgeting provided that it will be addressed as a unique and interdependent healthcare entity (5).

Our analysis focusing on the health economics of KT does not include the social costs and financial benefits that the regional community may undoubtedly enjoy. The overall considerations on such beneficial aspects of successful KT would require an accurate evaluation of the return to usual activities not only of the patients with ESKD but also of the positive impact that may be observed on the immediate families.

The methodology we suggest may potentially be applied to any KT program with adequate corrections to the parameters determining the KTCoV. The tariffs paid by commissioners to HP for KT services may vary between regions and countries; similarly, the actual HD/PD cost may be different producing different savings. Therefore, despite the fact that the same method may be applied, it may produce different KTCoV that consequently may be lower or actually higher than the one we have calculated. As importantly, in the same healthcare service that we have analyzed in our study, the actual tariffs may be revised by the commissioners, as well as HD/PD costs may be affected by discount rates and inflation. Necessarily, the application of the methodology we suggest for the calculation of a reliable eGrSav will require regular financial ad clinical outcome auditing to obtain a well-grounded calculation. Although a necessary regular validation of costs and clinical outcomes may be interpreted as a limitation, financial planning offices will easily source the relevant information from HP and regulatory bodies, guaranteeing a solid and reliable calculation of the KTCoV and eGrSav.

In conclusion, our study identifies that in Sicily, a number of critical areas would require the implementation of simultaneous interventions to reverse the current trend of performance. The application of recently proposed health economics metrics applied to the activity of the KT program in Sicily, followed by a benchmark analysis with other programs active in comparable territories, indicates that a progressively improved efficiency of the KT activity could be associated with increased savings that may subsequently lead to potential reinvestments in the ODT services, wider healthcare services, and new technologies aimed to reduce the chronic shortage of organs available for SOT (29).

We trust that our analysis may contribute to advance future dialogs between stakeholders of the services as the timing for the implementation of adequate strategies appears already critical because of the constant reduction of KT activity that was observed in the years preceding the SARS-CoV-2 pandemic; necessarily, it requires now the highest level of attention.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

RC, FL, LG, EC, IC, LT, DS, and GT: rationale of the study and original draft of the manuscript. RC, EF, LT, IC, and RC: final revision. SG, DP, CM, MV, MC, and IC: data collection and interpretation. CM and RA: literature review. LG, FL, and EF: editing. RC, LT, and EC: supervision. LG, IC, and RA: logistics. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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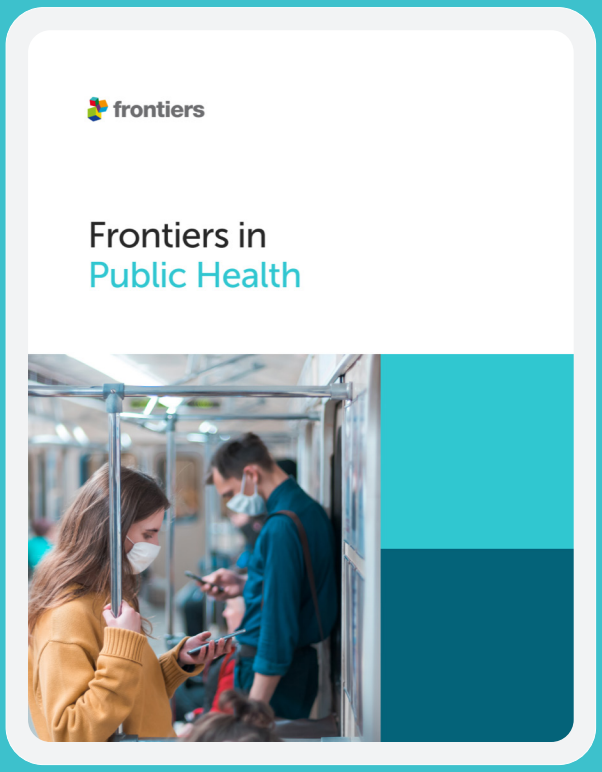

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