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Solid Organ Transplantation During COVID-19 Pandemic: An International Web-based Survey on Resources' Allocation

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Background. Solid organ transplants (SOTs) are life-saving interventions, recently challenged by coronavirus disease 2019 (COVID-19). SOTs require a multistep process, which can be affected by COVID-19 at several phases. **Methods.** SOT-specialists, COVID-19-specialists, and medical ethicists designed an international survey according to CHERRIES guidelines. Personal opinions about continuing SOTs, safe managing of donors and recipients, as well as equity of resources' allocation were investigated. The survey was sent by e-mail. Multiple approaches were used (corresponding authors from Scopus, websites of scientific societies, COVID-19 webinars). After the descriptive analysis, univariate and multivariate ordinal regression analysis was performed. **Results.** There were 1819 complete answers from 71 countries. The response rate was 49%. Data were stratified according to region, macrospecialty, and organ of interest. Answers were analyzed using univariate-multivariate ordinal regression analysis and thematic analysis. Overall, 20% of the responders thought SOTs should not stop (continue transplant without restriction); over 70% suggested SOTs should selectively stop, and almost 10% indicated they should completely stop. Furthermore, 82% agreed to shift resources from transplant to COVID-19 temporarily. Briefly, main reason for not stopping was that if the transplant will not proceed, the organ will be wasted. Focusing on SOT from living donors, 61% stated that activity should be restricted only to "urgent" cases. At the multivariate analysis, factors identified in favor of continuing transplant were Italy, ethicist, partially disagreeing on the equity question, a high number of COVID-19-related deaths on the day of the answer, a high IHDI country. Factors predicting to stop SOTs were Europe except-Italy, public university hospital, and strongly agreeing on the equity question. **Conclusions.** In conclusion, the majority of responders suggested that transplant activity should be continued through the implementation of isolation measures and the adoption of the COVID-19-free pathways. Differences between professional categories are less strong than supposed.

(*Transplantation Direct* 2021;7: e669; doi: 10.1097/TXD.0000000000001115. Published online 11 February, 2021.)

Received 28 August 2020. Revision received 31 October 2020.
Accepted 7 November 2020.

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This study was supported in part by a research grant of the Catholic University of Rome and by a special grant from the Italian Society of Organ Transplantation. The authors of this manuscript have no conflicts of interest to disclose as described by *Transplantation Direct*.

A.W.A. and F.G. did concept and design. A.W.A., S.A., G.B., P.B., F.G., F.G., P.M., G.D.R., S.S., and A.V. participated in analysis and interpretation of data.

A.W.A., F.G., and S.S. drafted of the article. A.W.A., G.d.R., and A.V. did statistical analysis. A.W.A. and F.G. obtained funding. S.A., A.W.A., P.B., G.B., F.G., F.G., G. D.R., P.M., S.S., and A.V. did critical revision of the article for important intellectual content. A.W.A. and P.B. did supervision.

A.W.A. had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data management.

*A list of "COVID-19 and Solid Organ Transplant Study Group" is given in "Acknowledgments" footnote.

Supplemental digital content (SDC) is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (www.transplantationdirect.com).

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ISSN: 2373-8731

DOI: 10.1097/TXD.0000000000001115

BACKGROUND

On March 12, 2020, the coronavirus disease 2019 (COVID-19) was declared by the WHO as a worldwide pandemic. Since then, the infection risk has increased dramatically. COVID-19-related mortality is particularly high in solid organ transplant (SOT) recipients (12%–21% for liver,^{1–3} 14%–30% for kidney,^{4–12} and 27%–33% for heart transplants).^{13–15} These facts led to restrictive approaches in the management of donors and recipients to maintain a safe level of activity (ie, temporary suspension or reduction, transplant of the more urgent cases).

SOTs require a multistep process, which can be affected by COVID-19 at several phases (workup and waiting time, hospitalization, early and long-term follow-up) with the involvement of different healthcare professionals and the prompt need for dedicated resources. The main issues posed by the pandemic include decisions around whether SOTs should continue; to establish rules transplant priority; and to identify strategies to mitigate infectious risk. Decisions may vary within and across countries, depending on the local ability to mobilize human and capital resources for the pandemic. Reports from national registries and reviews have shown that transplant activity significantly decreased in Europe, America, Asia, and Australia.^{16–24}

Health systems have shifted resources to this emergency, challenging the availability of hospital means (intensive care unit [ICU] beds, healthcare providers, blood products) for the management of other complex diseases. As health urgencies, COVID-19 patients and patients waiting for transplants are competing for resources.^{25–28} According to the principle of equity,²⁹ everyone should have a fair opportunity to attain their full health potential, and no one should be disadvantaged from achieving this potential. Ideally, SOT programs should draw on this principle to prioritize transparently recipient selection and to optimize donor-to-recipient matching.^{30–33} There is wide variability across countries in terms of different types of health systems, doctor subspecialties involved in SOT or COVID-19 patient care, organs of interest, and rates of SOT activity. Whether these factors influence the decision of continuing or not is unknown. Economic (gross domestic product [GDP], inequality-adjusted human development index [IHDI]) and epidemiological factors (daily deaths and confirmed cases) may also impact national and regional pandemic management.³⁴

This survey was designed to provide an international snapshot about opinions on resources' allocation and management of COVID-19 risk in SOTs. The implementation of some of them may inform practice and policies in the absence of "ad hoc" studies.

MATERIALS AND METHODS

Survey Design

The Fondazione Policlinico Universitario "Agostino Gemelli" IRCCS working group designed the survey according to the CHERRIES guidelines³⁵ after the outbreak of COVID-19 in Asia and at the beginning of infection spread in Italy. The group included SOT-specialists (surgeons, referring doctors, transplant physicians, transplant coordinators, ICU transplant doctors), COVID-19-specialists (ICU doctors, infectious disease doctors, pulmonologists, internists), and medical ethicists focused in transplant-related issues.

The working group decided the modality of identification of responders. The group included 14 researchers (4 transplant surgeons, 2 referring doctors, 1 transplant physician, 3 intensivists, 1 pneumologist, 1 infectiologist, 1 internal medicine doctor, 1 medical ethicist). The working group members were from Italy (5), United Kingdom (3), Spain (2), United States (2), Japan (1), and New Zealand (1). Before making the survey live, the link and the progression between questions were tested. The survey was approved by the local Institutional Review Board. Information about the consent and the time of response were registered. All data were anonymous. Additional information is available at ClinicalTrials.gov (NCT048367896).

Recruitment of Responders and Administration of Survey

Multiple strategies were adopted to recruit potential responders according to recent literature.^{36,37} The initial recruitment was by the identification of corresponding authors of papers reported in 2019 in the Scopus-Elsevier database. Three categories of authors were identified: transplant specialists (A), critical care specialists (B), and transplant ethicists (medical ethicist, medical practitioner) (C). For each A and B categories, the first 2000 e-mail addresses of corresponding authors were downloaded, whereas for category C, only the first 250 addresses were downloaded. There were 451 duplicate addresses. The survey was then e-mailed to 3799 addresses. Eighty-seven e-mails returned back as unknown. The valid address number was then 3712. This number was used as the denominator for the calculation of the response rate. The survey language was English.

The survey was also published on websites of several scientific societies as reported in the acknowledgments section, and the hyperlink was published in 2 international COVID-19 transplant webinars. The survey was hosted on the CASTOR ECD platform from March 24, 2020, to April 17, 2020 (<https://c19-transplant.castoredc.com/>). The option to forward the link by e-mail was allowed. According to the American Association for Public Opinion Research, only answers with at least 80% of questions were considered complete and then analyzed.³⁸

Survey Sections

The survey included 3 sections (Table 1).

Section 1

Nine demographic questions (self-identified gender, country, local health system specification, capacity and other characteristics of the local hospital, clinical specialty, years and level of experience, organ of interest).

Section 2

Twelve questions about transplant policy during the COVID-19 pandemic (including 2 questions on the perception about equity/inequity and 1 question on the consent to be transplanted during the pandemic).

Section 3

Three technical domains (screening, isolation, and pathway) were considered. The survey included skip logic and branching. Additionally, 2 comment boxes were provided to elucidate reasons guiding decisions about resources' allocation.

Questions and Dependent Measures

The main questions were as follows:

- a. "Given the COVID-19 outbreak, should transplant activities be stopped?" with 3 possible answers (completely, selectively, and not at all).
- b. "I feel that the current policy to allocate most resources to COVID-19 meets the equity of access in healthcare for different diseases" with 4 possible alternative answers (strongly agree, partially agree, partially disagree, and strongly disagree).

Regrouping and Stratification Methodology

The answers were stratified according to the following criteria:

- a. *Arbitrary subdivision in country macroregions* (Italy, Europe except-Italy, Americas, Africa-Asia-Australia). Italy (N = 600) was separately considered from Europe except Italy (N = 499); North America (N = 261), Central America (N = 5), and South America (N = 80) were grouped together, as well as Asia (N = 156), Africa (N = 27), and Australia (N = 17).
- b. *Arbitrary subdivision in areas of interest* (transplant area, COVID-19 area, transplant ethicist area). Transplant area included transplant surgeons, referring doctors, transplant physicians, transplant coordinators, transplant ICU doctors. COVID-19 area contained COVID-19 ICU doctors, infectious disease doctors, pulmonologists, and internists.
- c. *Organ of interest*. In the transplant area, a further stratification according to the organ of interest was made (kidney or kidney-pancreas, liver, liver and kidney, cardiothoracic organs).

Daily Correlations Between Demographic, Epidemiological Data and Answers

The 3 answers to the main question were correlated with the following variables collected by databanks (number of deaths and number of infected cases in each country on day of the survey filling,³⁹ 2019-IHDI and 2019-GDP⁴⁰) and with the data entered by responders (demographic data, macroregions, specialty data, organ of interest, and rating of the agreement on the equity policy according to a 4 level Likert scale: strongly agree, partially agree, partially disagree, and strongly disagree).

International Study Group of Collaborators and Interpretation of the Results Through Free-text Analysis

Following the preliminary analysis, a confidential draft including tables and figures was e-mailed to 638 responders giving their willingness to participate in data interpretation. Ninety-two (14.4%) of them commented on the results of the survey and were included in the study group of collaborators. Responders were not reinterviewed. Two authors (FG and SS) independently analyzed free-text comments and identified 3 overarching themes. The themes described the prevalent viewpoints regarding resources' allocation and SOT management during the pandemic.

Statistical Analysis

The study was performed according to guidelines for health estimates reporting and in respect of recommendations for

multivariable analysis in SOT.^{41,42} Regarding epidemiological and economic parameters, data augmentation and wrangling were performed using Julia (1.4.0).⁴³ Missing data were not imputed. After the descriptive analysis, univariate and multivariate ordinal regression analysis was performed. Variables with a $P < 0.2$ at univariate analysis were included in the multivariate analysis. The strength of the relationship was expressed as generalized R^2 . B-coefficients, SE, R^2 , and area under the curve obtained by receiver operating characteristic curve were reported. Statistics were performed using SPSS (25.0), JMP (14.0), and R (3.6.3). The $P < 0.05$ was considered significant.

Analysis of free comment boxes was performed thematically⁴⁴ using the Nvivo (12.0) package.

RESULTS

There were 1819 complete surveys from 71 countries (Figure 1). The response rate in terms of ratio between the number of responders at least to 1 question and the number of valid e-mail addresses was 49.0%. Overall, 1243/1819 responders (68.3%) answered all the questions. Seventy-seven point three percent of the included participants answered the main question (IQR, 72.9-87.0).

Main Descriptive Analysis

The main descriptive crude analysis is reported in Table 1. Most responders were transplant surgeons (32.3%), heads of the team (47.7%), used in public university hospitals (63.5%), or in countries with public health system with universal coverage (72.5%). Regarding the transplant policy, overall, 90.7% of responders suggested to continue transplant activity (selectively 70.3%, without restriction 20.4%), and 9.3% suggested to stop completely the activity during pandemic. The main reason for not stopping was to avoid organ wasting. However, a large number of responders suggested to weight case by case the transplant risk/benefit ratio. The main reason for selectively stop was the need to warrant transplant in very sick candidates (patients with acute organ failure or advanced chronic diseases and short-life expectancy). Finally, the main reason for completely stopping was the absence of safety due to the potential higher risk of Severe Acute Respiratory Distress Syndrome Coronavirus 2 (SARS-CoV-2) infection and COVID-19 mortality in the context of immunosuppression.

Notably, the majority of responders agreed on the need of double test screening at the admission (oropharyngeal swab/serology), pretransplant isolation, and COVID-19-free ICUs. Finally, they suggested to stop mainly kidney and kidney-pancreas transplants.

Stratification According to the 3 Main Question Answers

The characteristics of responders according to the 3 main-question answers are reported in Table 2 and in Figure 2A. There were differences related to regions, experience levels, health systems, posttransplant ICU management, and feeling of equity in resources' distribution.

Importantly, responses from Italy included a higher prevalence of "continue activity without restriction" and a lower prevalence of "completely stop" than in other countries, even during the highest acuity of COVID-19.

Stratification According to Nations and Regions

A more in-depth stratification according to each nation and each region is reported in Figure 3 and in Table S1 (SDC, <http://links.lww.com/TXD/A310>). In Europe excluding-Italy, there was the highest proportion of transplant-area doctors (76.1%). In the 3 remaining regions, a higher proportion of

COVID-19-area doctors were observed. Medical ethicists were a minority across all the regions. The most represented category in the transplant area was liver transplantation. Overall, among responders, 19.8% suggested not to stop SOTs. In this group, Italy showed the highest proportion (37.6%) of “not at all” answers.

TABLE 1.

Question and answers

No.		Question	Answers	Rate (%)	Reply rate to each question (%)
1.1	Demographic	Self-identified gender	Female	38.3	93.9
			Male	61.7	
1.2	Demographic	Country			90.4
1.3	Demographic	In your country, which kind of health system do you have?	Public health system with universal coverage	72.5	90.3
			Mainly a public health system, but without universal coverage	12.6	
			Mainly private health system	14.4	
			Only private health system	0.5	
1.4	Demographic	What is your hospital capacity?	≤500 beds	21.4	88.5
			>500 beds	78.6	
1.5	Demographic	What is your position?	Transplant surgeon	32.3	99.7
			Transplant physician/referring doctor	24.5	
			ICU doctor/anesthetist	20.7	
			Ethicist	4.6	
			Transplant coordinator/nurse	3.6	
			Pulmonologist/infectious disease specialist	3.2	
			Internist doctor	3.0	
			Other (researcher, psychologist, resident, etc...)	8.1	
1.6	Demographic	What is your level of experience	Trainee	10.7	85.9
			Appointed	41.6	
			Head of team/Clinical Lead	47.7	
1.7	Demographic	How many years of experience do you have in clinical work?	≥10	74.9	85.6
			<10	25.1	
1.8	Demographic	What type of hospital do you work?	Public University Hospital	63.5	84.9
			Private University Hospital	15.1	
			Public Hospital	14.7	
			Private Hospital	6.7	
2.1	TRANSPLANT POLICY	Given the COVID-19 outbreak, should organ transplantation programs be stopped?	Completely	9.3	87.0
			Selectively	70.3	
			Not at all	20.4	
2.1.1 ^b	TRANSPLANT POLICY	If you think transplant programs should be stopped, please specify why? Here you need to provide the option to select more than 1 answer	Transplant in this phase is unsafe due to the potential higher risk of SARS-CoV-2 infection in the context of immunosuppression with potential higher mortality	76.0	7.8
			SARS-CoV-2 infection may be more severe in the early posttransplant period	38.7	
			SARS-CoV-2 could reduce the survival chance in case of postoperative pulmonary complications	32.1	
			Other (please specify)	25.5	
2.1.1.1	TRANSPLANT POLICY	If you have answer other please specify:			1.9
2.1.2 ^b	TRANSPLANT POLICY	If you think transplant programs should be stopped selectively, please choose 1, or more than 1 option below:	Transplantation should be avoided in areas with a high COVID-19 rate (eg, Wuhan, North of Italy, Iran, South Korea, and Spain)	29.0	57.9
			Transplantation should be avoided if limited intensive care unit beds,	41.5	
			Transplantation should be offered only to very sick candidates, including acute organ failures or advanced chronic diseases with short-life expectancy (from few days to few weeks)	62.0	
			Transplantation should be offered only to patients that fully fill 3 conditions (very-low perioperative risk, high risk of dropout from the list, and an implemented SARS-CoV-2-free pathway)	36.0	
			Transplantation should be provided only in a hospital with an implemented SARS-CoV-2-free pathway	34.7	

Continued next page

TABLE 1. (Continued)**Question and answers**

No.		Question	Answers	Rate (%)	Reply rate to each question (%)
2.1.3 ^b	TRANSPLANT POLICY	If you think transplant programs should be SELECTIVELY stopped, please choose 1, or more than 1 option below:	Stop deceased donor kidney transplants Stop deceased donor kidney transplants, unless urgent conditions Stop deceased donor kidney transplants EXCEPT in hyperimmune recipients, taking the risk of higher doses of immunosuppressive therapy Stop deceased donor kidney-pancreas transplants Stop deceased donor liver transplants Stop deceased donor liver transplants EXCEPT in very-high-risk recipients Stop deceased donor liver transplants EXCEPT in very-low-risk recipients Stop deceased donor THORACIC transplants Stop deceased donor THORACIC (HEART, LUNG, and HEART/LUNG) transplants EXCEPT in high-risk recipients	15.8 48.7 21.5 32.5 5.8 41.2 12.2 10.4 39.1	55.6
2.1.4 ^b	TRANSPLANT POLICY	If you think that transplantation programs should NOT be stopped, please choose 1, or more, reasons below:	COVID-19 infectious risk is similar before and after transplantation In case of transplant from deceased donor, if the transplant will not proceed the organ will be wasted Transplant risk/benefit ratio should be weighted case by case Posttransplant immunosuppressive treatment may prevent severe pulmonary damage in case of COVID-19 infection	11.2 30.5 77.5 9.9	16.3
2.2	TRANSPLANT POLICY LIV-ING DONOR	Given the possibility to plan Living Related transplantation, in which of the following circumstances they should be performed during COVID-19 pandemia?	In urgent cases In all the scheduled cases Never	60.9 8.3 30.8	77.3 ^a
2.3	WORKUP for LIV-ING DONOR	Should workup of both Donor and Recipient (eg, imaging, functional evaluation) for Living Related Transplantation program be postponed avoiding the access to the hospital services and exposure to COVID-19 risk?	Yes No No, maintained in urgent cases	46.4 7.3 46.3	75.6 ^a
3.1	EQUITY	Please rank the following statement "I feel the current policy to allocate most resources to COVID-19 meets the equity of access in healthcare for different diseases"	10 strongly agree—0 strongly disagree		69.3
3.2	EQUITY	Do you have any comments to the previous question?			20.4
3.3	EQUITY	Do you agree or disagree with the following statement: "In the present pandemic setting shifting resources from Transplantation to COVID-19 emergency is at the moment the best available strategy despite breaking the equity principles"	Strongly agree Partially agree Partially disagree Strongly disagree	33.4 48.9 13.1 4.6	68.8
2.8	CONSENT	Should the all candidates for transplantation sign an additional consent-form accepting a minimal EXTRA hospital-risk to take an additional risk of COVID-19 infection?	Yes No	79.4 20.6	72.9 ^a
2.5	SCREENING	Provided that all deceased donors are screened with a swab for COVID-19, would you recommend to test also all transplant recipients before grafting?	Yes No	94.3 5.7	74.2 ^a
2.5.1	SCREENING	If you answer YES, when recipients should be screened?	At listing On the day of the admission for the transplant Both	5.1 56.9 38.0	66.6 ^a
2.5.2	SCREENING	If you answer YES, how recipients should be screened?	Oral swab Serology Both	35.1 6.3 58.6	66.5 ^a
2.6	SCREENING	Should recipients be screened with dual test approach including swab and chest-CT scan in asymptomatic patients (better diagnostic accuracy) to exclude COVID-19 pneumonia before scheduled transplantation?	Yes No	69.9 30.1	73.3 ^a
2.9	SCREENING	All healthcare workers in the transplant center should be screened for COVID-19?	Yes No	79.9 20.1	72.9 ^a

Continued next page

TABLE 1. (Continued)

Question and answers

No.	Question	Answers	Rate (%)	Reply rate to each question (%)
2.7	ISOLATION How do you feel we should manage isolation in transplant patients?	Transplant candidates and transplanted patients should be isolated independently from the COVID-19 status Transplant candidates and transplanted patients should follow the same policy as for the general population Transplant candidates, recipients, and their carers should be routinely screened to diagnose a COVID-19 latent infection.	54.1 19.9 26.0	72.3 ^a
2.4	PATHWAY Regarding patients admitted to ICU after transplant, please choose which of the following options in your opinion describe the best management.	Patients who are in the postoperative period after transplant must be hospitalized in different ICUs from those with COVID-19 patients Patients who are in the postoperative period after transplant may be hospitalized in the same ICU only different staffs will look after them	90.1 9.9	74.3

^aNumbers of answers "I do not have an opinion" were excluded by % calculation.

^bMultiple-choice answer.

COVID-19, coronavirus disease 2019; ICU, intensive care unit; SARS-CoV-2, severe acute respiratory distress syndrome coronavirus 2.

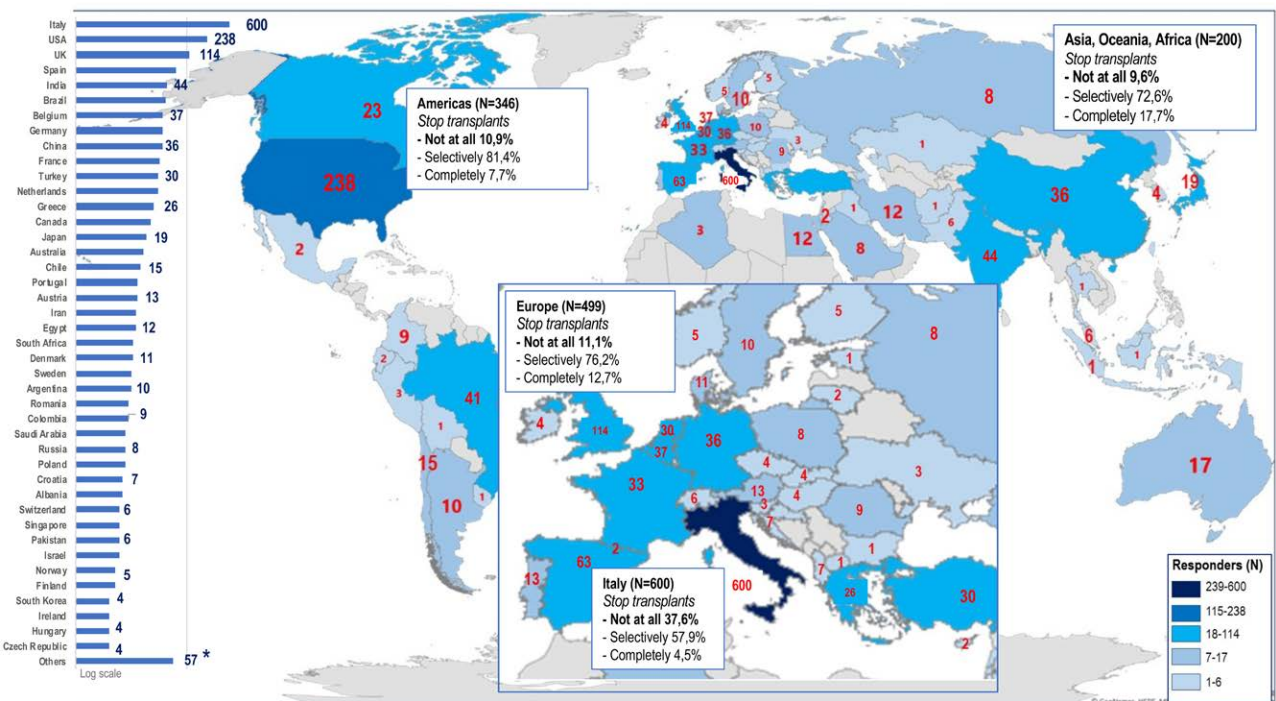
Overall, 70.7% of the responders suggested “selectively” stopping SOTs, and 9.5% suggested to “completely” stopping SOTs during the pandemic. Regarding resources’ distribution, 82.3% of responders “strongly [33.5%] or partially [48.8%] agreed” to temporarily shift the resources to COVID-19 patients. The highest proportion of “strongly partially disagree” was observed in Italy (22.4%), whereas the highest proportion of “strongly partially agree” was observed in the Americas (89.0%) (Figure 4).

Furthermore, 60.7% of responders suggested to restrict the activity to “urgent” cases of living-donor transplants. The highest proportion of “never stop living-donor-SOTs” was in Europe (38.4%), followed by the Americas (37.6%), Italy (25.7%), and Eastern countries (13.8%) (Figure 5).

Two further subanalyses were carried out about stopping transplants (red area regions versus all other regions in Italy and EAST-cost states versus all other states in United States) (Table S2, SDC, <http://links.lww.com/TXD/A310>).

Macrospecialty Stratification

Answers were also stratified according to macrospecialties of responders. In detail, 17.9% of responders from the transplant area and 23.3% of the COVID-19 area suggested not to stop “at all” SOTs. In the Ethicists’ group, this rate was 44.1% (Figure 2B; Table S3, SDC, <http://links.lww.com/TXD/A310>). Finally, 33.5% of the responders, stratified by specialty, strongly agreed with the equity of resources’ allocation (transplant area 34.7%, COVID-19 area 33.4%, medical Ethicists 9.8%).



*Others refers to 32 nations (3 with 4 responders, 3 with 3 responders, 10 with 2 responders, 16 with only one responder).

FIGURE 1. A total of 1819 participants to the survey from 71 nations.

TABLE 2.

Overall stratification according to 3 main question answers

	CONTINUE ACTIVITY		Selectively STOP		Completely STOP		Total	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Region								
Italy	200	37.6	308	57.9	24	4.5	532	100.0
Europe	51	11.1	349	76.2	58	12.7	458	100.0
Americas	34	10.9	254	81.4	24	7.7	312	100.0
Asia Africa Oceania	17	9.7	127	72.6	31	17.7	175	100.0
Experience level								
Trainee	45	29.2	90	58.4	19	12.3	154	100.0
Appointed	120	19.9	432	71.5	52	8.6	604	100.0
Head of Team	137	19.1	515	71.7	66	9.2	718	100.0
Health System								
Public, universal coverage	250	23.2	727	67.6	99	9.2	1076	100.0
Public, no universal coverage	29	15.9	131	72.0	22	12.1	182	100.0
Mainly private	22	10.3	175	82.2	16	7.5	213	100.0
Only private	1	16.7	5	83.3	0	0.0	6	100.0
ICU after transplant								
Different ICUs	239	20.1	832	69.9	120	10.1	1191	100.0
Same ICUs, different staffs	26	20.0	95	73.1	9	6.9	130	100.0
Equity resources distribution								
Strongly agree	38	9.2	288	69.4	89	21.4	415	100.0
Partially agree	132	21.7	455	74.7	22	3.6	609	100.0
Partially disagree	52	31.9	108	66.3	3	1.8	163	100.0
Strongly disagree	26	45.6	31	54.4	0	0.0	57	100.0

ICU, intensive care unit.

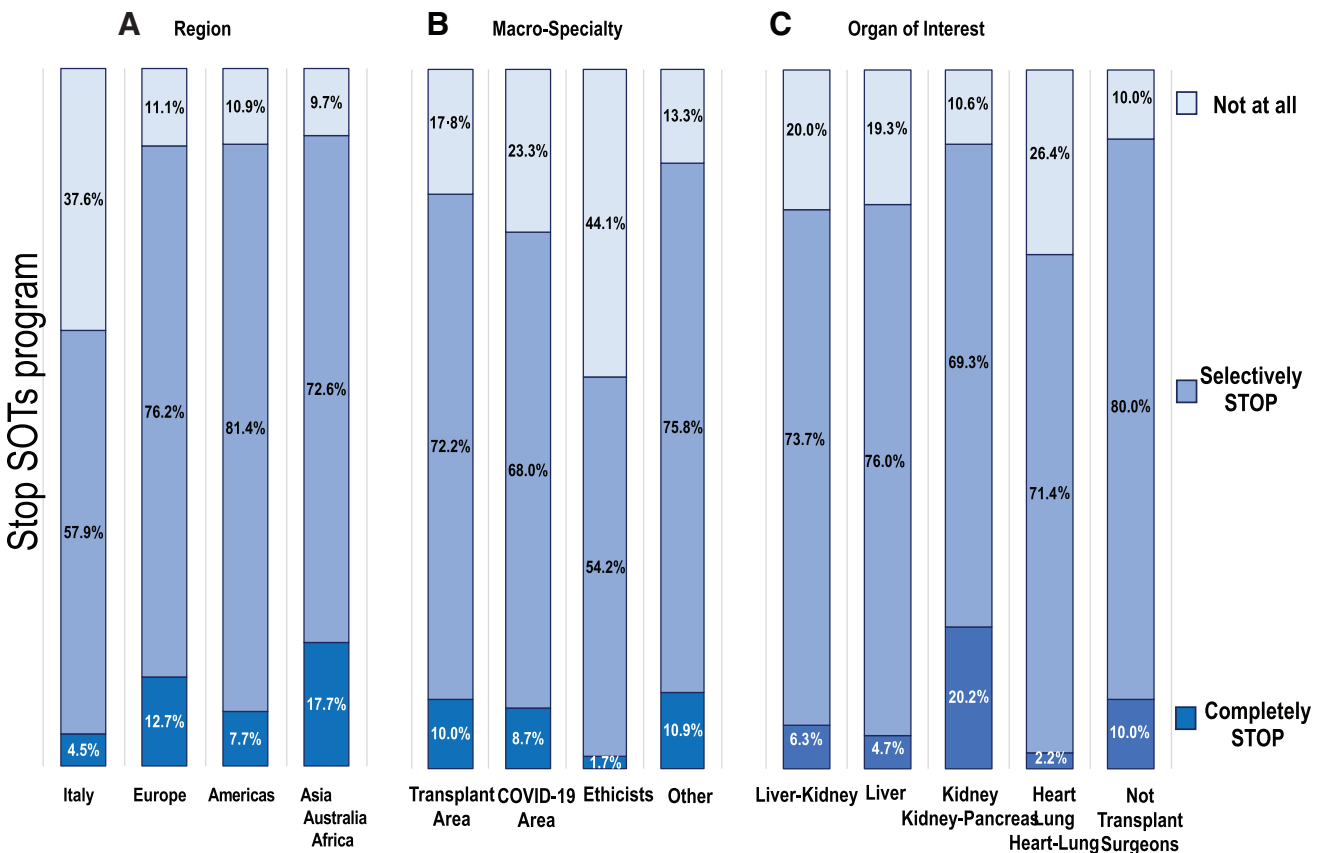


FIGURE 2. Stratification of answers in relation to “Stop SOTs program” according to region (A), macrospecialty (B), and organ of interest (C). COVID-19, coronavirus 2019; SOT, solid organ transplant.

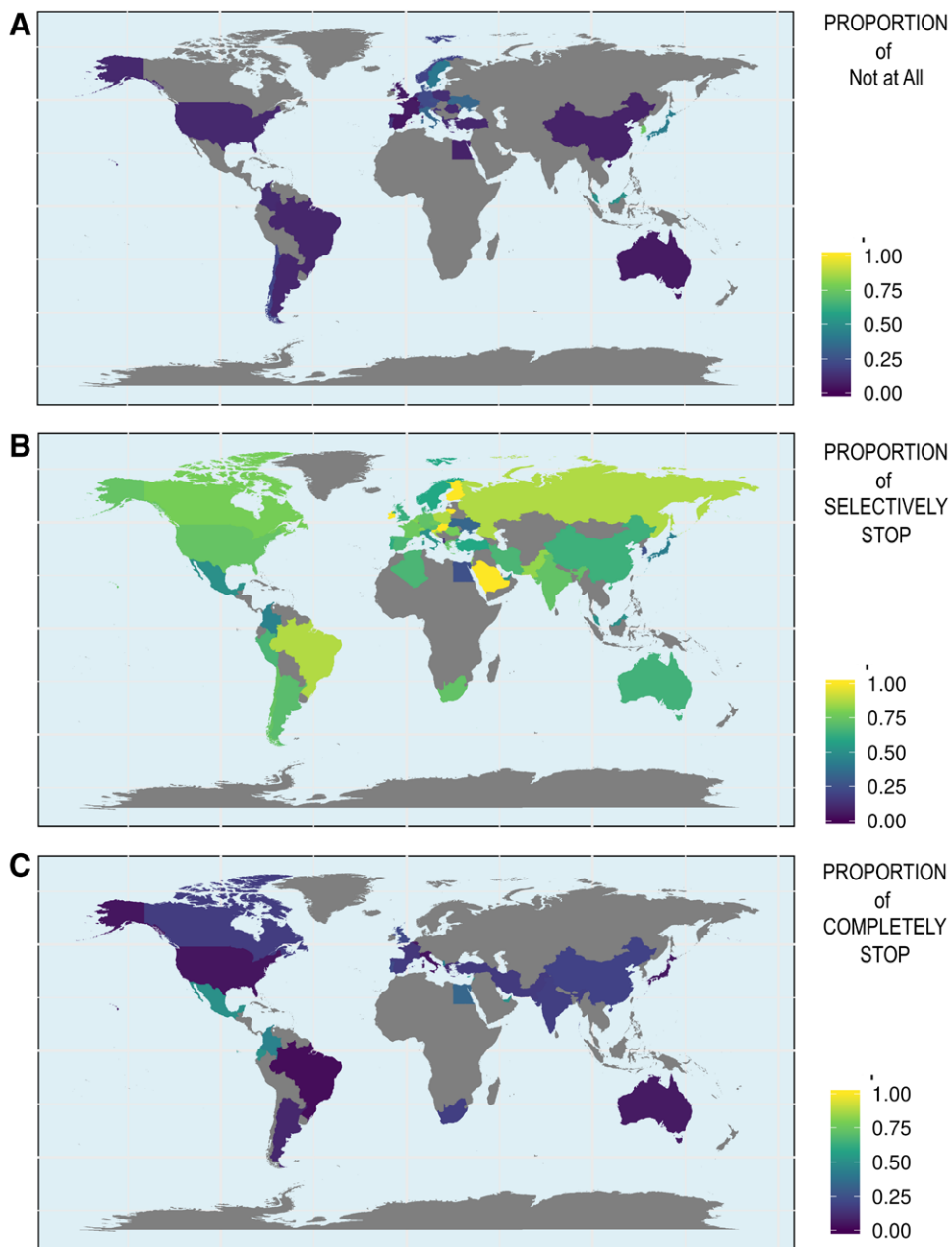


FIGURE 3. Color representation according to answer rates to the main question in each nation.

Organ Interest Stratification

Considering the stratification based on organ of interest, the intention not to stop “at all” was highest among cardiothoracic surgeons (26.4%), followed by liver-kidney (20.0%), liver (19.3%), kidney and kidney-pancreas (10.6%) transplant specialists (Figure 2C; Table S4, SDC, <http://links.lww.com/TXD/A310>).

Analysis of Epidemiological and Socioeconomic Data

Differences in the types of answers (to continue SOTs, to stop SOTs selectively, and to stop SOTs completely) depended on the daily number of deaths registered on the day of the answer. The trends of the daily number of infected persons and deaths for each region are illustrated in Figure 6A and B.

When the number of deaths decreased, the responders answered “selectively.” Notably, in Italy, even in the days with a high number of deaths, the responders selected the “not at all” option. Similar results were observed regarding the number of infected persons (Figure 7A). Median and IQR across the 3 answers to the main question were not different in the except Italy overall dataset (Figure 7B). Finally, responders selecting “completely” stop SOTs showed lower IHDI and lower GDP than others (Figure 7C).

Correlation Between Transplant Program Management and Equity

The visual correlation between stop SOTs and agreement on shifting resources to COVID-19 patients is illustrated in Figure 8. Overall, 44% of “not at all” responders were in

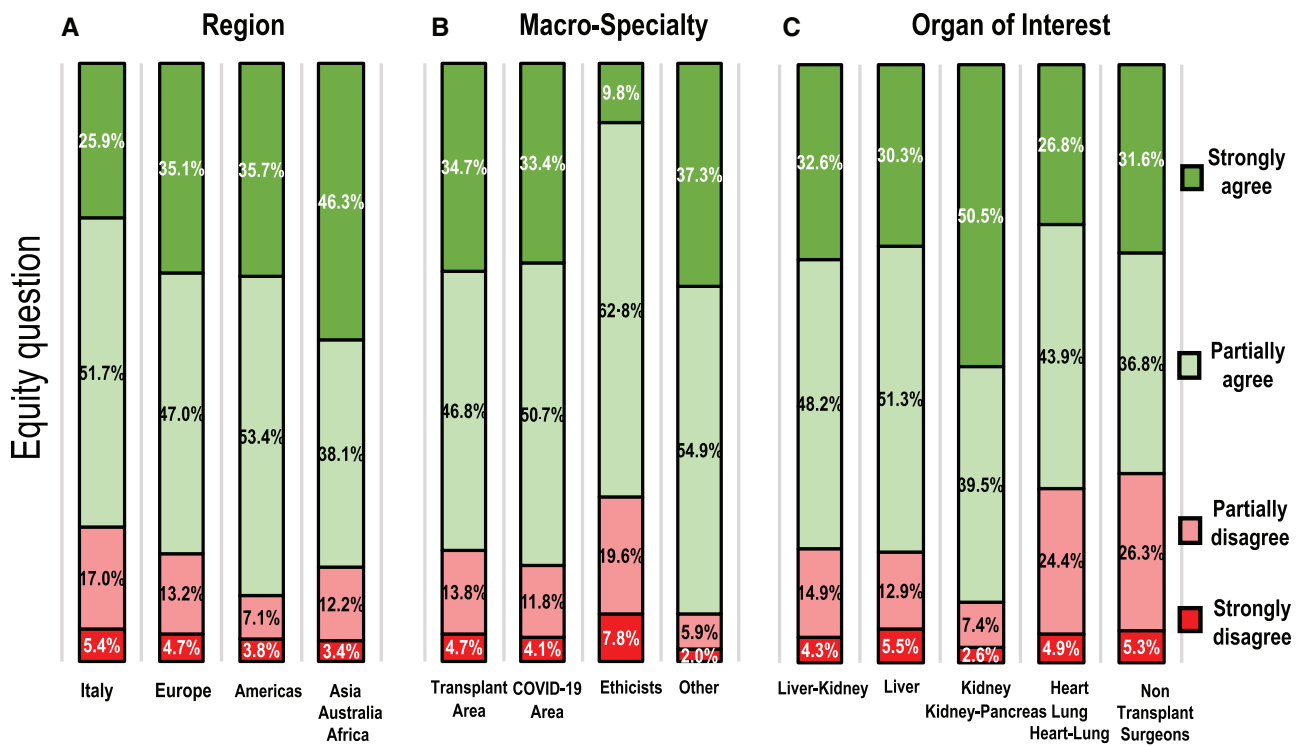


FIGURE 4. Stratification of answers in relation to “equity question” and according to region (A), macrospecialty (B), and organ of interest (C).

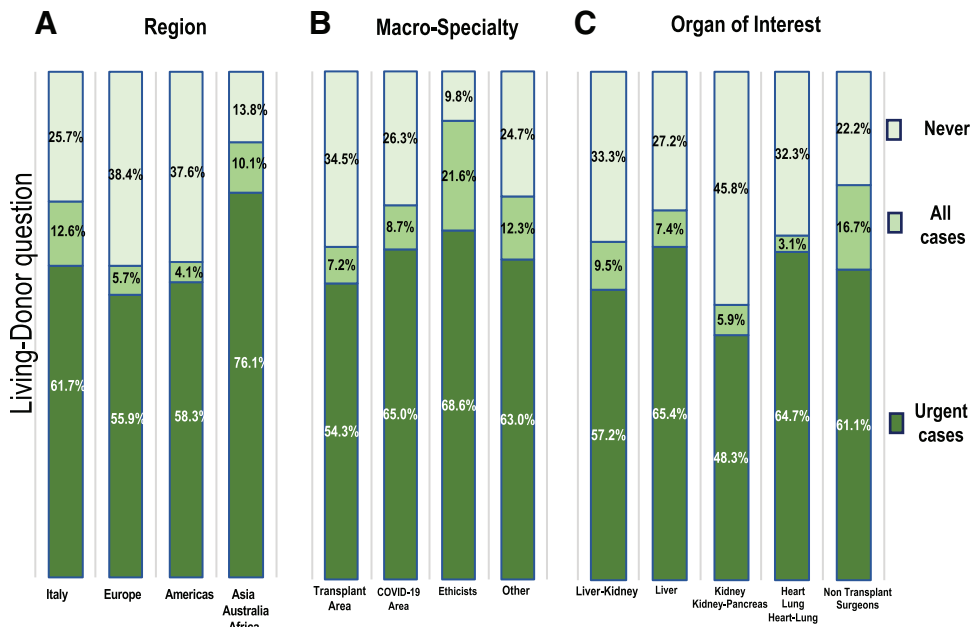


FIGURE 5. Stratification of answers in relation to the “living-donor question” and according to region (A), macrospecialty (B), and organ of interest (C).

the “strongly-disagree” group and 23% of the “completely” responders in the “strongly-agree” group.

Univariate-multivariate Ordinal Regression Analysis

The univariate ordinal regression analysis showed that the factors in favor of continuing transplants were Italy, public health systems with universal coverage, private university hospital or public hospital, to be ethicist, to have interest in cardi-thoracic or liver transplants, and experience >10 years. The

factors in favor of stopping transplant activity were Eastern countries or Europe except-Italy, public health systems without universal coverage, COVID-19-area or transplant-area doctors, kidney or kidney-pancreas specialists, and “strongly or partially agree” answer to the equity question (Table 3). Overall, a higher number of deaths associated to COVID-19 and higher IHDI were in favor of continuing SOTs.

At the multivariate analysis, the factors in favor of continuing transplant were Italy, to be ethicist, partially disagreeing on the

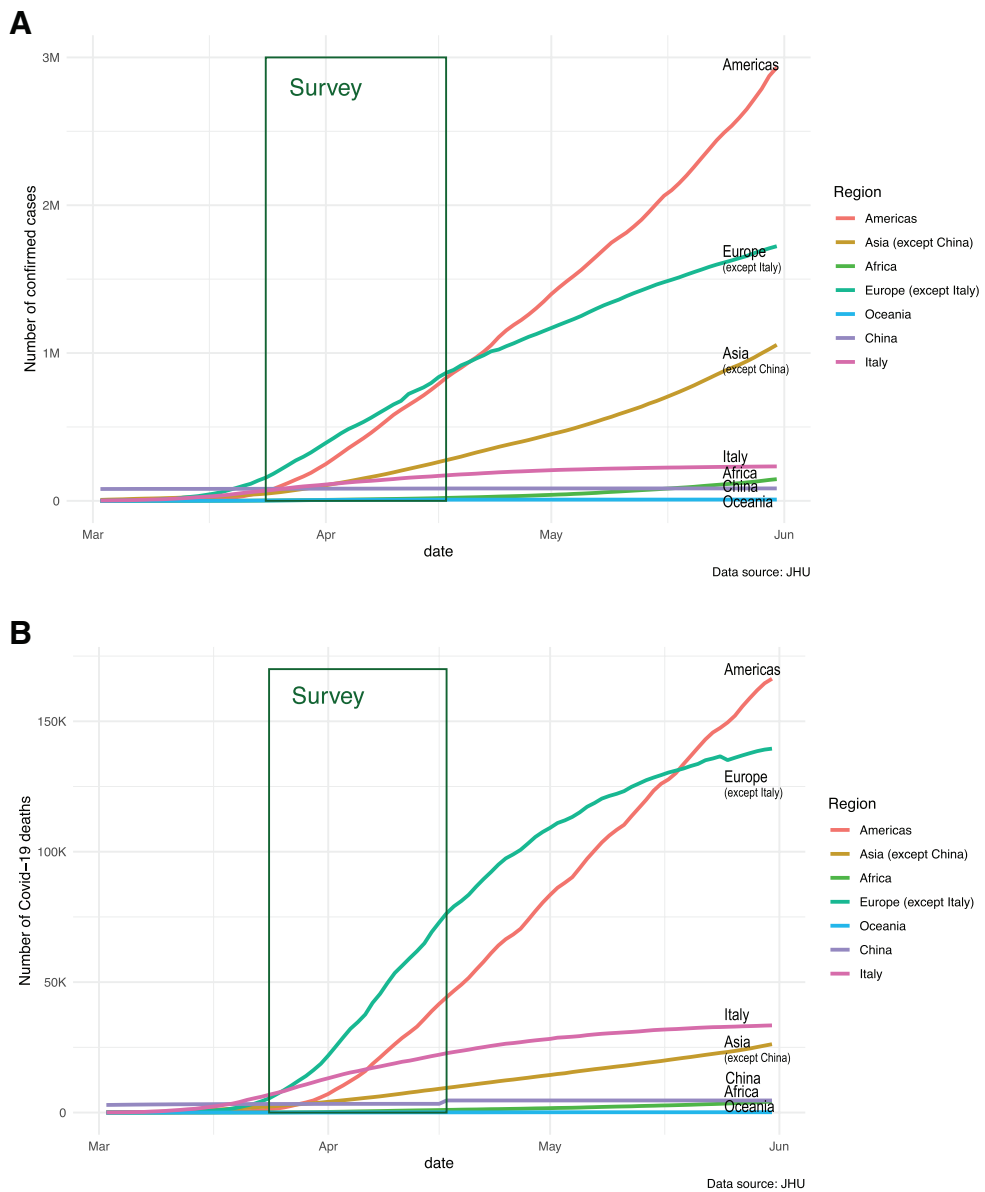


FIGURE 6. Trends of daily number of infected persons (A) and deaths (B) for each region are illustrated. Data from Asia except China, China, Africa, and Oceania have been reported separately. COVID-19, coronavirus 2019.

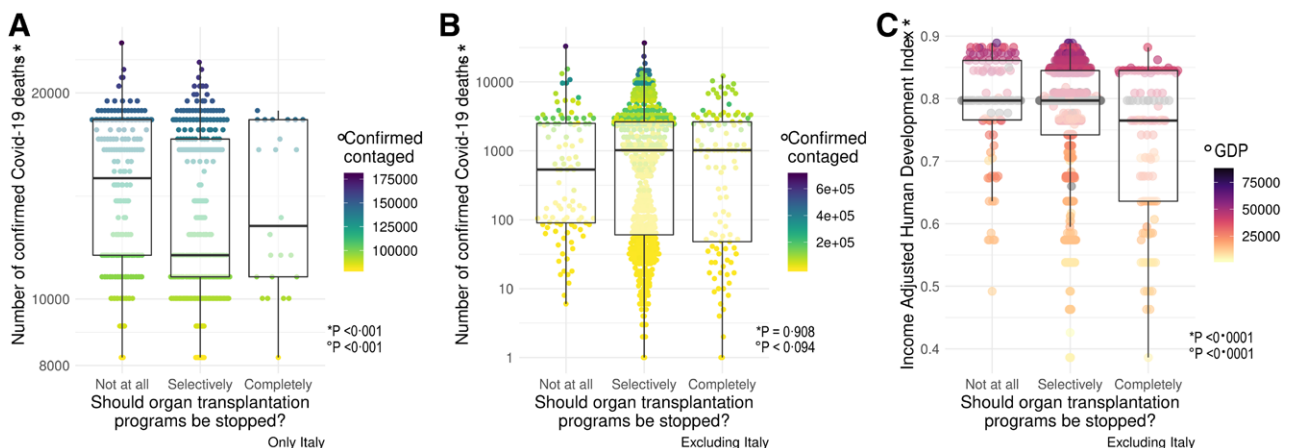


FIGURE 7. Contextual factors and the decision to stop transplant. A and B, Stratification of answers according to number of deaths and infected patients in Italy (A) and all country excluding Italy (B); C, Stratification according to Income Adjusted Human Development Index and to gross domestic product in all countries excluding Italy. COVID-19, coronavirus 2019; GDP, gross domestic product.

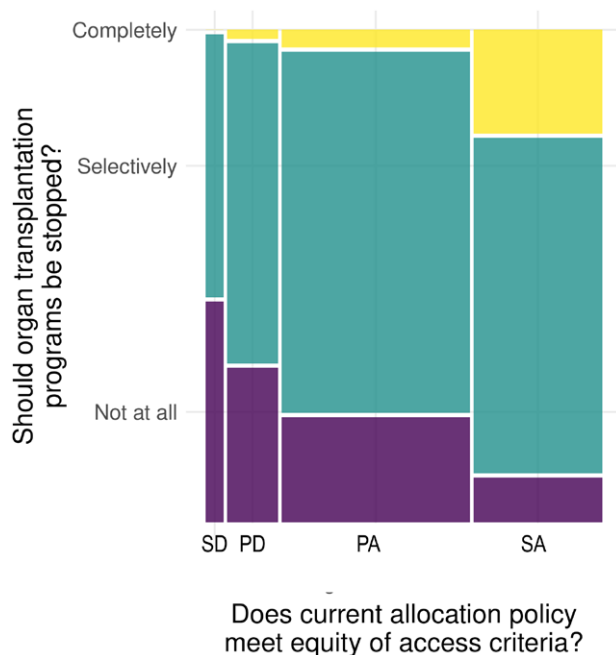


FIGURE 8. Stratification of answers to main question (should organ transplant SOT be stopped?) according to equity question. PA, partially agree; PD, partially disagree; SA, strongly agree; SD, strongly disagree; SOT, solid organ transplant.

equity question, a high number of COVID-19-related deaths on the day of the answer, a high IHDI country. Factors predicting to stop SOTs were as follows: Europe except-Italy, public university hospital, and strongly agreeing on the equity question.

Thematic Analysis of Free-text Comments

Three master themes (Normalizing Inequity, Political Stewardship, Collateral Damage) were identified and used to enhance the discussion of findings (Table S5, SDC, <http://links.lww.com/TXD/A310>).

DISCUSSION

Every year, millions of people around the world die from end-stage organ failure.^{45,46} A suitable organ is available only for a few of them. SOT is the optimal intervention for end-stage organ failure. Its potential to transform lives has been significantly affected by COVID-19 pandemic, and the transplant community has been faced with an unprecedented crisis and struggled with prompt solutions and guidance. Hospital capacity has been stretched mainly by the lack of COVID-19-free pathways and the delay to enact public health measures, including social distancing. However, the different rates of COVID-19 infection in the various countries may have driven the decision to continue or stop SOT programs. In many patients with kidney and pancreas diseases (life-enhancing transplant), second-line replacement therapies are available despite a low COVID-19 risk. Regarding renal replacement therapy, a COVID-19-related mortality rate similar to that of transplant has been reported in several studies.⁴⁷⁻⁴⁹ For other organs (liver, heart, lung), there is no alternative to proceed with a transplant.

This survey was designed to summarize the opinions of transplant professionals on strategies after the COVID-19

outbreak and to identify pathways for maintaining transplant activity safely. The survey was carried out during a 3-week period, and for each country, answers were correlated with daily deaths and socioeconomic and demographic data. Several national and international societies circulated the link to the survey, and the answers were stratified according to the level of experience of the respondent (trainee, appointed, head of team). Notably, the large majority of answers were from experienced specialists. The survey also described the perceptions regarding equity in resources' allocation, providing opinions about SOTs management, in the absence of strong scientific evidences. Equity is involved in several contexts during pandemic, such as the management of health resource for organ allocation in general, protocols about balancing individual transplantation benefits against risks, or decisions to pause transplant activities.

There are some concerns about the allocation of resources during the pandemic. Access to care has been restricted or even denied to several categories of patients with chronic disease (ie, cardiovascular or oncologic patients),⁵⁰⁻⁵² and patients waiting for a transplant are among them. Suspension or restrictions on transplant activities may contribute to inequities. The present survey intended to investigate whether it was fair and compliant with the equity principle to prioritize the allocation of health resources to respond to pandemic, shifting part of them (ie, access to ICU beds, operating room, blood bank products, and medications) to COVID patients instead of patients waiting for SOT. Furthermore, the extremely high mortality rate observed in COVID patients treated in ICUs is counterbalanced to the very-low ICU mortality rate of transplanted patients.^{53,54} According to these perspectives, the futility of care in some infectious patients may be avoided through an accurate triage.^{55,56}

Our data are a "snapshot" pairing the changes made in centers across the world when faced with COVID-19 and anticipate international society recommendations.^{22,24,57} Overall, nonurgent transplants were suspended in 10 out of 19 countries, and in 4 additional countries, a case-by-case decision strategy was implemented. There was a large degree of consensus in recommendations from national transplant societies to temporarily suspend elective living-donor program and reduce nonurgent deceased donor transplantation.^{22,24,57,58}

As an unprecedented pandemic, there was a paucity of evidence to guide decision making. Furthermore, the COVID-19 pandemic is an evolving and unpredictable scenario. More than 90% of the responders suggested to continue SOTs and this survey indicated the best path forward to safely identify who should be transplanted and how to safeguard the living donors and the recipients. The prevalent opinion was to reduce transplant activity, selectively stopping SOT and treating transplant patients in COVID-19-free units. This reflects the need to avoid transplants in hospitals with high numbers of infected patients and virus-free units. A high number of responders highlighted the need to maintain some level of activity, define criteria of urgency based on the COVID-19 extrarisk, and maximize benefit. Opinions were quite different among different healthcare providers, reflecting the lack of consensus related to responders' features (country, specialty, organ of interest, daily deaths, and economic context). Therefore, the transplant community should strongly consider particular circumstances such as hospital capacity, infection rate, and transplant-center network to allocate SOT activity

TABLE 3.**Univariate and multivariate analysis of answer options associated to the main question (stop transplant)**

Dependent variable	Univariate analysis					Multivariate analysis		
	β -coeff	SE	P	Generalized R ²	ROC curve ^a	β -coeff	SE	P
a. completely STOP (ref.)								
b. SELECTIVELY;								
c. NOT AT ALL								
Self-identified gender	0.087	±0.116	0.453					
World macroarea (ref d. OTHER)			0.000	0.123	0.643 (b)			0.001
ASIA, Australia, Africa	0.612	±0.153	0.000		0.690 (c)	0.109	±0.198	0.581
a. AMERICAS	0.081	±0.123	0.509			0.132	±0.176	0.455
b. EUROPE	0.302	±0.109	0.006			0.518	±0.153	0.001
c. ITALY	-1.224	±0.105	0.000			-1.259	±0.476	0.008
Health system (ref c private health system)			0.002	0.010	0.498 (b)			0.239
a. Public health system with universal coverage	-0.296	±0.086	0.001		0.565 (c)	-0.063	±0.141	0.656
b. Mainly a public health system, without universal coverage	0.130	±0.122	0.284			-0.226	±0.153	0.139
Hospital type (ref Private Hospital)			0.003	0.012	0.546 (b)			0.002
a. Public University Hospital	0.268	±0.092	0.004		0.554 (c)	0.438	±0.121	0.001
b. Private University Hospital	-0.083	±0.126	0.509			-0.099	±0.155	0.523
c. Public Hospital	-0.293	±0.128	0.022			0.251	±0.162	0.120
Hospital capacity (ref a) >500 beds	-0.092	±0.140	0.514					
Position macrogroup (ref other)			0.000	0.024	0.536 (b)			0.154
a. Medical ethicists	-0.970	±0.202	0.000		0.573 (c)	-0.525	±0.254	0.039
b. COVID area	0.054	±0.112	0.631			-0.036	±0.156	0.812
c. TRANSPLANT area	0.342	±0.098	0.001			0.007	±0.139	0.960
TX Speciality of interest (ref LTX-KTX)			0.000	0.070	0.710 (b)			
a. General surgeons	0.389	±0.427	0.362		0.588 (c)			
b. Cardiothoracic	-0.697	±0.217	0.001					
c. Kidney-pancreas	0.870	±0.183	0.000					
d. Liver	-0.297	±0.163	0.067					
Experience level (ref c. trainee)			0.253					
a. Appointed	0.071	±0.086	0.411					
b. Head of Team/Clinical Lead	0.125	±0.084	0.134					
Experience year (ref 10 y) >10 y	-0.320	±0.130	0.013	0.005	0.526 (b)	-0.039	±0.157	0.804
EQUITY CATEGORY (ref d. strongly disagree)			0.000	0.137	0.753 (b)			0.000
a. Strongly agree	1.486	±0.135	0.000		0.652 (c)	1.460	±0.141	0.000
b. Partially agree	0.030	±0.106	0.783			0.078	±0.115	0.495
c. Partially disagree	-0.464	±0.144	0.001			-0.380	±0.155	0.014
No. of deaths	-0.100	±0.009	0.000	0.109	0.609 (b)	-0.028	±0.020	0.164
Inequality-Adjusted Human Development Index	-3.104	±0.681	0.000	0.018	0.701 (c)	0.584 (b)	±1.016	0.000
					0.489 (c)			

Ref, reference; ROC, receiver operating characteristic.

Variable "TX Speciality of Interest" was excluded from multivariable analysis because it was answered only by a subgroup of Position macrogroup (TRANSPLANT area)

R² of the multivariable model was 0.274. ROC for "selectively stop" was 0.815. ROC for "not at all stop" was 0.771.

^aROC curves are identified by the number in bracket: b, selectively stop; c, not at all.

in COVID-19-free hospital. Finally, enrollment in a private or public healthcare system may play a role. A recent study reported that transplant activities decreased in both public and private healthcare systems, whereas at difference extent (91% in France, and 51% in United States).¹⁷

The main question regarded current SOT management in front of resources' limitations. Considering that the answers could be influenced by the local incidences of COVID-19, the answers were further correlated with the daily deaths in the country of the respondent. Theoretically, in areas where there is a low incidence of infection, the appetite to continue transplant activity may be higher. On the opposite, in areas with scarce ICU beds, reserving those for transplant care could be

difficult. The opinions of responders from Eastern countries and Europe were more in favor stopping SOTs, and the multivariate analysis confirmed these results. In countries with low GDP and IHDI, there are economic drivers where healthcare investment and expenditure per person are different and out-of-pocket expenses frequent even for life-saving intervention.⁵⁹ Additionally, low general to specialty doctor ratio in areas of Asia (ie, India)⁶⁰ explains why the healthcare workforce takes a more stringent view on conserving tends to spare resources. Conversely, in Europe, decision-making aligns more readily with the temporary nature of the pandemic, that is, inequity will be short-lived. It follows that while living-donor programs are well developed in Eastern countries due

to lower activity of deceased donor programs,⁶¹ responders in these regions more often wanted to stop transplants, likely due to resources' limitations for the care of living donors and recipients. In this regard, several solutions may be adopted, such as the identification of COVID-19 cluster with a temporary suspension and reduction or relocation of the transplant programs, especially when resources at the transplant centers may be constrained (ie, transplant of urgent cases, relocating transplant program in areas with low rate of SARS-CoV-2 infection).^{58,62}

Looking at the stratification of answers concerning "not stop," "selectively stop," or "completely stop," Italian responders, ethicists, and heart-lung transplant surgeons had the highest proportion of "not stop." Moreover, one-third of the responders strongly agreed that shifting resources from transplantation to COVID-19 is the best available strategy as an exceptional measure in an emergency. Accepting shifts in resources' allocation likely reflects a move in public health policy to an utilitarian approach when placed under pressure.⁶² This may explain the correlation between those selecting "strongly agree" to the equity question, also wanting to "stop" transplants.

The majority of responders suggested to define a safe COVID-19 pathway (outpatient visits, free ICUs, free wards, dedicated nurses and doctors aware of the additional risk due to the virus in the immunosuppressed patient). Although the effect of SARS-CoV-2 on the immunosuppression is presently unknown, experts' opinions suggest reducing the exposure to immunosuppressive drugs, particularly in COVID-19 patients.^{24,63,64} At some centers, lymphodepletive agents have been toned down to avoid excessive immunosuppression.^{4,65,66} Pulmonary complications are more frequent after transplant,⁶⁷ and available data suggest that 25% of transplanted patients with COVID-19 infection are critically ill.⁶⁸ Furthermore, SARS-CoV-2 exhibits the cytopathic effect on the liver and antiviral treatment may induce liver damage.⁶⁹ The importance of the COVID-19-free pathway has been subsequently reported in various settings.^{70–72} However, at the time of the survey administration, this topic was not yet clearly defined in the transplant literature. Presently, some programs resumed the activity and all of them implemented the virus-free pathway.^{73,74}

Open comments signaled the importance of a step-change in healthcare delivery to address these concerns. This included safeguarding not only units but also speciality workforce virus free to allow urgent cases to be taken forward.^{62,73,75} Furthermore, SOT programs could also consider continuing according to a model of priority based on the availability of alternative therapies (Thoracic Organs>Liver>Kidney-Pancreas>Kidney alone). Nevertheless, efforts should be made to continue all SOT programs implementing risk mitigation strategies to avoid graft wasting. We should also consider the differences among centers regarding implementation of free pathways and waiting list pressure. Overall, the fundamental principles on which healthcare systems are based should not be ignored and should be translated into regulations retaining egalitarianism in models of delivery.

Although a relevant percentage of responders suggest that living related programs should follow different criteria from deceased donor transplants, we are confident that isolation strategies and the implementation of COVID-19-free hospital pathways will allow safe transplant activity. Theoretically, rationing scarce healthcare resources is inequitable⁵⁹; nevertheless, our data suggested that some transient scaling back is

necessary during a pandemic for which no healthcare system was prepared.⁷⁶ Finally, we should note that responders call for government stewardship to establish better provision for timely COVID-19 and non-COVID-19 interventions, guiding choices for the next future. Utility, acceptable benefit, urgency, and equity principles should guide this process.^{26,76,77} At a local level, hospital capacity, infection rate, and transplant-center network may have peculiarities that may drive different strategic choices such as patient isolations in COVID-19 hubs or implementation of COVID-19 areas within the same hospitals. However, besides informing doctors involved in the care of transplant and COVID-19 patients, this survey may be of interest to health stewardship. We believe that there are main reasons for the reduced transplant activity^{16–21}: the high mortality rate reported in the transplant population and the low availability of healthcare resources during the first trimester in 2020. Notably, the mortality of ICU patients with COVID-19 ranges from 38%,⁵⁴ to 62%,⁷⁸ 67%,⁷⁹ and 78%.⁸⁰ Conversely, posttransplant 90-day mortality before the pandemic ranged from 2% to 6%.^{68,80–87} The implementation of isolation measures and the adoption of the COVID-19-free pathways will mitigate the posttransplant death risk, especially for transplant candidates who, for their better general conditions, are less prone to becoming sick. Regarding the availability of healthcare resources, many structural efforts have been made (new ICU dedicated beds, better isolation measures), and a more accurate triage procedure may lead to restore activity in respect of equity.

There are some caveats when interpreting the results. First, regional stratification may mask nuances within decision making across countries. The number of responders did not reflect the entire SOT activity in each country. Moreover, responders from Australia were combined with those from Asia and Africa as the least-worst possible grouping. Second, we recognize that a significant drawback of web-based surveys includes issues with "inferior" response rate when compared with traditional mail surveys.^{36–38} However, the communication strategy that we used may transform this limitation in a strength. Although the survey registered a response rate equal to 49%, we cannot calculate the number of professionals who were informed about the survey through scientific society websites, dedicated international webinars, and social media. We suppose that a relevant number of professionals who visualized the survey link opened the website only for curiosity, but they did not provided a valid questionnaire (ie, with answer in 80% of questions). As a matter of fact, we used multiple platforms to enhance the survey delivery to healthcare workers in different specialties. Of those completing the survey, comparable levels of responses were attained from major geographical regions, and there was diversity in the job roles of responders. Such characteristics may be more important in terms of generalizing the findings versus a true response rate per se. Finally, it should be emphasized that local contexts may lead to different nuances of each element of the questions depending on raw volume or proportion of cases in the local population. Similarly, the availability of beds for acute patients, besides per se reducing the deceased donor donation, may influence the attitudes toward suspension of living-donor transplants or overall transplant activity. Despite these limitations, the issue of resources' allocation during the pandemic is an important novel aspect. Additional strengths of the study are to have weighted responses against the contextual daily SARS-CoV-2

burden, and the multidisciplinary nature of the study, spanning medicine, economics, and ethics.

In conclusion, most responders suggested that transplant activity should be continued during a pandemic through a virus-free pathway. They also accept a temporary shift from the equity principle. Differences among professional categories, although present, were less marked than supposed.

ACKNOWLEDGMENTS

The authors thank the president of the Italian Society of Organ Transplantation, SITO (Ugo Boggi); the president of the European Society of Organ Transplantation, ESOT (Vassilios Papalois); the president of the International Liver Transplant Society, ILTS (Claus Niemann); the president of the Società Italiana di Gastroenterologia ed Endoscopia Digestiva (Domenico Alvaro); the secretary of the Associazione Italiana Studio Fegato, AISF (Salvatore Petta); the president of the Società Italiana Anestesia Analgesia Rianimazione e Terapia Intensiva, SIAARTI (Flavia Petrini) for promoting the survey. We would also like to acknowledge the tremendous effort of members of the COVID-19 and Solid Organ Transplant international study group for the interpretation of survey analysis and critical revision of the manuscript.

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