





ORIGINAL ARTICLE

SARS-CoV-2 infection and early mortality of waitlisted and solid organ transplant recipients in England: A national cohort study

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Patients waitlisted for and recipients of solid organ transplants (SOT) are perceived to have a higher risk of contracting severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and death; however, definitive epidemiological evidence is lacking. In a comprehensive national cohort study enabled by linkage of the UK transplant registry and Public Health England and NHS Digital Tracing services, we examined the incidence of laboratory-confirmed SARS-CoV-2 infection and subsequent mortality

Abbreviations: COVID-19, coronavirus disease 2019; IQR, interquartile range; NHSBT, National Health Service Blood and Transplant; ONS, Office of National Statistics; PHE, Public Health England; SARS-CoV-2, severe acute respiratory syndrome coronavirus-type 2 pathogen; SOT, solid organ transplant; UK, United Kingdom.

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in patients on the active waiting list for a deceased donor SOT and recipients with a functioning SOT as of February 1, 2020 with follow-up to May 20, 2020. Univariate and multivariable techniques were used to compare differences between groups and to control for case-mix. One hundred ninety-seven (3.8%) of the 5184 waitlisted patients and 597 (1.3%) of the 46 789 SOT recipients tested positive for SARS-CoV-2. Mortality after testing positive for SARS-CoV-2 was 10.2% (20/197) for waitlisted patients and 25.8% (154/597) for SOT recipients. Increasing recipient age was the only variable independently associated with death after positive SARS-CoV-2 test. Of the 1004 transplants performed in 2020, 41 (4.1%) recipients have tested positive for SARS-CoV-2 with 8 (0.8%) deaths reported by May 20. These data provide evidence to support decisions on the risks and benefits of SOT during the coronavirus disease 2019 pandemic.

KEYWORDS

clinical research/ practice, complication: infectious, epidemiology, health services and outcomes research, infection and infectious agents - viral, infectious disease, organ transplantation in general, patient survival, registry/ registry analysis

1 | INTRODUCTION

Severe acute respiratory syndrome coronavirus-type 2 pathogen (SARS-CoV-2), the causative agent for coronavirus disease 2019 (COVID-19), was first diagnosed in the United Kingdom (UK) on January 29, 2020. By May 16, >240 000 had tested positive for infection with more than 34,000 deaths due to COVID-19.¹ Demographic factors such as sex, age, ethnicity, and comorbidity (eg, diabetes, obesity) were associated with higher mortality in the UK population.²⁻⁴

Solid organ transplant (SOT) recipients or patients waitlisted for such transplants were considered to be at high risk of infection or poor outcomes following COVID-19 due to proportionately higher rate of underlying comorbidities, the need for frequent contact with medical care settings, and requirement for systemic immunosuppression. On March 22, 2020, Public Health England (PHE) issued guidance classifying SOT recipients as “clinically extremely vulnerable” and advised additional nonpharmaceutical interventions to reduce the risk of SARS-CoV-2 infection such as “shielding,” where patients undergo strict self-isolation even within multiperson households.⁵

Single-center or regional experiences describing COVID-19 mortality rates in transplant recipients have been published.⁶⁻¹⁵ While such reports provide a limited assessment of the impact of COVID-19 on SOT recipients, inclusion of a large “at risk” population with a high degree of data completeness is essential to more accurately quantify risk. Furthermore, there is a paucity of data on the impact of the pandemic on patients waitlisted for organ transplantation. This is the clinically most appropriate risk comparator group for SOT recipients, rather than the general population, because they share more similar comorbidity and risk profiles for SARS-CoV-2 infection and associated mortality. Availability of high-quality data

on outcomes following SARS-CoV-2 infection in waitlisted vs SOT recipients is essential for clinicians and patients to make informed decisions, especially as transplant centers consider re-opening or restoring transplant activity back to prepandemic activity levels.

We report on the first national registry-based cohort analysis describing the incidence of SARS-CoV-2 infection and all-cause mortality in both patients waitlisted for transplants and SOT recipients.

2 | MATERIALS AND METHODS

2.1 | Study population

The at-risk cohorts of interest were all patients resident in England who were either active on the wait-list for any deceased donor SOT, or were a SOT recipient with a functioning graft, as of February 1, 2020. Patients who were suspended on the wait-list on that date or recipients of tissue or cell transplants (eg, cornea, sclera, bone, bone marrow, hepatocyte) were not included. Patients who were on the wait-list on February 1 but were subsequently transplanted before May 20, 2020 were classified within the SOT recipient group. Patients on the wait-list for, or recipients of, islet transplants were reported jointly with solid organ pancreas-alone transplants. Any recipient of more than 1 simultaneous organ transplant (other than simultaneous pancreas-kidney transplants) was defined as receiving a multi-organ transplant.

In both cohorts, the outcome variables of interest were (1) laboratory-confirmed SARS-CoV-2 infection and (2) among those positive for SARS-CoV-2, vital status, and date of death if applicable. Patients were followed for outcomes of interest from February 1 to May 20, 2020.

Testing for SARS-CoV-2 was performed using PHE-validated, real time-polymerase chain reaction test kits with a probe specific for B-betacoronavirus (target E gene) and SARS-CoV-2 (target S gene). This enabled parallel detection of B-betacoronavirus and SARS-CoV-2-specific RNA.

2.2 | Study design and data sources

This was a national cohort study enabled by linkage of 3 national registries in England. National Health Service Blood and Transplant (NHSBT) database is the central repository that holds records, including identifiable information and demographics, on all patients waitlisted for a deceased donor SOT or in receipt of a SOT in the United Kingdom. The NHSBT database includes data on patients from all 4 nations in the United Kingdom (population ≈66 million) with the majority of the population in England (population ≈56 million). Access to a valid NHS number, a unique identifier for all patients in England with care provided on the NHS, enabled accurate data linkage. Forty-seven (0.9%) of the 5 184 waitlisted patients and 803 (1.7%) of the 46 789 SOT recipients had a missing NHS number and were excluded from outcome analyses. The at-risk cohorts were identified from the NHSBT database.

COVID-19 is designated as a “notifiable disease” and Public Health England (PHE) centrally collects reports on all patients living in England who test positive for SARS-CoV-2 under the Health Protection Regulations 2010, with a statutory requirement to report within 3 days. Merger of the at-risk cohorts identified from the NHSBT dataset with the PHE database was performed using 2 unique identifiers (NHS number and date of birth).

The NHS Digital Tracing Service records the vital status of all patients under the care of the NHS in England. The service records date of death either from hospital admission care episodes (for in-hospital deaths) or by linkage with the UK Office for National Statistics for deaths occurring outside the hospital. The NHS Digital Tracing Service only records date of death and does not collect information on cause of death. The death data reported in this study describes all-cause mortality and does not exclusively describe COVID-19-associated mortality.

The merged NHSBT and PHE dataset comprising all laboratory confirmed SARS-CoV-2 infected waitlisted patients or SOT recipients in England was securely linked with the NHS Digital Tracing Service using 3 unique identifiers (NHS number, date of birth, and sex). The final dataset therefore had near real-time, complete mortality information on all waitlisted and transplanted patients who tested positive for SARS-CoV-2 in England.

2.3 | Statistical analysis

Demographic characteristics (type of organ awaited/received, sex, age, ethnicity, and NHS region) were summarized for waitlisted patients, SARS-CoV-2-positive wait-list patients, SARS-CoV-2-positive

wait-list patient deaths, SOT recipients, SARS-CoV-2-positive SOT recipients, and SARS-CoV-2-positive SOT recipient deaths. In addition, type of donor and year of transplant were also summarized for SOT recipients, SARS-CoV-2-positive SOT recipients, and SARS-CoV-2-positive SOT recipient deaths.

Differences in characteristics for SOT recipients vs waitlisted patients were tested univariately using the χ^2 and Kruskal-Wallis tests.

Cumulative number of SOT recipients and waitlisted patients testing positive for SARS-CoV-2 and subsequent all-cause mortality in England was compared to the general English population using data provided by the UK Government (<https://coronavirus.data.gov.uk/>).

Kaplan-Meier estimates of patient survival for those testing positive for SARS-CoV-2 were compared for SOT recipients vs waitlisted patients using the log-rank test.

Multiple logistic regression analyses were used to identify factors associated with testing positive for SARS-CoV-2 in the SOT cohort and factors associated with SARS-CoV-2-positive recipient deaths in the SARS-CoV-2-positive SOT cohort. Variables included in the multivariable models were type of organ received, sex, age, ethnicity, NHS region, type of donor, and year of transplant. *P* values of <0.1 were judged to be significant. The multivariable analysis excluded 25 recipients with missing sex data.

Analyses were undertaken using SAS version 9.4 (SAS Institute Inc, Cary, NC).

2.4 | Ethical approval

The analyses described in this article were carried out at NHSBT, who maintain the UK Transplant registry on behalf of transplant centers in the United Kingdom. NHSBT are reliant on the General Data Protection Regulation Article 6(1)(e) – Performance of a public task. This lawful basis requires specific exemptions under Article 9(2)(h) and also (i) and (j). This allows NHSBT to use patient identifiable information for service evaluation without the consent of patients.

3 | RESULTS

On February 1, 2020 there were 46 145 SOT recipients alive with a functioning graft and 5 615 patients on the active wait-list for a deceased donor SOT. Six hundred forty-four patients received a SOT between February 1 and May 20, 2020, 431 of whom were active on the wait-list on February 1, 2020, leaving 46 789 SOT recipients and 5 184 waitlisted patients for analysis (Figure 1). The majority of recipients had received a kidney-only transplant (69.5%), and most patients were waiting for a kidney-only transplant (79.0%) (Table 1). The demographic characteristics of SOT recipients and waitlisted patients are also shown in Table 1. The median (interquartile range [IQR]) age of recipients was 56 (43-65) years vs 53 (41-61) years in the waitlisted cohort. SOT recipients

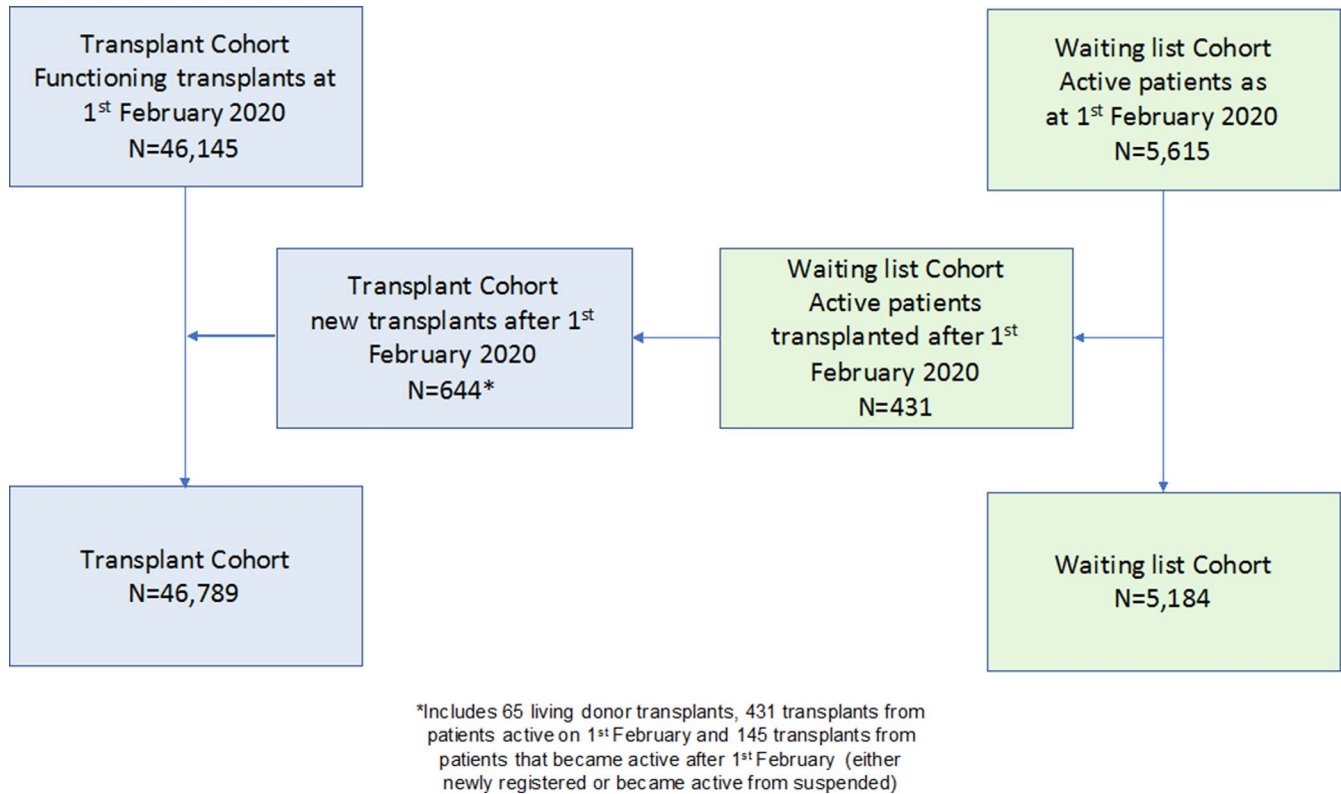


FIGURE 1 Flowchart of study cohorts

were more likely to be older ($P = .001$), white ($P < .001$), and have a history of liver disease ($P = .001$) than those patients on the wait-list (Table 1). The majority (66.9%) of recipients had their transplants prior to 2016, with 1004 (2.1%) being transplanted in 2020 up to May 20 (Table 2).

The risks of testing positive for SARS-CoV-2 were higher for those on the wait-list than for SOT recipients. As of May 20, 2020, 197 patients (3.8%) on the wait-list and 597 (1.3%) of SOT recipients tested positive for SARS-CoV-2. However, of those testing positive, the all-cause mortality risk during the follow-up period was 10.2% (20/197) for waitlisted patients and 25.8% (154/597) for SOT recipients.

Figure 2 shows the cumulative number of SARS-CoV-2-positive patients and subsequent all-cause mortality by time, with data on the general population in England for comparison. The first SOT recipient with SARS-CoV-2-positive status was notified on March 1, 2020. After a steep rise in incidence through March and April, the disease incidence and all-cause mortality in both waitlisted and SOT recipients plateaued in early May 2020. The median (IQR) duration between the positive result and death was 10.5 (6.5-15) days for the wait-list cohort, and 7.5 (4-12) days for SOT recipients ($P = .14$). A Kaplan-Meier plot of patient survival from date of positive SARS-CoV-2 shows estimated 30-day survival for both patient groups ($P < .0001$) (Figure 3). The median (IQR) follow-up from the date of the positive SARS-CoV-2 result to the end of the study period was 36 (13-47) and 44 (30-52) days for the waitlisted and SOT recipient groups, respectively.

The risk of having a confirmed SARS-CoV-2 infection varied by organ type, with the highest infection rates in those waiting for simultaneous pancreas-kidney, intestinal, and kidney transplants (4.4%-6.2%) (Figure 4). Infection rates were lower in transplanted patients (0.7%-1.7%). Despite these lower infection rates, the overall risk of becoming SARS-CoV-2 positive and then dying during the study period were similar between waitlisted and transplanted patients across different organ types (0.0%-0.5%), as mortality rates in infected patients were higher in SOT recipients. The median (IQR) age of recipients and waitlisted patients with SARS-CoV-2 was 59 (49-67) and 53 (45-62) years, respectively. The median (IQR) age of recipients and wait-list patients dying after testing positive for SARS-CoV-2 was 64.5 (58-70) and 59 (50.5-62) years, respectively.

Risk factors associated with the development of SARS-CoV-2 infection and subsequent mortality were examined within the SOT recipient group only, as there were insufficient cases for similar analyses to be undertaken on the wait-list cohort. SARS-CoV-2 infection was significantly more likely in transplant recipients who had received a kidney transplant ($P < .0001$), were older ($P < .0001$), non-white ($P < .0001$), lived in the London NHS region ($P < .0001$), had a deceased donor transplant ($P < .0001$), or had been transplanted in a more recent year ($P < .0001$). Multivariable logistic regression analysis showed that all of these variables were associated with a significantly increased risk of SARS-CoV-2 infection (Table 3). The only variable independently associated with death in those recipients with a positive SARS-CoV-2 test was age. Compared to a reference group aged 50-59 years, odds ratios (95% confidence intervals) were

TABLE 1 Organ type and demographic characteristics of solid organ transplant recipients with a functioning graft and patients on the active waiting list on February 1, 2020 in England, and SARS-CoV-2 infections and subsequent mortality between February 1 and May 20, 2020

	Recipients			SARS-CoV-2 + recipients			SARS-CoV-2 + recipient deaths			Waiting list patients			SARS-CoV-2 + wait-list patients			SARS-CoV-2 + wait-list patient deaths		
	N	%	N	%	% of recipients	N	%	% of cases	% of recipients	N	%	% of wait-list	N	%	% of cases	N	%	% of wait-list
Organ type																		
Kidney	32 503	69.5	470	78.7	1.4	124	26.4	0.4	79.0	179	90.9	4.4	18	10.1	0.4			
SPK	1469	3.1	19	3.2	1.3	4	21.1	0.3	2.8	9	4.6	6.2	—	—	—			
Pancreas ^a	251	0.5	3	0.5	1.2	—	—	—	0.4	—	—	—	—	—	—			
Liver	8734	18.7	64	10.7	0.7	13	20.3	0.1	6.3	6	3.0	1.8	1	16.7	0.3			
Heart	2194	4.7	23	3.9	1.0	6	26.1	0.3	5.2	—	—	—	—	—	—			
Lung	1318	2.8	13	2.2	1.0	6	46.2	0.5	5.5	2	1.0	0.7	1	50.0	0.4			
Intestinal	121	0.3	2	0.3	1.7	—	—	—	0.3	1	0.5	5.9	—	—	—			
Multi-organ	191	0.4	3	0.5	1.6	1	33.3	0.5	0.5	—	—	—	—	—	—			
Sex																		
Male	28 372	60.6	387	64.8	1.4	107	27.6	0.4	58.4	121	61.4	4.0	15	12.4	0.5			
Female	18 392	39.3	210	35.2	1.1	47	22.4	0.3	41.4	76	38.6	3.5	5	6.6	0.2			
Unknown	25	0.1	—	—	—	—	—	—	0.2	—	—	—	—	—	—			
Age group (y)																		
0-17	1703	3.6	3	0.5	0.2	—	—	—	3.3	3	1.5	1.8	—	—	—			
18-29	2899	6.2	21	3.5	0.7	—	—	—	6.5	7	3.6	2.1	1	14.3	0.3			
30-39	4737	10.1	40	6.7	0.8	—	—	—	12.5	21	10.7	3.2	1	4.8	0.2			
40-49	7311	15.6	93	15.6	1.3	15	16.1	0.2	18.6	40	20.3	4.1	2	5.0	0.2			
50-59	11 806	25.2	142	23.8	1.2	31	21.8	0.3	29.4	61	31.0	4.0	6	9.8	0.4			
60-69	11 294	24.1	195	32.7	1.7	67	34.4	0.6	22.5	51	25.9	4.4	9	17.6	0.8			
70+	7039	15.0	103	17.3	1.5	41	39.8	0.6	7.2	14	7.1	3.7	1	7.1	0.3			
Ethnicity																		
White	34 816	74.4	334	55.9	1.0	79	23.7	0.2	62.2	68	34.5	2.1	7	10.3	0.2			
Asian	5453	11.7	129	21.6	2.4	38	29.5	0.7	19.6	58	29.4	5.7	6	10.3	0.6			
Black	2620	5.6	95	15.9	3.6	27	28.4	1.0	11.8	48	24.4	7.8	3	6.3	0.5			
Other	1287	2.8	18	3.0	1.4	5	27.8	0.4	4.7	17	8.6	7.0	2	11.8	0.8			
Unknown	2613	5.6	21	3.5	0.8	5	23.8	0.2	1.7	6	3.0	6.7	2	33.3	2.2			
Region																		
North West	7372	15.8	58	9.7	0.8	12	20.7	0.2	15.2	15	7.6	1.9	1	6.7	0.1			

(Continues)

TABLE 1 (Continued)

	Recipients			SARS-CoV-2 + recipients			SARS-CoV-2 + recipient deaths			Waiting list patients			SARS-CoV-2 + wait-list patients			SARS-CoV-2 + wait-list patient deaths		
	N	%	N	%	N	% of recipients	N	% of cases	% of recipients	N	%	N	%	N	%	N	% of cases	% of wait-list
North East and Yorkshire	5611	12.0	61	10.2	1.1	0.4	22	36.1	0.4	676	13.0	11	5.6	1	9.1	1	1.6	0.1
Midlands	8357	17.9	91	15.2	1.1	0.3	24	26.4	0.3	1007	19.4	28	14.2	3	10.7	3	2.8	0.3
East of England	5467	11.7	69	11.6	1.3	0.3	18	26.1	0.3	429	8.3	19	9.6	—	—	—	4.4	—
London	8458	18.1	217	36.3	2.6	0.7	58	26.7	0.7	1291	24.9	103	52.3	12	11.7	12	8.0	0.9
South East	6967	14.9	72	12.1	1.0	0.2	13	18.1	0.2	573	11.1	16	8.1	3	18.8	3	2.8	0.5
South West	4557	9.7	29	4.9	0.6	0.2	7	24.1	0.2	419	8.1	5	2.5	—	—	—	1.2	—

Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus-type 2; SPK, simultaneous pancreas-kidney.

^aIncludes islet patient.

0.37 (0.19-0.72), 1.86 (1.13-3.04), and 2.37 (1.35-4.16) for recipients aged 0-49, 60-69, and 70 + years, respectively.

4 | DISCUSSION

The COVID-19 pandemic has had a major impact on health services of many countries and disrupted most clinical programs, including organ donation and transplantation, with intensive-care facilities facing extreme pressure due to a surge of COVID-19 admissions.¹⁶⁻¹⁹ Given the absence of definitive data on the risks of SARS-CoV-2 infections posttransplant, patients on the wait-list for a transplant and clinical teams are unsure of the relative safety of transplantation vs remaining on the wait-list. Many transplant programs are either suspended or have significantly curtailed their activity.

The analyses presented are derived from the largest and most comprehensive dataset yet available on the incidence of and outcomes after SARS-CoV-2 infection in SOT recipients during the pandemic. Furthermore, it is also the first national study from a country with significant rates of infection and deaths from COVID-19 to comprehensively examine the survival of patients on the national deceased donor wait-list over the same period, providing a more valid comparator group for risk-benefit assessment of undertaking transplantation than using general population data.⁴

We found that a higher proportion of waitlisted patients tested positive for SARS-CoV-2 than SOT recipients did (3.8% vs 1.3%). Since the highest proportion of patients on the list are waiting for a kidney transplant, it is possible that the inability of many hemodialysis patients to self-isolate due to requirement to travel 3 times/wk to a dialysis facility and remain in proximity to other patients and healthcare staff may contribute to a higher risk of COVID-19. After an initial rapid rise in numbers of affected patients, the number of new infections appears to have plateaued by May 2020.

While the overall risk of infection in waitlisted patients was higher, SOT recipients who tested positive for SARS-CoV-2 had a higher all-cause mortality during the follow-up period compared to waitlisted patients (25.8% vs 10.2%). Among the patients transplanted in 2020 (ie, during the pandemic), the incidence of SARS-CoV-2 infection was 4% with a subsequent risk of death of <1% within the follow-up period. Increasing age, nonwhite ethnicity, and living in London were associated with higher incidences of SARS-CoV-2 infection in SOT recipients. No patient aged <18 years is recorded as having died after confirmed SARS-CoV-2 infection. These findings are in accordance with studies of the general population in the United Kingdom.^{4,20} Other variables also associated with increasing risks of SARS-CoV-2 infection in posttransplant patients include recent transplantation, while liver transplant recipients had a reduced infection risk. These results may reflect the relatively high burden of immunosuppression in early posttransplant patients, and that recipients of liver transplants generally require less immunosuppression than other forms of SOT.

The only variable independently associated with death in SOT recipients with a positive SARS-CoV-2 test was age. Increasing age

	Recipients		SARS-CoV-2 + recipients			SARS-CoV-2 + recipient deaths		
	N	%	N	%	% of recipients	N	%	% of recipients
Year of transplant								
Before 2016	31 281	66.9	348	58.3	1.1	92	26.4	0.3
2016	3242	6.9	46	7.7	1.4	15	32.6	0.5
2017	3497	7.5	40	6.7	1.1	10	25.0	0.3
2018	3823	8.2	42	7.0	1.1	13	31.0	0.3
2019	3942	8.4	80	13.4	2.0	16	20.0	0.4
2020 ^a	1004	2.1	41	6.9	4.1	8	19.5	0.8
Donor type								
DBD	27 207	58.1	340	57.0	1.2	92	27.1	0.3
DCD	8354	17.9	146	24.5	1.7	36	24.7	0.4
Living	11 230	24.0	111	18.6	1.0	26	23.4	0.2

TABLE 2 Year of transplant and donor type in transplant recipients with a functioning graft on February 1, 2020 in England, and SARS-CoV-2 infections and subsequent mortality between February 1 and May 20, 2020

Abbreviations: DBD, donation after brain death; DCD, donation after circulatory death; SARS-CoV-2, severe acute respiratory syndrome coronavirus-type 2.

^aIncludes patients transplanted between February 1 and May 20, 2020 as per Figure 1.

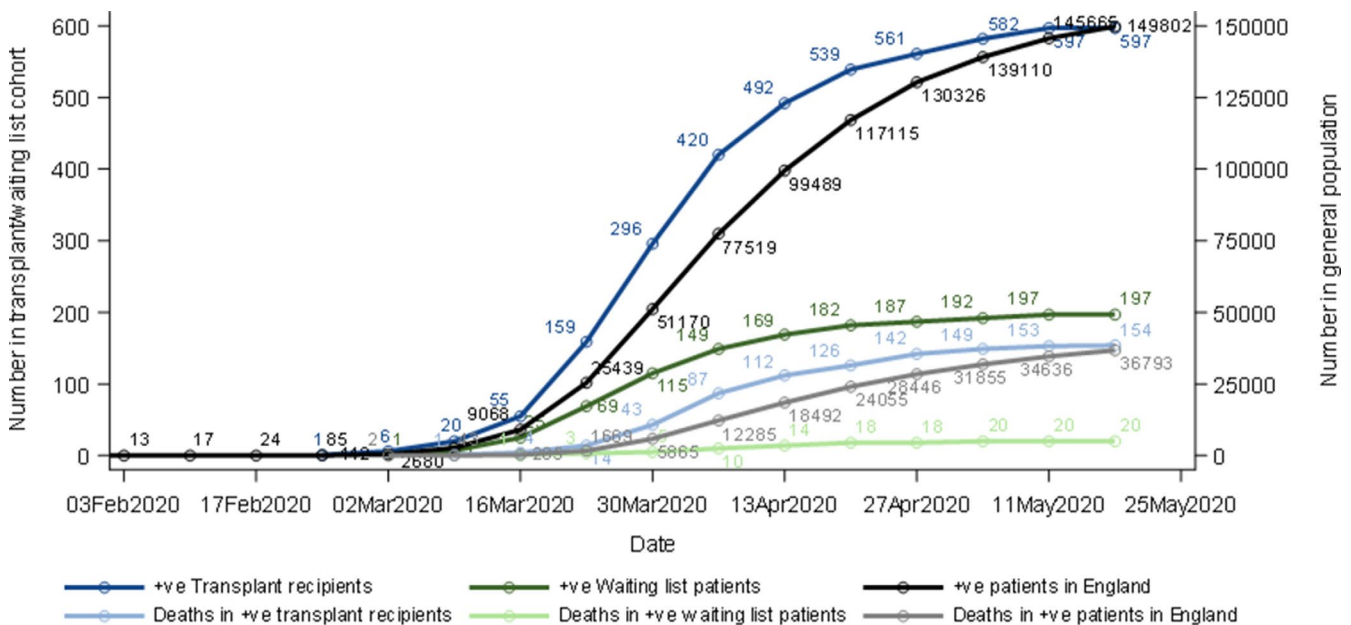


FIGURE 2 Cumulative number of solid organ transplant recipients and waitlisted patients with positive severe acute respiratory syndrome coronavirus-type 2 swabs and subsequent all-cause mortality in England, February 1 to May 20, 2020, compared to the general English population

has been identified as a strong risk factor for COVID-19-related deaths in other studies,^{3,4} and therefore this finding was unsurprising. Although our dataset did not adequately capture comorbidity data, it is notable that increasing rates of comorbidities do not appear to explain the apparent association between increasing age and death from SARS-CoV-2 infection, as 2 large studies from the United Kingdom show that age is an independent risk factor for death even after adjustment for multiple major comorbidities.^{3,4} Transplant clinicians will need to take these findings into account

when considering the suitability of older patients to undergo transplantation in countries with a high incidence of SARS-CoV-2 infection.

This study also supports the assumption that SOT recipients are at high risk of death after SARS-CoV-2 infection, with 154 (25.8%) of 597 patients dying during the study period. Although this mortality rate is similar to that of the general UK population with SARS-CoV-2, the median age of transplant recipients with SARS-CoV-2 infection in our study was far lower (59 years vs 73 years).³

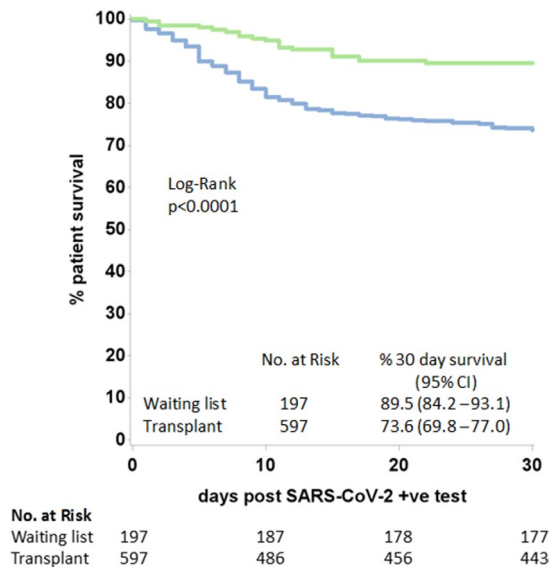


FIGURE 3 Patient survival from the date of SARS-CoV-2-positive swab in wait-list patients and solid organ transplant recipients. CI, confidence interval; SARS-CoV-2, severe acute respiratory syndrome coronavirus-type 2

To our knowledge, the only other national transplant registry that has reported on COVID-19-related deaths identified 21 Swiss SOT recipients between March 9 and April 6 who tested positive for SARS-CoV-2.¹⁴ After a median follow-up of 33 days, 2 patients died. In Spain, Domínguez-Gil et al noted that 363 SOT recipients had developed COVID-19, but no mortality data or denominator

were presented.¹⁸ Deaths on the Spanish national wait-list were reported at a rate of 1.3 per week during the pandemic (8 in total), compared to a prepandemic rate of 1.4 deaths per week, but without further information on whether those who died had COVID-19. The OpenSAFELY study included 20 130 organ transplant recipients but only 49 in-hospital deaths from COVID-19 were identified, with the general UK population as the comparator group.⁴

Many of the previous studies on the outcomes of SOT recipients with COVID-19 have focused on a single organ type, with the majority on kidney transplant recipients. Of those studies that have included more than 10 renal transplant patients, mortality rates varied from 6%⁷ to 67%.⁶ The largest study thus far on kidney transplant recipients reported on a voluntary Spanish registry of 868 patients on renal replacement therapy with COVID-19 between March 18 and April 11, including ≈290 renal transplant recipients.²¹ There were no linkages to central registries of death or notifiable disease. The mean age of all patients was 67 years, and the transplant population was younger than those on dialysis. Eighty-five percent of patients were admitted to the hospital, and 23% of patients died (18.6% of transplant recipients vs 24.9% of those on dialysis). Age was found to be a risk factor for death after COVID-19 in both transplant and dialysis patients.

Latif et al described outcomes of COVID-19 in 28 heart transplant recipients in New York City with 25% mortality,²² while a series of 13 patients from Michigan found that 2 patients (15%) died.²³ Six of 23 heart transplant recipients with SARS-CoV-2 infection died in our study. Reports of COVID-19 outcomes in lung transplant recipients have been limited, with a small number of case-series of fewer than 5 patients.^{12,24} The largest series of 17 lung patients comes from 2

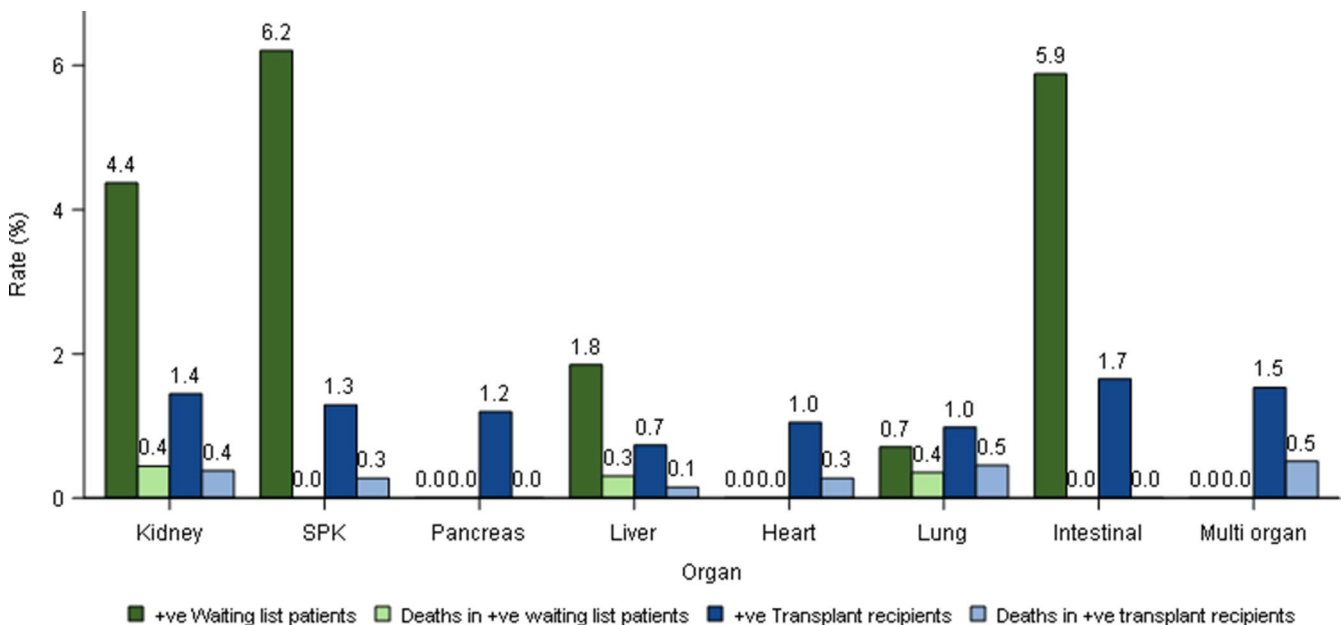


FIGURE 4 Risk of becoming SARS-CoV-2, severe acute respiratory syndrome coronavirus-type 2–positive and subsequent death for waiting-list and solid organ transplant recipients by organ type, February 1 to 20, May 2020. SPK, simultaneous pancreas-kidney

TABLE 3 Odds ratios and 95% confidence intervals for candidate risk factors associated with testing positive for SARS-CoV-2 infection in solid organ transplant recipients

	Odds ratio	95% confidence interval	P value
Organ type			
Kidney	1.00		
SPK	1.02	0.64-1.65	.9
Pancreas ^a	1.08	0.34-3.40	.9
Liver	0.53	0.40-0.70	<.001
Heart	0.94	0.61-1.44	.8
Lung	0.84	0.48-1.47	.5
Intestinal	1.86	0.45-7.71	.4
Multi-organ	1.20	0.38-3.79	.8
Age group (y)			
0-17	0.16	0.05-0.49	.002
18-29	0.68	0.43-1.07	.09
30-39	0.68	0.47-0.97	.03
40-49	1.03	0.79-1.35	.8
50-59	1.00	—	
60-69	1.57	1.26-1.96	<.001
70+	1.46	1.12-1.90	.005
Ethnicity			
White	1.00	—	
Asian	1.94	1.55-2.42	<.001
Black	2.41	1.85-3.15	<.001
Other	1.13	0.70-1.85	.6
Unknown	0.71	0.46-1.11	.14
NHS region			
London	1.00	—	
North West	0.58	0.43-0.79	.0004
North East and Yorkshire	0.43	0.32-0.59	<.0001
Midlands	0.55	0.42-0.71	<.0001
East of England	0.65	0.49-0.87	.004
South East	0.56	0.42-0.74	<.0001
South West	0.35	0.24-0.53	<.0001
Year of transplant			
Before 2016	1.00	—	
2016	1.22	0.89-1.66	.2
2017	0.98	0.70-1.36	.9
2018	0.91	0.66-1.27	.6
2019	1.60	1.24-2.06	.0003
2020	3.65	2.60-5.12	<.0001
Donor type			
DBD	1.00	—	

(Continues)

centers in New York City, though survival outcomes for this group are not reported.⁹ We found that 6 of 13 lung transplant recipients with SARS-CoV-2 died.

TABLE 1 (Continued)

	Odds ratio	95% confidence interval	P value
DCD	1.09	0.89-1.33	.4
Living	0.78	0.62-0.98	.03

Abbreviations: DBD, donation after brain death; DCD, donation after circulatory death; NHS, National Health Service; SARS-CoV-2, severe acute respiratory syndrome coronavirus-type 2; SPK, simultaneous pancreas-kidney.

^aIncludes islet recipients.

Similarly, mortality rates from COVID-19 in liver transplant recipients have not been widely described. An international collaborative from 21 countries reported a 23% mortality rate from COVID-19 in 39 liver transplant patients,²⁵ while a 21% mortality rate in 24 SARS-CoV-2-positive liver recipients was identified in a survey of Italian liver transplant programs.²⁶ Our results suggest that liver transplant recipients have a lower SARS-CoV-2 infection rate than recipients of other solid organ transplants, though larger analyses with longer follow-up are needed. To our knowledge, no COVID-19-related deaths have previously been reported in heart, lung, or liver transplant wait-list populations.

The strengths of our study include a complete national dataset of the at-risk population, accurate identification of all at-risk patients who tested positive for SARS-CoV-2, near real-time ascertainment of all-cause mortality in at-risk patients, and analysis of outcomes between waitlisted and transplanted patients. It highlights the value of routine, national, embedded data collection allowing systems to analyze comprehensive data and respond accordingly.

We acknowledge the weaknesses of this study. Although the NHSBT database holds data on SOT recipients and waitlisted patients in Wales, Scotland, and Northern Ireland, this study examined patients residing in England only, as linkages with the relevant notifiable diseases and mortality registries in other nations were not in place at the time of writing. Given the notifiable disease status, data on patients testing positive for SARS-CoV-2 were reported and collated centrally and available for analysis but data on patients testing negative were not available. Due to the relatively low number of events in the waiting-list group, multivariable analyses comparing the mortality rates between the 2 cohorts were not possible. Our analysis does not include the indication for SARS-CoV-2 testing, symptoms, hospital or intensive-care unit admissions, and treatments of COVID-19. We expect that the overwhelming majority of patients with SARS-CoV-2-positive tests had symptoms, as tests were predominantly done in hospitalized patients during the study period in the United Kingdom. As such, there was a selection bias toward sicker, symptomatic, and hospitalized patients. The study period was short, and further follow-up will be needed to determine definitive case-fatality rates. We were unable at this time to report on excess mortality in the study cohorts. Direct comparisons of SARS-CoV-2 positivity and subsequent mortality between the waitlisted and transplanted groups are limited by inherent demographic, biological,

and behavioral differences (eg, age, immunosuppressive burden, comorbidities, access to testing, challenges in self-isolating in those on unit dialysis) and should be treated with caution. Finally, while we could ascertain all-cause mortality in patients testing positive for SARS-CoV-2, we were unable to access cause of death as certified. The linked dataset did not provide cause of death information. Given the restriction of access for swab testing to symptomatic hospitalized patients and short median time (10.5 days for waitlisted and 7.5 days for SOT recipients) between a positive swab result and death, COVID-19-associated mortality is inferred but not proven by cause of death as certified.

In conclusion, analyses from this large, comprehensive national dataset will enable transplant clinicians and their patients to have a more accurate risk assessment of incidence of and outcomes following SARS-CoV-2 infection, with the first-of-its-kind analysis of risk in waitlisted and SOT recipient groups. Such information will help clinical teams decide on reinstating organ transplant programs and patient selection, and will aid patient consent discussions. Future work should include longer follow-up, further case-mix adjustment and multivariable analyses, along with more detailed understanding of the impact of pharmacological and nonpharmacological interventions on SARS-CoV-2 infection and mortality rates in waitlisted patients and SOT recipients.

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DISCLOSURE

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

AUTHOR CONTRIBUTIONS

RR and CC aided in the conception of the study and the statistical design of the study, and co-wrote the manuscript. LM aided in the conception of the study, designed the study, performed the statistical analyses, and critically reviewed the manuscript. IU-L, DT, JC, PF, JP, IC, LB, RB, JD, GCO, MB, JA, DH, AM, DM, DG, and JLRF aided in the conception of the study, and critically reviewed the writing of the manuscript. All authors agree to be accountable for the work and have given final approval for publication.

DATA AVAILABILITY STATEMENT

Non-identifiable data that supports the findings of this study are available from the corresponding author upon reasonable request. Any data release can only be completed after appropriate information governance clearances

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