

Health-related quality of life, uncertainty and coping strategies in solid organ transplant recipients during shielding for the COVID-19 pandemic

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Abbreviations:

BAME: Black, asian and minority ethnic

BMI: Body Mass Index

CARMS: Clinical Audit Registration and Management System

COSMO: COVID-19 Snapshot Monitoring

COVID-19: Coronavirus disease 2019

EQ-5D-5L: EuroQol-5 dimension-5 level

HRQoL: Health related quality of life

HSE: Health Survey England

IMD: Index of Multiple Deprivation

ITU: Intensive treatment unit

MERS-CoV: Middle East Respiratory syndrome coronavirus

NHS: National Health Service

NICE: National Institute of Clinical Excellence

PRO: Patient reported outcomes

PIS: Patient information sheet

REDCap: Research Electronic Database Capture program

RT-PCR: Reverse transcription – polymerase chain reaction

SF- MUIS: Short form Mishel Uncertainty in Illness scale

SOT: Solid Organ Transplant recipient

USA: United States of America

UK: United Kingdom

VAS: Visual analogue scale

Abstract

Strict isolation of vulnerable individuals has been a strategy implemented by authorities to protect people from COVID-19. Our objective was to investigate health-related quality of life (HRQoL), uncertainty and coping behaviours in solid organ transplant (SOT) recipients during the COVID-19 pandemic. A cross-sectional survey of adult SOT recipients undergoing follow-up at our institution was performed. Perceived health status, uncertainty and coping strategies were assessed using the EQ-5D-5L, Short-Form Mishel Uncertainty-in-Illness scale (SF-MUIS) and Brief Coping, respectively. Interactions with COVID-19 risk perception, access to healthcare, demographic and clinical variables were assessed. The survey was completed by 826 of 3,839 (21.5%) invited participants. Overall, low levels of uncertainty-in-illness were reported, and acceptance was the major coping strategy (92%). Coping by acceptance, feeling protected, self-perceived susceptibility to COVID-19 were associated with lower levels of uncertainty. Health status index scores were significantly lower for those with mental health illness, compromised access to healthcare, a perceived high risk of severe COVID-19 infection and higher levels of uncertainty. A history of mental health illness, risk perceptions, restricted healthcare access, uncertainty and coping strategies were associated with poorer HRQoL in SOT recipients during strict isolation. These findings may allow identification of strategies to improve HRQoL in SOT recipients during the pandemic.

INTRODUCTION

Due to the highly contagious nature of COVID-19, governments have implemented various strategies promoting self-isolation and social distancing of the general population to mitigate viral spread [1-3]. The impact of strictly isolating vulnerable individuals during the pandemic to prevent infection with COVID-19 are unknown at present, however, the well-being of vulnerable individuals may be at risk during long periods of strict isolation [2, 4, 5].

In March 2020, Public Health England introduced a 'shielding' policy, designed to protect individuals deemed clinically extremely vulnerable, such as oncology patients, individuals with respiratory disease, or patients taking immunosuppressive medications [6]. The '*shielding*' guidance advised clinically extremely vulnerable individuals to stay at home at all times between 23rd March and 31st July 2020 [7]. Additionally, shielded individuals were asked to stay 2 meters away from others as much as possible, even from household members. With the exception of emergencies, they could not physically attend appointments with healthcare providers. Due to the unprecedented nature of the pandemic, these expedient decisions were based on epidemiological principals rather than established evidence.

Evidence from the Middle East respiratory syndrome coronavirus (MERS-CoV) outbreak previously identified immunosuppression as a risk factor for severe infection and death [8]. The early accounts of COVID-19 risk in immunosuppressed solid organ transplant (SOT) patients were conflicting. While a protective effect of immunosuppression against the sequelae of the cytokine storm associated with severe COVID-19 was proposed, others suggested an increased risk of severe COVID-19 [9-12]. In agreement with the latter, an increased mortality rate following symptomatic COVID-19 has been demonstrated in renal transplant recipients, in comparison to patients with renal disease awaiting transplant[13]. However, a multicentre study demonstrated that the severity of illness with COVID-19 in SOT recipients was related to age and other comorbidities [14]. In addition to the great deal of uncertainty concerning risk of infection and severity of illness, these individuals may also experience anxiety regarding their specific healthcare needs not being met due to restricted access to healthcare

during shielding. Increased anxiety has been demonstrated in other patient populations that were also required to undergo shielding [15, 16]. In addition, Smith et al demonstrated worsening mental health in patients with asthma undergoing shielding during the pandemic, and individuals with a history of anxiety or depression were more vulnerable [17]. Our study was designed in response to rapidly defined Public Health research priorities for people experiencing severe distress during the COVID-19 pandemic [18, 19].

We hypothesised that SOT recipients would have a higher level of self-perceived risk for severe COVID-19, leading to greater levels of uncertainty in illness and worse health-related quality of life (HRQoL). In addition, we hypothesised that social isolation from shielding would lead to higher levels of anxiety and depression, and consequently poorer HRQoL. Our aim was to investigate health-related quality of life (HRQoL), uncertainty and coping behaviours in solid organ transplant (SOT) recipients during the COVID-19 pandemic, and identify deleterious and advantageous coping strategies used in this population. This will enable identification of at-risk groups for potential harm during shielding for this or future pandemics, allowing targeted interventions to support these individuals.

PATIENTS AND METHODS

Study design and setting

A cross-sectional survey of all SOT recipients being managed at a tertiary level transplant centre in the Midlands region of the UK, servicing a population of 10 235 000 people. Patient-reported outcomes (PROs) were the primary outcome of interest. To optimise the quality of reporting, the SPIRIT-PRO Extension guidelines were adhered to and reported where possible [20]. The study protocol was approved by the Human Research Ethics Committee (20/HRA/2613) and data acquisition approved by our institution (CARMS-16123).

Participants

All adult (≥ 18 years) liver, renal, heart, and lung transplant recipients identified through departmental electronic databases, that were alive and undergoing follow-up at our transplant centre in June 2020 were eligible for this study. A sample size calculation was not performed as the entire target population was approached.

Data collection

All eligible transplant recipients were invited to participate via a postal invitation letter at the beginning of July 2020. The invitation included the participant information sheet (PIS), details of a uniform resource locator and participant-specific login details. This ensured only one online survey could be completed per recipient via the Research Electronic Data Capture (REDCap®) program [21]. A paper-based version of the consent and survey was provided upon request. Only English language versions of the study survey, including PRO tools, were provided and the use of a proxy to complete or translate the survey was permitted. The survey remained open for a 28-day period until the 31st July 2020, which coincided with the last day of the recommended shielding period by Public Health England.

Demographics and Clinical Data

Demographic, transplant and health characteristics, were self-reported by patients. COVID-19 infection was defined as reporting a positive COVID RT-PCR test, and suspected COVID-19 infection (in

absence of a negative or positive test) as a self-reported illness with the presence of two or more of the following COVID-19 key symptoms; temperature, persistent cough, and anosmia. Self-reported illness consistent with COVID-19 was included in our case definition due to lack of routine testing of individuals with mild symptoms.

Both non-white ethnicity and a lower socioeconomic status have been extensively reported in the scientific literature and media as being associated with poorer COVID-19 outcomes, therefore this group may have additional levels of concern or uncertainty [22, 23]. Data was collected on participants self-reported ethnicity and the Index of Multiple Deprivation (IMD) was used to assess socioeconomic status. The IMD quintile values, a measure of relative deprivation at small local area level, were calculated from each recipient's residential postcode using the English Indices of Deprivation 2019 [24].

PRO Measures

A single measurement with relevant PROs was performed with reference to the period of shielding (March-July 2020). The primary outcome measure was health-related quality of life (HRQoL) using the EQ-5D-5L questionnaire [25]. Secondary outcomes comprised levels of uncertainty and coping strategies, measured with the Short Form Mishel Uncertainty in Illness scale (SF-MUIS) and Brief COPE questionnaire [26][27]. These tools were chosen to minimise the participant response burden.

EQ-5D-5L is a standardised, non-disease-specific measure of self-perceived health status widely used around the world in clinical research and population health studies, and real-world clinical settings, being recommended by several health technology assessment bodies internationally [28]. It incorporates 5 domains (mobility, self-care, usual activities, pain and discomfort, and anxiety and depression), further including an assessment of overall health using a visual analogue scale (VAS; best imaginable health is 100, and worst imaginable health is 0). The EQ-5D-5L version (using 5 levels of response; e.g. not, slightly, moderately, severely, or extremely) is more sensitive and suffers less ceiling effect than the original 3-level instrument (EQ-5D-3L) [29]. It has been validated in multiple populations across geographical and disease areas [30]. The EQ-5D-5L instrument was used

according to the published instructions [31]. The five domain scores were used to calculate the health state index scores, ranging from less than 0 (where 0 is the value of a health state equivalent to dead; negative values representing values as worse than dead) to 1 (the value of full health), which were used in the analysis.

The SF-MUIS comprises 5 questions and assesses 4 components of uncertainty: ambiguity, complexity, inconsistency and unpredictability. This derives a score (range 5-25) with higher levels corresponding to increased levels of uncertainty-in-illness. In a validation study conducted in the Norwegian breast cancer population, the ordinal coefficient alpha for the SF-MUIS was 0.70, which is considered reasonably consistent. The correlation coefficient was 0.98, supporting excellent reliability of the scale. The Brief COPE evaluates 14 coping strategies (Table 4) by answering 28 items on a 4-point Likert scale (1 = “I haven’t been doing this at all” to 4 = “I’ve been doing this a lot”). In the original validation study [27], the Cronbach's alpha coefficient of each scale ranged from (0.50 to 0.90), showing acceptable to extremely good reliability [31]. The instrument was used according to the instructions available from the author [32].

Participants self-reported COVID-19 infection status, shielding behaviour, risk perceptions and public trust were assessed using items from the World Health Organisations (WHO) standard protocol: COVID-19 Snapshot Monitoring (COSMO Standard), using both Likert and VAS scales [33]. Items regarding the protective behaviour of shielding and public trust were modified to represent the UK-specific recommendations and healthcare system, as recommended. Access to and perceptions of primary, secondary, and tertiary healthcare services were assessed. Participants’ concerns were investigated by allowing selection from a standard list of concerns derived from a general population survey on the mental health impact of the COVID-19 pandemic [18].

Population comparisons

EQ-5D-5L domains and index scores were compared with the general population in England using the Health Survey for England 2017 (HSE), which comprised a multi-stage, stratified, random probability

sample of 7 997 adults respondents. Disease-specific comparison was achieved with four post-transplant cohorts, after crosswalk from EQ-5D-5L to EQ-5D-3L according to NICE guidelines [34-37]. These four cohorts consisted of patients that were in the early or late post-operative period following either renal or liver transplantation and were compared to subgroups of the study population accordingly [34, 35, 38, 39].

The rate of self-reported COVID-19 positive cases were compared to national registry data on SOT recipients, compiled by the UK transplant regulatory body (NHS Blood and Transplant) and divided into geographic regions [40]. Shielding adherence data was compared to National UK Shielding Behavioural Survey conducted in July 2020 by the Office for National Statistics. This survey included 4 081 clinically extremely vulnerable sampled through the National Shielding Helpline [41].

Statistical analysis

Analyses were performed using STATA/SE v16.1 (College Station, Tx: StataCorp LLC). Explanatory variables for primary and secondary outcomes, such as demographics, transplantation and immunosuppression details, shielding behaviours, perceptions of COVID-19 risk, self-reported COVID-19 infection status, and access to healthcare, were pre-specified.

The relationship between EQ-5D-5L_{index} score (primary outcome) and explanatory variables was assessed using a backward stepwise selection process with an alpha-to-remove of ≥ 0.1 as criteria for inclusion in a multivariable linear regression model. Age, sex, ethnicity, IMD and BMI were forced into the model. A similar backward stepwise linear regression model was built for SF-MUIS uncertainty scale.

A two-sample t-test or Chi-square test was performed, as appropriate, to assess for statistically significant differences between comparison population datasets, and for differences in age, gender, type of organ transplanted, time since transplantation, ethnicity, first language, and IMD between survey responders and non-responders.

Patient and public involvement

Patient and public involvement was first initiated during the design stage of the study, through consultation and pilot testing. Feedback and opinion on the questionnaire design, methods of administration, and time required to participate were obtained.

RESULTS

Baseline demographics

826 of the 3 839 (21.5%) SOT recipients invited to participate completed the entire survey and were included in the analysis (Figure 1). The median age of responders was 60 years, and 57% (470/826) were male (Table 1). Time since transplant was more than five years in 61%, and 72% had undergone a liver transplant. 28% reported ≥ 2 co-morbidities (including renal dialysis, cardiac, respiratory, diabetes, hypertension), 20% had a history of a mental health illness, with depression being the most frequent (88/826). Most responders were on two or more immunosuppressive medications (67%). Responders were more likely to be older, had longer duration post-transplantation, be of a white ethnicity, and to have a higher IMD (Supplementary Table 1).

Shielding and COVID-19 infection

The adherence levels to different components of the shielding advice are shown in Table 2. Comparable to national data, communication of official advice to shield for clinically extremely vulnerable individuals had been highly successful in reaching our responders (95% vs 96%, $p = 0.17$, Supplementary Table 2)[42]. 96% declared adherence with shielding advice, which was significantly lower than the 99% adherence observed at a national level ($p < 0.001$). Adherence to the recommendation to stay home at all times was significantly better in our cohort.

Eight (1%) responders tested positive for COVID-19, and 16 (2%) declared a combination of 2 or more key symptoms for COVID-19. Twelve patients reported that their symptoms required hospital admission, but no recipients reported admission to the intensive treatment unit (ITU) or need for ventilatory support. A comparison with NHSBT registry data, showed no significant difference between our survey and either the national or regional level transplant registry infection rate in SOT recipients (Supplementary Table 3).

Perception of risk and public trust

The probability of contracting COVID-19 was perceived as extremely likely or somewhat likely in a minority of responders (27%), and a perceived high level of knowledge regarding how to protect themselves from COVID-19 was reported (median Visual analogue scale (VAS) 94/100) (Table 3). However, a high perceived susceptibility to COVID-19 infection was reported (median VAS 78/100), and responders believed they would be severely unwell with COVID-19 (median VAS 91/100). 24% of responders reported their access to healthcare had been compromised during shielding, putting them at potential risk. Compared to local healthcare facilities and government, SOT recipients had the greatest confidence in their transplant centre to manage COVID-19 well (median 95/100) (Table 3).

Uncertainty levels and coping strategies

Median uncertainty-in-illness during shielding for COVID-19, measured by the SF-MUIS score, was 11 (range 5 – 24), and was considered low. The frequency of coping strategies used are shown in Table 4. Acceptance was the most frequently used coping strategy (92%, mean 3.25, SD 0.8, on a 4-point Likert scale), followed by active coping, self-distraction and planning. The least reported coping strategies were substance abuse, behavioral disengagement, denial and self-blame. The Cronbach-alpha value for the SF MUIS and Brief COPE responses was 0.66 and 0.77, respectively.

Perceived health status

Comparing EQ-5D-5L domains and index scores for shielded SOT recipients to age-matched UK population controls, health was equivalent in the youngest and eldest cohorts (18-24 years, and >75 years), however significantly poorer for SOT recipients in the 35-74 age range for the majority of health domains (Table 5). Median EQ-5D-5L_{index} score for age categories were consistently lower in SOT recipients but did not reach statistical significance (Figure 2). The Cronbach-alpha value for the EQ-5D-5L was 0.88.

Comparing overall EQ-5D-3L index scores, perceived health status was worse for SOT recipients during shielding, than for pre-pandemic age-matched general population cohorts. Comparing perceived

health status with disease-specific controls, did not reveal consistent results. EQ-5D-3L VAS in liver transplant recipients during shielding were equivalent to pre-pandemic controls in the early post-transplant period (<2years), but with a trend to worse outcomes than the pre-pandemic group in the late period (>2years after liver transplantation). Conversely, perceived health status (EQ-5D index score) showed a trend towards better EQ-5D VAS scores in a smaller subgroup of renal transplant recipients during shielding compared to a pre-pandemic renal transplant cohort ≥ 2 years after transplantation (Figure 3)[34-36].

Multivariable linear regression model of EQ-5D-5L_{index} scores revealed a significant relationship between several explanatory variables, as shown in Table 6. A previous history of mental health illness, and being underweight or obese were significantly associated with lower EQ-5D-5L_{index} scores. Additionally, reporting not knowing whether they had been infected with COVID-19, perception of high likelihood of severe COVID-19 infection, compromised access to health-care, higher levels of uncertainty in illness, and a coping strategy of behavioural disengagement were also associated with lower EQ-5D-5L_{index} scores. Conversely, increasing deprivation index, chronic respiratory comorbidity, a coping strategy of self-distraction and positive reframing, and perceived safe access to their hospital despite not needing to attend were associated with higher EQ-5D-5L_{index} scores.

Uncertainty-in-illness

Regression analysis revealed an association between increasing uncertainty and compromised access to healthcare, coping strategies of denial, substance abuse, behavioural disengagement and planning (Table 7). Moderate deprivation, renal transplant recipients, higher EQ-5D-5L_{index} scores, a low perceived risk of contracting COVID-19, public trust and an acceptance coping strategy were associated with lower levels of uncertainty.

DISCUSSION

This large cross-sectional study of unselected solid organ transplant recipients focused on identifying risk factors for poor health-related quality of life during shielding for the COVID-19 pandemic. A poorer self-perception of health status in shielded SOT recipients was most significantly associated with a previous history of mental health illness, being overweight, reporting compromised access to healthcare and a coping strategy of behavioural disengagement. Increased uncertainty was also associated with poorer health status index scores, compromised access to healthcare, and several coping strategies (denial, substance abuse, behavioural disengagement and planning).

Overall, our study population showed resilience with low levels of uncertainty, the ability to use acceptance, self-distraction and positive reframing as coping strategies and to adhere to protective behaviours.

The main concepts of illness uncertainty, coping strategies and quality of life, have previously been described to be interrelated and incorporated in a theoretical framework. This is the first study to report these in detail in a shielded transplant population during the COVID pandemic (Figure 4) [43-47].

SOT recipients perceived themselves to be at high risk of contracting COVID-19 and experiencing a severe course of illness. Although, these perceptions may not be inappropriate, accurately quantifying risk, e.g. through methods such as cognitive re-appraisal and pro-active protective health behaviours, can reduce levels of fear and ensure it is proportional to the degree of threat [48-51]. In accordance, adherence levels to shielding were high and responders generally felt they knew how to protect themselves from COVID very well. This was accompanied by low levels of uncertainty, comparable to previous pre-pandemic transplant cohorts [52]. Previous studies suggest that structure providers, such as credible authorities, can decrease uncertainty directly by promoting interpretation and congruency of events [53]. The overarching public health recommendation of shielding for clinically extremely vulnerable individuals in England may have decreased uncertainty in our study population by promoting a clear interpretation of events. This was evidenced in our study by high levels of public trust, high adherence to shielding and high confidence in the effectiveness of shielding. However, no international

comparison cohort of SOT recipients was available to compare uncertainty levels and health status under different public health approaches [19]. Survey respondents expressed the highest level of confidence in the transplant service healthcare professionals to manage issues with COVID-19 well. These findings suggest that transplant units may be optimally positioned to promote interpretation of public health interventions aimed at improving the effectiveness and tolerability of shielding.

Acceptance was a frequent coping strategy in our patient cohort, and is suggested to be beneficial in times of uncertainty and improve psychological flexibility [19] [54, 55]. Our data support previous findings in transplant recipients of strong protective coping strategies to reduce uncertainty and focus on opportunities. SOT recipients may have developed strong coping strategies of acceptance and reframing with positive associations by their earlier experiences surrounding their transplantation. Previous studies have suggested that this may point at probabilistic perspectives on life, accepting uncertainty as a natural part of it [56, 57]. In contrast, avoidance coping strategies (denial, behavioural disengagement and substance abuse), often associated with psychological rigidity, was significantly related to poorer health and increased uncertainty in our study. The identified risk factors for poor HRQoL and higher levels of uncertainty may help target interventions for individuals at higher risk (such as previous mental health illness and obesity), as well as at specific items or components of the healthcare system (such as psychological support). Techniques such as sign-posting and encouraging activities balancing pleasure, mastery, and social connection have been described to reduce behavioural disengagement [49-51]. Health providers could, for example, improve access to video rather than telephone consultations, to provide a greater sense of social interaction and engagement.

Unintended harm caused by shielding has previously been reported in shielded patients. The Office of National Statistics reported 785,000 (35%) of shielded patients experiencing worsening mental health and wellbeing, and 6% reporting much worse mental health [58]. The general public has similarly experienced reductions in social interaction through 'lockdowns', and population surveys report stress and anxiety ranging from 20-53%, and depression rates of 2.7-37.8% [59-65]. The shielded population

represent the most extreme end of this spectrum with regard to restrictions. While our data are unable to exactly quantify the impact of shielding on perceived health status in SOT, a cautious comparison of our cohort with data from a pre-pandemic general population cohort suggested poorer health status index scores in shielded SOT recipients. However, comparisons of subgroups of shielded transplant recipients with pre-pandemic transplant cohorts at equivalent stages post-transplant were difficult to interpret. Previous studies show poorer HRQoL specifically in the first 6 months post-transplant, while improving and stabilising significantly after this period [34-36, 66]. Our results may suggest these changes in HRQoL are equivocal and mild in a majority, but an ideal comparison group of non-shielded SOT recipients during the pandemic was lacking in our study population or nationally. International recruitment would have been hampered by major differences in policies and language barriers. The survey data was collected during the pandemic in a cross-sectional manner, and therefore a direct comparison to pre-pandemic levels was not achievable. It is possible that associations of HRQoL and uncertainty was pre-existing and unrelated to the COVID pandemic.

Reuken *et al* surveyed 394 SOT recipients, and included 112 wait-list candidates, and 394 immediate household contacts during shielding for COVID-19 as controls [67]. They identified high levels of fear of COVID-19 infection in SOT recipients. This study was limited by its use of non-validated tools, and therefore interstudy comparison is not possible.

A limitation of the present study is the significantly higher proportion of non-responders from black, Asian and minority ethnic (BAME) groups, potentially related to language barriers. Including multi-lingual versions was however not possible due to our PRO tools not being validated in different languages [68, 69]. Subsequent studies need to ensure inclusion of at risk groups, such as BAME, by including translated or culturally validated measures. The survey response rate was 21.5% which is below the generally accepted 60% threshold for survey research, and the possibility responders do not accurately represent the target population exists [70]. However, the number of respondents in this study exceeded the threshold of 351 that has been previously reported to be representative of a population of approximately 4,000 [70, 71]. Selection bias may have impacted the results of this study, an often unintended consequence of a cohort study design with an effect size and direction that is difficult to

predict [72]. The method of delivering the survey by postal letters and invitation to participate online have likely contributed and may have imparted bias. However, alternate methods such as providing the survey at outpatient visits, was not possible due to shielding requirements.

Conclusive evidence of which patients are most vulnerable to severe COVID-19 disease and would benefit most from shielding is currently lacking. We relied on self-reported COVID infection rates at a time that confirmatory testing was not implemented and our study obtained no responses from recipients with severe COVID infection. The national NHSBT registry data on showed similarly low COVID-19 infection rates in SOT, however, our study carries a significant risk of responder bias for this parameter.

In conclusion, our findings demonstrate a self perceived health status that is below average in shielded SOT recipients, a subgroup of clinically extremely vulnerable individuals. Our study shows a resilient population reliant on acceptance and adherence to protective behaviour. Strategies to improve outcomes during shielding for the pandemic may be targeted at identified risk groups, reducing uncertainty and prevention of maladaptive coping strategies. Provision of continuity of care, information and clear guidance during different stages of the pandemic may increase public trust and address the specific concerns of individuals deemed clinically extremely vulnerable to COVID-19.

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Data sharing agreement:

Data collected for this study, including individual participant data and the data data dictionary, will be made available to others at publication. The data will be in anonymised form to protect participants privacy. The authorship agrees to provide access to all additional study documents.

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Tables

Table 1: Baseline characteristics of respondents of the COVID Transplant Survey

| | N (%) |
|--|--------------|
| Total number of respondents | 826 |
| Age in years (median, IQR) | 60 (50.67) |
| Sex Male | 470 (57) |
| Ethnicity | .. |
| White | 766 (93) |
| BAME | 54 (7) |
| Prefer not to answer | 6 (1) |
| Index of Deprivation | .. |
| 1 (Least Deprived) | 111 (13) |
| 2 | 127 (15) |
| 3 | 134 (16) |
| 4 | 155 (19) |
| 5 (Most Deprived) | 196 (24) |
| Not available | 103 (12) |
| Medical comorbidities | .. |
| Diabetes | 140 (17) |
| Hypertension | 456 (55) |
| Heart disease | 74 (9) |
| Chronic lung disease | 65 (8) |
| End stage renal failure | 6 (1) |
| Number of medical comorbidities per recipient | .. |
| 0 | 228 (28) |
| 1 | 364 (44) |
| 2 | 173 (21) |
| ≥3 | 61 (7) |
| BMI | .. |
| Normal weight | 277 (34) |
| Underweight | 14 (2) |
| Overweight | 268 (32) |
| Obese | 203 (25) |
| Invalid entry | 64 (8) |
| Mental Health Illness (Yes) | 166 (20) |
| Anxiety | 16 (2) |
| Depression | 88 (11) |
| PTSD | 43 (5) |
| Other | 19 (2) |
| Organ Transplanted | .. |
| Liver | 593 (72) |
| Kidney | 146 (17) |
| Heart or Lung | 87 (11) |
| Time since transplant | .. |
| <1 year | 58 (7) |
| 1-2 years | 74 (9) |
| 2-5 years | 188 (23) |

| | |
|-----------------------------------|----------|
| > 5 years | 506 (61) |
| Level of Immunosuppression | .. |
| No immunosuppression | 1 (0) |
| Monotherapy | 269 (33) |
| Dual therapy | 360 (44) |
| Triple therapy or more | 196 (23) |
| Steroids (Yes) | 312 (38) |
| Missing | 3 (0) |

* BAME = Black, Asian and minority ethnic

Table 2: Solid organ transplant recipient shielding during the COVID-19 pandemic: advice received, shielding adherence, and elements followed.

| | N (%) |
|---|-----------------|
| Total Number of Respondents | 826 |
| Received government advice regarding shielding (Yes) | 793 (96) |
| No | 26 (3) |
| Unsure | 7 (1) |
| Followed government advice to shield (Yes) | 793 (96) |
| Point shielding commenced | .. |
| Before advice received | 656 (79) |
| After advice received | 149 (18) |
| Decided not to shield | 21 (3) |
| Adherence to all recommended elements of Shielding | .. |
| Yes | 587 (71) |
| No | 13 (2) |
| Partially | 226 (27) |
| Staying home at all times | .. |
| Yes | 587 (71) |
| No | 13 (2) |
| Partially | 226 (27) |
| Avoided gatherings | .. |
| Yes | 794 (96) |
| No | 9 (1) |
| Partially | 23 (3) |
| Avoided contact with symptomatic people | .. |
| Yes | 812 (98) |
| No | 8 (1) |
| Partially | 6 (1) |
| Observed social distancing within household | .. |
| Yes | 349 (42) |
| No | 321 (39) |
| Partially | 156 (19) |
| Number of members in household | .. |
| Lives alone | 121 (15) |
| One other person | 425 (51) |
| 3 to 5 people | 270 (33) |
| 6 or more people | 10 (1) |

Table 3: COVID-19 risk perceptions and access to services

| | N (%) |
|--|---------------|
| Total Number of Respondents | 826 |
| What do you consider to be your own probability of getting infected with COVID-19?* | .. |
| Extremely likely | 78 (9) |
| Somewhat likely | 145 (18) |
| Neither likely or unlikely | 229 (28) |
| Somewhat unlikely | 251 (30) |
| Extremely unlikely | 123 (15) |
| Perceived risks and beliefs (visual analogue scale 0-100)* | .. |
| How susceptible do you consider yourself to be to an infection with COVID-19? † | 78.0 (50-95) |
| How severe do you think contracting COVID-19 would be for you? ‡ | 91.0 (80-100) |
| Do you know how to protect yourself from COVID-19? § | 94.0 (83-100) |
| For me avoiding an infection with COVID-19 in the current situation is? †† | 75.0 (50-88) |
| During shielding for COVID-19 I had safe and reliable access to: | .. |
| Getting my prescriptions | .. |
| Yes | 721 (87) |
| No | 17 (2) |
| Partially | 88 (11) |
| Visiting my GP | .. |
| Yes | 266 (32) |
| No | 53 (6) |
| Did not attend | 507 (61) |
| Visiting the health-care facilities at my local hospital | .. |
| Yes | 223 (27) |
| No | 46 (6) |
| Did not attend | 557 (67) |
| Visiting the health-care facilities at my transplant unit | .. |
| Yes | 125 (15) |
| No | 37 (4) |
| Did not attend | 630 (76) |
| Not applicable as local hospital is transplant unit | 34 (4) |
| How much confidence do you have in the below individuals and organisations that they can handle COVID-19 well? (visual analogue scale 0-100)* | .. |
| The specialist doctors and nurses of the transplant unit? ‡‡ | 95.0 (80-100) |
| Your own family doctor/GP? ‡‡ | 75.0 (50-90) |
| Your local hospital? ‡‡ | 75.0 (50-90) |
| Department of Health? ‡‡ | 52.0 (41-80) |
| The Government? ‡‡ | 50 (22-72) |
| Has your access to healthcare been compromised due to shielding, putting you at potential risk? | .. |
| Yes | 201 (24) |
| No | 625 (76) |

* Questions adapted from the World Health Organisations (WHO) tool for behavioural insights on COVID-19 to assess risk perceptions, behaviours, trust and knowledge[33].

† 0 = not susceptible, 100 = very susceptible

‡ 0 = not severely unwell, 100 = severely unwell

§ 0 = don't know at all, 100 = know very well

†† 0 = extremely difficult, 100 = extremely easy

‡‡ 0 = no confidence, 100 = very confident

Table 4: Coping strategies used by shielded solid organ transplant recipients (Brief COPE)

| Coping Strategy | Likert Scale | | Percentage reporting Likert 2, 3 or 4 points* | |
|---------------------------|--------------|------|---|-------|
| | Mean | SD | Mean | SD |
| Substance abuse | 1.16 | 0.46 | 11.4% | 0.013 |
| Behavioural disengagement | 1.29 | 0.56 | 19.1% | 0.060 |
| Denial | 1.33 | 0.60 | 21.6% | 1.144 |
| Self-blame | 1.38 | 0.66 | 23.7% | 0.160 |
| Religion | 1.45 | 0.85 | 25.4% | 0.013 |
| Venting | 1.58 | 0.69 | 40.7% | 0.190 |
| Instrumental support | 1.79 | 0.77 | 54.6% | 0.091 |
| Humour | 1.92 | 0.92 | 55.5% | 0.043 |
| Emotional support | 2.23 | 0.89 | 70.9% | 0.056 |
| Positive reframing | 2.23 | 0.92 | 71.0% | 0.053 |
| Planning | 2.31 | 0.92 | 70.8% | 0.076 |
| Self-distraction | 2.57 | 0.95 | 78.5% | 0.031 |
| Active coping | 2.66 | 0.90 | 78.9% | 0.049 |
| Acceptance | 3.25 | 0.80 | 91.7% | 0.028 |

*2=I've been doing this a little bit; 3=I've been doing this a medium amount; 4=I've been doing this a lot

Table 5: Health-related quality of life in shielded solid organ transplant (SOT) recipients compared to UK population** (using EQ-5D-5L***)

| EQ5D Domains | 18-24 years | | 25-34 years | | 35-44 years | | 45-54 years | | 55-64 years | | 65-74 years | | > 75 years | |
|-------------------------------|------------------|---------------|------------------|---------------|------------------|---------------|------------------|---------------|------------------|---------------|------------------|---------------|------------------|---------------|
| | COVID-Transplant | UK population | COVID-Transplant | UK population | COVID-Transplant | UK population | COVID-Transplant | UK population | COVID-Transplant | UK population | COVID-Transplant | UK population | COVID-Transplant | UK population |
| | N=15 (%) | N=422 (%) | N=50 (%) | 977 (%) | N=70 (%) | 1196 (%) | N= 162 (%) | 1218 (%) | N=232 (%) | 1243 (%) | N= 247 (%) | 1124 (%) | N=49 (%) | 851 (%) |
| Mobility | | | | | | | | | | | | | | |
| 1 | 15 (100) | 377 (89) | 41 (82) | 887 (91)* | 47 (67) | 1042 (87)* | 109 (67) | 975 (80)* | 140 (60) | 919 (74)* | 138 (56) | 743 (66)* | 19 (39) | 417 (49) |
| 2 | 0 (0) | 31 (7) | 4 (8) | 61 (6) | 9 (13) | 89 (7) | 23 (14) | 118 (10) | 32 (14) | 162 (13) | 49 (20) | 163 (15) | 11 (22) | 180 (21) |
| 3 | 0 (0) | 10 (2) | 5 (10) | 20 (2) | 11 (16) | 35 (3) | 24 (15) | 64 (5) | 38 (16) | 84 (7) | 42 (17) | 124 (11) | 8 (16) | 129 (15) |
| 4 | 0 (0) | 3 (1) | 0 (0) | 8 (1) | 2 (3) | 26 (2) | 5 (3) | 51 (4) | 20 (9) | 69 (6) | 18 (7) | 86 (8) | 9 (18) | 112 (13) |
| 5 | 0 (0) | 1 (0) | 0 (0) | 1 (0) | 1 (1) | 4 (0) | 1 (1) | 10 (1) | 2 (1) | 9 (1) | 0 (0) | 8 (1) | 2 (4) | 13 (2) |
| Self care | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| 1 | 14 (93) | 409 (97) | 46 (92) | 944 (97) | 56 (80) | 1146 (96)* | 134 (83) | 1121 (92)* | 177 (76) | 1108 (89)* | 205 (83) | 990 (88)* | 37 (76) | 714 (84) |
| 2 | 1 (7) | 5 (1) | 3 (6) | 22 (2) | 6 (9) | 24 (2) | 14 (9) | 39 (3) | 26 (11) | 62 (5) | 25 (10) | 69 (6) | 3 (6) | 69 (8) |
| 3 | 0 (0) | 6 (1) | 1 (2) | 8 (1) | 4 (6) | 15 (1) | 9 (6) | 40 (3) | 25 (11) | 44 (4) | 12 (5) | 50 (4) | 7 (14) | 42 (5) |
| 4 | 0 (0) | 2 (0) | 0 (0) | 3 (0) | 3 (4) | 9 (1) | 4 (2) | 14 (1) | 4 (2) | 20 (2) | 2 (1) | 14 (1) | 1 (2) | 18 (2) |
| 5 | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (1) | 2 (0) | 1 (1) | 4 (0) | 0 (0) | 9 (1) | 3 (1) | 1 (0) | 1 (2) | 8 (1) |
| Usual activities | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| 1 | 13 (87) | 368 (87) | 35 (70) | 872 (89)* | 41 (59) | 1040 (87)* | 108 (67) | 981 (81)* | 126 (54) | 931 (75)* | 138 (56) | 787 (70)* | 21 (43) | 489 (57) |
| 2 | 1 (7) | 41 (10) | 8 (16) | 67 (7) | 13 (19) | 82 (7) | 26 (16) | 112 (9) | 44 (19) | 160 (13) | 58 (23) | 173 (15) | 11 (22) | 172 (20) |
| 3 | 0 (0) | 8 (2) | 6 (12) | 28 (3) | 10 (14) | 43 (4) | 21 (13) | 64 (5) | 38 (16) | 91 (7) | 34 (14) | 97 (9) | 11 (22) | 115 (14) |
| 4 | 1 (7) | 4 (1) | 1 (2) | 9 (1) | 3 (4) | 25 (2) | 5 (3) | 48 (4) | 13 (6) | 46 (4) | 12 (5) | 50 (4) | 6 (12) | 54 (6) |
| 5 | 0 (0) | 1 (0) | 0 (0) | 1 (0) | 3 (4) | 6 (1) | 2 (1) | 13 (1) | 11 (5) | 15 (1) | 5 (2) | 17 (2) | 0 (0) | 21 (2) |
| Pain and discomfort | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| 1 | 10 (67) | 316 (75) | 33 (66) | 720 (74) | 28 (40) | 742 (62)* | 73 (45) | 657 (54)* | 85 (37) | 599 (48)* | 107 (43) | 445 (40) | 17 (35) | 312 (37) |
| 2 | 5 (33) | 64 (15) | 12 (24) | 175 (18) | 21 (30) | 303 (25) | 51 (31) | 342 (28) | 72 (31) | 374 (30) | 75 (30) | 378 (34) | 17 (35) | 246 (29) |
| 3 | 0 (0) | 34 (8) | 4 (8) | 56 (6) | 15 (21) | 103 (9) | 30 (19) | 148 (12) | 52 (22) | 185 (15) | 51 (21) | 203 (18) | 11 (22) | 205 (24) |
| 4 | 0 (0) | 7 (2) | 1 (2) | 21 (2) | 4 (6) | 35 (3) | 8 (5) | 48 (4) | 21 (9) | 62 (5) | 13 (5) | 85 (8) | 3 (6) | 73 (9) |
| 5 | 0 (0) | 1 (0) | 0 (0) | 5 (1) | 2 (3) | 13 (1) | 0 (0) | 23 (2) | 2 (1) | 23 (2) | 1 (0) | 13 (1) | 1 (2) | 15 (2) |
| Anxiety and depression | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. |

| | | | | | | | | | | | | | | |
|---|--------|----------|---------|-----------|---------|-----------|---------|-----------|----------|-----------|----------|-----------|---------|----------|
| 1 | 7 (47) | 265 (63) | 19 (38) | 669 (68)* | 30 (43) | 825 (69)* | 70 (43) | 833 (68)* | 116 (50) | 879 (71)* | 149 (60) | 831 (74)* | 36 (73) | 609 (72) |
| 2 | 2 (13) | 89 (21) | 17 (34) | 182 (19) | 22 (31) | 235 (20) | 64 (40) | 222 (18) | 70 (30) | 217 (17) | 67 (27) | 193 (17) | 7 (14) | 157 (18) |
| 3 | 5 (33) | 48 (11) | 10 (20) | 96 (10) | 12 (17) | 96 (8) | 22 (14) | 104 (9) | 37 (16) | 95 (8) | 24 (10) | 83 (7) | 6 (12) | 65 (8) |
| 4 | 1 (7) | 14 (3) | 4 (8) | 28 (3) | 2 (3) | 31 (3) | 4 (2) | 37 (3) | 6 (3) | 35 (3) | 6 (2) | 11 (1) | 0 (0) | 17 (2) |
| 5 | 0 (0) | 6 (1) | 0 (0) | 2 (0) | 4 (6) | 9 (1) | 2 (1) | 22 (2) | 3 (1) | 17 (1) | 1 (0) | 6 (1) | 0 (0) | 3 (0) |

*P value<0.05

**UK population data derived from Health Survey England 2017

*** representing 5 levels of response for each domain; e.g. not=1, slightly, moderately, severely, or extremely=5.

Table 6: Linear regression analysis (ordinary least squares) of health-related quality of life (EQ-5D-5L_{index}) for shielded solid organ transplant recipients during the COVID-19 pandemic

| Variables (r^2 0-41) (n=826) | Category | EQ-5D-5L index | | |
|---|------------------------------------|----------------|---------------|---------|
| | | β (Coef) | 95% CI | P-value |
| Age distribution (years) (18-24 years = reference group) | 25-34 | 0.02 | -0.08 – 0.12 | 0.715 |
| | 35-44 | -0.05 | -0.15 – 0.04 | 0.298 |
| | 45-54 | -0.02 | -0.11 – 0.07 | 0.699 |
| | 55-64 | -0.07 | -0.16 – 0.02 | 0.141 |
| | 65-74 | -0.04 | -0.13 – 0.04 | 0.324 |
| | >75 | -0.09 | -0.19 – 0.01 | 0.066 |
| Sex (Female = reference group) | Male | -0.01 | -0.03 – 0.02 | 0.553 |
| Ethnicity | BAME | 0.02 | -0.03 – 0.07 | 0.414 |
| (White = reference group) | Prefer not to answer | 0.05 | -0.09 – 0.18 | 0.515 |
| Index of multiple deprivation (1 = reference group; least deprived) | 2 | 0.00 | -0.04 – 0.05 | 0.936 |
| | 3 | 0.05 | 0.01 – 0.10 | 0.017 |
| | 4 | 0.05 | 0.01 – 0.09 | 0.026 |
| | 5 (most deprived) | 0.07 | 0.02 – 0.11 | 0.002 |
| | Not available | 0.00 | -0.04 – 0.05 | 0.898 |
| Body Mass Index (Kg/m2) (Normal weight = reference group) | Underweight | -0.10 | -0.19 - -0.01 | 0.028 |
| | Overweight | -0.00 | -0.03 – 0.03 | 0.838 |
| | Obese | -0.05 | -0.08 - -0.02 | 0.004 |
| Self-reported comorbidities | End stage renal disease (Dialysis) | 0.23 | 0.09 – 0.37 | 0.001 |
| | Mental Health Illness (Yes) | -0.12 | -0.16 - -0.09 | 0.000 |
| | Chronic respiratory disease | 0.03 | 0.01 – 0.05 | 0.014 |
| Self-reported COVID infection | | | | |
| (No = reference group) | Don't know | -0.04 | -0.07 - -0.00 | 0.031 |
| Uncertainty | Mishel Score (SF-MUIS) | -0.01 | -0.01 - -0.00 | <0.001 |
| Coping Strategies (Brief COPE) | Self-distraction | 0.02 | 0.00 – 0.03 | 0.033 |
| | Positive reframing | 0.02 | 0.00 – 0.03 | 0.022 |
| | Disengagement | -0.09 | -0.11 - -0.06 | 0.000 |
| Perceptions | | | | |
| <i>Compromised access to health care</i> | | | | |
| (No = reference group) | Yes | -0.05 | -0.08 - -0.02 | 0.001 |
| <i>Safe and reliable access to hospital</i> | Yes | 0.06 | 0.00 – 0.12 | 0.040 |
| (No = reference group) | Did not attend | 0.10 | 0.05 – 0.15 | <0.001 |
| <i>Trust in Local hospital</i> | | <0.01 | 0.00 - 0.00 | 0.013 |

* β coefficient rounded off to two decimal places

Table 7: Linear regression analysis of uncertainty in illness (SF-MUIS) for shielded solid organ transplant recipients during the COVID-19 pandemic

| Variables (r^2 0.35) (n=826) | Category | Mishel score | | |
|---|-----------------------------|----------------|---------------|---------|
| | | β (Coef) | 95% CI | P-value |
| Age distribution (years) | 25-34 | -0.38 | -2.04 – 1.28 | 0.653 |
| (18-24 years = reference group) | 35-44 | -0.74 | -2.35 – 0.87 | 0.369 |
| | 45-54 | -1.42 | -2.96 – 0.11 | 0.068 |
| | 55-64 | -0.34 | -1.85 – 1.16 | 0.654 |
| | 65-74 | 0.22 | -1.29 – 1.73 | 0.778 |
| | >75 | -0.70 | -2.37 – 0.97 | 0.411 |
| Sex (Female = reference group) | Male | -0.27 | -0.68 – 0.14 | 0.197 |
| Ethnicity | BAME | 0.45 | -0.38 – 1.28 | 0.292 |
| (White = reference group) | Prefer not to answer | 1.63 | -0.67 – 3.93 | 0.166 |
| Index of multiple deprivation | 2 | 0.09 | -0.65 – 0.83 | 0.817 |
| (1 = reference group; least deprived) | 3 | -0.74 | -1.49 – 0.00 | 0.051 |
| | 4 | -0.67 | -1.40 – 0.06 | 0.073 |
| | 5 (most deprived) | -0.28 | -0.99 – 0.43 | 0.434 |
| | Not available | -0.18 | -0.98 – 0.62 | 0.667 |
| Body Mass Index (Kg/m2) | Underweight | 0.31 | -1.25 – 1.87 | 0.698 |
| (Normal weight = reference group) | Overweight | -0.02 | -0.50 – 0.47 | 0.950 |
| | Obese | -0.07 | -0.61 – 0.47 | 0.795 |
| | Missing | -0.72 | -1.50 – 0.07 | 0.075 |
| Organ transplanted | Kidney | -0.66 | -1.17 – -0.14 | 0.012 |
| Number of comorbidities | ≥ 3 | 0.88 | 0.12 – 1.65 | 0.023 |
| Symptoms: Muscle aches | | 2.54 | 0.22 – 4.86 | 0.032 |
| Health related Quality of Life | EQ-5D-5L index | -1.96 | -3.05 – -0.87 | <0.001 |
| Coping Strategies (Brief COPE) | Behavioural disengagement | 0.57 | 0.15 – 0.99 | 0.008 |
| | Substance abuse | 0.49 | 0.05 – 0.92 | 0.028 |
| | Denial | 0.48 | 0.11 – 0.85 | 0.010 |
| | Planning | 0.45 | 0.21 – 0.68 | < 0.001 |
| | Acceptance | -0.36 | -0.63 – -0.09 | 0.010 |
| Perceptions (No = reference group) | | | | |
| <i>Access to health care compromised?</i> | Yes | 0.90 | 0.42 – 1.39 | <0.001 |
| <i>Access to prescriptions?</i> | Yes | 1.73 | 0.34 – 3.13 | 0.015 |
| | Partially | 2.52 | 1.02 – 4.02 | 0.001 |
| <i>Susceptibility to infection with COVID-19? †</i> | | -0.01 | -0.02 – -0.00 | 0.036 |
| <i>Knows how to protect self from COVID-19? §</i> | | -0.02 | -0.03 – -0.00 | 0.009 |
| Perception of probability of getting infected with COVID-19? | | | | |
| (Extremely unlikely = reference group) | Extremely likely | 0.97 | 0.20 – 1.74 | 0.014 |
| | Neither likely nor unlikely | 0.85 | 0.37 – 1.33 | 0.001 |
| Confidence individuals and organisations can handle COVID-19 well? | | | | |
| | Doctor/GP | -0.01 | -0.02 – -0.01 | 0.000 |
| | Department of health | -0.01 | -0.02 – -0.00 | 0.047 |
| | Government | -0.01 | -0.02 – -0.00 | 0.005 |

† 0 = not susceptible, 100 = very susceptible, § 0 = don't know at all, 100 = know very well

* β coefficient rounded off to two decimal places

Figure Legends:

Figure 1: COVID Transplant Survey Consort Diagram

Figure 2: Age-matched shielded solid organ transplant recipient health-related quality of life compared to the general population of UK (Health Survey England 2017) (median EQ-5D-5L_{index} score and interquartile range).

Figure 3: Shielded solid organ transplant recipient mean EQ-5D-3L_{index} or VAS scores compared to relevant published data. The entire COVID Transplant cohort EQ-5D-3L_{index} was lower than the general population of England as per Health Survey England results. The group of patients in the study cohort that had undergone a liver transplantation were compared to the results of Ratcliffe et al in which all 213 participants were surveyed at 24 months post liver transplant. The patients in the COVID transplant cohort that were more than 2 years from transplant are compared to Russell et al (>36 months post transplant). Similar comparisons were done with the renal transplant subgroup with Li et al (6 months post transplant) and Cleemput (Median 16.7 months post transplant, IQR 7.9-38.6)

Figure 4: COVID Transplant Survey Infographic.

Antecedents and outcomes of the COVID Transplant Survey, showing identified predictors of vulnerability (*left pane*), low levels of uncertainty-in-illness and appraisal of the context (*middle pane*), supportive and maladaptive coping strategies (*right pane*), and health-related quality of life compared to a pre-pandemic English population (*far right pane*). HRQOL= Health related quality of life

Adapted from: Wright et al. Curr Pain Headache Rep 2009, and Mishel et al. Image J Nurs Sch 1990