Psychosocial evaluation of candidates for solid-organ transplantation

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Abbreviations

AASLD – American Association for the Study of Liver Diseases (AASLD)
ARLD – Alcohol-related liver disease
CI – Confidence interval
ISHLT – International Society for Heart and Lung Transplantation
KDIGO – Kidney Disease: Improving Global Outcomes
OR – Odds Ratio
PACT – Psychosocial Assessment of Candidates for Transplantation
QOLT – Quality of life therapy
RCT – Randomised controlled trial
SIPAT – Stanford Integrated Psychosocial Assessment for Transplant
SRTR – Scientific Registry of Transplant Recipients
TERS – Transplant Evaluation Rating Scale
Abstract

Transplant candidates should undergo an assessment of their mental health, social support, lifestyle and behaviours. The primary aims of this ‘psychosocial evaluation’ are to ensure transplantation is of benefit to life expectancy and quality of life, and to allow optimisation of the candidate and transplant outcomes. The content of psychosocial evaluations is informed by evidence regarding pre-transplant psychosocial predictors of transplant outcomes. This review summarises the current literature on pre-transplant psychosocial predictors of transplant outcomes across differing solid-organ transplants, and discusses the limitations of existing research. Pre-transplant depression, substance misuse, and non-adherence are associated with poorer post-transplant outcomes. Depression, smoking and high levels of prescription opioid use are associated with reduced post-transplant survival. Pre-transplant non-adherence is associated with post-transplant rejection, and non-adherence may mediate the effects of other psychosocial variables such as substance misuse. There is evidence to suggest social support is associated with likelihood of substance misuse relapse after transplantation but there is a lack of consistent evidence for an association between social support and post-transplant adherence, rejection or survival across all organ transplant types.

Psychosocial evaluations should be undertaken by a trained individual and should comprise multiple consultations with the transplant candidate, family members, and healthcare professionals. Tools exist which can be useful for guiding and standardising assessment, but research is needed to determine how well scores predict post-transplant outcomes. Few studies have evaluated interventions designed to improve psychosocial functioning specifically pre-transplant. We highlight the challenges of carrying out such research and make recommendations regarding future work.
Introduction
Prior to transplant listing, organ transplant candidates are evaluated for medical, surgical and psychosocial suitability. A psychosocial evaluation comprises a comprehensive assessment of an individual’s mental health, social support network, lifestyle and behaviours, to identify factors that may adversely impact the success of transplantation. The evaluation provides the opportunity to intervene before, during and after transplantation to reduce harm, mitigate risk and optimise graft and recipient survival, the recipient’s level of functioning and their quality of life. In this Overview article we discuss the multiple aims of a psychosocial evaluation as part of the assessment for solid-organ transplantation, before providing an overview of both the required content and the practical process of undertaking such an assessment. As this review is across solid-organ transplantation, rather than focused on a single transplant type, we compare the literature for psychosocial predictors of transplant outcomes between different organ transplants and discuss how international guidelines on psychosocial evaluation compare. We discuss whether pre-transplant psychosocial variables can accurately predict post-transplant outcomes, highlighting the limitations of existing research in this field. We then consider the process of undertaking psychosocial evaluation in clinical practice: who should undertake assessment and whose contributions should be included, the methods of assessing the required content and the use of standardised assessment tools to guide evaluation. We suggest where further research is required to inform this process and to further assess the performance of standardised tools. Finally, we summarise the evidence regarding pre-transplant interventions designed to improve psychosocial functioning to allow successful transplantation or to improve transplant outcomes. We detail the challenges of carrying out such research and make recommendations regarding future work.

In order to identify all relevant literature, we searched PubMed and Embase (Ovid) in January 2021 using free-text terms and the following MeSH terms and Subject Headings “organ transplantation”, “transplantation”, “social support”, “patient compliance” (PubMed), “medication adherence” (PubMed),
“medication compliance” (Embase), “psychosocial support systems” (PubMed), and “psychosocial care” (Embase). Searches were limited to English language articles, human studies, and solid-organ transplantation (articles referring to non-solid-organ transplantation were excluded). References of identified articles were also searched for relevant papers. We did not review research regarding the psychosocial assessment of living solid-organ donors.

**Aims of psychosocial evaluation**

The primary aims of evaluation are to ensure transplantation is anticipated to be of benefit to the candidate in terms of life expectancy and quality of life, to optimise the candidate for transplantation, and to optimise short, medium and long-term transplant outcomes. The assessment is also an opportunity to understand and manage the expectations of the transplant candidate and family members.

At a population level, whilst certain pre-transplant psychosocial problems are associated with poorer post-transplant outcomes, for an individual with psychosocial problems transplantation is still likely to provide better outcomes when compared to the alternative. However, decisions related to solid-organ transplantation have implications for other potential recipients on the waiting list. Deceased-donor organ transplantation utilises a limited resource and another aim of psychosocial evaluation is to ensure optimal use of this resource. The importance of resource scarcity in decision making differs across organ transplant types due to differences in deceased-donor organ availability, opportunities for living donor transplants, and the availability of life-sustaining organ replacement therapies such as dialysis. A decision may be made to delay transplantation for a specific individual until after intervention to address psychosocial difficulties. Such decisions to delay transplantation must be based on evidence that pre-transplant intervention does improve transplant outcomes. A decision may be made that as a result of identified problems the candidate is not suitable for transplantation when organ availability is limited, and the evaluation therefore provides an opportunity to plan and provide care for who are assessed as not suitable for transplantation."
Content of evaluation: pre-transplant psychosocial predictors of transplant outcomes

The content of a psychosocial assessment is summarised in Table 1. This content is determined by knowledge of how pre-transplant psychosocial status relates to psychosocial and clinical outcomes following transplantation, and evaluation must identify risk factors for poor outcomes. The core components assessed in a pre-transplant psychosocial evaluation are i) cognitive function, ii) mental health, iii) substance misuse, iv) social support and v) therapy adherence. We discuss the evidence regarding transplant outcomes and their association with these core components It is important to highlight that whilst some variables may be modifiable (e.g. tobacco use) other variables (e.g. social support networks) may be difficult to change.

Cognitive function

A psychosocial evaluation should include a cognitive assessment to ensure an individual has the capacity to understand and make decisions regarding therapeutic options, is able to consent to investigations and treatments, and can adhere to transplant treatment plans. Candidates with non-progressive learning or cognitive disability should not be excluded from transplantation. The limited research available provides evidence that transplantation can be undertaken successfully in individuals with learning disabilities. A matched cohort study of kidney transplant recipients found that whilst patient survival is reduced in recipients with learning disabilities compared to individuals without (survival at 5 years 81% versus 94%, p<0.05), survival rates were high.

Some individuals whose cognitive functioning is impaired in part by their organ failure (e.g. hepatic encephalopathy) may see an improvement in cognitive functioning following transplantation. However, some impairments may remain or worsen in the long term, particularly in older recipients. Individuals with cognitive impairment that limits therapeutic adherence may be suitable for transplantation if caregivers are available to support this, thus social support may mitigate some of the effects of cognitive impairment.
Mental health problems are common in people with organ failure for whom transplantation may need to be considered. A meta-analysis of 28 studies found that 23% of people on dialysis treatment have depression diagnosed by clinical interview\(^7\), with similar findings in people with liver cirrhosis\(^8\). A pre-transplant mental health assessment should include evaluation of an individual’s past and current psychiatric and psychological disorders, their current mental state, and a cognitive evaluation to ensure capacity to make decisions regarding transplantation.

Several studies across different solid-organ transplants have suggested that pre-transplant mental health problems are associated with poorer post-transplant mental health. A meta-analysis of 27 studies in heart, liver, kidney, lung and pancreas transplant recipients found that depression measured before or early after transplantation is associated with an increased risk of mortality after transplant\(^9\). Associations with other outcomes have not been investigated across all organ types. There is evidence in kidney transplantation (meta-analysis of 3 studies) that depression is associated with an increased risk of death-censored graft loss. In heart transplant recipients, a history of suicide attempts has been found to be associated with an increased risk of post-transplant infection and death after heart transplantation\(^10\).

Associations between pre-transplant anxiety and transplant outcomes also appear to differ across organ types. In liver and lung transplant recipients there is evidence that individuals with anxiety or a mood disorder pre-transplant experience lower quality of life and more psychological distress than those without pre-transplant anxiety or mood disorder\(^11\)\(^12\). In a meta-analysis of six studies in heart transplant recipients, anxiety has not been found to be associated with post-transplant mortality or morbidity\(^9\).

There is no strong evidence that pre-transplant mania, psychosis or other mental health problems are associated with poorer transplant outcomes, but research is very limited. There is evidence in heart transplant recipients that a pre-transplant history of any psychiatric illness is associated with an increased risk of post-transplant Post-Traumatic Stress Disorder\(^13\).
In an analysis of a cohort of US kidney transplant recipients individuals with a pre-transplant history of psychosis or mania had a similar risk of death, graft loss and rejection when compared to people with no history of psychosis or mania. Whilst none of the guidelines on transplant candidate evaluation recommend that psychiatric disorder is an absolute contraindication to transplantation they are considered as contraindications insofar as they are uncontrolled or unstable, affect an individual’s decision-making capacity or ability to adhere to a medical regimen, are not mitigated by other factors, or put the candidate at unacceptable risk post-transplant. The current limited research may therefore suffer from selection bias if individuals with psychosis or mania are less likely to be considered suitable for referral or listing for transplantation.

**Substance misuse**

Pre-transplant substance use (including tobacco, alcohol and recreational drug use) is strongly correlated with post-transplant substance use, including non-adherence to post-transplant substance use restrictions. Therefore, pre-transplantation individuals are often required to demonstrate adherence with substance use restrictions, particularly when native organ failure has resulted from substance misuse. Alcohol

Most of the research with respect to alcohol use and transplantation is with respect to liver transplantation. Previous alcohol use disorder is common in liver transplant candidates, as it is associated with the development of alcohol-related liver disease (ARLD). Advanced ARLD is a well-accepted indication for liver transplantation and the overall survival rates in the UK and elsewhere are as good as many other indications. In individuals transplanted for ARLD, rates of graft loss due to resumption of alcohol post-transplant are 2% at 10 years, which is better than graft loss rates in those transplanted because of Hepatitis C, Primary Sclerosing Cholangitis, and Autoimmune Hepatitis. In some countries a minimum period of 6-months abstinence from alcohol prior to liver transplant listing is required: this period i) allows evaluation of whether there can be sufficient spontaneous recovery of liver function to avoid the need for transplantation, ii) enables individuals to receive help addressing addiction issues, and iii) may reduce the proportion of patients returning to alcohol consumption post-transplantation. A 6-month abstinence is
not required for transplant evaluation: the American Association for the Study of Liver Diseases (AASLD) guidelines recommend early referral for transplant evaluation to facilitate assessment and setting of addiction treatment goals\textsuperscript{15}. However, some individuals with a severe form of decompensated ARLD, acute alcoholic hepatitis, will continue to deteriorate despite medical therapy and die within 3 months. Early liver transplantation without requiring 6-months abstinence has been demonstrated to improve survival in a highly selected sub-group of individuals with severe alcoholic hepatitis\textsuperscript{22}. Liver transplantation for this indication is expanding: 1-year patient survival is 77-94\%, similar to other indications, and return to harmful drinking is recorded at 10-17\%\textsuperscript{22,23}.

Sustained harmful alcohol consumption after liver transplantation is associated with reduced long-term survival, whatever the original indication for transplantation\textsuperscript{21,24,25}. For individuals receiving a liver transplant for ARLD, alcohol use relapse after liver transplantation is estimated to occur in 10-50\% of cases\textsuperscript{21,26,27}, with 10-15\% resuming heavy drinking\textsuperscript{28}. Alcohol relapse is more likely in people who lack social support, have young children, have mental health problems, and in people who have been abstinent for a shorter period prior to transplantation\textsuperscript{21,29,30}. Longer pre-transplant abstinence is associated with a longer time to relapse\textsuperscript{21}.

Individuals without alcoholic liver disease may of course have alcohol use disorder but correlates of alcohol use remain under-investigated in solid-organ transplant recipients other than liver transplantation. There is evidence in kidney transplantation that alcohol abuse at the time of transplantation is associated with an increased risk of post-transplant mortality/reduced survival post-transplant\textsuperscript{10,31}. Findings from heart transplantation are mixed, with some studies finding evidence of an association between a history of alcohol abuse and post-transplant survival\textsuperscript{10} whilst others have not\textsuperscript{32}; any retrospective analyses will suffer from selection bias in terms of those selected for transplantation.

**Tobacco**

Smoking is associated with an increased risk of malignancy\textsuperscript{33} and reduced overall survival\textsuperscript{34,35} in all solid-organ transplant recipients as it is in the general population. The International Society for Heart and Lung
Transplantation (ISHLT) guidelines state that active tobacco smoking is a contraindication to heart and lung transplantation\textsuperscript{1}. There is little evidence regarding the optimal duration of abstinence prior to transplantation, but the shorter the period of abstinence before heart, lung or other types of transplantation, the higher the risk of relapse post-transplant\textsuperscript{1,36-38}. Lung transplant candidates are generally required to be smoke-free for a minimum of 6-months before being listed for transplantation\textsuperscript{39,40}. A relapse in tobacco use after lung transplantation appears to be low (4\% in one retrospective cohort study of 455 lung transplant recipients) With respect to other solid-organ transplants, there is inconsistency regarding the impact of pre-transplant smoking on listing: a recent survey found that tobacco smoking was an absolute contraindication to transplantation at 38\% of kidney, 15\% of liver, and 50\% of pancreas programs in the USA\textsuperscript{41}. National and international guidelines for both liver\textsuperscript{15} and kidney\textsuperscript{2} transplantation recommend that transplant candidates do not smoke tobacco. The Kidney Disease: Improving Global Outcomes (KDIGO) Transplant Candidate guidelines recommend that candidates abstain from tobacco use for a minimum of 1 month prior to wait-listing or living-donor kidney transplantation\textsuperscript{2}, and some liver transplant centres make smoking cessation a condition for transplant listing\textsuperscript{15}.

**Cannabis**

0.5-10\% of transplant candidates are reported to use cannabis\textsuperscript{42,43}. Cannabis use is associated with an increased likelihood of the misuse of and dependency on other substances, including alcohol and tobacco, which in turn are associated with an increased risk of medication non-adherence\textsuperscript{44}. Whilst there is limited research in heart transplant candidates, cohort studies in kidney and liver recipients have not demonstrated associations between cannabis use pre- or post-transplant and survival rates\textsuperscript{43,45}. In an analysis of kidney transplant recipients in the USA’s Scientific Registry of Transplant Recipients (SRTR) and Medicare records, cannabis dependence or abuse was diagnosed in only 0.5\% of recipients in the year before transplant, and 0.3\% in the year after transplant\textsuperscript{42}. Pre-transplant cannabis dependency or abuse was associated with post-transplant psychosocial problems including alcohol abuse, other drug abuse, non-
adherence, schizophrenia, and depression, but was not associated with death or graft failure in the first year after transplant.

**Opioids**

There are limited data on the prevalence of injecting drug use in transplant candidates but estimates in liver transplant candidates have been reported to be <5%\(^46\). High levels of prescription opioid use before transplantation have been found to be associated with poorer post-transplant outcomes in kidney and liver transplant recipients. In a linked registry analysis in the USA, 29% of kidney transplant recipients had received prescriptions of opioids in the year prior to transplantation\(^47\). Individuals with the highest quartile of opioid use had an adjusted risks of post-transplant death 2.3 times higher and of all-cause graft loss 1.8 times higher than non-users\(^47\). In a similar linked registry study of liver transplant recipients, compared with those with no opioid use, those with high levels of prescription opioid use during transplant listing had increased mortality over 5 years after liver transplant\(^48\).

The risk of substance misuse relapse is high both in and outside the transplant population, and patients should be assessed by substance abuse specialist teams and offered treatment prior to possible transplantation.

The 2020KDIGO Transplant Candidate guidelines recommend that patients should not be accepted for transplantation if they have ongoing substance use disorder (despite appropriate treatment) that adversely impacts decision-making or increases the level of post-transplant risk higher than is acceptable to the transplant program\(^2\). What constitutes an acceptable risk is however not specified.

**Social support**

The term ‘social support network’ describes the network through which an individual receives (and provides) social support, which comprises emotional, physical, practical, informational, and relational assistance\(^49\). There is no single standard method of measuring social support. Assessments can include measures of perceived social support, which describes an individual’s own subjective perception of
available support, and/or measures of received support, which is a more objective assessment of the quantity and quality of the informational, tangible, and emotional support received.

Social support is recognized as an important social determinant of health\textsuperscript{50}: lack of social support has been associated with adverse health behaviour and poor physical and mental health outcomes, especially among individuals from areas of high socioeconomic deprivation\textsuperscript{50,51}. Social support does appear to be associated with substance use relapse after transplantation: a meta-analysis of 54 studies in solid-organ transplant recipients with a history of substance misuse found that poorer social support showed small but significant associations with substance use relapse\textsuperscript{30}. It is less clear whether social support is associated with post-transplant medication adherence: in a meta-analysis of 32 studies in all recipients\textsuperscript{52}, social support was not found to be associated with post-transplant medication adherence, but there was significant heterogeneity between the included studies in terms of population, organ type, and measure of social support (perceived versus received). Liver transplant recipients with higher social support experienced higher odds of medication adherence post-transplant (Odds Ratio (OR) 1.34, 95% CI 1.01, 1.77), but this association was not found amongst other solid-organ transplants. Whilst individual studies have reported associations between social support and post-transplant adherence in heart and lung recipients\textsuperscript{53}, this has not been replicated in other studies, and the association was not found in meta-analysis of multiple studies. Most of the studies included in the meta-analyses assessed social support after transplantation: among the 3 studies which assessed social support prior to transplantation, social support was not associated with post-transplant adherence (OR 1.00, 95% CI 0.83, 1.19).

Research investigating the relationship between social support and clinical outcomes is inconsistent. In the previously referenced meta-analysis of 32 studies, among high quality studies, social support was not predictive of likelihood of rejection, or transplant survival\textsuperscript{52}. Due to the paucity of studies examining pre-transplant social support, this systematic review included studies that assessed social support pre- and post-transplantation, and most studies used measures of perceived rather than received social support. However, the relationship between social support and post-transplant clinical outcomes did appear to vary
by organ transplant type. Social support was associated with a higher odds of better clinical outcomes (survival) for heart recipients (OR 1.58, 95% CI 1.13, 2.20) but there was not evidence to support this association in other transplant recipients. As mentioned earlier, social support may be important in mitigating the impact of other factors, particularly in individuals whose capacity for independent self-care may be compromised, such as individuals with cognitive impairment.

Across organ transplants the evidence regarding an association between social support and post-transplant adherence, rejection or survival is inconsistent. As a result international guidance on evaluation of transplant candidates differs. The KDIGO kidney transplant candidate guidelines state that ‘there is little evidence suggesting that the absence of social support is an absolute contraindication to transplantation.’ In contrast, the ISHLT guidelines for cardiothoracic transplantation\textsuperscript{1} and the AASLD guidelines regarding liver transplantation\textsuperscript{15} both state that a lack of social support is a contraindication to transplantation. There is evidence from the USA that in clinical practice social support is used to determine transplant eligibility: a discrete choice experiment reported that transplant providers were most likely to choose a candidate who had social support (in the form of a person to care for them post-transplantation) compared to those who did not (OR 1.68, 95% CI 1.50, 1.86)\textsuperscript{54}. A survey of 551 USA transplant providers undertaken by the same researchers found that transplant providers exclude between 10% and 22% of transplant candidates from transplantation due to an assessment that they lack social support\textsuperscript{55}. The researchers found that there was uncertainty about using social support to make transplant decisions: 42% were only somewhat or not at all confident using social support to determine transplant suitability\textsuperscript{55}.

**Adherence**

The term medication adherence describes an individual patient’s medication use and health-related behaviour according to an agreed therapeutic strategy\textsuperscript{56,57}. The World Health Organisation defines medication adherence as ‘the extent to which a person’s behaviour corresponds with the agreed recommendations of a healthcare provider’\textsuperscript{58}. Three distinct aspects are described: initiation of treatment
(whether the patient starts taking the medication at all), implementation (whether medication doses are delayed, omitted, or extra doses are taken), and discontinuation (when the patient stop taking the medication)\textsuperscript{59}. The relevance of assessment of adherence in the evaluation of potential organ transplant recipients is that not taking medications post-transplant as prescribed is associated with transplant failure. Medication adherence has been estimated to be responsible for at least 15\% (range 3-36\%) of graft failures and 50\% (range 20-73\%) of late acute rejections\textsuperscript{60-63}. Qualitative work has found that both healthcare professionals and members of the general population think that adherence should be considered when allocating deceased-donor organs\textsuperscript{64,65}.

Solid-organ transplant recipients who report pre-transplant non-adherence have been reported to have a 3.1\textsuperscript{66} to 7.9\textsuperscript{67} times higher likelihood of post-transplant non-adherence than those who report adherence. However, these studies use self-reported measures, and these associations may therefore represent willingness to report non-adherence rather than an indication of true non-adherence. Pre-transplant most patients are not on the immunosuppression medication that is standard post-transplant, and therefore the adherence being measured pre-transplant is to a different aspect of treatment than being measured post-transplant.

The following variables, identifiable in the pre-transplant psychosocial evaluation, have been reported to be associated with non-adherence after solid-organ transplantation:

- Patient-related factors (younger age\textsuperscript{68,69} and older age\textsuperscript{70-72}, male sex\textsuperscript{68,73}, Black ethnicity\textsuperscript{74}, previous poor adherence\textsuperscript{66,69}, self-efficacy and self-care agency\textsuperscript{75}, substance abuse\textsuperscript{16,32}) and
- Socioeconomically-related factors (lower socioeconomic status\textsuperscript{76}, lack of social support\textsuperscript{57,68,73,77}, limited health literacy\textsuperscript{78}, higher education level\textsuperscript{67}, unemployment\textsuperscript{68} or full-time employment\textsuperscript{79}

However, the current evidence base, from which these associations have been reported, has several major limitations. Findings are not consistent: as detailed earlier, in a recent systematic review, among high quality studies, social support was not predictive of medication adherence\textsuperscript{52}. The variables listed above are
not independent: there is likely to be confounding (e.g. between age and ethnicity\cite{80,81}), interaction (e.g. between forgetfulness and frequency of dosing), and variables may be on the same causal pathway, that is one may mediate the effect of another (e.g. in some countries lack of adequate healthcare insurance may mediate the relationship between low socioeconomic status and adherence). Finally, investigating the relationships between variables and poor adherence in those already listed for a transplant is at risk of self-selection (or ‘collider’) bias\cite{82}: for example, if individuals who have a higher education level are more likely to be listed for transplantation\cite{83-85}, as are those with good adherence, investigating the association between education and adherence in a population of those on the transplant list may find an inverse association between the two variables as demonstrated in this study\cite{67}, that is not reflected in a population of people being assessed for transplant listing.

**Methods of psychosocial assessment**

Having outlined which variables are associated with post-transplant outcomes and therefore need to be assessed in a psychosocial evaluation, we will now discuss the practical process of evaluation. To our knowledge there is little to no empirical evidence as to the process of psychosocial evaluation, who should undertake psychosocial evaluation, and how and when to address issues identified. Where guidance exists, it is in the form of consensus guidance based largely on expert opinion\cite{1}. Such guidelines recommend that evaluations are undertaken by an individual trained in sensitively and accurately assessing the multiple domains outlined above\cite{1}. Independent mental health professionals and social workers may be best qualified to undertake such evaluations\cite{2}. Assessment should comprise of multiple consultations with the potential transplant candidate alone (when the patient’s medical status allows) as well as consultations with family members, friends, and healthcare professionals if possible. The importance of collateral history is especially important when a patient’s cognitive state is compromised by organ failure, but the involvement of a patient’s family and friends provides an opportunity to engage for support post-transplantation, and, for some organs, allows discussion regarding living donation. Psychosocial
assessment should incorporate some assessment of an individual’s cognitive function: if, based on the evaluation or patient history, cognitive impairment is suspected, use of a standardized, validated screening tool (e.g. Mini-Mental State Examination, Montreal Cognitive Assessment) should be considered in order to aid in assessing cognitive status and in decisions about whether to refer the patient for more extensive evaluation.

Subjective measurements of adherence involve a healthcare professional or patient’s self-reported evaluation of their behaviour, often evaluated using a questionnaire. Objective measures of pre-transplant therapy adherence include i) comparisons of the patient medication requests with prescribed use and predicted need for repeat dispensing \(^{86}\) ii) assessments of the number/proportion of clinical appointments and treatment sessions missed, and iii) observed adherence to a restriction or abstinence, for example evidence of alcohol or smoking avoidance, adherence to dietary and fluid restrictions.

Few transplanting hospitals have a protocol in place to assess pre-transplant adherence. A survey of 79 US kidney transplant hospitals found that only 51% of respondents had any knowledge of a protocol to evaluate pre-transplant adherence in people with kidney disease, and of these, only 10% used a standardized assessment questionnaire \(^{87}\). The most common means of assessing pre-kidney transplant adherence was the number of missed haemodialysis sessions. However, non-adherence in one domain of treatment may not predict non-adherence in another. The ability to avoid something (e.g. manage a fluid restriction on dialysis, avoid alcohol prior to liver transplant) may be a poor predictor of an ability to actively do something (e.g. take immunosuppressant medication). In addition, whether a pre-transplant behaviour needs to be sustained post-transplant affects the likelihood of pre-transplant behaviour predicting post-transplant behaviour for example, fluid restriction on dialysis is not required after kidney transplantation.

To standardise the overall assessment, make it more objective, and allow quantitative evaluation, a large number of scales and checklists have been developed. These can be useful for guiding the evaluation and
summarising findings. These are not completed by patients but are used by the assessor to ensure all content domains have been assessed and summarised\textsuperscript{1}. Three commonly used instruments are described below:

- **Stanford Integrated Psychosocial Assessment for Transplant (SIPAT)\textsuperscript{88,89}**

  The SIPAT was developed in the USA to assess a patients' transplant readiness, social support, psychological stability, and substance abuse. It provides an overall risk severity score intended to predict post-transplant behaviour, psychosocial support viability and effectiveness, treatment adherence, substance abuse, and recidivism and mental health. The SIPAT is undertaken by healthcare workers who are assessing the patient for transplantation\textsuperscript{88}, but there is no patient self-assessment or report. In the original publication, higher scores correlated with higher psychosocial risk. When evaluated in 217 transplant recipients however, post-transplant organ failure, mortality and treatment adherence were not associated with the pre-transplant SIPAT scores\textsuperscript{89}. Whilst this study reported some evidence that higher SIPAT scores were correlated higher rates of rejection, hospitalizations, infection rates, psychiatric decompensation, and support system failure\textsuperscript{89}, concerns have been raised regarding the study's power, retrospective analysis, and risk of selection bias\textsuperscript{90}. A further study did not find evidence that SIPAT scores were associated with mortality and treatment non-adherence\textsuperscript{91}.

- **Psychosocial Assessment of Candidates for Transplantation (PACT)\textsuperscript{92}**

  The PACT scale is a single page 10-item rating scale\textsuperscript{92} completed by a healthcare professional. Two of the ten items, the initial and the final rating, are based on the clinician's judgment of a candidate’s quality for transplantation. The remainder asks the clinician to score: Family/Support System Stability; Family/Support System Availability; Psychopathology, Stable Personality Factors; Risk for Psychopathology; Healthy Lifestyle, Ability to Sustain Change in Lifestyle, Drug/Alcohol Use; Compliance with Medications and Medical Advice; and Relevant Knowledge/ Receptiveness to Education. Higher scores mean lower psychosocial risk. In a retrospective cohort study of 538 liver
transplant recipients, PACT score was not associated with mortality in the whole sample, but there
was evidence that in women lower PACT scores were associated with increased mortality (p=0.003)
even after adjustments for age, marital status, and body mass index. In a study of 164 heart
transplant recipients, individuals with low pre-transplant scores (<2) were not allowed to be
transplanted until their scores increased (to ≥ 2). Low initial pre-transplant scores (<2) were
associated with an increased likelihood of a new episode of depression post-transplant, but, after
addressing the primary psychosocial issues before transplant, post-transplant length of stay, organ
rejection, and survival were the same as those without prior psychosocial concerns.

- Transplant Evaluation Rating Scale (TERS)

The Transplant Evaluation Rating Scale (TERS) consists of 10 items rated on a 3-point scale and
provides a single summary score that is meant to indicate a patient's current level of functioning.
Higher scores on the TERS represent a poorer rating. A German retrospective study generated TERS
scores from previously conducted psychosocial assessments of 146 living-donor kidney transplant
recipients, and found no correlation between TERS score and medical outcomes at 1 year post-
transplant. In a small study of 50 heart transplant wait-listed patients, higher TERS scores were
associated with a higher mortality pre-transplant but post-transplant mortality was not
investigated.

A potential strength of such rating scales is that as an objective tool they could be used to help patients
recognise and engage with issues, rather than engage with the judgement of an individual healthcare
provider. However, there is insufficient evidence regarding the validity (content, criterion-related and
construct validity) and reliability (internal consistency, inter-rater reliability, and temporal stability) of
existing scales; detailed psychometric analysis is required. There is also insufficient evidence regarding how
well scale scores predict post-transplant outcomes, alone and alongside other assessments. As a result,
consensus guidelines do not recommend a specific score determining suitability for transplantation, or
using these tools in isolation. It is not known what level of psychosocial risk as measured by these scales
should preclude transplantation, nor is it known whether scores can be changed through intervention, and whether measurable change on the scale correlates with better post-transplant outcomes. However, the tools can be useful as heuristic tools to aid assessment and reporting of findings.\(^1\)

Findings from the complete psychosocial evaluation should be shared with the multidisciplinary transplant team and include recommendations regarding the need for and timing of treatment and interventions, in particular whether intervention is required or possible pre- or post-transplant.

**Interventions**

Few studies have evaluated pre-transplant interventions designed to improve psychosocial functioning to allow successful transplantation or to improve transplant outcomes. In transplant candidates with psychosocial problems Quality of life therapy (QOLT) has been found to be effective at improving pre-transplant function. QOLT is a cognitive–behavioural treatment that targets happiness and life satisfaction in multiple life domains (e.g. relationships, self-esteem). Therapist-delivered QOLT has been evaluated in RCTs in people awaiting lung transplantation\(^98\) and kidney transplantation\(^99\) in the USA. Both studies suggested quality of life could be improved prior to transplantation using this intervention\(^98,99\). An RCT of a telephone intervention in which people awaiting liver transplantation participants were taught coping skills and uncertainty management strategies, found no impact on illness uncertainty, depression, anxiety, self-efficacy, or quality of life, when compared to a liver disease education package\(^100\).

Identified mental health problems should be treated with pharmacological and non-pharmacological therapies which have been found to be effective outwith transplantation. Among those with depression, there is evidence that people using antidepressants at the time of liver transplantation have a lower rate of acute cellular rejection compared with those not taking antidepressants (13% vs. 40%, adjusted Hazard Ratio=0.14 (0.03, 0.62))\(^101\). Overall, the literature suggests that in liver, heart and kidney transplant recipients, depression and anxiety early after transplant bear a stronger relationship to morbidity and
mortality outcomes than depression and anxiety occurring before transplant. This suggests that treatment of depression pre-transplant is related to better post-transplant outcomes than if it is untreated or develops de novo post-transplant. In addition to anti-depressant treatment, patients with diagnosed and treated depression may have developed support systems, effective coping strategies, and be in receipt of effective optimized psychological and psychiatric treatment, whereas those who develop new problems post-transplantation may lack these existing management strategies.

Transplant candidates who have substance use problems should receive treatment prior to transplantation to help them achieve a required period of abstinence, to lower substance use relapse risk before and after transplantation, and to improve clinical outcomes. Written policies regarding post-transplant expectations, and detailed plans regarding the management of substance replacement therapy and relapses on the waiting list and post-transplant should be available at all transplant units, and ideally consensus agreed internationally. For those with opioid use disorder, there is good evidence that long-term maintenance treatment with methadone or buprenorphine is the most effective treatment, reducing the risk of ongoing opioid use, overdose, death, and healthcare costs, while improving social function and health. The AASLD guidelines recommend that people should continue on opioid replacement therapy prior to and peri-transplantation to prevent relapse and should not be tapered off as a requirement for listing. In a retrospective study of people who had received a liver transplant for ARLD, people who received treatment for substance abuse before and after transplantation had a lower likelihood of alcohol relapse than people who received only pre-transplant substance abuse treatment, and those who received no substance abuse treatment. However, this needs to be evaluated in an RCT, as findings may result from selection bias, that is better outcomes are found in those willing to engage with post-transplant treatment rather than an effect of the treatment itself.

Interventions designed to improve adherence exist, but most of these target adherence post-transplant, and few have been shown to be effective. Several RCTs in kidney transplant recipients have reported
increased adherence from educational-behavioural interventions including personalised one-to-one education sessions\textsuperscript{110,111}, group multi-disciplinary team education sessions\textsuperscript{112}, and individualised strategies to link adherence to established daily routines, environmental cues, and supportive people alongside adherence feedback\textsuperscript{113}. Whilst none of these has been evaluated pre-transplant, identifying transplant candidates who may benefit from such interventions after transplantation is an important component of the transplant psychosocial evaluation. Many studies have evaluated the effect of additional support by pharmacists, including pharmaceutical counselling, resolving medication-related problems, and providing feedback on observed adherence\textsuperscript{114,115}. Findings are inconsistent, and some researchers have reported increased adherence but no impact on transplant outcomes\textsuperscript{114,116,117}. After psychosocial evaluation, any intervention recommended as required prior to transplantation should be accompanied by clear goals, specific statements as to what evidence will be used to assess progress, and a specific time period for intervention delivery and assessment\textsuperscript{1}.

\textbf{Future research}

Large multicentre prospective studies looking at pre-transplant psychosocial predictors of specific post-transplant outcomes are required, including the determination of the validity and reliability of both standardized psychosocial assessment tools and cognitive assessment tools. Healthcare-related (rather than patient-related) factors are particularly understudied in the area of adherence-research.

Adequately powered RCTs are required of interventions to improve adherence and psychosocial status pre-transplant, to see whether these interventions can improve transplant access and outcomes for those with psychosocial challenges. Such trials would benefit from ‘process evaluations’ to investigate to what extent interventions are delivered as intended, and to understand how and why the interventions do or do not
work\textsuperscript{118}. However standard RCTs may suffer from ‘the streetlight effect’ in particular with respect to recruiting to adherence intervention trials. This term describes bias that occurs when researchers investigate something where it is easiest rather than where it is most important. ‘The streetlight effect’ can describe research being conducted in the wrong group (the researchers investigate people who are easiest to recruit but are not representative of the population of interest), and/or an intervention trial measuring the wrong set of outcomes (for example measuring adherence, substance use, or perceived social support as an end-point rather than recipient and transplant survival)\textsuperscript{119}. ‘The streetlight effect’ is particularly relevant to adherence research highlighted in a recent systematic review of immunosuppressant adherence interventions\textsuperscript{119}. It is hard to recruit poorly adherent individuals to clinical trials: it is much easier to recruit and follow adherent patients. Studies that primarily enrol adherent patients can improve adherence (from very good to excellent) relatively easily because such patients are able to adhere to study procedures. It is also easier to measure surrogate end-points in transplant psychosocial research: investigating changes in transplant outcomes requires much larger sample sizes. As a result of these challenges, alternatives to a standard clinical RCT should therefore be considered. These could include evaluations that do not require individual participant recruitment such as rapid-cycle, randomized testing approaches based on both research and quality improvement methodology in a learning health system, as has recently been described in the USA\textsuperscript{120}. Intervention approaches could be combined to create multicomponent ‘complex’ interventions that target multiple reasons for poor psychosocial health or non-adherence at various ecological levels. Outcomes measured need to be those that matter to patients – including graft health, life participation, life-expectancy, and likelihood of infection and cancer – rather than simply adherence or substance use\textsuperscript{121}. Better ascertainment of patients’ perspectives and needs through qualitative work would help to identify patient priorities and potential modifiable factors. The optimal timing of intervention delivery needs to be determined and research needs to ascertain when the benefits of delaying transplantation to improve psychosocial variables outweigh the risks. Long-term follow up is required to see if positive changes are sustained.
Summary
Potential transplant candidates should undergo psychosocial evaluation as standard to enable the initiation of support and treatment pre- and post-transplant, and to ensure the best allocation of a limited resource. Ideally the goal of evaluation should not be to preclude patients with psychosocial and adherence challenges from a life sustaining therapy. Rather, pre-transplant evaluation should be a driver for multi-disciplinary intervention to allow successful transplantation for all who need it and to improve post-transplant outcomes. Collaboration between the transplant team and the medical psychology or psychiatry professionals is essential, to facilitate referral for assessment and intervention. Further intervention research in this field has the potential to both increase the candidacy of patients for transplantation and improve post-transplant outcomes.

References


81. UK Renal Registry 22nd Annual Report - data to 31/12/2018. Chapter 1 - Adults starting renal replacement therapy (RRT) for end-stage kidney disease (ESKD) in the UK in 2018. Available at:
During the First Three Years After Heart Transplantation.


### Table 1. Content of the psychosocial assessment

- Motivation for transplantation and post-transplant requirements
- Understanding of the transplant process and expectations of the outcome
- Current mental state examination, including cognitive evaluation to ensure capacity to make decisions regarding transplantation
- Past and current psychiatric and psychological disorders
- Past and current substance use and evidence of dependency
- Past and current adherence to recommended treatment and lifestyle
- Past and current social situation (e.g. living circumstances, important relationships)
- Availability and stability of the social network to meet any post-transplant care needs