Psychiatric Aspects of Organ Transplantation and Donation

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Abstract

Purpose of the review—Psychiatrists and other mental health professionals typically assist with evaluating and treating psychiatric and behavioral issues in transplant candidates, recipients and living organ donors. In this review recent findings on specific psychiatric issues in adult solid organ transplant candidates and recipients, as well as living donors are discussed as well as their relevance to clinical practice.

Recent findings—Patients with complex mental health and addiction histories can have outcomes similar to patients without these disorders but may require specialized pre-transplant preparation or post-transplant interventions to optimize their outcomes. Specific attention to the preparation and wellbeing of living donors is needed.

Summary—As transplant programs increasingly consider patients with complex mental health histories, psychiatrists and mental health professionals evaluating and treating these patients need to consider plans for early identification and treatment. Psychiatric care provided across the pre- to post-operative periods will best address the longitudinal care needs of patients with mental health disorders. Abstinence from substances and complete adherence to medical directives provides the best chance for optimal outcomes. Treatment of depression may improve transplant outcomes. Research is needed to identify effective interventions and the best strategies to engage patients to improve adherence.

Keywords

psychiatric disorders; substance use; adherence; living donation; solid organ transplantation

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Introduction

Solid organ transplantation is the standard of care for patients with advanced organ disease and certain cancers. However, the need for donated organs substantially exceeds the supply. By the end of 2014, nearly 130,000 patients were waitlisted in the US while <30,000 received transplants. Each year 10-15% of candidates die on the waitlist, which has increasingly led to the use of living organ donors. In order to optimize outcomes in this situation of scarce resources, candidates must be carefully selected for transplantation.

Improvements in pre-operative management (e.g., mechanical circulatory support [MCS] for heart transplant candidates), surgical innovations (e.g., the use of laproscopic surgery for kidney transplant) and the development of less toxic immunosuppressive medications have resulted in reduced long-term morbidity and mortality for transplant recipients. However, increasing evidence suggests that psychiatric and behavioral factors affect pre-transplant selection and long-term post-transplant outcomes. The critical need for transplant recipients to adopt lifelong self-care management behaviors has led to the development of psychotherapeutic and behavioral interventions for improving sustained adherence to all facets of the post-transplant regimen.

Psychiatrists and other mental health professionals typically assist with evaluating and preparing patients and living donors for possible transplantation/donation and to address psychiatric and behavioral issues as they arise. Here we will review recent findings on specific psychiatric issues in adult solid organ transplant candidates and recipients, as well as living donors and discuss their relevance to clinical practice.

Mood and Psychotic Disorders

Rational selection of transplant candidates maximizes benefit to patients and society and ensures public trust in the process of organ allocation, an important facet of which is the consideration of equity for disadvantaged patients. However there is neither a standard psychosocial evaluation process nor selection criteria across transplant centers and different criteria may be considered relevant depending on the transplanted organ. Each transplant program must decide on specific psychosocial criteria and the relevance of these criteria for individual patients, often with input from mental health professionals. Concerns still exist that patients with pre-existing serious mental illness (SMI; including schizophrenia and other psychotic disorders, bipolar disorder, major depressive disorder, and severe posttraumatic stress disorder) may be less likely to be adherent to post-transplant care. Some guidelines consider a preexisting psychotic disorder as a relative contraindication to transplantation (1).

In response to these concerns, Evans et. al analyzed health services data for 822 solid organ transplants in the national Veteran Administration system and found that 17% of transplant recipients suffered from SMI, while 30% carried other mental health diagnoses. The study found no difference in attendance at follow-up appointments, frequency of filling immunosuppressant prescriptions, or 3-year mortality among those with SMI, another mental health diagnosis, or no mental health diagnosis(2). Similarly, Price et al.'s recent review found no evidence of poorer post-transplant adherence in patients with psychotic

disorders than in patients without(1). Recent publications indicate a consensus opinion that psychiatric disorders must be well controlled before transplantation and that psychosocial supports must be optimized to help patients cope with the stresses of transplantation and remain adherent to follow-up care (3, 4)

Although there is little evidence that SMIs impact adherence in organ transplants, recent studies continue to demonstrate a negative effect of clinically significant depression and depressive symptoms (measured with standard rating scales) on transplant outcomes when assessed both before(5) and following transplantation(5, 6). In one of the few studies that examined depression and anxiety disorders prospectively using a DSM-IV-R structured interview in a cohort of lung transplant recipients, post-transplant depression predicted not only poorer patient and graft survival but also the development of bronchiolitis obliterans syndrome(7). Anxiety was not significantly associated with these poorer outcomes. A recent meta-analysis of the literature indicates that depression, either pre- or post-transplant, has a strong negative impact on post-transplant survival(8). Morbidities are infrequently studied but appear also to be predicted by the presence of depression. The small literature on anxiety's impact on outcomes is mixed, although many studies indicate that anxiety is not related to outcomes. Some studies suggest that treating psychiatric disorders could lessen the impact of depression (9), but further research is needed.

Substance Use and Disorders

Substance use is a common concern for transplant programs specifically due to the negative affect of substances on health and organ function. This is of particular concern in patients who have received transplanted organs, as substance use and the accompanying psychosocial problems place patients and transplanted organs at risk from direct toxicity of the substance, increased risk of infection due to risky behaviors, and increased incidence of nonadherence to immunosuppressants leading to organ rejection (10). In general, a 6-month period of abstinence from use of substances is required before transplantation although not all substances are considered equally across different types of organ transplant programs with regard to this requirement. For example, although there is general consensus regarding the need for abstinence from alcohol use among individuals with histories of abuse, no matter what the type of transplant program, heart and lung transplant programs also require abstinence from tobacco use while abdominal transplant programs may not impose this requirement.

Cannabis use has grown with the advent of medical prescribing and legalization in certain states. As yet, there is no consensus across transplant centers as to how this will affect selection criteria. While some transplant programs exclude patients who are actively using marijuana (11), this remains controversial. A prior Current Opinions review suggested that potential cannabis effects (e.g., increased infection risk, cancer, and psychological effects) may negatively impact transplant outcomes (12), but no studies have examined this since then. Beyond recreational cannabis use, psychiatrists should evaluate for substance use disorders, educate patients about the medical and psychological outcomes of substance abuse, and provide assistance towards addiction treatment.

Rodrigue et al. compared liver transplant (LT) patients who received substance abuse counseling at various points in the transplant process and found that those who received treatment before and after transplant had significantly lower relapse rates than those who received no treatment or treatment only pre-transplant (16% vs. 41% or 45%, respectively) (13). Risk factors for relapse into problem drinking include: shorter pre-transplant abstinence, more attempts to quit drinking, history of treatment for psychological problems, noncompliance with medical follow-up post-transplant, smoking post-transplant, and a first-degree relative with alcohol abuse(14, 15). Positive relationships in the patient's life were negatively correlated with relapse(16). A pre-transplant screening tool has been developed to predict relapse into any amount of alcohol use after transplantation(17).

A recent controversial study from Europe demonstrating successful outcomes for carefully selected patients with acute alcoholic hepatitis (AAH) (18), has created discussion about transplanting patients with very short abstinence. AAH occurs in the context of active drinking and typically has a rapidly deteriorating course that would not allow six months of abstinence to be achieved. Some transplant programs are beginning to consider, evaluate, and even transplant such patients. Psychiatrists should be prepared to evaluate and provide treatment recommendations for short abstinence patients, keeping in mind that limited time and potential encephalopathy and/or physical debility could impede engagement in treatment. Weinrieb et al. determined that LT candidates often do not perceive a need for addiction counseling and that motivational interviewing techniques may be helpful to facilitate addiction treatment engagement (19). For those too ill to complete rehabilitation pre-LT, contracting for ongoing post-LT addiction counseling may be considered. One study examined the impact of embedding an alcohol addiction treatment unit (AAU) within the liver transplant team. This unit focused on the assessment, selection and monitoring of candidates with alcohol use disorders providing collaborative care pre- and post-LT (20). LT recipients managed by the AAU appeared to have less post-LT alcohol recidivism (16.4% vs. 35.1%) and improved survival (20), but recidivism results were not adjusted for time since LT. Within the AAU treated group there was no difference in relapse based on more or less than 6 months pre-LT abstinence, suggesting that transplanting patients with <6 months abstinence might be considered in selected patients managed by an AAU. Ongoing monitoring even on the LT waitlist is needed, as up to 25% of waitlisted alcoholic patients may drink (19); measuring random blood alcohol levels may be potentially effective for identifying the majority of those who are drinking (21).

Cognitive Impairment

Assessing cognitive function in transplant candidates is essential to identifying deficits that could compromise patients' capacity to comprehend and participate in decision-making before surgery and, if permanent, to understand and adhere to post-transplant treatment directives. Caregivers are also affected by patients' cognitive deficits, as the burden of assisting with following medical directives or even basic activities of daily living could become their responsibility. Psychiatrists can play an important role in identifying cognitive impairment as assessment of cognition is part of a complete psychiatric evaluation. While serial cognitive assessment is recommended for evaluating the effects of disease progression over time, prospective studies with this design are infrequently undertaken.

In heart transplantation, the increasing use of MCS as a bridge to transplant may reduce cognitive impairment from low cardiac output while simultaneously introducing adverse neurological and psychiatric events. More recently, non-pulsatile flow MCS devices have demonstrated significant improvements in reducing morbidity and mortality and are half as likely as the older, pulsatile flow devices to be associated with neurological dysfunction and psychiatric episodes (22). A prospective study of cognitive functioning in continuous flow devices demonstrated that compared to baseline pre-implantation continuous flow MCS recipients had improved memory and no cognitive decline through 16 months post-implantation (23). Their psychological and quality of life status also remained stable pre-to post-implantation although quality of life was reduced (23).

LT candidates may experience cognitive impairment due to hepatic encephalopathy (HE), a typically fluctuating cluster of neuropsychiatric and behavioral symptoms that are potentially reversible following transplantation. Overt encephalopathy is easier to identify on clinical exam, but because minimal HE (MHE) requires cognitive testing to elicit the symptoms, it often goes undiagnosed and untreated. Nevertheless, MHE can impair functioning and safety (e.g., driving). Although a variety of neurocognitive screening tools can identify MHE, they are often not employed due to lack of clinical time and expertise required for implementation, scoring and interpretation, especially in the gastroenterology clinics where LT candidates are commonly managed. One study validated a smartphone application for delivering the Stroop cognitive screening test to detect MHE against a standard battery of neurocognitive tests for MHE (24). Although the intent of the Stroop screening app is to supplement clinical judgment as point-of-care testing, a self-scoring algorithm and mobile device app potentially allows prospective monitoring even from home.

Although organ dysfunction-related cognitive impairment may be reversed by transplantation, other central nervous systems insults may arise after transplant (e.g., post-operative delirium, neuropsychiatric side effects of immunosuppressants). In a prospective study of cognitive impairment in lung transplant patients, while 45% were impaired pre-transplant, 57% showed neurocognitive impairment at discharge from the transplant hospitalization(25). Although early new onset neurocognitive impairment associated with delirium tended to improve at follow-up three months later, 80% of those who were impaired pre-transplant remained impaired at follow-up. However, on repeat testing, cognitive impairments tended to improve over the months following transplant. Older age and lower education were associated with poorer neurocognitive performance across timepoints(25). Similar findings are reported in a cross sections study of lung recipients showing 67% had mild cognitive impairment(26). In a cohort of LT patients, features of cognitive impairment characteristic of HE largely resolved after transplant(27). New onset cognitive impairments emerged by one year post-transplant in 70% of recipients and were not related to a history of encephalopathy or prior alcohol use. The cognitive decline continued up until12 months after transplant suggesting the actual surgery was not the main trigger. Cognitive impairments were also associated with poorer quality of life(27).

Adherence to the Post-transplant Regimen

Lifelong adherence to the post-transplant regimen is difficult given the complexity of the regimen. Generally, it involves taking multiple medications on a precise schedule and self-monitoring and reporting on physical signs and symptoms. Unfortunately despite these requirements non-adherence is not uncommon, tends to increase over time, and leads to poorer outcomes(28). Although pre-transplant evaluations can identify individuals who may require assistance with adherence, pre-transplant predictors of post-transplant adherence have been difficult to identify(28).

Due to extent and critical nature of nonadherence the bulk of recent research in transplant psychiatry addresses efforts to understand and prevent it (see Table 1). The kidney transplant literature has shown that mood and perception of self-efficacy are associated with adherence(43). Other recent work has emphasized the need for patient involvement in selection of treatment. Much of this work is through observational studies and there is a need for randomized control trials to thoroughly test the efficacy of adherence methods and tools. Many of the studies do however highlight the importance of increasing patient education and allowing them, with support, to make decisions regarding their care(44). Technological developments have facilitated patient self-monitoring of diseases such as diabetes and depression. In organ transplantation, technology-based interventions hold promise for improving patient self-monitoring and adherence to post-transplant care, ideally increasing patients' involvement in their care.

Living Donor Issues

Living donors make a personal sacrifice by undergoing surgery to provide a part or whole organ to enhance the welfare of another. Their safety and wellbeing are priorities in organ transplantation. Most studies examine donor outcomes to identify the types and predictors of poorer outcomes with the intent to educate clinicians who perform the psychosocial evaluations and inform future interventions. Chen et al.'s study of living lung donors found that, while donation was well tolerated with no limitations in daily activity and preserved pulmonary function, donors experienced increased dyspnea, decreased health-related quality of life, and, in donors whose recipients died, decreased sleep quality(45). A separate study by the same group showed that living donor parents who donated a kidney to their adult child suffered more depression and anxiety and had worse physical functioning than living sibling donors(46). A study of quality of life among living donors showed that although the incidence of depression and anxiety among living donors post-donation is comparable to that of age- and gender-matched peers, increased stressors, more complicated recovery, and ambivalence to donation increase the risk of these conditions(47). Several studies conclude that many donors do not retain enough information about the procedure to make an informed decision to donate, that computer-based education can alert transplant teams to potential donors who lack sufficient understanding to give informed consent, and that home-based education of donors and recipients can increase willingness to be a living donor(48-50).

Because ambivalence has been associated with poorer outcomes after donation Dew et al conducted a pre-donation randomized controlled intervention trial using motivational

interviewing (MI) to address residual ambivalence among donors. The MI intervention reduced pre-donation ambivalence and following donation those in the intervention reported fewer perceived physical symptoms, less pain and fatigue post-donation and a lower incidence of anxiety but not depression(51).

Conclusions

These recent studies reflect a willingness of transplant programs to consider candidates with complex mental health and addiction histories. While psychiatrists and mental health providers are benefitted by the available observational studies that identify psychosocial risk factors for poorer mental health and transplant outcomes, interventions targeting known risk factors are lacking. Pre-transplant studies are uncommon but could address issues with early identification of problems and preparation for transplantation. This timeframe is critical to addressing substance use disorders. Preserving the wellbeing of living organ donors requires greater attention to consenting and preparation prior to the donation surgery. Following transplant careful attention to mood disorders and cognitive limitations is needed. Cognitive impairment can worsen in the immediate aftermath of transplantation and may improve over time but may not normalize and sometimes may be worse than baseline. Strategies to empower recipients to manage their new organ, particularly in tandem with the help of multidisciplinary transplant teams are needed. These studies need to address more than just one aspect of adherence and need to consider the problem of increasing non-adherence over time.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

References

1. Price A, Whitwell S, Henderson M. Impact of psychotic disorder on transplant eligibility and outcomes. Current opinion in organ transplantation. 2014; 19(2):196–200. [PubMed: 24553499]

2**. Evans LD, Stock EM, Zeber JE, et al. Posttransplantation Outcomes in Veterans With Serious Mental Illness. Transplantation. 2015 This is a very large study comparing patients with mental health disorders to patients without, showing that outcomes for patients with serious mental illness are not different and thus mental health disorders should not be considered a contraindication to transplant.

3. Corbett C, Armstrong MJ, Parker R, et al. Mental health disorders and solid-organ transplant recipients. Transplantation. 2013; 96(7):593–600. [PubMed: 23743726]

4. Stewart KE, Hart RP, Gibson DP, et al. Illness apprehension, depression, anxiety, and quality of life in liver transplant candidates: implications for psychosocial interventions. Psychosomatics. 2014; 55(6):650–8. [PubMed: 24360533]

5. Smith PJ, Blumenthal JA, Carney RM, et al. Neurobehavioral functioning and survival following lung transplantation. Chest. 2014; 145(3):604–11. [PubMed: 24233282]

6. Farmer SA, Grady KL, Wang E, et al. Demographic, psychosocial, and behavioral factors associated with survival after heart transplantation. The Annals of thoracic surgery. 2013; 95(3):876–83. [PubMed: 23374446]

7. Rosenberger EM, DiMartini AF, DeVito Dabbs AJ, et al. Psychiatric Predictors of Long-Term Transplant-Related Outcomes in Lung Transplant Recipients. Transplantation. In press.

8. Dew, MA.; Myaskovsky, L.; Greenhouse, JB., et al., editors. Transplantation. Systematic review and meta-analysis of psychiatric distress as a risk factor for morbidity and mortality in organ transplantation. in press

9. Rogal SS, Dew MA, Fontes P, et al. Early treatment of depressive symptoms and long-term survival after liver transplantation. American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons. 2013; 13(4):928–35.

10. Parker R, Armstrong MJ, Corbett C, et al. Alcohol and substance abuse in solid-organ transplant recipients. Transplantation. 2013; 96(12):1015–24. [PubMed: 24025323]

11. Martin P, DiMartini A, Feng S, et al. Evaluation for liver transplantation in adults: 2013 practice guideline by the American Association for the Study of Liver Diseases and the American Society of Transplantation. Hepatology (Baltimore, Md). 2014; 59(3):1144–65.

12. Coffman KL. The debate about marijuana usage in transplant candidates: recent medical evidence on marijuana health effects. Current opinion in organ transplantation. 2008; 13(2):189–95. [PubMed: 18685302]

13. Rodrigue JR, Hanto DW, Curry MP. Substance abuse treatment and its association with relapse to alcohol use after liver transplantation. Liver transplantation : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society. 2013; 19(12):1387–95.

14. Deruytter E, Van Steenkiste C, Trepo E, et al. Liver transplantation for alcoholic liver disease: a retrospective analysis of recidivism, survival and risk factors predisposing to alcohol relapse. Acta gastro-enterologica Belgica. 2013; 76(3):282–90. [PubMed: 24261021]

15. Egawa H, Nishimura K, Teramukai S, et al. Risk factors for alcohol relapse after liver transplantation for alcoholic cirrhosis in Japan. Liver transplantation : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society. 2014; 20(3):298–310.

16. Dom G, Wojnar M, Crunelle CL, et al. Assessing and treating alcohol relapse risk in liver transplantation candidates. Alcohol and alcoholism (Oxford, Oxfordshire). 2015; 50(2):164–72.

17. Rodrigue JR, Hanto DW, Curry MP. The Alcohol Relapse Risk Assessment: a scoring system to predict the risk of relapse to any alcohol use after liver transplant. Progress in transplantation (Aliso Viejo, Calif). 2013; 23(4):310–8.

18. Mathurin P, Moreno C, Samuel D, et al. Early liver transplantation for severe alcoholic hepatitis. The New England journal of medicine. 2011; 365(19):1790–800. [PubMed: 22070476]

19. Weinrieb RM, Van Horn DH, Lynch KG, et al. A randomized, controlled study of treatment for alcohol dependence in patients awaiting liver transplantation. Liver transplantation : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society. 2011; 17(5):539–47.

20**. Addolorato G, Mirijello A, Leggio L, et al. Liver transplantation in alcoholic patients: impact of an alcohol addiction unit within a liver transplant center. Alcoholism, clinical and experimental research. 2013; 37(9):1601–8. This study examines the impact of an embedded addiction unit within the transplant program. They demonstrate the ability to provide continuity of addiction care and also that their collaborative care with the transplant team may have allowed more acceptance of patients with addictions.

21. Bholah H, Bate J, Rothwell K, et al. Random blood alcohol level testing detects concealed alcohol ingestion in patients with alcoholic liver disease awaiting liver transplantation. Liver transplantation : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society. 2013; 19(7):782–3.

22. Kirklin JK, Naftel DC, Kormos RL, et al. Fifth INTERMACS annual report: risk factor analysis from more than 6,000 mechanical circulatory support patients. The Journal of heart and lung

transplantation : the official publication of the International Society for Heart Transplantation. 2013; 32(2):141–56.

23. Mapelli D, Cavazzana A, Cavalli C, et al. Clinical psychological and neuropsychological issues with left ventricular assist devices (LVADs). Annals of cardiothoracic surgery. 2014; 3(5):480–9. [PubMed: 25452908]

24**. Bajaj JS, Thacker LR, Heuman DM, et al. The Stroop smartphone application is a short and valid method to screen for minimal hepatic encephalopathy. Hepatology (Baltimore, Md). 2013; 58(3):1122–32. This study validates a simple neurocognitive screening test for minimal hepatic encephalopathy. The investigators are working to overcome challenges of identifying MHE in clinical practice and additionally the smartphone app they developed may allow monitoring outside of the point-of-care setting.

25. Smith PJ, Rivelli S, Waters A, et al. Neurocognitive changes after lung transplantation. Annals of the American Thoracic Society. 2014; 11(10):1520–7. [PubMed: 25375275]

26. Cohen DG, Christie JD, Anderson BJ, et al. Cognitive function, mental health, and health-related quality of life after lung transplantation. Annals of the American Thoracic Society. 2014; 11(4): 522–30. [PubMed: 24605992]

27. Tryc AB, Pflugrad H, Goldbecker A, et al. New-onset cognitive dysfunction impairs the quality of life in patients after liver transplantation. Liver transplantation : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society. 2014; 20(7):807–14.

28. De Geest S, Burkhalter H, Bogert L, et al. Describing the evolution of medication nonadherence from pretransplant until 3 years post-transplant and determining pretransplant medication nonadherence as risk factor for post-transplant nonadherence to immunosuppressives: the Swiss Transplant Cohort Study. Transplant international : official journal of the European Society for Organ Transplantation. 2014; 27(7):657–66. [PubMed: 24628915]

29. Massey EK, Meys K, Kerner R, et al. Young Adult Kidney Transplant Recipients: Nonadherent and Happy. Transplantation. 2015

30. Massey EK, Tielen M, Laging M, et al. Discrepancies between beliefs and behavior: a prospective study into immunosuppressive medication adherence after kidney transplantation. Transplantation. 2015; 99(2):375–80. [PubMed: 25606787]

31. Epstein FR, Kale PP, Weisshaar DM. Association between the chance locus of control belief with self-reported occasional nonadherence after heart transplantation: a pilot study. Transplantation. 2014; 98(1):e4. [PubMed: 24978040]

32. Hugon A, Roustit M, Lehmann A, et al. Influence of intention to adhere, beliefs and satisfaction about medicines on adherence in solid organ transplant recipients. Transplantation. 2014; 98(2): 222–8. [PubMed: 24926826]

33. Serper M, Patzer RE, Reese PP, et al. Medication misuse, nonadherence, and clinical outcomes among liver transplant recipients. Liver transplantation : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society. 2015; 21(1):22–8.

34. Supelana C, Annunziato RA, Schiano TD, et al. Medication level variability index predicts rejection, possibly due to nonadherence, in adult liver transplant recipients. Liver transplantation : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society. 2014; 20(10):1168–77.

35. Lalic J, Velickovic-Radovanovic R, Mitic B, et al. Immunosuppressive medication adherence in kidney transplant patients. Medical principles and practice : international journal of the Kuwait University, Health Science Centre. 2014; 23(4):351–6.

36. Nevins TE, Robiner WN, Thomas W. Predictive patterns of early medication adherence in renal transplantation. Transplantation. 2014; 98(8):878–84. [PubMed: 24831921]

37. Eisenberger U, Wuthrich RP, Bock A, et al. Medication adherence assessment: high accuracy of the new Ingestible Sensor System in kidney transplants. Transplantation. 2013; 96(3):245–50. [PubMed: 23823651]

38. Denhaerynck K, Schmid-Mohler G, Kiss A, et al. Differences in Medication Adherence between Living and Deceased Donor Kidney Transplant Patients. International journal of organ transplantation medicine. 2014; 5(1):7–14. [PubMed: 25013673]

39**. Joost R, Dorje F, Schwitulla J, et al. Intensified pharmaceutical care is improving immunosuppressive medication adherence in kidney transplant recipients during the first post-transplant year: a quasi-experimental study. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association. 2014; 29(8):1597–607. This study showed with increased patient education and follow up there was better adherence.

40*. McGillicuddy JW, Gregoski MJ, Weiland AK, et al. Mobile Health Medication Adherence and Blood Pressure Control in Renal Transplant Recipients: A Proof-of-Concept Randomized Controlled Trial. JMIR research protocols. 2013; 2(2):e32. This study is interesting in its approach of incorporating technological interventions that can help monitor adherence and make more precise, faster medication adjustments. Will need further studies to see how that translates into long term patient outcomes. [PubMed: 24004517]

41. DeVito Dabbs A, Dew MA, Myers B, et al. Evaluation of a hand-held, computer-based intervention to promote early self-care behaviors after lung transplant. Clinical transplantation. 2009; 23(4):537–45. [PubMed: 19473201]

42**. Chisholm-Burns MA, Spivey CA, Graff Zivin J, et al. Improving outcomes of renal transplant recipients with behavioral adherence contracts: a randomized controlled trial. American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons. 2013; 13(9):2364–73. Randomized control trial that showed that intervention not only improved adherence, but that increased adherence allowed for better outcome for patients and less healthcare utilization.

43. Calia R, Lai C, Aceto P, et al. Emotional self-efficacy and alexithymia may affect compliance, renal function and quality of life in kidney transplant recipients: Results from a preliminary cross-sectional study. Physiology & behavior. 2015; 142:152–4. [PubMed: 25680476]

44. Popoola J, Greene H, Kyegombe M, et al. Patient involvement in selection of immunosuppressive regimen following transplantation. Patient preference and adherence. 2014; 8:1705–12. [PubMed: 25525347]

45. Chen F, Oga T, Sakai H, et al. A prospective study analyzing one-year multidimensional outcomes in living lung transplant donors. American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons. 2013; 13(11):3003–9.

46. Chen P, Luo Q, Peng L. Anxiety and decreased social support underline poorer quality of life of parent living kidney donors. Asia-Pacific psychiatry : official journal of the Pacific Rim College of Psychiatrists. 2013

47. Jowsey SG, Jacobs C, Gross CR, et al. Emotional well-being of living kidney donors: findings from the RELIVE Study. American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons. 2014; 14(11):2535–44.

48. Freeman J, Emond J, Gillespie BW, et al. Computerized assessment of competence-related abilities in living liver donors: the Adult-to-Adult Living Donor Liver Transplantation Cohort Study. Clinical transplantation. 2013; 27(4):633–45. [PubMed: 23859354]

49. Ismail SY, Luchtenburg AE, Kal VGJA, et al. Modifiable factors in access to living-donor kidney transplantation among diverse populations. Transplantation. 2013; 96(6):586–90. [PubMed: 23799425]

50. Timmerman L, Ismail SY, Luchtenburg AE, et al. Exploring Knowledge About Dialysis, Transplantation, and Living Donation Among Patients and Their Living Kidney Donors. International journal of behavioral medicine. 2015

51*. Dew MA, DiMartini AF, DeVito Dabbs AJ, et al. Preventive intervention for living donor psychosocial outcomes: feasibility and efficacy in a randomized controlled trial. American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons. 2013; 13(10):2672–84. One of few interventional studies addressing outcomes for living donors, this study uses motivational techniques to

improve outcomes. This is particularly important as living donors put themselves at risk for no tangible benefit to themselves in order to help others.

Key Points

- Patients with complex substance and mental health disorders can achieve good post-transplant outcomes with expert management perhaps optimally delivered through mental health provider/teams embedded within the transplant service to provide collaborative longitudinal care

- Psychiatric distress and disorders should be screened for and treated to improve quality of life and wellbeing if not potentially reducing the risk for poorer survival and increased morbidity post-transplant.

- In addition to interventions that target a specific facet of behavior, such as medication-taking, adherence interventions that are individually tailored to the specific and possibly multiple needs of transplant recipients are required. These may be especially necessary for complex patients who may require more intensive strategies.

Table 1

Recent Studies of Adherence in Transplant Patients

Study (first author year)	Brief description	Transplant Type	Age Group	Type of Adherence Behaviors	Outcome Measures Pre/ Post transplant?	Results
Studies of patient perception as to importance of adherence to treatment recommendations						
Massey 2015(29)	Cross-sectional interview based study of transplant experience	Renal	20-30	Medication adherence	Post, questionnaires about coping, medication adherence, QoL scales	Study showed a conflicting picture of patient's perception of their adherence and their actual adherence to medication.
Massey 2015(30)	Prospective cohort study of illness perception and perceived importance of adherence	Renal	18 and above	Medication adherence	Pre/Post, questionnaires via skilled interview	Non-adherence increased with time along with ambivalence as to the importance of medication
Epstein 2014(31)	Pilot cross sectional study of self report measuring the effect that the perceived locus of control has on adherence	Heart	18 and above	Medication adherence	Post, questionnaires to measure adherence as well as thoughts about locus of control	Study showed that patients that have low self-efficacy and feel that they have no control over their treatment course have an increased risk of non-adherence.
Hugon 2014(32)	Observational study of how intention to adhere and beliefs about medication efficacy affect adherence	Solid organ	42-68	Medication adherence	Post, questionnaires related to adherence and QoL measures	Those with higher satisfaction and positive beliefs about medication have better adherence. Living alone, heart tx, and being on everolimus were independent risk factors for non-adherence
Serper 2015(33)	Observational study of adherence in liver transplant and clinical outcomes	Liver	18 and above	Medication adherence	Post, interviews, medical record review and medication levels	Those with lower health literacy, more complicated medication regimens, and lower socioeconomic status had lower adherence. Those who had more treatment knowledge and could demonstrate how to take medications had reduction in post transplant readmissions.
Studies of adherence via quantitative monitoring						
Supelana 2014(34)	Retrospective study of medication level variability and its ability to predict rejection	Liver	18 -80	Medication adherence	Post, study consecutive blood levels of tacrolimus to make a medication level variability index (MLVI)	MLVI was higher in those with biopsy confirmed rejection as compared with other non rejecting liver biopsies
Lalic 2014(35)	Observational study of the effect that different immunosuppressants have on adherence.	Renal	18 and above	Medication adherence	Post, medication levels and adherence questionnaires	Glomerular Filtration Rate and Tacrolimus levels were lower in non-adherent patients in comparison to other medication regimens.

Study (first author year)	Brief description	Transplant Type	Age Group	Type of Adherence Behaviors	Outcome Measures Pre/Post transplant?	Results
Nevins 2014(36)	Prospective observational study of medication adherence through electric medication monitors	Renal	Adults	Medication adherence	Post, percent of days adherent per month by electronic monitoring, clinical outcomes	Missing as few as two days of medicine in the early post-transplant months predicted later poorer adherence and was associated with more frequent and earlier acute rejection and graft loss
Eisenberger 2013(37)	Uncontrolled pilot study of accuracy of ingestible sensory system in monitoring adherence in renal transplant	Renal	35-68	Observation of new technology	Post, system of phone app, adhesive monitor and medication with ingestible sensor system.	Showed that this technology allows for precise measurement of intake, quantity, and timing of intake of drugs.
Denhaerynck 2014(38)	Cross sectional observational study of adherence of recipients from either living or nonliving donors	Renal	18 and above	Medication adherence	Post, medication adherence assessed by self report or electronic monitoring via the MEMS-V track cap system	Non adherence is greater in those who received transplants from living donors
Studies of adherence Interventions						
Joost 2014(39)	Prospective study with sequential control group measuring efficacy of intensive program run by pharmacist on adherence	Renal	18 and above	Medication adherence	Pre and post, meetings with pharmacist, questionnaires, monitoring via medication event monitoring system	Study showed that implementation of program significantly increased adherence
McGillicuddy 2013(40)	Small pilot randomized control trial of efficacy of apps for medication adherence and BP monitoring in non-adherent patients	Renal	30-65	Medication adherence	Post,3 month study of mobile phone app, electronic medication tray, bluetooth enabled BP monitor, smart phone (android)	Intervention group showed improvements in medication adherence and BP and physicians could make more adjustments in medications to manage BP more effectively. No long term outcome measures
De Vito Dabbs 2014(41)	Randomized control trial of mobile app Pocket Path (personal assistant for tracking health)	Lung	adult	Treatment adherence	Post, mobile phone app, tracked readmission and number of critical values tracked	Pocket Path was shown to be helpful in promoting self-care, but did not significantly reduce readmission or post transplant complications.
Chisholm-Burns 2014(42)	Randomized controlled trial of pharmacist intervention using contracting and individualized strategies with follow-up every 3 months	Renal	21 and older	Medication adherence	Post, baseline characteristics and adherence, pharmacy refill records and healthcare utilization	Those in the intervention had better adherence by the 6 months which continued over the follow-up period and had less healthcare utilization