Psychiatric Transplant Evaluation

Psychiatry in Medical Settings | February 2017

Shehzad K. Niazi, MD, FRCPC
Objectives

1. Recognize the role of transplant psychiatrist
2. Understand the role of transplant psychiatrist
3. From “alive or dead” to “how well they are living”
4. Recognize factors affecting psychiatric medications in transplant pts

Recognize the impact of psych. comorbidities on outcomes
Mayo Clinic Transplant Center

More than 200 physicians, three centers (Arizona, Florida, Rochester) and about 1800 transplants a year

<table>
<thead>
<tr>
<th></th>
<th>MCF</th>
<th>MCA</th>
<th>MCR</th>
<th>Total to date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>3122</td>
<td>1070</td>
<td>2835</td>
<td>7027</td>
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<tr>
<td>Heart</td>
<td>292</td>
<td>279</td>
<td>623</td>
<td>1194</td>
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<tr>
<td>Lungs</td>
<td>548</td>
<td>5</td>
<td>234</td>
<td>787</td>
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<tr>
<td>Kidneys</td>
<td>1853</td>
<td>3036</td>
<td>5539</td>
<td>10428</td>
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<tr>
<td>Pancreas</td>
<td>195</td>
<td>297</td>
<td>494</td>
<td>986</td>
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</tbody>
</table>

Solid organs only; composite tissue grafts, BMT and pediatric transplant volumes not included

Data from Mayo Clinic Transplant Centers: accessed on 01/18/2017
**Milliman: It costs pretty penny!**

### TABLE 2: ESTIMATED U.S. AVERAGE 2014 BILLED CHARGES PER TRANSPLANT

<table>
<thead>
<tr>
<th>Transplant</th>
<th>30 Days Pre-Transplant</th>
<th>Procurement</th>
<th>Hospital Transplant Admission</th>
<th>Physician During Transplant</th>
<th>180 Days Post-Transplant Discharge</th>
<th>Op Immuno-Suppressants And Other Rx</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td><strong>Single-Organ/Tissue</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Bone Marrow - Allogeneic</td>
<td>$57,600</td>
<td>$55,700</td>
<td>$479,600</td>
<td>$23,400</td>
<td>$290,300</td>
<td>$24,000</td>
<td>$930,600</td>
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<tr>
<td>Bone Marrow - Autologous</td>
<td>56,300</td>
<td>10,700</td>
<td>212,300</td>
<td>10,800</td>
<td>81,800</td>
<td>6,100</td>
<td>378,000</td>
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<tr>
<td>Cornea</td>
<td>0</td>
<td>0</td>
<td>20,000</td>
<td>8,600</td>
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<td>0</td>
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<tr>
<td>Heart</td>
<td>50,900</td>
<td>97,200</td>
<td>771,500</td>
<td>88,600</td>
<td>198,400</td>
<td>35,600</td>
<td>1,242,200</td>
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<td>Intestine</td>
<td>78,900</td>
<td>92,100</td>
<td>952,900</td>
<td>112,400</td>
<td>272,700</td>
<td>38,200</td>
<td>1,547,200</td>
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<tr>
<td>Kidney</td>
<td>23,200</td>
<td>84,400</td>
<td>119,600</td>
<td>20,500</td>
<td>66,800</td>
<td>19,800</td>
<td>334,300</td>
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<tr>
<td>Liver</td>
<td>37,300</td>
<td>95,000</td>
<td>399,100</td>
<td>53,100</td>
<td>128,900</td>
<td>25,700</td>
<td>739,100</td>
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<tr>
<td>Lung - Single</td>
<td>21,800</td>
<td>90,200</td>
<td>435,200</td>
<td>44,600</td>
<td>165,800</td>
<td>27,400</td>
<td>785,000</td>
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<td>Lung - Double</td>
<td>30,700</td>
<td>129,700</td>
<td>566,900</td>
<td>59,100</td>
<td>219,800</td>
<td>31,500</td>
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<td>Pancreas</td>
<td>12,100</td>
<td>93,800</td>
<td>104,300</td>
<td>18,800</td>
<td>67,700</td>
<td>20,800</td>
<td>317,500</td>
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<tr>
<td><strong>Multiple-Organ</strong></td>
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<tr>
<td>Heart-Lung</td>
<td>88,500</td>
<td>168,700</td>
<td>1,607,100</td>
<td>108,700</td>
<td>304,200</td>
<td>36,400</td>
<td>2,313,600</td>
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<tr>
<td>Intestine With Other Organs</td>
<td>88,600</td>
<td>236,400</td>
<td>1,045,400</td>
<td>132,800</td>
<td>297,400</td>
<td>44,100</td>
<td>1,844,700</td>
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<tr>
<td>Kidney-Heart</td>
<td>76,100</td>
<td>136,000</td>
<td>1,162,100</td>
<td>132,500</td>
<td>296,500</td>
<td>37,100</td>
<td>1,840,300</td>
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<tr>
<td>Kidney-Pancreas</td>
<td>35,900</td>
<td>123,300</td>
<td>227,000</td>
<td>35,200</td>
<td>114,700</td>
<td>22,500</td>
<td>558,600</td>
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<tr>
<td>Liver-Kidney</td>
<td>60,800</td>
<td>161,500</td>
<td>644,500</td>
<td>86,700</td>
<td>210,300</td>
<td>26,500</td>
<td>1,190,300</td>
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<tr>
<td>Other Multi-Organ</td>
<td>76,700</td>
<td>177,600</td>
<td>926,100</td>
<td>116,500</td>
<td>288,600</td>
<td>35,300</td>
<td>1,620,80</td>
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</table>
Heart: $1,242,200
Double Lung: $1,037,700
Liver: $739,100
Kidney: $334,300
BMT Allogenic: $930,600

Heart-Lung: $2,313,600
## Alive | Dead

### How well are patients living?

**Milliman**

**TABLE 8: PATIENT SURVIVAL RATES BY TYPE AND YEAR OF TRANSPLANT**

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>HEART</td>
<td>87%</td>
<td>88%</td>
<td>80%</td>
<td>79%</td>
<td>75%</td>
<td>72%</td>
<td>N/A</td>
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<tr>
<td>INTESTINE</td>
<td>74%</td>
<td>79%</td>
<td>54%</td>
<td>59%</td>
<td>52%</td>
<td>48%</td>
<td>34%</td>
</tr>
<tr>
<td>KIDNEY</td>
<td>93%</td>
<td>96%</td>
<td>85%</td>
<td>91%</td>
<td>74%</td>
<td>85%</td>
<td>48%</td>
</tr>
<tr>
<td>LIVER</td>
<td>86%</td>
<td>86%</td>
<td>78%</td>
<td>78%</td>
<td>69%</td>
<td>72%</td>
<td>53%</td>
</tr>
<tr>
<td>LUNG</td>
<td>86%</td>
<td>83%</td>
<td>68%</td>
<td>63%</td>
<td>56%</td>
<td>47%</td>
<td>27%</td>
</tr>
<tr>
<td>PANCREAS</td>
<td>81%</td>
<td>79%</td>
<td>63%</td>
<td>63%</td>
<td>55%</td>
<td>46%</td>
<td>41%</td>
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<tr>
<td>HEART-LUNG</td>
<td>N/A</td>
<td>66%</td>
<td>N/A</td>
<td>50%</td>
<td>N/A</td>
<td>39%</td>
<td>N/A</td>
</tr>
<tr>
<td>KIDNEY-PANCREAS</td>
<td>96%</td>
<td>95%</td>
<td>89%</td>
<td>90%</td>
<td>84%</td>
<td>86%</td>
<td>67%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>BONE MARROW - AUTOLOGOUS</td>
<td>85%-89%</td>
<td>83%-87%</td>
<td>67%-71%</td>
<td>64%-68%</td>
<td>54%-58%</td>
<td>51%-55%</td>
</tr>
<tr>
<td>BONE MARROW - ALLOGENEIC</td>
<td>61%-65%</td>
<td>58%-62%</td>
<td>48%-52%</td>
<td>46%-50%</td>
<td>43%-47%</td>
<td>42%-46%</td>
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</table>

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Psychiatric Comorbidities: Pre Transplant

- Advanced Lung Diseases
- Advanced Liver Disease
- Advanced Cadiac Diseases

Incidence of Mood Disorder:
- Advanced Lung Diseases: 25
- Advanced Liver Disease: 40
- Advanced Cadiac Disease: 50

Psychiatric Comorbidities: Post Transplant

- Kidney: 20
- Liver: 30
- Heart: 63

Treatment can improve outcomes

Impact on Outcomes: Liver Transplant

10 Years Post LT

- Low Depression: 66%
- Increasing Depression: 46%
- High Depression: 43%

Impact on Outcomes: Liver Transplant
Cumulative incidence of death after liver transplant for patients ≥ 65 years old with and without anxiety disorder

Unpublished data from Mayo Clinic Florida
Impact on Outcomes: Lung Transplant

Increased mortality at 12-year F/U in 111 Lung TX recipients

The Psychosocial Assessment of Candidates for Transplantation (PACT): A Cohort Study of its Association with Survival among Lung Transplant Recipients. (Submitted data) Mario J. Hitschfeld, MD et al
**Allogeneic Hematopoietic Stem Cell Transplantation**

TERS Prospectively Predicts Inferior Overall Survival Outcome for High Risk Scoring Patients Undergoing Allogeneic Hematopoietic Stem Cell Transplantation. Speckhart, D PhD et al

Median f/u 48 months of 438 BMT recipients

68% | 42%

Treatment can improve outcomes

56 | 32 | 52

167 Liver TX recipients were followed for median of 9.5 years

What does a transplant psychiatrist do?
Transplant Psychiatrist

Screen for absolute and relative psychiatric contraindications

Evaluate donors

Treat psychological conditions before & after transplant.

Educate patient, caregivers and other providers
A. Pt’s readiness level
   - Knowledge of Illness
   - Knowledge of Transplant
   - Desire for Treatment
   - Compliance
   - Lifestyle Factors

B. Social Support
   - Availability
   - Functionality
   - Physical living space

C. Psychological Stability & Psychopathology
   - Depression, Anxiety, Mania, Psychosis, Neurocognitive, Personality, Truthfulness, deception & Overall Risk for Psychopathology

D. Effect of Substance Use
   - Alcohol use & Risk for relapse
   - Substance Use & Risk for relapse
   - Nicotine Use
• Inadequate social support system
• Active illicit substance use
• Active alcohol dependence/abuse
• Active nicotine abuse
• Active manic or psychotic symptoms that may impair adherence

• Current suicidal ideation (in a pt with a h/o multiple suicidal attempts)
• Dementia (requires a formal diagnosis)
• Non-adherence with treatment
• History of recidivism of substance abuse after previous organ TX
Immunosuppressant Medications

- **Calcineurin Inhibitors:**
  - Cyclosporine (Gengraf, Neoral): encephalopathy, seizures, tremors, neuropathy
  - Tacrolimus (Prograf): Tremors, Headaches

- **Antiproliferative Agents:**
  - Azathioprine (Imuran): Not widely used nowadays
  - Mycophenolate Mofetil (Cellcept): nausea, gastritis, diarrhea, Leukopenia and thrombocytopenia

- **mTOR Inhibitors:**
  - Sirolimus (Rapamycin)
  - Everolimus (Zortress)

- **Prednisone**
Steroids

- Neuropsychiatric effects of steroids: 2-60%\(^1\)
- Associated with Affective, Behavioral and Cognitive changes

Symptomatic treatment \(^2\)
- Manic symptoms
  - Mood stabilizer
  - Atypical antipsychotic
- Depressive symptoms
  - Mood stabilizer
  - SSRIs
- Psychotic symptoms
  - Atypical antipsychotic

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CYP3A4 SUBSTRATES

Sirolimus
Everolimus
Cyclosporine
Tacrolimus

CYP3A4 INHIBITORS

Fluvoxamine
Nefazadone
Ketoconazole
Itraconazole
Fluconazole

Cimetidine
Clarithromycin
Erythromycin
Grapefruit juice
Pomegranate juice

Carbamazepine
Oxcarbazepine
St. John’s Wort
Modafinil
Rifampin

Rifabutin
Ritonavir
Phenobarbital
Phenytoin

CYP3A4 INDUCERS

Sirolimus
Everolimus
Cyclosporine
Tacrolimus

CYP3A4 INHIBITORS

Fluvoxamine
Nefazadone
Ketoconazole
Itraconazole
Fluconazole

Cimetidine
Clarithromycin
Erythromycin
Grapefruit juice
Pomegranate juice

Carbamazepine
Oxcarbazepine
St. John’s Wort
Modafinil
Rifampin

Rifabutin
Ritonavir
Phenobarbital
Phenytoin
Medication Selection

- **Mirtazapine:**
  - Reduced clearance in Liver disease and CrCl < 40 mL/min

- **Escitalopram & Citalopram:**
  - Hepatic impairment use up to 10 mgs/day for Escitalopram and 20 mgs for Citalopram.
  - No dose adjustment in mild to moderate renal impairment but use lower dose in severe impairment

- **Sertraline:**
  - Renal impairment does not require dose adjustment
  - Use lower dose in hepatic impairment
Medication Selection

• **Fluoxetine:**
  - Use lower dose in hepatic impairment
  - No dosage routinely necessary in renal impairment

• **Vilazodone:**
  - Does not require adjustment in renal or hepatic impairment
  - Increase dose with strong CYP3A4 inducer and lower dose with strong CYP3A4 inhibitors

• **Vortioxetine:**
  - Use in severe hepatic impairment is not recommended

• **Duloxetine:**
  - Avoid in hepatic impairment and when CrCl < 30 mL/min
Medication Selection

• **Lamotrigine:**
  - Use 25% lower dose in moderate to severe hepatic impairment

• **Divalproex Sodium:**
  - Does not require adjustment in renal impairment
  - Do not use in patients with hepatic insufficiency

• **Carbamazepine:**
  - Do not use in severe hepatic impairment/active
  - 50% starting dose and increase slow when CrCl < 30 mL/min

• **Lithium:**
  - High risk of toxicity in renal disease
Medication Selection

• **Quetiapine:**
  - Start at 12.5-25 mgs and increase slowly in hepatic impairment
  - Increase dose with strong CYP3A4 inducer and lower dose with strong CYP3A4 inhibitors

• **Olanzapine:**
  - Does not require adjustment in renal impairment.

• **Aripiprazole:**
  - No adjustment in renal or hepatic impairment
  - Increase dose with strong CYP3A4 inducer and lower dose with strong CYP3A4 inhibitors
  - Increase dose with strong CYP2D6 inducer and use 50% dose with strong CYP2D6 inhibitors
Medication Selection

• **Risperidone:**
  - Start at 0.5 mgs and increase slowly in hepatic and renal impairment

• **Lurasidone:**
  - Do not exceed 80 mgs if CrCl < 50 mL/min or when hepatic impairment is present

• **Asenapine:**
  - Contraindicated in severe hepatic impairment
  - CrCl 15-90 mL/min: no adjustments necessary

• **Haloperidol**
QTc

Adapted from Joseph F. Goldberg, M., MS; Carrie L. Ernst, MD, Managing the SIDE EFFECTS of PSYCHOTROPICS MEDICATIONS. 1st ed. 2012: APPI. 496. (%ages rounded for simplification*)
Consider Medical Comorbidities

<table>
<thead>
<tr>
<th>Metabolic Complications after Liver Transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>COMPLICATIONS</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
</tr>
<tr>
<td>Diabetes</td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
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<tr>
<td>Chronic Kidney Disease</td>
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</table>

Comprehensive assessment Pre TX and ongoing care by transplant psychiatrist is critical

Psych. comorbidities increase morbidity & mortality

Symptomatic Rx of side effects of immunosuppressant medications can improve QOL

Drug-Drug interactions and contextual factors need to be considered when selecting psychiatric medications in TX pts