A Meta-analysis of Determinants and Outcomes of Medication Adherence in Adult Solid Organ Transplantation

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Disclosures

• Cynthia L. Russell has no disclosures.
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- *on behalf of the B-serious consortium*
Objectives

• Describe the background of determinants and outcomes of medication adherence in the adult transplant population.
• Discuss the methods used in this meta-analysis.
• Analyze the results of the meta-analysis.
• Evaluate the conclusions reached from the meta-analysis.
Definitions

Adherence
• The extent to which a person’s behavior (taking medications, following a recommended diet and/or executing life-style changes) corresponds with the agreed recommendations of a health care provider

Medication Non-Adherence
• Deviation from the prescribed medication regimen sufficient to influence adversely the regimen’s intended effect

Medication Adherence

The process by which patients take their medications as prescribed

1. Initiate
   - Patient does not initiate treatment
     - Binary (Yes/No)

2. Implement
   - Taking dimension
     - Timing dimension
   - Drug holidays
   - Dose reduction

3. Persist
   - Patient discontinues treatment
     - Time to event

Vrijens et al., British Journal of Clinical Pharmacology, 2012; 73(5):691-705
The Scope of the Problem

- Medication non-adherence
  - $300 billion/year in avoidable costs of hospitalizations, nursing home admissions, and premature deaths
  - 33-69% of hospital admissions due to medication non-adherence - $100 billion a year
  - Transplant medical costs - $33,000 in first 3 years after transplant
  - Graft failure – increased 6 to 7 fold

Prevalence of Medication Non-Adherence

<table>
<thead>
<tr>
<th>Area</th>
<th>N</th>
<th>Point Estimate (95% CI)</th>
<th>Q</th>
<th>Fail-Safe N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taking immunosuppr. medics</td>
<td>46</td>
<td>22.6 (19.6, 25.5)</td>
<td>3484.7*</td>
<td>18,230</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>49</td>
<td>3.4 (2.8, 4.0)</td>
<td>1193.7*</td>
<td>14,047</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>26</td>
<td>3.6 (2.6, 4.6)</td>
<td>2914.3*</td>
<td>1,741</td>
</tr>
<tr>
<td>Illicit drug use</td>
<td>11</td>
<td>0.9 (0.5, 1.4)</td>
<td>20.8</td>
<td>115</td>
</tr>
<tr>
<td>Attending clinic appointments</td>
<td>19</td>
<td>5.8 (4.2, 7.3)</td>
<td>303.5*</td>
<td>1,269</td>
</tr>
<tr>
<td>Exercise</td>
<td>18</td>
<td>19.1 (14.9, 23.2)</td>
<td>308.1*</td>
<td>1,883</td>
</tr>
<tr>
<td>Following diet</td>
<td>12</td>
<td>25.0 (18.3, 31.7)</td>
<td>148.4*</td>
<td>836</td>
</tr>
<tr>
<td>Blood work and tests</td>
<td>8</td>
<td>12.0 (7.0, 16.9)</td>
<td>191.9*</td>
<td>324</td>
</tr>
<tr>
<td>Monitoring vital signs</td>
<td>6</td>
<td>20.9 (12.2, 29.6)</td>
<td>81.3*</td>
<td>216</td>
</tr>
<tr>
<td>Global nonadherence</td>
<td>9</td>
<td>14.3 (8.7, 20.0)</td>
<td>214.3*</td>
<td>579</td>
</tr>
</tbody>
</table>

22.6 cases per 100 persons per year

Factors Associated with Medication Non-Adherence in Adult Transplantation

Medication Non-adherence

<table>
<thead>
<tr>
<th># of Studies</th>
<th>Pooled ES $r$ (95% CI)</th>
<th>Q</th>
<th>Fail Safe N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>19</td>
<td>-.01 (-.03, .02)</td>
<td>14.6</td>
</tr>
<tr>
<td>Age</td>
<td>15</td>
<td>-.06 (-.13, .02)</td>
<td>55.6*</td>
</tr>
<tr>
<td>Education</td>
<td>12</td>
<td>.02 (-.04, .08)</td>
<td>24.7*</td>
</tr>
<tr>
<td>Nonwht ethn</td>
<td>7</td>
<td>.06 (.01, .12)</td>
<td>8.5*</td>
</tr>
<tr>
<td>Poorer soc supp</td>
<td>15</td>
<td>.10 (.03, .17)</td>
<td>17.9</td>
</tr>
<tr>
<td>Poorer per hlth</td>
<td>7</td>
<td>.15 (.03, .26)</td>
<td>27.4*</td>
</tr>
</tbody>
</table>

Limited correlates examined
Outcomes not explored

Research Gap

• Numerous primary studies have examined determinants and outcomes of medication adherence in adults with solid organ transplant, however no meta-analyses have examined both determinants and outcomes in this population.

• World Health Organization’s Multi-level Model nested within Socio-ecological theory was used to guide this study.
Aims of Study

• To investigate the relationship between socio-economic, patient-related, treatment-related, condition-related, and health care team/system-related factors and post-transplant medication non-adherence in adults with lung, heart, liver and kidney organ transplantation

• To investigate the relationship between post-transplant medication non-adherence and clinical, economic outcomes & health-related quality of life in adults with lung, heart, liver and kidney organ transplantation
Methods

• Following standard methodology for systematic review and meta-analysis (http://www.crd.york.ac.uk/PROSPERO), we conducted electronic searches of PubMed (1947-2012), Ebscohost CINAHL (1981-2012), Ovid PsycINFO (1967-2012) and EMBASE.COM (1947-2012). No language limits were used.

• From 4060 citations meeting inclusion criteria, 3324 abstracts were screened. Of these, 482 full-text articles were accessed and reviewed for eligibility.

• After eliminating 408 studies, 68 studies were included in the review. Data were abstracted from each article by pairs of the authors. Meta-analyses were conducted on factors/outcomes of NA examined in 5 or more studies.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Organ Transplant Type</strong></td>
<td></td>
</tr>
<tr>
<td>Liver (%)</td>
<td>10.4</td>
</tr>
<tr>
<td>Kidney (%)</td>
<td>74.0</td>
</tr>
<tr>
<td>Heart (%)</td>
<td>13.0</td>
</tr>
<tr>
<td>Lung (%)</td>
<td>2.6</td>
</tr>
<tr>
<td><strong>Continent</strong></td>
<td></td>
</tr>
<tr>
<td>North-America (%)</td>
<td>55.8</td>
</tr>
<tr>
<td>Europe (%)</td>
<td>33.8</td>
</tr>
<tr>
<td>Asia (%)</td>
<td>3.9</td>
</tr>
<tr>
<td>Other (%)</td>
<td>5.2</td>
</tr>
<tr>
<td><strong>Sample Size</strong></td>
<td></td>
</tr>
<tr>
<td>Median IQ Range</td>
<td>137</td>
</tr>
<tr>
<td>Range</td>
<td>20 - 15,525</td>
</tr>
<tr>
<td><strong>Participant % Male Gender</strong></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>63.1 ± 12.0</td>
</tr>
<tr>
<td>25th and 75th IQ Range</td>
<td>82-255</td>
</tr>
<tr>
<td><strong>Participant Mean Age</strong></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>48.1 ± 7.2</td>
</tr>
<tr>
<td>Range</td>
<td>32.2 – 61.7</td>
</tr>
</tbody>
</table>
Results: Sociodemographic Factors

13 additional Sociodemographic factors were found but were studied < 5 times

p < .05
Results: Patient-Related Factors

- Higher Sense of Mastery/Self-efficacy
- Higher Self-care Agency
- Positive Medication Beliefs and Attitudes
- Greater Knowledge of Diagnosis and Treatment
- More Side-effect Symptom Occurrence
- Depressive Symptoms Post-transplant
- Higher Locus of Control

52 additional Patient-related factors were found but were studied < 5 times

*p < 0.05
p < 0.001
Results: Treatment-Related Factors

Longer Time Since Transplant
Number of Transplant Medications

32 additional Treatment-related factors were studied but < 5 times

p<.001
Results: Condition-Related Factors

48 additional Condition-related factors were studied but < 5 times
Association of Medication Non-Adherence with Outcomes

p < .001

25 additional outcomes were studied but < 5 times
## Results: Healthcare/System-Related Factors

<table>
<thead>
<tr>
<th>Factors</th>
<th># of papers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Support from the healthcare provider</td>
<td>2</td>
</tr>
<tr>
<td>Type of health insurance</td>
<td>2</td>
</tr>
<tr>
<td>Continent of transplant surgery</td>
<td>1</td>
</tr>
<tr>
<td>State or country of transplant surgery</td>
<td>2</td>
</tr>
<tr>
<td>Transplant center</td>
<td>3</td>
</tr>
<tr>
<td>Distance from the transplant center (travel time)</td>
<td>1</td>
</tr>
<tr>
<td>Having health insurance</td>
<td>1</td>
</tr>
<tr>
<td>Frequency of follow-up (number of visits)</td>
<td>1</td>
</tr>
</tbody>
</table>

**Total = 11**
Summary
Medication Non-Adherence

Protective
- Higher sense of mastery/self-efficacy
- Higher self-care agency/ability
- Greater knowledge of diagnosis and treatment
- Positive medication beliefs/attitudes
- Having diabetes pre-transplant

Increased Risk
- More side-effect symptom occurrence
- Longer time since transplant

Medication Non-adherence
- Late acute rejection (2.356 times as likely)
Discussion

• Support multilevel determinants’ contributions to NA-WHO model as an organizing framework is supported.

• Published research continues to remain focused on the patient- and micro-level (health care provider, social support).
Discussion

• First to provide strong evidence that medication non-adherence worsens the longer the recipient is from the transplant date and that having diabetes prior to transplant is protective for medication non-adherence.

• Medication non-adherence results in a 2.3 times increased risk for late acute rejection.

• Many factors with heterogeneity in study findings
  – Varied instruments used to measure factors and medication non-adherence

• Most study statistics were correlations (r-values) – estimates were made in conversion to odds ratios
Conclusions

- WHO organizing framework nested within Socio-ecological theory is supported.
- Future research should focus on health care organization and health care system influences.
- All potential correlates and outcomes of medication non-adherence should be included in future intervention studies.
- Standardized definitions of correlates and outcomes should be developed to decrease heterogeneity across studies.
Thank you!!

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References


References


- PROSPERO International Prospective Register of Systematic Reviews. (2012). from http://www.crd.york.ac.uk/PROSPERO


Questions?