Impact of Managed Problem Solving Antiretroviral Adherence Intervention on HIV Copy-Years

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  – DDCRF

• Industry
  – BMS
  – Abbott
Problem Solving for Adherence

- Depression is major adherence barrier
- Multifactorial nature of both depression and non-adherence
- Problem solving already adapted
  - Cancer and HIV respite care
  - Obesity
Problem Solving Therapy vs. Treatment

• Therapy requires training
  – Many sessions
  – Patients need motivation
  – Added burden of homework

• Treatment
  – Goal is just solving problems
  – Problem solver is part of team
Conceptual Framework

Adherence and Implementation Feedback

Clinician  Interventionist  Patient

**Tools:** medical information, facilitating routines, memory aids, social supports enhancement, mental health resources, toxicity management
Defining the Problem
Brainstorm
Decision re: Plan
Implement Plan
Assessment and Modification

Plan

Assessment Cycle

Assess

Improve

Analyze
MAPS Study Design

• Train interventionists to deliver MAPS
  – College graduate
  – Familiar/comfortable with HIV topics
  – Health background not necessary

• Randomize 1:1 to MAPS vs. Usual Care (UC)
Eligibility Criteria

- HIV-1 infection
- Age $\geq$ 18 years
- HIV VL $\geq 10^3$ copies/ml
- Any CD4 count
- Not living in care facility
- Able to consent
- Initiating an active regimen
Baseline Screening

• Assessment of adherence barriers
  – Knowledge of regimen
  – Knowledge of desirable adherence
  – Plans if doses missed
  – Depression
  – Substance Use
Delivery of Intervention

• **Initial visit**
  – Duration 60-90 min

• **3 monthly follow-up visits with adherence feedback via MEMS**
  – Duration 45-60 min

• **Weekly phone calls for 3 mo**
  – Duration 5-20 min

• **Monthly refill calls for 1 yr**
  – Duration 1-5 min
Outcomes

• **Primary: adherence**
  - Measured continuously using MEMS
  - Summarized quarterly: % doses taken

• **Secondary: HIV VL**
  - Measured quarterly
  - VL<75 copies/ml
  - HIV copy-years = average viral load over each quarter x 3 months, and summed over the year
ITT vs. AT

• Intent to Treat
  – Primary analysis approach
  – Strategy trial-all subjects evaluated

• As Treated
  – Secondary analysis approach
  – Provides useful data on patients remaining in care
Assessed for eligibility (n=218)

Excluded (n=38)
- Not meeting inclusion criteria (n=21: 14 inappropriate regimen, 7 viral load < 1000 copies/ml)
- Declined to participate (n=10)
- Enrolled in another study with adherence intervention (n=7)

Enrollment

Randomized (n=180)

Allocated to MAPS (n=91)

Allocated to UC (n=89)

Allocation

Follow-Up

Lost to follow-up (n=33)
- No longer willing to follow protocol (n=8)
- Lost to clinical care (n=11)
- Moved away from study center (n=8)
- Death (n=1)
- Other (incarcerated, stopped rx) (n=5)

Lost to follow-up (n=23)
- Not willing to follow protocol (n=2)
- Lost to clinical care (n=13)
- Moved away from study center (n=1)
- Death (n=1)
- Other (incarcerated, stopped rx) (n=6)
<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>MAPS (n=91)</th>
<th>UC (n=89)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (range), yrs</td>
<td>43 (20-65)</td>
<td>42 (19-60)</td>
</tr>
<tr>
<td>Male sex</td>
<td>52 (57%)</td>
<td>56 (63%)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>80 (88%)</td>
<td>73 (82%)</td>
</tr>
<tr>
<td>White</td>
<td>9 (10%)</td>
<td>15 (17%)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (2%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Treatment naïve</td>
<td>40 (44%)</td>
<td>32 (36%)</td>
</tr>
<tr>
<td>Baseline VL (log_{10} copies/ml)-Q25,75</td>
<td>3.24 (2.46, 4.32)</td>
<td>3.47 (2.35, 4.40)</td>
</tr>
<tr>
<td>Baseline CD4 count cells/mm(_3)- Q25,75</td>
<td>287 (146, 370)</td>
<td>244 (116, 379)</td>
</tr>
</tbody>
</table>
Adherence Results

• MAPS associated with higher adherence
  – ITT: Odds of being in a higher category of adherence 1.78 (1.07-2.96) for MAPS vs. UC
  – AT: Odds of being in a higher category of adherence 2.33 (1.35-4.05) for MAPS vs. UC
VL Results

- **MAPS - higher odds of UDVL**
  - ITT: Odds of UDVL=1.48 (0.94-2.31) favoring MAPS
  - AT: Odds of UDVL=1.98 (1.15-3.41) favoring MAPS

- **MAPS - lower HIV copy-years**
  - ITT: MAPS: 1.54 vs. UC: 2.02 log copy-years, p=0.046
  - AT: MAPS: 1.36 vs. UC: 1.87 log copy-years, p=0.027
Limitations

• **Generalizability**
  - Specialty clinic population
  - Use of MEMS for feedback

• **Evidence for effect**
  - Mixed conclusion on virologic effect

• **Bias**
  - Unclear how dropouts affected true impact of intervention
Conclusions and Next Steps

- MAPS effective at improving adherence and virological outcome
  - Refine and disseminate
- Adapt to VA System
  - MAPS-EXTRA
  - Use pharmacy refill system
- Modify approach to use for retention
  - PREPARE
Acknowledgements

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### Adherence Results by Quarter

<table>
<thead>
<tr>
<th>Median adherence (Q25,75) (missing=0%)</th>
<th>MAPS</th>
<th>UC</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1</td>
<td>0.61 (0,0.95)</td>
<td>0.52 (0, 0.85)</td>
<td>&gt;0.5</td>
</tr>
<tr>
<td>Q2</td>
<td>0.64 (0, 0.94)</td>
<td>0.42 (0.02, 0.81)</td>
<td>0.45</td>
</tr>
<tr>
<td>Q3</td>
<td>0.60 (0, 0.93)</td>
<td>0.39 (0.01, 0.78)</td>
<td>0.2</td>
</tr>
<tr>
<td>Q4</td>
<td>0.69 (0.21, 0.91)</td>
<td>0.39 (0.04, 0.79)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Median adherence (Q25,75) (missing=missing)</th>
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<th>UC</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1</td>
<td>n=58, 0.90 (0.63,1.0)</td>
<td>n=61, 0.78 (0.51,0.97)</td>
<td>0.046</td>
</tr>
<tr>
<td>Q2</td>
<td>n=60, 0.90 (0.66,0.98)</td>
<td>n=68, 0.60 (0.27,0.89)</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td>Q3</td>
<td>n=65, 0.86 (0.56,0.97)</td>
<td>n=69, 0.58 (0.26, 0.91)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Q4</td>
<td>n=76, 0.77 (0.47,0.92)</td>
<td>n=77,0.50 (0.13, 0.83)</td>
<td>&lt;0.002</td>
</tr>
</tbody>
</table>
## VL Results by Quarter

<table>
<thead>
<tr>
<th>Proportion with UDVL (missing=failure)</th>
<th>MAPS</th>
<th>UC</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1</td>
<td>53/91 (58%)</td>
<td>42/89 (47%)</td>
<td>0.14</td>
</tr>
<tr>
<td>Q2</td>
<td>53/91 (58%)</td>
<td>47/89 (53%)</td>
<td>0.46</td>
</tr>
<tr>
<td>Q3</td>
<td>52/91 (57%)</td>
<td>39/89 (44%)</td>
<td>0.07</td>
</tr>
<tr>
<td>Q4</td>
<td>54/91 (59%)</td>
<td>45/89 (51%)</td>
<td>0.24</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Proportion with UDVL (missing=missing)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1</td>
<td>53/68 (78%)</td>
<td>42/67 (63%)</td>
<td>0.052</td>
</tr>
<tr>
<td>Q2</td>
<td>53/62 (86%)</td>
<td>47/70 (67%)</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Q3</td>
<td>52/69 (75%)</td>
<td>39/59 (66%)</td>
<td>0.25</td>
</tr>
<tr>
<td>Q4</td>
<td>54/72 (75%)</td>
<td>45/76 (59%)</td>
<td>0.04</td>
</tr>
</tbody>
</table>