The Effect of Antidepressant Treatment on HIV and Depression Outcomes:
Results from the SLAM DUNC Randomized Controlled Trial

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Motivation

• Depression is highly prevalent and predicts worse adherence, outcomes

• Does depression treatment improve adherence and HIV outcomes?
  – Meta-analysis: Yes (Sin 2013)
  – RCTs of CBT and adherence support: Yes (Safren 2009, 2012; Simoni 2013)
  – RCTs of antidepressants: No (Pyne 2011; Tsai 2013)
The SLAM DUNC Study

Strategies to Link Antidepressant and Antiretroviral Management at Duke, UAB, NOC, and UNC

Key questions:
1. Will high-quality antidepressant treatment improve ARV adherence and clinical outcomes?
2. Can evidence-based antidepressant management be integrated efficiently and effectively into HIV care?

Pence 2012
SLAM DUNC Study

- **Population**: HIV clinic attendees with current major depression
- **Sites**: Duke ID; UAB 1917 Clinic; Northern Outreach Clinic; UNC ID
- **Follow-up**: 12 months
- **Primary Outcome**: ARV adherence at 6 months (unannounced pill count)
- **Intervention**: Measurement-Based Care Depression Care Managers provide decision support to HIV providers to ensure adequate antidepressant prescription and management
- **Comparison**: Usual care
Measurement-Based Care

Evidence-based guidelines

Depression care manager

Assessment Follow up

Patient

Decision support

Supervision Quality assurance

Consult

Psychiatrist

Consult

HIV care provider

Treatment plan

Nurse
Social worker
Medical assistant

Adams 2012
<table>
<thead>
<tr>
<th>Enrollment</th>
<th>over 33 months, 2 sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>9,765 screened for depression</td>
<td></td>
</tr>
<tr>
<td>1,852 positive screens (19%)</td>
<td></td>
</tr>
<tr>
<td>1,628 assessed for eligibility (88%)</td>
<td></td>
</tr>
<tr>
<td>Not recommended by provider: 649 (40%)</td>
<td></td>
</tr>
<tr>
<td>Patient declined: 431 (26%)</td>
<td></td>
</tr>
<tr>
<td>Patient not eligible: 360 (22%)</td>
<td></td>
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<tr>
<td>186 enrolled in study (11%)</td>
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</tbody>
</table>

No screening log data

118 enrolled

304 total

Pence 2015
## Who enrolled?

<table>
<thead>
<tr>
<th></th>
<th>Intervention (n=149)</th>
<th>Usual Care (n=155)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Mean (SD) or %</strong></td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>43 (10)</td>
<td>45 (10)</td>
</tr>
<tr>
<td>Male gender</td>
<td>75%</td>
<td>65%</td>
</tr>
<tr>
<td>Black non-Hisp.</td>
<td>56%</td>
<td>68%</td>
</tr>
<tr>
<td>CD4, cells/mm³</td>
<td>607 (371)</td>
<td>569 (354)</td>
</tr>
<tr>
<td>VL &lt; 48 c/mL</td>
<td>72%</td>
<td>69%</td>
</tr>
<tr>
<td>ARV adherence*</td>
<td>86% (23%)</td>
<td>87% (22%)</td>
</tr>
</tbody>
</table>

* Self report, past 30 days, visual analog scale
Psychiatric comorbidities

SLAM DUNC study enrollees (n=304)

- Major depression, no comorbidities: 18%
- Substance abuse / dependence: 29%
- Dysthymia: 48%
- Anxiety: 56%
- All three: 10%
Antidepressant prescription and dosing
Intervention arm participants (n=149)
Comparing antidepressant prescription and dosing between arms

Intervention arm (n=149)  Usual care arm (n=155)

Study Month  Study Month

No AD  Low dose  Medium dose  High dose
Retention for pill count adherence, by month

Retention
Adherence (pill count) over time

Primary endpoint
$p = 0.61$
Adherence (self report) over time

Self-reported ARV adherence

<table>
<thead>
<tr>
<th>Months</th>
<th>Intervention</th>
<th>Usual care</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>145</td>
<td>132</td>
</tr>
<tr>
<td>3</td>
<td>91</td>
<td>94</td>
</tr>
<tr>
<td>6</td>
<td>98</td>
<td>92</td>
</tr>
<tr>
<td>9</td>
<td>77</td>
<td>71</td>
</tr>
<tr>
<td>12</td>
<td>81</td>
<td>69</td>
</tr>
</tbody>
</table>

p = 0.59
Virologic suppression over time

Viral load < 50 copies (%)

Intervention Usual care 95% CI

p = 0.07
Appointment adherence over time

Observations

Intervention Usual care 95% CI

p = 0.56
Suicidality over time

Observations

<table>
<thead>
<tr>
<th>Months</th>
<th>0</th>
<th>3</th>
<th>6</th>
<th>9</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual care</td>
<td>129</td>
<td>91</td>
<td>98</td>
<td>79</td>
<td>81</td>
</tr>
<tr>
<td>95% CI</td>
<td>139</td>
<td>97</td>
<td>92</td>
<td>72</td>
<td>69</td>
</tr>
</tbody>
</table>

p < 0.01
Depression scores over time

Observations

<table>
<thead>
<tr>
<th>Months</th>
<th>Intervention 128</th>
<th>Usual care 139</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>128</td>
<td>139</td>
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p < 0.01
Depression-Free Days

Mean difference:
29 days
(95% CI: 1-57 days)

p = 0.04
Interpretation

Can evidence-based antidepressant management be integrated efficiently and effectively into HIV care?

→ Yes

• Well received, implemented faithfully
• Appears to have increased AD initiation, dose escalation
• Reduced depression morbidity, shortened duration of depression
Interpretation

Will high-quality antidepressant treatment improve adherence and clinical outcomes?

→ No

(in these general clinic populations)

• No impact on HIV measures
Why?

• Participants not selected for low adherence
  – Goal was to estimate effect of clinic-wide integration of depression treatment
  – Ceiling effect?

• 89% of depressed patients did not enroll
  – Who was willing to enroll?
  – A lot of unaddressed psychological distress

• Anxiety / PTSD / substance use comorbidities?
Further directions?

• Could combination of counseling and medications
  – reach more patients
  – address comorbidities / adherence
  – increase impact?

• Could motivational interviewing enhance engagement in mental health treatment?
Many thanks to...

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**Site leads / co-investigators:**
- Overall: Brad Gaynes
- UAB: Michael Mugavero, James Willig, Jim Raper, Teena McGuinness
- UNC: Byrd Quinlivan, Amy Heine
- Duke: Nathan Thielman, Julie Adams, Kristen Shirey, Chris Conover, Liz Turner
- NOC: Michelle Ogle

**Many other staff**
- Providers and clinical staff
- Patients
References


Summary of related RCTs

Safren 2009; Safren 2012; Simoni 2013

- Impact on ARV adherence
- Poorer adherence / viral control at baseline
- Depression and adherence counseling

Pyne 2011; Tsai 2013; Pence 2015

- No impact on ARV adherence
- Better adherence / viral control at baseline
- Depression treatment was primary focus
Randomization

• Tension in design: Randomize patients or providers?
  – If randomizing patients: Potential for contamination
  – If randomizing providers: Potential for referral bias
Decision: Pseudo-Cluster Randomization

Providers

Provider Group A

Randomized 1:1

Provider Group B

Patients randomized 80%/20%

Patients randomized 20%/80%

MBC

Usual care

MBC

Usual care

Teerenstra 2006
Missing data had minimal impact on effect estimates

<table>
<thead>
<tr>
<th>Effect estimate at 6 months: Intervention vs. usual care</th>
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</tr>
<tr>
<td>ARV adherence, pill count (%)</td>
</tr>
<tr>
<td>Kept visit proportion* (%)</td>
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<tr>
<td>Depressive severity (0-50)</td>
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<tr>
<td>Mental health QOL (0-100)</td>
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</table>

* Over 12 months
Predictors of retention

• Retention associated with baseline…
  – ARV adherence, VL, CD4, appt adherence
  – Depressive severity
  – Self efficacy, coping
  – Alcohol / substance use

• Retention NOT associated with
  – Study arm
  – Site
  – Demographics
What have we learned?

- Reach could still be expanded
- Patients are psychiatrically (and medically) complex
- DCM model is definitely feasible and perceived as high-value
- Providers are generally on board and convinced of importance, but need support
Provider perspectives

“I’ve always known [depression care is] an important part of the care but I think just having the support, especially of the counseling team in the clinic readily available, immediately accessible has been a huge addition to the clinic. Because I am not confident that antidepressants alone are adequate for the types of depression that we frequently see. They need a supportive environment. The ones who have come away happiest have regular meetings, regular support with the SD staff.”
“[Adherence is] a hard thing to change. I don’t think there’s going to be a huge effect but I think that probably there were enough people who responded that there was a difference. … Adherence is influenced by so many things that … are not even under the control of the person, that I think it’s going to be very hard to show a tremendous difference. But I think it’s going to be helpful for a lot of people and we may learn that there’s certain people that it’s helpful for just like any intervention.”
“[Integration of MBC into the clinic] was probably the biggest achievement. … Originally I think there was a lot of resistance, you know, how are we going to have this happen. But I think it’s been great and I think we’ll miss having the care manager in the clinic and providing that support and safety net that you can go to and ask questions and be a resource. “
Patient perspectives

“The program really did help me a lot be open up with myself to realize I wasn’t hurting nobody but myself and . . . basically I can say it has helped me a lot to be able to open up and talk to someone and not hide things that’s going on in my life.”
Patient perspectives

“I can say, thanks to that SLAM DUNC program, it helped me a lot because it taught me how to deal with people, it started teaching me anyway how to deal with life on [life’s] terms”
SLAM DUNC: Measurement-Based Care

- Start treatment at low dose
- Interim contacts: Measure side effects

Week 0
2
4
6
8
10
12

CDPs: Measure depressive symptoms; provide decision support to HIV provider around adjustment of antidepressant dose / treatment

- Remission: Recommend maint. phase
- No remission: Recommend new treatment plan

Adams 2012