Effects of a real-time reminder intervention on retention in HIV treatment among pregnant and postpartum women in a low-resource setting: The Uganda WiseMama Study

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Abstract #220

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Conflict of Interest Disclosure

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has no real or apparent conflicts of interest to report.
Background

• HIV in Uganda:
  • High burden country: 7.1% prevalence among adults; 8% in pregnant women
  • Rapid scale-up of WHO’s Option B+ initiative to provide antiretroviral therapy (ART) to HIV+ pregnant women
  • Over 95% of HIV+ pregnant women on ART by 2015

• ART retention & high adherence: critical for success
  • For women’s health and elimination of mother-to-child transmission of HIV

• Obstacle: HIV+ pregnant and postpartum women (PPPW) face particular challenges related to ART retention and adherence
Real-time feedback: previous research

- Real-time wireless pill containers (WPC)
  - Web-linked medication container that sends electronic signal to central server at each opening
  - Allows reminders to be sent in response to adherence behavior (e.g. non-openings)

- Patient experience with WPC
  - Feasible/acceptable in Uganda and China (2010, 2013)
  - Positive effect of triggered reminders + counseling with WPC-generated data on adherence in China (2015)
Given the need for ART retention and adherence support among PPPW, we wanted to know…

Could triggered reminders (via WPC) combined with data-informed counseling improve ART retention and adherence in this vulnerable population?
The Uganda WiseMama Study

Primary Objective

- To generate efficacy data of triggered reminders plus data-informed counseling (‘real-time feedback’) on ART retention and adherence among HIV-positive pregnant and postpartum women

- Today: Results on efficacy of real-time feedback on ART retention
WiseMama study design
(‘real-time feedback’ intervention)

Intervention design and timeline

Eligible patients* → Adherence Monitoring

Intervention: Reminders & Adherence Feedback

Comparison: Usual Care (No reminders/Adherence feedback)

No Reminders/feedback

Month 0: Enrollment in Study

Month 1: Randomization of Enrolled Patients

≈ Month 7: End of Active Intervention (postpartum M3)

Month 10: End of Follow-up Period
Postpartum M6

*HIV+ pregnant women

Pre-intervention Period (1 month)

Intervention Period (≈ 6 months)

Post-Intervention Follow-up Period (3 months)
Methods: Enrollment

- Eligibility: ART-naïve pregnant women >18 years, 12-26 weeks of gestation, attending 2 clinics where ANC/HIV integrated care provided:
  - Entebbe Grade B Hospital
  - Mityana District Hospital
- Once daily regimen: (Tenofovir, 3TC, Efavirenz)
What happened in intervention arm?

1. SMS reminder to cell phone if WPC unopened within 1 hour of dose time
   - Subjects chose one of 10 possible reminders; examples:
     - Time for prayers
     - Hello, it’s time
     - Don’t forget to watch the news

2. WPC-generated data used in counseling sessions
   - At monthly clinic visits, WPC report given to subject
   - Subjects <95% adherence in previous month given counseling using report

What happened in comparison arm?

- No reminder messages
- WPC report NOT shared with subject
Methods: Data collection

• Baseline characteristics collected at enrollment.
• From randomization – postpartum month 3, we documented whether each clinician-scheduled ANC/HIV clinic visit was completed within one month of the scheduled date.
• If the scheduled visit was missed by >1 month, a study team member set a ‘scheduled’ date 1 month ahead for study purposes, after which the next visit would be ‘missed’.
Methods: Measures

• We compared ART retention between the 2 arms at conclusion of intervention period (postpartum month 3) using 3 measures:
  
  a) ‘full retention’: proportion that attended all scheduled monthly ART visits and delivered at the HIV/ANC care hospital
  
  b) ‘visit retention’: proportion of scheduled visits attended
  
  c) ‘postpartum retention’: proportion retained in care at three months postpartum, defined by proportion missing ≤ 1 clinic visit (of 3 total scheduled) in postpartum period
Results: WiseMama Study Overview

**Enrollment:**
June 2015-Jan 2016

1 Month Pre-Intervention period:
June 2015–Feb 2016

**Intervention period:**
Randomization through 3 months post-partum

Baseline
165 HIV+ pregnant women enrolled

- Entebbe = 84
  - 16 w/d by study:
    - 8: missed M1 visit
    - 5: poor signal
    - 2: refused meds
    - 1: miscarried
  - 1: withdrew
  - 1: ‘compassionate use’

- Mityana = 81
  - 14 w/d by study:
    - 5: missed M1 visit
    - 4: poor signal
    - 3: miscarried
    - 1: refused meds
    - 1: not HIV+

66 randomized
- 35: Intervention
  - 7: lost to f/up
  - 28 completed intervention

- 31: Control
  - 10: lost to f/u
    - 1: w/d by study (refused meds)
  - 20 completed intervention

67 randomized
- 34: Intervention
  - 2: died
    - 1: w/d
    - 2: lost to f/u
  - 29 completed intervention

- 33: Control
  - 2: lost to f/u
  - 31 completed intervention

66 included in ITT analysis
65 included in ITT analysis (excluding 2 who died)
### Background characteristics at randomization (n=133)

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th></th>
<th>Comparison</th>
<th></th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean/% (SD)</td>
<td></td>
<td>Mean/% (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>25.6 (6.8)</td>
<td></td>
<td>25.2 (4.6)</td>
<td></td>
<td>0.73</td>
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<tr>
<td>Gestation age (weeks)</td>
<td>20.4 (5.0)</td>
<td></td>
<td>21.9 (4.2)</td>
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<td>0.06</td>
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<tr>
<td>Married</td>
<td>71.0 (45.7)</td>
<td></td>
<td>76.6 (42.7)</td>
<td></td>
<td>0.47</td>
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<tr>
<td>Education level completed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>44.9 (50.1)</td>
<td></td>
<td>39.1 (49.2)</td>
<td></td>
<td>0.50</td>
</tr>
<tr>
<td>Secondary</td>
<td>49.3 (50.4)</td>
<td></td>
<td>54.7 (50.2)</td>
<td></td>
<td>0.54</td>
</tr>
<tr>
<td>First pregnancy</td>
<td>24.6 (43.4)</td>
<td></td>
<td>31.3 (46.7)</td>
<td></td>
<td>0.40</td>
</tr>
<tr>
<td>Multiparous women, previous pregnancies</td>
<td>2.2 (1.4)</td>
<td>3.0 (2.1)</td>
<td>0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Someone else knew status at enrollment</td>
<td>43.5 (49.9)</td>
<td>40.6 (49.5)</td>
<td>0.74</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disclosed to husband/partner at enrollment</td>
<td>31.9 (46.9)</td>
<td>23.4 (42.7)</td>
<td>0.28</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean adherence, pre-intervention period</td>
<td>78.5 (23.9)</td>
<td>75.9 (24.5)</td>
<td>0.53</td>
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</tbody>
</table>
Results: ‘Full retention’

Proportion that attended all scheduled clinic visits and delivered at the hospital where they received ANC/HIV care

<table>
<thead>
<tr>
<th></th>
<th>Full retention</th>
<th>Pre-delivery period</th>
<th>Delivery at study hospital</th>
<th>Post-delivery period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevented (n=67)</td>
<td>49.3 (50.4)</td>
<td>80.6 (39.8)</td>
<td>89.6 (30.8)</td>
<td>59.7* (49.4)</td>
</tr>
<tr>
<td>Comparison (n=64)</td>
<td>53.1 (50.3)</td>
<td>85.9 (35.0)</td>
<td>81.3 (39.3)</td>
<td>67.2** (47.3)</td>
</tr>
</tbody>
</table>

Full retention, and components of full retention n=131

- Full retention was low; no significant difference between arms
- Sharp decline between pre-delivery and post-delivery: *p<0.01; **p<0.05
- Delivery at ANC/HIV hospital site was relatively high
- Similar patterns at each study site; retention somewhat higher at Mityana site

*No differences significant at $\alpha = 0.05$
Results: ‘Visit retention’

Proportion of scheduled visits attended

- Visit retention: just over 80%;
- No difference between arms;
- Visit retention declined between pre- and post-delivery periods ($p< 0.001$);
- This pattern was consistent across sites.
Results: ‘Postpartum retention’:
Proportion ‘retained in care’ at postpartum month 3

• 81% retained in care at postpartum month 3; no difference between arms
• Higher proportion retained at Mityana site
Why no improvement in retention?

Real-time feedback did not address structural and interpersonal barriers

- Quantitative analysis of retention barriers found two significant positive factors on retention:
  - **Disclosure**: having disclosed HIV status to partner increased attendance at scheduled visits by 8.6% overall and by 18.6% in the postpartum period
  - **Education**: women with secondary education or higher completed 13.3% more visits overall and 22.7% in postpartum period

- Qualitative analysis of post-intervention focus group discussions found more issues, suggests reasons for post-delivery decline:
  - **Travel to hospital clinics**: expensive, time-consuming, burdensome due to child-caring responsibilities
  - **Motivation to stay on ART high during pregnancy**: women wanted to avoid HIV transmission to child; became busier after delivery
In their own words:

• Disclosure:

[Non-disclosure] can affect the woman since the woman comes monthly to the hospital to pick up her medication. The husband may begin asking questions as to why she has to come to the hospital… this may affect the woman and maybe she misses her appointments.

• Cost of transport:

I think transport is the main barrier to accessing HIV care. The month may end without you getting any money for transport and you totally fail to get money to transport you on the appointment day, hence not accessing care.

• Burden of post-partum HIV care:

When you are pregnant, you are just alone and it’s not as difficult coming back to the clinic, but after giving birth … [and] given the long distance, you find you have to carry the baby and this makes it very hard.

• Reduced motivation postpartum:

When I was pregnant, I was so worried about my baby, so I stayed in care because I did not want to infect my unborn baby and I also worried about my health …. I would not be strong enough to give birth to my baby….
Conclusions

• Real-time feedback did not improve ART retention among pregnant and postpartum women in two clinic sites in Uganda.

• This population experiences substantial challenges being retained in ART care, especially postpartum.

• Future studies should explore structural and other barriers rigorously and design interventions that address them.

• We plan to analyze quantitative data collected at multiple time points during the trial to contribute to this discussion.
WiseMama Study Team & Acknowledgements

Boston University School of Public Health
• Lora Sabin (PhD)
• Lisa J Messersmith (PhD)
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• Philip Aroda (BA)

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Extra in case needed
Results: ‘Full retention’ by sites

Proportion that attended all scheduled clinic visits and delivered at the hospital where they received ANC/HIV care

- Similar patterns present at each study site
- Retention somewhat higher at Mityana site

### Full retention: Entebbe
- n=66
- Intervention (n=35)
- Comparison (n=31)

<table>
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<tr>
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<tr>
<td>Full retention</td>
<td>45.7 (50.5)</td>
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<td>80.0 (40.6)</td>
<td>57.1 (50.2)</td>
</tr>
<tr>
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<td>71.0 (46.1)</td>
<td>58.1 (50.2)</td>
</tr>
</tbody>
</table>

### Full retention: Mityana
- n=65
- Intervention (n=32)
- Comparison (n=33)

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</thead>
<tbody>
<tr>
<td>Full retention</td>
<td>53.1 (50.7)</td>
<td>75.0 (44.0)</td>
<td>90.0 (29.2)</td>
<td>100.0 (0.0)</td>
</tr>
<tr>
<td></td>
<td>62.5 (49.2)</td>
<td>60.6 (49.6)</td>
<td>90.0 (29.2)</td>
<td>75.8 (43.5)</td>
</tr>
</tbody>
</table>

*No differences significant at α = 0.05