Rapporteur Session: Adherence Track

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Track 1 Rapporteur Team: Dr. Laura Packel, Dr. Teri Senn, Dr. Mark Rubert

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Disclosures

I have received research grants from:

• The National Institute of Mental Health

I have no conflicts to declare.
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Adherence Track: Our Lens

Context:

• Ambitious goals to end the epidemic are now possible
  – Globally, 81% of people on ART virally suppressed (UNAIDS, 2017)
  – In 2016, 85% of Ryan White HIV/AIDS Program recipients virally suppressed (Mandsager et al., 2018)

• Value of implementation science widely recognized

• Adherence support and monitoring a science of its own

Needs:

• Marginalized and/or vulnerable populations underserved, ‘youth bulge’ on horizon

• Intrinsic motivation for adherence is high among most PLWH
  – Achievement of global goals will require focusing on major psychosocial, structural and economic barriers to care
  – PLWH in care but not suppressed account for 20% of transmissions (CDC, 2019)

• Balancing adherence monitoring with need for positive, safe, non-judgmental care
Adherence Track: Our Approach

**Domain**

**Research Question**

**Potential Tools & Approaches**

**INNOVATE**

- How might we use new technologies and data to maximize and measure the therapeutic and preventative effects of ARV agents?

**INTEGRATE**

- How might we integrate quality ART services into existing health programs and health systems to maximize efficiency and impact?

**MOTIVATE**

- How might we motivate, encourage, and nudge people, communities, providers, and organizations to use ART as intended?

- **New product formulations**
- **New modes of delivery**
- **Advances in adherence monitoring**
- **Novel study designs**

- **Implementation science**
- **Client-centered care**
- **Differentiated care**
- **Community-based delivery**
- **Integration with ancillary services**
- **Integration with youth programs and schools**

- **Behavioral science /Behavioral economics**
- **New service delivery models**
- **Methods to overcome barriers (e.g., stigma)**
- **Engagement with different health cadres**
Emotional, psychological, and social well-being = healthier patients with better adherence

- Fitzsimmons et al. [#2000] find adult PLWH in 4 U.S. clinics (n=708) who reported optimal social support were less likely to have a detectable viral load.

- Among 401 MSM in NYC [Horvath et al. [#2040], depression and social support associated, and enacted stigma associated with detectable viral load.

- Momplaisir et al. [#2038] find depression in the third trimester among 1,367 pregnant women in the U.S. predictive of prenatal and postpartum adherence and suppression.

- In a systematic review of studies in LMICs, those with anxiety have 59% [29%, 96%] higher odds of poor ART adherence (Velloza J, et al., #1073).
Low Antiretroviral Therapy Adherence in A National Pediatric Cohort with HIV in the United States

- Retrospective cohort, Medicaid enrollees
- Ages 2-19, n=4,627
- 58% of children and adolescents w/ at least 1 year of follow-up had no ART exposure in 2011-2012
- 55% of children and adolescents who were enrolled in Medicaid (low income/disabled) and received an ART regimen for HIV in 2011 and 2012 did not present good ART adherence.

Co-authors: Zhang T., Shireman T.I., Youn B., Lee Y. and Wilson I.B.
### Adherence Interventions: Level of Action

<table>
<thead>
<tr>
<th>Level of Action</th>
<th>Intervention Example</th>
<th>Adherence 2019</th>
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<tbody>
<tr>
<td><strong>Policy</strong></td>
<td>Same-day ART start</td>
<td>Same day ART initiation in TZ [Mchaumi et al., #2001]</td>
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<td>South Africa Central Chronic Medicine Dispensing Program [Bassett et al.]</td>
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<td><strong>Organization</strong></td>
<td>Provider training</td>
<td><strong>InfoPlus Adherence</strong> [Puttkammer et al., #2025]</td>
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<td><strong>Community</strong></td>
<td>Reduce stigma</td>
<td>Patient Navigation [Health et al., #1044]</td>
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<td><strong>Household</strong></td>
<td>Family programs</td>
<td><strong>Suubi+Adherence</strong>, family-based economic support [Dvalishvili et al., #2051]</td>
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<td><strong>Interpersonal</strong></td>
<td>Peer support</td>
<td>SMS+treatment supporters [Nachega et al., #1074]</td>
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<td><strong>Individual</strong></td>
<td>Behavioral science</td>
<td>ThriveSS [Driffin], After school clubs in SA [Atujuna]</td>
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#### mHealth:
- **Rango** [Ventuneac et al., #2022]
- **MESA** [Outlaw et al., #2023]

#### Self-Management:
- [Moucheraud et al., #2024]

#### Mental Health:
- Depression screening & tx [Pence et al., #1003, #1031]
- Resilience for Black MSM [Teti et al., #1106]
# Noteworthy Interventions

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<tr>
<th>Study</th>
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<th>Effectiveness Outcomes</th>
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<tr>
<td>MESA [Outlaw et al., #2023]</td>
<td>2-session mHealth program for U.S. youth (16-24), 7 sites</td>
<td>RCT (n=125); MESA associated with: ↓ VL, ↑ information, motivation, and self-efficacy</td>
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<td>InfoPlus Adherence [Puttkammer et al., #2005]</td>
<td>Adults at 2 clinics in Haiti; clinic-based EMR alerts for providers + tailored counseling</td>
<td>Quasi-experimental (n=146); ↑ adherence, ↓ unsuppressed VL vs. historical control</td>
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<td>Self-Management [Moucheraud et al., #2014]</td>
<td>Self-management support for adults in Tanzania &amp; Uganda</td>
<td>Quasi-experimental (n=1,112); ↑ appointment attendance in TZ only</td>
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Implementation Science: Bridging the “know-do gap”

Adapted from presentations by Geng E, Odeny T. Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. Implement Sci. 2009;4:50.
## Noteworthy interventions... with an eye toward implementation

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<td>Implementation Outcomes (CFIR)</td>
<td>• Intervention characteristics</td>
<td>• Inner setting • Implementation characteristics • External setting</td>
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Global Introduction of TLD

Benefits of TLD (Tenofovir disoproxil fumarate + Lamivudine + Dolutegravir) vs NNRTI-based regimens:

- Higher barrier to resistance (Clutter DS et al., 2016)
- Faster viral suppression (Walmsley SL et al., 2013)
- Better tolerability (Walmsley SL et al., 2013)
- Lower cost

Adherence still matters!

- 80-90% of those failing NNRTI-based ART have resistance (Steegen K, et al., 2016; WHO 2017)
- Now, most likely, rates of virologic failure will be lower with TLD
  - A higher proportion of failures will be due to poor adherence
  - Adherence threshold unknown

Source: Suzanne McCluskey, MD
Should monitoring procedures change?

Current WHO Algorithm

- ** VL >1000**
  - Intensified counseling
  - Repeat VL
    - ** Repeat VL <1000**
      - Continue 1st line
    - ** Repeat VL >1000**
      - Change to 2nd line

This algorithm was designed for NNRTI-based regimens.

Should an adherence assessment or biomarker be included?

Sources: Suzanne McCluskey, MD
New adherence screening tools and validation studies in new populations

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<th>Investigators</th>
<th>Scale</th>
<th>Population</th>
<th>Design &amp; Performance</th>
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<td>Dandachi et al., #2003</td>
<td>3-item self-report (Wilson <em>et al</em>)</td>
<td>9 sites in U.S., 336 PLWH experiencing homelessness with substance use and MH disorders</td>
<td>Cross-sectional; good internal consistency; correlated with VS</td>
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<td>Nguyen et al., #2005</td>
<td>3-item self-report (Wilson <em>et al</em>)</td>
<td>108 adults in Cape Town, South Africa with history of adherence problems</td>
<td>Prospective cohort; scale correlated with 12-mo Wisepill adherence trajectories</td>
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<td>Azhar et al., #2004</td>
<td>Provider estimate of <em>pre-ART</em> readiness</td>
<td>176 PLWH in Los Angeles</td>
<td>Prospective cohort nested in RCT; measure correlated with optimal early ART adherence</td>
</tr>
<tr>
<td>Christopoulos et al.,  #2052</td>
<td>10-item self-reported index of engagement</td>
<td>2,767 PLHW in 7 U.S. clinics</td>
<td>Cross-sectional; higher scores associated with increased odds of VS</td>
</tr>
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VS: viral suppression; PLWH: people living with HIV; MH: mental health; RCT: randomized controlled trial
Clinical Cutoffs for a 10-item patient engagement screener [Christopoulos et al., #2052]

• **High Risk** for Disengagement
  - 48% greater odds of missing any visits over the next 12 months*
  - 57% greater odds of missing the next scheduled appointment*
  - 226% greater odds of unsuppressed VL over next 12 months*

• **Moderate Risk** for Disengagement
  - 28% greater odds of missing any visits over the next 12 months*
  - 85% greater odds of unsuppressed VL over next 12 months*

• **Low Risk** for Disengagement

* Compared to low-risk group
Injectable ART: Two phase 3 studies (ATLAS and FLAIR) find cabotegravir (CAB) plus rilpivirine (RPV) non-inferior to daily oral ART (Orkin C et al., Swindells S, et al., CROI 2019)

- 97% and 99% of PLWH preferred monthly injections over daily oral ART, respectively
- In Kenya, Simoni et al. [#2039] find injectable options acceptable, esp. those delivered by a provider and if no more than monthly; however, clinic attendance and implementation approach a concern

Implants: Preclinical potency and efficacy high, with favorable long-acting pharmacokinetics (uLA-DTG; TAF; MK-8591)

- Implant clinical safety & acceptability on horizon
- 80% of U.S. youth living with HIV willing to use implantable method (Weld ED et al., 2019)

Long-acting ART is compelling to PLWA due to stigma, fear of inadvertent disclosure, psychological burden of disease, and convenience (Margolis D)

Adapted from presentations by Margolis D, Weld E.
Long-Acting ART: The Promise

- Less frequent dosing; no need for daily adherence
- Shifts burden of adherence from patient to provider
- Provides freedom, partially allays psychological burdens
- If implemented with a client-centered and human rights perspective, potential to achieve more equitable ART outcomes

Adapted from presentations by Margolis D, Weld E.
Contraceptive CHOICE Project illustrates benefits of a diverse mix of methods and removal of barriers to uptake

Pregnancy, Birth, and Abortion Rates among U.S. Teenage Girls and Women, as Compared with CHOICE Participants, Stratified According to Age and Race

Long-Acting ART: The Promise and Challenges

- Less frequent dosing; no need for daily adherence
- Shifts burden of adherence from patient to provider
- Provides freedom, partially allays psychological burdens
- If implemented with a client-centered and human rights perspective, potential to achieve more equitable ART outcomes

- Unique safety considerations, longer term data needed
- Shifts burden of adherence from patient to provider \((\text{INNOVATE!})\)
- Need for implementation studies \((\text{INTEGRATE!})\)
- Could exacerbate disparities – no data in vulnerable populations
- Who will pay? What is the added value?
- Behavioral approaches remain foundational \((\text{MOTIVATE!})\)
People First

Adherence monitoring tools
- Self-report
- Pharmacy-based
- Viral suppression
- Electronic methods
- Hair/urine/saliva
- Digital smart pills
- More on the horizon...

Ethics of adherence monitoring
- Privacy
- Trust/relationships
- Autonomy
- Ancillary care obligations

Adapted from Haberer J, Campbell J, Chai P, Schmidt H, Wilson I.
Thank you!