Gary S. Reiter, MD & Andrew Kaplan, MD - Memorial Lecture

Lifetime Adherence: The Role of the Provider in Maximizing the Odds of HIV Treatment Success

Gerald Friedland MD
Yale University School of Medicine

Adherence 2018 • June 8-10 • Miami
Gary Reiter provided HIV care both as a front line caring and compassionate clinician and as a hospital administrator. He established the first HIV/AIDS clinic for people living with HIV in an underserved semi urban and rural population in Western Massachusetts. (1955-2003)

Andy Kaplan, was on the faculty at the University of North Carolina and UCLA as a wonderful clinician, teacher and creative and committed HIV molecular virologist. Along with other accomplishments, he was among the first to describe protease inhibitor mutations. (1959-2006)
Lifetime Adherence: The Role of the Provider in Maximizing the Odds of HIV Treatment Success

- Expanding the definition of provider

- Adherence and maximizing and broadening HIV treatment success
  - The importance of TRUST
  - Reaching the “hard to reach”
  - Challenges in HIV pandemic
    - Co-morbidities
    - Aging

- Lifetime providers’ adherence?
  - Passing the baton
Expanding the definition of Provider

AIDS as a teacher

1. Compassion
2. Competence
3. Comprehensiveness
4. Co-morbidities
5. Continuity
6. Colleagues
7. Courage
8. Creating new knowledge
9. Combinations
10. Community-Activism

11. Cost-effectiveness
Who are the providers?

- Providers are all with direct contact with PLWH or at risk, including:
  - Prevention, Care and Treatment doctors
  - nurses
  - social workers
  - pharmacists
  - community health workers
  - mental health workers
  - substance use counselors
  - clergy
  - family members and loved ones
  - Peers
  - lawyers
  - activists
Multidisciplinary colleagues and collaboration

- HIV Treatment Adherence:
- The Intersection of Biomedical, Behavioral, and Social Science Research with Clinical Practice
Who are the providers?

• How many remember the exact time and place and first person living with HIV that you encountered as a provider?

• What are the personal characteristics that have defined and attracted providers (all of us) to work in and with HIV/AIDS?
  Qualities of humanism, empathy, equity, social justice, human rights, intellectual challenge and responsibility
  (Camus, “simple human decency”)

• The response to HIV/AIDS can serve as a model for other diseases and epidemics.
  – Including those that are now infecting our political and national life
Maximizing and Broadening Treatment Success

Trust

• Incarcerated men and women 10% of PLWH in CT

• PLWH prisoners eligible for ART recruited in 1996

• Acceptance and adherence by self-report and pharmacy clinical information obtained from chart review

• Adherence defined as having taken 80% of ART.

• Acceptance (80%) and adherence to (84%) ART high.

• Identify the therapeutic process necessary to promote acceptance of and adherence to ART
**Importance of TRUST**

**Acceptance of and Adherence to ART**

Altice, Mostashari, Thompson, Friedland  JAIDS 2001

<table>
<thead>
<tr>
<th></th>
<th>A O R</th>
<th>p value</th>
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<tbody>
<tr>
<td><strong>Acceptance</strong></td>
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</tr>
<tr>
<td>TRUST in Physician Scale</td>
<td>0.08</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MISTRUST Medications</td>
<td>0.30</td>
<td>&lt;0.001</td>
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<td></td>
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<tr>
<td><strong>Adherence</strong></td>
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<tr>
<td>Side Effects</td>
<td>0.09</td>
<td>0.001</td>
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<tr>
<td>Complexity of ART regimen</td>
<td>0.33</td>
<td>0.01</td>
</tr>
<tr>
<td>Social Isolation</td>
<td>0.08</td>
<td>0.005</td>
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8% increase in acceptance for each unit increase in 11 item Trust in Physician Scale (Anderson and Dietrick)

Three fold reduction for those mistrustful of medications

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Target 1: 90% of HIV+ people diagnosed

Target 2: 90% of diagnosed people on ART

Target 3: 90% of people on ART with HIV RNA suppression

HIV Positive People: 36.9 million
Diagnosed: 33.2 million
On ART: 29.5 million
Viral Suppression: 26.9 million

Maximizing and Broadening Treatment success
Reaching out to the Hard to Reach

These goals won’t be achieved without special and sustained attention to hard to reach populations and social determinants of health and disease

- People in remote and/or underserved urban and rural areas locally and globally
- People who inject drugs or use alcohol
- People with mental illness
- People living in vulnerable personal, social and economic situations
- People who are imprisoned or detained in jails

This requires reaching out into the communities and special settings in which populations live and in doing so as a provider team
Superiority of Directly Administered Antiretroviral Therapy Compared to Self-Administered Therapy among HIV-Infected Drug Users: A Prospective, Randomized, Controlled Trial


- Community based intervention of DAART vs self-administered ART in PWID
- PWID received supervised therapy 5 X/wk delivered in a mobile community based health care van
- Outcomes: reduction in HIV-1 RNA level to ND @ 6 mos
  mean change from baseline CD4+
Superiority of Directly Administered Antiretroviral Therapy over Self-Administered Therapy among HIV-Infected Drug Users: A Prospective, Randomized, Controlled Trial

**VL Response**

Proportion of patients achieving virological success, %

- DAART (n = 88) vs SAT (n = 52)

**CD4 Response**

Mean change in CD4 T cell count, cells/μL

- DAART (n = 88) vs SAT (n = 53)

**Graphs**

- Mean change in viral load, log_{10} copies/mL

- Months from baseline

<table>
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<th>Impaired SAT</th>
<th>0</th>
<th>1</th>
<th>3</th>
<th>8</th>
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<tr>
<td>Values</td>
<td>0</td>
<td>10</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>DAART</td>
<td>21</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Mean SAT</td>
<td>-1.0.30</td>
<td>-0.41</td>
<td>-0.29</td>
<td></td>
</tr>
<tr>
<td>Values DAART</td>
<td>-0.77</td>
<td>-1.01</td>
<td>-1.18</td>
<td></td>
</tr>
<tr>
<td>Mean P value</td>
<td>.11</td>
<td>.17</td>
<td>.00</td>
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P = .017 (VL Response), P = .002 (CD4 Response)
Maximizing and Broadening Treatment success
Reaching out to the Hard to Reach
addressing co-morbidities

- Relapse to drug & alcohol use occurs quickly after release associated with recidivism and loss of Viral Suppression
- Worked with prisoners directly before released into the community
- RCTs with extended-release naltrexone (approved for opioid and alcohol use disorders)
  1. Opioid use disorders - NEW HOPE
  2. Alcohol use Disorders - INSPIRE
- Achieved significant improvement in relapse and VS at < 50 copies/mL
Change in Viral Suppression (<50 copies/mL) from Baseline to 6 months: NEW HOPE (Opiate use)

- XR-NTX:
  - Baseline: 37.9%
  - 6 months: 60.6%
  - P=0.002

- Placebo:
  - Baseline: 55.6%
  - 6 months: 40.7%
  - P=0.294

Source: Springer et al. CROI Abstract 96. Boston, MA. March 6, 2018
ATHENA (Adherence Through Home Education and Nursing Assessment): A Randomized Controlled Trial examining the effectiveness of a home nursing and peer intervention designed to improve adherence to HAART

Results

Subjects with ≥ 90% adherence

(Extended Mantel-Haenszel Test: 5.41, p=.02)

Williams A et al, J Acquir Immune Defic Syndr & Volume 42, Number 3, July 2006
Moral of the story

• Patients are more complicated than HIV and their regimens
• A picture is worth a thousand words
• A home or community visit or project is worth a thousand pictures

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Broadening Treatment success
Co-morbidities

**HIV prevalence** and **TB incidence** in South Africa: 1990 - 2013


Note: The lines are based on fitted mathematical models developed by E Gouws (HIV) and A Grobler (TB)
Co-morbidities - TB and HIV Integration

SAPIT trial outcome: Mortality rates

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<tr>
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<th>Integrated Treatment Arm n = 431</th>
<th>Sequential Treatment Arm n = 214</th>
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<tbody>
<tr>
<td>Number of deaths</td>
<td>24</td>
<td>26</td>
</tr>
<tr>
<td>Person-years of follow-up</td>
<td>469</td>
<td>224</td>
</tr>
<tr>
<td><strong>Mortality rate per 100 person-years</strong></td>
<td><strong>5.1</strong></td>
<td><strong>11.6</strong></td>
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56% lower mortality with integrated TB-HIV treatment
Tugela Ferry-Msinga Sub District Rural KwaZulu-Natal

Tugela Ferry-Msinga
- 180,000 traditional Zulu people
- Extreme poverty
  - Poorest sub district in South Africa
- High TB and HIV burden
- District Hospital-COSH; Philanjalo-NGO
- HIV/TB ART initiation - Sizonqoba study
- First site of national roll out of ART
- Site of uncovering epidemic of XDR-TB
Community based HIV/TB integrated intensive case finding in congregate and home based settings

- Feasible & acceptable
- Multiple sites
  - >20,000 adults
  - 10% HIV positive
  - 3% with active TB
- 30% DR TB
- Community Health Care Workers and Task shifting
- Linkage to care
- Strengthening care continuum
Where are the men?

- Shebeens offer opportunity for HIV testing among high risk young men and women
- Identify and link those with HIV to care
- Offer prevention, incl PrEP
Maximizing and Broadening Treatment success
Reaching out to the Hard to Reach
Community and peer based strategies

Peer Group Monthly Regimen Construction
Tugela Ferry, South Africa

Adherence Clubs as models of ART delivery & Adherence Support
Cape Town, South Africa
Broadening Treatment success - HIV and Aging:—
Improving and sustaining quality of life

• The gratifying longer survival with HIV, has
  resulted in increasing the # and % of older adults
  living with HIV in all regions of the world.

• Approximately 30% of adults living with HIV
  in high income countries are 50 or over.

• More than 10% of adults living with HIV in
  low- and middle-income countries are 50 or over

• HIV  ART and aging comorbidities affect
  morbidity and mortality

• Treatment success should be measured not just
  by VL and CD4 but by Quality of Life for
  PLWH, the goal is aging well with HIV.

Althoff, K , Smit, M, Reiss, P, Justice, A
Current Opinion in HIV AIDS: 2016 - Vol
11 - 5 - p 527–536
Lifetime Provider adherence

• Lifetime—what of providers’ lifetimes’?
• Sustaining our own healthy selves and productive work to the end of HIV/AIDS
• Recognize the importance of mentoring and need for passing the baton to the next and the generation and beyond
Curriculum

General Primary Care - Residents can go to YOBM to access the 3-year outpatient general ambulatory medicine case-based curriculum. Residents will be reviewing these topics at precinic conferences.

HIV Primary Care - The HIV Training Track curriculum was developed using tools and material that will describe the framework to the residents in order to achieve competency and expertise in caring for HIV-infected patients.

Entrustable Professional Activities (EPAs)
The three year Yale HIV training track curricular goals and objectives are based on the 12 following Entrustable Professional Activities (EPAs) that we believe are necessary to be an outstanding independent provider of HIV primary care at the end of the HIV residency training.

Goals and Objectives
The overall goal of the Yale HIV Training Track is to provide Yale primary care residents with the opportunity to enhance their knowledge of HIV disease and associated opportunistic infections, and to provide a venue for them to develop expertise and appropriate professional attitudes regarding a primary care role...
Strategies for lifelong treatment success

- Continue and strengthen what we have done well
  - Including community and peer activities
- Develop and deploy new strategies: Rapid initiation, Differential Service Delivery. Task shifting. One size need not fit all
- New long acting and safe and acceptable medication
- Encourage use of new tools-but to supplement, not replace the fundamentally human content of HIV care
- Robust implementation research
- Quality of life not just quantity
- Address and fix social determinants which are at the root of HIV risk and essential for successful adherence and treatment
Thank You

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- Lydia Barakat
- Sandra Springer
- AIDs Program staff

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- Kogie Naidoo
- Nesri Padayatchi
- Wm Sturm

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- Smatosa Khosa
- Neel Gandhi
- Sarita Shah
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- Jason Andrews
- DDCF ICRFs
- J & J Scholars

People and communities in The Bronx, New Haven and South Africa