Antiretroviral *therapy*
Adherence in Adolescents and Young Adults

K Rivet Amico, PhD
Center for Health, Intervention and Prevention
University of Connecticut
ART ADHERENCE IN ADOLESCENCE/YOUNG ADULTHOOD - Why focus on this?

1) It is a sizable population
   • 4.9 Million (of 33.4 million) people living with HIV are youth

2) It is a growing population
   • 40% of all new infections are among 15-24 year-olds;
   • An estimated 2,500 youth become infected with HIV every day

IN THE US...

Between 56,000 and 80,600 individuals between 13 and 24 are living with HIV

1 in 4 new infections are in youth ages 13 to 24

22% increase from 2008-2010 among young gay males (African American and Latino)
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3) It is a unique population
   • Poorer outcomes than adults in general
Compared to adults, adolescents and young adults in US have:
- Poorer retention
- More delay in ART start
- Lower suppression (6% vs. 30%)
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   • Poorer outcomes than adults in general
   • Adolescents and young adults are **NOT SHORT VERSIONS OF ADULTS**
     • Distinct patterns in cognitive and emotional development
Distinct patterns in cognitive and emotional development

Executive Functioning

- Concrete → Abstract
- Immediate → Delayed
- Impulsive → Planning
- Invulnerable → Self-preserving
- Influence → Independent

Gradual development of the cognitive control system (DLPFC, dorsal ACC, and parietal cortex)

Gradual development of social brain network (mPFC, TP, subgenual ACC, and insula)

Flexible frontotemporal engagement, depending on motivational salience of context

Motivational and goal flexibility (shifting priorities)

Increased social-affective influences on goals and behaviour

Puberal changes in the limbic system (ventral striatum and amygdala): increases in sensation-seeking, novelty-seeking, and motivational salience of peer contexts

Positive growth trajectories:
- Diminished goals (e.g. adaptive exploration, mature long-term goals and social competence)

Negative growth trajectories:
- Diminished goals (e.g. depression and social withdrawal)
- Excessive motivation towards negative goals (e.g. substance use and excessive risk-taking)

http://www.nature.com/nrn/journal/v13/n9/fig_tab/nrn3313_F3.html
Distinct patterns in cognitive and emotional development

Adolescent Thinking
- Concrete
- Abstract
- Immediate
- Delayed
- Impulsive
- Planning
- Invulnerable
- Self-preserving
- Influence
- Independent

Executive Functioning

TIME OF PARADOXES
- Dependent and Rebellious
- Suspicious and Gullible
- Overly confident and Insecure
- Needy and Independent
- Unique and Wanting to fit in

WINGS TO FLY AND CHAINED TO THE GROUND
### Stages of Development

**Erikson’s Stage Theory in its Final Version**

<table>
<thead>
<tr>
<th>Age</th>
<th>Conflict</th>
<th>Resolution or “Virtue”</th>
<th>Culmination in old age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infancy (0-1 year)</td>
<td>Basic trust vs. mistrust</td>
<td>Hope</td>
<td>Appreciation of interdependence and relatedness</td>
</tr>
<tr>
<td>Early childhood</td>
<td>Autonomy vs. shame</td>
<td>Will</td>
<td>Acceptance of the cycle of life, from integration to disintegration</td>
</tr>
<tr>
<td>Play age (3-6 years)</td>
<td>Initiative vs. guilt</td>
<td>Purpose</td>
<td>Humor; empathy; resilience</td>
</tr>
<tr>
<td>School age (6-12 years)</td>
<td>Industry vs. inferiority</td>
<td>Competence</td>
<td>Humility; acceptance of the course of one’s life and unfulfilled hopes</td>
</tr>
<tr>
<td>Adolescence (12-19 years)</td>
<td>Identity vs. Confusion</td>
<td>Fidelity</td>
<td>Sense of complexity of life; merging of sensory, logical and aesthetic perception</td>
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<tr>
<td>Early adulthood</td>
<td>Intimacy vs. Isolation</td>
<td>Love</td>
<td>Sense of the complexity of relationships; value of tenderness and loving freely</td>
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<tr>
<td>Adulthood (26-64 years)</td>
<td>Generativity vs. stagnation</td>
<td>Care</td>
<td>Caritas, caring for others, and agape, empathy and concern</td>
</tr>
<tr>
<td>Old age (65-death)</td>
<td>Integrity vs. Despair</td>
<td>Wisdom</td>
<td>Existential identity; a sense of integrity strong enough to withstand physical disintegration</td>
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- Experimentation sex, drugs, alcohol, love, testing rules, pushing boundaries
- Forming identity
- Crisis is NORMAL

**WHO AM I?**
**DO I FIT IN?**

[Handwritten note: I'm depressed, sad, hurt, confused, lonely, unloved, judged, misunderstood, insignificant, broken, dying, insignificant. Fine.]
Stages of Development

- Experimentation: sex, drugs, alcohol, love, testing rules, pushing boundaries
- Forming identity
- Crisis is NORMAL

Ethnic/Racial Identity

Gender/Sexual Identity

Moral Identity Development

Religious/Faith Identity Development

HIV

Erikson's Stage Theory

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WHO AM I? DO I FIT IN?

I'm ____________

Fine.
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   • Poorer outcomes than adults in general
   • Adolescents and young adults are NOT SHORT VERSIONS OF ADULTS
     • Distinct patterns in cognitive and emotional development
   • Highly variable by culture
Adolescence by region

Cultures vary dramatically on what characterizes childhood and adolescence, and when and how it “ends” for which gender and class.
ART ADHERENCE IN ADOLESCENCE/YOUNG ADULTHOOD - Why focus on this?

Because **4.9 million people living with HIV are youth** and the population is growing all over the world, concentrated in Sub Saharan Africa and among young Black MSM in US, and are **poorly virally suppressed** as a cohort and the strategies and interventions developed for adults may be inappropriate for the **cognitive/emotional development** of youth or their life circumstances.
ADHERENCE

Adherence “Extent to which one’s behaviors coincides with medical or health advice”

Collaborative
Active

Compliance “Accurate implementation of a regimen set by health professional”

Top down
Passive

• Resistance
• Exhaust Tx Options
• Mortality

• Execution
• Persistence
• Gaps
ADOLESCENT NON-ADHERENCE

- Across conditions: 11% to 90% demonstrate inadequate adherence
  - 40-50% Asthma medication
  - 25% injections, 29% glucose monitoring, 71% diabetes specific diet

HIV REGIMEN NON-ADHERENCE IN ADOLESCENTS AND YOUNG ADULTS

- REACH- 59% did not reach “good adherence” criteria
- 2009 US Meta: 30% - 72% suboptimally adherent
- 2014 Meta: 38% suboptimally adherent
  - 30% Asia and Africa
  - 40%-50% Europe and Americas

Taddeo Egedy Frappier 2008 Paediatrics & Child Health
Reisner et al 2009 TopHIVMed
Kim et al 2014 AIDS
# ADOLESCENT NON-ADHERENCE

## Correlates of Adherence and Non-adherence

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<td>- Higher caregiver education</td>
<td>- Life satisfaction</td>
<td>- History of adverse effects</td>
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<tr>
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<td>- Lower sexual risk/no STI since dx</td>
<td>- Lower levels of psychological distress</td>
<td>- Time on ART</td>
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<td>- [social support inconsistent]</td>
<td>- Concrete over abstract reasoning</td>
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# Adolescent Non-Adherence

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<td>inconsistent]</td>
<td>Stigma/discrimination</td>
<td>distress</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Alcohol/drug use</td>
<td>Concrete over abstract</td>
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**Amplified Barriers in Time of Stress**

**Transition to adult care**

- Reisner et al 2009 TopHIVMed
- Thurston et al 2014 CogBehPractice

**TOP 3 REASONS**
1. Forgetting
2. No meds with me
3. Change in routine
Use of logic or pointing out dire consequences of inaction tend to fall flat...
...because of NORMAL and APPROPRIATE propensity to “test evidence” and abstraction and independence lending themselves to discounting “authority”
Use of logic or pointing out dire consequences of inaction tend to fall flat... ...because of NORMAL and APPROPRIATE propensity to “test evidence” and abstraction and independence lending themselves to discounting “authority.”

Interventions to support adherence and on-going access to ART through attendance in care must be youth appropriate.
ADOLESCENT YOUNG ADULT ADHERENCE

INTERVENTIONS- What works for youth?

2009 Review of RCTs-- 7 Studies
• DOT [3 studies]
• Regimen Simplification [1 study]
• Education and Counseling [2 studies] TREAT and Family Group + Reminder device
• Reminder calls [1 study]

FAR fewer interventions targeting youth and adolescents than adults.
Even fewer when considering interventions OUTSIDE of the US
ADOLESCENT YOUNG ADULT ADHERENCE

INTERVENTIONS- RECENT LITERATURE on What works for Youth?

Motivational Interviewing based (MI)
Cognitive Behavioral
Incentives
Technology+ (cell phones)
Motivational Interviewing based (MI)

Specifically avoids direct challenging or assuming shared goals.
Allows for expression of opposition as an opportunity to assist in development.
Promotes autonomy and self-directedness.
ATOLEDSCENT ADHERENCE

INTERVENTIONS- Motivational Interviewing- PILOT

Motivational Enhancement System for Adherence (MESA): Pilot Randomized Trial of a Brief Computer-Delivered Prevention Intervention for Youth Initiating Antiretroviral Treatment

Sylvie Naar-King, PhD, Angulique Y. Outlaw, PhD, Moussa Sarr, MD, MPH, Jeffrey T. Parsons, PhD, Marvin Belzer, MD, Karen MacDonell, PhD, Mary Tanney, CRNP, MPH, Steven J. Ondersma, PhD, and The Adolescent Medicine Network for HIV/AIDS Interventions

On a scale of 1 to 5, where 1 is not at all important right now, and 5 is the most important thing in your life, how important is it to you to take your medication exactly as prescribed by your doctor?

A: Not at all or never important
B: A little bit or sometimes important
C: Pretty important or often important
D: Very important or usually important
E: Extremely or always important

Naar-King et al 2013 J Ped Psych

Courtesy of Angulique Outlaw
ADOLESCENT YOUNG ADULT ADHERENCE

INTerventions- RECENT LITERATURE on What works for Youth?

Motivational Interviewing based (MI)

Cognitive Behavioral

- Specifically teaches regulation
- Targets relaxation
- Assists in developing problem solving skills
- Normalization of ‘errors’ in perception with skills to address them
ADOLESCENT ADHERENCE

INTERVENTIONS- Cognitive Behavioral- PILOT
Positive Steps (Adaptation of LifeSteps)
• Youth/young adults on ART- 2 cases presented
• 5 1-hour individual sessions with MA or Doctoral Clinicians
• Video testimonials, text message at dose times through 2-weeks prior to end of study (Stick with it, You are worth it)
• Values Activity- generates own motivators

Examples
Belonging
Courage
Fun
Hope
Humor
Making others proud
My culture
Safety
Sexuality

Thurston et al 2014 CogBehPractice
ADOLESCENT ADHERENCE

INTERVENTIONS - Trauma Informed Cognitive Behavioral Therapy Enhanced

ADHERENCE-enhanced TI-CBT delivered by Indigenous Youth Leaders

Trauma

Depression

ART Adherence Barriers

Parental Adherence Problem Solving

CD4

Viral Load

Pill Count

Self-report

Logistics

Youth Knowledge, Attitudes, Skills

Caregiver Attitudes/ Behavior

Gender Based Violence

Historical

HIV/AIDS

Loss

Trauma Informed Cognitive Behavioral Therapy Enhanced

Youth indigenous leaders co-lead groups for HIV+ youth

Explore gender roles, adjustment to living with HIV and trauma

Geri Donenberg
ADOLESCENT YOUNG ADULT ADHERENCE

INTERVENTIONS- RECENT LITERATURE on What works for Youth?

Motivational Interviewing based (MI)

Cognitive Behavioral

Incentives

Immediate reward structure
ADOLESCENT ADHERENCE

INTERVENTIONS- Incentives (+++)- PILOT

Incentive Scheme (IS) Foster et al 2014
- 11 PaHIV youth (~19 yo) transitioning to young adult clinic with CD4<200 cell/uL off ART (suspended)
- Pilot multidisciplinary team (including peer support)
- Gift vouchers- VL and attendance to Motivational Interviewing (MI) Sessions

<table>
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<tr>
<th>Started ART</th>
<th>VL response and attended for MI</th>
<th>Voucher value</th>
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<tbody>
<tr>
<td>Week 2</td>
<td>Fall in VL</td>
<td>£ 25</td>
</tr>
<tr>
<td>Week 4</td>
<td>Fall in VL</td>
<td>£ 25</td>
</tr>
<tr>
<td>Week 8-16</td>
<td>VL &lt;50</td>
<td>£ 50</td>
</tr>
<tr>
<td>3 months suppressed</td>
<td>Sustained VL &lt;50</td>
<td>£ 25</td>
</tr>
<tr>
<td>6 months suppressed</td>
<td>Sustained VL &lt;50</td>
<td>£ 25</td>
</tr>
<tr>
<td>12 months suppressed</td>
<td>Sustained VL &lt;50</td>
<td>£ 50</td>
</tr>
<tr>
<td>Total</td>
<td>VL suppression for 12 months</td>
<td>£ 200</td>
</tr>
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Foster et al 2014 AIDS Pt Care and STDs
ADOLESCENT ADHERENCE

INTERVENTIONS- Incentives (+++) - PILOT

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Foster et al 2014 AIDS Pt Care and STDs
ADOLESCENT YOUNG ADULT ADHERENCE

INTERVENTIONS- RECENT LITERATURE on What works for Youth?

Use technologies common in life of youth
Help with executive functioning- reminders
Build sense of social support
Immediate intervention potential

Technology+ (cell phones)
ADOLESCENT YOUNG ADULT ADHERENCE

INTERVENTIONS - Technology

**ATN** 24 weeks of daily cell phone support - **PILOT**

Funded phone places (direct pay to service provider)

37 participants 15-24yo with poor adherence or delayed ART start

Conversations (5m) focused on
- Reminder to take medications
- Problem solving adherence needs/challenges
- Referrals

*Belzer et al 2013 (AIDS BEHAV): ATN pilot*
ADOLESCENT YOUNG ADULT ADHERENCE

INTERVENTIONS

- **Specialty Camps**  Gillard Witt Watts 2011 QualHealthResearch
- **Adolescent Impact**  Chandwani et al 2011 AIDSEducPrev
- **VideoConferencing- Telehealth**  Saberi et al. 2013 AIDSPtCareSTDs
- **STAR TRACK- ST-AMP**  Hailey Arscott 2013 JANAC
- **UNICEF project for HIV-positive adolescents.**  (L. Cluver)
- **FACES (Family AIDS Care and Education Services Kisumu, Kenya)**

Once Daily
Regimen simplification

Discussion

Knowledge

Organization Tools

Reminders/Alarm
ADOLESCENT ADHERENCE

SUMMARY

• Adolescents and young adults are a priority population but continue to be underrepresented in research and evidence base

• Several kinds of interventions are promising but field continues to be dominated by small pilot studies and community programs that lack evaluation components

• Strategies to better support perinatally infected and behaviorally infected youth, in general and as they transition to adult care are needed

• Adherence support strategies specific to youth and their NORMAL COURSE of development

• Much to learn....many excellent advocates but we need to have adolescence and youth highlighted as a priority and REPRESENTED in the research.
Children/youth deserve more than just being kept alive

- Sarah Bernays, Prudence Jarrett, Katharina Kranzer, Rashisa Ferrand

_The Lancet_ 2014

Thank you
• S. Hosek
• A. Outlaw
• G. Donenberg
• LG. Bekker

• All the adolescents and youth participating in research and practice based trials!

**Future Fighters**
(Youth CAB, DTHF)- courtesy of LG Bekker