Retention and adherence: evidence-based strategies.

Dr Catherine Orrell

Desmond Tutu HIV Centre

University of Cape Town

Desmond Tutu HIV Foundation

Masibambane Ngezandla

Adherence in sub-Saharan Africa

3 large reviews of the antiretroviral adherence literature to date:

- Bärnighausen, Lancet 2011
- Thompson, Annals of Internal Medicine 2012
- Chaiyachati, AIDS 2014

Approaches to managing adherence

Review

The Lancet, 2011

Interventions to increase antiretroviral adherence in sub-Saharan Africa: a systematic review of evaluation studies

Till Bärnighausen, Krisda Chaiyachati, Natsayi Chimbindi, Ashleigh Peoples, Jessica Haberer, Marie-Louise Newell

Lancet Infect Dis 2011; 11: 942–51
Published Online October 25, 2011
DOI:10.1016/S1473-3099(11)70181-5

Africa Centre for Health and Population Studies, University of KwaZulu-Natal, Mtubatuba, South Africa
(T Bärnighausen MD, N Chimbindi MSc,

The success of potent antiretroviral treatment for HIV infection is primarily determined by adherence. We systematically review the evidence of effectiveness of interventions to increase adherence to antiretroviral treatment in sub-Saharan Africa. We identified 27 relevant reports from 26 studies of behavioural, cognitive, biological, structural, and combination interventions done between 2003 and 2010. Despite study diversity and limitations, evidence suggests that treatment supporters, directly observed therapy, mobile-phone text messages, diary cards, and food rations can effectively increase adherence in sub-Saharan Africa. However, some interventions are unlikely to have large or lasting effects, and others are effective only in specific settings. These findings emphasise the need for more research, particularly for randomised controlled trials, to examine the effect of context and specific features of intervention content on effectiveness. Future work should assess intervention targeting and selection of interventions based on behavioural theories relevant to sub-Saharan Africa.

The Lancet, 2011

Intervention categories:

- education and counselling,
- treatment supporters,
- text messages / reminder devices
- DOTs
- food supplements
- health system approaches

Systematic literature review; adherence interventions only.

Any ART study with adherence outcome and a comparator group.

Sub-Saharan Africa only.

26 studies (16/26 show benefit)

Approaches to managing adherence

Clinical Guidelines

Guidelines for Improving Entry Into and Retention in Care and Antiretroviral Adherence for Persons With HIV: Evidence-Based Recommendations From an International Association of Physicians in AIDS Care Panel

Melanie A. Thompson, MD; Michael J. Mugavero, MD, MHSc; K. Rivet Amico, PhD; Victoria A. Cargill, MD, MSCE; Larry W. Chang, MD, MPH; Robert Gross, MD, MSCE; Catherine Orrell, MBChB, MSc, MMed; Frederick L. Altice, MD; David R. Bangsberg, MD, MPH; John G. Bartlett, MD; Curt G. Beckwith, MD; Nadia Dowshen, MD; Christopher M. Gordon, PhD; Tim Horn, MS; Princy Kumar, MD; James D. Scott, PharmD, MEd; Michael J. Stirratt, PhD; Robert H. Remien, PhD; Jane M. Simoni, PhD; and Jean B. Nachega, MD, PhD, MPH

Annals of Internal Medicine, 2012

Intervention categories:

- ART strategies (pill number, dosing)
- education and counselling,
- peer support,
- interactive reminder devices and
- health system / service delivery

Systematic literature review: **linkage**, **retention** and adherence.

Any study with adherence as an outcome, including a comparator arm.

325 studies; global

Quality of the body of evidence

Quality of Body of Evidence	Interpretation
Excellent (I)	**RCT** evidence without important limitations **Overwhelming** evidence from observational studies
High (II)	RCT evidence with important limitations **Strong evidence** from observational studies
Medium (III)	RCT evidence with critical limitations **Observational** study evidence without important limitations
Low (IV)	Observational study evidence with important or critical limitations

Strength of Recommendations

Strength of Recommendation	
Strong (A)	**Almost all** patients should receive the recommended course of action.
Moderate (B)	**Most** patients should receive the recommended course of action. However, other choices may be appropriate for some patients.
Optional (C)	There may be **consideration** for this recommendation on the basis of individual patient circumstances. Not recommended routinely.

Approaches to managing adherence

Interventions to improve adherence to antiretroviral therapy: a rapid systematic review

Krisda H. Chaiyachati[a], Osondu Ogbuoji[b], Matthew Price[b], Amitabh B. Suthar[c], Eyerusalem K. Negussie[c] and Till Bärnighausen[b,d]

Introduction: Access to antiretroviral treatment (ART) has substantially improved over the past decade. In this new era of HIV as a chronic disease, the continued success of ART will depend critically on sustained high ART adherence. The objective of this review was to systematically review interventions that can improve adherence to ART, including individual-level interventions and changes to the structure of ART delivery, to inform the evidence base for the 2013 WHO consolidated antiretroviral guidelines.

Design: A rapid systematic review.

Methods: We conducted a rapid systematic review of the global evidence on interventions to improve adherence to ART, utilizing pre-existing systematic reviews

AIDS, 2014

Intervention categories:

- education,
- cognitive-behavioural interventions,
- treatment support,
- active reminder devices and
- DOTs …and combinations

Rapid systematic review (utilises previous reviews), adherence interventions only.

RCT, NRCT: before-after cohort and case-control studies.

124 studies (75/124 show adh. benefit).

Global.

Linkage to care:

Monitor entry and retention.

- **Systematic monitoring of linkage** should be done for all diagnosed (II A)
- **Systematic monitoring of retention** is recommended for all patients (II A) – retention is associated with improved outcome. Use what is available: medical records, administrative databases, pharmacy data etc.

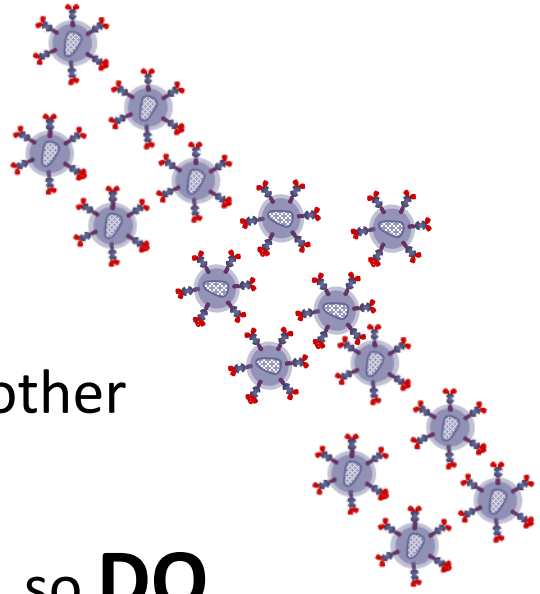
Notice if a visit is missed…

Adherence monitoring:

Monitor adherence and retention.

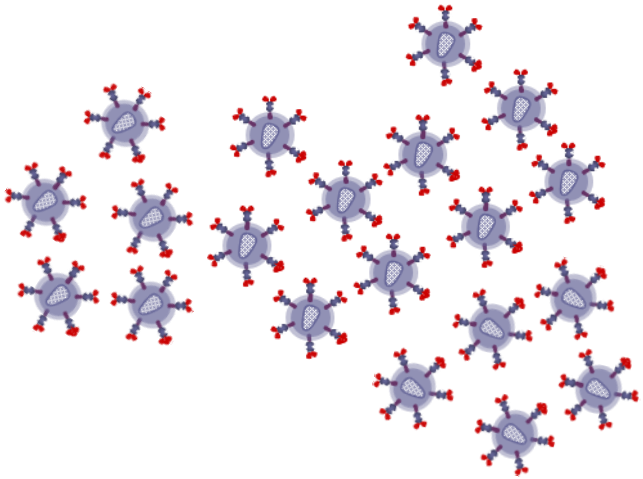
- **Self-reported adherence** should be obtained routinely in all patients (II A)
- **Pharmacy refill data** are recommended for adherence monitoring when medication refills are not automatically sent to patients (II B)
- The following are not routinely recommended, but can be useful:
  - Use of DAART in routine ART care (IA)
  - Drug concentrations in biological samples (III C)
  - Pill counts performed by staff or patients (III C)
  - Electronic Drug Monitors for clinical use (I C)

Adherence monitoring:



Use the viral load.

- WHO recommends **VL monitoring** with other adherence measures.
- Raised viral load indicates a risk of failure, so **DO** something.
- 56-68% can re-suppress with an adherence intervention.



Adherence interventions are successful

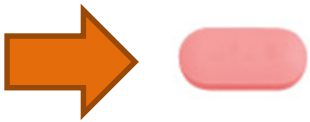
Study	Year	n	Intervention	Outcome
Berki-Benhaddad	2006	15	Personal adh support	Ave decrease VL by 2.3 log
Calmy	2007	232	Counseling, pill boxes, support group, treatment partner	77% achieved VL<400
DeFino	2004	45	Counseling, pill boxes, alarm reminders, repeat education…	Ave decrease VL by 0.6 log
Khan	2013	40	Structured adh counseling, including families	78% achieved resuppression
Orrell	2007	43	Pill box, dosing diaries, counseling, home visit	68% achieved resuppression
Parker	2013	200	Intensive adh counseling	48% achieved resuppression
Pirkle	2009	56	1 month mDAART, weekly f/u visits	36% decreased VL by >1 log
Wilson	2009	40	Counseling and education	90% resuppression

Bonner, JAIDs 2013

Interventions to improve adherence:

ART strategies:

- Among regimens of similar efficacy and tolerability, **once-daily regimens** are recommended for treatment-naive patients beginning ART (II B).
- **Simplify** where possible…
- Among regimens of equal efficacy and safety, **fixed-dose combinations** are recommended to decrease pill burden (III B).



Thompson et al.

Adherence interventions:

Counselling and education:

- Individual ART **education** is recommended (IIA); can be done in a group (IIC).
- Providing **one-on-one adherence support** to patients through adherence counselling approaches is also recommended.
- **Multidisciplinary education and counselling** intervention can be useful too – use the skills of the team: nurse, Dr, CCW, psychologist (IIIB)
- Positive outcome: 79-88% adherence; 21-63% biological.

Thompson, Bärnighausen and Chayachati.

Adherence interventions:

Peer support:

- Offering **peer / treatment support** may be considered (IIIC) .
- Some discrepant findings… 62% had a positive adherence outcome, 19% positive biological outcome.
- Treatment supporter role is not clear.

Thompson, Bärnighausen and Chayachati.

Adherence interventions:

Cognitive behavioural therapy:

Chaiyachati reports 60 studies; 67% had a positive adherence outcome and 20% a positive biological outcome.

Includes motivational interviewing, self-efficacy and skills building, stress management, patient empowerment.

Chayachati.

Adherence interventions:

Interactive reminder devices:

- **Reminder devices (e.g. pillboxes)** and use of **communication technologies** with an interactive component are recommended. (IB)

Thompson, Bärnighausen and Chayachati.

Adherence interventions:

Interactive reminder devices:

8 recent RCT using SMS messaging…

Only 5 noted improved adherence; only 2 showed biological improvement.

Successes to date include:

- Weekly messaging
- Interactive component
- Targeting those with poor adherence

Adherence interventions:

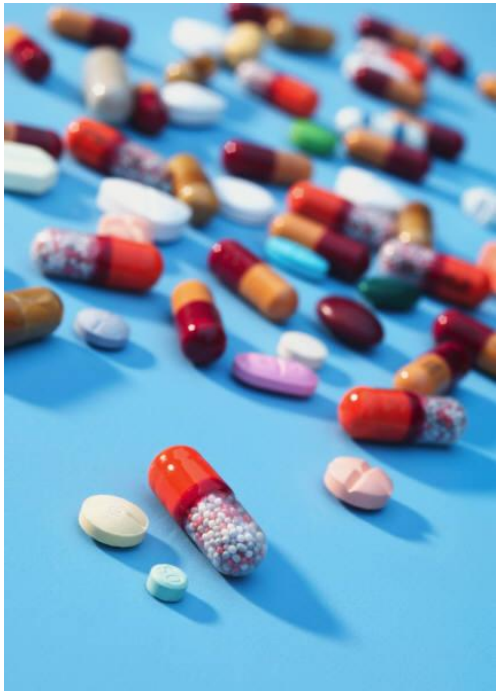
Health system approaches:

- Using **nurse- or counsellor-based care** is recommended where resources are limited: task – shifting. (IIB)
- **Monthly food supplementation** packages improve early adherence to first-line antiretroviral therapy and are recommended. (IIB)

43% of seven studies showed biological improvement.

Thompson, Bärnighausen and Chayachati.

Adherence interventions:



Health system approaches:

- DOTS vs no DOTS: discrepant findings

Thompson: DAART not recommended in routine clinical settings (IA)

Chaiyachati: of 20 studies, 85% showed adherence benefit; 30% biological.

Bärnighausen: assess within context!

Vulnerable populations:

- Mentally ill (including anxiety and depression)
- Pregnant women
- Children and adolescents
- Substance use

Summary 1

- Simplify the treatment to be taken…
- Education and counseling is beneficial.
- Monitor adherence on treatment: PR, SR.
- Notice if people miss visits.
- Use the viral load! Target interventions to those not doing well.
- Consider the use of food supplementation / reminders…
- Watch for high-risk groups; consider use of DOTs.

Summary 2

Still room for more learning:

- For each intervention with a significant outcome there is one without.
- Many studies use only subjective adherence measures and have only shown short-term benefit;
- Lack of cost-effectiveness information;
- Little data on vulnerable populations;
- Value of single vs. combination adherence interventions (prevention);
- Improving long-term adherence / retention.

What works to improve adherence?

Develop your adherence toolkit:

- Medication factors,
- Service / provider factors,
- Patient factors

We can do a lot with what we have already!

Acknowledgements

- Desmond Tutu HIV Centre team
- Melanie Thompson and IAPAC guideline team

University of Cape Town