Adherence to ART

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Adherence is the key

• Two main reasons for treatment failure:
  – Non-adherence
  – Viral resistance

• Virological, immunological & clinical failure occurs in:
  – Non-adherent patients
  – Patients exposed to multiple regimens over a long period of time
  – Inadequate drug levels
  – Pre-existing drug resistance
Adherence is the key

- Optimising adherence is arguably the single most important way to ensure excellent therapeutic outcomes in children & adults with HIV infection and delay the progression to clinical and virological failure.

- Within the public sector we have limited treatment options for children.
Definition of good adherence

• Early adult studies suggested that adherence of at least 95% is associated with a good virological response, and delays the emergence of viral resistance

• Prospective study in adults, n=81
  – 5/23 (22%) with an adherence rate $\geq 95\%$ had virologic failure
  – Failure occurred in 61% of those with adherence rates of 80% - 94.9%
  – Failure increased to 80% in those with < 80% adherence

• Paediatric studies: 75 – 100%

Methods of monitoring adherence

• Directly observed therapy
• Caregiver / patient self-report
• Medication return (pill counts)
• Pharmacy refill records
• Appointment keeping
• Electronic pill monitoring
• Plasma drug level testing
• Viral load monitoring
Directly observed therapy

- Theoretically associated with 100% adherence

- Cons
  - Highly labour intensive
Caregiver / patient self report

• Types
  – Clinician interview
  – Questionnaires e.g. PACTG 3-day recall
  – Medication diaries

• Pros
  – Convenient, inexpensive

• Cons
  – Less accurate than more objective measures
  – Subject to bias as caregivers may inflate their adherence reports

• Research findings
  – Significant association between CSR and 6 month VL outcome

Michaels D, PhD thesis, February 2008
Medication return / pill counts

• Pros
  – May be more accurate than self report
  – May increase accuracy when combined with reminder calls or visits

• Cons
  – Labour intensive
  – Although an objective measure ‘medicine dumping’ may occur

• RCWMCH study, n=122
  – 91 (79%) achieved MR adherence ≥ 90%
  – Undetectable VL : 62/80 (78%) with annual MR adherence ≥ 90% vs 2/8 (25%) with lower MR adherence, OR=10.3, CI 1.92-55.7, p=0.005

Adherence monitoring

- Pharmacy refill records: This is sometimes used in conjunction with medication return
- Appointment keeping: not particularly useful
- Electronic monitoring:
  - offers more detailed assessment than medication return or pharmacy refill records; may provide details of the pattern of poor adherence.
  - Local study: provides accurate measure of adherence in children on liquid formulations

Viral load monitoring

- Traditionally used to assess treatment success or failure
- Not a primary measure of adherence
- Can be used as an objective measure of adherence in association with other measures e.g. MR, self report, etc.
- It is possible to have virological failure in the face of good adherence, particularly if there are existing resistant strains present
# VL monitoring & recommended action

<table>
<thead>
<tr>
<th>Viral load</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 400 c/mL</td>
<td>Routine VL monitoring and adherence support</td>
</tr>
</tbody>
</table>
| 400-1000 c/mL    | - Repeat VL after 6 months  
                    - Step-up adherence support if VL remains between 400-1000 c/mL                                                                       |
| >1000 c/mL       | - Step-up adherence support  
                    - Repeat VL after 3 months  
                    - If <400 c/mL resume routine monitoring  
                    - If between 400 and 1000 c/mL continue adherence support & repeat VL after 6 months  
                    - If >1000 c/mL despite intensified adherence support, and child is on a NNRTI-based regimen switch to 2nd line therapy provided that adherence is good  
                    - If >1000 c/mL and child on LPV/r-based regimen:  
                      • Reinforce adherence [it is very difficult to fail a LPV/r-based regimen]  
                      • Switch to 2nd line regimen if VL >5000 c/mL, only if adherence is good & consider drug resistance testing if available  
                    - If child received unboosted PI, do resistance testing if available and change to 2nd line regimen if VL >1000 c/ml |
Understanding non-adherence
Socio-demographic factors

- Age, race and gender have not been shown to be predictors of adherence.
- Being transiently housed (homeless shelters and single occupancy hostels) was not associated with adherence.
- Profiling may lead to overestimates of adherence (rich) or underestimates (poor).
Factors associated with poor adherence

- Caregiver depression and other untreated affective disorders adversely associated with adherence
- Active substance abuse associated with decreased adherence
- Non-adherent patients: Caregivers are less certain about how the medication works
- More complex the regimen the less adherent the patient
What makes a regimen more complex?

• The number of pills or medication
• How many times per day you take meds
• Crushing, mixing, dissolving, measuring
• Does it need food or an empty stomach?
• The timing – Do you have to take it while at school?
• The need for refrigeration
Side effects and adherence

• Patients may discontinue medication to avoid side effects.

• However, when they perceive their illness as life threatening, patients are prepared to tolerate side effects.
Education

• Research from PACTG programmes in the USA:
  – 10% paediatric patients weren’t clear of their regimen immediately after the clinic visit where it was prescribed
  – 10% of paediatric patients did not know how to take their medication
  – 18% of paediatric patients did not know the name of their drugs
  – 2% of paediatric patients could not state the dosing instructions that they were given

• Interventions using pharmacists to educate patients had a positive effect on their adherence (review of 21 studies)
Clinician factors impacting adherence

• Stability
• Availability
• Style: clinical, personal
• Assessment skills
• Communication skills
• Flexibility
• Cultural sensitivity
Family factors influencing adherence

• Caregivers
  – Mental health, physical health, substance abuse, past experiences

• Child
  – Age (developmental not chronological), temperament

• Home environment
  – Privacy, disclosure and support, additional stresses, responsibilities
# Age and adherence

## Infancy
- Dependence on caregiver
- Prematurity
- HIV-related feeding difficulties
- Pills versus suspensions
- Side effects: diarrhoea, vomiting, nausea, etc

## Pre-school children
- Dependence on caregiver
- Refusal of child
- Taste and texture
- Lack of routine
- Change of caretaker
- Daycare or school attendance
## Age and adherence (2)

### School-aged children
- Taste / texture / amount
- Timing
- Hiding the meds
- Lack of control
- Lack of supervision
- Disclosure status
- Understanding HIV

### Adolescents
- Pill burden
- Responsibility for self
- Side effects on activities
- Peer pressure
- Affective disorders
- Disclosure status
- They feel that they are invincible
- Increased risk taking behavior
What can we do to improve matters?
Education / communication

- Use terminology they can understand
- Use metaphors that fit in with cultural beliefs
- Draw pictures
- Use models
- Have them draw pictures
- Repeat over time
- Have them teach you
Give them feedback

- Show them their CD4 counts, viral load results & growth charts
- Praise them for a job well done
- Provide incentives such as sticker charts
- Talk to them about long term goals that include staying on medication
- Encourage two-way honesty about adherence
Simplify medication

- Minimize pill burden
  - Use combination pills when available
- Rationalize dose frequency
- Minimize dietary instructions
- Assess readiness to swallow pills
  - Do not assume that a patient is old enough to swallow pills
Link medication to daily activities

• Carefully assess home life & family routine
• Choose options that fit their lives:
  – Consider school
  – Consider caregiver’s job
  – Does medication require refrigeration
  – When do they eat?
• Identify activities that will trigger them to take their medication e.g. brushing teeth
• Changes in normal routine may affect adherence
Manage side effects

• Follow up with the patient 1-2 weeks after starting new medication
• This is when most problems occur
• Offer support and treatment as needed
• Sometimes they need to be talked through the first few days with daily calls
• Persevere with Kaletra
Provide tools

- Pill boxes
- Sticker charts
- Colour coding
- Reminder calls
- Buddy system: community adherence support
- Diaries
- Alarms

Consistency

• Educate caregivers on consistency and routine
• Infants who hate medication will get use to it if doses are regular and consistent
• Prepare them for the struggle and tears but encourage them to stick with it
• As soon as a child sees that he/she can control whether they get medication through tantrums, he/she will stop taking it