

# A multi-faceted approach to adherence – a broader perspective

Wits Institute (formerly RHRU and ECHO)

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**RHRU**

Reproductive Health & HIV Research Unit  
of the University of the Witwatersrand, South Africa.



# Adherence in HIV prevention trials

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- Adherence to investigational product is critical in trials of biomedical interventions to prevent HIV (Padian, 2008)
- Without adequate adherence, the true efficacy of these interventions cannot be determined (Weiss, 2008)
- The majority of current or ongoing HIV prevention trials rely on user-dependent adherence
- Despite high levels of HIV treatment adherence in our setting, these levels may not be translated to high levels of adherence to preventive interventions in healthy volunteers

# HIV prevention trials face particular prevention challenges

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- **Trials recruit healthy volunteers who may have little incentive to adhere to products of unknown efficacy**
  - Altruism, access to personal health and behavioural benefits have been reported previously as main reasons for participation (Colfax, 2005; Kenyon, 2006)
  - Compensation is also more important in some settings (Shaffer, 2006)
- **Measurement of adherence still relies largely on user-dependent measures e.g. self-report, pill count**
  - Also require adherence to pharmacy refill visits and return of pill bottles
- **Protocol often require adherence to additional preventive behaviours e.g. condom use, avoidance of genital cleansing, coital use of product**
  - Links between product adherence and sexual behaviour create additional challenges

# Research questions

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- What motivates trial participation in South African women and how does this influence trial participation?
- How good are our existing adherence measures?
- Can we do more to predict who will adhere well and who will require support?



# Methods

A proof-of-concept, randomised, double-blind, placebo-controlled trial of daily acyclovir 400mg BD vs. placebo for 3 months among co-infected women not requiring HAART

- **During the trial**

- Monthly visit data collected on adherence by pill count and self-report

- **Post-trial**

- in-depth interviews with trial participants (n=32)
- Analysis of trial data to assess baseline predictors of poor adherence (<90% doses taken) (n=300)



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**What motivates trial participation in South African women and how does this influence trial participation?**



# Reasons for participation

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- Participants motivated by desire to access health information and to gain control of their health
  - Access to information, testing and treatment were all mentioned
- Although women did discuss HIV and HSV-2 specifically, they were more likely to speak of wanting to improve their health more generally
- Compensation was not a motivating factor for most women

# Reasons for participation

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“ I joined the study because I wanted to know about my health; it was not because of the money” (Participant #20)

“My aim for coming to the clinic was to get something to help me. I found what I was looking for because the medication that I received helped my problem. My aim was not to receive money when I came here. If it was just because I wanted the money then it would have been better if I had just stayed at home”  
(Participant #16)



# Reasons for participation

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- **Altruism** was not a major determining factor for trial participation
  - Only a single participant noted that she was motivated to assist the research process
- Overall, the decision to participate was a **rational health decision** in the face of perceptions of general reproductive ill-health in the community
- While most said their **partners** were aware of their participation, few mentioned that male partners had assisted in decision to participate
- Participants more often sought advice about participation from **female relatives** or friends
- **Perceived personal benefits** outweighed any negative attitudes towards research in the community
  - Many specifically said that they would not listen to anyone who attempted to sabotage their participation

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**How good are our existing adherence measures?**



# Measuring adherence during the trial

	Month 1 N=299 n (%)	Month 2 N=298 n (%)	Month 3 N=298 n (%)
<b>Missed visits</b>	<b>20 (7)</b>	<b>26 (9)</b>	<b>28 (9)</b>
<b>Adherence data from pill counts</b>			
No. of pill boxes returned at follow up	261 (94)	258 (95)	253 (94)
Percentage of expected doses taken			
<90%	41 (14)	36 (12)	36 (12)
90-100%	232 (84)	232 (85)	224 (83)
Not returned	6 (2)	4 (1)	10 (3)
<b>Self-reported adherence data from questionnaire</b>			
No. of consecutive doses missed			
<9	258 (87)	250 (84)	253 (85)
>=10	20 (7)	19 (6)	15 (5)

# Post-trial interviews confirmed reported adherence during the trial

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- Participants reported missing a few doses and compensation strategies
- Reasons for missed doses matched reasons reported during the trial viz. Change in routine, travel, side effects



- A small number linked their motivation to adhere to study drugs to a perception that their health had improved since enrolment in the study
- No participants reported pill sharing and many noted that it was an unwise strategy if one was concerned about one's own health and that of partners, family or friends
- Participants reflected that lying about their adherence would limit the degree to which they could measure health improvements or manage health problems

# Post-trial interviews confirmed reported adherence during the trial

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- "I was scared [to tell clinic staff I had missed a dose]. I thought they would shout at me but they did not shout at me - they showed me how to take them so I could see if they were going to help". (Participant #6)*
- "I was honest because I told them [clinic staff] I was taking my pills and I was honest about it. The other thing is that I never missed to take my pills and my husband used to set the alarm so the time it started to go off I knew it was the time for me to take my pills". (Participant #19)*
- "I think the nurses helped me to take my pills because they used to encourage me to take my medication if I want to become better. Moreover, the nurses were fine by me. (Participant #8)"*

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**Can we do more to predict who will adhere well and who will require support?**



# Predictors of poor adherence

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- Poor adherers (<90% doses taken)
  - 58% aged 25-34 years
  - 83% single
  - 84% secondary/tertiary education
  - 57% >1 week outside JHB in past year
  - 14% >1 current partner
  - 70% condom use at last sex act
  - 12% history of GUD in past 3 months
  - 47% <6 months since HIV diagnosis



# Predictors of poor adherence

<b>Risk factor</b>	<b>Adjusted OR</b>	<b>95% CI</b>	<b>p</b>
<b>Age (years)</b>	0.95	0.91 – 1.00	0.038
<b>Mobility</b>			
<=1 week outside JHB in past year	1.00	Ref	
>1 week outside JHB in past year	2.44	1.41 – 4.21	0.001
<b>Number of current sexual partners</b>			
<=1	1.00	Ref	
>1	2.51	1.03 – 6.09	0.043
<b>Time since HIV diagnosis</b>			
<6m prior to enrolment	1.00	Ref	
>=6m & <3yrs prior to enrolment	0.52	0.27 – 1.01	0.054
>=3 years prior to enrolment	0.74	0.38 – 1.42	0.363

# Conclusions

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- Women's participation in this clinical trial was overwhelmingly motivated by a desire to better manage and understand their health while accessing quality healthcare
- High levels of drug adherence can be achieved when study activities are highly applicable to participants or fill an unmet need
- Women's motivation to improve their health influenced their adherence to study visits and study drug which in turn enhanced adherence assessments
  - Adherence measures observed in the trial were corroborated in post-trial interviews
- It is important to appreciate the linkages between visit adherence and product adherence

# Conclusions

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- Trial staff play a critical role in supporting adherence through quality care and knowledge
- Participants who are less likely to adhere to study drug can be identified on demographic factors alone
  - Younger age, travel >1 week, having >1 sex partner predict poor adherence
  - Importantly neither clinical indicators nor randomisation arm were associated with poor adherence
- Future trials that involve daily dosing may benefit from the lessons learned in the acyclovir trials, despite some differences in trial populations

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