Improving adherence to antiretroviral medications using triggered cell-phone reminders with the Wisepill Device: The China Adherence through Technology Study (CATS) Abs

Abstract #493

June 9, 2010

Lora Sabin,¹ Mary Bachman DeSilva,¹ Christopher J Gill,¹ Zhong Li,² Taryn Vian,¹ Xie Wubin,² Cheng Feng,³ Xu Keyi,⁴ Jessica Haberer,⁵ David Bangsberg,⁵ Allen L. Gifford^{1,6}

¹Boston University, Boston, MA, USA
²FHI 360, Beijing, China
³Global Health Strategies, Beijing, China
⁴Ditan Hospital, Beijing, China
⁵Massachusetts General Hospital, Boston, MA, USA
⁶ Edith Nourse Rogers Memorial VA Hospital, Bedford, MA, USA



Rapid ART scale up in China

- China: relatively stable HIV epidemic
 - Roughly 780,000 PLWHA currently
 - Border epidemics still growing most rapidly
- Scale-up of ART: impressive
 - National free ART program started in 2002
 - By March 2014, 287,000 on ART
- The tools exist to eliminate HIV, but...
 - Non-adherence appears common
 - Non-adherence contributes to drug resistance
 - Ways to improve adherence urgently needed

Sources: China MoH (2012), China NCAIDS personal communication (2014)

Previous China research and electronic drug monitoring (EDM) feedback

- Our previous work in Dali
 - EDM-informed counseling significantly improved ART adherence and CD4 counts
 - Conclusion: EDM-guided adherence support works, but is limited it doesn't provide real-time behavioral feedback
- Real-time monitoring (via Wisepill)
 - Web-linked medication container that sends electronic signal to central server at each opening
 - Allows reminders to be sent at specific times
- Patient experience with Wisepill
 - Wisepill feasible/acceptable in Uganda (2010)
 - Wisepill feasible/acceptable in China (2013)



So we hypothesized...

Could *real time* reminders (via Wisepill) combined with data-informed counseling improve ART adherence?

Study objectives

Primary Objectives

• To generate efficacy data of real-time feedback on adherence

Secondary Objectives

• To generate efficacy data of real-time feedback on CD4 count, HIV viral load

CATS study design ('real-time feedback' intervention)

Intervention design and timeline



What happened in intervention arm?

1. SMS reminder to cell phone if device unopened within 30 minutes of dose time

Patients chose one of 10 possible reminders; examples: *Carry on, carry on! Be healthy, have a happy family.*:)

2. Wisepill data used in counseling sessions

- At monthly clinic visits, Wisepill report given to patient
- Patients <95% adherence given counseling using report

What happened in comparison arm?

•No reminder messages

•Wisepill report NOT shared with patient

Study endpoints

Impact on adherence (primary endpoint)

- $\% \ge 95\%$ adherent post-intervention (M 9)
- Mean adherence in Month 9

Adherence measure ('on time' measure):

doses taken +/- 1 hour of scheduled time

prescribed doses

Impact on clinical markers

- CD4 (cells/µl) mean change: M3 to M9
- Undetectable Viral load (UDVL) (RT PCR: <50 copies/ml): % UDVL in M9



Patients' characteristics at randomization

	Intervention	Comparison	
Characteristic	N (%) or Mean (SD) (N=62)	N (%) or Mean (SD) (N=57)	p-value
Gender (male)	41 (66.1)	35 (61.4)	NS
Age (years)	36.5 (10.7)	38.8 (9.9)	NS
Married	24 (38.7)	38 (66.7)	**
Education level			NS
Primary only	14 (22.6)	13 (22.8)	
Middle/secondary school	34 (54.8)	35 (61.4)	
Beyond Secondary School	14 (22.6)	9 (15.8)	
Currently employed (yes)	35 (56.5)	31 (54.4)	NS
Monthly income (yuan) (n=64)	2593 (2456)	3333 (5950)	NS

*p<0.05; ** p<0.01

Patients' characteristics at randomization

	Intervention	Comparison	
	N (%) or	N (%) or	
	Mean (SD)	Mean (SD)	
Characteristic	(N=62)	(N=57)	p-value
CD4 count at baseline	386 (150)	367 (192)	NS
UDVL at baseline (N=118)	42 (67.7)	54 (94.7)	***
Time on ART (months)	29.5 (32.3)	33.3 (27.5)	NS
Twice/daily regimen (vs. once a			
day regimen)	38 (61.3)	45 (79.0)	*
Used injectable street drug (ever)	7 (11.3)	8 (14.0)	NS
Used non-injectable drug (ever)	8 (12.9)	9 (15.8)	NS
Presumed transmission route			*
Sex with HIV+ man	37 (59.7)	18 (31.6)	
Sex with HIV+ woman	9 (14.5)	15 (26.3)	
Shared needles	5 (8.1)	7 (12.3)	
Blood	2 (3.2)	5 (8.8)	
Don't know/other	9 (14.5)	5 (21.1)	

*p<0.05; ** p<0.01

Impact of the intervention Comparison of mean monthly adherence: pre-intervention vs. final intervention month

	Pre-intervention (M 3)		Final intervention month (M 9)		
	Intervention Mean, % (SD)	Comparison Mean, % (SD)	Intervention Mean, % (SD)	Comparison Mean, % (SD)	
Measure	n=61	n=55	n=61	55	
On-time	91.7 (15.4)	92.6 (11.3)	96.4 (6.1)	89.2 (16.1)**	
Porportion taken	93.9 (13.0)	95.4 (9.6)	97.6 (3.5)	92.2 (14.9)*	

*p<0.05 **p<0.01 At Month 3, no significant differences between intervention and comparison arms.

At Month 9, large increase in adherence in intervention arm, regardless of measure; no significant increase in comparison arm.

Impact of the intervention Comparison of mean adherence: pre-intervention period vs. intervention period

	Pre-intervention (M 1-3)		Intervention (M 4-9)	
	Intervention Mean, % (SD)	Comparison Mean, % (SD)	Intervention Mean, % (SD)	Comparison Mean, % (SD)
Measure	n=61	n=55	n=61	n=55
On-time	91.6 (12.0)	93.2 (10.4)	96.3 (5.9)	89.5 (14.5)**
Porportion taken	94.7 (9.0)	95.4 (9.0)	97.5 (3.7)	93.2 (10.5)**

*p<0.05; ** p<0.01

At Month 3, no significant differences between intervention and comparison arms.

At Month 9, large increase in adherence in intervention arm, regardless of measure; no significant increase in comparison arm.

Adherence over time, stratified by baseline adherence (low vs. high)

Monthly adherence by adherence category at Month 3, intervention vs. control (on-time measure)



Proportion of subjects achieving adherence $\ge 95\%$

Effect of Real Time Feedback on rates of optimal adherence in Month 9



Biological impact of intervention

	Intervention	Comparison	
Mean change in CD4 (x1000 cells/ml)	+ 53	+ 33	
Not significant			
No change in UDVL (nearly 100% UDVL at baseline)			

Analysis of late doses: the effect of reminders among subjects who hit 30 minute mark without taking dose



One patient, 6 months of intervention: Wisepill data are powerful!





Doses taken on time (78%)

Doses taken late (22%)

Conclusions

We found:

- Real-time feedback intervention a personalized intervention that delivers triggered reminders + data-informed counseling as back up – improved on-time adherence
- Results especially promising with low adherers
- No evidence of impact on CD4 counts

CATS team & acknowledgements

• BU CGHD

- Lora Sabin (PhD)
- Mary Bachman DeSilva (ScD)
- Allen Gifford (MD)
- Christopher Gill (MD)
- Taryn Vian (PhD)
- Ariel Falconer (MPH)

• FHI 360/China

- Zhong Li (MS)
- Cheng Feng (PhD) (former China Country Director)
- Xie Wubin (MPH)

We gratefully acknowledge support from the National Institute for Drug Abuse. We appreciate help from: Shoshana Kahana, Richard Denisco, Bram Brooks, Mark Harrold, Evan Hecht, & Katherine Semrau. We thank most sincerely all the individuals in Nanning who participated in this research.



- Guangxi Provincial CDC ART Clinic (Nanning)
 - Lan Guanghua (MD)
 - All clinic staff members
- Ditan Hospital
 - Xu Keyi (MD)
- Harvard University/Mass General Hospital
 - David Bangsberg (MD)
 - Jessica Haberer (MD)

Extra slides in case needed

Effect of intervention on adherence (proportion taken measure)

Monthly adherence by adherence category at Month 3, intervention vs. control (proportion taken measure)



Proportion at optimal adherence levels $(\geq 90\%)$

Effect of Real Time Feedback on rates of adherence in Month 9



Proportion of subjects achieving adherence $\geq 80\%$

Effect of Real Time Feedback on rates of adherence in Month 9



Changes in counseling frequency among intervention subjects, stratified by baseline adherence



Low adherers (n=22)

High adherers (n=38)



First visit of intervention period