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HIV TREATMENT
AND PREVENTION
ADHERENCE

Association Between Barriers to Antiretroviral Therapy Adherence and Plasma HIV RNA among AIDS Clinical Trials Group Study Participants

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Disclosures

- I have no conflict of interest

Introduction

- HIV is a chronic disease and life-long ART is required. Therefore, it is imperative to:
  - understand barriers to adherence over time
  - examine association between adherence barriers and HIV treatment goals to develop effective ART adherence interventions

Introduction

- Prior research has heavily focused on commonly reported barriers to determine intervention targets.

- Forgetting to take ART is one of the most commonly stated adherence barriers. Therefore, many studies have examined use of reminder devices but most have not revealed significant changes in adherence.

Objectives

1. Examine the association between specific adherence barriers and the cumulative number of barriers and virologic detectability

2. Establish the relative importance of each adherence barrier in explaining virologic detectability

Study Design

- Secondary analysis of longitudinal data collected as part of ACTG ART studies

- Include: all ACTG ART studies that were conducted in US, used ACTG adherence barriers questionnaire at 12 weeks (+/-4 weeks), collected data on demographics and plasma HIV RNA at 24 weeks (+/-4 weeks)

- Exclude: studies that examined non-oral ART, assessed impact of treatment interruption before 24 weeks (+/-4 weeks), or recruited less than 10 participants

ACTG Studies

- Identified 11 ACTG studies:
  - 4 ART naïve: ACTG 371, 384, 746, A5073
  - 7 ART experienced: ACTG 372, 398, 400, A5025, A5116, A5126, A5143
- Enrollment period range= 1997-2003
- Concluded between 2002 and 2012 (median= 2009)
- Mean 280 participants enrolled per study (range= 25-987)
- Mean duration= 93 weeks (range= 24-220)

Variables

- Outcome: HIV RNA at 24 weeks (+/-4 wks)
  - Dichotomized: detectable vs. undetectable

- Predictor: adherence barriers at 12 weeks (+/-4 wks)
  - Dichotomized (yes/no) and summed and categorized (0= no adherence barriers; 1= 1-4 barriers; 2= 5-14 barriers)

- Potential confounders: age, sex, race/ethnicity, HIV risk factor, and study protocol number

In the **past month**, how often have you **missed taking your medications** because you:

(Check one

Please check one box for each question.

	Never	Rarely	Some-Times	Often
1. Were away from home?	☐ 0	☐ 1	☐ 2	☐ 3
2. Were busy with other things?	☐ 0	☐ 1	☐ 2	☐ 3
3. Simply forgot?	☐ 0	☐ 1	☐ 2	☐ 3
4. Had too many pills to take?	☐ 0	☐ 1	☐ 2	☐ 3
5. Wanted to avoid side effects?	☐ 0	☐ 1	☐ 2	☐ 3
6. Did not want others to notice you taking medication?	☐ 0	☐ 1	☐ 2	☐ 3
7. Had a change in daily routine?	☐ 0	☐ 1	☐ 2	☐ 3
8. Felt like the drug was toxic/harmful?	☐ 0	☐ 1	☐ 2	☐ 3
9. Fell asleep/slept through dose time?	☐ 0	☐ 1	☐ 2	☐ 3
10. Felt sick or ill?	☐ 0	☐ 1	☐ 2	☐ 3
11. Felt depressed/overwhelmed?	☐ 0	☐ 1	☐ 2	☐ 3
12. Had problem taking pills at specified times (with meals, on empty stomach, etc.)?	☐ 0	☐ 1	☐ 2	☐ 3
13. Ran out of pills?	☐ 0	☐ 1	☐ 2	☐ 3
14. Felt good?	☐ 0	☐ 1	☐ 2	☐ 3

Analysis

1. Demographics and adherence barriers at 12 week

2. Bivariate logistic regression: association between each barrier at 12 wks and undetectable HIV RNA at 24 wks and association between total number of barriers and HIV RNA

3. Multivariate logistic regression: association between barriers and undetectable HIV RNA while adjusting for potential confounders

4. Dominance analysis: assess the relative importance of 14 barriers at 12 wks in association with HIV RNA at 24 wks (all possible subsets regression was used to rank importance of each barrier)

Mean age, years (SD)		**39.3 (9.2)**
Male, N (%)		1,275 (85.2)
Race/ethnicity, N (%)		
	White	756 (50.5)
	Black	426 (28.5)
	Latino	264 (17.7)
	Other	50 (3.3)
HIV risk factor, N (%)		
	MSM	798 (61.0)
	Heterosexual	316 (24.1)
	Needle sharing	69 (5.3)
	Transfusion	28 (2.1)
	Other/do not know	98 (7.5)
Treatment naïve, N (%)		792 (52.9)
Mean CD4+ cell count, cells/mL (SD)		402.2 (265.2)
Plasma HIV RNA below limit of quantification, N (%)		694 (46.5)

N= 1,496

Adherence Barriers, N (%)	
Away from home	328 (21.9)
Simply forgot	293 (19.6)
Change in daily routine	292 (19.5)
Fell asleep/slept through dose time	282 (18.9)
Busy with other things	255 (17.1)
Felt sick or ill	186 (12.4)
Problem taking pills at specified time	181 (12.1)
Wanted to avoid side effect	133 (8.9)
Felt depressed/overwhelmed	127 (8.5)
Felt good	111 (7.4)
Not want others to notice you taking medications	105 (7.0)
Felt like the drug was toxic/harmful	82 (5.5)
Too many pills to take	79 (5.3)
Ran out of pills	48 (3.2)

Summed adherence barriers, N (%)	
0 (no ACTG barriers reported)	845 (56.5)
1 (1-4 ACTG barriers reported)	446 (29.8)
2 (≥5 ACTG barriers reported)	205 (13.7)

N= 1,496

Adherence barriers	OR (95% CI)	p-value
Away from home	0.88 (0.68-1.13)	0.32
Busy with other things	0.95 (0.72-1.26)	0.73
Simply forgot	0.99 (0.76-1.30)	0.95
Too many pills to take	0.43 (0.27-0.68)	<0.001
Wanted to avoid side effect	0.54 (0.38-0.77)	0.001
Not want others to notice you taking medications	0.94 (0.62-1.43)	0.77
Change in daily routine	0.82 (0.63-1.07)	0.14
Felt like the drug was toxic/harmful	0.44 (0.28-0.70)	<0.001
Fell asleep/slept through dose time	0.84 (0.64-1.10)	0.20
Felt sick or ill	0.49 (0.36-0.66)	<0.001
Felt depressed/overwhelmed	0.58 (0.40-0.84)	0.004
Problem taking pills at specified time	0.71 (0.52-0.98)	0.04
Ran out of pills	1.26 (0.67-2.37)	0.48
Felt good	0.80 (0.54-1.19)	0.27

N= 1,496

Summed adherence barriers		0.02
1 (1-4 ACTG barriers reported)	0.85 (0.67-1.09)	0.20
2 (≥5 ACTG barriers reported)	0.64 (0.46-0.87)	0.005

Multivariate Analyses

- Significantly associated with lower odds of undetectable HIV RNA
  - **"Felt sick or ill"**: OR=0.53, 95% CI=0.37-0.76, p<0.001
- Marginally associated with lower odds of undetectable HIV RNA controlling for confounders
  - **"Too many pills to take"**: OR=0.59, 95% CI=0.36-0.96, p=0.06
  - **"Felt like drug was toxic/harmful"**: OR=0.61, 95% CI=0.37-1.04, p=0.07

Dominance Analysis

- Relative importance of each barrier in association with virologic detectability:

  1. felt sick or ill
  2. had too many pills to take
  3. felt like the drug was toxic/harmful
  4. wanted to avoid side effects
  5. felt depressed/overwhelmed
  6. ran out of pills
  7. were busy with other things
  8. had problem taking pills at specified times
  9. simply forgot
  10. did not want others to notice you taking medication
  11. felt good
  12. had a change in daily routine
  13. fell asleep/slept through dose time
  14. were away from home

Discussion

- Those with a higher number of barriers had lower odds of virologic suppression

- Individual barriers were reported at low frequency

- Majority of participants did not report any barriers
  - Limited awareness of barriers, social desirability bias, or questionnaire not adequately capturing other important barriers
  - 53% of participants not virologically suppressed at 12 wks and 34% not suppressed at 24 wks, therefore identification and understanding of barriers is critical

Discussion

- Barriers related to ART, e.g., high pill burden or perceived/actual medication adverse effects, and feeling depressed/overwhelmed, significantly associated with virologic detectability

- Despite being some of the least frequently reported barriers, these ranked the highest in their relative importance

- Other frequently reported barriers, such as forgetfulness, were not associated with virologic detectability and were ranked low in relative importance

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Discussion

- Findings challenge notion that the justification for an intervention to overcome an adherence barrier be based on the frequency of reporting that barrier

- This reasoning may result in ineffective interventions and an inefficient allocation of time and financial resources

Limitations

- Secondary analysis of data collected for other purposes and containing missing data

- Self-reported adherence barriers
  - Prone to recall and social desirability bias
  - May not address other barriers not listed in questionnaire

- Study period (1997-2003) prior to the introduction of newer and better tolerated ART; therefore, results may not be fully generalizable to present ART era

Conclusion

- Currently, ART regimens are more potent, require fewer daily pills, and have improved tolerability

- However, lifelong adherence is still a significant concern

- Assessment of adherence barriers and examination of correlation between barriers and plasma HIV RNA for newer regimens should be conducted in order to design and develop interventions that may be better at improving HIV treatment outcomes

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