Are Intervention (vs Control) Arm Participants in ART Adherence-Promotion Interventions More Likely to Overestimate Adherence? *Findings from the MACH14 Study*

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Collaborators

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For MACH14 Investigators

Background

- Typically, intervention arm participants in ART adherence-promotion trials are exhorted to adhere to their prescribed ART regimens, possibly creating demand characteristics that would lead to overestimates of adherence. Subsequently, self-reports of adherence are often considered unacceptable, or not rigorous, in determining intervention efficacy.
- For example, in evaluating adherence interventions for possible dissemination, the CDC relegated outcomes based on self-reported adherence to the category of "good" but not "best" evidence of efficacy, which was reserved for purportedly more objectives assessment methods.

AIMS

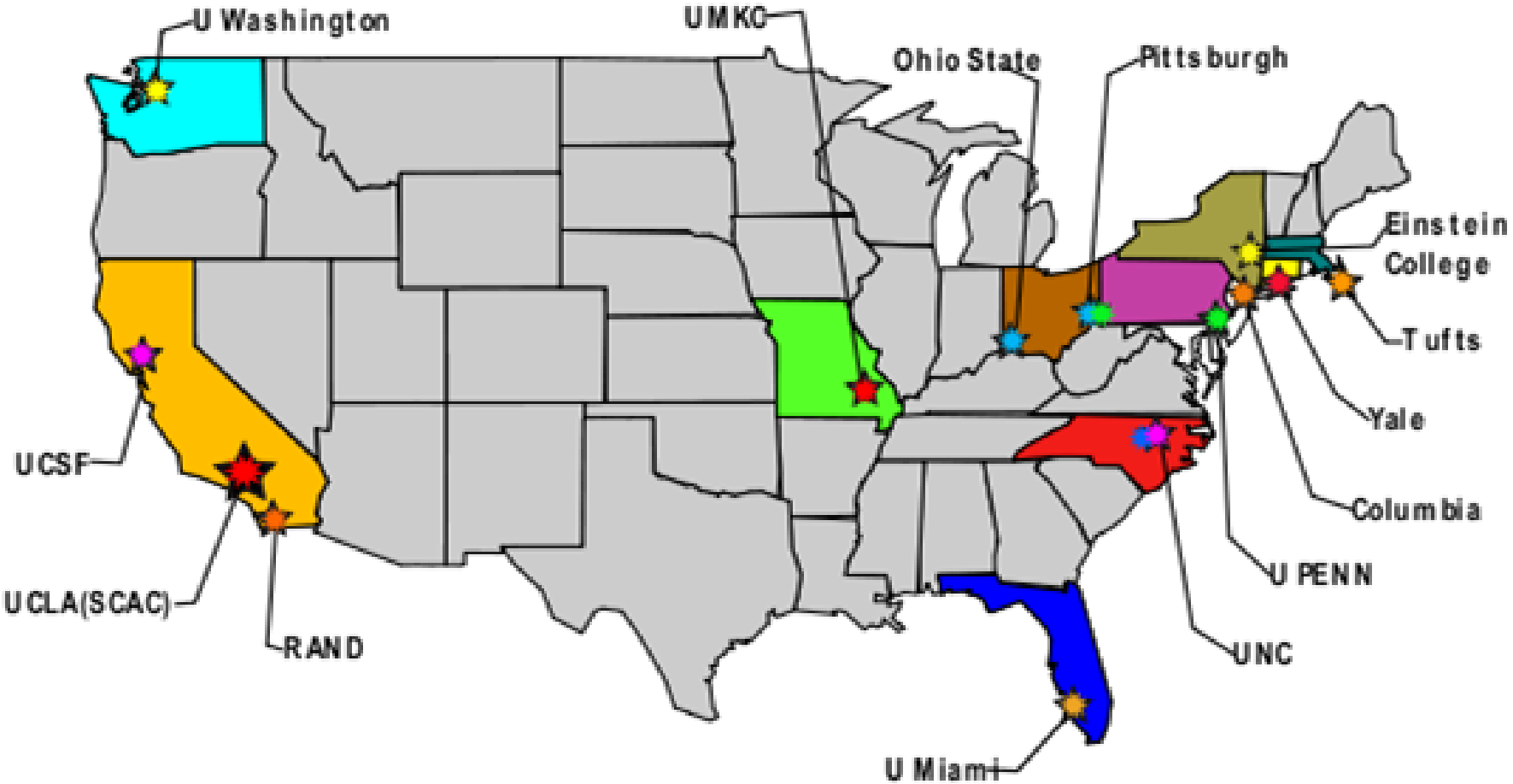
- Determine whether intervention arm assignment (intervention versus control) moderates the association between self-reported adherence and (a) MEMS adherence or (b) VL.

Multi-site Adherence Collaboration in HIV among 14 Institutions (MACH14)

Honghu Liu, PI &
David Bangsberg, Co-PI

NIMH National Institute of Mental Health
Transforming the understanding and treatment of mental illness through research

14 Study Sites



Pooled data from 16 studies with 2817 PLWHA

Principal Investigator	Institute	Study Name	Project Period	Number of Patients	Length of Follow-up
Julia Arnsten	Einstein College of Medicine	HIV Epidemiology Research on Outcomes (HERO Adherence Study)	1998-2004	104	6 months
David Bangsberg	UCSF	Research in Access to Care in the Homeless (REACH)	1997-2002	107	60 months
Judith Erlen	University of Pittsburgh	Adherence to Protease Inhibitors	1998-2003	215	13 months
Judith Erlen	University of Pittsburgh	Improving Adherence to Antiretroviral Therapy	2003-2008	347	19 months
Kathy Goggin	University of Missouri-Kansas City	ART Adherence: Enhanced Counseling and Observed Therapy	2004-2008	162	48 weeks
Robert Gross	University of Pennsylvania	Adherence to Protease Inhibitors in HIV	2005-2006	76	16 weeks
Honghu Liu	UCLA	Adherence and Efficacy of Protease Inhibitor Therapy (ADEPT)	2000-2003	145	48 weeks
Carol Golin	UNC Chapel Hill	Directly Observed Therapy (DOT)	2000-2005	102	48 weeks
Carol Golin	UNC Chapel Hill	Participating And Communicating Together (PACT)	1999-2004	155	12 weeks
Robert Remien	Columbia University & NYSPI	Serodiscordant Couples, Medical Adherence and HIV Risk Couples Study (SMART)	2000-2004	215	32 weeks
Nancy Reynolds	Ohio State University	AIDS Clinical Trail Group (ACTG) 731	1998-2003	109	64 weeks
Marc Rosen	Yale University	Rewards Improve Medication Compliance for HIV Treatment (REWARDS)	2002-2005	97	36 weeks
Neil Scheneiderman	University of Miami	Behavioral Management and Stress Responses in HIV/AIDS	1997-2003	404	18 months
Jane Simoni	University of Washington	Peer and Pager Support to Enhance Antiretroviral Adherence (PAL)	2002-2008	224	9 months
Glenn Wagner	RAND	California Co-operative Treatment Group (CCTG) 578	2000-2002	199	48 weeks
Ira Wilson	Tufts University	Understanding and Improving Adherence in HIV Disease	2001-2003	156	24 months

Key Measures

Self-reported adherence was assessed at immediate post-intervention for the previous 3 days, averaged across medication.

The MEMS adherence estimate for the exact corresponding interval was calculated for each participant.

VL data matching closest to the self-reported adherence date were used.

Measures of Socio-Demographics

- Race/ethnicity
  - Black/African-American
  - Hispanic/Latino
  - White/Caucasian
- Sex
  - Male
  - Female
- Age
  - Continuous, in years
- Study site
  - One of 14 sites
- Education
  - <=8th grade/some HS but did not graduate
  - HS graduate/some college but no degree
  - Completed college/>4 year college degree
- Homosexual Orientation
  - Yes
  - No
- Naïve to ARV medications at baseline
  - Yes
  - No

**All self-reported and assessed at baseline.*

Analytic Approach

Two regression models predicting:

VL and MEMS

Main effects for:

Arm, self-reported adherence

AdhXarm interaction

Models were adjusted for:

Age, sex, race/ethnicity, educ, sexual orientation

Analytic Sample

N = 1711

The analytic sample included the 1711 participants in 9 of the 16 studies who had non-missing data on relevant variables:

- Intervention arm (*n*=1055)
- Control (*n*=656) arm

Sample Characteristics

- Race/ethnicity
  - 49% Black/African-American
  - 11% Hispanic/Latino
  - 30% White/Caucasian
- Sex
  - 70% Male
  - 30% Female
- Age
  - 41.0 (SD=8.3) years
- Study site
  - Nine of 14 sites
- Naïve to ARV at baseline
  - 15% are naïve
- Education
  - 23%
    <=8th grade/some HS but did not graduate
  - 64%
    HS graduate/some college but no degree
  - 13%
    Completed college/>4 year college degree
- Homosexual orientation
  - 42% are homosexual

**All self-reported and assessed at baseline.*

RESULTS

Overall Model for MEMS Adherence Outcome N=709

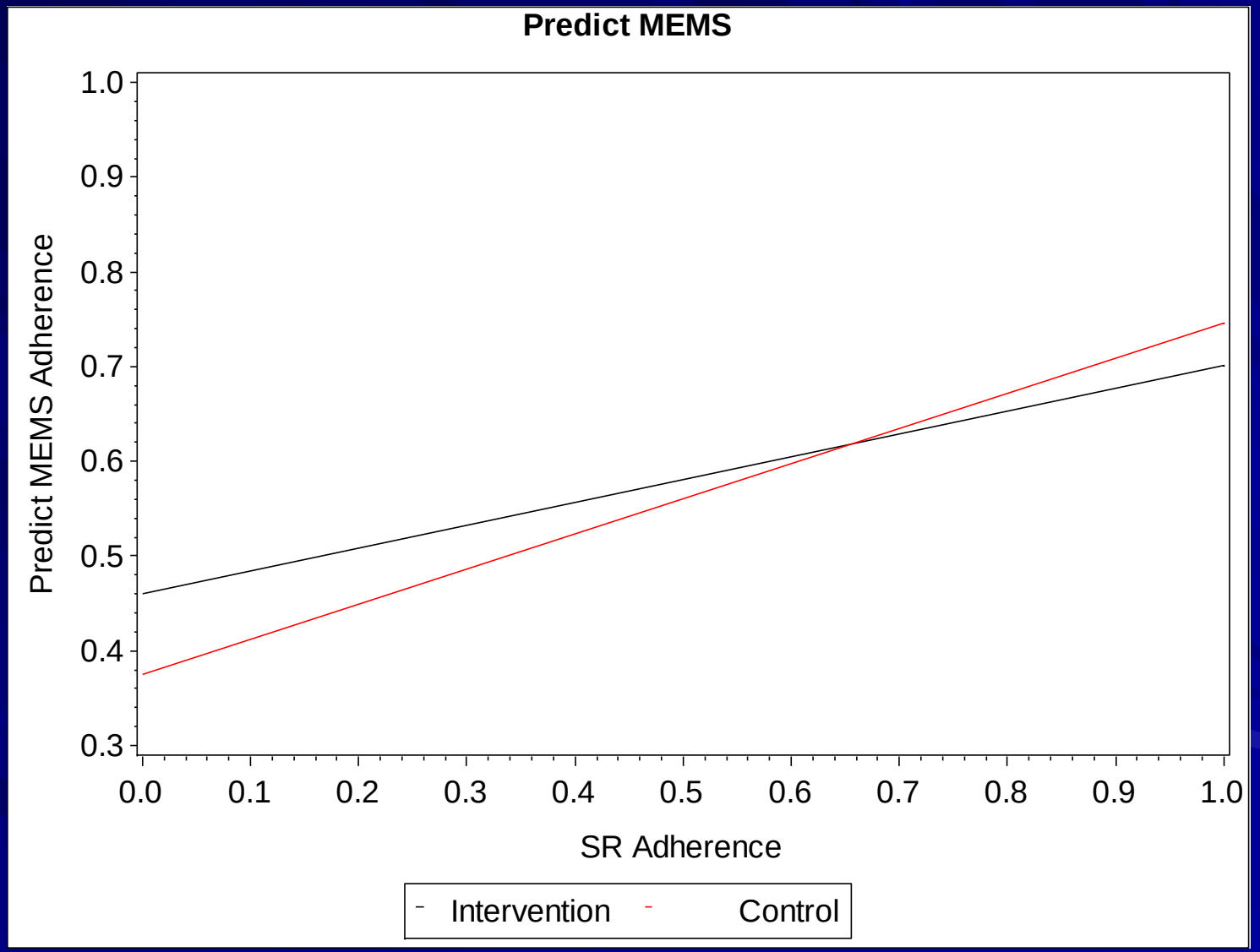
Parameter	Estimate	SD	Pr > |t|
SR3DADH	**0.230**	**0.098**	**0.0192**
Intervention	**-0.083**	**0.126**	**NS**
SR3DADH*intervention	**0.124**	**0.130**	**NS**
Age	0.004	0.002	0.0349
Female	0.023	0.034	NS
African American	-0.035	0.032	NS
Latino	-0.089	0.053	NS
Asian/Other	0.049	0.038	NS
Less than HS	-0.029	0.050	NS
High School	-0.029	0.040	NS
Not naive to ARV	0.037	0.045	NS
Homosexual Orientation	0.054	0.032	NS

Association of SR and MEMS Adherence, by group

- For a 1 percent increase in self-report adherence, MEMS adherence increased by:
  - 0.35% in the intervention group
  - 0.23% in the control group

- This difference was not statistically significant.

Overall Model for MEMS Adherence Outcome



Betas for Associations in Individual Studies

MEMS ADHERENCE

Study	N	SR ADH(SD)	SR X INT(SD)
3	107	0.11 (0.15)	-0.28 (0.20)
4	151	0.03 (0.13)	0.36 (0.26)
6	7	NA	
9	93	**0.46 (0.15)**	0.13 (0.21)
10	22	-0.43 (0.32)	-0.82 (0.70)
11	4	NA	
12	116	0.35 (0.14)	0.11 (0.69)
13	96	0.36 (0.22)	0.20 (0.27)
14	113	Only intervention group	
Total	**709**	**0.23 (0.10)**	**0.12 (0.34)**

Overall Model for VL Outcome N=856

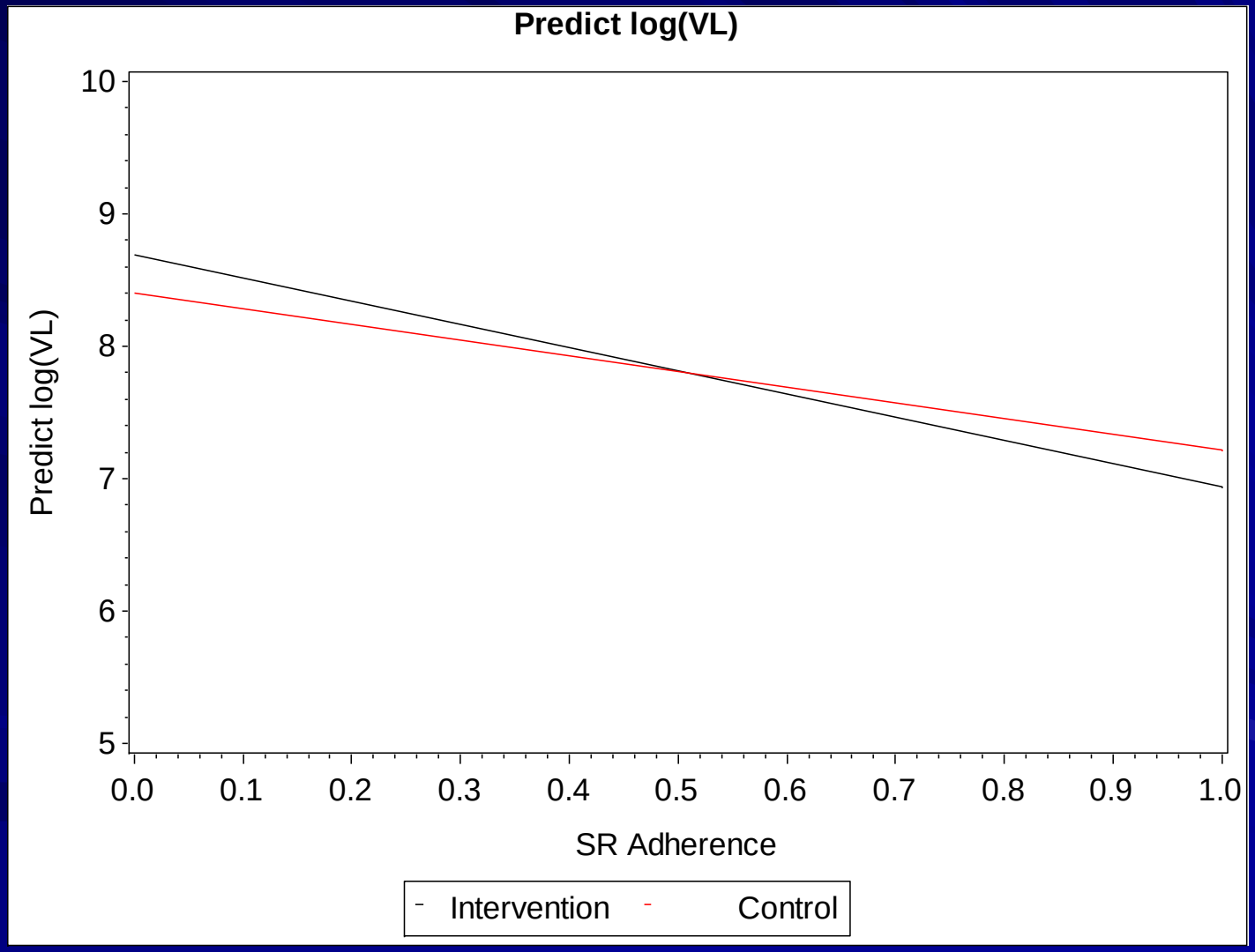
Parameter	Estimate	SD	Pr > |t|
SR3DADH	**-1.526**	**0.577**	**0.0084**
Intervention	**-0.186**	**0.696**	**NS**
SR3DADH*intervention	0.442	0.719	NS
Age	-0.011	0.008	NS
Female	-0.320	0.197	NS
African American	0.337	0.176	NS
Latino	-0.175	0.195	NS
Asian/Other	0.785	0.266	0.0033
Less than HS	0.415	0.249	NS
High School	-0.056	0.183	NS
Not naive to ARV	0.527	0.175	0.0027
Homosexual Orientation	-0.401	0.192	0.0368

Association of SR adherence and VL, by group

- For a 1 percent increase in self-report adherence, viral load decreased by:
  - 1.3% in the intervention group
  - 1.4% in the control group

- This difference was not statistically significant.

Overall Model for VL Outcome



Betas for Associations in Individual Studies

Log VL

Study	N	SR ADH(SD)	SR X INT(SD)
3	105	-0.51 (2.41)	0.49 (2.55)
4	34	3.47 (1.78)	-2.91 (1.61)
6	6	NA	
9	122	-1.15 (1.69)	2.06 (1.89)
10	96	-2.48 (1.51)	2.10 (1.60)
11	7	NA	
12	224	**-2.56 (0.93)**	0.62 (1.19)
13	113	**-2.09 (0.73)**	-0.64 (1.13)
14	149	Only intervention group	
Total	**856**	**-1.53 (0.58)**	**0.44 (0.72)**

Summary

The association between self-reported ART adherence and (a) MEMS adherence as well as (VL) was not moderated by intervention arm assignment in these adherence-promotion trials.

Limitations

- To enhance power, we used the 3-day adherence measure. Results may vary with other measures of self-reported adherence.
- We used linear models, but the associations may be non-linear.
- There was variation in time between self-reported adherence assessment and VL results that was not taken into account in this preliminary analysis.
- We may need to control for additional covariates (e.g., regimen type, dosing schedule).

Discussion

- Findings suggest self-reported adherence in ART adherence promotion intervention trials is not differentially affected by study arm (at least according to the criterion outcomes of MEMS adherence and VL).
- Although self-reported adherence has been shown to inflate adherence estimates relative to more “objective” measures, it apparently is not subject to demand characteristics in intervention arm procedures.
- Self-report may constitute a valid outcome for the purposes of intervention efficacy evaluations.

Thank you!

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For more information or

to join the ART adherence research listserv