Comparing adherence items of missed doses with different timeframes and their associations with viral load in routine clinical care

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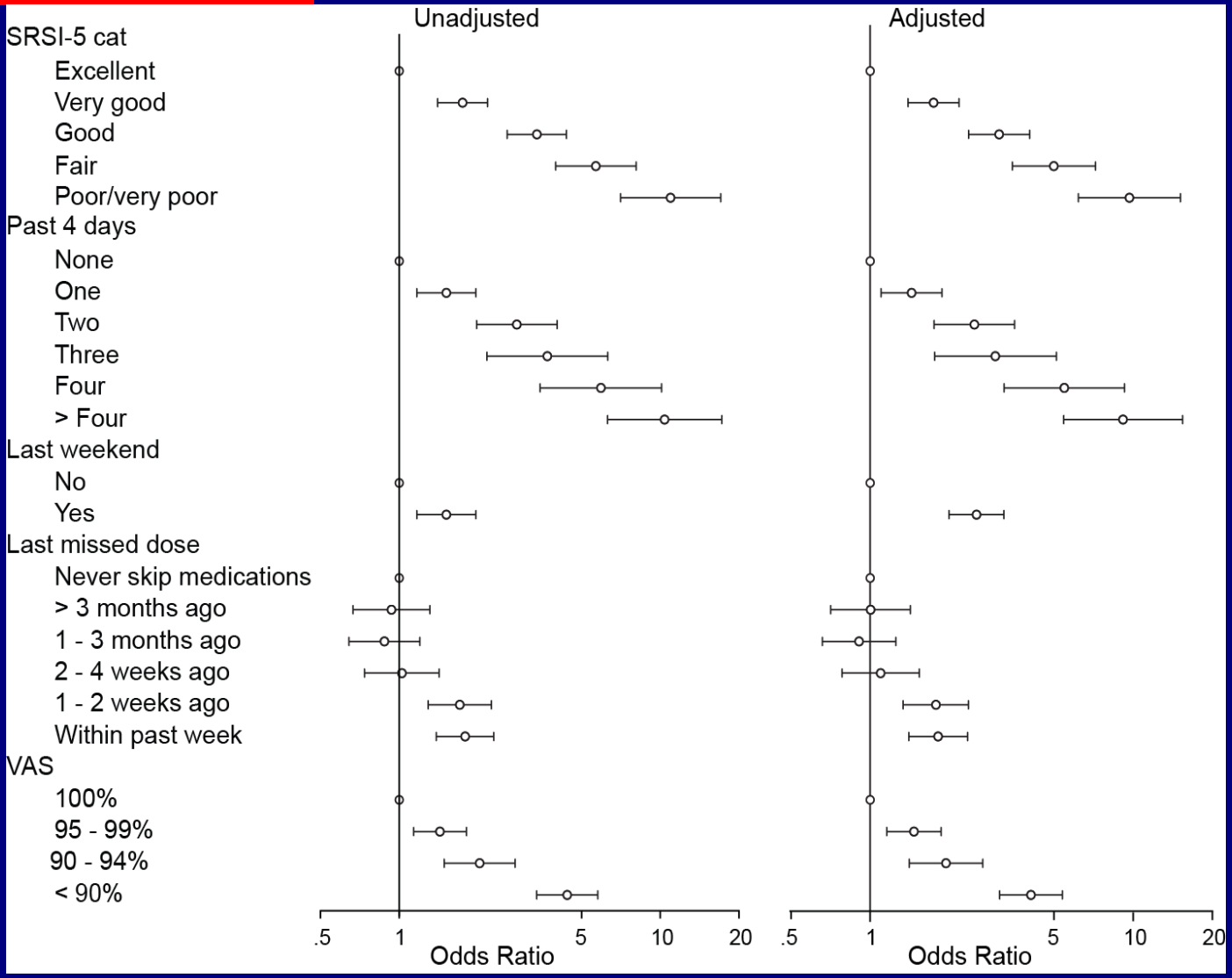
Why do it?

- Patient-reported outcomes (PROs) such as medication adherence integrated into routine clinical can:
  - Enhance patient-provider communication
    - Patients more honest to CASI than they are to a provider, less social desirability bias. More likely to report to CASI poor adherence, substance abuse, depression, risk behavior than to provider (even when provider receives the results). (Provider estimates of adherence consistently unreliable)
  - Improve care
    - Previously presented data from the UW Madison clinic demonstrating that routine integration of the clinical assessment improved provider awareness and/or actions for domains such as adherence, at-risk alcohol use, substance use, and depression but not sexual risk behavior
  - Facilitate clinical research

Even Brief Or Single-Item Adherence Measures Can Be Very Useful



Miss complex patterns of adherence behavior

Goal: more targeted discussion of patient needs, as well as real-time adherence intervention *before* patients suffer virological failure and the potential consequences of ARV resistance mutations

Similar pattern of findings looking at VL or unsafe sex in setting of detectable VL

Missed doses items

- Medication adherence items often ask how many doses have been missed over a specific time period
- Questions remain regarding optimal timeframes for asking about adherence in clinical care settings
- Some very nice data (e.g. Lu et al.,) included several item formats (rating scale, etc.) but did not include direct comparisons of a number of timeframes such as the 14 and 60 day windows using the same missed dose format
- To determine which timeframe is most useful, we compared adherence calculated from 4-, 7-, 14-, 30-, and 60-day missed dose self-report items with VL
- We confirmed these findings in subset sensitivity analyses of patient groups potentially at increased risk for poor adherence including those with depression, at-risk alcohol use, and substance use

Methods

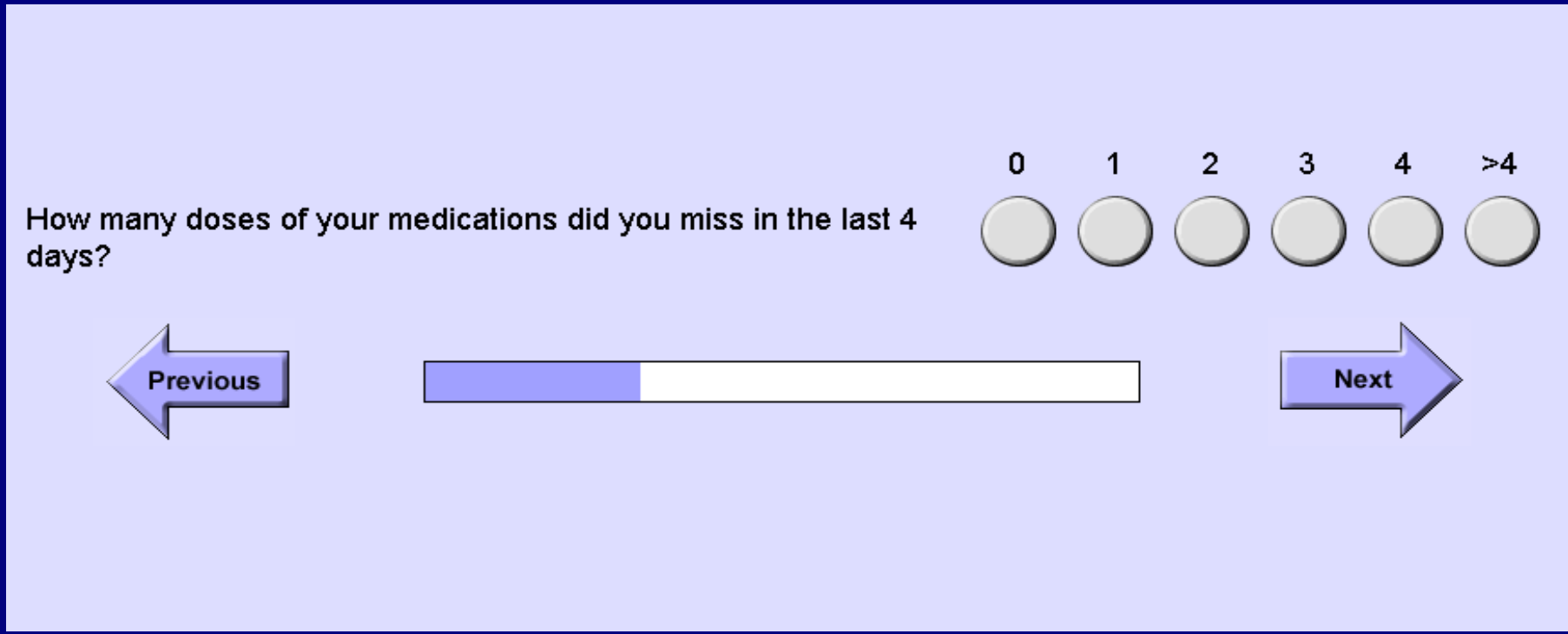
- UW HIV Madison clinic
- 873 individuals on ART
- 4-, 7- 14- 30-, 60-day missed dose items integrated into ongoing clinical PRO assessment
- Correlations between adherence calculated from each timeframe with other timeframes
- Convergent validity as measured by correlations between adherence from each timeframe and VL
- Logistic and linear regression, Baysian model averaging using adherence from different timeframes to predict VL
- VL as outcome as this is what we are truly trying to predict in clinical care (ideally before it occurs)

Instruments

Domain	Instrument
ARV adherence	ACTU-4, VAS, 30-day rating
Depression	PHQ-9 from PRIME-MD
Anxiety	PHQ-4
Alcohol use	AUDIT-C (AUDIT and MINI if at-risk)
Substance use	ASSIST
Health related quality of life	EuroQOL-5D
Symptom burden	HIV Symptoms Index (HIV-SI)
Body morphology	Adapted from FRAM instrument
HIV Risk Behavior	HRAP

Routine clinical care, limited exclusion criteria (only available in English and Spanish, exclude those who appear intoxicated or cognitively impaired). Assessments on tablet PCs with touch screens every 4-6 months, contains between 69 and 127 items depending on responses and skip patterns. Developed and integrated at the UW Madison clinic and have now expanded throughout the CNICS network with >30,000 assessments completed to date among patients as part of clinical care visits.

Assessment



The interface is designed for ease of navigation with questions displayed with large, easy to read type, and clearly labeled radio buttons to indicate responses, no typing to answer questions or navigate, and no keyboard available. No double or ambiguous answers by allowing only one response per question but permits mistakes to be easily corrected.

4, 7, 14, 30, 60 day missed dose items

Item	Mean Adherence (%)	Standard Deviation	Median Adherence	Percentage who missed any dose (%)
4-day	93	18	100	23
7-day	95	12	100	26
14-day	95	12	100	36
30-day	96	7	100	47
60-day	97	5	99	54

Item	4-day	7-day	14-day	30-day	60-day
4-day	1				
7-day	0.79	1			
14-day	0.71	0.88	1		
30-day	0.62	0.81	0.85	1	
60-day	0.49	0.69	0.69	0.88	1

The mean age of study patients was 45 (SD 9) years, 86% were men, and mean current $CD4^+$ cell count was 514 (SD 290) cells/mm^3. 95% were undetectable (VL<40)

4, 7, 14, 30, 60 day missed dose items

	Detectable VL (binary)				Detectable VL (continuous log)			
	All	Patients reporting current substance use	Patients reporting current depression	Patients reporting at-risk alcohol use	All	Patients reporting current substance use	Patients reporting current depression	Patients reporting at-risk alcohol use
Item	Correlation	Correlation	Correlation	Correlation	Correlation	Correlation	Correlation	Correlation
4-day	-0.16	-0.21	-0.29	-0.29	-0.16	-0.19	-0.27	-0.31
7-day	-0.21	-0.17	-0.31	-0.27	-0.20	-0.16	-0.29	-0.28
14-day	-0.25	-0.18	-0.37	-0.26	-0.25	-0.17	-0.34	-0.27
30-day	-0.18	-0.14	-0.24	-0.19	-0.17	-0.14	-0.21	-0.20
60-day	-0.14	0.01	-0.08	-0.06	-0.14	0.01	-0.07	-0.05

Logistic Regression: Outcome is undetectable VL. For all: the 14 day item was significant, and adding the others did not significantly improve the R^2.
Among current substance users and those with at-risk alcohol, the 4-day item had the largest R^2
Linear regression: Outcome VL (log). For all: the 14 and 30 day item were significant and adding the others did not significantly improve the R^2.
Among those with at-risk alcohol use, the 4, 14, and 30 day item all significantly contributed to the R^2.
BMA models: 14 days for all or depressed, 30 days among drug users, shorter windows for those with at-risk alcohol use

Findings

- High rates of adherence among patients in clinical care in the current treatment era reported by all timeframes although likely not surprising given 95% were undetectable. Integrated into clinical care, not part of an adherence study or trial with consequences for patients that would encourage or enhance over-reporting
- Shorter timeframes did not report higher adherence than longer timeframes
- Longer timeframes, particularly increases up to 30 days capture increasing numbers of patients as having missed doses (23% for 4-day vs. 58% for 60-day items)
- Fewer patients reported missed doses with shorter timeframes than longer timeframes (more at ceiling), larger SD, greater impact on adherence for each missed dose
- Adherence from 14 day item largest correlations with VL and highest predictive ability, in some groups also the 30 day item
- Among those with at-risk alcohol use, shorter timeframes had higher correlations or more predictive ability

Strengths and limitations

- Limitations:
  - Only in English and Spanish, 1 site
  - Did not include qualitative work to further define why the patients answered as they did
  - Other item formats may have less numeracy issues
  - Findings may not necessarily apply to timeframes for other types of formats besides missed dose items, prior published data suggest 30 day for self-rating item

- Strengths:
  - Compared timeframes using the exact same item format
  - Collected as part of an existing integrated assessment as part of routine clinical care therefore more generalizable than a study with specific criteria

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