Measuring Retention in HIV Care: The Elusive Gold Standard

Michael Mugavero,[1] Andrew Westfall,[1] Anne Zinski,[1] Jessica Davila,[2] Mari-Lynn Drainoni,[3] Lytt Gardner,[4] Jeanne Keruly,[5] Faye Malitz,[6] Gary Marks,[4] Lisa Metsch,[7] Tracey Wilson,[8] Thomas Giordano,[2] for the Retention in Care (RIC) Study Group*

[1]University of Alabama at Birmingham, [2]Baylor College of Medicine,[3]Boston University Medical Center, [4]Centers for Disease Control and Prevention, [5]Johns Hopkins University, [6]Health Resources and Services Administration, [7]University of Miami, [8]State University of New York, Downstate Medical Center

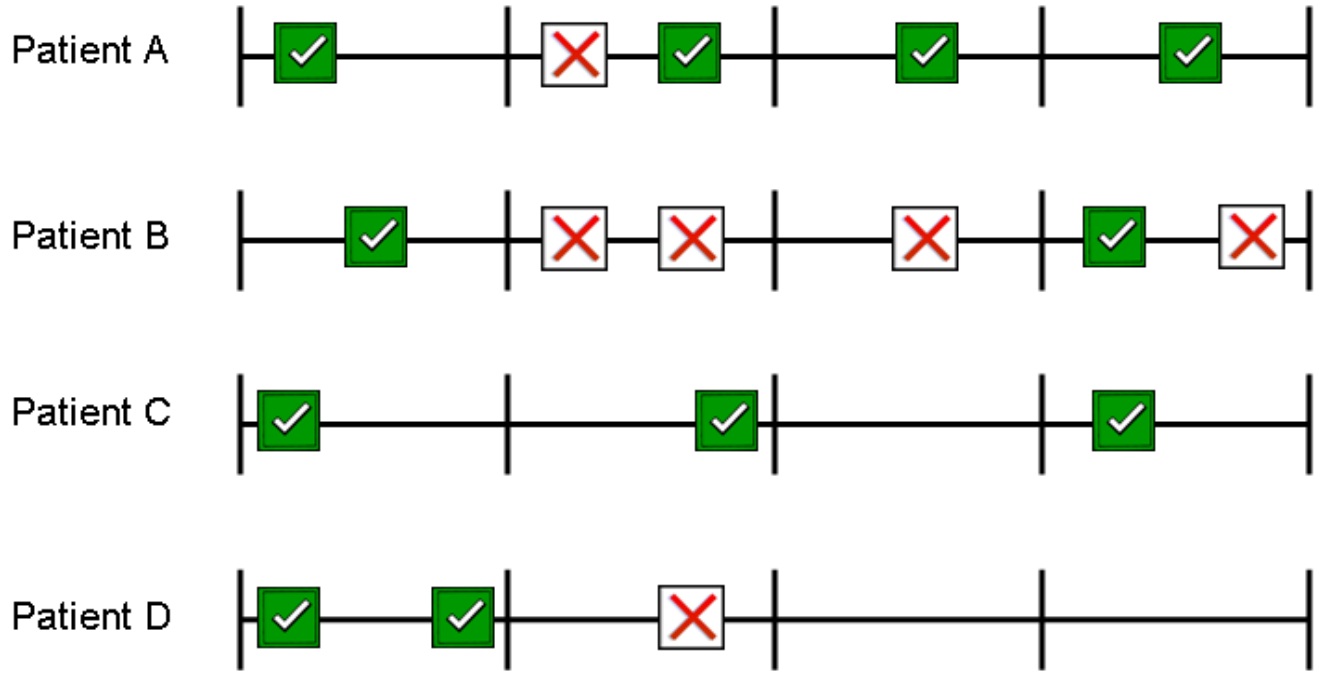
CDC Centers for Disease Control and Prevention

7th International Conference on HIV Treatment and Prevention Adherence

U.S. Department of Health and Human Services HRSA Health Resources and Services Administration

Background

- Measuring retention in care is complex
  - Multiple visits at varying intervals over time
- Numerous retention measures employed
  - Missed visit ("no show") & kept visit measures
  - Each associated w/ biological & clinical outcomes
  - Most studies focus on a single measure
- Degree to which measures are related to one another and to outcomes largely unexplored



	Missed Visits	Appt. Adherence	Visit Constancy	Gap in Care	HRSA HAB Measure
Patient A	Yes; 1	80%	100%	No	Yes
Patient B	Yes; 4	33%	50%	Yes	Yes
Patient C	No; 0	100%	75%	No	Yes
Patient D	Yes; 1	67%	25%	Yes	No

Mugavero, Davila, Nevin & Giordano. *AIDS Pt Care STDs* 2010;24

Methods

- Study aims:
  - Evaluate correlation among 6 retention measures
  - Evaluate prognostic value of measures in predicting plasma viral load (VL) suppression
- Design:
  - Retention in Care (RIC) Intervention Study
    - Six academically-affiliated HIV clinics
    - Phase I (Clinic-wide) & Phase II (Behavioral RCT)
  - Current study: Clinic-wide cohort design during 12 months preceding Phase I RIC intervention

Methods

- Study period: May 2008 – April 2009

- Eligibility criteria:
  - Attended ≥1 primary HIV care appointment in the year preceding study period
  - ≥1 scheduled primary HIV care appointment during 1st six months of study period
  - Criteria employed to identify established clinic patients in whom retention could be measured

Methods

- Principal outcome:
  - VL suppression (<400 c/mL) at end of study period
    - 12-month VL suppression
    - VL nearest 30 April 2009 (± 120 days)

- Principal exposures:
  - Six commonly used retention measures
    - Scheduled visits w/ primary HIV medical provider
    - Calculated based upon kept and no show visits

Methods

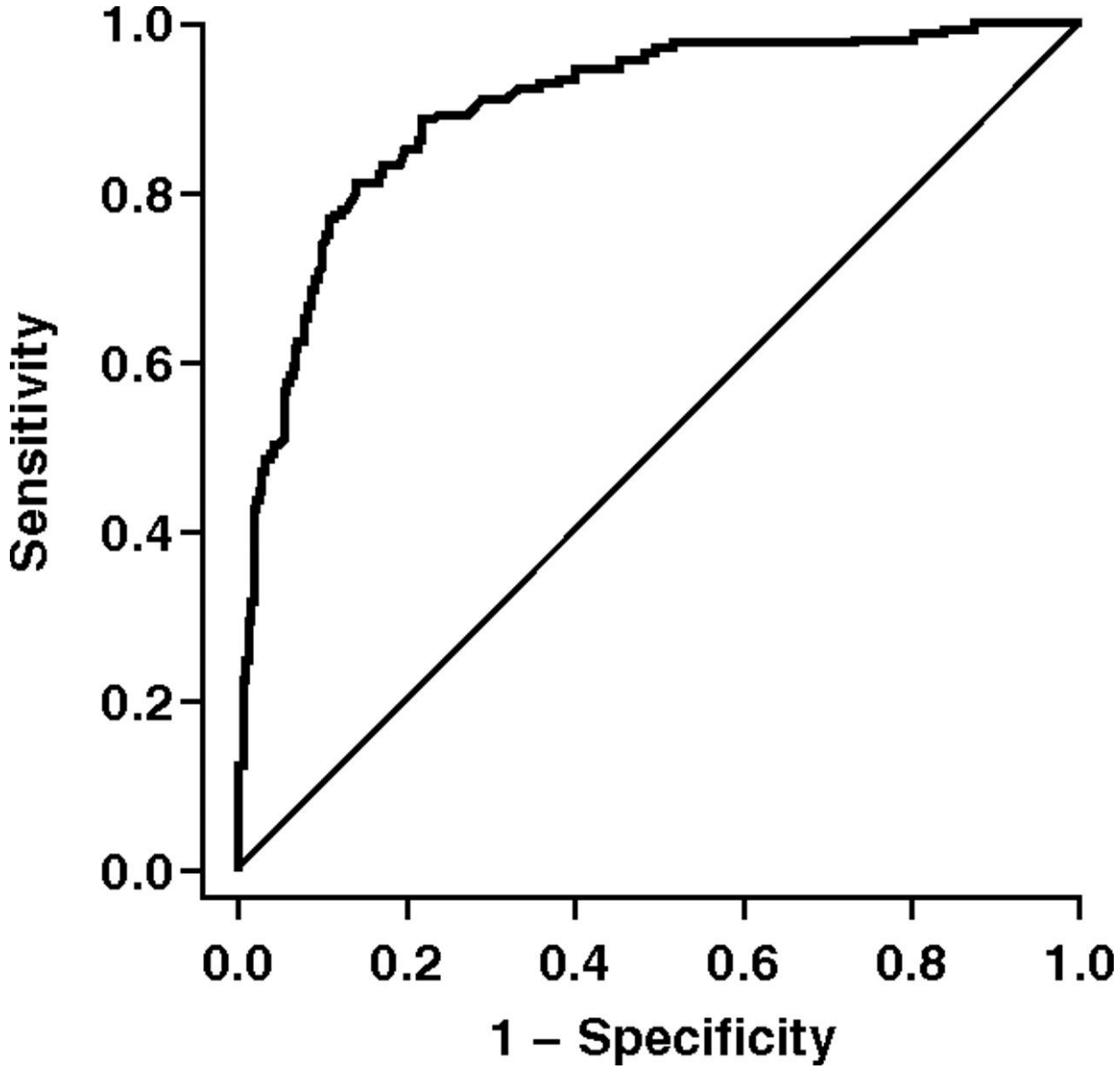
- Statistical analyses:
  - Spearman rank correlation: compare measures
  - Logistic regression for each measure (VL<400 c/mL)
    - C-statistic: discriminatory capacity of measures
      - Prognostic value to assign pts to correct 12-mo VL state
      - Range 0.5 – 1.0 ('coin toss' – perfect discrimination)
      - Estimate of area under ROC curve
  - Primary analyses: pts w/ missing 12-mo VL excluded
  - Sensitivity analyses: pts w/ missing 12-mo VL=failure

Methods: Retention measures

Measure	Description
Missed visits: count	Number of “no show” visits accrued (count measure)
Missed visits: dichotomous	≥1 “no show” visit (dichotomous measure, ‘no’ = retained)
Visit adherence	Proportion of kept visits / (kept + “no-show” visits) (continuous measure, range=0.0-1.0)

Methods: Retention measures

Measure	Description
Missed visits: count	Number of “no show” visits accrued (count measure)
Missed visits: dichotomous	≥1 “no show” visit (dichotomous measure, ‘no’ = retained)
Visit adherence	Proportion of kept visits / (kept + “no-show” visits) (continuous measure, range=0.0-1.0)
4-month constancy	Number of 4-month intervals with at least 1 kept visit (categorical measure, range=0-3)
6-month gap	≥189 days elapsed between sequential kept visits (dichotomous measure, ‘no’ = retained)
HRSA HAB	2 kept visits separated by ≥90 days (dichotomous measure, ‘yes’ = retained)


1.0
0.8
0.6
0.4
0.2
0.0
Sensitivity
0.0
0.2
0.4
0.6
0.8
1.0
1 – Specificity

Baseline characteristics (n=10,053)

Age (years)	46.0 ± 10.0
Gender	
Male	6549 (65.1%)
Female	3465 (34.5%)
Transgender	39 (0.4%)
Race	
Black	6435 (64.0%)
White	3004 (29.9%)
Other/Unknown	614 (6.1%)
Ethnicity	
Hispanic	1880 (18.7%)
Non-Hispanic	8066 (80.2%)
Missing/Unknown	107 (1.1%)
Risk transmission group	
MSM	2837 (28.2%)
MSM + IDU	230 (2.3%)
IDU	1318 (13.1%)
Heterosexual	4947 (49.2%)
Other/Missing/Unknown	721 (7.2%)

Data presented as mean ± standard deviation or n (%)

Baseline characteristics (n=10,053)

Site	
Baylor College of Medicine	2904 (28.9%)
Boston University Medical Center	1053 (10.5%)
Johns Hopkins University	1883 (18.7%)
SUNY Downstate Medical Center	922 (9.2%)
University of Alabama at Birmingham	1307 (13.0%)
University of Miami	1984 (19.7%)
Baseline plasma HIV RNA (log_{10} c/mL)	2.59 ± 1.17
Baseline CD4+ T lymphocyte count (cells/μL)	456 ± 296

Data presented as mean ± standard deviation or n (%)

"No show" visits (range=0-14)	1.5 ± 1.7
Zero	3327 (33.1%)
One	2895 (28.8%)
Two	1730 (17.2%)
≥ Three	2101 (20.9%)
Visit adherence	0.69 ± 0.30
0-24%	837 (8.4%)
25-50%	1103 (11.1%)
50-74%	2835 (28.4%)
75-99%	1951 (19.6%)
100%	3244 (32.5%)
4-month visit constancy (intervals with ≥ 1 kept visit)	
Zero	760 (7.6%)
One	1448 (14.4%)
Two	2768 (27.5%)
Three	5077 (50.5%)
6-month gap (≥ 189 days between sequential kept visits)	
No (Retained)	6805 (67.7%)
Yes (Not retained)	3248 (32.3%)
HRSA HAB measure (2 kept visits >90 days apart)	
Retained	7761 (77.2%)
Not retained	2292 (22.8%)
12-month plasma HIV RNA	
≤ 400 copies/mL	6304 (62.7%)
> 400 copies/mL	1931 (19.2%)
Missing	1818 (18.1%)

Data presented as mean ± standard deviation or n (%)

Spearman rank correlation matrix

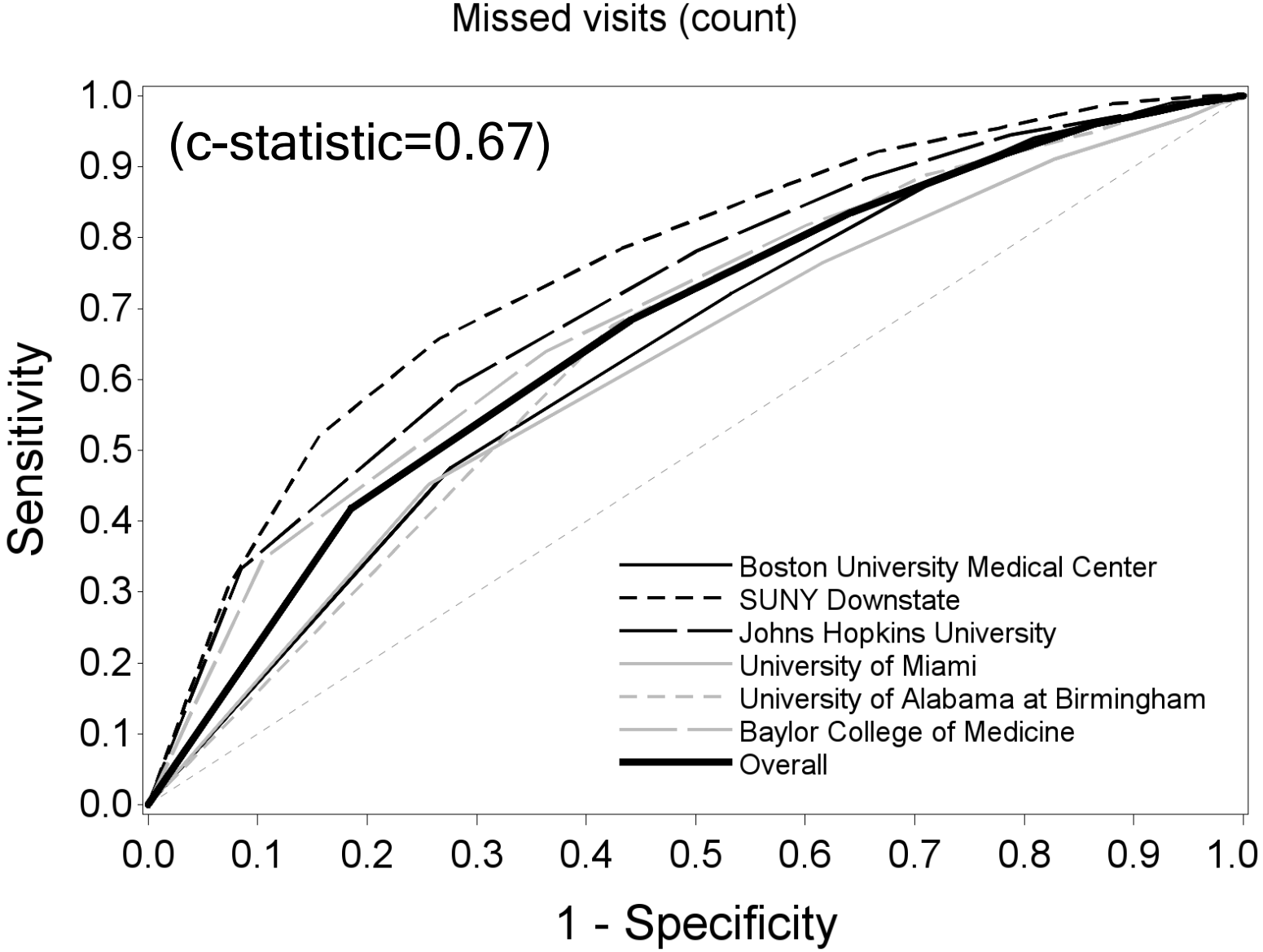
	Missed visits (count)	Missed visits (dichotomous)	Visit adherence	4-month constancy	6-month gap	HRSA HAB measure
Missed visits (count, range=1-14)	1					
Missed visits (dichotomous)	0.84	1				
Visit adherence (continuous, range=0.0-1.0)	0.85	0.83	1			
4-month constancy (categorical, range=0-3)	0.21	0.26	0.57	1		
6-month gap (dichotomous)	0.20	0.25	0.51	0.76	1	
HRSA HAB measure (dichotomous)	0.16	0.22	0.53	0.77	0.72	1

Association of retention measures with 12-month VL suppression (<400 c/mL)

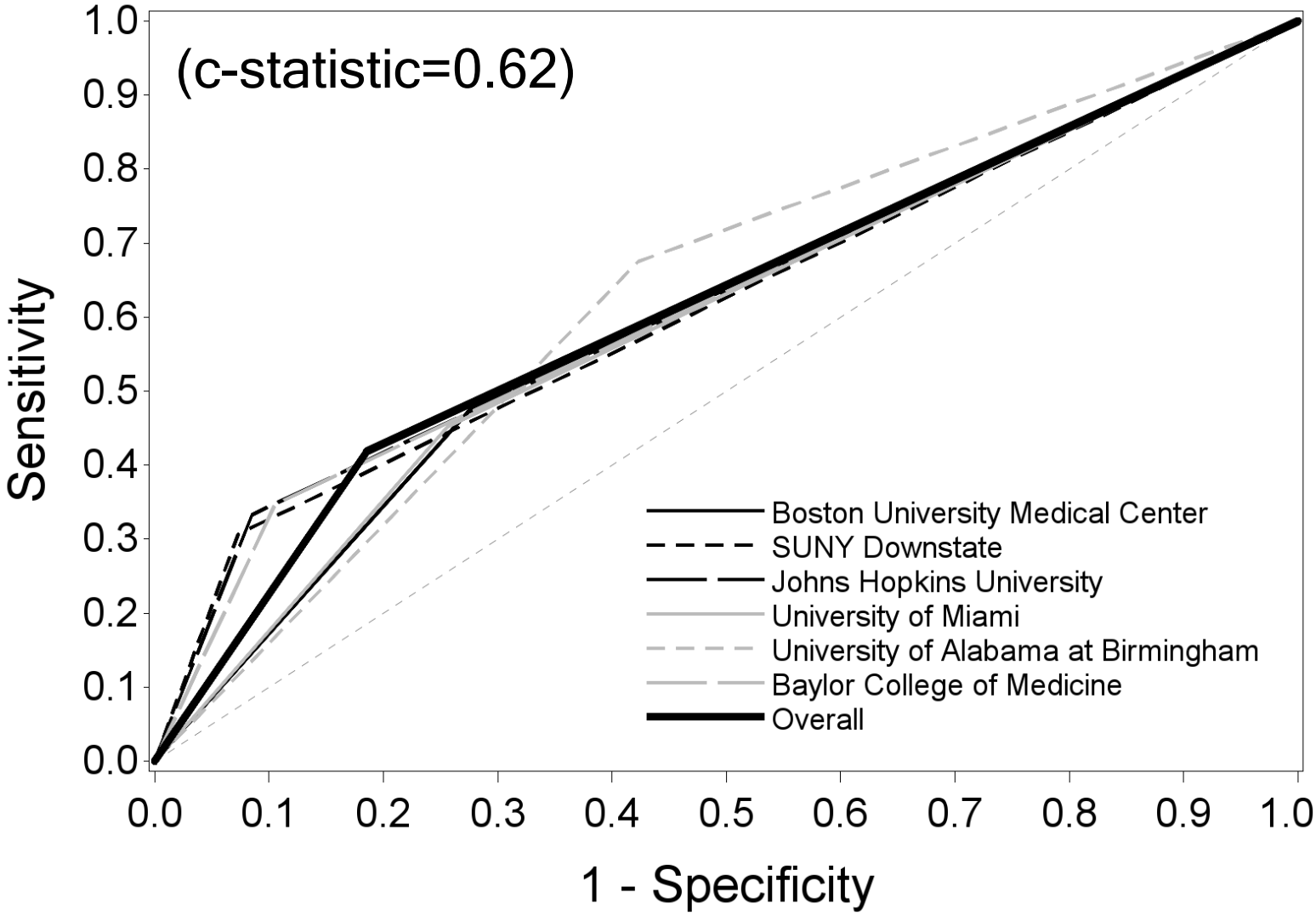
	Odds Ratio [a]	95%CI	C-statistic	Sn [b]	Sp [b]
Missed visits (count)	0.73	0.71-0.75	0.67	68.4%	55.9%
Missed visits (dichotomous)	3.16	2.79-3.59	0.62	41.9%	81.5%
Visit adherence	3.87	3.49-4.29	0.69	68.1%	61.4%
4-month visit constancy	2.77	2.52-3.05	0.63	64.6%	57.9%
6-month gap	2.96	2.65-3.31	0.61	82.0%	39.4%
HRSA HAB measure	3.81	3.33-4.35	0.59	91.2%	26.8%

[a] OR presented per missed visit (count), per 0.5 increase for visit adherence & 4-month constancy, and "retained" for dichotomous retention measures: missed visits, 6-month gap, and HRSA HAB measure

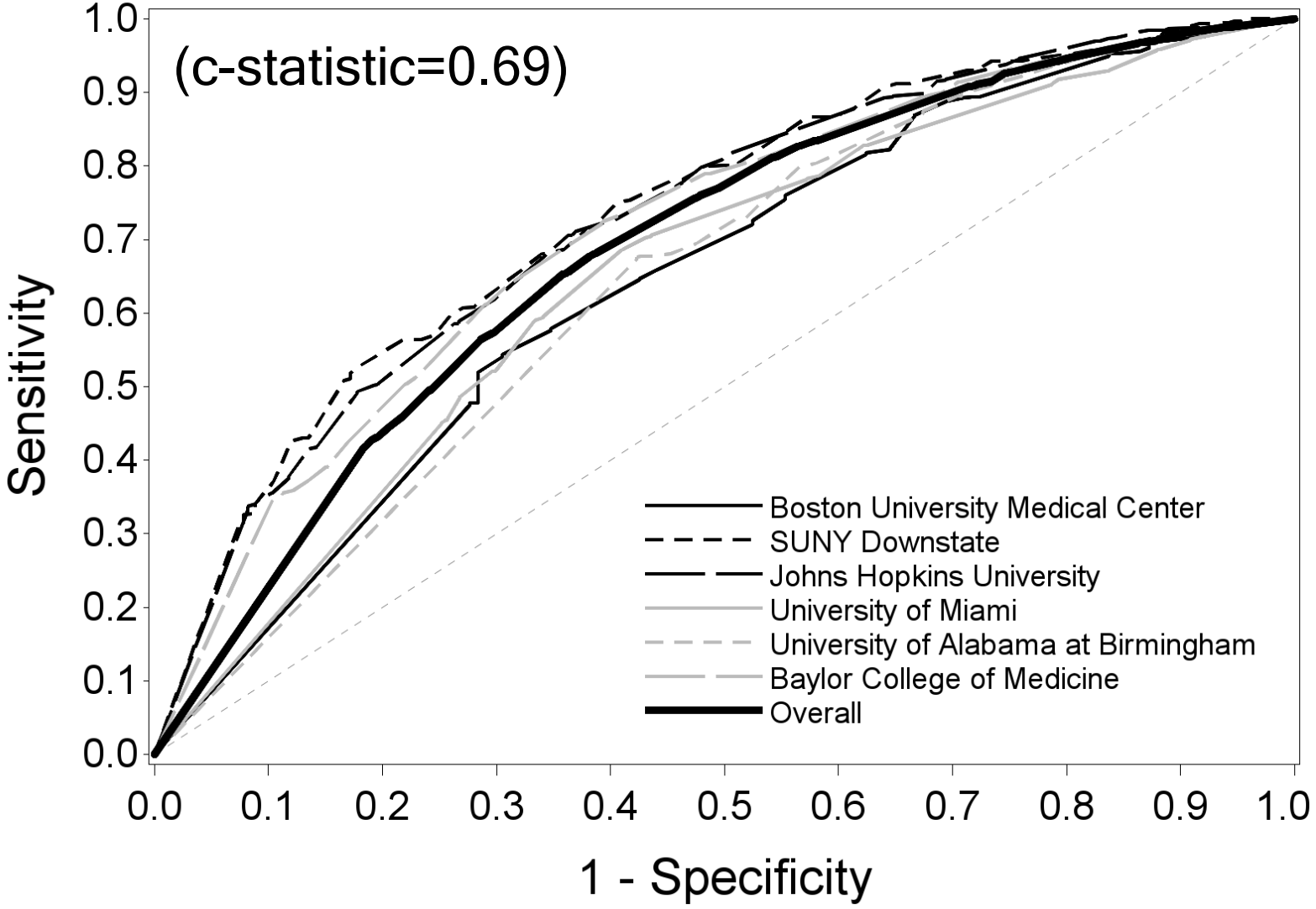
[b] Sn and Sp for cut-points for "retained" of: ≤ 1 missed visits (count), ≥ 70% visit adherence, and attended visits in all 3 intervals for 4-month constancy, and per "retained" for dichotomous measures


Missed visits (count)
(c-statistic=0.67)
Sensitivity
1 - Specificity
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
Boston University Medical Center
SUNY Downstate
Johns Hopkins University
University of Miami
University of Alabama at Birmingham
Baylor College of Medicine
Overall

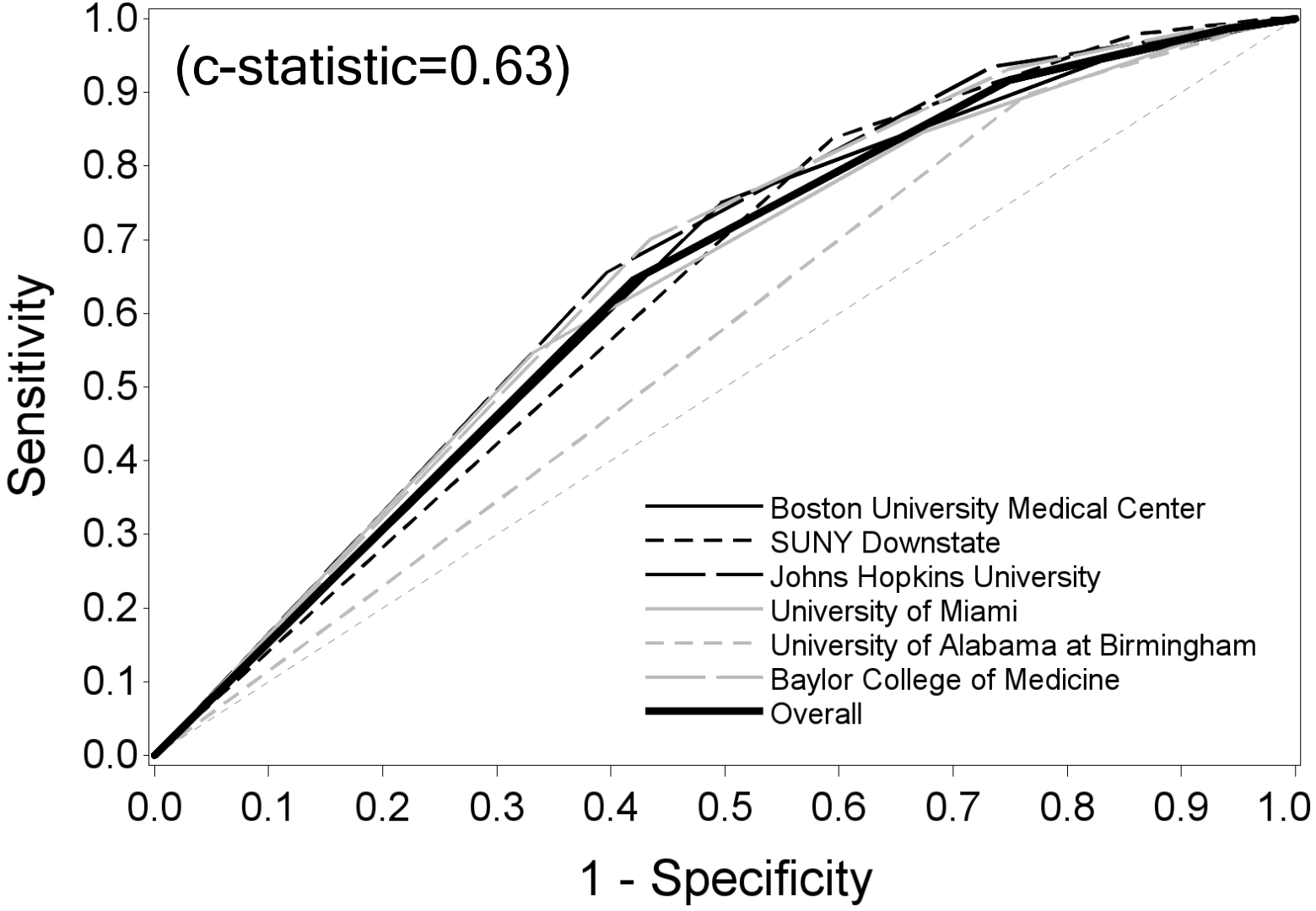
Missed visits (dichotomous)

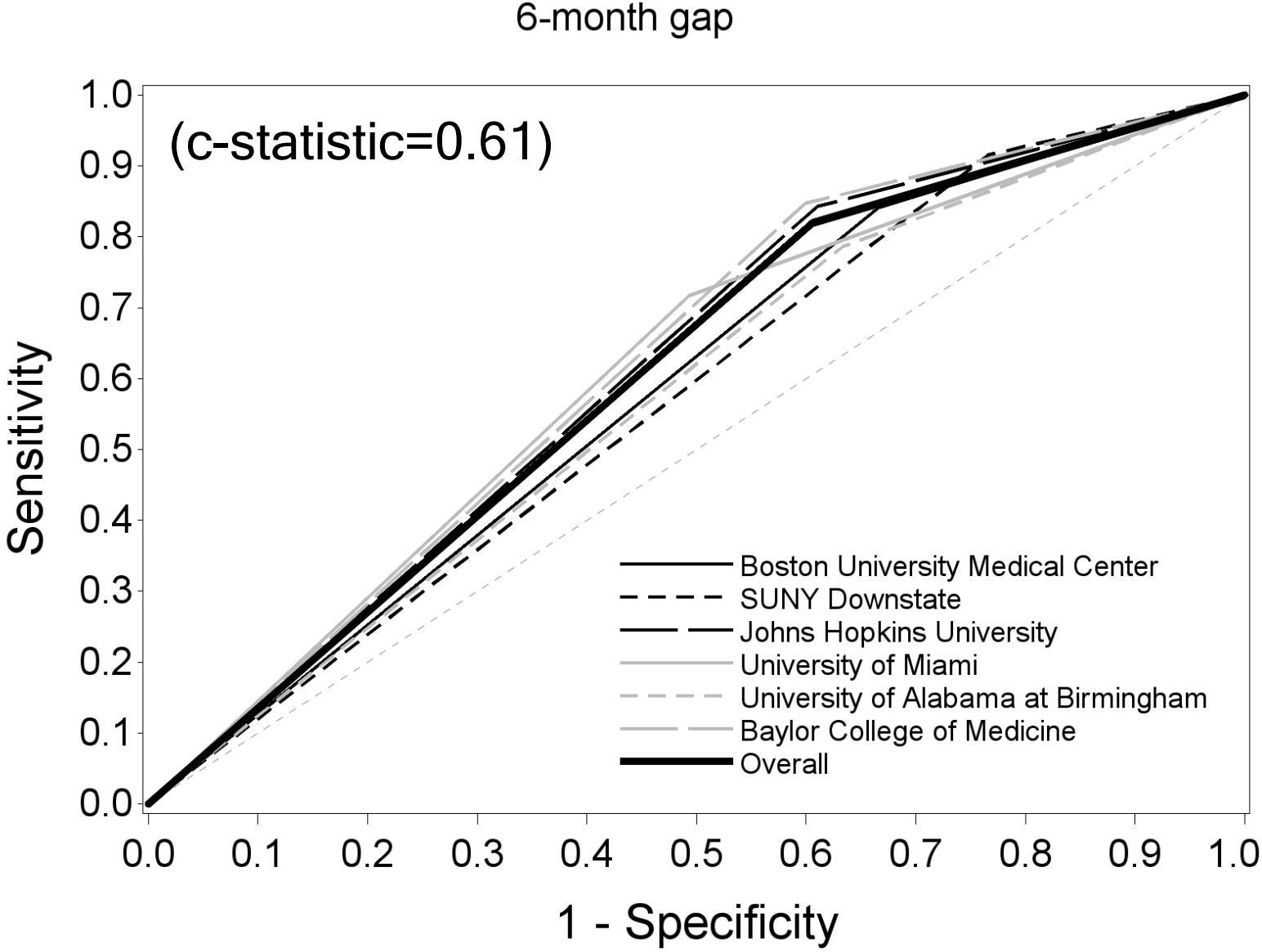


Visit adherence

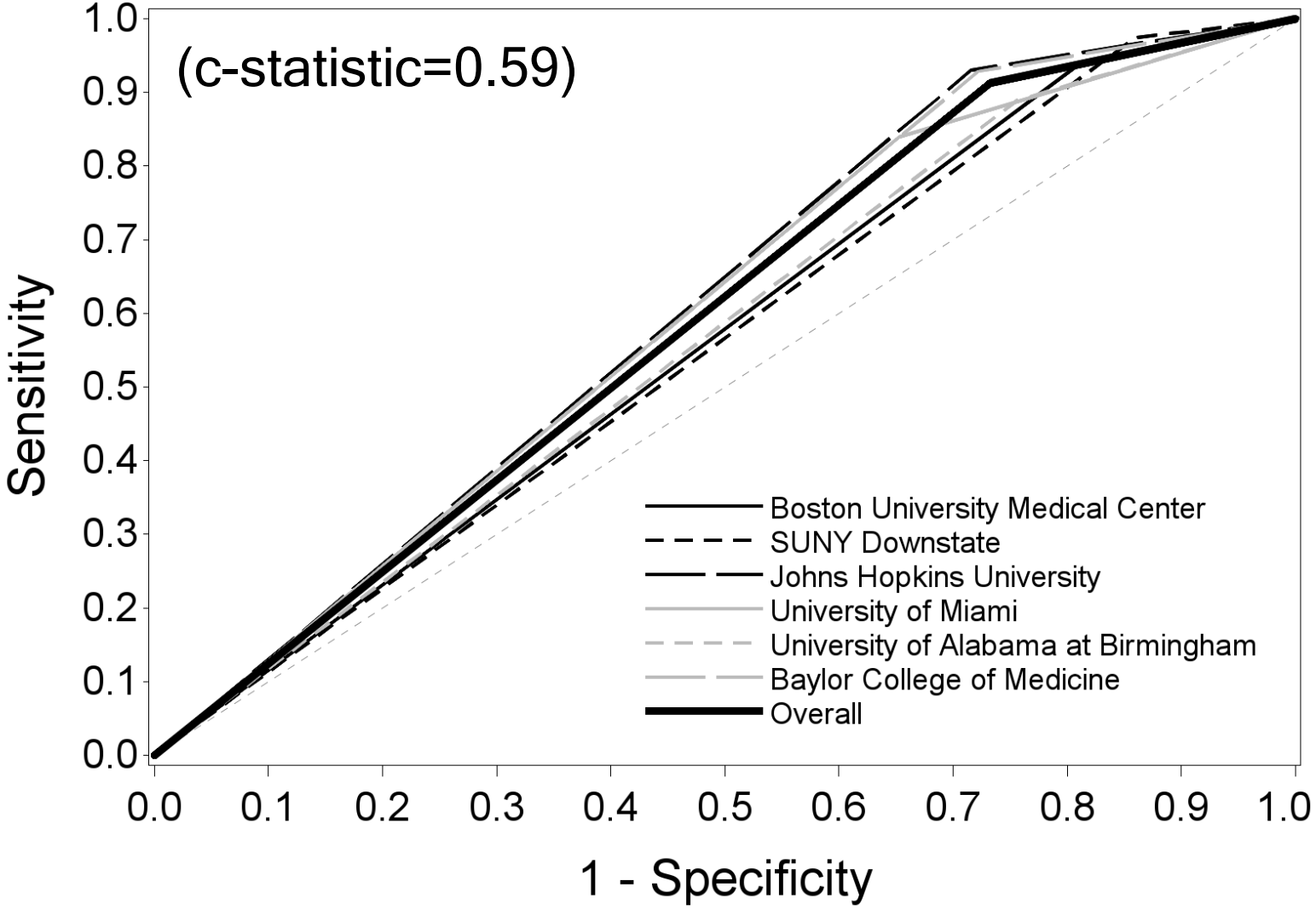


4-month visit constancy




6-month gap
(c-statistic=0.61)
Sensitivity
1 - Specificity
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
Boston University Medical Center
SUNY Downstate
Johns Hopkins University
University of Miami
University of Alabama at Birmingham
Baylor College of Medicine
Overall

HRSA HAB measure



Sensitivity analyses (M=F)
12-month VL suppression (<400 c/mL)

	Odds Ratio [a]	95%CI	C-statistic
Missed visits (count)	0.77	0.75-0.79	0.64
Missed visits (dichotomous)	3.20	2.91-3.53	0.62
Visit adherence (continuous)	5.13	4.72-5.58	0.73
4-month visit constancy	5.35	4.94-5.79	0.74
6-month gap	5.88	5.37-6.44	0.69
HRSA HAB measure	9.02	8.10-10.06	0.69

[a] OR presented per missed visit (count), per 0.5 increase for visit adherence & 4-month constancy, and "retained" for dichotomous retention measures: missed visits, 6-month gap, and HRSA HAB measure

Conclusions

- Considerable variability among six measures in categorizing “retention”
- Wide range of correlation across measures
  - Missed visit measures highly correlated (0.72-0.77)
  - Kept visit measures highly correlated (0.83-0.85)
  - Correlation lower across these two groups (0.16-0.57)
- All six measures had significant association ($P<0.001$) with 12-month VL suppression

Limitations

- Observational study: cannot ascribe causality
- Exclusion of patients new to care
- ART exposure not systematically captured during 12-month study period
- Relatively short observation period
- Modest discriminatory capacity of measures
  - ➢ Augmented by ART receipt & adherence?

The Elusive Gold Standard

Future Perspectives for HIV Adherence Assessment and Intervention

Margaret A. Chesney, PhD

Summary: There is no "gold standard" for the assessment of adherence to HIV/AIDS medications. Similarly, there is no single optimal tool that enhances adherence to HIV/AIDS treatment regimens. This article presents a model that provides a heuristic for selecting adherence assessment approaches and intervention strategies based on the purpose for which each is to be used. First, a broad distinction is made between research and clinical settings. Second, with each of these settings, the selection of assessments and interventions is based on the extent to which the focus is on HIV/AIDS in general or on adherence in particular. Examples applying the model are provided. Finally, new dimensions are discussed for expanding the model, with particular attention to applying the model to the resource-limited settings that are so important in efforts to reduce the morbidity and mortality associated with the global threat of HIV/AIDS.

Key Words: HIV, adherence, AIDS

(*J Acquir Immune Defic Syndr* 2006;43:S149–S155)

Implications

- No clear gold standard to measure ‘retention’
- Each measure may have value and utility according to setting and circumstance
- Merit in using a missed and a kept visit based measure in research settings
- Measures capturing different constructs?
  - Missed visit based → “Adherence”
  - Kept visit based → “Persistence”

Acknowledgments

Boston University Medical Center
Mari-Lynn Drainoni (PI)
Cintia Ferreira
Lisa Koppelman
Maya McDoom
Michal Naisteter
Karina Osella
Glory Ruiz
Paul Skolnik
Meg Sullivan (PI)

SUNY Downstate Medical Center
Sophia Gibbs-Cohen
Elana Desrivieres
Mayange Frederick
Kevin Gravesande
Susan Holman
Harry Johnson
Tonya Taylor
Tracey Wilson (PI)

University of Alabama-Birmingham
Scott Batey
Stephanie Gaskin
Michael Mugavero (PI)
Jill Murphree
Jim Raper
Michael Saag (PI)
Suneetha Thogaripally
James Willig
Anne Zinski

Baylor College of Medicine
Monisha Arya
David Bartholomew
Tawanna Biggs
Hina Budhwani
Jessica Davila
Christine Jacobsen
Tom Giordano (PI)
Nancy Miertschin
Shapelle Payne
William Slaughter

Johns Hopkins University
Mollie Jenckes
Jeanne Keruly (PI)
Angie McCray
Mary McGann
Richard Moore (PI)
Melissa Otterbein
LiMing Zhou

University of Miami
Carolyn Garzon
Jesline Jean-Simon
Kathy Mercogliano
Lisa Metsch (PI)
Allan Rodriguez (PI)
Gilbert Saint-Jean
Marvin Shika

Mountain Plains AETC
Lucy Bradley-Springer
Marla Corwin

Federal
Laura Cheever, HRSA
Faye Malitz, HRSA
Robert Mills, HRSA
Jason Craw, CDC/ICF
Lytt Gardner, CDC
Sonali Girde, CDC/ICF
Gary Marks, CDC

We thank the study participants, providers, clinical and research personnel at the six study sites as well as the CDC and HRSA administrative and data management teams.

Supported by CDC & HRSA via CDC contracts: 200-2007-23685, 200-2007-23690, 200-2007-23689, 200-2007-23687, 200-2007-23684, 200-2007-23692. MJM supported by 5K23MH082641-05

Questions?