Determinants of Adherence to Antiretroviral Therapy differ between Africa and Asia

Rimke Bijker [1] Awachana Jiamsakul [2] Margaret Siwale [3] Sasisopin Kiertiburanakul [4] Cissy Kityo [5] Praphan Phanuphak [6] Tobias F Rinke de Wit [1] Oon Tek Ng [7] Raph L Hamers [1] PASER-TASER Cohort Collaboration

[1] Amsterdam Institute for Global Health and Development Academic Medical Center Amsterdam The Netherlands [2] The Kirby Institute Sydney Australia [3] Lusaka Trust Hospital Lusaka Zambia [4] Ramathibodi Hospital Mahidol University Bangkok Thailand [5] Joint Clinical Research Centre Kampala Uganda [6] HIV-NAT/Thai Red Cross AIDS Research Centre Bangkok Thailand [7] Tan Tock Seng Hospital Singapore

Corresponding author: Rimke Bijker *rimkebijker@hotmail.com*
Website: *aighd.org/projects/paser/*

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Background

- Adherence to antiretroviral therapy (ART) has been poorly studied among HIV-infected populations in resource-limited settings.
- We studied determinants of adherence in the Sub-Saharan African and Asia-Pacific regions.

Methodology

- In a cohort collaboration in Africa (6 countries, 13 sites) and Asia (5 countries, 11 sites) adherence was assessed using the WHO-validated Adherence Visual Analogue Scale (VAS) at each clinic visit, during the first 24 months of 1st-line ART.
- The main outcome was suboptimal mean adherence (SubAdh), defined as mean VAS<95% for each 6-month period. We used generalized estimating equations multivariable regression, adjusting for number of adherence assessments, site type and calendar year.
- Because region-of-residence showed significant interaction with a substantial number of independent variables at the 10% level, all analyses were performed with separate models for Africa and Asia.
- The association between suboptimal adherence and virological treatment failure was assessed using Chi-square test.
- Additional analyses studied:
  - 36 months follow-up data (available for 15 of 24 ART sites).
  - The effect of individual antiretroviral drugs (in participants receiving an NNRTI-based regimen).
  - The effect of country income status (without stratification by region). Site characteristics possibly related to site resourcing (number of assessments, site type and sector) were removed from the model.

Results

Figure 1 & Table 1

- In the first 24 months of follow-up, 23,074 VAS assessments were performed in 3,913 participants; median per participant was 7 (IQR 6-8) in Africa (n=2,409) and 8 (IQR 5-9) in Asia (n=1,504).

Figure 2

- Of 12,889 mean adherence scores, 6.5% (832/12,889) were classified as SubAdh, with 7.3% (614/8,398) in Africa versus 4.9% (218/4491) in Asia (Chi2, p<0.001).

Table 2

- In Africa (but not in Asia), factors associated with SubAdh were male sex (OR 1.4, 95%CI 1.1-1.6) and any concomitant medication (1.9, 1.2-3.1); attending a non-government facility (0.7, 0.5-0.9) and older age were associated with less SubAdh. In Asia, relative to heterosexuals, SubAdh was lower in men who have sex with men (0.5, 0.3-0.9) and higher in injecting drug users (3.5, 2.1-5.8). In both regions, longer ART duration was associated with better adherence.
- A sensitivity analysis that accounted for attrition, using last observation carried forward methods, suggested that adherence improvement with ART duration was not entirely due to attrition bias or missing data.
- SubAdh was strongly associated with virological failure (≥400 c/mL) at month 12 and 24 (Chi2, p<0.001).
- The additional analyses showed that:
  - The protective effect of longer ART duration extended to at least 36 months (n=2361)
  - Type of ART regimen was not associated with SubAdh (n=3771).
  - Participants from high or upper-middle income countries had a 24% (95%CI 7-38%) reduced risk of SubAdh, compared to low or lower-middle income countries (p=0.007).

conclusions

- **Cross-regional di erences may be partly related to health system resources, although social desirability bias cannot be excluded.**
- **Interventions to improve adherence need to be locally tailored and should particularly target the rst ART years.**

Figure 1a PASER sites

Africa *Participants (n=2409): Zambia (21%) South Africa (23%) Uganda (24%) Kenya (17%) Zimbabwe (8%) Nigeria (7%)*

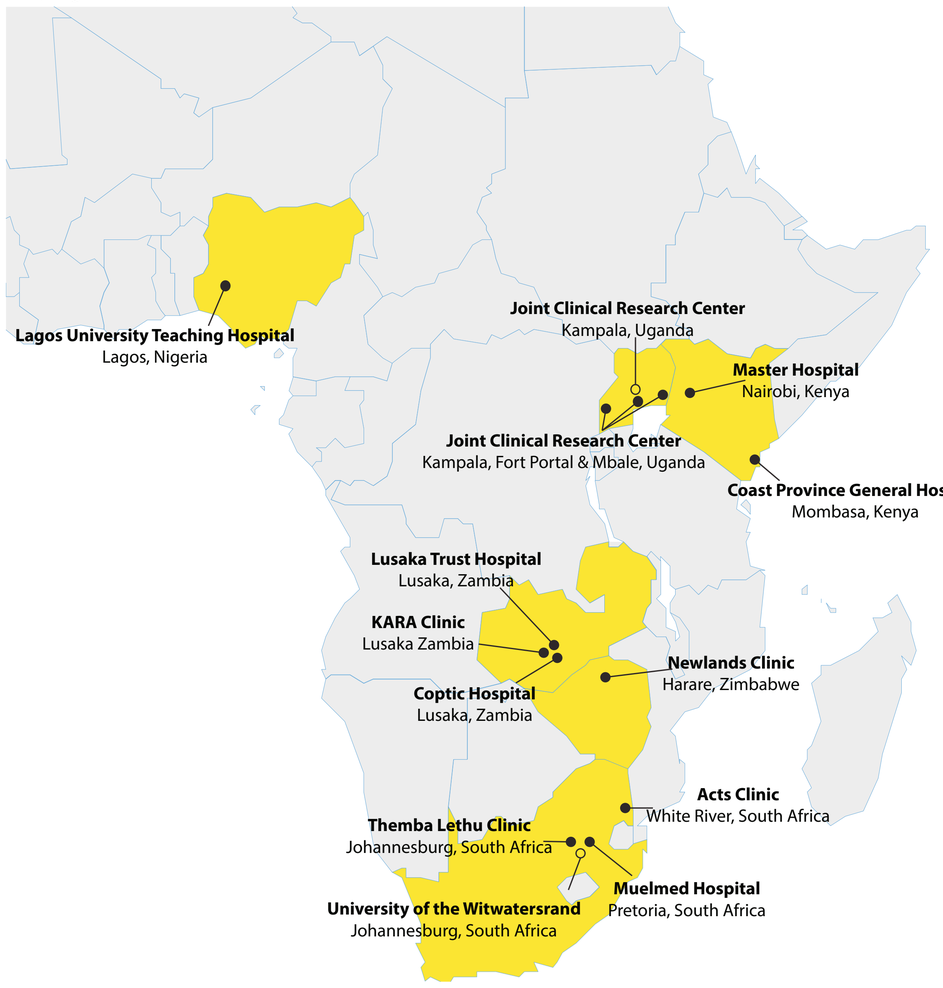


Figure 1b TASER sites

Asia *Participants (n=1504): Hong Kong (12%) Indonesia (2%) Malaysia (21%) Philippines (8%) Thailand (57%)*

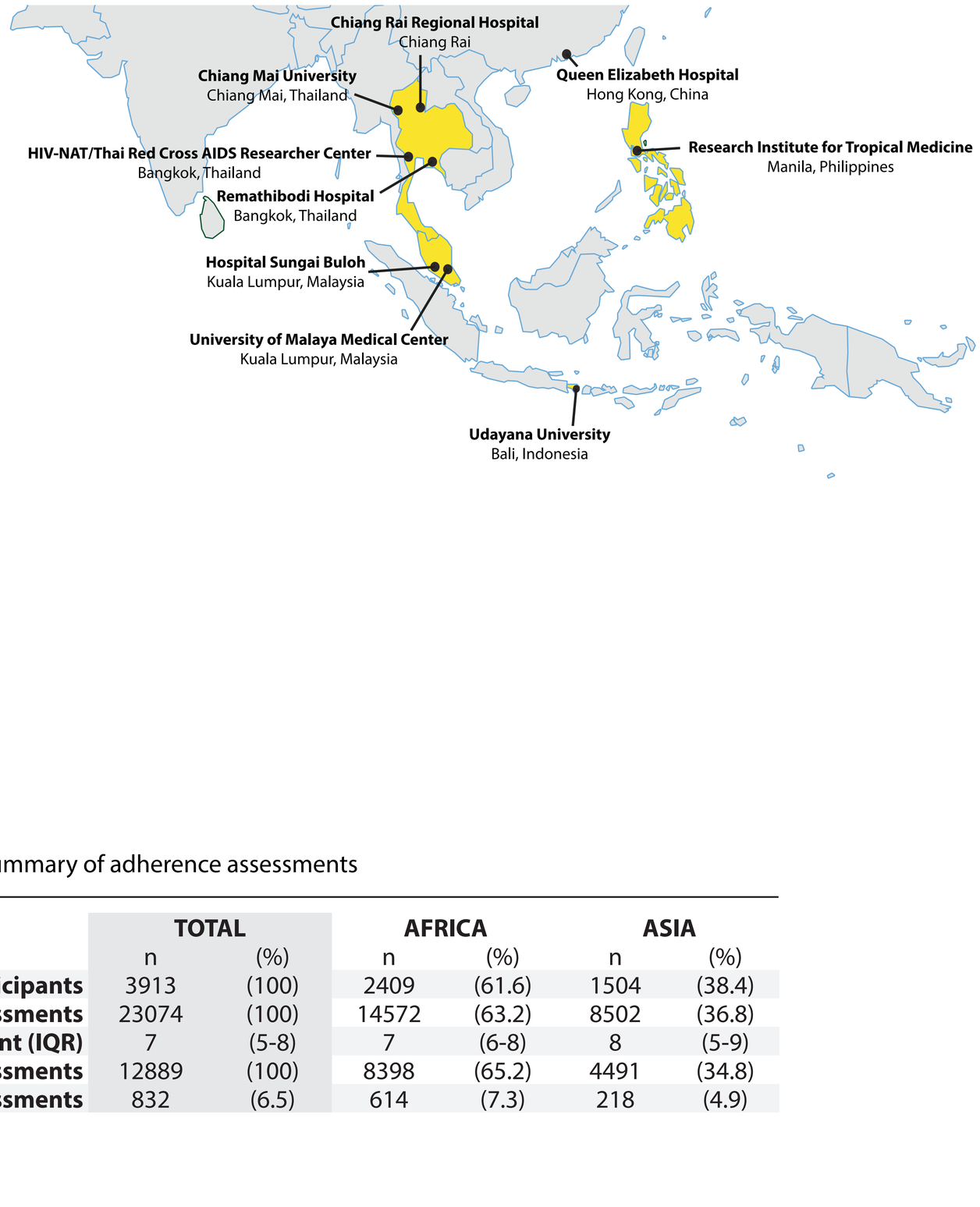


Table 1 Summary of adherence assessments

	TOTAL		AFRICA		ASIA	
	n	(%)	n	(%)	n	(%)
Participants	3913	(100)	2409	(61.6)	1504	(38.4)
Adherence assessments	23074	(100)	14572	(63.2)	8502	(36.8)
Median adherence assessments/participant (IQR)	7	(5-8)	7	(6-8)	8	(5-9)
Number of mean adherence assessments	12889	(100)	8398	(65.2)	4491	(34.8)
Number of suboptimal mean adherence assessments	832	(6.5)	614	(7.3)	218	(4.9)

Note *Adherence assessed using 30-day Visual Analogue Scale*

Table 2 Factors associated with mean adherence <95% stratified by region

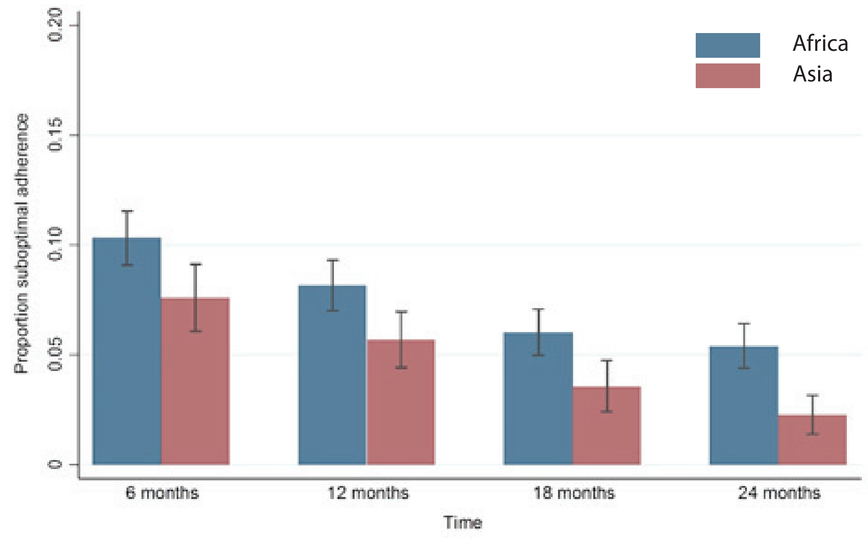
	Africa				Asia				Interaction
DETERMINANT	**OR**	**95% CI**		**p-value**	**OR**	**95% CI**		**p-value**	**p**
GENDER									
Female	1.00				1.00				
Male	1.35	1.11 -	1.65	**0.002**	1.12	0.76 -	1.66	0.572	0.400
AGE									
18-29	1.00				1.00				
30-39	0.73	0.57 -	0.94	**0.016**	0.82	0.52 -	1.29	0.393	
≥40	0.66	0.51 -	0.87	**0.003**	0.70	0.44 -	1.12	0.138	0.745
EXPOSURE CATEGORY									
Heterosexual contact	1.00				1.00				
MSM	[a]				0.51	0.31 -	0.86	**0.012**	†
IDU	-				3.47	2.09 -	5.75	**<0.001**	†
Unspecified	0.78	0.72 -	0.85	**<0.001**	0.46	0.09 -	2.37	0.351	0.964
PRE-ART AIDS EVENT									
No	1.00				1.00				
Yes	1.07	0.72 -	1.38	0.608	0.81	0.55 -	1.19	0.287	0.212
PRE-ART CD4 CELL COUNT[b]									
<50	1.00				1.00				
50-99	1.28	0.94 -	1.76	0.116	1.09	0.67 -	1.80	0.724	0.553
100-199	1.04	0.79 -	1.37	0.771	1.02	0.65 -	1.61	0.920	0.973
≥200	1.14	0.85 -	1.52	0.627	0.62	0.36 -	1.06	0.081	**0.047**
PRE-ART HIV VIRAL LOAD[c]									
<10000	1.00				1.00				
10000-99999	1.31	0.96 -	1.79	0.090	0.46	0.27 -	0.80	**0.006**	0.001
≥100000	1.16	0.85 -	1.57	0.352	0.75	0.45 -	1.25	0.273	0.152
ART REGIMEN									
NNRTI-based	1.00				1.00				
Other	2.02[d]	1.23 -	3.32	**0.005**	0.64	0.29 -	1.44	0.301	0.017
CONCOMITANT MEDICATION									
No	1.00				1.00				
Yes	1.90	1.16 -	3.12	**0.013**	1.15	0.81 -	1.62	0.436	0.133
SECTOR									
Government									
Non-government	0.69	0.54 -	0.88	**0.003**	[e]				[e]
ART DURATION									
6 months	1.00				1.00				
12 months	0.74	0.61 -	0.91	**0.004**	0.86	0.63 -	1.17	0.327	0.484
18 months	0.53	0.43 -	0.67	**<0.001**	0.60	0.41 -	0.87	0.007	0.714
24 months	0.49	0.39 -	0.63	**<0.001**	0.43	0.28 -	0.64	<0.001	0.425

Note *Analysis with Generalized Estimating Equation to model the probability that a participant was in the suboptimal adherence group. Therefore, an OR of >1 indicates an increased odds of suboptimal adherence, compared with the odds for the reference group. Corrected for: n° of assessments, site type and calendar year.*

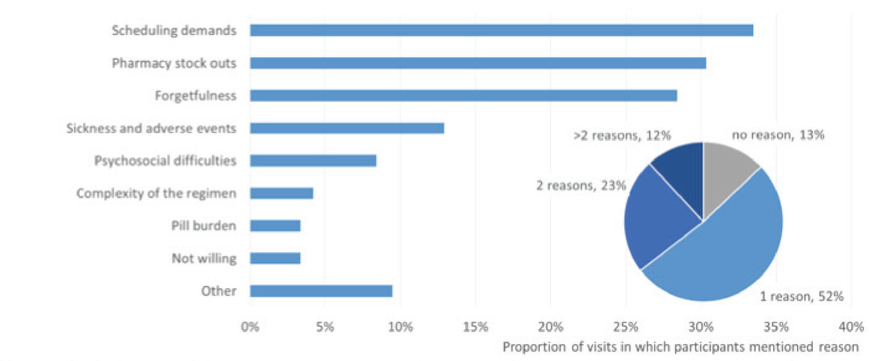
[a]MSM category in Africa included in unspecified due to limited n° of observations; [b]CD4 cells/µL; [c]HIV-RNA c/mL; [d]26 African participants on other regimen; [e]All facilities in Asia were governmental; † too few observations to estimate association, omitted from model.

NNRTI = *non-nucleoside reverse transcriptase inhibitor* **MSM** = *men who have sex with men*
IDU= *injecting drug use* **PMTCT** = *prevention of mother-to-child-transmission*

Figure 2 Suboptimal adherence over time across regions in participants who initiated first-line ART (n=3913)



Box 1 Exploration of reasons for suboptimal adherence mentioned by participants in Africa



Note 1 *In Africa, participant-reported reasons for suboptimal adherence were explored. In case of suboptimal adherence at any given site visit, reasons were recorded using a category-based questionnaire. Pre-defined and open answers were categorized. A descriptive analysis was performed on reasons given by 235 different participants during 1045 visits in which suboptimal adherence was reported.*

Note 2 *More than one reason could be mentioned per visit, therefore the sum of all proportion is greater than 1*

affiliations

PASER PAN-AFRICAN STUDIES TO EVALUATE RESISTANCE
TASER Studies to Evaluate Resistance
Amsterdam Institute for Global Health and Development
aighd
amc Academisch Medisch Centrum Universiteit van Amsterdam
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