

Supplementary Appendix

Using a Medication Event Monitoring System to Evaluate Self-report and Pill Count for Determining Treatment Completion with Self-administered, Once-weekly Isoniazid and Rifapentine

Authors: Nigel A. Scott¹, Claire Sadowski^{1,2}, Andrew Vernon¹, Bert Arevalo³, Karlyn Beer¹, Andrey Borisov¹, Joan A. Cayla⁴, Michael Chen¹, Pei-Jean Feng¹, Ruth N. Moro¹, David P. Holland⁵, Neil Martinson⁶, Joan-Pau Millet^{7,8}, Jose M. Miro^{9,10}, Robert Belknap¹¹

March 2023

Author Affiliations:

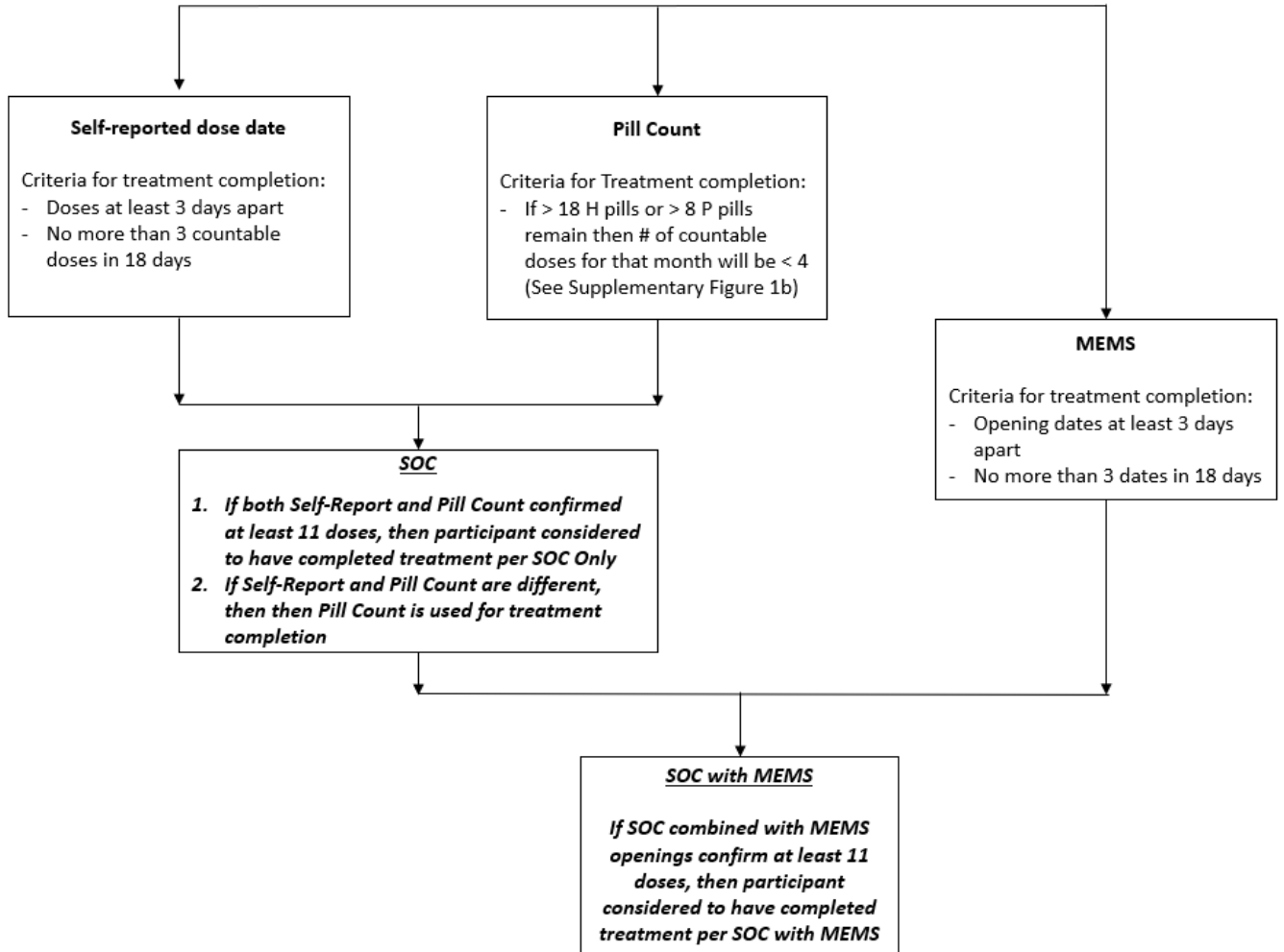
1. U.S. Centers for Disease Control & Prevention, Atlanta, GA, USA
2. Oak Ridge Institute for Science and Education, Oak Ridge, TN, USA
3. Westat, Rockville, MD, USA
4. Foundation of TB Research Unit of Barcelona, Barcelona, Spain
5. Emory University, Atlanta, GA, USA
6. Perinatal HIV Research Unit (PHRU), University of the Witwatersrand, South Africa and Johns Hopkins University Center for TB Research, Baltimore, MD, USA
7. Agència de Salut Pública de Barcelona, Spain
8. CIBER de Epidemiología y Salud Pública (CIBERESP), Madrid, Spain
9. Infectious Diseases Service. Hospital Clinic-IDIBAPS. University of Barcelona, Barcelona, Spain
10. CIBERINFEC, Instituto de Salud Carlos III, Madrid, Spain
11. Public Health Institute at Denver Health, Denver, CO, USA

Corresponding author:

Nigel A. Scott, M.S., Division of TB Elimination, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, 1600 Clifton Road, NE, MS-E10, Atlanta, GA 30329, USA.

Email: NScott@cdc.gov

Supplementary Figure 1a. Determination of Treatment Completion by Self-report, Pill count and MEMS



H – Isoniazid: One dose = 900mg (3 pills x 300mg)
 P – Rifapentine: One dose = 900mg (6 pills x 150mg)
 SOC – Standard of Care
 MEMS – medication event monitoring system.

Supplementary Figure 1b. Determination of Treatment Completion by Pill count

1

Review number of tablets remaining in the **P** blister packs and circle the corresponding number of Doses

# P tablets left in blisters	Doses
27-32	0
21-26	1
15-20	2
9-14	3
0-8	4

2

Review number of pills remaining in the **H** bottle and circle the corresponding number of Doses

# H pills left in bottle	Doses
28-30	0
25-27	1
22-24	2
19-21	3
0-18	4

3

Is the number of Doses (1 & 2 above) the same for both P and H?

Yes

No

Choose the smallest number of circled doses
 (e.g., If # tabs left in blister packs is 10 (3 doses),
 and # of pills left in bottle is 12 (4 doses), then "# doses" = 3, not 4)

Notes:

Algorithm estimates the number of doses per month

P – Rifapentine

H - Isoniazid

Supplementary Table 1. Percentage Treatment Completion by Standard of Care vs. Standard of Care with MEMS by Arm and Sites within U.S.

Enrollment Site	Treatment Completion							% Difference of Total in SAT SOC vs. SOC with MEMS (95% CI) ¹
	DOT	SOC			SOC with MEMS			
		SAT	SAT-r	Total in SAT	SAT	SAT-r	Total in SAT	
Site A	41/50 (82.0)	45/52 (86.5)	43/52 (82.7)	88/104 (84.6)	43/52 (82.7)	42/52 (80.8)	85/104 (81.7)	2.9 (-0.3, 6.1)
Site B	22/25 (88.0)	20/24 (83.3)	26/27 (96.3)	46/51 (90.2)	20/24 (83.3)	24/27 (88.9)	44/51 (86.3)	3.9 (-1.4, 9.2)
Site C	25/31 (80.7)	21/32 (65.6)	22/30 (73.3)	43/62 (69.4)	20/32 (62.5)	20/30 (66.7)	40/62 (64.5)	4.8 (-0.5, 10.2)
Site D	16/17 (94.12)	14/18 (77.8)	12/14 (85.7)	26/32 (81.3)	14/18 (77.8)	11/14 (78.6)	25/32 (78.1)	3.2 (-2.9, 9.2)
Site E	48/54 (88.9)	44/56 (78.6)	44/58 (75.9)	88/114 (77.2)	42/56 (75.0)	43/58 (74.1)	85/114 (74.6)	2.6 (-0.3, 5.6)
Site F	3/6 (50.0)	3/4 (75.0)	1/2 (50.0)	4/6 (66.7)	3/4 (75.0)	1/2 (50.0)	4/6 (66.7)	0.0 ²
Site G	7/8 (87.5)	5/6 (83.3)	4/5 (80.0)	9/11 (81.8)	5/6 (83.3)	4/5 (80.0)	9/11 (81.8)	0.0 ²
Site H	24/29 (82.8)	25/29 (86.2)	18/24 (75.0)	43/53 (81.1)	24/29 (82.8)	17/24 (70.8)	41/53 (77.4)	3.8 (-1.4, 8.9)
Site I	37/41 (90.2)	35/41 (85.4)	30/39 (76.9)	65/80 (81.3)	33/41 (80.5)	29/39 (74.4)	62/80 (77.5)	3.8 (-0.4, 7.9)

1 Wald 95% confidence interval for the difference in proportion between SOC and SOC with MEMS

2 Wald 95% confidence interval for the difference in proportion cannot be calculated

DOT – Directly Observed Therapy.

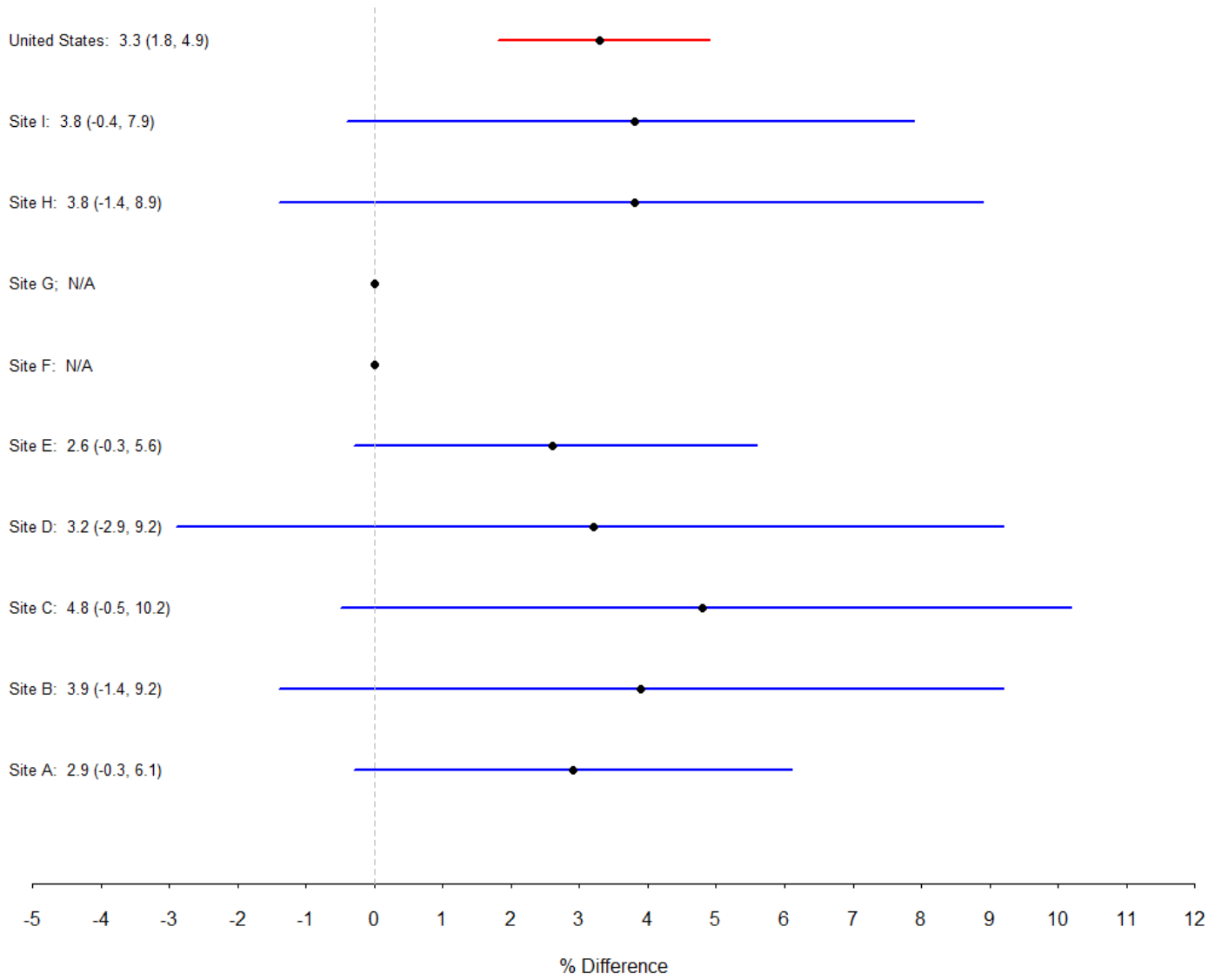
SAT – Self-Administered Therapy.

SAT-r – Self-Administered Therapy with text message reminders

SOC – Standard of Care.

MEMS – Medication Event Monitoring System.

Supplementary Figure 2. Percent Difference in Treatment Completion: SOC vs SOC with MEMS by Sites within U.S., - with their 95% C.I.



Supplementary Table 2. Univariable and Multivariable Analyses of Factors Associated with Difference between Self-report and Pill Count Treatment Completion Compared with MEMS-based Treatment Completion. (South Africa Population Only)

Characteristics	# With Discordance*	# w/o Discordance*	Univariable				Multivariable			
			OR	Lower 95% CI	Upper 95% CI	P-value	OR	Lower 95% CI	Upper 95% CI	P-value
Part of Household Cluster	2	4	0.93	0.16	5.40	0.93				
Female	9	15	1.05	0.36	3.12	0.92				
Age 35 years or older	4	11	0.57	0.16	2.06	0.39				
Born Outside Country of Enrollment	1	0	5.35	0.06	512.08	0.47				
Indication for LTBI Treatment										
Contact of a person with infectious TB	13	34	ref	ref	ref	ref				
Recent LTBI screening test conversion	0	0	-	-	-	-				
Fibrosis	0	0	-	-	-	-				
HIV infection	1	0	7.70	0.08	746.49	0.66				
Positive results on LTBI screening test	7	2	7.67	1.49	39.42	0.47				
Occupation – Unemployed	18	24	2.70	0.69	10.59	0.16				
Did Not Complete High School	11	12	2.15	0.72	6.44	0.17				
Homeless	0	0	-	-	-	-				
Drug Use	2	0	9.35	0.22	401.45	0.24				
Resident of Correctional Facility	0	0	-	-	-	-				
Alcohol Use	15	17	2.66	0.85	8.32	0.09				
Alcohol Abuse	10	11	2.03	0.67	6.14	0.21				
Current Smoker	12	13	2.29	0.77	6.85	0.14				
Smoke Ever	13	13	2.77	0.91	8.37	0.07				
Diabetes	0	0	-	-	-	-				
Liver Disease	0	0	-	-	-	-				
HIV Positive	2	2	1.77	0.23	13.58	0.58				

Characteristics	# With Discordance*	# w/o Discordance*	Univariable				Multivariable			
			OR	Lower 95% CI	Upper 95% CI	P-value	OR	Lower 95% CI	Upper 95% CI	P-value
Concomitant Medications at Baseline	5	6	1.56	0.41	5.92	0.51				
SMS	7	21	0.37	0.12	1.14	0.08				
Treatment Arm										
	SAT	14	15	ref	ref	ref	ref			
	SAT w/reminders	7	21	0.37	0.12	1.14	0.08			

DOT – Directly Observed Therapy.

SAT – Self-Administered Therapy.

*Discordance: a mismatch in treatment completion status, where participants were deemed to have completed treatment per SOC but were found to have not completed treatment according to SOC with MEMS.

Supplementary Table 3. Percentage Treatment Completion by SOC vs. SOC with MEMS by Arm and Enrollment Country

Enrollment Country	Treatment Completion										% Difference of Total in SAT SR+PC vs. SR+PC+MEMS (95%CI) ¹
	DOT	SR Only			SR + PC			SR + PC + MEMS			
		SAT	SAT-r	Total in SAT	SAT	SAT-r	Total in SAT	SAT	SAT-r	Total in SAT	
United States	223/261 (85.4)	214/262 (81.7)	202/251 (80.5)	416/513 (81.1)	212/262 (80.9)	200/251 (79.7)	412/513 (80.3)	204/262 (77.9)	191/251 (76.1)	395/513 (77.0)	3.3 (1.8, 4.9)
Spain	33/35 (94.3)	23/32 (71.9)	29/33 (87.9)	52/65 (80.0)	23/32 (71.9)	29/33 (87.9)	52/65 (80.0)	22/32 (68.8)	28/33 (84.8)	50/65 (76.9)	3.1 (-1.1, 7.3)
Hong Kong	14/15 (93.3)	11/14 (78.6)	16/16 (100.0)	27/30 (90.0)	11/14 (78.6)	16/16 (100.0)	27/30 (90.0)	11/14 (78.6)	16/16 (100.00)	27/30 (90.0)	0 (0,0)
South Africa	24/26 (92.3)	26/29 (89.7)	22/28 (78.6)	48/57 (84.2)	25/29 (86.2)	21/28 (75.0)	46/57 (80.7)	11/29 (37.9)	14/28 (50.0)	25/57 (43.9)	36.8 (24.3, 49.4)
Total	294/337 (87.2)	274/337 (81.3)	269/328 (82.0)	543/665 (81.7)	271/337 (80.4)	266/328 (81.1)	537/665 (80.8)	248/337 (73.6)	249/328 (75.9)	497/665 (74.7)	6.1 (4.2, 7.8)

Notes: SR – Self-report; PC – Pill Count; MEMS – Medication Event Monitoring System

Wald 95% confidence interval for difference of Total in SAT is based on repeated measures linear model

DOT – Directly Observed Therapy.

SAT – Self-Administered Therapy.

SAT-r – Self-Administered Therapy with text message reminders

Supplementary Table 4. Baseline Characteristics by Country and Arm

Characteristics		Overall (SAT + SAT-r)				SAT				SAT-r			
		ESP n=65	HKG n=30	USA n=513	ZAF n=57	ESP n=32	HKG n=14	USA n=262	ZAF n=29	ESP n=33	HKG n=16	USA n=251	ZAF n=28
Part of Household Cluster		2 (3.1)	9 (30.0)	37 (7.2)	6 (10.5)	2 (6.3)	2 (14.3)	24 (9.2)	2 (6.9)	0 (0.0)	7 (43.8)	13 (5.2)	4 (14.3)
Female		23 (35.4)	19 (63.3)	263 (51.3)	35 (61.4)	11 (34.4)	12 (85.7)	127 (48.5)	11 (37.9)	12 (36.4)	7 (43.8)	136 (54.2)	24 (85.7)
Age 35 years or older		34 (52.3)	18 (60.0)	311 (60.6)	15 (26.3)	16 (50.0)	9 (64.3)	156 (59.5)	10 (34.5)	18 (54.5)	9 (56.3)	155 (61.8)	5 (17.9)
Race													
	White	43 (66.2)	0 (0.0)	304 (59.3)	0 (0.0)	22 (68.8)	0 (0.0)	153 (58.4)	0 (0.0)	21 (63.6)	0 (0.0)	151 (60.2)	0 (0.0)
	Black/African American	4 (6.2)	0 (0.0)	105 (20.5)	57 (100.0)	2 (6.3)	0 (0.0)	60 (22.9)	29 (100.0)	2 (6.1)	0 (0.0)	45 (17.9)	28 (100.0)
	Asian or Other Race	18 (27.7)	30 (100.0)	104 (20.3)	0 (0.0)	8 (25.0)	14 (100.0)	49 (18.7)	0 (0.0)	10 (30.3)	16 (100.0)	55 (21.9)	0 (0.0)
Born Outside Country of Enrollment		42 (64.6)	11 (36.7)	341 (66.5)	1 (1.8)	24 (75.0)	6 (42.9)	176 (67.2)	1 (3.4)	18 (54.5)	5 (31.3)	165 (65.7)	0 (0.0)
Indication for LTBI Treatment													
	Contact of a person with infectious TB	45 (69.2)	28 (93.3)	114 (22.2)	47 (82.5)	22 (68.8)	12 (85.7)	56 (21.4)	21 (72.4)	23 (69.7)	16 (100.0)	58 (23.1)	26 (92.9)
	Recent LTBI screening test conversion	0 (0.0)	0 (0.0)	65 (12.7)	0 (0.0)	0 (0.0)	0 (0.0)	34 (13.0)	0 (0.0)	0 (0.0)	0 (0.0)	31 (12.4)	0 (0.0)
	Fibrosis	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
	HIV infection	2 (3.1)	1 (3.3)	0 (0.0)	1 (1.8)	1 (3.1)	1 (7.1)	0 (0.0)	0 (0.0)	1 (3.0)	0 (0.0)	0 (0.0)	1 (3.6)
	Positive results on LTBI screening test	18 (27.7)	1 (3.3)	333 (64.9)	9 (15.8)	9 (28.1)	1 (7.1)	172 (65.6)	8 (27.6)	9 (27.3)	0 (0.0)	161 (64.1)	1 (3.6)
Occupation													
	Employed	40 (61.5)	25 (83.3)	327 (63.7)	15 (26.3)	19 (59.4)	10 (71.4)	161 (61.5)	8 (27.6)	21 (63.6)	15 (93.8)	166 (66.1)	7 (25.0)

Characteristics		Overall (SAT + SAT-r)				SAT				SAT-r			
		ESP n=65	HKG n=30	USA n=513	ZAF n=57	ESP n=32	HKG n=14	USA n=262	ZAF n=29	ESP n=33	HKG n=16	USA n=251	ZAF n=28
	Unemployed	25 (38.5)	5 (16.7)	186 (36.3)	42 (73.7)	13 (40.6)	4 (28.6)	101 (38.5)	21 (72.4)	12 (36.4)	1 (6.3)	85 (33.9)	21 (75.0)
	Did Not Complete High School	30 (46.2)	3 (10.0)	152 (29.6)	23 (40.4)	14 (43.8)	1 (7.1)	74 (28.2)	12 (41.4)	16 (48.5)	2 (12.5)	78 (31.1)	11 (39.3)
	Homeless	3 (4.6)	0 (0.0)	32 (6.2)	0 (0.0)	1 (3.1)	0 (0.0)	15 (5.7)	0 (0.0)	2 (6.1)	0 (0.0)	17 (6.8)	0 (0.0)
	Drug Use	5 (7.7)	0 (0.0)	24 (4.7)	2 (3.5)	2 (6.3)	0 (0.0)	11 (4.2)	1 (3.4)	3 (9.1)	0 (0.0)	13 (5.2)	1 (3.6)
	Resident of Correctional Facility	0 (0.0)	0 (0.0)	8 (1.6)	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.6)	0 (0.0)
	Alcohol Use	19 (29.2)	22 (73.3)	275 (53.6)	32 (56.1)	11 (34.4)	8 (57.1)	134 (51.1)	17 (58.6)	8 (24.2)	14 (87.5)	141 (56.2)	15 (53.6)
	Alcohol Abuse	1 (1.5)	0 (0.0)	23 (4.5)	21 (36.8)	0 (0.0)	0 (0.0)	11 (4.2)	11 (37.9)	1 (3.0)	0 (0.0)	12 (4.8)	10 (35.7)
	Current Smoker	28 (43.1)	3 (10.0)	105 (20.5)	25 (43.9)	15 (46.9)	1 (7.1)	52 (19.8)	14 (48.3)	13 (39.4)	2 (12.5)	53 (21.1)	11 (39.3)
	Diabetes	1 (1.5)	1 (3.3)	50 (9.7)	0 (0.0)	1 (3.1)	0 (0.0)	23 (8.8)	0 (0.0)	0 (0.0)	1 (6.3)	27 (10.8)	0 (0.0)
	Liver Disease	1 (1.5)	2 (6.7)	28 (5.5)	0 (0.0)	0 (0.0)	1 (7.1)	14 (5.3)	0 (0.0)	1 (3.0)	1 (6.3)	14 (5.6)	0 (0.0)
	HIV Positive	3 (4.6)	1 (3.3)	0 (0.0)	4 (7.0)	1 (3.1)	1 (7.1)	0 (0.0)	1 (3.4)	2 (6.1)	0 (0.0)	0 (0.0)	3 (10.7)
	Concomitant Medications at Baseline	33 (50.8)	15 (50.0)	315 (61.4)	11 (19.3)	14 (43.8)	7 (50.0)	167 (63.7)	6 (20.7)	19 (57.6)	8 (50.0)	148 (59.0)	5 (17.9)

Notes:

SAT – Self-Administered Therapy.

SAT-r – Self-Administered Therapy with text message reminders

ESP – Spain; HKG – Hong Kong; USA – United States of America; ZAF – South Africa.

