

# Monitoring self-reported adherence to antiretroviral therapy in public HIV care facilities in Brazil

# A national cross-sectional study

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# Abstract

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Introduction: Patient adherence to antiretroviral therapy (ART) is critical for HIV treatment success. Monitoring rates of adherence in public HIV outpatient care facilities can improve outcomes in Brazil where ART is universally available.

Methods: We conducted a national cross-sectional survey of ART adherence in 2010. Participants were selected using a multistage probability sample. First, HIV outpatient care facilities were stratified according to 7 Organizational Quality Classification (OQC) groups and regions. Second, 1 or 2 facilities were selected per region for each OQC group. Finally, patients were randomly selected at each facility. In a first component, patients were invited to answer to a web-based questionnaire (WebAd-Q), a validated self-reported tool that includes 3 questions on adherence to ART in the past 7 days (time scheduling-timing, drug regimenmedication, and pill counts - dose), herein named indicators of potential nonadherence (IPN). In addition, a subsample of participants were interviewed in order to obtain further data on sociodemographic and clinical characteristics (second component). The proportion of each IPN was estimated using weighted data to account for the sampling design with 95% confidence interval (CI) and descriptive analysis was carried out.

Results: Fifty-five facilities were chosen and 2424 patients completed the WebAd-Q in the first component of the study, while 598 patients were interviewed for the second component. The weighted proportions of the IPN were 50.9%, 31.8%, and 19.5%, for timing, medication, and dose, respectively, while11.7% had all 3 indicators, varying from 5.9% in the Southeast and 21.9% in the Northeast regions. Overall, 61.1% of the patients had at least 1 IPN (95% CI: 58.5–63.7%). Patients reporting depression symptoms, illicit drug use and those who missed medical appointments had worse nonadherence outcomes.

Conclusions: Overall, there was a high proportion of all indicators IPN and timing was the main component associated with low adherence. Although these indicators may not necessarily indicate individual nonadherence, they represent a worrisome scenario in the public Brazilian HIV care facilities. On a routine basis, these facilities can identify gaps in providing counseling and ART orientation to their clientele and develop innovative strategies to prevent nonadherence.

Abbreviations: AIDS = acquired immune deficiency syndrome, ART = antiretroviral therapy, CI = confidence interval, DIAHV = Department of STI/AIDS and Viral Hepatitis, Ministry of Health, HAART = highly active antiretroviral therapy, HIV = human immunodeficiency virus, IPN = indicators of potential nonadherence, OQC = Organizational Quality Classification, STI = sexually transmitted infection, WebAd-Q = Qualiaids Web Adherence Questionnaire.

Keywords: antiretroviral therapy, Brazil, health services research, HIV/AIDS, national survey, nonadherence

Medicine (2018) 97:S1(e9015)

Editor: Ismaël Maatouk.

Funding: This study was developed in partnership with the Qualiaids Research Team (University of Sao Paulo), the Research Group on Epidemiology and Health Evaluation (Federal University of Minas Gerais), and the Research Group on Epidemiology of Medications (Regional University of Blumenau). This research was supported by the Department of STI, HIV/AIDS and Viral Hepatitis, Ministry of Health (DIAHV/MoH) through technical cooperation with UNESCO (United Nations Educational, Scientific and Cultural Organization), project CSV 124/2009. M.A.S. was supported by a FAPESP (São Paulo Research Foundation) doctoral research grant in Preventive Medicine (process no. 2012/20578-4), and a FAPESP doctoral internship research grant (process no. 2013/06186-9).

The authors have no conflicts of interest to disclose

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Received: 6 November 2017 / Accepted: 9 November 2017

http://dx.doi.org/10.1097/MD.0000000000009015

# 1. Introduction

Patient adherence to antiretroviral therapy (ART) is critical to ensure the effectiveness of HIV treatment. Since the advent of highly active antiretroviral therapy (HAART), high levels of adherence have been consistently associated with improved virologic, immunologic, and clinical outcomes,<sup>[1-3]</sup> with consequent increase in survival<sup>[4–6]</sup> and quality of life.<sup>[7,8]</sup>

Even though recent and more potent regimens indicate the possibility of achieving satisfactory outcomes at moderate levels of adherence,<sup>[9,10]</sup> the assumption that higher adherence levels lead to improved outcomes remain valid.<sup>[11–13]</sup> However, ART consists of a lifelong, complex treatment, which often involves side effects. As a result, patient adherence is inconsistent and tends to decline over time.<sup>[6,14]</sup> Even with more tolerable and simpler regimens currently available, adherence remains challenging for HIV programs worldwide.<sup>[15]</sup>

In view of this context, recent international guidelines for the organization of HIV care highly recommend routine monitoring of adherence in clinical settings.<sup>[16–19]</sup> Adherence monitoring is critical to guide treatment planning and prevent virologic failure during medical follow-up.<sup>[20]</sup> In addition, routine adherence measurement is a valuable tool in managing HIV programs in public health facilities, including the implementation of interventions to promote and support adherence and routine evaluation of program and facilities' performance.<sup>[21–24]</sup> Furthermore, adherence assessment is a key element in the implementation of treatment-as-prevention strategies along with efforts to improve outcomes in all stages of the HIV treatment cascade.<sup>[25]</sup>

Currently, there are approximately 405,000 individuals receiving ART at approximately 1024 human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) referral facilities through the Brazilian universal public health system.<sup>[26,27]</sup> This number should increase in the coming years considering the introduction of treatment as prevention strategies and the constant updates in treatment guidelines to include HIV-infected individuals regardless of CD4+ cell counts.<sup>[28,29]</sup>

Despite efforts of the Department of STI, HIV/AIDS and Viral Hepatitis, Ministry of Health (DIAHV/MoH) to disseminate strategies to promote and sustain patients' adherence,<sup>[30,31]</sup> its assessment is not a standard practice in most facilities and Brazil still lacks standardized, valid, and feasible measures for routine use in public HIV care facilities.<sup>[32,33]</sup>

To address this gap, a self-reported tool to monitor ART and screen for potential nonadherence in the Brazilian public HIV care facilities has been recently developed and validated—the *Qualiaids Web Adherence Questionnaire* (*WebAd-Q*).<sup>[34]</sup> The *WebAd-Q* was developed to be a practical tool for routine use, capable of addressing different dimensions of adherence, that is, scheduling, drug regimen, and dose. In the validation study, the *WebAd-Q* measures were associated with viral load, and performed well in comparison to concurrent measures (i.e., electronic monitoring, pill counting, self-report interview).<sup>[34]</sup>

The WebAd-Q focus on indicators at the facility level, rather than on medically oriented individual adherence. It allows for periodic screening of a healthcare facility clientele so that staff managers can continuously assess service performance and define effective strategies to promote adherence in each facility. In this paper, we present overall descriptive results of a national application of the WebAd-Q in the Brazilian public HIV care facilities.

# 2. Methods

#### 2.1. Study design

National cross-sectional survey of adherence conducted in 2010 among HIV-infected patients receiving ART in public HIV outpatient care facilities in Brazil. Patients should be 18 years old or over and facilities should have been registered with the DIAHV/MoH as of 2007 (N=636).<sup>[35]</sup> Pregnant women were excluded from the study. The study was divided into 2 components: Overall assessment of adherence; application of a semi-structured interview in a subset of participants from the first component in order to assess potential determinants of nonadherence.

#### 2.2. Sampling procedures

A 2-stage probability sampling procedure was used in the survey: selection of facilities; and selection of participants. For the first stage, 2 characteristics were taken into account, an Organizational Quality Classification (OQC) of each facility<sup>[35]</sup> and the 5 main Brazilian geographical regions (North, Northeast, Central-West, South, and Southeast), plus the States of São Paulo and Rio de Janeiro which were treated separately due to their large contributions to AIDS cases in the country.<sup>[36]</sup> The OQC was determined by a previous national assessment of structural (e.g., access to care, infrastructure, human resources, availability of medications, exams, and referral service) and process characteristics (e.g., reception of new patients, counseling, medical and nurse care, multidisciplinary team, adherence-focused activities, work flows and protocols, coordination, professionals' training and updating, data monitoring, evaluation and planning, patient and civil society participation), ranging from Group 1 (highest OQC) to Group 6 (lowest OQC).<sup>[35]</sup> A seventh group includes facilities with unknown OOC.<sup>[35]</sup>

# 2.3. Selection of facilities

Within each OQC group we selected 1 or 2 facilities from each region according to the distribution of patients receiving HIV care. One facility was selected when the region contained up to 20% of patients receiving HIV care within each OQC group. Otherwise, 2 facilities were selected. The facilities were selected using simple random sampling proportional to the size of each facility within each region and OQC group. Overall, 55 facilities were selected, ranging from 5 to 9 per OQC group.

#### 2.4. Selection of participants

We anticipated a sample size of 336 participants per OQC group plus an estimated nonparticipation rate of 12.0% considering an estimated prevalence of adherence of 70.0% (95% CI: 65.0–75.0%) and a significant level of 0.05. Once the facilities were selected, we used simple probability sampling proportional to the number of patients receiving ART within each OQC group. The minimum sample size for each facility was set at 5 participants, yielding a total of 2646 patients to be recruited for the first component of the study. A subset of 598 participants was randomly selected proportional to the number of patients under ART in each region for further interview during the second component.

#### 2.5. Data collection and measures

Treatment adherence was assessed using the WebAd-Q, a previously validated self-reported tool developed to monitor

an overall measure of adherence in Brazilian public HIV care facilities.<sup>[34]</sup> Two healthcare providers from each selected facility participated in a 1-day training regarding the patients' recruitment process and invitation to participate in the study according to standardized procedures. Patients selected for the first component answered to the *WebAd-Q* in private rooms in the healthcare facilities, and no personal data were collected.

The WebAd-Q is an anonymous self-administered web-based questionnaire designed as a computer animated cartoon. It contains 3 questions, each one corresponding to one dimension of ART adherence: Timing: "In the last 7 days, have you taken any of your regimen drugs at times other than those scheduled by your doctor?"; Medication: "In the last 7 days, have you failed to take any of your regimen drugs?"; and Dose: "In the last 7 days, have you taken less or more pills of any of your regimen drugs?" Possible answers were "Yes," "No," or "I do not know/Do not recall." The answer "No" is an indicator of adherence and the answers "Yes" and "I do not know/Do not recall" are indicators of potential nonadherence (IPN).

For the second component (subset sample) a brief questionnaire was applied by face-to-face interviews. The interviews were conducted by trained members of the research team. Data on sociodemographic (age, gender, skin color, socioeconomic class), on ART (e.g., side effects, difficulties with treatment, missed medical appointments, time since HIV diagnosis and ART), substance use (e.g., illicit drugs and alcohol). Self-rated quality of life and anxiety and depression symptoms were also obtained. Depression and anxiety were assessed by the Hospital Anxiety and Depression scale (HAD) previously tested and validated in Brazil<sup>[37]</sup> and quality of life by the WHOQOL-HIV.<sup>[38]</sup>

#### 2.6. Statistical analysis

In this report we present descriptive data on the first component and selected characteristics of the second component of the study. We analyzed the frequency distribution of the answers to the *WebAd-Q* according to each dimension with 95% confidence intervals (CIs). We also analyzed the accumulation of the 3 dimensions (i.e., timing, medication, dose), as follows: nonadherence in only 1 dimension; nonadherence in any combination of 2 dimensions; nonadherence in all 3 dimensions; and nonadherence in at least 1 of the 3 dimensions. Categories 1 and 2 were irrespective of which dimension reported.

The proportions were weighted to account for the sampling design (i.e., the probability of facilities and patients being selected) using SAS statistical software by means of the complex sampling analysis procedure (SURVEYFREQ). The OQC groups were considered the strata level.

#### 2.7. Ethics statement

This study was approved by the Research Ethics Committee from the Faculty of Medicine, University of São Paulo (Protocol no.: 1140/09) and by local Ethical Review Boards when requested by the healthcare facilities. Participants who agreed to participate in the study provided written informed consent. Confidentiality of participants' identity was maintained. For the second component an additional written informed consent was also obtained.

#### 3. Results

Fifty-five public HIV care facilities from 7 Brazilian regions participated in the study. A total of 2604 patients were invited to

# Table 1

Sample distribution of facilities and patients according to the Organizational Quality Classification (OQC) and regions.

	Facilities, n (%)	Patients, n (%)
OQC		
1	9 (16.4)	357 (14.7)
2	8 (14.5)	398 (16.4)
3	7 (12.7)	367 (15.1)
4	9 (16.4)	367 (15.1)
5	9 (16.4)	370 (15.3)
6	5 (9.1)	219 (9.0)
Not classified	8 (14.5)	346 (14.3)
Regions		
São Paulo (SP)	9 (16.4)	386 (15.9)
Rio de Janeiro (RJ)	8 (14.5)	490 (20.2)
Northeast	8 (14.5)	462 (19.1)
North	5 (9.1)	200 (8.3)
Southeast (excluding SP and RJ)	5 (9.1)	135 (5.6)
South	14 (25.5)	560 (23.1)
Central-West	6 (10.9)	191 (7.9)
Total	55 (100.0)	2424 (100.0)

answer the WebAd-Q and 2424 (93.1%) completed the questionnaire during the first component. Of those invited to participate in the study, 97 (3.7%) declined and 54 (2.1%) did not meet the eligibility criteria. Lack of time was the main reason for declining to participate. Problems with administration of the questionnaire (incomplete or duplicated data) accounted for 29 (1.1%) exclusions. Table 1 shows the distribution of the sample according to facilities and patients.

Overall, 50.7% of the patients reported timing nonadherence while lower proportions were observed for medication and dose (32.2% and 20.3%, respectively) (Table 2). Although some heterogeneity was found for regions (42.2–59.4% for timing; 26.4–34.3% for medication; 12.9–30.5% for dose) and OQC (42.3–60.3% for timing; 21.9–36.8% for medication; 3.4–23.3% for dose), there was no indication of statistically significant differences (CI overlapping).

When taking the number of indicators reported, 61.1% (95% CI: 57.8–64.4%) of the patients reported at least 1 dimension (Table 3) and decreasing proportions were shown for only 1, 2, or all 3 dimensions, respectively. However, only Rio de Janeiro and the Northeast regions showed proportions with nonoverlapping CI for the presence of all 3 dimensions.

The analysis of the subset sample (second component), indicated that most variables had similar trends for each dimension of nonadherence (Table 4). Higher proportions were found among women, those at younger age, nonwhite, with lower schooling and lower social class, with moderate to severe depression or anxiety, low self-rated quality of life, and those who reported current alcohol or illicit drug use. In addition, participants with more recent HIV diagnosis and ART, who reported missing any medical appointment in the last six months and adverse reactions also showed higher proportions of the nonadherence indicators. However, only missing medical appointments showed nonoverlapping CI in each of the 3 dimensions, while depression symptoms and illicit drug use showed nonoverlapping CI for the timing dimension only. Similar results were also seen for those with nonadherence in at least 1 of the dimensions, but only depression symptoms and missing appointments were statistically different (Table 5).

# Table 2

Weighted proportions of the WebAd-Q dimensions (nonadherence indicators) by regions and Organizational Quality Classification (OQC), Brazil 2010.

		Timing	Medication	Dose
	N <sup>*</sup>	Wtd% (95% Cl) $^{\dagger}$	Wtd% (95% Cl) <sup>†</sup>	Wtd% (95% Cl) $^{\dagger}$
Overall	2424	50.7 (47.2–54.1)	32.2 (28.9–35.6)	20.3 (17.4–23.2)
Regions				
São Paulo (SP)	386	55.9 (50.4-61.4)	31.4 (26.2-36.6)	19.1 (14.6-23.5)
Rio de Janeiro (RJ)	490	52.4 (45.9-58.8)	26.4 (21.0-31.9)	13.7 (9.6–17.8)
Northeast	462	59.4 (49.4-69.4)	41.9 (31.7–52.1)	30.5 (21.2-39.8)
North	200	56.9 (48.1-65.7)	34.3 (25.9–42.8)	26.2 (18.7-33.6)
Southeast (excluding SP and RJ)	135	45.8 (35.7–55.9)	29.7 (20.3-39.1)	12.9 (5.9–19.9)
South	560	42.2 (35.0-49.4)	31.0 (23.8–38.1)	19.2 (12.9-25.4)
Central-West	191	49.3 (40.5–58.2)	31.1 (22.9–39.3)	23.5 (15.7–31.2)
OQC				
1	357	60.3 (54.1-66.6)	34.1 (27.9-40.2)	21.4 (15.9-26.9)
2	398	42.5 (30.0-54.9)	21.9 (14.9-29.0)	17.6 (8.2-27.1)
3	367	45.2 (37.1–53.3)	30.6 (23.3-37.8)	19.7 (13.5-26.0)
4	367	42.3 (28.6-56.1)	36.8 (22.6-51.0)	23.3 (10.7-35.8)
5	370	46.8 (40.6-53.1)	31.2 (25.3–37.1)	18.8 (13.7-23.9)
6	219	48.2 (39.8-56.5)	27.1 (19.6–34.6)	3.4 (7.9-18.9)
Unclassified	346	54.4 (48.7-60.1)	32.4 (27.0-37.8)	20.8 (16.2-25.4)

CI = confidence interval, WebAd-Q = Qualiaids Web Adherence Questionnaire.

 $^{\ast}$  Numbers according to the first component of the study.

<sup>+</sup>Weighted proportions (95% confidence interval).

# 4. Discussion

The national application of the WebAd-Q Questionnaire showed high proportions of nonadherence indicators in Brazil, either analyzing the 3 dimensions separately or in accumulation— 61.1% had at least 1 nonadherence indicator and timing was the most common one, suggesting that complying with recommended ART schedules is still a challenge in Brazil. National data on nonadherence in Brazil are still scarce. Before the present study, only 1 study has estimated national measures of adherence in Brazil, in 2001.<sup>[39]</sup> In that report, individual adherence was measured using a more traditional concept of nonadherence, that is, patients who reported taking less than 95% of the prescribed regimen during the 3 days before the interview. Approximately one-quarter of the patients were

#### Table 3

Weighted proportions according to the number of nonadherence indicators by regions and Organizational Quality Classification (OQC), Brazil 2010.

			Number of nonad	herence indicators	
		Only one	Тwo	All three	At least one
	$N^*$	Wtd% (95% CI) $^{\dagger}$	Wtd% (95% CI) $^{\dagger}$	Wtd% (95% CI) $^{\dagger}$	Wtd% (95% Cl) <sup>†</sup>
Overall	2424	30.8 (29.8–31.7)	18.6 (17.7–19.4)	11.7 (11.0–12.5)	61.1 (57.8–64.4)
Regions					
São Paulo (SP)	386	28.6 (23.5-33.7)	22.7 (18.0-27.4)	10.8 (7.3-14.3)	62.1 (56.7-67.4)
Rio de Janeiro (RJ)	490	32.6 (26.5–38.8)	19.0 (14.1-23.8)	7.3 (4.3–10.3) <sup>‡</sup>	58.9 (52.5-65.3)
Northeast	462	28.3 (19.1-37.5)	18.8 (11.1-26.6)	21.9 (13.3–30.5) <sup>‡</sup>	69.1 (59.5-78.7)
North	200	38.5 (29.8-47.2)	20.3 (13.2-27.4)	12.7 (7.1–18.4)	71.6 (63.5–79.6)
Southeast (excluding SP and RJ)	135	33.7 (24.1-43.3)	18.5 (10.6-26.3)	5.9 (0.8-11.1)	58.1 (48.0-68.2)
South	560	31.7 (24.5-38.9)	14.8 (9.3-20.2)	10.4 (6.1–14.7)	56.8 (49.7-63.9)
Central-West	191	29.1 (21.3–36.9)	17.2 (10.8-23.6)	13.5 (7.0–20.0)	59.7 (51.0-68.5)
OQC					
1	357	34.5 (28.2-40.7)	22.2 (16.7-27.6)	12.3 (7.8–16.9)	69.0 (63.1-74.8)
2	398	22.3 (12.7-31.9)	17.3 (8.0-26.6)	8.4 (4.3-12.4)	48.0 (35.2-60.8)
3	367	25.9 (18.6–33.2)	19.0 (12.8-25.1)	10.6 (6.2-14.9)	55.4 (47.2-63.7)
4	367	37.9 (23.7-52.0)	18.7 (7.8-29.6)	9.0 (0.9-17.2)	65.6 (52.8-78.4)
5	370	27.2 (21.7-32.8)	14.9 (10.6–19.3)	13.2 (8.6–17.8)	55.4 (49.2-61.6)
6	219	28.5 (20.7-36.3)	17.2 (11.3-23.1)	8.6 (3.6-13.5)	54.3 (46.0-62.6)
Unclassified	346	30.4 (25.3–35.5)	20.2 (15.5–24.9)	12.3 (8.6–16.0)	62.8 (57.3–68.4)

CI = confidence interval.

 $^{*}$  Numbers according to the first component of the study.

<sup>†</sup> Weighted proportions (95% confidence interval).

<sup>+</sup>Confidence intervals do not overlap as compared to the overall proportion.

# Table 4

Weighted proportions of the *WebAd-Q* dimensions (nonadherence indicators) according to selected characteristics of the subset sample (n=598), Brazil 2010.

		Timing	Medication	Dose
	n*	Wtd% (95% CI) $^{\dagger}$	Wtd% (95% CI) $^{\dagger}$	Wtd% (95% CI)
Overall	598	65.1 (59.7–70.5)	36.3 (30.7-41.9)	12.9 (8.9–16.9)
Gender				
Male	361	62.3 (55.0-69.7)	34.6 (27.1-42.0)	10.8 (6.0–15.7)
Female	236	69.4 (61.4–77.4)	38.9 (30.3–47.4)	15.9 (9.1–22.6)
Age (years old)				()
<45	316	69.5 (62.2–76.7)	40.0 (32.1-47.9)	14.5 (8.8–20.2)
45+	282	59.7 (51.6–67.8)	31.7 (24.0–39.4)	10.9 (5.4–16.4)
Skin color	202	33.7 (31.0 07.0)	31.7 (Z=1.0 - 33.+)	10.3 (0.4 10.4)
White	266	62.0 (54.6–69.3)	29.7 (21.8–37.7)	8.3 (4.1–12.5)
			( )	( )
Nonwhite	331	67.4 (59.6–75.1)	40.9 (33.1–48.7)	16.3 (10.2–22.4)
Schooling (years)				
<8	282	67.2 (59.7–74.6)	36.7 (29.1–44.3)	10.8 (6.1–15.4)
8+	297	61.3 (53.1–69.5)	36.1 (27.5–44.8)	13.4 (7.0–19.9)
Social class				
A–B	155	57.7 (46.9–68.6)	35.1 (22.7–47.6)	10.6 (2.4–18.8)
C-D-E	437	66.8 (60.5-73.1)	36.2 (29.9-42.5)	13.7 (9.1–18.3)
Depression symptoms				
Moderate-severe	90	91.0 (85.3–96.6) <sup>‡</sup>	52.5 (37.9-67.1)	24.1 (12.2-36.0)
None-light	505	60.5 (54.4–66.6)	33.1 (27.1–39.2)	11.1 (6.8–15.3)
Anxiety symptoms	000			
Moderate-severe	123	70.5 (58.7-82.3)	31.6 (21.6–41.7)	13.4 (6.2–20.7)
None-light	474	64.0 (57.9–70.0)	37.3 (30.9–43.7)	12.8 (8.2–17.4)
0	474	04.0 (07.9-70.0)	57.5 (50.9-45.7)	12.0 (0.2-17.4)
Self-rated quality of life	101			
Good-very good	421	58.4 (51.6–65.1)	32.4 (25.8–39.0)	10.3 (6.2–14.5)
Low-very low	176	77.6 (69.1–86.0)	43.8 (33.5–54.2)	17.8 (9.4–26.2)
Current alcohol use				
Yes	283	71.7 (64.4–79.0)	37.4 (28.8–46.0)	14.8 (8.4–21.2)
No	315	59.4 (51.8-67.1)	35.3 (28.0–42.7)	11.2 (6.3–16.2)
Current illicit drug use				
Yes	100	84.2 (76.5–91.8) <sup>‡</sup>	42.8 (27.3–58.3)	20.8 (8.1–33.6)
No	498	61.2 (55.2-67.3)	35.0 (29.1-40.9)	11.3 (7.3–15.3)
Time since HIV diagnosis		× ,	× ,	
<90 mo	254	67.7 (59.4–76.0)	39.4 (30.5-48.2)	15.2 (8.7–21.6)
90+ mo	339	62.6 (55.7–69.4)	32.9 (26.4–39.3)	10.5 (5.9–15.1)
Time since on ART	000	02.0 (00.1 00.1)	02.0 (20.1 00.0)	10.0 (0.0 10.1)
<90 mo	301	68.0 (60.5–75.6)	39.5 (31.3–47.7)	15.0 (9.0–21.0)
< 90 mo 90+ mo		· · · · · · · · · · · · · · · · · · ·		
	294	61.0 (53.5–68.4)	31.7 (24.9–38.5)	10.0 (5.5–14.5)
Missed any medical appointment (6	,			
Yes	151	83.5 (76.4–90.6)*	54.4 (43.7–65.1)*	25.1 (14.5–35.7)
No	447	59.5 (52.9–66.1)	30.7 (24.3–37.1)	9.1 (5.3–12.9)
Any ARV adverse reaction (6 mo)				
Yes	224	70.3 (62.1–78.5)	40.9 (31.1–50.8)	16.2 (8.6–23.8)
No	360	61.7 (54.6-68.9)	33.3 (26.5-40.1)	10.2 (5.8–14.5)

ART = antiretroviral therapy, CI = confidence interval, HIV = human immunodeficiency virus, WebAd-Q = Qualiaids Web Adherence Questionnaire.

"Numbers according to the second component of the study.

<sup>+</sup> Weighted proportions (95% confidence interval).

\* Confidence intervals do not overlap within each variable comparison.

considered nonadherent (24.9%; 95% CI: 23.0–26.9%). Other studies of ART adherence among adult patients in Brazil show large variations in nonadherence rates across the country, varying from 10.7% to 86.0%,<sup>[33,40–57]</sup> depending on study design (e.g., cross-sectional, longitudinal), target populations (e.g., general population, alcohol and drug users, patients initiating ART), measurement tools (e.g., self-reports, pharmacy records, pill counts, patient records), and adherence definitions (e.g., percentage of doses taken, time between medication refills). Similar to international studies,<sup>[58,59]</sup> this methodological heterogeneity limits proper comparison among studies. Results from the subset sample are also corroborated by findings from studies approaching individual barriers to ART adherence, including depression symptoms and illicit drug use.<sup>[60]</sup> Also, missing medical appointments has been consistently associated with worse HIV treatment outcomes<sup>[61–64]</sup> which is in itself an important indicator of nonadherence.<sup>[22,23]</sup> Individual factors associated with nonadherence may vary across facilities and regions, thus demanding specific measures suitable for each scenario. However, contrary to our previous findings,<sup>[65]</sup> there was no clear indicators in this study and differences found between regions are still inconclusive. Further analyses are

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# Table 5

Weighted proportions according to the number of nonadherence indicators by selected characteristics of the subset sample (n=598), Brazil 2010.

		Number of nonadherence indicators				
		Only one	Тwo	All three	At least one	
	n <sup>*</sup>	Wtd% (95% CI) <sup>†</sup>	Wtd% (95% CI) <sup>†</sup>	Wtd% (95% CI) <sup>†</sup>	Wtd% (95% CI) <sup>†</sup>	
Overall	598	28.8 (23.7-34.0)	23.4 (18.4–28.3)	12.9 (8.9–16.9)	65.1 (59.7–70.6)	
Gender						
Male	361	27.8 (20.9-34.6)	23.7 (16.9–30.5)	10.8 (6.0–15.7)	62.3 (55.0-69.7)	
Female	236	30.5 (22.4–38.6)	23.0 (15.8–30.1)	15.9 (9.1–22.6)	69.4 (61.4-77.4)	
Age (years old)		× ,		. ,	, , , , , , , , , , , , , , , , , , ,	
<45	316	29.5 (22.5-36.5)	25.5 (18.2–32.7)	14.5 (8.8–20.2)	69.5 (62.2-76.7)	
45+	282	28.1 (20.3–35.8)	20.8 (14.4–27.2)	10.9 (5.4–16.4)	59.7 (51.6-67.8)	
Skin color		× ,		· · · · · ·	,	
White	266	32.3 (24.5-40.0)	21.4 (13.9-29.0)	8.3 (4.1–12.5)	62.0 (54.6-69.3)	
Nonwhite	331	26.5 (19.5–33.4)	24.6 (18.0-31.2)	16.3 (10.2–22.4)	67.4 (59.6-75.1)	
Schooling (years)	001		2 (1010 0112)			
<8	282	30.5 (23.1–37.8)	25.9 (19.0–32.9)	10.8 (6.1–15.4)	67.2 (59.7–74.6)	
8+	297	25.2 (18.1–32.3)	22.7 (15.0–30.4)	13.4 (7.0–19.9)	61.3 (53.1–70.0)	
Social class (Abep)	201	20.2 (10.1 02.0)		10.1 (1.0 10.0)	01.0 (00.1 70.0)	
A–B	155	22.6 (14.5-30.7)	24.5 (12.4–36.6)	10.6 (2.4-18.8)	57.7 (46.9-68.6)	
C-D-E	437	30.6 (24.3–36.8)	22.6 (17.3–27.9)	13.7 (9.1–18.3)	66.8 (60.5–73.1)	
Depression symptoms	-107	00.0 (24.0 00.0)	22.0 (11.0 21.0)	10.7 (0.1 10.0)	00.0 (00.0 70.1)	
Moderate-severe	90	38.5 (23.7–53.2)	28.4 (15.2–41.7)	24.1 (12.2–36.0)	91.0 (85.3–96.6) <sup>3</sup>	
None-light	505	27.4 (21.9–32.9)	22.1 (16.7–27.4)	11.1 (6.8–15.3)	60.5 (54.4–66.6)	
Anxiety symptoms	505	27.4 (21.5 52.5)	22.1 (10.7 27.4)	11.1 (0.0 10.0)	00.0 (04.4 00.0)	
Moderate-severe	123	38.9 (26.4–51.4)	18.2 (10.8–25.6)	13.4 (6.2–20.7)	70.5 (58.7–82.3)	
None-light	474	26.6 (21.0–32.3)	24.5 (18.8–30.3)	12.8 (8.2–17.4)	64.0 (57.9–70.0)	
Self-rated quality of life	4/4	20.0 (21.0-52.5)	24.3 (10.0-30.3)	12.0 (0.2-17.4)	04.0 (07.9-70.0)	
Good-very good	421	26.0 (20.2-31.8)	22.1 (16.0-28.1)	10.3 (6.2–14.5)	58.4 (51.6-65.1)	
Low-very low	176	33.7 (23.6–43.9)	26.1 (17.3–34.8)	17.8 (9.4–26.2)	77.6 (69.1–86.0)	
Current alcohol use	170	55.7 (25.0 <del>-</del> 45.9)	20.1 (17.5–54.0)	17.8 (9.4–20.2)	77.0 (09.1–00.0)	
Yes	283	34.3 (26.1-42.5)	22.6 (14.9–30.2)	14.8 (8.4–21.2)	71.7 (64.4–79.0)	
No	315	24.1 (17.6–30.6)	24.1 (17.6–30.6)	11.2 (6.3–16.2)	59.4 (51.8–67.1)	
Current illicit drug use	310	24.1 (17.0-30.0)	24.1 (17.0-30.0)	11.2 (0.3–10.2)	39.4 (31.0-07.1)	
Yes	100	41.4 (26.5–56.3)	21 0 (7 6 26 2)	20.8 (8.1–33.6)	04 0 (76 5 01 0)	
No	498	26.3 (20.9–31.7)	21.9 (7.6–36.3) 23.7 (18.5–28.9)	20.8 (8.1–33.0) 11.3 (7.3–15.3)	84.2 (76.5–91.8) 61.2 (55.2–67.3)	
	490	20.3 (20.9–31.7)	23.7 (10.3–20.9)	11.3 (7.3–15.3)	01.2 (00.2-07.0)	
Time since HIV diagnosis <90 mo	254	28.3 (20.2–36.3)	24.3 (16.1–32.5)	15.2 (8.7–21.6)	67.7 (59.4–76.0)	
< 90 mo 90+ mo		(		· · ·	( /	
	339	29.7 (23.1–36.2)	22.4 (17.0–27.8)	10.5 (5.9–15.1)	62.6 (55.7–69.4)	
Time since on ART	201	20 E (21 2 2E 0)	04 E (17 1 01 0)	15.0 (0.0, 01.0)		
<90 mo	301 294	28.5 (21.2-35.9)	24.5 (17.1–31.8)	15.0 (9.0-21.0)	68.0 (60.5–75.6)	
90+ mo		29.3 (22.1–36.4)	21.7 (15.9–27.6)	10.0 (5.5–14.5)	61.0 (53.5–68.4)	
Missed any medical appointr	. ,				00 5 (70 4 00 0)	
Yes	151	29.1 (19.2–39.0)	29.3 (20.3–38.3)	25.1 (14.5–35.7)	83.5 (76.4–90.6)	
No Ann ADV a durant in (C	447	28.8 (22.7–34.9)	21.6 (15.7–27.5)	9.1 (5.3–12.9)	59.5 (52.9–66.1)	
Any ARV adverse reaction (6	/				70.0 (00.4 70.4)	
Yes	224	29.3 (21.0-37.6)	24.7 (15.6–33.9)	16.2 (8.6–23.8)	70.3 (62.1–78.4)	
No	360	28.4 (21.6-35.2)	23.1 (17.1–29.1)	10.2 (5.8–14.5)	61.7 (54.6–68.9)	

ART = antiretroviral therapy, CI = confidence interval, HIV = human immunodeficiency virus.

\* Numbers according to the second component of the study.

<sup>+</sup> Weighted proportions (95% confidence interval).

\* Confidence intervals do not overlap within each variable comparison.

needed to better understand the influence of facility and patient characteristics on the nonadherence indicators.

The WebAd-Q methodology provides data for continuous evaluation of HIV care facilities by measuring ART nonadherence indicators in different dimensions during the 7 days previous to a regular follow-up medical visit. If periodically obtained, WebAd-Q measures could help guide providers in respect to which adherence dimensions tend to be more problematic among their clientele.

The findings of our study must be interpreted with caution due to potential limitations. This was a cross-sectional sample, and direct causal associations and changes in the nonadherence indicators over time among facilities and regions cannot be observed. However, these can be partially overcome if facilities decide to apply the *WebAd-Q* on a regular basis, or through periodic surveys. In addition, we should note that the *WebAd-Q* may not be a direct measure of individual nonadherence. However, it has been shown to be associated with viral load (i.e., indicators of nonadherence were associated with higher viral load) and with traditional adherence measures<sup>[34]</sup> and, thus, can be considered a robust and valid tool for screening nonadherence in HIV care facilities in Brazil. Finally, although the patients answered the *WebAd-Q* anonymously, adherence measures collected in a standardized research protocol may not entirely correspond to measures obtained in routine care, and additional data should be obtained to corroborate the findings, including CD4+ cell counts, viral load, and ARV resistance assays.

In conclusion, the results obtained in this national study represent a worrisome scenario in the public Brazilian HIV care facilities with regard to adherence to ART. On a routine basis, these facilities can identify gaps in providing counseling and ART orientation to their clientele and develop innovative strategies to prevent nonadherence, including training and update workshops of staff.

# **Author contributions**

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#### Acknowledgments

The authors gratefully acknowledge review suggestions of Paul D. Cleary and the T32 Interdisciplinary HIV Prevention Training Program—Center for Interdisciplinary Research on AIDS (CIRA), Yale School of Public Health.

#### References

- Bangsberg DR, Perry S, Charlebois ED, et al. Non-adherence to highly active antiretroviral therapy predicts progression to AIDS. AIDS 2001;15:1181–3.
- [2] Paterson DL, Swindells S, Mohr J, et al. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. Ann Intern Med 2000;133:21–30.
- [3] Gross R, Bilker WB, Friedman HM, et al. Effect of adherence to newly initiated antiretroviral therapy on plasma viral load. AIDS 2001;15: 2109–17.
- [4] Focà E, Odolini S, Sulis G, et al. Clinical and immunological outcomes according to adherence to first-line HAART in a urban and rural cohort of HIV-infected patients in Burkina Faso, West Africa. BMC Infect Dis 2014;14:153.
- [5] Rai S, Mahapatra B, Sircar S, et al. Adherence to antiretroviral therapy and its effect on survival of HIV-infected individuals in Jharkhand, India. PLoS ONE 2013;8:e66860.
- [6] Lima VD, Harrigan R, Bangsberg DR, et al. The combined effect of modern highly active antiretroviral therapy regimens and adherence on mortality over time. J Acquir Immune Defic Syndr 2009;50:529–36.
- [7] Wang H, Zhou J, He G, et al. Consistent ART adherence is associated with improved quality of Life, CD4 counts, and reduced hospital costs in central China. AIDS Res Hum Retroviruses 2009;25:757–63.
- [8] Mannheimer SB, Matts J, Telzak E, et al. Quality of life in HIV-infected individuals receiving antiretroviral therapy is related to adherence. AIDS Care 2005;17:10–22.
- [9] Viswanathan S, Justice AC, Alexander GC, et al. Adherence and HIV RNA suppression in the current era of highly active antiretroviral therapy. J Acquir Immune Defic Syndr 2015;69:493–8.
- [10] Bangsberg DR. Less than 95% adherence to nonnucleoside reversetranscriptase inhibitor therapy can lead to viral suppression. Clin Infect Dis 2006;43:939–41.
- [11] Parienti JJ, Ragland K, Lucht F, et al. Average adherence to boosted protease inhibitor therapy, rather than the pattern of missed doses, as a predictor of HIV RNA replication. Clin Infect Dis 2010;50: 1192–7.
- [12] Nachega JB, Hislop M, Dowdy DW, et al. Adherence to nonnucleoside reverse transcriptase inhibitor-based HIV therapy and virologic outcomes. Ann Intern Med 2007;146:564–73.

- [13] San Lio MM, Carbini R, Germano P, et al. Evaluating adherence to highly active antiretroviral therapy with use of pill counts and viral load measurement in the drug resources enhancement against AIDS and malnutrition program in Mozambique. Clin Infect Dis 2008;46:1609–16.
- [14] Wilson IB, Bangsberg DR, Shen J, et al. Heterogeneity among studies in rates of decline of antiretroviral therapy adherence over time: results from the multisite adherence collaboration on HIV 14 study. J Acquir Immune Defic Syndr 2013;64:448–54.
- [15] Ortego C, Huedo-Medina TB, Llorca J, et al. Adherence to highly active antiretroviral therapy (HAART): a meta-analysis. AIDS Behav 2011; 15:1381–96.
- [16] Thompson MA, Mugavero MJ, Amico KR, et al. Guidelines for improving entry into and retention in care and antiretroviral adherence for persons with HIV: evidence-based recommendations from an International Association of Physicians in AIDS Care panel. Ann Intern Med 2012;156:817–33.
- [17] Amico KR, Zuniga JM, Wilson IB, et al. Provider guidance for linking patients to antiretroviral therapy adherence interventions: recommendations from an IAPAC advisory committee on adherence monitoring and support. J Int Assoc Provid AIDS Care 2013;12:79–83.
- [18] World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. Geneva: WHO; 2013. Available at: http://www.who.int/iris/bitstream/10665/85321/1/ 9789241505727\_eng.pdf?ua=1. Accessed 5 November 2017.
- [19] Centers for Disease Control and Prevention, Health Resources and Services Administration, National Institutes of Health, et al. Recommendations for HIV Prevention with Adults and Adolescents with HIV in the United States, 2014. CDC: Atlanta; 2014. Available at: http://stacks. cdc.gov/view/cdc/26062. Accessed 5 November 2017.
- [20] Bangsberg DR. Preventing HIV antiretroviral resistance through better monitoring of treatment adherence. J Infect Dis 2008;197(suppl 3): S272–8.
- [21] Chalker J, Wagner A, Tomson G, et al. Urgent need for coordination in adopting standardized antiretroviral adherence performance indicators. J Acquir Immune Defic Syndr 2010;53:159–61.
- [22] Chalker JC, Andualem T, Gitau LN, et al. Measuring adherence to antiretroviral treatment in resource-poor settings: the feasibility of collecting routine data for key indicators. BMC Health Serv Res 2010; 10:43.
- [23] Ross-Degnan D, Pierre-Jacques M, Zhang F, et al. Measuring adherence to antiretroviral treatment in resource-poor settings—the clinical validity of key indicators. BMC Health Serv Res 2010;10:42.
- [24] Garfield S, Clifford S, Eliasson L, et al. Suitability of measures of selfreported medication adherence for routine clinical use: a systematic review. BMC Med Res Methodol 2011;11:149.
- [25] Nachega JB, Uthman OA, del Rio C, et al. Addressing the Achilles' heel in the HIV care continuum for the success of a test-and-treat strategy to achieve an AIDS-free generation. Clin Infect Dis 2014;59(suppl 1): S21–7.
- [26] Brazil. Ministry of Health. Health Surveillance Secretariat. STD/AIDS Department. Boletim Epidemiológico HIV/Aids 2015. Brasilia: Ministry of Health; 2015. Available at: http://www.aids.gov.br/pt-br/ pub/2015/boletim-epidemiologico-hivaids-2015. Accessed 5 November 2017
- [27] Brazil. Ministry of Health. Qualiaids Research Team. Qualiaids System. Available at: http://www.qualiaids.fm.usp.br. Accessed 5 November 2017.
- [28] Brazil. Ministry of Health. Health Surveillance Secretariat. STD/AIDS Department. Protocolo Clínico e Diretrizes Terapêuticas para o Manejo da Infecção pelo HIV em Adultos. Brasilia: Ministry of Health; 2013. Available at: http://www.aids.gov.br/pt-br/pub/2013/protocolo-clinicoe-diretrizes-terapeuticas-para-manejo-da-infeccao-pelo-hiv-em-adultos. Accessed 5 November 2017.
- [29] Joint United Nations Programme on HIV/AIDS (UNAIDS). 90-90-90: an ambitious treatment target to help end the AIDS epidemic. Geneva: UNAIDS; 2014. Available at: http://www.unaids.org/sites/default/files/ media\_asset/90-90-90\_en\_0.pdf. Accessed 5 November 2017.
- [30] Brazil. Ministry of Health. Health Surveillance Secretariat. National STD/AIDS Program. Manual de adesão ao tratamento para pessoas vivendo com HIV e Aids. Brasilia: Ministry of Health; 2008. Available at: http://bvsms.saude.gov.br/bvs/publicacoes/manual\_adesao\_tratamento\_ hiv.pdf. Accessed 5 November 2017.
- [31] Brazil. Ministry of Health. Health Surveillance Secretariat. National STD/AIDS Program. Diretrizes para o fortalecimento das ações de adesão ao tratamento para pessoas que vivem com HIV e Aids. Brasilia:

Ministry of Health; 2007. Available at: http://bvsms.saude.gov.br/bvs/ publicacoes/diretrizes\_tratamento\_aids.pdf. Accessed 05 November 2017.

- [32] Caraciolo JMM, Santa-Helena ET, Basso CR, et al. Interventions to enhance HAART adherence in HIV/AIDS health services in the State of Sao Paulo, Brazil, 2007. Saude Soc 2009;18(suppl 2):S79–83.
- [33] Rocha GM, Machado CJ, Acurcio FA, et al. Monitoring adherence to antiretroviral treatment in Brazil: an urgent challenge. Cad Saude Publica 2011;27(suppl 1):S67–78.
- [34] Vale FC, Santa-Helena ET, Santos MA, et al. Development and validation of the WebAd-Q Questionnaire to monitor adherence to HIV therapy. Rev Saude Publica 2018;52: *In press.*
- [35] Brazil. Ministry of Health. Health Surveillance Secretariat. National STD/AIDS Program. Avaliação da assistência ambulatorial aos adultos vivendo com HIV/AIDS. Qualiaids: Relatório 2007/2008. Brasilia: Ministry of Health; 2008. Available at: http://www.qualiaids.fm.usp.br/ aplicacoesanteriores.html. Accessed 5 November 2017.
- [36] Brazil. Ministry of Health. Health Surveillance Secretariat. STD/AIDS Department. SICLOM: Medication Logistics Control System [web homepage]. Available at: http://azt.aids.gov.br/gerencial. Accessed 5 November 2017.
- [37] Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983;67:361–70.
- [38] World Health Organization. Department of Mental Health and Substance Dependence. WHOQOL-HIV Instrument. WHO, 2002. Available at: http://www.who.int/mental\_health/media/en/613.pdf. Accessed 5 November 2017.
- [39] Nemes MIB, Carvalho HB, Souza MF. Antiretroviral therapy adherence in Brazil. AIDS 2004;18(suppl 3):S15–20.
- [40] Brazil. Ministry of Health. Health Surveillance Secretariat. STD/AIDS Department. Adherence to antiretroviral therapy in Brazil: studies collection of the project ATAR. Brasilia: Ministry of Health; 2010. 406 p
- [41] Leite LHM, Papa A, Valentini RC. Body image dissatisfaction and adherence to antiretroviral therapy in people with HIV/AIDS. Rev Nutr 2011;24:873–82.
- [42] Felix G, Ceolim MF. The profile of women with HIV/AIDS and their adherence to the antiretroviral therapy. Rev Esc Enferm USP 2012; 46:884–91.
- [43] Fonseca LC, Martins FJ, Vieira RC, et al. Evaluation of inadequate antiretroviral treatment in patients with HIV/AIDS. Rev Soc Bras Med Trop 2012;45:151–5.
- [44] Gutierrez EB, Sartori AM, Schmidt AL, et al. Measuring adherence to antiretroviral treatment: the role of pharmacy records of drug withdrawals. AIDS Behav 2012;16:1482–90.
- [45] Silveira MP, Guttier MC, Pinheiro CA, et al. Depressive symptoms in HIV-infected patients treated with highly active antiretroviral therapy. Rev Bras Psiquiatr 2012;34:162–7.
- [46] Bonolo FP, Ceccato MGB, Rocha GM, et al. Gender differences in nonadherence among Brazilian patients initiating antiretroviral therapy. Clinics (Sao Paulo) 2013;68:612–20.
- [47] Fiuza MLT, Lopes EM, Alexandre HO, et al. Adherence to antiretroviral treatment: comprehensive care based on the care model for chronic conditions. Esc Anna Nery 2013;17:740–8.

- [48] Teixeira C, Dourado ML, Santos MP, et al. Impact of use of alcohol and illicit drugs by AIDS patients on adherence to antiretroviral therapy in Bahia, Brazil. AIDS Res Hum Retroviruses 2013;29:799–804.
- [49] Batista Jd, Albuquerque MF, Santos ML, et al. Association between smoking, crack cocaine abuse and the discontinuation of combination antiretroviral therapy in Recife, Pernambuco, Brazil. Rev Inst Med Trop Sao Paulo 2014;56:127–32.
- [50] Calvetti PU, Giovelli GRM, Gauer GJC, et al. Psychosocial factors associated with adherence to treatment and quality of life in people living with HIV/AIDS in Brazil. J Bras Psiquiatr 2014;63:8–15.
- [51] Camargo LA, Capitao CG, Filipe EMV. Mental health, family support and treatment adherence: associations in the context of HIV/AIDS. Psico-USF 2014;19:221–32.
- [52] Moraes DCA, Oliveira RC, Costa SFG. Adherence of men living with HIV/AIDS to antiretroviral treatment. Esc Anna Nery 2014;18:676–81.
- [53] Silva AC, Reis RK, Nogueira JA, et al. Quality of life, clinical characteristics and treatment adherence of people living with HIV/ AIDS. Rev Lat Am Enferm 2014;22:994–1000.
- [54] Tufano CS, Amaral RA, Cardoso LR, et al. The influence of depressive symptoms and substance use on adherence to antiretroviral therapy. A cross-sectional prevalence study. Sao Paulo Med J 2015;133:179–86.
- [55] Galvao MTG, Soares LL, Pedrosa SC, et al. Quality of life and adherence to antiretroviral medication in people with HIV. Acta Paul Enferm 2015;28:48–53.
- [56] Padoin SMM, Züge SS, Aldrighi JD, et al. Women in antiretroviral therapy: sociodemographic, behavioral and medication treatment profiling, Santa Maria, Rio Grande do Sul State, Brazil, 2011. Epidemiol Serv Saúde 2015;24:71–8.
- [57] Silveira MP, Maurer P, Guttier MC, et al. Factors associated with therapeutic success in HIV-positive individuals in southern Brazil. J Clin Pharm Ther 2015;40:192–5.
- [58] Simoni JM, Kurth AE, Pearson CR, et al. Self-report measures of antiretroviral therapy adherence: a review with recommendations for HIV research and clinical management. AIDS Behav 2006;10:227–45.
- [59] Williams AB, Amico KR, Bova C, et al. A proposal for quality standards for measuring medication adherence in research. AIDS Behav 2013; 17:284–97.
- [60] Shubber Z, Mills EJ, Nachega JB, et al. Patient-reported barriers to adherence to antiretroviral therapy: a systematic review and metaanalysis. PLoS Med 2016;13:e1002183.
- [61] Mugavero MJ, Lin HY, Willig JH, et al. Missed visits and mortality among patients establishing initial outpatient HIV treatment. Clin Infect Dis 2009;48:248–56.
- [62] Mugavero MJ, Lin HY, Allison JJ, et al. Racial disparities in HIV virologic failure: do missed visits matter? J Acquir Immune Defic Syndr 2009;50:100–8.
- [63] Zhang Y, Dou Z, Sun K, et al. Association between missed early visits and mortality among patients of china national free antiretroviral treatment cohort. J Acquir Immune Defic Syndr 2012;60:59–67.
- [64] Walburn A, Swindells S, Fisher C, et al. Missed visits and decline in CD4 cell count among HIV-infected patients: a mixed method study. Int J Infect Dis 2012;16:e779–85.
- [65] Nemes MI, Castanheira ER, Helena ET, et al. Treatment adherence, access and AIDS assistance quality in Brazil. Rev Assoc Med Bras 2009;55:207–12.