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Intentionality of medication nonadherence among individuals living with HIV/AIDS in Hong Kong

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Abstract

Adherence to antiretroviral therapy is essential to treatment success for individuals living with HIV/AIDS. Despite the wealth of studies in examining antiretroviral nonadherence, few have distinguished between intentional and unintentional nonadherence. The present study attempted to identify factors associated with adherence, intentional nonadherence, and unintentional nonadherence among HIV+ individuals using a longitudinal design. Dietary instructions and medication schedule were also included to measure the subtleties of antiretroviral adherence. One hundred and two HIV+ patients who were under antiretroviral therapy were recruited in an outpatient clinic in Hong Kong at baseline and 6 months follow-up. Using the conventional adherence rate, only 12 (11.8%) of participants reported having missed/ altered medication in the past four days. However, using a more comprehensive assessment, only 27 (26.5%) of participants were classified as adherers. Results showed that adherers were significantly older and had higher adherence self-efficacy than those who were unintentional or intentional nonadherers. Participants classified as unintentional nonadherers had longer length of diagnosis and started medication longer than adherers and intentional nonadherers. Participants classified as intentional nonadherers had worse mental health, higher level of self-stigma, and reported higher score in avoidant coping than adherers and unintentional nonadherers. They also

scored higher in physical symptoms than adherers. Findings highlight the importance of a reliable, comprehensive measurement for adherence and extend on previous adherence literature that intentional and unintentional nonadherence are separate entities and are associated with different factors. Future research should understand the intentions behind nonadherence and this would serve as an important guide in the development of interventions aimed at improving antiretroviral adherence for HIV+ patients.

.ce, uni Keywords: HIV/AIDS, intentional nonadherence, unintentional nonadherence,

antiretroviral therapy, Hong Kong

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Introduction

Antiretroviral therapy in HIV

The advent of antiretroviral therapy has greatly transformed the lives for persons living with HIV/AIDS (PLWA). While antiretroviral therapy has resulted in remarkable decrease in AIDS-related morbidity and mortality (Garcia de Olalla et al., 2002; Jain et al., 2003; Lohse, Hansen, Gerstoft, & Obel, 2007; McNaghten, Hanson, Jones, Dworkin, & Ward, 1999), an extremely high level of adherence (e.g. <95%) is required to guarantee treatment effectiveness due to rapid replication and mutation rate of HIV (Bangsberg et al., 2000; Montaner et al., 1998; Paterson et al., 2000). *Factors associated with antiretroviral adherence*

As adherence to antiretroviral medication is essential for clinical effectiveness, research in this area has burgeoned over the past decades (Chesney, Ickovics, Hecht, Sikipa, & Rabkin, 1999; Ramirez Garcia & Cote, 2003). Review of the literature has identified various factors that are associated with antiretroviral nonadherence. These include the complexity of the regimen, treatment side effects, and disruptive schedules (Battaglioli-DeNero, 2007; M. O. Johnson & Folkman, 2004; M. O. Johnson & Neilands, 2007). Psychosocial factors associated with nonadherence include psychological distress, poor social support, and low self efficacy (Kalichman, Ramachandran, & Catz, 1999; Malcolm, Ng, Rosen, & Stone, 2003; Roberts & Mann,

2000; Schonnesson, Diamond, Ross, Williams, & Bratt, 2006; Sorensen et al., 1998; Wagner, Remien, Carballo-Dieguez, & Dolezal, 2002). HIV-related stigma is also associated with poorer adherence (Pryor, Reeder, & Landau, 1999; Remien & Rabkin, 2001; Ware, Wyatt, & Tugenberg, 2006). Despite the research endeavors in identifying factors associated with nonadherence, adherence to antiretroviral therapy remains suboptimal. The prevalence of nonadherence ranges from less than 80% to as low as 3%, depending on different operational definitions, studying populations, and methodologies (Walsh, Dalton, & Gazzard, 1998).

Intentionality of antiretroviral nonadherence

One reason for less than optimal adherence might be the failure of studies in distinguishing between intentional and unintentional nonadherence. It is suggested that intentional and unintentional nonadherence are separate entities and they occur for different reasons (Lehane & McCarthy, 2007b; Wroe, 2002). Studies in various health conditions showed that whereas concerns about side effects, stigma associated with medications, and perceiving the medication as unnecessary were associated with intentional nonadherence, cognitive impairments, access to medications, interruptions in one's patterns of medication intake, and forgetfulness were associated with unintentional nonadherence (Ayalon, Arean, & Alvidrez, 2005; M. J. Johnson, Williams, & Marshall, 1999; Lehane & McCarthy, 2007a; Remien et al., 2003; Wroe,

2002). One study in HIV/AIDS also highlighted that severe symptoms were associated with intentional nonadherence (Heath, Singer, O'Shaughnessy, Montaner, & Hogg, 2002). Despite this, intentionality of nonadherence in HIV/AIDS has received very little attention.

Measuring nonadherence

Medication adherence is a complex concept that requires detailed, sophisticated assessment (Hill, Kendall, & Fernandez, 2003; Hugen et al., 2002; Samet, Sullivan, Traphagen, & Ickovics, 2001; Sankar, Nevedal, Neufeld, & Luborsky, 2007; Wilson, Tchetgen, & Spiegelman, 2001). However, majority of studies have focused only on the administration of prescribed dose, and have classified participants into adherers or nonadherers based on whether they take a certain percentage of prescribed medication during a time period (Catz, Kelly, Bogart, Benotsch, & McAuliffe, 2000; Chesney et al., 2000; Garcia de Olalla et al., 2002; Knobel et al., 2002). Despite the fact that adherence to instructions regarding dietary requirements, amount and schedule of medications, and lifestyle habits may also substantially influence the efficacy of medication regimens (Altice & Friedland, 1998; Murphy, Marelich, Hoffman, & Steers, 2004; Stone et al., 2001), they have not been well incorporated into the measurement of medication adherence. One recent study employed a more extensive measurement by including more aspects of adherence and found this to be valid and

reliable (Reynolds et al., 2007). Ideally, these perspectives should be assessed along with the amount of prescribed medications taken.

The present study

The present study aimed to identify factors associated with adherence, intentional nonadherence, and unintentional nonadherence among PLWA in Hong Kong using a more extensive measurement of adherence. Comprehensive, feasible and accurate measures of adherence are important to identify patients who do not adhere to medication for various reasons and to design and evaluate interventions to improve medication adherence among PLWA.

Methods

Procedure

Participants were recruited at the AIDS outpatient clinic in Hong Kong. Potential participants were identified by nurses and were approached by a trained interviewer. Inclusion criteria included: 1) aged 18 years or older; 2) having been tested HIV-positive for at least one month; 3) being currently on antiretroviral medication. Interested participants were invited to for a structured interview. Based on their dates of next medication appointment, participants were followed up approximately six months after the initial interview. Upon completion of each interview, participants were given a supermarket voucher of HK\$50 (approx. US\$6.40) as a token of

appreciation. The study has been approved by the local Institutional Review Board prior to commencement.

Measures

The following measures were administered at Time 1:

Adherence Self-efficacy. Adherence self-efficacy was measured by a single item from the AIDS Clinical Trial Group (ACTG) adherence measure(Chesney et al., 2000). Item was measured on a 4-point Likert Scale ranging from 0 to 4, with higher scores showing higher self-efficacy. In the present study, participants who scored 4 were classified as reporting high level of self-efficacy.

Self-Stigma. A self-stigma scale was used to assess the level of perceived stigma of participants (Mak et al., 2007). It is a 22-item scale which measures three dimensions of self-stigma (affective, behavioral, and cognitive). Responses are rated on a 6-point Likert scale ranging from 1 to 6, with higher scores indicating greater level of self-stigma. The Cronbach's alpha of the scale was .87 in the present study.

Coping. Coping was measured by the Brief COPE, a 28-item scale that measures 14 types of cognitive or behavioral coping processes (Carver, 1997; Carver, Scheier, & Weintraub, 1989). Items were measured on a 4-point Likert Scale ranging from 1 to 4, with higher score indicating greater use of the coping strategies. In the present study, items were grouped into three subscales: problem-focused,

emotion-focused, and avoidant coping (Carver et al., 1989). The Cronbach's alphas of the three subscales were .71, .73, and 81, in the present study.

Mental health. The 38-item Mental Health Inventory (MHI) was used to assess the level of mental health of participants (Veit & Ware, 1983). Items are rated on a 6-item scale ranging from 1 to 6, with higher score indicating better mental health. The Cronbach's alpha of the scale was .82 in the present study.

Physical symptoms. Physical symptoms were assessed by a 20-item checklist developed by Folkman and colleagues (Folkman, Chesney, Collette, Boccellari, & Cooke, 1996). A 5-point Likert scale ranging from 0 to 4 was provided for each item, with higher scores indicating more severe physical symptoms. The Cronbach's alpha of the scale was .81 in the present study.

The following measure was administered at Time 2.

Medication Adherence. The ACTG adherence measure (Chesney et al., 2000) was adopted and modified for the purposes for the present study. Participants were asked to list the details of medications they were currently prescribed and the time and dosage of medications they have taken in the past four days. Additional questions asked participants how well they followed the dietary instructions, whether they always remembered to take their medication, and whether they skipped medication over the past weekend. Participants were also asked to rate their frequency of missing

medication and frequency of taking doses 2 hours earlier or later. Participants who reported ever skipping or alternating medications were presented with a list of reasons why people may miss taking medications and were asked to choose the reason(s) that applied to them.

Results

Participants

Out of the 126 participants who have completed the initial interview, one hundred and two participants (81.0%) completed the follow-up interview. The mean lapse between the initial and follow-up interview was 6.89 months (SD = 1.88). Majority of the participants were male (87.3%).Their mean age was 41.9 years (SD =10.04). More than two-thirds of them (70.0%) were in advanced AIDS stage and they have been diagnosed for an average of 5.18 years (SD = 3.24). The mean reported daily pill count was 7.09 (SD = 3.52).

To assess whether the participants who were retained in the follow-up differed from those who are lost, Chi-square tests and independent *t*-tests were conducted on major demographic and medical factors measured at Time 1. Results showed no significant difference on major demographic and medical variables, with the exception that participants who were retained had slightly lower CD4 count (338.05

cells/mm³) than those who were lost (436.04 cells/mm³). The demographic and medical information of participants are presented in Table 1.

Rate of medication adherence

The conventional adherence rate, calculated by the number of missing doses divided by number of does prescribed, was very high, with only twelve participants (11.8%) reported having missed doses in the past four days. However, when asked whether they always remembered to take their medication, only 74 (72.5%) reported 'always' and an additional 10 (9.8%) reported 'most of the time'. When asked how often they missed taking their medication, only 34 (33.3%) reported 'never' and 43 (42.2%) reported 'seldom'. Also, when asked how often they take medications two hours earlier or later, only 28 (27.5%) reported 'never' and 34 (33.3%) reported 'seldom'. Finally, when asked when was the last time they missed medication, 8 (7.8%) reported that it was within the past week, 11 (10.8%) 1-2 weeks ago, 11 (10.8%) 2-4 weeks ago, 12 (11.8%) 1-3 months ago, 16 (15.7%) more than three months ago, and 40 (39.2%) reported they never skip or miss medication.

To account for dietary instructions and alternating doses in medication adherence, participants who reported remembering taking medication most of the time; and following the time and dose of medications and their dietary instructions most of the time in the past 4 days; not having skipped medication over the past weekend; and

rarely missing or alternating doses were classified as *adherers*. Participants who were not classified as adherers were further divided as *intentional nonadherers* or *unintentional nonadherers* based on their reason of missing medications (refer to the following section). Using the above criteria, only 27 (26.5%) participants were classified as adherers and 75 (73.5%) were classified as nonadherers.

Factor analysis of reason for medication nonadherence

To determine the factor structure of medication nonadherence, exploratory factor analysis was conducted on the reasons for missing medication. Results from exploratory factor analysis, using the maximum likelihood estimation method, produced a 2-factor solution (Table 2). Specifically, feeling good for not taking pills, avoiding side effects, feeling difficult for taking pills at specific time, and having too many pills to take were loaded on factor 1, while being away from home, out of pills, being busy with other things, forgetting, having slept, and not feeling well were loaded on factor 2.

Based on the result of factor analysis, participants who have chosen higher proportion of reasons listed in factor 1 were classified as intentional nonadherers, while those who have chosen higher proportion of reasons listed in factor 2 were classified as unintentional nonadherers. Using the above criteria, 53 (52.0%) participants were classified as unintentional nonadherers, while 21 (20.6%) participants were classified as intentional nonadherers.

Difference in demographic and medical status between groups

Results from one-way ANOVA revealed significant group difference on age, F(1,100) = 4.94, *p*<.01. Post hoc analysis showed that adherers were significantly older at baseline. In addition, results of Kruskal-Wallis tests indicated significant group differences on time since starting medication, H(2) = 9.06, *p*<.01, and length of diagnosis, H(2) = 11.72, *p*<.05. Follow up Mann-Whitney U tests showed that unintentional nonadherers had longer length of diagnosis and have started medication longer.

Difference in psychosocial variables between groups

Result from one-way ANOVA showed significant group difference on self-stigma, F(1, 100) = 7.58, p < .001, avoidant coping, F(1, 100) = 5.09, p < .01, physical symptoms, F(1, 100) = 3.08, p < .05, and mental health, F(1, 100) = 6.25, p < .001. Post hoc analyses revealed that intentional nonadherers had significantly higher level of stigma and avoidant coping, and worse mental health than unintentional nonadherers and adherers at baseline. They also reported significantly more severe physical symptoms than adherers. In addition, results from chi-square test showed a significant group difference in adherence self-efficacy, χ^2 (2) = 19.08, p < .001. Follow up analyses indicated that while all adherers reported high level of

adherence self-efficacy, only slightly more than half of unintentional nonadherers (55%) and intentional nonadherers (52.5%) showed high level of adherence self-efficacy.

Discussion

Factors associated with adherence

The present study aimed to examine factors associated with antiretroviral adherence, intentional nonadherence, and unintentional nonadherence among PLWA in Hong Kong. Participants who were older at baseline tended to report excellent adherence at follow-up. It is important to note that while previous studies suggested that older age was associated with cognitive dysfunction that might result in poor adherence rate (Cherner et al., 2004; Chesney et al., 2000; Hardy et al., 1999), the mean age of the participants in the present study were under 50s and age-related declines in cognition do not typically start at that age. In fact, older age and its association with better adherence have been documented in recent literature (Barclay et al., 2007; Hinkin et al., 2002; Hinkin et al., 2004; Solomon & Halkitis, 2008). As excellent adherence rate would require strict adherence to dietary, dosage, and time restrictions, participants at older age may need less alternation in their daily activities or lifestyles to accommodate to such restrictions or find alternations in lifestyle less troublesome. Therefore, they may be more able to follow the instructions and be more likely to show excellent adherence to medication.

Participants who had excellent adherence also showed high level of self-efficacy regarding adherence to medication. It is conceivable that patients who believed that they could follow the medication regimen would report excellent adherence rate (Barclay et al., 2007; Molassiotis et al., 2002; Wolf et al., 2007). Result suggests that interventions should not just focus on practicing adherence behaviors, it is also important to increase their belief in their ability to follow the medication regimens (Battaglioli-DeNero, 2007; Chesney et al., 2000).

Factors associated with unintentional nonadherence

In the present study, participants with longer length of diagnosis and started medication longer at baseline were more likely to be classified as unintentional nonadherers at follow up. This is consistent with studies suggesting that adherence rate among patients decrease over time (Barclay et al., 2004; Deschamps et al., 2004; Mannheimer, Friedland, Matts, Child, & Chesney, 2002). One possible explanation may be the gradual decrease in motivation in adhering to the medication. It can also be assumed that the longer one is diagnosed and on medications, the more likely that they will experience lifestyle disruptions that inevitably affect their medication taking. *Factors associated with intentional nonadherence*

Participants who were classified as intentional nonadherers had significantly poorer mental health, higher level of self-stigma, and reported higher use of avoidant

coping strategies at baseline. Participants with poorer mental health might have poor access to health care, or have less ability in integrating complex medication regimens into their daily activities (Ickovics et al., 2001; Tucker et al., 2004). In addition, while taking medication in the public may signify a person's serostatus status, individuals with high level of stigma may skip their medication to avoid disclosure of serostatus (Edwards, 2006; Ware et al., 2006).

The finding that avoidant coping is associated with intentional nonadherence is in line with previous literature (Halkitis, Parsons, Wolitski, & Remien, 2003; Singh et al., 1999; Weaver et al., 2005). Individuals who use avoidant coping strategies may choose to escape the stressors when dealing with the disease and therefore, be less likely to take an active role in their medication management. In contrast, the use of approach coping (problem-focused and emotion-focused coping) strategies was not related to adherence. This suggests that minimizing the use of avoidant coping strategies should the prioritized in improving antiretroviral adherence rate.

Participants with more severe physical symptoms at baseline were more likely to be intentional nonadherers compared to adherers. Result is consistent with previous study that physical symptoms were related to poorer adherence (Ammassari et al., 2001; Gonzalez et al., 2007; Holzemer et al., 1999). Since avoiding side effects represented a factor of intentional nonadherence, it could be conjectured that

participants might discontinue their medication to minimize the severity of symptoms. It would also be possible that physical limitations caused by symptoms made participants difficult in following the medication regimen.

Limitations of the study

Antiretroviral adherence was assessed using self-report measure in the present study. There has been discussion that self-report assessment might underestimate the nonadherence rate compared to other objective measures, such as pill counts, Medication Events Monitoring System (MEMS), pharmacist report, or biological markers (Chesney et al., 1999; Samet et al., 2001). Future studies should seek to assess adherence rate using multiple measures (Hill et al., 2003). In addition, nonadherence in the present study was defined by a new set of more extensive, arbitrary criteria. Although this is believed to be a more comprehensive measure for nonadherence, more studies are needed to test the validity of this new measure. Nevertheless, it is important to point out that a similar approach of measuring nonadherence was employed by recent study (Reynolds et al., 2007) and was proved to be reliable.

Implications and conclusions

Results of the present study highlight the need of a more comprehensive measurement of antiretroviral adherence, and the importance of distinguishing the

reasons behind intentions for nonadherence and targeting different variables for patients who may not adhere to medication due to different reasons. To minimize intentional nonadherence, intervention should target on symptom control, improving patients' mental health, stigma reduction, and reducing the use of avoidant coping strategies. Education is also warranted to remind adherence among patients with longer length of diagnosis and medication history to minimize unintentional nonadherence. To promote adherence behavior, improving self-efficacy in medication taking would be particularly vital. Individualized assessment and tailored education would be important to remove the specific barriers to adherence and to increase general antiretroviral adherence rates.

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Retained Participants				Participa	Difference	
()	n = 102)	(n = 25)	groups		
Μ	SD	%	Μ	SD	%	0
41.85	10.04		40.80	5.83		t(124) = .50
						$\chi^2(1) = .72$
		87.3			80.8	
		12.7			19.2	
						$\chi^2(3) = 4.53$
		12.8			28.0	
		68.8			64.0	
		16.7			8.0	
		2.0			0.0	
						$\chi^2(2) = .72$
		49.4			53.8	
		36.7			38.5	
		13.9			7.6	
5.18	3.24		5.88	2.63		t(123) =99
						$\chi^2(2) = .48$
		12.0			12.0	
		18.0			24.0	
		70.0			64.0	
338.0	210.7		436.0	224.7		t(123) = -2.06*
1.70	1.08		2.0	1.96		t(123) = -1.03
	Retaine (/ M 41.85 5.18 5.18 338.0 1.70	Retained Partici (n = 102) M SD 41.85 10.04 5.18 3.24 338.0 210.7 1.70 1.08	Retained Participants $(n = 102)$ $\%$ MSD $\%$ 41.8510.0487.312.712.868.816.72.049.436.73.245.183.2412.018.070.0338.0210.71.701.08	Lost $(n = 102)$ $(n = 102)$ M SD $\%$ M 41.85 10.04 40.80 41.85 10.04 40.80 87.3 12.7 12.8 12.8 68.8 16.7 2.0 49.4 36.7 3.24 5.88 13.9 5.18 3.24 5.88 12.0 18.0 70.0 338.0 210.7 436.0 1.70 1.08 2.0	Lost Participate $(n = 102)$ $(n = 25)$ MSD%MSD41.8510.0440.805.8341.8510.0440.805.8312.712.887.312.712.868.816.72.049.436.713.95.183.245.882.6312.012.018.070.0338.0210.7436.0224.71.701.082.01.96	Lost Participants $(n = 102)$ $(n = 25)$ M SD % M SD % 41.85 10.04 40.80 5.83 80.8 12.8 87.3 12.7 80.8 19.2 12.8 28.0 68.8 64.0 16.7 8.0 16.7 2.0 0.0 0.0 0.0 0.0 5.18 3.24 5.88 2.63 7.6 5.18 3.24 5.88 2.63 12.0 18.0 24.0 24.0 24.0 70.0 436.0 224.7 12.0 338.0 210.7 436.0 224.7 1.06

Table 1. Demographics and medical status of retained and lost participants as measured at Time 1.

* *p*<.05, ** *p*<.01, *** *p*<.001



	F1	F2
Factor 1 (19.8% of total variance explained)		
Feeling good for not taking pills	.71	
Avoiding side effects	.68	
Feeling difficult for taking pills at specific time	.52	
Having too many pills to take	.35	
Factor 2 (14.8% of total variance explained)		
Being away from home without pills		.62
Out of pills		.56
Being busy with other things		.48
Forgetting		.46
Having Slept		.41
Not feeling well		.31

Table 2.	Factor	analysis	of rea	asons for	medication	nonadherence
1 4010 2.	I GOLOI	and join	01 100	100110 101	moutoutom	momaanerenee

Variables at Time 1	adherer (<i>n</i> =2		(n=27) Unintentional nonac (n=53)			nadherer	Intenti	onal nona (<i>n</i> =21)	adherer	Difference between groups	
	Μ	SD	%	Μ	SD	%	Μ	SD	%		Post hoc
Demographic information											
Age	46.77	11.90		40.83	8.28		38.43	10.09		F(1,100) = 4.94 **	A>I. A>U
Gender											
Male			88.9%			86.8%			85.7%	$\chi^2(2) = .12$	-
Female			11.1%			13.2%			14.3%		
Education										$\chi^2(4) = 2.94$	-
Primary school or below			66.7%			81.1%			66.7%		
Secondary school			7.4%			5.7%			9.5%		
College			25.9%			13.2%			23.8%		
Graduate school or above											
Marital status											
Single			34.6%			49.1%			71.4%	$\chi^2(4) = 6.61$	-
Married/cohabited			46.2%			35.8%			23.8%		
Separated/divorced/widowed			19.2%			15.1%			4.8%		
Medical Status											
Disease stage during time of study										$\gamma^{2}(A) = 4.54$	_
Asymptomatic			37%			13.2%			21.1%	χ (+) = +.5+	
Symptomatic			25.9%			15.2%			15.8%		
AIDS			20.9%			13.1 % 71 7%			63.2%		
CD4 count (in cells/mm ³)	264.15	123.72	/0.1/0	377.45	244.78	/ 1./ /0	332.26	190.23	03.270	F(1.99) = 2.67	_
No. of physical complications	1.96	.94		1.74	1.16		1.26	.93		F(1,99) = 2.45	-
¥ ¥ _	Median		Median			Median					
Time since starting medication (in years)	3.25			6.58			4.50			H(2)=9.06**	U>A, U>I
Length of diagnosis (in years)	3.	83		6	.67		4.	67		H(2)=11.72**	U>A, U>I

Table 3 Difference in demographic and medical status between groups as measured at Time 1

Time 1 Variables	adherer (<i>n</i> =27)			Uninte	entional no $(n-53)$	nadherer	Intentional nonadherer $(n-21)$			Difference betwee	en groups
	М	SD	%	М	(<i>n</i> =33) SD	%	М	(n-21) SD	%		Post hoc
Self-stigma	3.78	.96		3.22	.92		4.11	.74		$F(1, 100) = 7.58^{***}$	I>A, I>U
Emotion-focused coping	2.64	.49		2.58	.45		2.71	.39		F(1, 100) = .57	-
Problem-focused coping	2.46	.70		2.59	.59		2.70	.37		F(1, 100) = 1.03	-
Avoidant coping	1.94	.09		2.04	.06		2.36	.09		F(1, 100) = 5.09 **	I>A, I>U
Physical symptoms	.88	.77		1,11	.74		1.43	.79		F(1, 100) = 3.08*	I>A
Mental health	4.62	.77		4.49	.70		3.90	.81		$F(1, 100) = 6.25^{**}$	A>I, U>I
Adherence self-efficacy											
% of participants with high			100			52.8			55.0	$\chi^2(2) = 19.08^{***}$	A>I, A>U
adherence self-efficacy											

Table 4 Difference in psychosocial variables between groups as measured at Time 1