Investigating the potentially important role of psychological flexibility in adherence to antiretroviral therapy in people living with HIV

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Abstract:

Antiretroviral therapy (ART) has significantly improved immune health and survival rates in HIV, but these outcomes rely on near perfect adherence. While many psychosocial factors are related to sub-optimal adherence, effectiveness of associated interventions are modest or inconsistent. The Psychological Flexibility (PF) model underlying Acceptance and Commitment Therapy (ACT) identifies a core set of broadly applicable transdiagnostic processes that may be useful to explain and improve non-adherence. However, PF has not previously been examined in relation to ART adherence. Therefore, this cross-sectional study (*n*=275) explored relationships between PF and intentional/unintentional ART non-adherence in people with HIV. Adults with HIV prescribed ART were recruited online. Participants completed online questionnaires assessing self-reported PF, adherence and emotional and general functioning. Logistic regressions examined whether PF processes were associated with intentional/unintentional non-adherence. Fifty-eight percent of participants were classified as nonadherent according to the Medication Adherence Rating Scale, of which 41.0% reported intentional and 94.0% unintentional non-adherence. Correlations between PF and adherence were small. PF did not significantly explain intentional/unintentional non-adherence after controlling for demographic and disease factors. Further clarification of the utility of PF in understanding ART non-adherence is warranted using prospective or experimental designs in conjunction with more objective adherence measures.

Keywords:

HIV AIDS, adherence, antiretroviral treatment, psychological flexibility, acceptance and commitment therapy (ACT).

1. Introduction

The human immunodeficiency virus (HIV) remains a global health concern (UNAIDS, 2014; WHO, 2014). Antiretroviral therapy (ART) slows disease progression and reduces transmission, being widely available in well-resourced countries (Ambrosioni, Calmy, & Hirschel, 2011; Ingersoll & Cohen, 2008; Jones, Taylor, Wilkin, & Hammer, 2007). However, on average people living with HIV (PLWHIV) only take around 70% of prescribed doses (Malta, Strathdee, Magnanini, & Bastos, 2008; Simoni et al., 2006).

Individual, treatment and healthcare provider factors contribute to ART non-adherence (García & Côté, 2003). Common ART side-effects (Raines, Radcliffe, & Treisman, 2005) do not consistently correlate with non-adherence (Carrieri et al., 2006; Harzke et al., 2004; Molassiotis et al., 2002). Rather, studies show a wide range of psychosocial factors share small to medium associations with ART non-adherence (Catz, Kelly, Bogart, Benotsch, & McAuliffe, 2000; Gonzalez, Batchelder, Psaros, & Safren, 2011; Harzke et al., 2004; Ingersoll & Heckman, 2005; Ironson et al., 2005; Katz et al., 2013; Langebeek et al., 2014; Molassiotis et al., 2002; Ortego et al., 2011; Uthman, Magidson, Safren, & Nachega, 2014). Most variables included in these studies are guided by Social cognitive models (SCM), which theorise that non-adherence is driven by intentions and beliefs about illness and treatments (Munro, Lewin, Swart, & Volmink, 2007). Growing evidence suggests that such models lack explanatory power in predicting ART adherence (Brandes & Mullan, 2014; Horne et al., 2013; Rich, Brandes, Mullan, & Hagger, 2015). Therefore, unsurprisingly, SCM-informed

treatment trials aiming to improve adherence also show inconsistent/modest efficacy (Binford, Kahana, & Altice, 2012; Chaiyachati et al., 2014; Conn, Ruppar, Enriquez, & Cooper, 2016). It has been theorised that this is because such models underestimate the impact of emotional, behavioural, motivational and wider socio-economic contextual processes on adherence (Michie, Van Stralen, & West, 2011). Further, it has been argued that SCMs are better placed to explain intentional rather than unintentional non-adherence (i.e. forgetting (Lehane & McCarthy, 2007)), where adherence depends on conscious costs-benefit expectations/evaluative processes (Edwards, 1954). Although unintentional non-adherence could be due to impaired memory, it might also reflect a socially desirable response, change in mood, disease and treatment burden or access (Lehane, 2007; Molloy, 2014). Therefore, disentangling causes of intentional/unintentional non-adherence may be challenging (Gadkari & McHorney, 2012).

The Psychological Flexibility model (PF) (Hayes, Strosahl, & Wilson, 1999) provides an alternative behavioural/psychosocial framework to understand ART non-adherence stemming from philosophical assumptions and basic theory that are distinct from SCMs (Hayes, Barnes-Holmes, & Roche, 2001; Vilardaga, Hayes, & Schelin, 2007). Described as a transdiagnostic theory of "normal" human behaviour (McCracken & Morley, 2014), PF incorporates emotional, motivational and attentional processes that may be lacking in SCM. PF is "the capacity for an individual to persist with, or change, behaviour in a manner that includes conscious and open contact with thoughts and feelings, appreciates what situations afford, and serves one's goals and values" (Scott & McCracken, 2015, p.91). PF incorporates six interacting sub-processes, including 'mindfulness and acceptance' and 'motivational'

elements: Acceptance, defusion, self-as-context, present moment awareness, values and committed action (Hayes, Luoma, Bond, Masuda, & Lillis, 2006).

Psychological *inflexibility* could explain intentional and unintentional non-adherence to ART. According to Hayes et al.'s (2011) "Open, Aware, and Active/Engaged" facets, PLWHIV may lead a person to behavioural patterns that contribute to non-adherence:

(i) Avoid situations, thoughts, feelings or bodily sensations ("Closed") to reduce/eliminate side-effects or anxiety and/or shameful thoughts and feelings related to taking ART.

(ii) Become overly influenced by difficult thoughts and feelings related to ART, unable to take a different perspective ("Unaware"), dwelling on life before their diagnosis and worrying about the future.

(iii) Fail to identify and pursue valued life directions/goals, and instead persist in unhelpful behaviour ("Inactive/Disengaged"), such as skipping doses and not connecting with how adhering might serve their long-term values/goals (e.g., being independent).

Arguably, experiential avoidance and lack of present moment awareness could occur in and outside of conscious awareness. Therefore, PF does not distinguish between intentional/unintentional non-adherence. PF assumes that effective action, e.g., being adherent, can happen despite difficult thoughts or feelings, low self-efficacy, or contradicting illness/treatment beliefs. HIV studies indicate PF is strongly associated with better self-reported illness management, mental health and quality of life (Chartier et al., 2010; Delaney & O'Brien, 2012; Landstra, Ciarrochi, Deane, & Hillman, 2013).

Acceptance and Commitment Therapy (ACT) is the treatment approach most directly focused on increasing PF (Hayes et al., 2006). Rather than modifying content, frequency or intensity of beliefs or feelings typical of traditional cognitive-behaviour therapy and SCM-informed approaches (Conn et al., 2016; Easthall, Song, & Bhattacharya, 2013), ACT helps to decrease their literal influence and set current behaviour against a person's values to encourage a more Open, Aware and Engaged stance (Hayes, Levin, Plumb-Vilardaga, Villatte, & Pistorello, 2013). Consequently, clarity of an individual's informed decisions about treatment could be enhanced. For example, willingness to experience side-effects or negative thoughts about ART, alongside valued-goals around "being healthy", may facilitate adherence.

Evidence supporting ACT for improved general/social functioning has grown in LTCs (Graham, Gouick, Krahé, & Gillanders, 2016; Hann & McCracken, 2014). A small, uncontrolled ACT feasibility trial for PLWHIV shows trends towards reductions in viral load and increases in $CD4^+$ counts post-treatment (Moitra, Herbert, & Forman, 2011). ACT may improve engagement in medical care for newly diagnosed PLWHIV (Moitra, Chan, & Stein, 2015) and reduce stigma (Skinta, Lezama, Wells, & Dilley, 2014). While one study (Berghoff et al., 2018) has identified small relationships between experiential avoidance, non-adherence and strained patient–provider interactions, few have examined other PF subprocesses, intentional/unintentional non-adherence and general functioning.

1.1. Study aims and hypotheses

This study examined the associations between components of PF, self-reported adherence and general functioning. Current evidence suggests an interaction between non-adherence, cognitive impairment, depression and regimen complexity (Hinkin et al., 2002). Therefore, examining PF processes in explaining non-adherence and HIV-related functioning, independent of these variables is important. The following hypotheses were tested:

(i) PF components will be positively associated with adherence, independent of demographic and illness characteristics.

(ii) PF components will be positively associated with general functioning.

2. Materials and methods

This international cross-sectional survey (Bristol Online Surveys) recruited *n*=283 PLWHIV 18+ years of age currently prescribed ART (July 2016-2017). The study was approved by Research Ethics Committee King's College London (August 2016: HR-15/16-2496). Informed consent was obtained online. Participants were recruited via online HIV organisations, charities, Facebook and Twitter, identified through NAM AIDSMAP e-atlas (http://www.aidsmap.com/e-atlas). The NAM AIDSMAP e-atlas database includes HIV-

related charities and organisations globally. Eight cases were excluded (underage (*n*=1), not prescribed ART (*n*=4), incomplete survey (*n*=3).

2.1. Measures

2.1.1. Self-reported medication adherence measure

The *Medication Adherence Report Scale (MARS-5)* (Horne, Hankins, & Jenkins, 2001) measures medication-taking behaviour. The MARS-5 shows good internal reliability and test-retest reliability (α=0.83) in other long-term health conditions (LTCs) (Salt, L, Peden, & Horne, 2012), despite showing mixed associations with more objective adherence measures (Jónsdóttir et al., 2010; Tommelein, Mehuys, Van Tongelen, Brusselle, & Boussery, 2014). It has not yet been used with PLWHIV, but unlike other scales distinguishes intentional/unintentional non-adherence (Chesney et al., 2000; Morisky, Green, & Levine, 1986). Adherence was defined as a score of 25 (100%). Unintentional non-adherence reflected a subscale-score <5 and intentional non-adherence a subscale-score <20 (de Vries et al., 2014; Moon, Moss-Morris, Hunter, & Hughes, 2017).

2.1.2. Psychological flexibility processes

Currently, there is no single measure that assessed all PF processes. Therefore, validated self-reported instruments assessed the “Open, Aware, and Active” facets (Hayes et al., 2011).

The *Acceptance and Action Questionnaire (AAQ-II)* measures experiential avoidance with good validity/reliability (Bond et al., 2011; Fledderus, Oude Voshaar, ten Klooster, & Bohlmeijer, 2012). Higher scores reflect greater psychological inflexibility.

The *Committed Action Questionnaire (CAQ-8)* (McCracken, Chilcot, & Norton, 2015) has shown promising validity/reliability in chronic pain (McCracken et al., 2015). Higher scores reflect greater committed action.

The *Short Form Experiences Questionnaire (SF-EQ)* assesses cognitive defusion and self-as context processes with good psychometric properties in people with chronic pain (McCracken, Barker, & Chilcot, 2014). Higher scores indicate better cognitive defusion/self-as-context.

2.1.3. Demographic and disease variables

Demographic and disease factors may be related to a person's level of ART adherence (Carrieri et al., 2006). Age, ethnicity, gender, sexual orientation, education level, current employment, relationship status and time since diagnosis were included. The *British Columbia Cognitive Complaints Inventory* (BC-CCI) (Iverson & Lam, 2013) was used to rate perceived common cognitive impairments during the past week (Steinbrink et al., 2013). A preliminarily validation demonstrated good internal consistency. Higher scores indicate worse impairment.

2.1.4. Mood

The *Patient Health Questionnaire (PHQ-4)* recorded self-reported symptoms of anxiety/depression (Kroenke, Spitzer, Williams, & Löwe, 2009) and has acceptable psychometric properties (Löwe et al., 2010). Higher scores indicate greater distress.

2.1.5. Functioning

The *Work and Social Adjustment Scale (WSAS)* (Mundt, Marks, Shear, & Greist, 2002) measured everyday life interference caused by HIV. Higher scores indicate worse illness adjustment. The WSAS demonstrates high internal consistency (Mundt et al., 2002). Established cut-offs were not used because a scaling error occurred.

2.2. Statistical analyses

All continuous variables were checked for normality violations (George and Mallery, 2010). The MARS-5 total score (Skewness=-3.24, SE=.17; Kurtosis=13.37, SE=.34) and intentional sub-scale distributions (Skewness=-3.77, SE=.15; Kurtosis=4.29, SE=.04) were both highly negatively skewed. Therefore, established binary cut-offs were used. Pearson's correlations, t-tests and ANOVAs (and non-parametric equivalents: Cramer's *V* for categorical variables, Pearson biserial correlations p_b for continuous variables) examined associations or differences between the MARS-5 total and intentional/unintentional non-adherence scores with participant demographic, disease and PF predictors.

Multiple binomial regressions examined relationships between PF sub-processes and intentional/unintentional non-adherence, after controlling for demographic and disease variables. Demographic and disease variables significantly related with non-adherence (p<.05) at the bivariate level were entered in the first step of the models. PF processes were entered in the following step. The proportion of explained variance was assessed using Nagelkerke R^2 (pseudo R^2). The -2 Log Likelihood statistic (-2LL) assessed model fit. Cases were excluded if ≥20.0% scale item data were missing. Diagnostic checks confirmed the validity of all regression models. Analyses were conducted using SPSS Version 24.

2.3. A priori power analysis

No previous studies investigated relationships between PF and self-reported adherence in PLWHIV. Therefore, an *a priori* power analysis using G*Power version 3.1.9.2. (Faul, Erdfelder, Lang, & Buchner, 2007) indicated a minimum of 78 participants to detect a medium R^2 effect size of 0.15 based on studies of other psychosocial adherence correlates in HIV (Langebeek et al., 2014), with 80.0% power at a two-tailed α-level of .05 using a multiple linear regression fixed model, including 15 predictor variables.

3. Results

3.1 Demographics and adherence rates

Participants (N=275) were mostly white-Caucasian (74.0%) and male (72.0%) in their late forties, from the UK (46.0%) and US (52.0%). The group was divided according to MARS-5 cut-offs and sample characteristics can be found in Table 1 (adherence=25, unintentional

non-adherence = <5 and intentional non-adherence = <20 on respective subscales, in line with other LTC samples (de Vries et al., 2014; Moon et al., 2017). Significant differences were found in the cognitive complaints and relationship status variables.

[TABLE 1 HERE]

3.2 Adherence and general functioning

General functioning showed a small significant relationship with the dichotomised MARS-5 total and intentional nonadherent subscale scores (Table 2). However, it did not correlate with unintentional non-adherence. Medium to large relationships between the WSAS, PF processes, anxiety and depression fell in expected directions.

[TABLE 2 HERE]

3.3 Intentional/unintentional non-adherence

Variables associated with intentional non-adherence were gender (V=.177, p=.01, 95%CI=[.06,.29], relationship status (V=.233, p=.022, 95%CI=[.16,.34]), perceived cognitive complaints (r_b=.25, p<.01), anxiety (r_b=.223, p<.01) and depression (r_b=.185, p<.01). Variables associated with unintentional non-adherence included years since diagnosis ($M_{\text{nonadherent}}$ =16.75, $SD_{\text{nonadherent}}$=10.65; M_{adherent}=13.60, SD_{adherent}=12.06, r_b=-.144, p=.01) and perceived cognitive complaints (Table 1). These variables were entered in the first step of the regression models as covariates.

All biserial relationships between PF processes and the dichotomised adherence outcomes were in expected directions (Table 2). However, intentional non-adherence showed only a small significant association with experiential avoidance and committed action and was unrelated to cognitive defusion or self-as-context. Similarly, unintentional non-adherence was only related to committed action.

The first logistic regression tested PF model components in predicting intentional non-adherence controlling for demographic and disease variables (Table 3). Demographic and disease variables accounted for 19.2% (Nagelkerke R^2=.192) of the variance in intentional non-adherence, significantly improving the model fit ($\chi^2(6)=37.66$, p<.01). Specifically, cohabitation (OR=.11, 95% CI=[.02,.49]) was associated with decreased odds of intentional non-adherence, and having more cognitive complaints (OR=1.10, 95% CI=[1.02,1.19]) was associated with increased odds of intentional non-adherence. Adding PF processes did not significantly improve the model fit ($\Delta\chi^2$ (2)=1.49 (p=.47, 2LL=264.53), only explaining a further 0.7% (Nagelkerke ΔR^2=.007) of the variance.

[TABLE 3 HERE]

The second logistic regression tested PF model components in predicting unintentional non-adherence controlling for demographic and disease variables (Table 4). Demographic and disease variables accounted for 11.9% (Nagelkerke R^2=.119) of the variance in unintentional non-adherence, significantly improving the model fit ($\chi^2(7)=25.39$, p<.01). Being married or civil partnered (OR=.45, 95%CI=[.23,.86]) or widowed (OR=.16, 95%CI=[.04,.59]) was associated with decreased odds of unintentional non-adherence.

Conversely, more years since diagnosis (OR=1.02., 95% CI=[1.00,1.04]) and more cognitive complaints (OR=1.08, 95% CI=[1.02,1.14]) were associated with increased odds of unintentional non-adherence. Adding committed action did not significantly improve the model fit ($\Delta\chi^2(1)=693$ $p=.40$, 2LL=349.53, Nagelkerke $\Delta R^2=.003$).

[TABLE 4 HERE]

4. Discussion

This is the first published study investigating PF processes in conjunction with intentional/unintentional ART non-adherence and general functioning in PLWHIV. Overall, small, significant bivariate relationships indicated greater PF was associated with better adherence. Yet, PF was not significantly associated with self-reported intentional/unintentional non-adherence after controlling for demographic and disease variables, with little difference between non-adherence-subtypes. The most potent predictors of non-adherence were being single, more time since diagnosis and perceived cognitive problems. The former emphasises the importance of contextual factors, while the latter is consistent with evidence showing poorer cognitive performance is associated with non-adherence (Lovejoy & Suhr, 2009). Similar to other psychological variables in LTCs (Kardas, Lewek, & Matyjaszczyk, 2013), these findings suggest PF processes have some, albeit limited, explanatory power in understanding ART non-adherence in PLWHIV. HIV-specific psychological processes appear to be bigger drivers of non-adherence than general psychological factors (Catz et al., 2000; Fekete, Williams, & Skinta, 2018; Rachlis, Mills, & Cole, 2011).

There are several possible reasons why PF processes showed small correlations with self-reported non-adherence. First, self-reporting biases may have occurred and/or cut-offs used might not capture variability in PF, emotional or general functioning. Conversely, PF measures could be too 'broad-brush' to predict non-adherence, such that adherence behaviours might reflect only one among many other valued-actions. Constructing a non-adherence-specific PF scale that is sufficiently sensitive but does not inadvertently overlap with adherence instruments remains challenging. Future research should use additional objective ART adherence measures.

Second, it is plausible that participants provided an average rating over a self-selected timeframe on MARS-5 and PF scales, which is unspecified on both instruments. Arguably, retrospective bias can also arise (Moskowitz & Young, 2006). Using an adherence measure validated in PLWHIV with established cut-offs and a specific timeframe may help (e.g., (Chesney et al., 2000). Whilst further validation of the MARS-5 and its intentional/unintentional non-adherence cut-offs in PLWHIV is warranted, our findings indicate PF does not distinguish between them. One alternative might be to use objective momentary assessments of adherence, PF and general functioning within ecological momentary assessment (EMA) studies (Moitra & Gaudiano, 2016). This approach captures dynamic changes over time and across contexts. EMA methods also examine within-individual and group-level relationships between variables in conjunction with relevant events or changes in routine (Hektner, Schmidt, & Csikszentmihalyi, 2007).

The medium to large relationships observed between PF processes, general and emotional functioning are consistent with other LTC studies (Graham et al., 2016; Kashdan

& Rottenberg, 2010; Veehof, Trompetter, Bohlmeijer, & Schreurs, 2016), supporting the transdiagnostic applicability of PF. ACT may help PLWHIV manage distress since approximately 30.0% receiving ART report anxiety/depression (Lowther, Selman, Harding, & Higginson, 2014). Depression is a consistent predictor of ART non-adherence (Gonzalez et al., 2011) but this study found small/negligible relationships between self-reported non-adherence, emotional and general functioning. This contrasts with the expectation that less than perfect adherence triggers low mood and reduces functioning or vice-a-versa. Perhaps when ART adherence is more strongly associated with mood and/or functioning, PF processes may play a stronger role in predicting adherence. There is an implicit assumption that non-adherence-related symptom deterioration equates to reduced engagement in valued activities. However, ACT trials in LTCs show reductions in distress, indicating that people can live valued lives despite the presence of difficult symptoms and prognoses (Graham et al., 2016), which may of course include PWLHIV making a valued-choice to not adhere.

4.1 Limitations

Causation cannot be inferred due to the cross-sectional design of the study. Additionally, the MARS-5 is not validated in PLWHIV and including objective biomarkers to assess adherence would have been preferable. Online recruitment may have introduced self-selection bias. Indeed**,** over 70.0% of the sample was white and male, which is unrepresentative of PLWH. Furthermore, the sample was split between English-speaking UK and US residents. The generalisability of findings to non-Western countries requires investigation. Other psychosocial factors that also play a significant role in adherence for

PLWHIV, such as economic circumstances, stigma and lack of social support, were not assessed thus limiting generalisability of findings. Finally, the study did not distinguish between disease severity, PLWHIV and those with AIDS or different treatment regimens.

4.2 Treatment Implications and Conclusions

This evaluation did not provide evidence that the PF model is more suitable than existing SCMs in explaining non-adherence to ART. Therefore, ACT, which is the treatment approach most directly linked to increasing PF, may not be more suited to addressing non-adherence than existing behaviour change approaches informed by SCMs. However, this is the first evaluation and further research with sensitive HIV-specific proximal measurements and longitudinal methods may provide more clarity.

Currently, studies focusing specifically on ART adherence are mostly small, uncontrolled and have not measured PF processes. Assessment of contextual factors alongside key therapeutic mechanisms in larger trials after EMA investigations will further clarify the utility of the PF model. Moderation analyses will help determine who may benefit and identify at risk groups.

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Table 1 Participant characteristics according to MARS-5 cut-offs (N= 275)

	Adherent (according to MARS-5 cut-off) (*n*=113, 41.1%)	Nonadherent (according to MARS-5 cut-off) (*n*=162, 58.9%)	*p* value
Mean age (SD)	47.79 (12.93)	48.29 (11.66)	.74
Gender (%)			.20
Cisgender man	86 (77.5)	115 (70.1)	
Cisgender woman	24 (21.6)	45 (27.4)	
Transgender woman	0	3 (1.8)	
Other	1 (0.9)	1 (0.6)	
Country (%)			.08
UK	46 (40.7)	83 (51.2)	
Non-UK)	66 (58.4)	78 (48.1)	
White ethnicity (%)	82 (72.5)	122 (75.3)	.15
Employment status (%)			.53
Full time	48 (42.4)	75 (46.2)	
Part time	10 (8.4)	23 (14.1)	
Education	6 (5.3)	(2.4)	
Homemaker	0	1 (0.6)	
Retired	14 (12.3)	19 (11.7)	
Unemployed	32 (28.3)	38 (23.4)	
Other)	(0.8)	(0.6)	
Relationship status (%)			.048*
Single	45 (39.8)	85 (52.4)	
Married or civil partnership	31 (27.4)	24 (14.8)	

Separated or divorced			
Cohabiting	6 (5.3)	13 (8.0)	
Widowed	15 (13.2)	25 (15.4)	
Other)	8 (7.0)	6 (3.7)	
	6 (5.3)	8 (4.9)	
Sexual orientation (%)			.06
Gay	62 (54.8)	97 (59.8)	
Bisexual	15 (13.2)	7 (4.3)	
Straight	32 (28.3)	53 (32.7)	
Other)	3 (2.6)	5 (3.0)	
Mean disease duration (*SD*)	13.61 (12.27)	16.57 (10.64)	.039*
Depression PHQ-4 (%)	74 (65.0)	121 (75.0)	.62
Anxiety PHQ-4 (%)	73 (65.0)	123 (76.0)	.30
Mean Cognitive Complaints			
BC-CCI (SD)	9.90 (4.22)	11.34 (4.88)	.01*
Intentionally nonadherent			
MARS-5 (%)	NA	67 (41)	NA
Unintentionally nonadherent			
MARS-5 (%)	NA	152 (94)	NA

BC-CCI (British Columbia Cognitive Complaints Inventory); PHQ-4 (Patient Health Questionnaire four items: screen 'yes/caseness' for values >3); MARS-5 (Medication Adherence Rating Scale five items: 'adherence' 25 and 'nonadherence' <25).

Table 2: Summary of bivariate correlations (sample sizes range from *n*=252 to *n*=275)

	MARS-5 Unintent	WSAS	BC-CCI	AAQ II	CAQ- 8	SF-EQ	PHQ-4 dep	PHQ-4 anx
MARS-5 Intent	NA	*.18***	*.25***	*.18***	*-.22***	*-0.15*	*.22***	*.18***
MARS-5 Unintent		*0.031*	*.18***	*0.04*	*-.14**	*-0.09*	*0.06*	*0.07*
WSAS			.63***	.49***	-.42***	-.34***	.50***	.44***
BC-CCI				.48***	-.44***	-.38***	.47***	.48***
AAQ-II					-.64***	-.61***	.70***	.65***
CAQ-8						.63***	-.57***	-.56***
SF-EQ							-.55***	-.59***
PHQ-4 dep								.71***

Italics = point biserial Pearson's correlations; **Correlation is significant <.01 (2-tailed); *Correlation is significant <.05 (2-tailed); AAQ-II (Acceptance and Action Questionnaire II); BC-CCI (British Columbia Cognitive Complaints Inventory); CAQ-8 (Committed Action Questionnaire eight items), MARS-5 (Medication Adherence Rating Scale five items total score), MARS-5 Intent (Medication Adherence Rating Scale five items intentional nonadherence subscale score), MARS-5 unintent (Medication Adherence Rating Scale five items unintentional nonadherence subscale score), PHQ-4 total (Patient Health Questionnaire four items), PHQ-4 dep. (Patient Health Questionnaire four items depression subscale), PHQ-4 anx. (Patient Health Questionnaire four items anxiety subscale), SF-EQ (Shortened version of the Experiences Questionnaire total score); WSAS (Work and Social Adjustment Scale).

Table 3 Multiple binomial logistic regression to predict intentional nonadherence (MARS-5)

Step 1: Demographic and disease variables	*n*=272		R^2=.192	
χ^2 (6) = 37.66 (*p*<.001)				
-2LL = 266.03				
	b	**Bca 95% CI**	**OR**	**OR 95% CI**
Relationship status[1]				
Single vs. Married / Civil partnership	-.19	-1.07, .55	.81	.38, 1.74
Single vs. Separated or divorced	.12	-1.21, 1.18	1.13	.37, 3.40
Single vs. Cohabiting	-2.20*	-20.65, -1.05*	.11	.02, .49
Single vs. Widowed	-.76	-20.76, .60	.46	.11, 1.85
Single vs. Other	-.72	-20.21, .43	.48	.10, 2.36
Cognitive Complaints (BC-CCI)	.10*	.03, .19*	1.11	1.03, 1.19
Depression (PHQ-4)	.16	-.06, .43	1.18	.93, 1.49
Anxiety (PHQ-4)	-.01	-.26, .23	.98	.78, 1.23
Step 2: Psychological flexibility processes				R^2=199
$\Delta\chi^2$ (2) = 1.49 (*p*= .47)				
-2LL = 264.53				
	b	**Bca 95% CI**	**OR**	**OR 95% CI**
Psychological inflexibility (AAQ-II)	-.01	-.07, .04	.98	.933, 1.03
Committed action (CAQ-8)	-.02	-.08, .02	.97	.931, 1.01

Adherent=0, Nonadherent=1;[1]Single reference group=0; χ^2 Chi-squared goodness of fit; $\Delta\chi^2$ (Chi-squared goodness of fit); *b*= beta value; Bca 95% bootstrapped CI (beta value 95% confidence intervals with 1000 samples); *beta is significant <.05 (2-tailed); OR (standardized odds ratio); OR 95% CI (standardized odds ratio 95% confidence intervals); -2LL(-2 Log Likelihood statistic); R^2 (Nagelkerke R^2 / pseudo R^2); AAQ-II (Acceptance and Action Questionnaire II); CAQ-8 (Committed Action Questionnaire eight items) BC-CCI (British Columbia Cognitive Complaints Inventory); PHQ-4 (Patient Health Questionnaire four items).

Table 4 Multiple binomial logistic regression to predict unintentional nonadherence (MARS-5)

Step 1: Demographic and disease variables	*n*=274			R^2=. 119
χ^2 (7) = 25.39 (*p*<.001)				
-2LL = 350.22				
	b	**Bca 95% CI**	**OR**	**OR 95% CI**
Relationship status[1]				
Single vs. Married / Civil partnership	-.79*	-1.50, -.16*	.45	.23, .86
Single vs. Separated or divorced	-.26	-1.35, .97	.76	.27, 2.18
Single vs. Cohabiting	-.02	-.82,.82	.97	.46,2.07
Single vs. Widowed	-1.78*	-3.71, -.55*	.16	.04.598
Single vs. Other	-.04	-1.33, 1.39	.95	.31, 2.95
Years since diagnosis	.02*	<.01, .05*	1.02	1.00,1.04
Cognitive Complaints (BC-CCI)	.07*	.02,.14*	1.08	1.02, 1.14
Step 2: Psychological flexibility processes				R^2=.122
$\Delta\chi^2$ (1) = .69 (*p*= .40)				
-2LL = 349.53				
	b	**Bca 95% CI**	**OR**	**OR 95% CI**
Committed action (CAQ-8)	-.01	-.04,.02	.98	.95, 1.01

Adherent=0, Nonadherent=1; [1]Single reference group=0; χ^2 Chi-squared goodness of fit; $\Delta\chi^2$ (Chi-squared goodness of fit); *b*= beta value; Bca 95% bootstrapped CI (beta value 95% confidence intervals with 1000 samples); *beta is significant <.05 (2-tailed); OR (standardized odds ratio); OR 95% CI (standardized odds ratio 95% confidence intervals); -2LL(-2 Log Likelihood statistic); R^2 (Nagelkerke R^2 / pseudo R^2); AAQ-II (Acceptance and Action Questionnaire II); CAQ-8 (Committed Action Questionnaire eight items) BC-CCI (British Columbia Cognitive Complaints Inventory); PHQ-4 (Patient Health Questionnaire four items).