Non-adherence to tamoxifen in breast cancer survivors: A 12 month longitudinal analysis

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Objective: Previous research has shown that up to 50% of breast cancer survivors prescribed tamoxifen do not take it as recommended, which is associated with increased risk of recurrence and mortality. Little research has attempted to identify modifiable psychosocial factors associated with tamoxifen non-adherence. This study aimed to examine how tamoxifen adherence rates change over a year and to identify modifiable predictors of non-adherence.

Methods: 345 breast cancer survivors who were in their first year of tamoxifen prescription were sent questionnaires at four points over a 12-month period. Questionnaires assessed demographic and clinical factors, side-effects, beliefs about the illness and medication, social support, distress and tamoxifen adherence. Adherence was assessed using the Medication Adherence Rating Scale. Latent Growth Modelling was used to identify predictors of tamoxifen non-adherence.

Results: Reported rates of non-adherence increased over time (37-48%). Several demographic, clinical and psychosocial variables were associated with non-adherence. Women who were non-adherent were more likely to be from a minority ethnic group, to have more negative medication beliefs and to have lower confidence in their ability to take tamoxifen.

Conclusions: These demographic and clinical variables can be used to identify women at higher risk of non-adherence. The modifiable psychosocial variables can be used as the basis for psychological interventions to improve adherence in this population. Interventions should focus on both intentional and unintentional non-adherence.

Keywords: adherence, illness perceptions, medication beliefs, theory of planned behaviour; tamoxifen, hormone therapy.

Introduction

Breast cancer is the most common cancer in the UK, accounting for 15% of all new cancer cases and is the third most common cause of cancer-related deaths (Cancer Research UK, 2018). Around three quarters of breast cancers are oestrogen receptor positive and can be treated with hormone therapy (HT) such as tamoxifen. Prescribed to breast cancer survivors for up to ten years after primary treatment, tamoxifen can reduce the risk of breast cancer recurrence by 40% and mortality by a third (EBCTCG, 1998; EBCTCG, 2011). However, up to 50% of women take less than 80% of the prescribed dosage, which is known as non-adherence, or stop treatment early, known as non-persistence, both of which are associated with increased odds of recurrence and mortality (Barron, Cahir, Sharp & Bennett, 2013; Brito, Portela, Leite de Vasconcellos, 2014; Hershman et al., 2011; Hsieh, Chen, Cheung, Chang & Yang, 2014; Partridge, Wang, Winder & Avon, 2003; van Herk-Sukel et al., 2010). Non-adherence can be either intentional, where the patient makes a deliberate decision not to take their medication, or unintentional, where they may forget to take it, or misunderstand the instructions.

Previous research into predictors of tamoxifen non-adherence has largely focussed on clinical and demographic factors and has identified few consistent predictors beyond the experience of side-effects (Cahir, Guinan, Dombrowski, Sharp & Bennett, 2015; Kadakia et al., 2016; Moon, Moss-Morris, Hunter, Carlisle & Hughes, 2017; Pan et al., 2018). Irrespective of poor predictability, clinical and demographic factors have somewhat limited utility in this context as they are not amenable to modification through intervention, although they can identify those at increased risk of non-adherence. Recent studies assessing modifiable psychosocial factors found that social support, positive medication beliefs and high self-efficacy for medication taking are associated with increased odds of adherence (Brett et al., 2018; Hershman et al., 2016; Huiart et al., 2012; Kimmic et al., 2015). However, the majority of this research is cross-sectional and longitudinal studies are scarce.

Furthermore, previous research often lacks a theoretical framework with clearly specified psychosocial mechanisms of non-adherence, which may contribute to the poor success of previous interventions to improve adherence (Holmes, Hughes & Morrison, 2014; Horne et al., 2005). A recent cross-sectional study has supported the utility of using two common social cognition models of health behaviour as a framework for understanding tamoxifen non-adherence (Moon, Moss-Morris, Hunter & Hughes, 2017b).

The Common Sense Model (CSM) posits that an individual forms beliefs about their illness and treatment that will influence coping strategies, such as medication adherence (Leventhal et al., 2012). These illness representations include perceptions about the identity (symptoms), causes, consequences, timeline, level of understanding (coherence) and amount of control a person feels over an illness and are continually amended in a self-regulatory process as the individual develops more knowledge and experience of their illness and treatment over time. The continual self-regulatory nature of the model lends itself to the understanding of the experience of long-term conditions which require ongoing management. In terms of treatment perceptions, it is hypothesised that perceptions of how necessary treatment is to wellbeing, and concerns patients have about the medication will affect adherence. These illness and treatment perceptions are associated with adherence in several conditions (Chen, Tsai & Choi, 2011; Horne & Weinman, 2002), including two longitudinal studies assessing adherence to hormonal therapy in breast cancer survivors (Fink, Gurwitz, Rakowski, Guadagnoli & Silliman, 2006;Corter, Broom, Porter, Harvey, & Findlay, 2018).

Another set of determinants used to predict medication adherence have been drawn from the Theory of Planned Behaviour (TPB). The TPB was developed largely to explain preventative health behaviours and focuses more on performance of the desired behaviour than on the individual's ongoing cognitive or emotional management of an illness and appraisal of the associated behaviours. The TPB is formed of the patient's intentions to adhere, their general attitudes about medication taking, their beliefs about others' attitudes towards medication taking (subjective norm), and their confidence in their ability to take the medication (perceived behavioural control) (Ajzen, 1991); a

concept which is closely aligned to self-efficacy. Despite recent criticisms with the model (Sniehotta, Presseau & Araujo-Soares, 2014), there is a significant body of evidence showing that constructs such as attitudes and perceived behavioural control explain large amounts of variance in medication adherence (Bane, Hughes & McElnay, 2006; Chisholm, Williamson, Lance & Mulloy, 2007;), and that interventions based on these constructs are able to improve medication adherence and screening attendance (O'Carroll, Chambers, Dennis, Sudlow & Johnston, 2013; Sheeran & Orbell, 2000). One study has used the TPB in HT adherence and found TPB variables could explain 66% of the variance in intentions to adhere, and were associated with past medication taking behaviour (Hurtado-de-Mendoza et al., 2019).

Although there are some similarities between the main constructs of these models, there are also important differences, particularly in how they conceptualise long-term medication management. The CSM's self-regulatory process focuses on how perceptions of the illness and treatment influence specific coping behaviours such as the decision to take medication which are appraised and modified in relation to the ongoing incorporation of new knowledge and experience that the individual develops over time. Conversely, the TPB focuses on patients' attitudes and confidence in performing the behaviour itself, alongside social influences to predict engagement in behaviour, in isolation from perceptions of the associated illness. These complementary concepts have been shown to be associated with treatment adherence in isolation (Corter et al., 2018; Fink et al., 2006; Hurtado-de-Mendoza et al., 2019), leading researchers to suggest that using both models may increase the explanatory power to predict health behaviours (Holmes et al., 2014; Orbell, Hagger, Brown & Tidy, 2006; Sivell, Edwards, Elwyn & Manstead, 2011), which has been supported by three previous studies which have compared and combined elements from both models to successfully explain attendance at cervical screening follow-up (Orbell et al., 2006) and help-seeking (Hunter, Grunfeld & Ramirez, 2003) and treatment adherence (Moon et al., 2017b) in breast cancer. Therefore, the current study operationalized measurement variables from both models alongside additional psychosocial factors shown to be associated with tamoxifen adherence (Moon et al., 2017a; Cahir et al., 2015) to predict adherence to tamoxifen in breast cancer survivors.

Aims and hypotheses

This study aimed to examine how tamoxifen adherence rates change across a one-year period, and to identify modifiable predictors of non-adherence, using two social cognition models of health behaviour as a framework. Predictors of both intentional and unintentional non-adherence were identified, as understanding these different behaviours is important for improving overall non-adherence. We hypothesised that non-adherence rates would increase over time and that rates of unintentional non-adherence would be higher than intentional non-adherence. We also hypothesised that psychosocial factors such as medication beliefs will be related more to intentional non-adherence than to unintentional non-adherence.

Methods

Participants and procedure

The study was approved by the Northampton National Research Ethics Committee (REF 14/EM/1207). This longitudinal study was nested within a larger cross-sectional study of tamoxifen non-adherence (Moon et al., 2017b). Recruitment methods are described fully in the cross-sectional study. In short, women were recruited through National Health Service (NHS) outpatient clinics and online. Eligible participants were female, over the age of 18, had been diagnosed with primary breast cancer and had been prescribed tamoxifen. Women in their first year of treatment were included in the longitudinal study (n=345). Informed consent was obtained from all participants. Eligible patients consented to follow-up at recruitment.

Follow-up questionnaires were sent at 3, 6 and 12 months after completion of the baseline survey. Questionnaires were emailed or posted, depending on the participant's preference. If the questionnaire was not returned within two weeks, a reminder was sent, followed by a phone call two weeks later if the questionnaire was still not returned. Participants were not sent further questionnaires if they reported discontinuing tamoxifen at the previous time point or if they withdrew from the study.

Measures

Sociodemographic and clinical factors.

Self-reported data were collected on a range of demographic, illness and treatment related factors, including age, ethnicity, cancer stage and menopausal status.

Common Sense Model (CSM) variables.

The IPQ-BCS, a modified version of the Illness Perceptions Questionnaire, was used to measure illness perceptions, a key component of the CSM. The scale was modified for use in breast cancer survivors and has good psychometric properties (Moon, Moss-Morris, Hunter & Hughes, 2017c). It includes ten subscales; cure, risk of recurrence, tamoxifen consequences, breast cancer consequences, personal control, treatment control, illness coherence, emotional representations, tamoxifen identity and causal attributions. Medication beliefs were assessed using the Beliefs about Medicines Questionnaire-Specific (BMQ-Specific). The BMQ-Specific measures both perceived necessity for tamoxifen and perceived concerns about this medication. Patients' perceived cost benefit analysis was operationalised through a differential score calculated by subtracting necessity beliefs from concerns (Horne, Weinman & Hankins, 1999). A more positive necessity/concerns differential indicates that the patient's necessity beliefs outweigh their concerns.

Theory of Planned Behaviour variables.

TPB constructs (intentions to take tamoxifen, subjective norms, attitude and perceived behavioural control) were assessed by three items each, based on guidance from Azjen (2002) and Francis et al (2004). Items were scored on a seven-point Likert scale from strongly agree to strongly disagree. Each subscale showed good reliability (α=0.67–0.82), except for subjective norms (α=0.52), however all subscales were included in order to fully test the model.

Additional psychosocial factors.

Perceived social support was measured with the Multidimensional Scale of Perceived Social Support (Zimet, Dahlem, Zimet & Farley, 1988), with higher scores indicating higher levels of

support. Distress was measured using the general distress scale of the Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983; Norton, Cosco, Doyle, Done & Sacker, 2013). The additional concerns subscale of the FACT-ES was used to measure the extent to which patients experience a range of side-effects (from 'not at all' to 'very much') (Fallowfield, Leaity, Howell, Benson & Cella, 1999).

Adherence.

Adherence was measured using the Medication Adherence Report Scale (MARS), a self-report scale with five items scored on a five-point scale (Horne, Hankins & Jenkins, 2001). Participants report the extent to which they engage in adherence behaviours, scored from 'never' to 'always'. Higher scores indicate higher adherence rates. As the scale is often positively skewed towards high adherence, it is usually dichotomised, with participants scoring 24 or below being classed as non-adherent and participants scoring 25 being classed as adherent (de Vries et al., 2014; Timmers et al., 2016). Separate scores are generated for intentional (four items, range 4-20; ≤19 scored as non-adherent) and unintentional non-adherence (one item, range 1-5; ≤4 scored as non-adherent). Women who had discontinued tamoxifen were asked to provide a free text explanation as to why they discontinued. Women who reported discontinuing tamoxifen prematurely without the advice of their healthcare professional were classed as non-adherent for the analysis.

Statistical analysis

Statistical analyses were conducted in SPSS v21 and Mplus v7. Item level missing data within scales for covariates was negligible (<5%) and was replaced using mean substitution. Latent growth models (LGMs) were carried out to model the change in non-adherence rates over time and to identify factors associated with this change. Non-adherence was binary coded with adherence status being allowed to change from one time-point to the next. LGM assumes data is missing at random, which protects against bias due to differential non-response when variables relating to non-response are included in the analysis. Non-adherence at each of the four assessments was fixed to load onto the slope factor with values equal to the number of months since the baseline assessment (i.e. 0,3,6,12)

(see supplementary material). This allows for interpretation of co-efficients relating to time in months. Baseline covariates were added to the model as predictors of both the intercept and the slope.

The *intercept* indicates baseline levels of non-adherence by representing the point at which the slope intercepts the vertical axis. Variables with significant effects on the slope are therefore associated with baseline non-adherence. The *slope* represents the growth or change in non-adherence over time. These analyses were run for total non-adherence, and separately for both intentional and unintentional non-adherence. Three separate models were run to test: (1) variables from the CSM, (2) variables from the TPB, and (3) variables from both the CSM and the TPB. In addition to the model variables, the following variables were also entered as theory and previous literature suggests they may be associated with non-adherence in this population; age, menopausal status, ethnicity, job status, distress, side-effects and social support (Brett et al., 2018; Lambert, Balneaves, Howard, & Gotay, 2018; Moon et al., 2017a; Roberts et al., 2015). The variable *intentions* from the TPB was removed from the LGM analysis as it was positively skewed and showed high kurtosis. Plots were created to show the marginal means for covariates within the model. These plots illustrate how non-adherence rates change over time for +/- one standard deviation away from the mean.

Results

Response rate

The flow of participants through the study is summarised in Figure 1. The response rate to the initial questionnaire was 61%. 345 participants were sent 3-month follow-up questionnaires, with a 91% response rate (n=315). At 6 months, 332 participants were sent questionnaires, with an 86% response rate. At 12 months, 306 participants were sent questionnaires, with an 84% response rate. Thirty-nine women were not sent follow-up questionnaires as they withdrew from the study, were deceased or discontinued tamoxifen. The retention rate at 12 months was 75% of the original sample, and 84% of those who were sent all four questionnaires. Non-responders to the questionnaires across time points were more likely to be younger, from a minority ethnic group, pre-menopausal, less

adherent and to have higher distress scores and higher side-effects scores at baseline (see supplementary material).

Participant demographics

Participant demographics are shown in Table 1. Most participants were white British (95%), had a partner (76%) and were employed (71%). Age ranged from 30–90 (*M* =52, *SD*=10.3). Participants mostly had Stage I (41%) or Stage II breast cancer (45%) and were premenopausal at diagnosis (55%).

Changes in adherence over time

At baseline, 37% of women were classed as non-adherent (MARS scores ≤ 24); this increased to 48% at 12 months. For intentional non-adherence, 7% were classed as non-adherent at baseline (scores ≤19) and this rose to 10% at 12 months. For unintentional non-adherence, 35% were non-adherent at baseline (scores ≤ 4) and 47% were non-adherent at 12 months (Figure 2). A one-way repeated measures ANOVA showed a significant effect of time, with adherence scores falling over the 12 months ($F(2.3, 513.4)=5.33$, p=.003). Post-hoc Bonferroni tests showed significant decreases between baseline and 6 months ($p=.037$) and baseline and 12 months ($p=.004$).

Discontinuation

Only 41 women (15%) reported that they discontinued tamoxifen across the study period. The majority reported that they were switched to another medication or that they discontinued on their doctor's orders, with only a small proportion reporting making their own choice to discontinue ($n=7$, 2%).

Changes in side-effects over time

Side-effect intensity increased significantly over time (F[2.8, 631.3]=2.37, p<.001). Post-hoc tests indicated significant increases between baseline (M=1.95, SD=0.59) and 12 months (M=2.15, SD=0.66, p<.001).

Latent growth modelling (LGM)

Dichotomous MARS scores (adherent/non-adherent) were used to model non-adherence in the LGM as the MARS scores were positively skewed. Linear and quadratic growth functions were both tested, with the linear growth pattern providing superior fit to the data, based on the Loglikelihood and BIC values (see supplementary material). The intercept represents the initial rate of non-adherence in the sample at baseline, and the slope represents monthly change in the rate of non-adherence in the sample over time.

Table 2 shows the results of the LGMs. The proportion of women classed as non-adherent increased at each time point. There was significant variance in the intercept (7.88, p=.002) but not the slope (0.09, p=.131).

In the LGM with CSM variables, ethnicity was the only factor with a significant effect on the intercept, with women who were from minority ethnic groups having eleven times higher odds of non-adherence than women who were white (Table 2). In terms of the slope of non-adherence, women with more positive necessity/concern differentials and who attributed more symptoms to tamoxifen had significantly lower odds of non-adherence over time. Marginal means plots show how the estimated proportions of non-adherence over the 12 months period differ for those with a positive necessity/concerns differential and those with a negative necessity/concerns differential (see supplementary material). Whilst the non-adherence rates at baseline are similar across the two groups, those with more negative medication beliefs have much higher rates of non-adherence over time than those with more positive medication beliefs.

The same analytic approach was run to test the TPB. As with the CSM model, ethnicity was significantly related to the intercept, with women who were from minority ethnic groups having

higher odds of non-adherence at baseline (Table 2). In addition to ethnicity, PBC over medication taking and social support also showed a significant effect on the intercept, with higher levels of PBC and higher rated social support being associated with lower odds of non-adherence. The marginal means plots show that whilst women with higher perceived behavioural control had lower odds of non-adherence at baseline, the slope of non-adherence over time did not differ at different levels of perceived behavioural control (supplementary material).

In the final model combining elements from both the CSM and the TPB, women who were from a minority ethnic group, who had lower perceived social support and lower perceived behavioural control over medication taking had higher odds of non-adherence at baseline. Again, having more positive medication beliefs was associated with lower odds of non-adherence over time, as was beliefs that breast cancer was cured, attributing more symptoms to tamoxifen and more positive attitudes towards tamoxifen.

Intentional / unintentional non-adherence

Additional analyses were run to determine whether the association between variables differs between unintentional and intentional non-adherence (Table 3). Being from a minority ethnic group, being younger, being employed, and perceiving lower levels of social support were associated uniquely with increased odds of unintentional non-adherence. Attributing symptoms to tamoxifen, lower coherence beliefs, and believing that psychological factors cause a recurrence were associated uniquely with increased odds of intentional non-adherence. Several factors were associated with both intentional and unintentional non-adherence; higher distress, more side-effects, less positive medication beliefs, lower PBC and less positive attitudes towards tamoxifen.

Discussion

This study is one of the first to identify modifiable psychosocial predictors of non-adherence to tamoxifen longitudinally. Results showed that less positive medication beliefs and lower perceived behavioural control (PBC) over medication taking were most consistently associated with increased

odds of non-adherence. Women from minority ethnic groups were also at higher odds of non-adherence. These results provide important information on how to support women taking tamoxifen.

Results showed that 37-48% of women were non-adherent, and that reported rates of non-adherence increased significantly over time, which is consistent with previous research (Seneviratne et al., 2015). These results highlight the need for interventions to support women throughout their treatment. Women who were non-adherent at baseline were less likely to return their follow-up questionnaires, indicating that the levels of non-adherence reported here may be lower than the true incidence of non-adherence. Furthermore, self-report questionnaires are often criticised for under-estimating non-adherence rates. Attempts were made to overcome this by setting a high cut off for non-adherence, as per previous recommendations (Huther et al., 2013; Stirratt et al., 2015).

Interestingly, rates of discontinuation were much lower than previous estimates, at around 15% in total, and only 2% for those who reported making their own decision to discontinue (Owusu et al., 2008). Previous research has been criticised for failing to consider the reasons why women discontinue treatment, and for classing women as non-persistent even if their clinician advised them to stop treatment or switched their medications (Guth, Myrick, Kilic, Eppenberger-Castori & Schmid, 2012). Accurate rates of non-persistence, where the patient initiates the decision to stop treatment, may be much lower than the 40-50% previously reported. However, the lower rates of discontinuation in this study may be due to the self-report measurement and follow-up attrition, therefore further research is needed to investigate this further and identify if the predictors of non-adherence identified here will transfer to prediction of non-persistence.

Whilst women are often told clinically that their side-effects will likely lessen over time, these results showed that self-reported side-effect intensity increased significantly over the twelve-month period. This highlights a need to develop ongoing support for women to manage their side-effects.

Women from minority ethnic groups were up to 26 times more likely to be non-adherent when controlling for other covariates. The proportion of women from minority ethnic groups was small, and the confidence intervals for this effect were wide; therefore caution should be taken when interpreting the results. However, this is an important finding, especially in light of research showing poorer clinical outcomes in women from minority ethnic groups compared to white women (Moller et al., 2016), and therefore future research is warranted to explore this further. Bivariate analyses also showed that women who were employed were more likely to be unintentionally non-adherent, which is consistent with other recent studies (Brett et al., 2018; Quinn, Fleming & Sullivan, 2016) and suggests that women who are working may need additional support in remembering to take their medication. In addition to this, women with lower perceived social support were at higher odds of non-adherence, and women with higher levels of distress at baseline were at increased odds of becoming non-adherent over time. Therefore, providing support with distress early on in treatment, and helping women build adequate social support, may prevent women from becoming non-adherent.

However, whilst the sociodemographic factors are important for identifying who may be at risk of non-adherence and require more support, these factors are not amenable to change. Whilst the CSM and the TPB only explained a modest proportion of the variance in non-adherence, using these two models has helped to identify a broader range of potentially modifiable psychosocial variables, which may provide useful targets for interventions to improve non-adherence. In terms of the CSM, having less positive medication beliefs, i.e. believing that concerns outweigh the necessity of the medication, were associated with increased odds of non-adherence over the 12 month follow-up, even when controlling for other covariates. This is comparable with previous research and highlights the importance of medication beliefs in understanding tamoxifen adherence (Brett et al., 2018; Fink et al., 2004). Previous studies have shown that medication beliefs can be altered through intervention, leading to improvements in medication adherence (Moon, Moss-Morris, Hunter, Goodliffe & Hughes, 2019; O'Carroll et al., 2013; Petrie et al., 2012).

Two other CSM variables also appear relevant to future adherence interventions. High scores on perceptions that breast cancer was cured were associated with lower odds of non-adherence over time. In addition, attributing more symptoms to tamoxifen had higher odds of intentional non-adherence at the intercept, but also lower odds of becoming non-adherent (total non-adherence) over time. This highlights the complex relationship between side-effects and non-adherence. Side-effects may be an initial driver of non-adherence, as often assumed, whereas over time symptoms resulting from oestrogen blocking, such as hot flushes, may be an indicator that the treatment is working (Cuzick et al., 2008), and may therefore be associated with lower odds of non-adherence. These results also highlight that whether or not symptoms are attributed to tamoxifen may be a more important determinant than the experience of symptoms themselves.

Three other illness perceptions could also be considered for future interventions to improve adherence. Perceiving severe consequences of tamoxifen, believing that psychological stress would cause a recurrence and lower coherence were all associated with increased odds of intentional non-adherence, but these did not remain significant in the multivariate analyses. Although perceptions of personal and treatment control as measured by the modified IPQ-R were not associated with non-adherence, perceived behavioural control (PBC) drawn from the TPB did appear to have relevance. PBC focuses more on the confidence in performing the medication taking behaviour itself (in this case, taking a daily tablet), whereas constructs of control within the IPQ-R focus on the extent to which the patient believes they can control their illness through this behaviour (i.e. whether taking tamoxifen will reduce the risk of recurrence).

Variables from the TPB also contributed to explaining non-adherence. Higher perceptions of PBC over medication taking were associated with decreased odds of non-adherence at the intercept. This is supported by previous research into medication adherence showing the importance of PBC and provides some support for the model, helping to counter some of the criticism the model has faced over recent years (Chisholm et al., 2007; Sniehotta et al., 2014). In addition to PBC, attitudes towards tamoxifen, such as tamoxifen being beneficial or pleasant, were also a significant predictor of non-

adherence both at baseline and over time. However, the current results do support the criticism that the TPB is unable to predict later behaviour, as attitudes towards tamoxifen was the only variable associated with non-adherence over time and may represent more perennial influences over long term medication taking. PBC was only related to non-adherence at baseline and had no effect on later non-adherence. This is somewhat expected, however, as the CSM is designed to explain long-term adjustment to illness and treatment whereas the PBC construct of the TPB refers more specifically to performing the specific behaviour which is more likely to relate to adherence at the same time point than 12 months later. However, it was not possible to fully test the model as the variable intentions to take tamoxifen was strongly skewed in this population, with most women reporting strong intentions to adhere.

Overall, neither the CSM nor the TPB provided a perfect fit for understanding non-adherence. There are likely additional factors affecting non-adherence which the current study is missing, especially when predicting later non-adherence. However, testing two complementary social cognition models provides a more complete analysis for explaining adherence to tamoxifen, and supports and extends previous studies that have found utility in assessing illness and treatment beliefs proposed by the CSM (Brett et al., 2018; Corter et al., 2008; Fink et al., 2004; Moon et al., 2017b) as well as attitudes towards and confidence in performing medication taking behaviour proposed by the TPB (Hurtado-de-Mendoza et al., 2019; Moon et al., 2017b) Constructs of both models remained important in explaining non-adherence when they were combined, suggesting that they measure distinct but important factors. Furthermore, there were hypothesised differences between the psychosocial factors with the CSM being related to intentional but not unintentional non-adherence. This has important implications for future interventions.

Clinical implications

Taken together, these results highlight women who may be at higher risk of non-adherence, such as those who are younger, from minority ethnic groups, who are employed and who have higher levels of distress. Clinicians can identify these women and give them additional support with their

medication taking and with managing distress. In addition to this, the results highlight ways in which adherence could be improved through intervention, by modifying the psychosocial variables identified in this study. Previous interventions based on modifying medication beliefs and increasing PBC have shown success at improving adherence rates (Moon et al., 2019; O'Carroll et al., 2013; Petrie, Perry, Broadbent & Weinman, 2012). Results showed that demographic factors, such as ethnicity, age and employment status were associated with unintentional non-adherence, whereas psychological factors such as perceptions around risk of recurrence tended to be associated more with intentional non-adherence. These results have important implications for understanding how to intervene and improve non-adherence. Finally, the results showed that instead of decreasing over time, the perceived impact of self-reported side-effects increased over the first 24 months. This is especially important considering qualitative research showing that some women feel dismissed by healthcare professionals and feel un-validated in their experience of side-effects (Moon, Moss-Morris, Hunter & Hughes, 2017d). Supporting women to manage their side-effects, as well as re-evaluating their weight in the decisional balance to minimise side-effect related concerns presents a potential target for intervention

Study limitations

Whilst retention rates were relatively high, significant differences were seen between responders and non-responders. Women who did not respond were more likely to be younger, from a minority ethnic group and to be more non-adherent at baseline, which is a common limitation with adherence research. There was little ethnic diversity in the sample, so future research should be conducted with a more representative sample in order to further explore the relationship between ethnicity and non-adherence. The research only focused on women prescribed tamoxifen, as tamoxifen was more widely prescribed when the study was designed. Future research could extend this to women prescribed aromatase inhibitors. Finally, there are criticisms associated with the use of self-report measures of non-adherence such as the MARS, which are known to over-estimate adherence rates. However, the MARS is designed to overcome some of these limitations by using language which normalises non-adherence. Furthermore, in order to counter the over-estimation of adherence, a high cut off point was used to dichotomise non-adherence, based on previous

recommendations (Huther et al., 2013; Stirratt et al., 2015). Whilst the MARS has shown good concordance with objective measures (O'Carroll et al., 2013), it is unclear if the levels of non-adherence reported here are associated with poor clinical outcomes. Whilst it was not possible in this study, future research could overcome these limitations by triangulating from multiple sources, such as pharmacy records, pill counts, or electronic monitoring.

To conclude, results show that reported rates of non-adherence increase significantly over a one-year follow-up period. Unintentional non-adherence was reported more frequently than intentional non-adherence and was associated with some unique predictors. A key sociodemographic predictor of non-adherence was ethnicity, with women from minority ethnic groups being at higher odds of non-adherence. The research has identified several potentially modifiable targets, such as medication beliefs and perceived behavioural control over medication taking, which can form the basis of interventions to improve non-adherence in this population.

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Conflict of interest

The authors declare that they have no conflict of interest.

References

Ajzen, I.(1991). The theory of planned behavior. *Organizational Behavior and Human Decision Processes 50,* 179-211.

Azjen, I. (2002). *Constructing a TPB questionnaire: Conceptual and methodological considerations. 2002.* Retrieved from: http://chuang.epage.au.edu.tw/ezfiles/168/1168/attach/20/pta_41176_7688352_57138.pdf

Aujla, N., Walker, M., Sprigg, N., Abrams, K., Massey, A., & Vedhara, K (2016). Can illness beliefs, from the common-sense model, prospectively predict adherence to self-management behaviours? A systematic review and meta-analysis. *Psychology & Health, 31*, 931-58. doi: 10.1080/08870446.2016.1153640.

Bane, C., Hughe, C.M., & McElnay, J.C. (2006). Determinants of medication adherence in hypertensive patients: an application of self-efficacy and the Theory of Planned Behaviour. *International Journal of Pharmacy Practice, 14,* 197-204. doi: 10.1211/ijpp.14.3.0006

Barron, T.I., Cahir, C., Sharp, L., & Bennett, K. (2013). A nested case-control study of adjuvant hormonal therapy persistence and compliance, and early breast cancer recurrence in women with stage I-III breast cancer. *British Journal of Cancer, 109.* 1513-21. doi: 10.1038/bjc.2013.518

Brandes, K., & Mullan, B.(2014). Can the common-sense model predict adherence in chronically ill patients? A meta-analysis. *Health Psychology Review,* 8, 129-53. doi: 10.1080/17437199.2013.820986

Brett, J., Fenlon, D., Boulton, M., Hulbert-Williams, N.J., Walter, F., Donnelly, P. et al. (2018). Factors associated with intentional and unintentional non-adherence to adjuvant endocrine therapy following breast cancer. *European Journal of Cancer Care, 27,* 1.doi: doi.org/10.1111/ecc.12601

Brito, C., Portela, M.C., & Leite de Vasconcellos, M.T. (2014). Factors associated to persistence with hormonal therapy in women with breast cancer. *Revista de Saude Publica, 48,* 284-95.

Cahir, C., Guinan, E., Dombrowski, S.U., Sharp, L., & Bennett, K. (2015). Identifying the determinants of adjuvant hormonal therapy medication taking behaviour in women with stages I–III breast cancer: a systematic review and meta-analysis. *Patient Education and Counselling*. Advanced Online Publication. doi: 10.1016/j.pec.2015.05.013

Cancer Research UK. (2018, March 15). *Breast Cancer Statistics.* Retrieved from: http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer#heading-Two

Chen, S.L., Tsai, J.C., Chou, K.R. (2011). Illness perceptions and adherence to therapeutic regimens among patients with hypertension: a structural modeling approach. *International Journal of Nursing Studies, 48,* 235-45. doi: 10.1016/j.ijnurstu.2010.07.005

Chisholm, M.A., Williamson, G.M., Lance, C.E., & Mulloy, L.L. (2007). Predicting adherence to immunosuppressant therapy: a prospective analysis of the theory of planned behaviour. *Nephrology Dialysis Transplantation, 22,* 2339-48. doi: 10.1093/ndt/gfm149

Corter, A.L., Broom, R., Porter, D., Harvey, V., Findlay, M. (2018). Predicting nonadherence to adjuvant endocrine therapy in women with early stage breast cancer. *Psycho-oncology, 27,* 2096-2103. doi: 10.1002/pon.5771

Cuzick, J., Sestak, I., Cella, D., Fallowfield, L., on behalf of ATAC Trialists' Group. (2008). Treatment-emergent endocrine symptoms and the risk of breast cancer recurrence: a retrospective analysis of the ATAC trial. *The Lancet Oncology, 9,* 1143-1148. doi: 10.1016/S1470-2045(08)70259-6

de Vries, S.T., Keers, J.C., Visser, R., de Zeeuw, D., Haaijer-Ruskamp, F.M., Voorham, J. et al. (2014). Medication beliefs, treatment complexity, and non-adherence to different drug classes in patients with type 2 diabetes. *Journal of Psychosomatic Research, 76,* 134-8. doi: 10.1016/j.jpsychores.2013.11.003

Early Breast Cancer Trialists' Collaborative Group (EBCTCG). (1998). Tamoxifen for early breast cancer: an overview of the randomised trials. *Lancet, 351,* 1451-67.

Early Breast Cancer Trialists' Collaborative Group (EBCTCG).(2011). Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials. *Lancet, 378,* 771-84. doi: 10.1016/S0140-6736

Fallowfield, L.J., Leaity, S.K., Howell, A., Benson, S., & Cella, D. (1999). Assessment of quality of life in women undergoing hormonal therapy for breast cancer: validation of an endocrine symptom subscale for the FACT-B. *Breast Cancer Research and Treatment, 55,* 189-99.

Fink, A.K., Gurwitz, J., Rakowski, W., Guadagnoli, E., & Silliman, R.A. (2004). Patient beliefs and tamoxifen discontinuance in older women with estrogen receptor--positive breast cancer. *Journal of Clinical Oncology, 22,* 3309-15. doi: 10.1200/JCO.2004.11.064

Francis, J.J., Eccles, M.P., Johnston, M., Walker, A., Grimshaw, J., Foy, R. et al. (2004). *Constructing questionnaires based on the theory of planned behaviour. A manual for health services researchers.* Centre for Health Services Research: Newcastle upon Tyne, UK.

Grunfeld, E.A., Hunter, M.S., Sikka, P., & Mittal, S. (2005). Adherence beliefs among breast cancer patients taking tamoxifen. *Patient Education and Counselling, 59,* 97-102. doi: 10.1016/j.pec.2004.10.005

Guth, U., Myrick, M.E., Kilic, N., Eppenberger-Castori, S., Schmid, S.M. (2012). Compliance and persistence of endocrine adjuvant breast cancer therapy. *Breast Cancer Research and Treatment, 131,* 491-9. doi: 10.1007/s10549-011-1801-y.

Hershman, D.L., Kushi, L.H., Hillyer, G.C., Coromilas, E., Buono, D., Lamerato, L. et al. (2016). Psychosocial factors related to non-persistence with adjuvant endocrine therapy among women with breast cancer: the Breast Cancer Quality of Care Study (BQUAL). *Breast Cancer Research and Treatment,157,* 133-43. doi: 10.1007/s10549-016-3788-x

Hershman, D.L., Shao, T., Kushi, L.H., Buono, D., Tsai, W.Y., Fehrenbacher, L., et al. (2011). Early discontinuation and non-adherence to adjuvant hormonal therapy are associated with increased mortality in women with breast cancer. *Breast Cancer Research and Treatment, 126,* 529-37. doi: 10.1007/s10549-010-1132-4

Holmes, E.A., Hughes, D.A., & Morrison, V.L. (2014). Predicting adherence to medications using health psychology theories: a systematic review of 20 years of empirical research. *Value in Health, 17,* 863-76. doi:10.1016/j.jval.2014.08.2671

Horne, R., Hankins, M., & Jenkins, R. (2001). The Satisfaction with Information about Medicines Scale (SIMS): a new measurement tool for audit and research. *Quality in Health Care, 10,* 135-40. doi: 10.1136/qhc.0100135

Horne, R., & Weinman, J. (2002). Self-regulation and Self-management in Asthma: Exploring The Role of Illness Perceptions and Treatment Beliefs in Explaining Non-adherence to Preventer Medication. *Psychology & Health, 17,* 17-32. doi: 10.1080/08870440290001502

Horne, R., Weinman, J., Barber, N., Elliott, R., Morgan, M., Cribb, A. et al. (2005). *Concordance, adherence and compliance in medicine taking.* National Co-ordinating Centre for NHS Service Delivery and Organisation: London.

Horne, R., Weinman, J., & Hankins, M. (1999). The beliefs about medicines questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication. *Psychology & Health, 14,* 1-24. doi: 10.1080/08870449908407311

Hsieh, K-P., Chen, L-C., Cheung, K-L., Chang, C-S., & Yang, Y-H. (2014). Interruption and Non-Adherence to Long-Term Adjuvant Hormone Therapy Is Associated with Adverse Survival Outcome of Breast Cancer Women - An Asian Population-Based Study. *Plos One 9.* doi: 10.1371/journal.pone.0087027.t001

Huiart, L., Bouhnik, A.D., Rey, D., Tarpin, C., Cluze, C., Bendiane, M.K. et al. (2012). Early discontinuation of tamoxifen intake in younger women with breast cancer: is it time to rethink the way it is prescribed? *European Journal of Cancer, 48,* 1939-46. doi: 10.1016/j.ejca.2012.03.004

Hunter, M.S., Grunfeld, E.A., & Ramirez, A.J. (2003). Help-seeking intentions for breast-cancer symptoms: A comparison of the self-regulation model and the theory of planned behaviour. *British Journal of Health Psychology, 8,* 319-33. doi: 135910703322370888

behaviour. *British Journal of Health Psychology, 8,* 319-333. doi: 135910703322370888 Hurtado-de-Mendoza, A., Cabling, M.L., Lobo, T., Dash, C., & Sheppard, V.B. (2018). Behavioural Interventions to Enhance Adherene to Hormone Therapy in Breast Cancer Survivors: A Systematic Literature Review. *Clinical Breast Cancer, 16,* 247-255. doi: 10.1016/j.clbc.2016.03.006

Hurtado-de-Mendoza, A., Carrera, P., Parrott, W.G., Gomez-Trillos, S., Perera, R.A., & Sheppard, V.B. (2018). Applying the theory of planned behaviour to examine adjuvant endocrine therapy adherene intentions. *Psycho-oncology, 28,* 187-194. doi: 10.1002/pon.4931

Hüther, J., von Wolff, A., Stange, D., Härter, M., Baehr, M., Dartsch, D.C. et al. (2013). Incomplete medication adherence of chronically ill patients in German primary care. *Patient Preference and Adherence, 7,* 237-44. doi: 10.2147/PPA.S38373

Kadakia, K.C., Snyder, C.F., Kidwell, K.M., Seewald, N.J., Flockhart, D.A., Skaar, T.C. et al. (2016). Patient-Reported Outcomes and Early Discontinuation in Aromatase Inhibitor-Treated Postmenopausal Women With Early Stage Breast Cancer. *The Oncologist, 21,* 539-46. doi 10.1634/theoncologist.2015-0349

Kimmick, G., Edmond, S.N., Bosworth, H.B., Peppercorn, J., Marcom, P.K., Blackwell, K. et al. (2015). Medication taking behaviors among breast cancer patients on adjuvant endocrine therapy. *The Breast, 24,* 630-6. doi: 10.1016/j.breast.2015.06.01

Lambert, L.K., Balneaves, L.G., Howard, A.F., & Gotay, C.C. (2018). Patient-reported factors associated with adherence to adjuvant endocrine therapy after breast cancer: an integrative review. *Breast Cancer Research & Treatment, 167,* 615 – 633. doi: 10.1007/s10549-017-4561-5

Leventhal, H., Bodnar-Deren, S., Breland, J.Y., Hash-Converse, J., Phillips, L.A., & Leventhal, E.A. et al. (2012). Modeling Health and Illness Behaviour: The approach of the Commonsense Model. In A.B. Baum, T.A. Revenson, & J. Singer J (Eds.), *Handbook of Health Psychology 2nd Edition* (pp 3-36). New York: Psychology Press, Taylor & Francis Group.

Lin, C-Y., Updegraff, J.A., & Pakpour, A.H. (2016). The relationship between the theory of planned behavior and medication adherence in patients with epilepsy. *Epilepsy & Behavior, 61,* 231-6. doi: 10.1016/j.yebeh.2016.05.030

Møller, H., Henson, K., Lüchtenborg, M., Broggio, J., Charman, J., Coupland, V. H., et al. (2016). Short-term breast cancer survival in relation to ethnicity, stage, grade and receptor status: National cohort study in England. *British Journal of Cancer, 115,* 1408-1415. doi: 10.1038/bjc.2016.335

Moon, Z., Moss-Morris, R., Hunter, M.S., Carlisle, S., & Hughes, L.D. (2017a). Barriers and facilitators of adjuvant hormone therapy adherence and persistence in women with breast cancer: a systematic review. *Patient Preference and Adherence, 11,* 305-22. doi: 10.2147/ppa.s126651

Moon, Z., Moss-Morris, R., Hunter, M.S., Goodliffe, S., & Hughes, L.D. (2019) Acceptability and feasibility of a self-management intervention for women prescribed tamoxifen. *Health Eduction Journal*. In Press.

Moon, Z., Moss-Morris, R., Hunter, M.S., & Hughes, L.D. (2017b). More than just side-effects: The role of clinical and psychosocial factors in non-adherence to tamoxifen. *British Journal of Health Psychology, 22,* 998-1018. doi: 10.1111/bjhp.12274

Moon, Z,, Moss-Morris, R., Hunter, M.S., & Hughes, L.D. (2017c). Measuring illness representations in breast cancer survivors (BCS) prescribed tamoxifen: Modification and validation of the Revised Illness Perceptions Questionnaire (IPQ-BCS). *Psychology & Health, 32*, 439-58. doi: 10.1080/08870446.2016.1275629

Moon, Z., Moss-Morris, R., Hunter, M.S., & Hughes, L.D. (2017d). Understanding tamoxifen adherence in women with breast cancer: A qualitative study. *Brtish Journal of Health Psychology, 22*, 978-97. doi: 10.1111/bjhp.12266

Norton, S., Cosco, T., Doyle, F., Done, J., & Sacker, A. (2013). The Hospital Anxiety and Depression Scale: A meta confirmatory factor analysis. *Journal of Psychosomatic Research, 74,* 74-81. doi: 10.1016/j.jpsychores.2012.10.010

O'Carroll, R.E., Chambers, J.A., Dennis, M., Sudlow, C., & Johnston, M. (2013). Improving adherence to medication in stroke survivors: a pilot randomised controlled trial. *Annals of Behavioural Medicine, 46,* 358-68.

Orbell, S., Hagger, M., Brown, V., & Tidy, J. (2006). Comparing two theories of health behavior: a prospective study of noncompletion of treatment following cervical cancer screening. *Health Psychology, 25,* 604-15. doi: 10.1037/0278-6133.25.5.604

Owusu, C., Buist, D.S.M., Field, T.S., Lash, T.L., Thwin, S.S., Geiger, A.M. et al. (2008). Predictors of tamoxifen discontinuation among older women with estrogen receptor-positive breast cancer. *Journal of Clinical Oncology, 26,* 549-5. doi: 10.1200/JCO.2006.10.1022

Pan, Y., Heisig, S.R., von Blanckenburg, P., Albert, U-S., Hadji, P., Rief, W. et al. (2018). Facilitating adherence to endocrine therapy in breast cancer: stability and predictive power of treatment expectations in a 2-year prospective study. *Breast Cancer Research and Treatment, 168,* 667-77. doi: 10.1007/s10549-017-4637-2

Partridge, A.H., Wang, P.S., Winer, E.P.,& Avorn, J. (2003). Nonadherence to adjuvant tamoxifen therapy in women with primary breast cancer. *Journal of Clinical Oncology, 21*, 602-6. doi: 10.1200/JCO.2003.07.071

Petrie, K.J., Perry, K., Broadbent, E., & Weinman, J. (2012). A text message programme designed to modify patients' illness and treatment beliefs improves self-reported adherence to asthma preventer medication. *Brtish Journal of Health Psychology, 17,* 74-84. doi: 10.1111/j.2044-8287.2011.02033.x

Quinn, E., Fleming, C., & O'Sullivan, M. (2016). Endocrine therapy adherence: a cross-sectional study of factors affecting adherence and discontinuation of therapy. *Irish Journal of Medical Science, 185,* 383-92. doi: 10.1007/s11845-015-1307-4

Roberts, M.C., Wheeler, S.B., & Reeder-Hayes, K. (2015). Racial/Ethnic and Socioeconomic Disparities in Endocrine Therapy Adherence in Breast Cancer: A Systematic Review. *Americal Journal of Public Health, 105,* e4-e15. doi: 10.2105/AJPH.2014.302490

Seneviratne, S., Campbell, I., Scott, N., Kuper-Hommel, M., Kim, B., Pillai, A., et al. (2015). Adherence to adjuvant endocrine therapy: is it a factor for ethnic differences in breast cancer outcomes in New Zealand? *Breast, 24*, 62-7. doi: 10.1016/j.breast.2014.11.011

Sivell, S., Edwards, A., Elwyn, G., & Manstead, A.S. (2011). Understanding surgery choices for breast cancer: how might the Theory of Planned Behaviour and the Common Sense Model contribute to decision support interventions? *Health Expectations, 14,* 6-19. doi: 10.1111/j.1369-7625.2009.00558.x

Sheeran, P,, & Orbell, S. (2000). Using implementation intentions to increase attendance for cervical cancer screening. *Health Psychology, 19,* 283. doi: 10.1007/s12160-013-9515-5

Sniehotta, F.F., Presseau, J., & Araújo-Soares, V. (2014). Time to retire the theory of planned behaviour. *Health Psychology Review, 8,* 1-7. doi: 10.1080/17437199.2013.869710

Stirratt, M.J., Dunbar-Jacob, J., Crane, H.M., Simoni, J.M., Czajkowski, S., Hilliard, M.E. et al. (2015). Self-report measures of medication adherence behavior: recommendations on optimal use. *Translational Behavioral Medicine, 5,* 470-82. doi: 10.1007/s13142-015-0315-2

Timmers, L., Boons, C.C.L.M., Mangnus, D., Van de Ven, P.M., Van den Berg, P.H., Beeker, A. et al. (2016). Adherence and Patients' Experiences with the Use of Capecitabine in Daily Practice. *Frontiers in Pharmacology, 7,* 310. doi: 10.3389/fphar.2016.00310

van Herk-Sukel, M.P., van de Poll-Franse, L.V., Voogd, A.C., Nieuwenhuijzen, G.A., Coebergh, J.W., & Herings, R.M. (2010). Half of breast cancer patients discontinue tamoxifen and any endocrine treatment before the end of the recommended treatment period of 5 years: a population-based analysis. *Breast Cancer Research and Treatment, 122,* 843-51. doi: 10.1007/s10549-009-0724-3

Zigmond, A.S., & Snaith, R.P. (1983). The HospitalAnxiety and Depression Scale. *Acta Psychiatria Scandinavica, 67,* 361-70. doi: 10.1111/j.1600-0447.1983.tb09716.x

Zimet, G.D., Dahlem, N.W., Zimet, S.G., & Farley, G.K. (1988). The Multidimensional Scale of Perceived Social Support. *Journal of Personality Assessessment, 52,* 30-41. doi: 10.1207/s15327752jpa5201_2

Table 1

Demographic and clinical characteristics of participants

	N (%)
Age	Range 30-90, *M*=51.7 (*SD*=10.3)
Age left full time education	Range 14-33, *M*=18, (*SD*=2.9)
Ethnicity	
White	325 (95%)
Other	19 (5%)
Job Status	
Employed	235 (71%)
Not employed	98 (29%)
Relationship status	
With partner	261 (76%)
Not with partner	82 (24%)
Menopausal status at diagnosis	
Premenopausal	175 (55%)
Menopausal / Post- Menopausal	144 (45%)
Months since prescribed tamoxifen	
< 1 month	28 (8%)
1-3 months	70 (20%)
3-6 months	93 (27%)
6-8 months	47 (14%)
8-12 months	100 (29%)
Stage at diagnosis	
Stage I	138 (41%)
Stage II	153 (45%)
Stage III	39 (11%)
Unsure	11 (3%)
Previous treatment	
Chemotherapy	163 (47%)
Radiotherapy	256 (74%)
Lumpectomy	219 (64%)
Single mastectomy	115 (33%)
Double mastectomy	16 (5%)

Table 2. Results of Latent Growth Models predicting non-adherence

	Common Sense Model		Theory of Planned Behaviour		Combined model	
	Effect on initial non-adherence OR (95% CI)	**Effect on slope**	**Effect on initial non-adherence OR (95% CI)**	**Effect on slope**	**Effect on initial non-adherence OR (95% CI)**	**Effect on slope**
Model slope	0.221		0.619		0.704	
Ethnicity (black/minority ethnic groups)	11.69* (1.29 - 110.61)	-0.01 (-0.35 – 0.32)	26.39** (2.12 – 328.3)	-0.10 (-0.47 – 0.26)	37.4** (2.77 – 504.7)	-0.15 (-0.52 – 0.22)
Job (employed)	3.22 (0.95 – 10.84)	0.18 (-0.01 – 0.36)	2.58 (0.77 – 8.65)	0.09 (-0.09 – 0.28)	3.26 (0.91 – 11.72)	0.14 (-0.06 – 0.33)
Menopausal status (post-menopausal)	1.37 (0.38 – 4.98)	-0.13 (-0.30 – 0.04)	1.70 (0.48 – 5.98)	-0.12 (-0.30 – 0.06)	2.05 (0.94 – 7.93)	-0.20* (-0.39 - -0.01)
Age	0.96 (0.90 – 1.03)	0.00 (-0.01-0.01)	0.97 (0.89 – 1.03)	-0.00 (-0.01 – 0.01)	0.97 (0.90 – 1.04)	0.00 (-0.01 – 0.01)
Distress	1.01 (0.91 – 1.12)	0.02 (-0.00 – 0.03)	0.98 (0.89 – 1.07)	0.01 (0.00 – 0.03)	0.99 (0.88 – 1.10)	0.01 (0.00 – 0.03)
Social support	0.73 (0.48 – 1.11)	-0.01 (-0.07 – 0.05)	0.65* (0.43 – 0.97)	-0.02 (-0.08 – 0.05)	0.61* (0.39 – 0.96)	-0.01 (-0.07 – 0.06)
Side effect intensity	0.97 (0.91 – 1.04)	0.00 (-0.01 – 0.01)	0.98 (0.93 -1.03)	0.00 (-0.01 – 0.01)	0.96 (0.90 – 1.03)	0.00 (-0.01 – 0.01)
Necessity-concerns differential	0.93 (0.83 – 1.04)	-0.03** (-0.05 - -0.01)			0.98 (0.88 – 1.12)	-0.02* (-0.04 - 0.00)
Risk of recurrence	0.95 (0.78 – 1.14)	-0.01 (-0.04-0.01)			0.95 (0.78 – 1.16)	-0.02 (-0.05 – 0.01)
Breast cancer consequences	0.97 (0.81 – 1.16)	0.01 (-0.02 – 0.03)			0.93 (0.77 – 1.12)	0.02 (-0.01 – 0.04)
Personal control	0.94 (0.45 – 1.18)	0.02 (-0.01 – 0.05)			0.98 (0.77 – 1.24)	0.02 (-0.01 – 0.05)
Treatment control	1.30 (0.94 – 1.80)	0.01 (-0.04 – 0.05)			1.22 (0.87 – 1.71)	0.01 (-0.04 – 0.06)
Coherence	0.94 (0.77 – 1.15)	0.01 (-0.03 – 0.03)			1.03 (0.83 – 1.28)	0.00 (-0.03 – 0.04)
Emotional representations	0.93 (0.80 - 1.09)	-0.00 (-0.02 – 0.02)			0.96 (0.82 – 1.13)	-0.00 (-0.03 – 0.02)
Cure	0.86 (0.72 – 1.04)	-0.02 (-0.05 – 0.00)			0.89 (0.73 – 1.08)	-0.03* (-0.06 – 0.00)
Tamoxifen consequences	1.13 (0.95 – 1.34)	0.02 (-0.01 – 0.05)			1.07 (0.89 – 1.29)	0.02 (-0.01 – 0.05)
Causal beliefs: health behaviour	1.04 (0.46 – 2.40)	-0.05 (-0.17 – 0.08)			0.80 (0.34 – 1.90)	-0.02 (-0.16 – 0.10)
Causal beliefs: psychological stress	1.25 (0.67 – 2.32)	-0.06 (-0.14 – 0.02)			1.53 (0.79 – 2.94)	-0.08 (-0.18 – 0.01)
Symptoms attributed to tamoxifen (identity)	1.04 (0.90 – 2.32)	-0.03* (-0.05- -0.00)			1.06 (0.91 – 1.23)	-0.03* (-0.05- 0.00)
Attitude towards tamoxifen			0.96 (0.90 – 1.03)	-0.01 (-0.02 – 0.00)	0.91 (0.98 – 1.05)	-0.01* (-0.02 – 0.00)
Subjective Norm			1.25 (0.75 – 2.06)	0.01 (-0.07 – 0.08)	1.31 (0.76 – 2.25)	0.01 (-0.07 – 0.09)
Perceived Behavioural Control			0.37*** (0.21 – 0.64)	-0.05 (-0.15 – 0.05)	0.34*** (0.19 – 0.62)	-0.02 (-0.11 – 0.07)

Note. *p<.05, **p<.01, ***p<.001. All covariates were measured at baseline.

Table 3. Results of Latent Growth Models predicting unintentional and intentional non-adherence

	Intentional non-adherence			Unintentional non-adherence		
	Effect on initial non-adherence OR 95% CI	**Change in non-adherence (slope)**	**Effect on slope**	**Effect on initial non-adherence OR 95% CI**	**Change in non-adherence (slope)**	**Effect on slope**
Ethnicity (black/minority ethnic groups)	0.99 (0.92 – 1.06)	0.22	-0.00 (-0.01 – 0.01)	11.65* (1.49 – 91.10)	0.11	0.02 (-0.27 – 0.31)
Job (employed)	1.26 (0.26 – 6.18)	0.16	-0.04 (-0.20 – 0.12)	3.79* (1.30 – 11.06)	0.04	0.09 (-0.05 -0.24)
Menopausal status (post-menopausal)	0.98 (0.92 -1.06)	0.24	0.00 (-0.01 – 0.01)	0.47 (0.16 – 1.34)	0.16	-0.10 (-0.23 – 0.03)
Age	0.99 (0.92 – 1.06)	0.02	0.00 (-0.01 – 0.01)	0.95* (0.90 – 0.99)	0.37	-0.01 (-0.01 – 0.00)
Distress	1.15** (1.05 – 1.28)	0.09	0.00 (-0.01 – 0.02)	1.04 (0.98 – 1.11)	-0.01	0.01** (0.00 – 0.02)
Social support	0.64 (0.37 – 1.08)	0.10	0.00 (-0.07 – 0.07)	0.66* (0.45 – 0.96)	0.24	-0.02 (-0.07 -0.03)
Side effect intensity	1.08* (1.02 – 1.15)	0.14	0.00 (-0.01 – 0.01)	1.02 (0.98 – 1.06)	-0.01	0.01* (0.00 – 0.01)
Necessity-concerns differential	0.76** (0.65 – 0.87)	0.10	0.00 (-0.02 – 0.02)	0.92 (0.84 – 1.01)	0.15	-0.02* (-0.03 – 0.00)
Risk of recurrence	0.98 (0.78 – 1.22)	0.14	0.00 (-0.03 – 0.02)	1.03 (0.89 – 1.20)	0.07	0.01 (-0.01 – 0.02)
Breast cancer consequences	1.23 (0.98 – 1.55)	0.08	0.00 (-0.02 – 0.03)	1.10 (0.96 – 1.27)	-0.07	0.02 (0.00 – 0.03)
Personal control	0.97 (0.77 – 1.23)	0.25	-0.01 (-0.03 – 0.02)	1.00 (0.85 – 1.18)	0.08	0.00 (-0.02 – 0.02)
Treatment control	0.76 (0.54 – 1.05)	0.13	0.00 (-0.04 – 0.04)	1.01 (0.82 – 1.24)	0.36	-0.02 (-0.04 – 0.01)
Coherence	0.78* (0.62 – 0.99)	-0.14	0.02 (-0.01 – 0.04)	0.88 (0.74 – 1.04)	0.17	0.00 (-0.03 – 0.02)
Cure	1.04 (0.81 – 1.33)	0.23	-0.01 (-0.03 – 0.02)	0.91 (0.77 – 1.06)	0.31	-0.01 (-0.03 – 0.01)
Emotional representations	1.04 (0.87 – 1.25)	0.09	0.00 (-0.02 – 0.02)	1.05 (0.93 – 1.18)	0.00	0.01 (-0.01 – 0.02)
Tamoxifen consequences	1.33** (1.09 – 1.64)	0.08	0.00 (-0.02 – 0.03)	1.09 (0.96 – 1.25)	-0.07	0.02* (0.00 – 0.04)
Causal beliefs: health behaviour	1.00 (0.37 – 2.68)	0.43	-0.09 (-0.20 – 0.02)	1.50 (0.78 – 2.90)	0.16	-0.01 (-0.10 – 0.07)
Causal beliefs: psychological stress	2.25* (1.03 – 4.92)	0.30	-0.06 (-0.14– 0.02)	1.37 (0.83 – 2.27)	0.14	-0.01 (-0.07 – 0.05)
Symptoms attributed to tamoxifen (identity)	1.20* (1.03 -1.40)	0.14	-0.01 (-0.02 – 0.01)	1.05 (0.95 – 1.17)	0.09	0.01 (-0.01 – 0.02)
Attitude towards tamoxifen	0.87** (0.79 – 0.96)	-0.17	0.01 (-0.01 – 0.02)	0.94* (0.89 – 1.00)	0.53	-0.01 (-0.02 – 0.00)
Subjective Norm	0.73 (0.40 – 1.32)	0.22	-0.02 (-0.08 - 0.05)	0.67 (0.44 – 1.02)	0.34	-0.04 (-0.09 – 0.02)
Perceived Behavioural Control	0.30*** (0.16 – 0.56)	0.05	-0.01 (-0.07 – 0.09)	0.52** (0.34 – 0.78)	0.43	-0.05 (-0.11 – 0.01)

Note. *p<.05, **p<.01, ***p<.001. All covariates were measured at baseline.

Figure 1. Participant retention

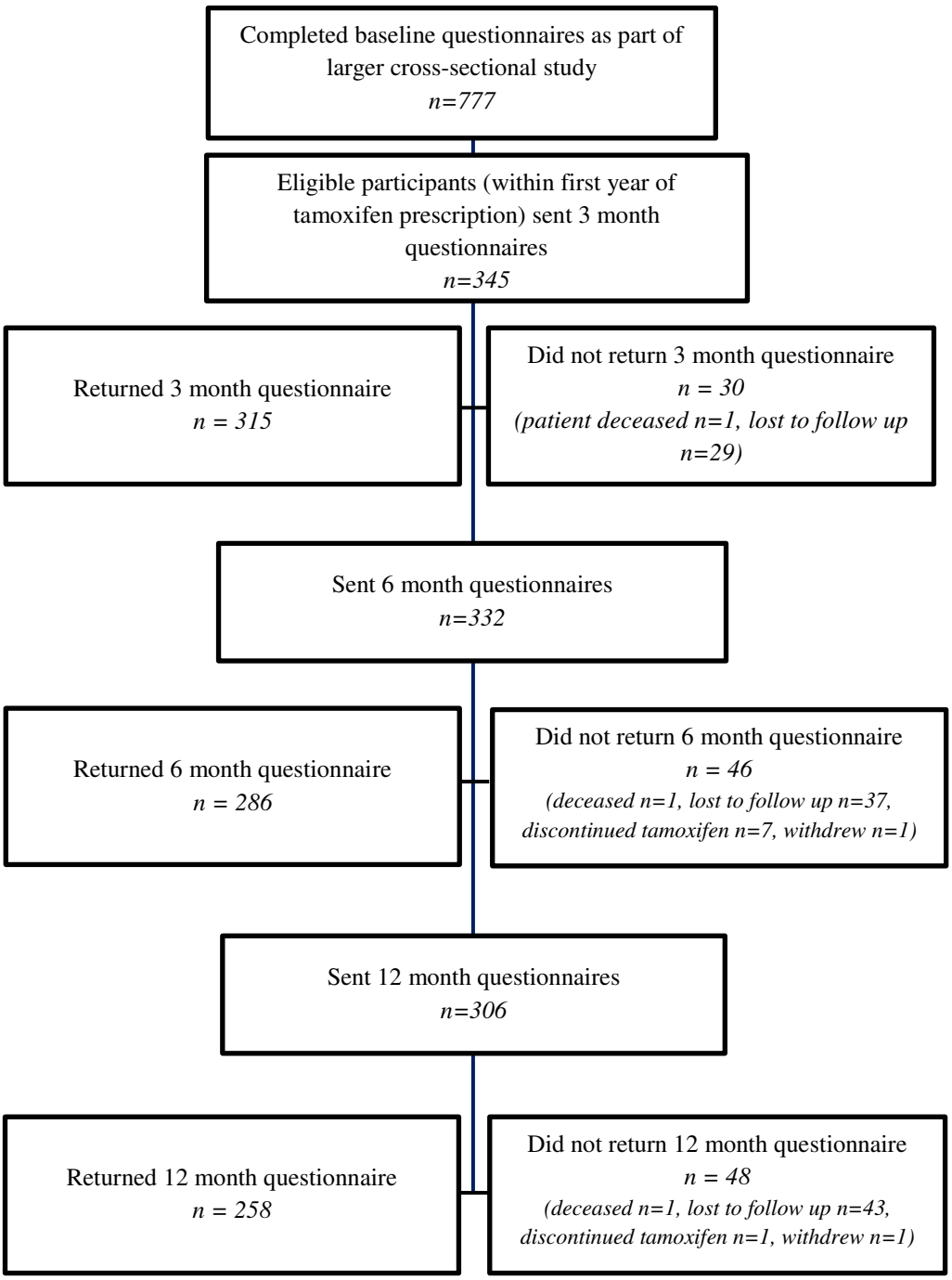
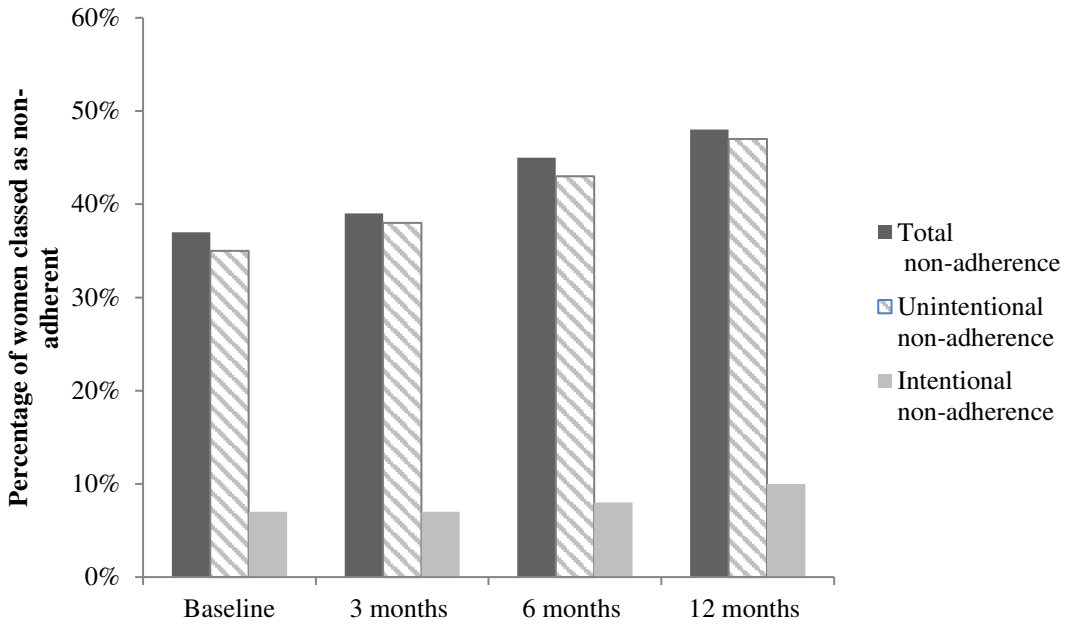


Figure 2. Percentage of women classed as non-adherent at each time point.



Note. Women can be classed as both intentionally non-adherent and unintentionally non-adherent.