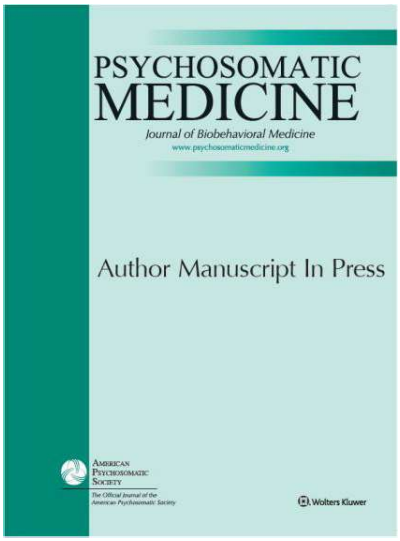

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Unraveling the prospective associations between mixed anxiety-depression and insomnia during the course of cognitive behavioral therapy

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Abstract

Objective: Previous studies have suggested that there is a reciprocal relationship betweenanxiety/depression and insomnia. However, little is known about the prospective relationships between these constructs across the course of cognitive behavioural therapy (CBT). The present study examined these relationships in clients who received short-term cognitive behavioral therapy in a primary care setting.

Methods: 653 clients (mean age = 37.8 [12.9], 26.4% men)with mild to moderate levels of anxiety and depression and a treatment duration of at least 7 weeks were included for analyses.The clients completed questionnaires measuring mixed anxiety-depression (MAD - Patient Health Questionnaire Anxiety and Depression Scale) and insomnia (3 items derived from the Karolinska Sleep Questionnaire representing core DSM-V criteria) on a session-to-session basis. The data were analysed using latent growth curve models and random intercept cross-lagged panel models.

Results: The results of the latent growth curve models showed that there was a significant decrease in both mixed anxiety-depression (cubic slope; B=.002, p<.001, quadratic slope; B=.036, p<.001, linear slope; B= -.205, p<.001) and insomnia (linear slope; B= -.080, p<.001) across treatment. A strong correlation (r=.838, p<.001) between the linear slopes indicated co-occurring change processes. The cross-lagged panel model showed that insomnia significantly predicted mixed anxiety-depression at the subsequent measurements (B=.190; p<.001), but not vice versa (B=.252; p=.343).

Conclusions: Changes in mixed anxiety-depression and insomnia are co-occurring processes during the course of CBT. Changes in insomnia predicted prospectively changes in mixed anxiety-depression, but not vice versa. Targeting insomniain the context of brief CBT in clients with mild to moderate anxiety and depression may thereforenot only further reduce symptoms of insomnia,but also symptoms of anxiety and depression.

Keywords: insomnia, anxiety, depression, cognitive behavioral therapy

List all acronyms

CBT = CognitiveBehavioral Therapy

CBT-I = CognitiveBehavioral Therapy for Insomnia

CFI = Comparative Fit Index

FIML = Full Information Maximum Likelihood

IAPT = Improving Access to Psychological Therapies

ICC = Intra-Class Correlation

MAD = Mixed Anxiety and Depression

MAR = Missing At Random (MAR)

MI = Measurement Invariance

MLR = Maximum Likelihood with Robust standard errors.

PHQ-ADS = Patient Health Questionnaire Anxiety and Depression Scale

PMHC = Prompt Mental Health Care

RI-CLPM = Random Intercept Cross Lagged Panel Model

RMSEA = Root Mean Square Error of Approximation

SRMR = Standardized Root Mean Square Residual

Introduction

Sleep and mental health problems are growing public health concerns, affecting millions of people around the world. Insomnia is the most common sleep disorder, with a prevalence of 10-15% in the general population(1, 2). Anxiety disorders and depression are the most common mental health disorders. Meta-analyses have estimated that the global prevalence of anxiety disorders is around 7% (3), whereas about 5% of the population has a major depressive disorder (4). Single studies applying less stringent criteria for classifying insomnia, anxiety and depression often report higher estimates, and comorbidity between these disorders are common (5, 6).

Traditionally, researchers and therapists have perceived insomnia as secondary to mental health problems such as depression and anxiety. However, the last decadesthere has been an increasing focus on insomnia as a primary diagnosis and as a predictor of poor mental health. Non-depressed individuals with insomnia have twice the risk of developing a depressive episode compared to non-depressed individuals without insomnia (7). Research also indicates that insomnia predicts anxiety (for a review, see 8). Several studies have found evidence for a bidirectional relationship between insomnia on the one hand and depression and anxiety on the other. Jansson-Frøjmark and Lindblom (9) found that anxiety and depression at baseline each increased the risk of new insomnia cases at follow-up one year later, whereas insomnia at baseline in turn increased the risk of new cases of anxiety and depression at follow-up. Sivertsen et al. (10) found that having either insomnia or depression at both baseline and follow-up entailed a six-fold risk of having developed the other disorder at follow-up. In a systematic review of studies on this topic, Alvaro, Roberts, & Harris (11)reported that the evidence thus far suggests a bidirectional relationship, although more longitudinal studies are needed to draw a definitive conclusion.

The aforementioned studies were primarily based on cohort designs with relatively long time-lags, typically using year as unit of measurement for time. Shorter time-lags would be of interest in situations when more rapid changes are to be expected, such as changes following an intervention.Cognitive Behavioural Therapy for insomnia (CBT-I) has been successful in the treatment of primary (12) and comorbid (13) insomnia, as well as reducing levels of both anxiety and depression (14, 15). Conversely, CBT for depression and anxiety also has an effect on insomnia. For example, Mason and Harvey (16) found that Internet-based CBT for anxiety and/or depression was associated with a decrease in anxiety and depression as well as

in insomnia symptoms, and Carney and co-workers (17) reported a significant decrease of insomnia following CBT treatment for depression. However, in the latter study half of those with a pre-treatment insomnia diagnosis still had residual insomnia post-treatment, despite remitting from depression.

To the best of our knowledge, no studies have measured both insomnia and anxiety/depressive symptoms repeatedly throughout the course of CBT treatment to investigate *trajectories* of these symptoms (how each develops over time) and the relationship between these two processes. There are, however, studies that have examined trajectories of depressive symptoms across treatment. Gunthert, Cohen (18) and Kashdan and Roberts (19) found that symptom relief throughout the course of cognitive therapy and group CBTwas best described as curvilinear, with an initial drop before levelling off. Furthermore, we are not familiar with any studies that have explored *cross-lagged relations* between insomnia and anxiety/depression from session to session during treatment (whether insomnia at one session predict anxiety/depression at the subsequent session and vice versa). However, there are studies that have examined cross-lagged relations between other measures over the course of CBT treatment, such as the relationship between fear, avoidance and physiological symptoms across CBT for social anxiety disorder (20).

It should be noted that many studies applying cross-lagged panel models do not account for stable individual differences, and thus fail to represent genuine within-person relations across time(21). The consequence may be inaccurate estimates of the reciprocal effects which may lead to false conclusions regarding the underlying causal relations between variables. As shown by Hamaker et al. (21), this can be avoided by separating the within-person process from stable between-person differences by means of a multilevel approach in which measurement occasions are nested within individuals.

For the current study, data from the Prompt Mental Health Care (PMHC) project were used(22, 23). PMHC is modelled after the English program Improving Access to Psychological Therapies (IAPT) (24), and is a free-of-charge, low-threshold, primary health care program, aimed at reaching adults with anxiety and mild to moderate levels of depression. Cognitive behavioural therapy (CBT) is provided by multidisciplinary teams of health care professionals. Therapy modes include face-to-face, group and guided self-help treatments, offered through a matched care model. Session-to-session data were collected as part of the evaluation of the PMHC program. A previous study based on the same dataset

showed that the program was associated with a clinically significant improvement in symptoms of anxiety and depression from pre-to post-treatment. The reliable recovery rate was 51.6%(23), which is on par with the IAPT target recovery rate (24). The session-to-session data were employedto investigate the trajectories of symptoms of mixed anxiety-depression (MAD) and insomniaover the course of treatment, using latent growth curve modelling. Based on preliminary analyses, we expected a linear-driven improvement during the course of treatment for both symptoms of mixed anxiety-depression (MAD) and insomnia(22). Furthermore, we explored cross-lagged relations between MADand insomnia from session to session, using a random intercept cross lagged panel model (RI-CLPM) (21), to see whether the relationship between MAD and insomnia could best be described as unidirectional or as reciprocal. Based on current evidence, we expected the latter.

Methods

Pilot samples

The study included 12 pilot sites, distributed across several geographical areas, both urban and rural, in Eastern, Western and Central Norway. All PMHC teams were interdisciplinary, and each team had at least one psychologist who carried the professional responsibility for the services provided. All employees had a minimum of three years with relevant higher education, and completed an additional one-year training in cognitive behavioural therapy under the auspices of the Norwegian Association for Cognitive Therapy. The CBT provided to the clients primarily focused on depression and anxiety symptoms. Central elements of CBT-I (sleep diary, stimulus control) were used very little in PMHC (<5%).

Procedures

All clients participated in an initial assessment. During these sessions, information about the study and treatment was provided to the clients, and the therapist collected the necessary data to decide whether PMHC could be the appropriate treatment. The therapist identified the relevance and severity of the mental problems, and the available client resources. A formal diagnosis was not provided. Clients with suspected or known severe psychiatric disorders,

severe substance abuse, and suicide risk were generally excluded from PMHC, and were referred to the general practitioner or more specialized mental health care services.

Participation was based on opt-in, where all eligible clients were invited, and informed written consent was obtained from each participant upon recruitment. The study was approved by the regional ethics committee for Western Norway (REK-vest 2014/597). For the present study, a prospective cohort design was used. The participants were asked to complete questionnaires at pre-treatment, before each session during the treatment, and at post-treatment. For each participant, the therapists were asked to complete a questionnaire at post-treatment about the therapy process.

Participants

Of the 1983 clients that received treatment at PMHC between October 2014 and April 2016, 1279 participated in the study, resulting in an overall participation rate of 64.5%. By April 2016, 970 participating clients had concluded treatment. For the present study, we aimed to examine the development of MAD and insomnia during the first 8 weeks of treatment. Eight weeks was chosen as a trade-off between substantial treatment duration and reasonable sample size. The observations of the included participantswere divided into time intervals as follows: **T1**=0 weeks (n=652, M_{time}=0, SD=0), T2=2 ±1weeks (n=325, M_{time}=2.1, SD=.5), T3=4 ± 1 weeks (n=318, M_{time}=4.1, SD=.5), T4=6 ± 1 weeks (n=300, M_{time}=6.1, SD=.5), and T5=8 ± 1 weeks (n=300, M_{time}=8.1, SD=.5). Measurements were averaged within a time interval in case a client had multiple observations within that specific interval. Clients with a treatment duration less than 7 weeks were excluded (n=118), as were clients for which the treatment duration was unknown due to missing data in the therapist questionnaire (n=199), leaving a total of n=653 clients for further analyses.The final sample (n=653) was comparable to the overall sample (n=970) with regard to sex, age, educational level (low, medium, high), marital status (having a partner vs. not having a partner), immigration background (defined as the clients or his/her parents being born outside Norway), employment status (see definition under 'measures'), and MAD/Insomnia symptoms at baseline (all p>.05). For the final sample (n=653), Little's missing completely at random test based on the demographic variables mentioned above, and longitudinal MAD/Insomniadata with missing values (T1-T5)produced a non-significant chi-squared value ($\chi^2(350)=330.6$, p=.77), which may point to follow-up data missing completely at random.

Measures

The Patient Health Questionnaire Anxiety and Depression Scale (PHQ-ADS) was used to measure MAD (25). The PHQ-ADS includes 16 items based on each of the DSM-IV criteria for depression and anxiety, and could range from 0 ("none of the time) to 3 ("all of the time"). This yielded a total sum score that ranged from 0 to 48. For estimation purposes, the sum score was averaged by the number of items. The PHQ-ADS has shown good psychometric properties (25). Cronbach's alpha based on PMHC data at baseline was .91. MAD was modeled as a manifest variable.

Symptoms of insomnia (labeled *insomnia* throughout the manuscript) were assessed by three items derived from the validated Karolinska Sleep Questionnaire (26). These core insomnia symptoms are based on the DSM-V criteria for insomnia disorder, which include 1) difficulties initiating sleep (sleep onset problems), 2) experiencing frequent nocturnal awakenings (sleep maintenance problems) and 3) daytime tiredness/sleepiness (functional impairment caused by the sleep problem). These items are also included in The Research Diagnostic Criteria for insomnia (27). All items were measured on a scale from 0 to 7 days, yielding a total score range of 0-21. Previous studies have used these three items as a continuous score as well (28, 29). Cronbach's alpha based on PMHC data at baseline was .65. Given this relatively low value for internal consistency, insomnia was modeled as a latent variable.Longitudinal measurement invariance (MI) was found for latent insomnia after testing and sequentially comparing configural, metric, scalar, residual, factor variance, and factor covariance invariance models. Results indicated that the intercept for item 3 at T1 and the factor covariances (f_{t2}, f_{t3}) and (f_{t4}, f_{t5}) should be estimated freely. All other parameters were constrained to be equal across time points in subsequent analyses.

Employment status was assessed by means of two questions, one multi-response item about employment status, and one multi-response item about sources of income (22). Based on these two questions, participants were placed into three categories: 1) in regular work, 2) in combined work and recipients of benefits, and 3) out of work with or without benefits. A similar categorization has been used in another Norwegian treatment study (30).

Statistical analyses

Descriptive statistics were calculated for manifest baseline and outcome variables. Intercorrelations were calculated for MAD and insomnia across time.

All subsequent models were estimated using full information maximum likelihood (FIML) estimation under the assumption of data missing at random (MAR) with robust standard errors (MLR). Model fit was assessed by using the Comparative Fit Index (CFI), the Root Mean Square Error of Approximation (RMSEA), and the Standardized Root Mean Square Residual (SRMR). A CFI≥.95, RMSEA≤.06, and SRMR≤.08 was considered indicative of good model fit(31). To compare nested models, we used the following guidelines based on the recommendations by Chen (32):a change of ≤-.010 in CFI, supplemented by a change of ≥.015in RMSEA or a change of ≥□.010 in SRMR would support the less restricted model (restricted model minus unrestricted model).

Unconditional growth models were estimated separately for MAD and insomnia over the five time points. Intercept only, linear, quadratic, and cubic functional forms were sequentially tested against each other using the same criteria for fit indices as described above. After establishing the best fitting unconditional growth models for MAD and insomnia, baseline covariates were added to examine whether these were associated with the individual growth factors. Unconditional and conditional parallel process models were estimated as well to determine whether the change processes of MAD and insomnia were co-occurring.

To estimate reciprocal relationships over time, a random intercept cross-lagged panel model was fitted to the data (21). As displayed in figure 2 the RI-CLPM model distinguishes between variance at the between-level and variance at the within-level to avoid ecological fallacy. All means were unconstrained with exception of mean insomnia at T1, which was set to zero for the purpose of identification as our model used latent insomnia scores instead of manifest insomnia scores. All other specifications were similar to previous applications of this model (21, 33, 34).

The random intercepts represented stable trait-like, relative individual differences for MAD and insomnia during the 8-weeks treatment period. The cross-lagged parameters indicated the extent to which deviations from an individual's expected MAD score could be predicted from preceding deviations from this individual's expected insomnia score while accounting for the individual's deviation of the preceding expected score on MAD (and vice versa). Expected

scores for individual *i* at time *t* are defined as the temporal group mean at time *t*plus the individual's trait-like deviations from this group mean as modelled by the random intercept.

The Statistical Package for Social Science version 23 for Windows and Mplus version 7.4were used for data analyses.

Results

Baseline characteristics and correlations

Of the 653 participants included in this study, 26.4% (n=170) were men. The average age was 37.8 (SD=12.9), and 37.9% (n=244) of the participants did not have a partner. With regard to educational level, 9.3% (n=60) of the sample had primary education only, 44.2% (n=285) had high school education, whereas 46.5% (n=300) had higher education. The percentage of participants with an immigrant background was 9.4% (n=61). Finally, 40.5% (n=261) was in regular work, 35.0% (n=226) in combined work and recipients of benefits, and 24.5% (n=158) was out of work with or without benefits. The average MAD score was 1.40 (SD=0.60) at baseline, while the average insomnia score was 3.73 (SD=1.92). For MAD (1.40 * 16 items = 22.40), this reflected symptoms at the moderate level(25), which is in line with the intended target population of PMHC and IAPT (23, 24). A similar categorization was difficult for the insomnia score as established norms were not available. Still, the average insomnia score in the current sample was higher than among healthy Swedish adults (rescaled average = 2.8)(29).

Observed means based on manifest scores with regard to MAD and insomnia indicated a monotone decrease between T1 (MAD_{t1}=1.40, SD=.60; $Insomnia_{t1}$=3.73, SD=1.92) and T5 (MAD_{t5}=.90, SD=.59; $Insomnia_{t5}$=3.01, SD=2.02). According to conventional guidelines, this corresponded to a large change in MAD (Cohen's d=.83) and close to a medium change in insomnia (Cohen's d=.38) during the initial 8-week treatment period.High correlations between time points with regard to respectively MAD ($.63\leq r\leq.86$) and insomnia ($.67\leq r\leq.87$) indicated relatively high degrees of stability across time. Correlations between MAD and insomnia across time were moderate to large ($.35\leq r\leq.61$).

As the data was collected at multiple sites (average cluster size = 54), intraclass correlations (ICCs) were calculated for the outcomes variables at each time point. ICC's were generally

very low (<.01), and accounting for the cluster effect of pilot site was therefore considered unnecessary.

Growth curve models for mixed anxiety-depression and insomnia

The best functional form for the unconditional MAD model was cubic with mean intercept (SE) = 1.402 (.023), mean linear slope = -.205 (.018), mean quadratic slope = .036 (.006), and mean cubic slope = -.002 (.000) (see Table S1, Supplemental Digital Content, http://links.lww.com/PSYMED/A542). For this model, the variance of the cubic slope factor was constrained to zero to avoid non-convergence. The trajectory of MAD was characterized by a monotone decrease during the 8-weeks treatment period with the decrease during the first two weeks being largest (see Figure 1). The best functional form for the unconditional insomnia model was linear with mean intercept = .000 (by default due to the latent variable specification) and mean linear slope = -.080 (.010), see figure 1 and Table S1, Supplemental Digital Content, http://links.lww.com/PSYMED/A542). This indicated a linear decrease in insomnia during the 8-weeks treatment period.

In the next step, baseline predictors were added to the selected growth curve models (Table 1). For MAD (CFI=1.000, RMSEA=.000, SRMR=.010), younger age, immigration background, and being in combined work and recipient of benefits was associated with higher levels of MAD at baseline. Immigration background was also associated with a lower linear slope. Together with the higher average baseline levels, this may indicate that treatment was less effective for clients with an immigrant background. For insomnia (CFI=.958, RMSEA=.034, SRMR=.046), female sex and being in combined work and recipient of benefits were associated with higher levels of insomnia at baseline.

Both the unconditional and the conditional parallel process models showed good model fit (see Table S2, Supplemental Digital Content, http://links.lww.com/PSYMED/A542). There was a strong significant correlation between the intercepts of MAD and insomnia indicating that clients with high levels of MAD at baseline were also more likely to have high levels of insomnia at baseline (r_{cond}=.838, p<.001). Similarly, there was a strong correlation between the linear slope parameters of MAD and insomnia, indicating that these two change processes were co-occurring and shared about 57% of their linear change variance (r_{cond}=.758, p<.001). All other associations between the growth parameters of these two processes were not statistically significant (Table S2). It should be noted that the variance of the quadratic and

cubic MAD slope factors were constrained to zero in both models to avoid convergence problems.

Random intercept cross-lagged panel model (RI-CLPM) for mixed anxiety-depression and insomnia

The unconditional RI-CLPM with unconstrained autoregressive and cross-lagged parameters showed adequate model fit (CFI=.986, RMSEA=.025, SRMR=.044) and served as a base model for the comparison with more constrained models. The subsequent models with constrained autoregressive parameters (□CFI=-.002, □RMSEA=.001, □SRMR=.003), and constrained autoregressive &cross-lagged parameters (□CFI=-.002, □RMSEA=.001, □SRMR=.004)fitted the data equally well as the base model. Therefore, the most restrictive model with constrained autoregressive & cross-lagged parameters was used to examine the parameters of interest in further detail.

Between 48.8% to 52.8% of the variance of MAD was explained at the between level. For insomnia, this percentage was between 50.0% and 60.5%.As displayed in Table 2, the results showed a strong correlation between MAD and insomnia at the between-person level (r=.601, p<.001). This correlation reflects stable between-client traits during the 8-weeks treatment period. That is, clients with higher average levels of MAD also showed higher average levels of insomnia.

There was a large correlation at the within-level at T1 (r=.622, p<.001). This indicates that the client's individual deviation from their own expected score on MAD at baseline was strongly linked to the individual's deviation from their own expected score on insomnia at baseline. The residual correlations from T2 to T5 were also high (r>.55, all p<.001), indicating that the within-person changes in MAD were strongly associated with the within-person changes in insomnia, and arelinked through other, unmeasured time-varying variables.

For both MAD and insomnia, the stability paths were positive and statistically significant (Table 2). This indicated that a client scoring above (or below) his/her expected score at one occasion was likely to score above (or below) his/her expected score at the next occasion. In addition, statistically significant cross-paths were found for insomnia (t-1) to MAD (t). That is within-person changes in insomnia predict within-person changes in MAD (B=.190, S.E.=.034, p<.001, see also Table 2). Thus, a client's deviation from his/her own score in MAD was predicted by this client's deviation in insomnia at the previous time point while

accounting for time-variant and time-invariant stability. Cross-paths in the opposite direction, MAD (t-1) to insomnia (t), were not statistically significant (B=.252, S.E.=.265, *p*=.34, see also Table 2).

Discussion

Our main findings from the latent growth curve models were, as expected, a decrease in insomnia (linear) and MAD (cubic) over the course of treatment. The latter is in line with studies that have reported a curvilinear trend for depressive symptoms over the course of treatment (18, 19). The mean observed scores on the PHQ-ADS indicate that the severity of MAD in the sample on average was moderate at baseline and mild at the end of treatment. A decrease in symptoms of both MAD and insomnia from baseline to the end of treatment is in line with what Mason and Harvey (16) reported from their study on internet-based CBT for anxiety and/or depression. The steeper decrease in MAD compared to the decrease in insomnia may reflect that the treatment was mainly targeted towards anxiety and/or depression.

The significant positive correlation between the intercepts of MAD and insomnia is in line with research reporting positive correlations or high prevalence of comorbidity between insomnia and mental distress(5-7, 9-11). The positive correlation between the linear slopes of MAD and insomnia may indicate a causal link whereby one or both of the processes influence the other, or alternatively that a third variable affect both processes. For the present study, receiving CBT treatment was likely to be one such a process.

We found that younger clients had higher levels of MAD compared to older clients. Despite some conflicting findings in the literature and the question of possible cohort effects, a literature review reported that there is some evidence for a decrease in anxiety and depression across the adult life span (35). Clients with an immigration background also had higher levels of MAD. Immigrants in Norway are reported to have poorer mental health compared to ethnic Norwegians (36), and they are often less likely to seek help for mental health problems (37). When it comes to insomnia, women had higher levels than men did. There is compelling evidence that women have an increased risk of insomnia compared to men (38). We did not find many indications that treatment response varied according to client characteristics. The exception was for immigrant background, in that clients with an immigration background had

a slower rate of change in MAD. This may indicate a lower treatment response in these clients. Treatment response may be affected by factors such as communication difficulties between the therapist and the client, and contradictions between the client's and the therapist's conceptions of the disease (39).

Our main finding from the cross-lagged analyses was that insomnia predicted MAD at the subsequent time point, but not vice versa. Thus, we did not find evidence for a bidirectional relationship between insomnia and MAD, contrary to what has been reported from previous studies the last decade (9, 40). These studies used a time lag of one and eleven years, respectively, and they were not conducted in a therapeutic setting. Moreover, the aforementioned studies did not explicitly model within- and between-person processes, which may lead to biased estimates of reciprocal effects (21).

Although previous studies have indicated that treatment was effective in reducing both mental health symptoms and insomnia(22, 23), the CBT provided to the clients was not specifically targeted towards insomnia (i.e., not CBT-I).Our finding that insomnia (t-1) predicted MAD (t) suggests that targeting insomniacould be an important part of treatment for anxiety and depression, because this may lead to a further decrease in both insomniaand MAD symptoms. Results from other studies have pointed in the same direction (41-44), most notably a recent large-scale randomized controlled trial among university students which found strong evidence thattreating insomnia leads to improved mental health(41).

Strengths and limitations

The main strengths of the present study are the collection of data at every session throughout treatment, a relatively large sample size, and the choice of methods to analyse these data. Numerous studies have examined the relationship between insomnia and anxiety/depression in the general population with a long time span, or in the clinical populationwith measurements pre and post treatment only.We examined cross-lagged relations between insomnia and MAD throughout the course of therapy using five repeated measurements. Structural equation modelling has several advantages compared to traditional approaches. These include the modelling of intra- and inter-individual differences, estimation of latent factors separated from error variance, and flexible methods for handling missing data (45).

Growth curve models permit investigating trajectories of symptoms and a RI-CLPM permits the investigation of genuine within-person cross-lagged relations across time.

There are also some limitations to the present study. Symptom assessment of MAD and insomnia were based on self-report only. It cannot be excluded that, for example, insomnia scores were somewhat inaccurate due to possible mood-dependence. For the replication of the current findings, increasing measurement accuracy by means of additional modes of assessment (e.g. clinical interview, diaries, actigraphy) is recommended. Moreover, the insomnia measure did not include a specific item on early morning awakenings, which may have affected its construct validity.

By investigating symptoms of mixed anxiety-depression rather than anxiety and depressive symptoms separately, there is a risk of missing important information concerning reciprocal relations that may be specific to the disorder. According to a retrospective population study, insomnia was in most cases present before or at the same time as symptoms of a mood disorder, whereas it was present at the same time or after an anxiety disorder(46).Similarly, in a study of adolescents with comorbid insomnia and depression/anxiety, insomnia occurred first in the majority of cases concerning depression, whereas it occurred after in the majority of cases concerning anxiety (47).

In the previously mentioned longitudinal studies where bi-directionality was assessed (9, 40), the Hospital Anxiety and Depression Scale (HADS) was used to measure anxiety and depression. A main difference between HADS and PHQ-ADS is that the latter includes one item related to sleep ("troubles falling or staying to sleep, or sleeping too much") and one item related to lack of energy ("feeling tired or having little energy"), whereas the former does not. Thus, there is some overlap between the two measures in the present study. However, a sensitivity analysis excluding the two items mentioned above had minimal impact on the results for the RI-CLPM (not shown).

The sample consisted of clients with anxiety and mild to moderate depression, undergoing CBT of a relatively short duration. The current findings may therefore be particular relevant to clients receiving treatment in primary health care settings through programs similar to PMHC, but may not be generalizable to clients with more severe symptoms or longer treatment periods. Although the latter is a limitation in itself, it should be noted that the potential group of clients that could benefit from CBT treatment in primary health care is assumed large (48). Increasing the availability of programs such as PMHC is therefore

important, not the least because many clients do not fulfil the criteria of severity of problems set by specialized mental health services.

Generalizability to the entire target group of PMHC may be compromised due to the relatively low participation rate of 64.5%. Although data for non-participants were unavailable, some selection among participants seems reasonable to assume (e.g. more females, less severe symptoms at baseline).

It has been shown that the length of the time lag can affect the cross-lagged regression coefficients (49). Finding the optimal time lag a-priori can be challenging as it depends on the actual size of the autoregressive and cross-lagged associations, which is typically information that is not available prior to data collection. In the present study, the intervals between occasions were on average 2 weeks. Based on the autoregressive and cross-lagged coefficients found in our study and the formula from Dormann & Griffin (49), the estimated optimal time lag was 1.22 weeks. This implies that the strength of our cross-lagged associations may be somewhat underestimated.

Conclusions

This study found that over the course of brief CBT, in clients with mild to moderate levels of MAD, clients' changesin insomnia predict changes in symptoms of mixed anxiety-depression, but not vice versa. Targeting insomnia in clients with comorbid insomnia and depression/anxiety may thus be vital for optimal effect of cognitive behavioural therapy for anxiety and/or depression. Based on our findings we recommend that therapists perform CBT-I or place larger emphasis on implementing elements from CBT-I in their therapeutic approach to clients with comorbid insomnia and anxiety/depression.

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FIGURE CAPTION

Figure 1. Unconditional average growth curves for mixed anxiety-depression and insomnia (bold line). The thin grey lines represent the estimated individual growth curves of 50 randomly selected participants.

Figure 2. Random intercept cross-lagged panel model of the relationship between mixed anxiety-depression and insomnia.

Figure 1

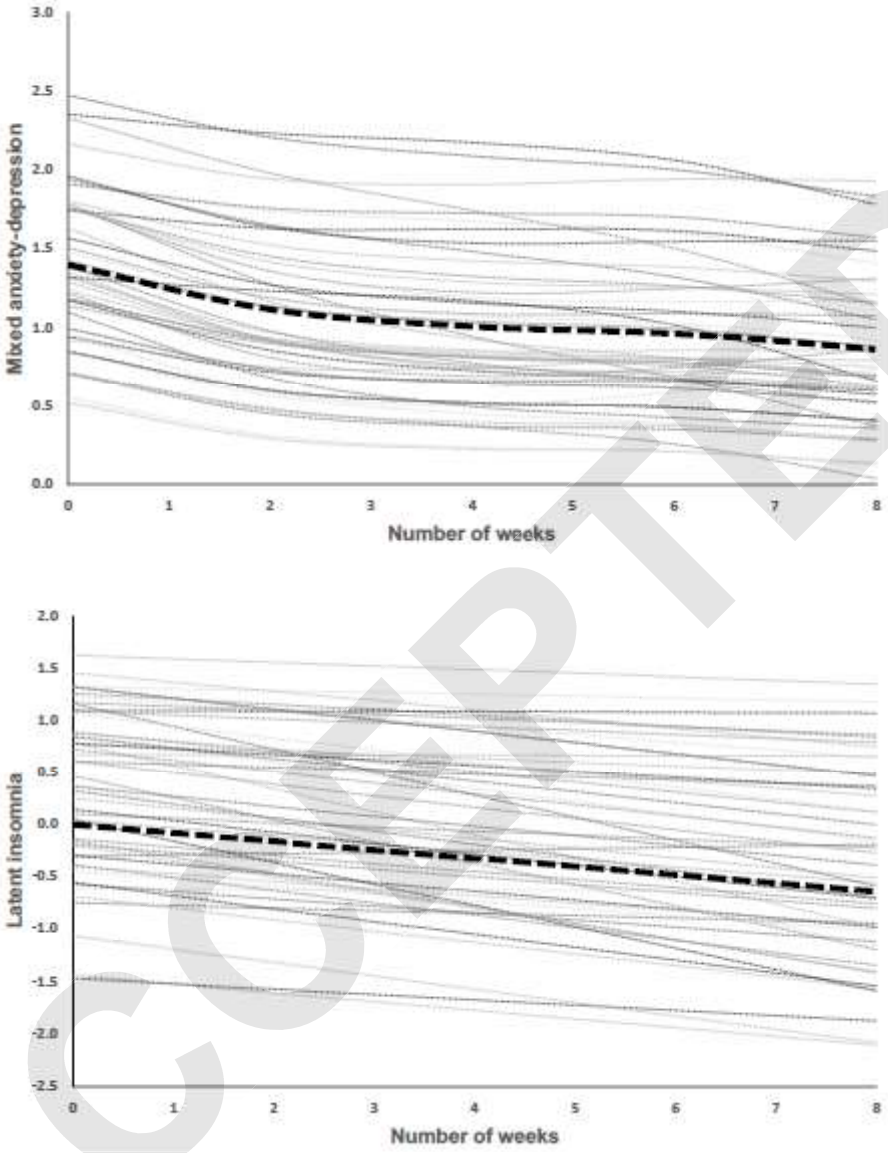

Figure 2

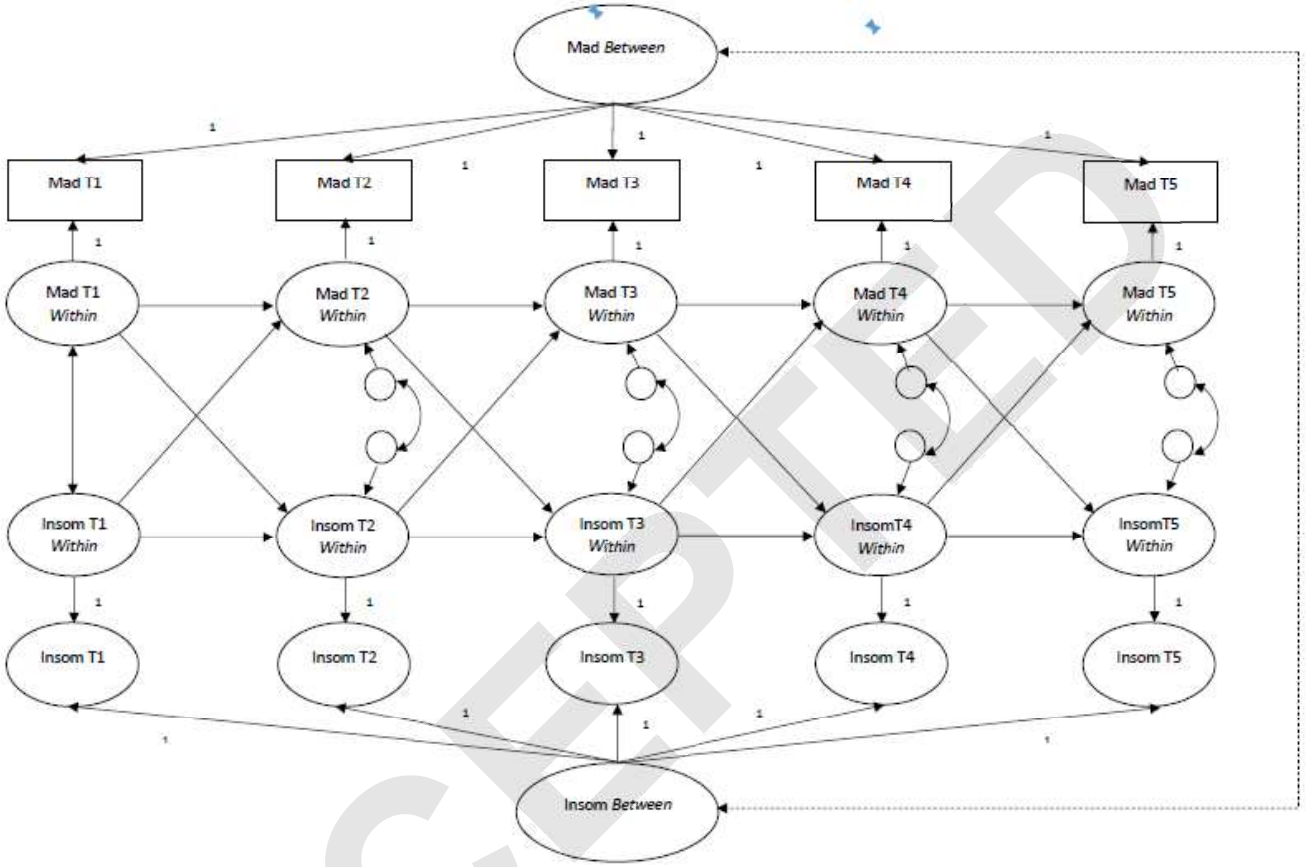

Table 1. Unstandardized predictors of MAD and insomnia growth curve trajectories (conditional growth model, robust maximum likelihood, N=629).

	Mixed anxiety-depression			**Insomnia**	
Baseline predictors	Intercept b *(SE)*	Linear slope b *(SE)*	Quadratic slope b *(SE)*	Intercept b *(SE)*	Linear slope b *(SE)*
Female sex	.078 (.053)	.026 (.023)	-.002 (.003)	.459 (.162)**	.000 (.022)
Age	-.007 (.002)***	.001 (.001)	.000 (.000)	.009 (.007)	.000 (.001)
Not having a partner	.004 (.048)	-.014 (.019)	.001 (.002)	.106 (.156)	-.004 (.022)
Immigration background	.209 (.078)**	-.035 (.033)*	.003 (.004)	.311 (.253)	-.029 (.037)
Educational level					
Middle vs low	-.067 (.086)	-.011 (.038)	.001 (.005)	.131 (.265)	-.029 (.030)
High vs low	-.162 (.085)	-.027 (.038)	.001 (.005)	-.003 (.265)	-.050 (.033)
Employment status†					
In combined work and recipient of benefits	.216 (.053)***	-.033 (.023)	.003 (.003)	.717 (.178)***	-.024 (.024)
Out of work with or without benefits	.076 (.061)	.055 (.028)	-.006 (.003)	.343 (.195)	.008 (.029)

†Reference category = regular work; ***$p<.001$ **$p<.01$ *$p<.05$.

Table 2. Parameter estimates of the unconditional random intercept cross-lagged panel model (robust maximum likelihood, N=653).

	Unstandardized b (SE)	**Standardized □(SE)**
Autoregressive		
Mad t2 ON Mad t1[†]	.237 (.110)[*]	.245 (.105)[*]
Mad t3 ON Mad t2	.237 (.110)[*]	.249 (.116)[*]
Mad t4 ON Mad t3	.237 (.110)[*]	.225 (.113)[*]
Mad t5 ON Mad t4	.237 (.110)[*]	.239 (.111)[*]
Sleep t2 ON Sleep t1	.733 (.113)[***]	.593 (.115) [***]
Sleep t3 ON Sleep t2	.733 (.113)[***]	.767 (.122) [***]
Sleep t4 ON Sleep t3	.733 (.113)[***]	.700 (.109) [***]
Sleep t5 ON Sleep t4	.733 (.113)[***]	.732 (.120) [***]
Cross-lagged		
Mad t2 ON Sleep t1	.190 (.034)[***]	.433 (.087)[***]
Mad t3 ON Sleep t2	.190 (.034)[***]	.562 (.104)[***]
Mad t4 ON Sleep t3	.190 (.034)[***]	.511 (.085)[***]
Mad t5 ON Sleep t4	.190 (.034)[***]	.541 (.089)[***]
Sleep t2 ON Mad t1	.252 (.265)	.093 (.102)
Sleep t3 ON Mad t2	.252 (.265)	.094 (.106)
Sleep t4 ON Mad t3	.252 (.265)	.085 (.098)
Sleep t5 ON Mad t4	.252 (.265)	.089 (.099)
Other		
Association (Mad t1, Sleep t1)	.254 (.100)[**]	.622 (.094)[***]

Residual association (Mad t2, Sleep t2)	.194 (.032)***	.666 (.063)***
Residual association (Mad t3, Sleep t3)	.098 (.028)***	.647 (.100)***
Residual association (Mad t4, Sleep t4)	.120 (.034)***	.555 (.105)***
Residual association (Mad t5, Sleep t5)	.118 (.024)***	.616 (.093)***
Between-person association ($Intercept_{MAD}$, $Intercept_{SLEEP}$)	.296 (.101)***	.601 (.087)***

†Mad = mixed anxiety-depression; ***$p<.001$ **$p<.01$ *$p<.05$.