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Symptoms of depression and insomnia in older age: A within-individual analysis over 20 years

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Abstract

Background: Depression and insomnia often co-occur, and precede one another. Possibly, insomnia gives rise to depression, and vice versa. We tested whether insomnia symptoms of an older individual are associated with later depressive symptoms in that older individual, and vice versa.

Methods: We performed a longitudinal analysis of data from a prospective cohort study in a large sample of community-dwelling older people ($N = 3081$), with measurements every three years, over a time period of 20 years. The within-individual longitudinal reciprocal relationship between symptoms of depression (Center for Epidemiological Studies Depression Scale), and symptoms of insomnia (three-item questionnaire, including difficulty initiating sleep, nightly awakenings, and early morning awakening) was modeled by means of a bivariate linear growth model. We tested whether symptoms of insomnia were associated with symptoms of depression three years later, and vice versa.

Results: Severity of symptoms of depression and insomnia and their within-individual average change over time were moderately correlated (correlation of intercepts: rho 0.41, 95% CI: 0.36 to 0.46 $p < 0.001$; correlation of slopes: rho 0.39, 95% CI: 0.25 to 0.52, $p < 0.001$). Symptoms of depression were not found to be associated with an additional risk of higher symptoms of insomnia three years later, and vice versa ($p = 0.329$ and $p = 0.919$, respectively). Similar results were found when analyses were corrected for covariates.

Conclusions: In older individuals, depression and insomnia are associated and tend to increase concurrently over time, but constitute no additional risk for one another over repeated three-year intervals. These findings contradict previous research that suggests that depression and insomnia are risk factors for one another over time. The current study stands out due to the longitudinal within-individual statistical approach, but is limited by the three-year interval between measures.

KEYWORDS
depression, depressive, elderly, insomnia, older, sleep

INTRODUCTION

Depression and insomnia are common, and affect about 1 in every 10 individuals.[1,2] Depression is a mental state characterized by depressed mood or loss of interest or pleasure, in combination with other symptoms such as problems concentrating or making decisions, fatigue, problems sleeping, alterations in appetite or body weight, feelings of worthlessness or excessive guilt, or thoughts of death or suicide, nearly every day.[3] Insomnia refers to a report of sleep initiation or maintenance problems despite adequate opportunity and circumstances to sleep, with daytime consequences, at least three times a week.[4] The conditions have negative effects on health, functioning, and well-being, and their prevalence and severity increases with age.[1,2] The syndromes of depression and insomnia show overlap, with insomnia being a symptom of depression, and depression and insomnia may co-occur.[3,5,6] Insomnia symptoms often precede a depressive episode, and insomnia symptoms frequently remain after resolution of a depression.[7–17] Hence, one may wonder whether insomnia gives rise to depression, and vice versa. Possibly, a sequential comorbidity model applies, which implies that a primary disorder (e.g., insomnia) or its treatment increase the onset of a secondary disorder (e.g., depression).[6] If so, timely treatment of insomnia may help to prevent future depression, and vice versa.

Key points

- In older individuals, both depression and insomnia are associated phenomena and tend to increase concurrently over time.
- Depression and insomnia constitute no additional risk for one another over time, as measured in three-year intervals during 20 years.

Why does this paper matter?

Our findings support the idea that depression and insomnia are closely related but independent phenomena. After adjustment for contemporal associations, no associations were found between symptoms of depression and insomnia three years later and vice versa. For this reason, treatments should focus on reduction of both depressive symptoms and insomnia concurrently.

In the present study, we tested whether insomnia symptoms of an older individual were associated with later depressive symptoms in that older individual, and vice versa (Figure 1). Such analyses call for specific

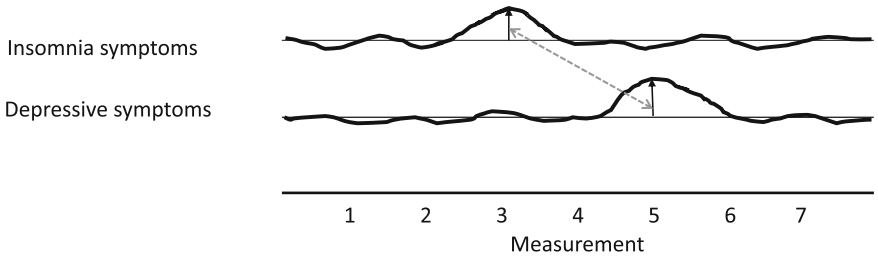

FIGURE 1 Graphical representation of the hypothesized cross-lagged association of symptoms in an older individual. For simplicity, the graph only includes the cross-lagged association between insomnia symptoms and future depressive symptom (indicated by the dashed arrow), and not the cross-lagged association between depressive symptoms and future insomnia symptoms. The solid arrows indicate a deviation in symptoms from the prospected course of symptoms

statistical analyses (bidirectional longitudinal association study of within-individual cross-lagged effects) that require large datasets, with multiple measures over time.

We used data from a large naturalistic cohort study in older adults, with measurements every three years over a 20-year period: the Longitudinal Aging Study Amsterdam (LASA)[18]; and modeled the bidirectional longitudinal association between symptoms of depression and insomnia using a bivariate linear growth model.[19–23]

Our findings could further improve the understanding of the interaction between depression and insomnia, and may guide the primary and secondary prevention of depression and insomnia in older people.

METHODS

Study population

Analyses were performed on data from the LASA, an ongoing prospective cohort study of older people in the community in the Netherlands. The study has been described in detail elsewhere.[18] The LASA cohort is a nationally representative sample of community-dwelling older adults aged 55 to 85 years living in three geographically distinct areas, with respondents from both urbanized and rural areas. A random sample of 3107 persons was included for the first examination in 1992–1993. Follow-up examinations took place every 3 years from 1995–1996 to 2011–2012, and included 2545, 2076, 1691, 1257, 985, and 763 persons, respectively. Attrition was mainly due to mortality.[18] The Medical Ethics Committee [removed for double-blind review], approved the study, and informed consent was obtained from all participants. All procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

In this study, individuals with at least one measurement on either symptoms of depression or symptoms of insomnia were included. This resulted in a total sample-size of 3081 for the unadjusted analysis.

Measurements

Symptoms of depression and insomnia were assessed every three years over a period of 20 years. The baseline and follow-up examinations will be referred to as 'waves'.

Symptoms of depression were measured using the CES-D (Center for Epidemiological Studies Depression Scale), a self-report scale of 20 items.[24] Total scores range from 0 to 60, with higher scores indicating more depressive symptoms. A score of 16 or higher is indicative of clinically relevant symptoms with high sensitivity and specificity for major depressive disorder.[24] The CES-D contains one question about sleep ('My sleep was restless.'). For assessing associations between symptoms of depression and insomnia, we used adjusted CES-D scores that did not take this sleep question into account. This was done to focus on the association of symptoms of depression with symptoms of insomnia irrespective of the contribution of insomnia to the construct of depression.

Symptoms of insomnia were measured using a three-item self-report questionnaire, including questions on the difficulty initiating sleep, nightly awakenings, and early morning awakening, which were rated as almost never, sometimes, frequently, or almost always. Total scores range from 0 to 12, with higher scores indicating more severe insomnia symptomatology.

Covariates included age, gender, education level, medication use (antidepressants, anxiolytics, hypnotics), use of alcohol, reported pain, and chronic diseases. Highest level of completed education (education level) was classified into nine categories, ranging from elementary not completed to university education. Information on medication use was provided by the participants. Use of alcohol was self-reported as the number of standardized drinks (containing approximately 10 gram of alcohol) per week. Pain was estimated using five items from the Nottingham Health Profile pain scale.[25] Total scores range from 5 to 10, with higher scores indicating more pain. Number of chronic diseases was assessed by self-report,[26] and cross-checked with the general practitioners of the participants.

Statistical analyses

A bivariate linear growth model was used to jointly model the longitudinal course of symptoms of depression and insomnia within the individual. In this model, cross-lagged effects between symptoms of insomnia and symptoms of depression can be included to test how deviations from an individual's typical course of insomnia symptoms influence later depressive symptoms.

The bivariate linear growth model is a special case of a structural equation model where the observed longitudinal courses of symptoms of depression and insomnia are assumed to be realizations of two underlying linear growth curves with unobserved (latent) intercepts and slopes, with intercepts and slopes of the two growth curves correlated.[19–23] The bivariate growth model allows both symptoms of depression and insomnia to act as dependent and independent variables in a single model.

In this situation, the correlation between symptoms insomnia and symptoms of depression is partitioned in a cross-sectional correlation (i.e., intercept correlation), the tendency of linear changes in both to be correlated (i.e., slope correlation), and the tendency of the linear change to be correlated with correlated with the level of symptoms (i.e., intercept-slope correlations).

Cross-lagged correlations (symptoms of depression at time t correlated with symptoms of insomnia at time t−1, and vice versa) were added to the bivariate linear growth model to test whether at the individual level higher scores on symptoms of depression were associated with higher scores of symptoms of insomnia and vice versa on the subsequent wave, beyond what could be expected based on the linear growth and, when applicable, values for the covariates alone. The cross-lagged effects were incorporated in the model by including symptoms of depression on the previous wave as a time-dependent covariate for symptoms of insomnia and vice versa.

Goodness of fit of the models (how well the model represents the data) was assessed by means of the model chi-square, the root mean square error of approximation (RMSEA), the comparative fit index (CFI), and the sample-size adjusted Bayesian information criterion (BIC). Higher chi-square values indicate better fit, with values ≥90 indicating good fit. RMSEA is a measure of absolute fit (relative to the perfect model), and lower values indicate better fit. It is generally presumed that a value between 0.05 and 0.08 suggests a reasonable fit, and that a value of <0.05 indicates a close fit. CFI is a comparative measure of fit (relative to a baseline model), and larger values indicate better fit. BIC is a criterion for model selection, to correct for overfitting with the addition of parameters to the model using penalties. Models with lower BIC are preferred. Added-value of the cross-lagged effects was evaluated by testing the statistical significance by means of the χ^2 difference test for nested models.

Regression coefficients for time-varying coefficients, residual variances for symptoms of depression and insomnia and between-construct residual correlations were restricted to be constant across waves. A graphical representation of the full model is given in Figure S1.

Sensitivity analyses were performed to test the robustness of the findings, and included analyses, including covariates and subgroup analyses.

To control for sources of between-participant variation, we included age at first wave, gender, their two-way interaction, and education level as time-invariant covariates acting on the intercept and slope of symptoms of insomnia and depression (adjusted[1] model). Education level was categorized into nine groups, ranging from elementary not completed to university education, and was included as a continuous independent variable in the models. To additionally control for possible sources of variance at the individual level, time-varying covariates were added to the model for repeatedly measured candidate confounders, including alcohol consumption, the number of comorbid chronic diseases, and pain scores (adjusted[2] model), as well as the use of antidepressants, anxiolytics, and hypnotics (adjusted[3] model). Regression coefficients for the contemporaneous effect of these time-varying covariates on symptoms of depression and insomnia were restricted to be constant across the waves. To facilitate interpretation of the regression coefficients for the adjusted models, regression coefficients were calculated with men as the reference category for gender, and age at first wave was centered at 65 years. Education level was centered at the mode, which was elementary education. Pain scores were centered at 5, which was the minimum value. No use of medication, no alcohol use, and no comorbid disease were the reference value for the other time-variant covariates.

To evaluate whether result was similar across subgroups of participants, the analyses were repeated for subgroups of participants defined by age at the first wave (below 70 years and 70 or older), gender, and occurrence of a clinically relevant depression during follow-up (participants with at least one wave CES-D ≥ 16 and participants with CES-D < 16 on all waves).

The bivariate linear growth models were fitted in M-plus version 7. Missing values on symptoms of depression and insomnia were considered missing at random, and were not imputed. Missing values on the time-varying covariates were imputed using a Last Observation Carried Forward (LOCF) approach. SPSS version 22.0 was used for the descriptive statistics. *p*-values <0.05 were considered significant.

RESULTS

Sample characteristics

In total 3081 individuals were included in the unadjusted analyses (3075 individuals in the adjusted[1] analyses, and 1939 in the adjusted[2] analyses). The sample-size decreased over time, mainly due to mortality.[18] At the first wave, the mean age was 70.7 years and 51.6% were women. The mode for education level was elementary education for all subsamples. At the first wave, the median symptoms of depression score were 6 and the median symptoms of insomnia score 6; 14.7% of the individuals experienced clinically relevant depressive symptoms (CES-D ≥ 16). At the first wave 1.9%, 6.1%, and

TABLE 1 Cohort characteristics

Baseline characteristics							
N	3081						
Age, mean (SD)	70.7 (8.7)						
Women, %	51.6						
Education level[a], % higher vocational, or university other	11.3 88.7						
Wave-specific descriptives							
Wave, number	1	2	3	4	5	6	7
Wave, year	1992–1993	1995–1996	1998–1999	2001–2002	2005–2006	2008–2009	2011–2012
N symptoms of insomnia	2224	2021	1689	1287	956	739	523
N symptoms of depression	3056	2212	1853	1453	1034	825	606
Symptoms of insomnia, median (IQR)	6 (4–7)	6 (4–7)	6 (4–7)	6 (4–7)	6 (4–7)	6 (4–7)	6 (4–7)
Symptoms of depression, median (IQR)	6 (2–11)	6 (2–11.75)	7 (3–13)	8 (4–13)	7 (4–13)	7 (3–12)	8 (4–14)
Clinically relevant depressive symptoms, %	14.7	15.0	17.4	17.1	16.2	15.2	19.6
Medication use, % antidepressants	1.9	2.7	4.1	5.0	5.0	4.6	6.0
anxiolytics	6.1	6.8	7.4	6.4	5.4	4.3	4.0
hypnotics	8.2	9.4	11.9	8.9	7.7	9.2	9. 1
Alcohol use, number of drinks per weeks, median (IQR)	3 (0.5–10)	3 (0–7)	3 (0.5–7)	3 (0.5–12)	2 (0.5–7)	2 (0.5–7)	2 (0–7)
Chronic diseases, number, median (IQR)	1 (0–2)	2 (1–2)	2 (1–3)	2 (1–3)	2 (1–3)	2 (1–3)	3 (2–4)
Pain, score, median (IQR)	5 (5–6)	5 (5–6)	5 (5–6)	5 (5–6)	5 (5–7)	5 (5–7)	5 (5–7)

Abbreviations: CES-D, Center for epidemiological studies depression scale; IQR, interquartile range; SD, standard deviation.
[a]Specific information on the nine education levels is included in Table S1.

TABLE 2 Model statistics and comparisons between models including or excluding cross-lagged effects

Model statistics				**Comparisons between models**		
fit indices				***p*-value for chi-square test for difference**		
Both cross-lagged effects included (1)	**Only cross-lagged Dep → Ins included (2)**	**Only cross-lagged Ins → Dep included (3)**	**No cross-lagged effects included (4)**	**1 versus 4**	**2 versus 4**	**3 versus 4**
χ^2: 305.7 (df: 100) RMSEA: 0.026 95% CI: 0.023–0.029 CFI: 0.978 BIC: 107438 Explained variances: R^2 Ins: [0.69, 0.76] R^2 Dep: [0.58, 0.67]	χ^2: 305.7 (df: 101) RMSEA: 0.026 95% CI: 0.022–0.029 CFI: 0.978 BIC: 107433 Explained variances: R^2 Ins: [0.69, 0.76] R^2 Dep: [0.58, 0.67]	χ^2: 306.6 (df: 101) RMSEA: 0.026 95% CI: 0.022–0.029 CFI: 0.978 BIC: 107434 Explained variances: R^2 Ins: [0.69, 0.76] R^2 Dep: [0.58, 0.67]	χ^2: 306.6 (df: 102) RMSEA: 0.026 95% CI: 0.022–0.029 CFI: 0.978 BIC: **107429** Explained variances: R^2 Ins:[0.69, 0.76] R^2 Dep:[0.58, 0.67]	0.62	0.33	0.96

Note: Model statistics and comparisons between models (Unadjusted analyses, $N = 3081$) R^2 are summarized as the range of R^2 of the different waves in the analysis. Smallest BIC in row is printed in bold.
Abbreviations: BIC, Bayesian information criterion; CFI, comparative fit index; CI, confidence interval; Dep, symptoms of depression; Ins, symptoms of insomnia; RMSEA, root mean square error of approximation.

8.2% of the participants used antidepressants, anxiolytics, or hypnotics (mainly benzodiazepines), respectively. The insomnia symptoms score and the use of anxiolytics and hypnotics remained stable over time, while the depression symptom score, the percentage of participants experiencing clinically relevant depressive symptoms,

TABLE 3 Model estimates for the model without cross-lagged effects

Estimates of model parameters							
Means				**Correlations (rho)**			
Intercept (Ins)	**Slope (Ins)**	**Intercept (Dep)**	**Slope (Dep)**	**Intercept (Ins) Intercept (Dep)**	**Slope (Ins) Slope (Dep)**	**Slope (Ins) Intercept (Dep)**	**Slope (Dep) Intercept (Ins)**
5.9***	0.095***	7.3***	0.55***	0.42***	0.41***	−0.11*	−0.062
(SE:0.042)	(SE:0.012)	(SE: 0.13)	(SE:0.037)	(SE: 0.024)	(SE:0.066)	(SE:0.050)	(SE: 0.048)

Note: Means and correlations (rho) are reported for the model without cross-lagged effects (Unadjusted analyses, $N = 3081$). * indicates $p < 0.05$; ** indicates $p < 0.01$; *** indicates $p < 0.001$; absence of */**/*** indicates not significant.
Abbreviations: Ins, symptoms of insomnia; Dep, symptoms of depression; SE, standard error.

and the use of antidepressants appeared to increase. The use of alcohol (median of 3 drinks per week at the first wave) decreased over time, while the number of chronic diseases (1 at the first wave) increased. Pain scores (median of 5 at the first wave) remained stable. Characteristics of the cohort and subsamples are presented in Tables 1 and S1, respectively.

Association of longitudinal courses of insomnia symptoms and depressive symptoms and tests for cross-lagged effects

The model that included both cross-lagged effects showed good fit (χ^2: 305.667, df = 100, $p < 0.0001$; RMSEA: 0.026, 95% CI: 0.023 to 0.029; CFI: 0.978) (Table 2). 'Good fit' means that the model represents the data well, and that the model results in predicted values close to the observed data values. Yet, the goodness of fit of the model was hardly affected when the cross-lagged effects were removed from the model (χ^2 difference test: delta = 0.96, df = 2, $p = 0.62$) (Table 2). The crossed-lagged effects were not found to be of added value (symptoms of depression on symptoms of insomnia in the subsequent wave: $p = 0.33$); symptoms of insomnia on symptoms of depression in the subsequent wave: $p = 0.96$) (Table 2). Apparently, intercept correlations, slope correlations, and intercept-slope correlations, drive the correlation between symptoms of depression and symptoms of insomnia. The contribution of cross-lagged associations is insignificant.

Table 3 shows the model parameters (mean intercepts, slopes, and correlations) for the model without cross-lagged effects. Mean score for symptoms of depression at the first wave was 7.31 (95% CI: 7.05 to 7.57) and mean score for symptoms of insomnia at the first wave was 5.85 (95% CI: 5.77 to 5.93). Symptom scores of depression and insomnia at the first wave were found to be positively associated (correlation of intercepts, rho: 0.42, 95% CI: 0.37 to 0.46, $p < 0.001$). In addition, changes in symptom scores of depression and insomnia over the waves were found to be positively associated (correlation of slopes, rho: 0.41, 95% CI: 0.28 to 0.54, $p < 0.001$). Symptom scores of depression at the first wave were negatively associated with changes in symptoms of insomnia over the waves (rho: −0.11, 95% CI: −0.21 to −0.01, $p = 0.027$). Symptom scores of insomnia at the first wave were not associated with the change in symptoms of depression over the waves (rho: −0.062, 95% CI: −0.16 to 0.03, $p = 0.020$). Mean slope for change in symptoms of depression was 0.55 points per wave (95% CI: 0.48 to 0.63, $p < 0.001$) and mean slope for change in symptoms of insomnia was 0.095 points per wave (95% CI: 0.071 to 0.12, $p < 0.001$), both indicating worsening with age.

Similar results were found when covariates were added to the model (adjusted[1] analyses included age at first wave, gender, education level; adjusted[2] analyses included adjusted[1] covariates plus number of comorbid chronic diseases, alcohol consumption, and reported pain; adjusted[3] analyses included adjusted[2] covariates plus use of antidepressants, anxiolytics, and hypnotics) or when analyses were restricted to subgroups based on age, gender, and the presence of clinically relevant depression during follow-up (Tables S2 and S3).

DISCUSSION

We tested whether insomnia symptoms of an older individual are associated with later depressive symptoms in that older individual, and vice versa, to delineate whether a sequential comorbidity model applies to symptoms of depression and insomnia. Such a model would suggest that timely treatment of insomnia may help to prevent future depression, and vice versa. The within-individual longitudinal reciprocal relationship between symptoms of depression, and symptoms of insomnia, was modeled by means of a bivariate linear growth model.

We found that depression and insomnia are associated and tend to increase concurrently over time, but constitute no additional risk for one another over

repeated three-year intervals. These findings contradict previous research that suggests that depression and insomnia are risk factors for one another over time.

Though previous research has been suggestive of cross-lagged effects between insomnia symptoms and depressive symptoms in the general population[8] and in older people,[7,9,10] we did not find that increased symptoms of depression and insomnia constitute additional risk for one another over repeated three-year intervals.

This discrepancy may be explained by the fact that previous studies assessed the cross-lagged effects between depression and insomnia using regression analyses, or estimates of relative risk.[7–10] Such analyses test the longitudinal relationship between depression and insomnia on a group level (between-individuals), that is, whether individuals with higher levels of insomnia at the baseline measure show higher levels of depression at the follow-up measure. If significant effects are identified, they are usually interpreted as being sequential, while this may not be the case.[27] It is possible that insomnia and depression are strongly correlated and stable concepts, and that identified effects merely reflect co-occurring changes in insomnia and depression. In this study, we modeled within-individual changes instead of between-individual changes, and corrected analyses for co-occurring changes in symptoms of depression and insomnia.[19–23,27]

Our differential findings may also be attributed to cohort-differences, differences in measurements, or differences in the time to follow-up. Previous studies on the cross-lagged effects between depression and insomnia generally followed-up after shorter time periods, and used a variety of sleep measures, ranging from sleep questionnaires to wrist-actigraphy measures, in various patient populations from around the globe.[7–10]

Although our findings do not suggest a sequential comorbidity model, we did find that symptoms of depression and insomnia were moderately associated in terms of their severity as well as their changes over time. These results underscore the idea that depression and insomnia are closely related phenomena.[6,28] Insomnia and depression share risk factors,[5,29] and both disorders are linked to serotonin and noradrenalin deficiencies, hyperactivity of the hypothalamic–pituitary–adrenal axis, hyperarousal, disturbed rapid eye movement (REM) sleep, and decreased slow-wave sleep.[30,31] In addition, effective treatment of insomnia has shown concurrent positive effects on mood in individuals with depression[32,33] and vice versa.[34]

The major strength of the current study is the statistical approach used, in addition to its large sample-size, and the long and frequent follow-up.

The primary limitation of our study is that assessment of symptoms of depression and insomnia was performed at three-year intervals. Even though depression appears to become more persistent with aging,[35] individuals may have had episodes of depression that may have been missed in this study.[36] Furthermore, if the cross-lagged influences of symptoms of depression on insomnia, and vice versa, play a role over shorter time intervals, we may have missed this effect. Future research using a within-individual approach in a dataset with measures around shorter intervals could aim to delineate whether cross-lagged associations between insomnia and depressive symptoms play a role at shorter time intervals.

Furthermore, there are limitations related to the measurement of the primary outcome measures and sensitivity of the analyses due to the naturalistic nature of the cohort.

Insomnia was assessed using a three-item, not validated, questionnaire. In addition, insomnia severity, and the effect of insomnia symptoms on daytime functioning or well-being, are not measured by this questionnaire, in contrast to the validated insomnia severity index.[37] Although, the questions refer to the core symptoms of insomnia, it is possible that symptoms are a result of other sleep disorders (e.g., sleep apnea, restless legs syndrome, or a circadian rhythm disorder) or external interference (e.g., noise). Finally, depression was assessed using the CES-D, which contains items on symptoms that could be related to other medical conditions than depression (e.g., appetite and energy level).

This study was conducted in a naturalistic cohort, in which treatment was not controlled, nor monitored. In sensitivity analyses, we corrected for use of antidepressant and sleep medication at the time of the measurement. Yet, we had no information on medication use between measurements, or other treatments, such as psychotherapy, continuous positive airway pressure (CPAP), or over-the-counter products (e.g., melatonin and Valeriana officinalis). Hence, results likely represent the natural course of symptoms in combination with treatment effects. Inherent to the study sample, mortality of participants contributed considerably to attrition. Although we confined our analyses to 7 waves due to a decrease in sample-size over time, effects of mortality on our findings, such as bias through selective attrition, cannot be excluded.

Lastly, the findings of this study are complicated by the conceptual nature and heterogeneity of the syndromes of depression and insomnia. The syndromes of depression and insomnia show conceptual overlap, with insomnia being a symptom of depression, which may affect the contemporal associations between depression and insomnia.[3] In this study, we strived to diminish the effects of conceptual overlap, by using adjusted depression scores that did not take sleep questions into account. Furthermore, depression, as well as insomnia, maybe

heterogeneous conditions in itself, with some subtypes of insomnia showing higher concurrence with depression, or specific depressive symptoms, than others.[38]

The current study demonstrates that symptoms of depression and insomnia are strongly associated, and both increase together over time, marking the commonality of both symptom clusters in older adults. However, this study demonstrates deviations in symptoms of depression and insomnia constitute no additional risk for one another over repeated three-year intervals within individuals. Hence, these results do not support a sequential comorbidity model on insomnia and depression. Instead, our findings support the recommendation that clinicians should be aware of the connection between depression and sleep problems, and that it might be beneficial to screen for and treat symptoms of depression when faced with symptoms of insomnia and vice versa. These findings also suggest that future research should test clinical interventions in which the evaluation and treatment for depression and insomnia are conjoined.

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CONFLICT OF INTEREST

All authors have no conflicts of interest to declare related to this study.

AUTHOR CONTRIBUTIONS

Annelies Brouwer, Peter M. van de Ven, and Marijke A. Bremmer conceived the research question addressed in this study. Annelies Brouwer and Peter M. van de Ven performed statistical analyses and drafted the manuscript. All authors helped with the design of the study, the interpretation of the results, and helped to draft the manuscript.

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The sponsor had no role in the design, methods, subject recruitment, data collections, analysis, and preparation of the article.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

Figure S1. Graphical representation of the bivariate linear growth model.

Table S1. Characteristics of analysis population in adjusted analyses.

Table S2. Fit indices and tests for cross-lagged effects.

Table S3. Model estimates.

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