

# Longitudinal associations between subjective cognitive impairment, pain and depressive symptoms in home-dwelling older adults: Modelling within-person effects

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## Abstract

**Objectives:** Cognitive impairment, pain and depressive symptoms are common and interrelated factors in older adults. However, the directionality and specificity of their association remains unclarified. This study explored whether these factors prospectively increase reciprocal risk and examined the longitudinal association between these factors and quality of life (QoL).

**Methods:** This study used longitudinal data from The Older Persons and Informal Caregivers Survey Minimal Data Set (TOPICS-MDS; the Netherlands). Older adults self-reported cognitive impairment, pain, depressive symptoms and QoL at baseline and after 6 and 12 months of follow-up. The Random Intercept Cross-Lagged Panel Model was used to assess the prospective association between the three factors, while a multilevel linear regression analysis in a two-level random intercept model was used to examine the longitudinal associations between the three factors and QoL at the within-person level.

**Results:** The data of 11,582 home-dwelling older adults with or without subjective cognitive impairment were analysed. At the within-person level, pain at 6 months was associated with subsequent depressive symptoms ( $\beta = 0.04$ ,  $p = 0.024$ ). The reverse association from depression to pain, and longitudinal associations between pain and subjective cognitive impairment and between depressive symptoms and subjective cognitive impairment were non-significant. Pain, depressive symptoms and subjective cognitive impairment showed a significant association with poor QoL 6 months later.

**Conclusions:** A directional relationship was observed from pain to depressive symptoms. Pain reduction holds a potential benefit in the prevention of depressive symptoms, ultimately optimising the QoL of older adults.

## KEYWORDS

cognitive impairment, depression, older adults, pain, quality of life

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### Key points

- Older adults have multiple chronic conditions, and subjective cognitive impairment, pain and depressive symptoms are common and interrelated factors which affect the quality of life.
- Home-dwelling older adults experiencing pain were more likely to report later depressive symptoms.
- Pain, depressive symptoms and subjective cognitive impairment were associated with subsequent poor quality of life.
- Pain reduction may help prevent depressive symptoms and poor quality of life.

## 1 | INTRODUCTION

Globally, the older adult population is increasing rapidly, from an estimated 9.3% in 2020 to 16.0% in 2050.<sup>1</sup> Older adults have multiple chronic conditions<sup>2,3</sup>; consequently, the salience of quality of life (QoL) of older adults is garnering attention in goals of care discussions and as an emerging public health issue. This requires a thorough understanding of QoL determinants to enable the identification of potential targets for interventions for optimising the QoL.<sup>4</sup> Depressive symptoms,<sup>5–11</sup> cognitive impairment,<sup>4–6,9</sup> and pain<sup>5,12–14</sup> have been associated with poor QoL.

Health and social care workers face challenges in prioritising target domains to optimise QoL because many older adults have multiple and concurrent unmet needs across the cognitive, physical<sup>15</sup> and psychological health domains.<sup>16</sup> Pain<sup>16–19</sup> and depressive symptoms<sup>20,21</sup> can result in unmet needs or cause a lack of wellbeing in people with cognitive impairment. Pain is a major trigger of neuropsychiatric symptoms including depression,<sup>21–24</sup> while depression is a modifiable risk factor for cognitive impairment.<sup>21,25,26</sup> Furthermore, depression is often present with pain,<sup>27</sup> while pain is associated with cognitive decline.<sup>26,28,29</sup> Findings from adolescents,<sup>30,31</sup> young and middle-aged adults<sup>32</sup> suggest a directional relationship from pain to depressive symptoms. However, evidence in older adults has remained inconclusive owing to a limited number of longitudinal evaluations.<sup>33</sup> Similarly, the directionality and specificity of the association between cognitive impairment, pain and depressive symptoms remain unclarified. Knowledge of these longitudinal associations will provide more insights into clustering and the possible causal factors for cognitive impairment, depressive symptoms and pain. This can help professional caregivers prioritise the factors to be addressed and undertake preventive and intervention measures, which eventually benefit older adults. Therefore, this study aimed to assess whether cognitive impairment, pain and depressive symptoms prospectively increase reciprocal risk and examine the longitudinal associations between them and QoL. Since we were interested in how cognitive impairment, pain and depressive symptoms are related to one another the following period within an individual, this study focussed on within-person effects of the three factors.

## 2 | MATERIALS AND METHODS

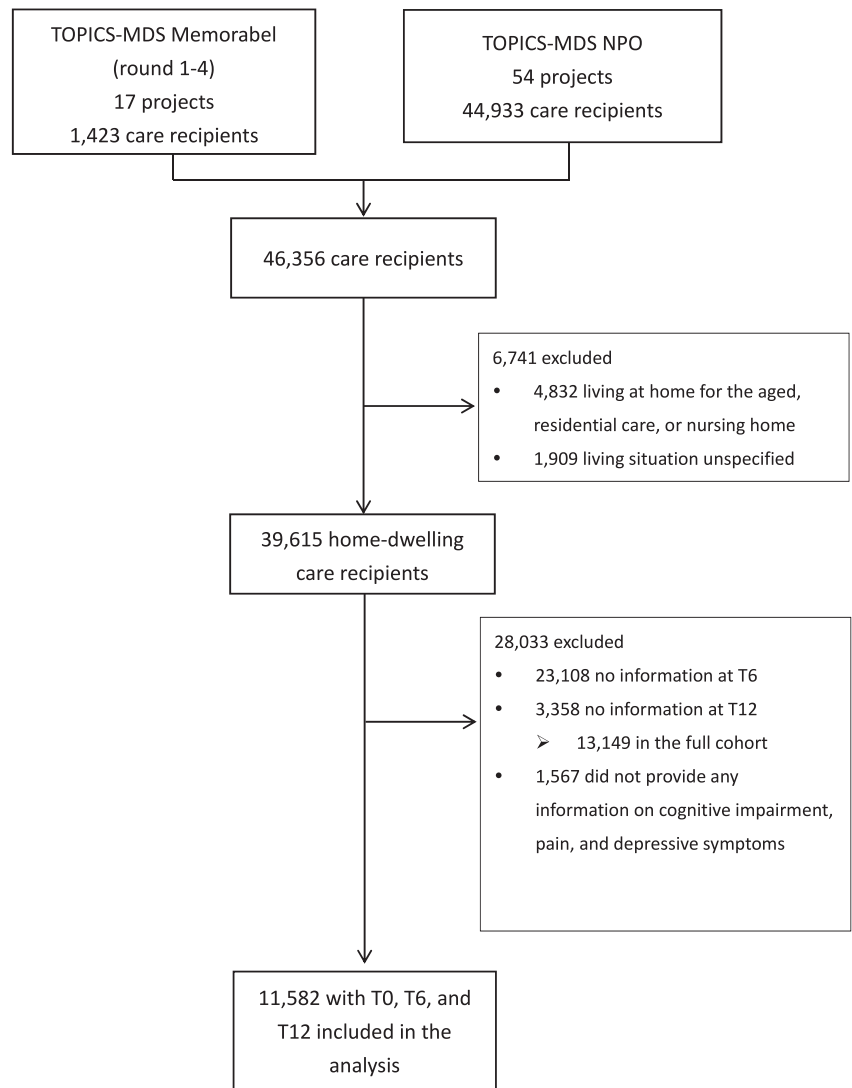
### 2.1 | Design and setting

This longitudinal study used data from The Older Persons and Informal Caregivers Survey Minimal Data Set (TOPICS-MDS) data repository. This repository includes data collected in two programmes funded by the Organisation of Health Research and Development (ZonMw—The Netherlands: the National Care for the Elderly Programme (Nationaal Programma Ouderenzorg, NPO), which contains nationwide information on the physical and mental health being of older persons and informal caregivers, and 'Memorabel', for dementia research).<sup>34</sup> Most of the participants were home-dwelling older adults and family caregivers rather than nursing home residents. The data were cleaned using a standardised protocol. Anonymised data were subsequently submitted to a central institution (Radboud university medical center, Nijmegen, the Netherlands) for further validation checks and creation of the pooled dataset. As of May 2023, 71 research projects in the NPO and Memorabel (rounds 1–4) programs have contributed data to TOPICS-MDS, via different study designs, sampling frameworks and inclusion criteria.<sup>34,35</sup>

### 2.2 | Participants

We selected home-dwelling older adults who had assessment at baseline and after 6 and 12 months of follow-up. The 6- and 12-month follow-up periods were chosen as the population that completed data at these time points was larger in TOPICS-MDS. However, since the deposit data did not include project identifiers, we could not specify if the care receiver was a dropout case or the project itself did not have follow-up assessment at 6 and/or 12 months. Of the 39,615 care recipients who were identified as home-dwelling individuals, 28,033 were excluded due to no information available in 6-month ( $n = 23,108$ ) or 12-month follow-up ( $n = 3358$ ) and missing information on all of cognitive impairment, pain, and depressive symptoms ( $n = 1567$ ). In total, 11,582 care recipients were included in the analysis (Figure 1). Based on publicly

**FIGURE 1** Flowchart of data extraction. As the deposit data did not include project identifiers, we could not specify if the care receiver was a dropout case or the project itself did not have follow-up assessment at 6 and/or 12 months. Based on publicly available information, 45 of 71 projects did not have 6-month follow-up assessment (25,313 care recipients at baseline), and 40 projects did not have 12-month follow-up assessment (12,916 care recipients at baseline). NPO, National Care for the Elderly Programme (Nationaal Programma Ouderenzorg); T0, baseline; T12, 12 months follow-up; T6, 6 months follow-up; TOPICS-MDS, The Older Persons and Informal Caregivers Survey Minimal Data Set.



available information, the 11,582 were assumed as participants from 16 studies, including six randomised controlled trials and three stepped-wedge randomised controlled trials and two intervention, two quasi-experimental and one pre-post study.

### 2.3 | Measurements

The primary outcome measure was QoL as reported by care recipients. Primary exploratory variables were self-rated cognitive impairment, pain, and depressive symptoms. The missingness at baseline ranged 4%–5% in QoL and 1%–3% in the three factors (Table 2). The missingness in subjective cognitive impairment at baseline was more likely to occur in participants with greater depressive symptoms ( $t(93.63) = 2.71, p = 0.008$ ), pain ( $t(60.77) = 2.52, p = 0.014$ ) and QoL ( $t(98.26) = 2.52, p = 0.013$ ) at baseline. The missingness in depressive symptoms at baseline was associated with greater pain at baseline ( $t(286.71) = 5.36, p < 0.001$ ). The missing in QoL at baseline was associated with greater

depressive symptoms ( $t(685.03) = 6.05, p < 0.001$ ) and pain at baseline ( $t(417.81) = 4.17, p < 0.001$ ). Thus, we assumed the type of missing as ‘missing at random’; the probability that data is missing depends on the variables observed within the dataset.

Respondents were asked to rate their current QoL based on a five-level response scale ranging from ‘poor = 5’ to ‘excellent = 1’. The question was phrased using wording similar to self-perceived health questions from the RAND-36.<sup>36</sup> In this study, the scores were reversed such that a higher score indicated better QoL.

Subjective cognitive impairment was assessed using the item ‘I have (no/moderate/extreme) problems with my memory, attention, and thinking’, in a modified version of the EuroQoL Five Dimensional (EQ-5D) instrument,<sup>37</sup> the EQ-5D+C.<sup>38</sup> While the conventional EQ-5D assesses five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression), the EQ-5D+C assesses an additional dimension, cognitive function. Each dimension has three levels (1 = no problems, 2 = moderate problems and 3 = extreme problems). Pain was assessed using the item from the EQ-5D+C: ‘I have (no/moderate/extreme) pain or other symptoms’.

Depressive symptoms were assessed using the RAND-36 mental health sub-scale.<sup>36</sup> This scale asks how often in the past 4 weeks an individual has felt the following: 'very nervous', 'calm and peaceful', 'down-hearted and blue', 'happy' and 'so down in the dumps nothing could cheer you up'. In the original scale, the response option ranging from 'none (6)' to 'all (1)'.<sup>36</sup> The TOPICS-MDS measurements used six-level response option ranging from 'never (6)' to 'always (1)'. Positive items are scored from zero to 100 and negative items are

scored in reverse. In the TOPICS-MDS data, depressive symptoms were assessed using the item 'down-hearted and blue', and scored from zero to 100 (1 = 100, 2 = 80, 3 = 60, 4 = 40, 5 = 20, and 6 = 0).

Demographic characteristics in this study comprised age, sex, country of birth, educational attainment, marital status, and self-reported dementia or depression in the last 12 months at baseline. The missingness in demographic variables ranged 0%–9% at baseline (Table 1).

**TABLE 1** Baseline characteristics of home-dwelling care recipients (N = 11,582).

	Number of responses	Value
Age in years, mean (SD)	11,177	76.8 (6.8)
Missing values	405	
Sex, n (%)	11,582	
Male		6688 (57.7)
Female		4894 (42.3)
Missing values	0	
Country of birth, n (%)	11,532	
Netherlands		10,849 (94.1)
Other country		683 (5.9)
Missing values	50	
Educational attainment, n (%)	11,475	
Less than six grades of primary school		398 (3.5)
Six grades of primary school		1583 (13.8)
More than primary school/primary school with uncompleted further education		1261 (11.0)
Practical training		2165 (18.9)
Secondary vocational education		3638 (31.7)
Pre-university education		896 (7.8)
University/higher professional education		1534 (13.4)
Missing values	107	
Marital status, n (%)	11,549	
Married		6216 (53.8)
Divorced		834 (7.2)
Widowed/partner deceased		3719 (32.2)
Single		544 (4.7)
Cohabiting		236 (2.0)
Missing values	33	
Diagnosis of depression in the last 12 months, n (%)	10,631	
Present		885 (8.3)
Not present		9746 (91.7)
Missing values	951	
Diagnosis of dementia in the last 12 months, n (%)	10,594	
Present		492 (4.6)
Not present		10,102 (95.4)
Missing values	988	

## 2.4 | Statistical analysis

Cross-sectional associations with presence of self-reported illness and health condition at baseline were calculated to examine the validity of the subjective cognitive impairment and depressive symptoms assessments. A Random Intercept Cross-Lagged Panel Model (RI-CLPM) analysis was used to investigate the direction and strength of the longitudinal associations between subjective cognitive impairment, pain, and depressive symptoms at the within-person level. The CLPM model considers the autoregressive effect within at least two waves of data with two variables  $X_t$  and  $Y_t$ , namely ( $X_1$  to  $X_2$  and  $Y_1$  to  $Y_2$ ), which is the effect of the variable on itself in a subsequent wave, and cross-lagged effect ( $X_1$  to  $Y_2$  and  $Y_1$  to  $X_2$ ), which is the effect of the variable on a crossed variable.<sup>39</sup> The RI-CLPM extends the standard CLPM via the addition of random intercepts as 'stable traits' for each measured variable, partialling between-person variance such that the cross-lagged associations represent only within-person changes over time.<sup>40</sup> The within-unit analysis in an RI-CLPM model used latent variables to control for time-invariant confounders (unobserved heterogeneity) such as baseline sociodemographic factors and comorbidities as well as environmental influences which were not necessarily observed in assessment. The RI-CLPM decomposes  $X$  and  $Y$  for persons  $i$  into three components:

$$X_{it} = \mu_{xt} + X_{Bi} + X_{Wit} \quad (1)$$

$$Y_{it} = \mu_{yt} + Y_{Bi} + Y_{Wit} \quad (2)$$

Subscripts  $i$  and  $t$  represent vectors of values for individuals and time, respectively. The time-specific means ( $\mu_{xt}$ ,  $\mu_{yt}$ ) reflect the means of all participants per timepoint. The between-person components (random intercepts,  $X_{Bi}$ ,  $Y_{Bi}$ ) capture an individual's time-invariant deviations using latent variables composed of repeated measures with factor loadings fixed to 1. The within-person components ( $X_{Wit}$ ,  $Y_{Wit}$ ) reflect the person specific deviations from their expected means at any one occasion. The fully specified RI-CLPM path diagram is shown in Supplementary Figure S1.

For each construct of interest, the observed variables at baseline and 6- and 12-month follow-up were regressed (with regression weights constrained to be equal) on the following: (a) a single time-invariant latent factor representing stable influences on the construct over the observation period ('random intercept') and (b) a time-varying latent factor for each time point, representing time-specific deviations in an individual's construct level at assessment. Subsequently, cross-lagged and auto-regressive parameters were specified and freely estimated between these time-varying latent factors, with the coefficients of these parameters interpreted as associations between within-person changes in subjective cognitive impairment/depressive symptoms/pain over that time interval. The correlations of the random intercepts were interpreted as those for between-person sources of variances in measured variables that were stable over time. Model fit indices were calculated and applied

to conventional thresholds as  $\chi^2/df < 2$ , comparative fit index (CFI)  $> 0.95$ , root mean square error of approximation (RMSEA)  $< 0.08$ , and the standardised root-mean-square residual (SRMR)  $< 0.05$ .<sup>41,42</sup> The ratio  $\chi^2/df$  means the magnitude of  $\chi^2$  with the expected value of the sample distribution, that is, the number of degrees of freedom. RMSEA is an absolute fit index, in that it assesses how far a hypothesized model is from a perfect model. CFI is an incremental fit index that compares the fit of a hypothesized model with that of a baseline model. SPMR evaluates the difference between the residuals of the sample covariance matrix and the hypothesised covariance model.

A multilevel linear regression analysis of the QoL at follow-up was performed according to a random intercept model with two-level structure (person and time of assessment) to examine the longitudinal associations between the three factors and QoL. A panel-data format was adopted in which the data of the same participant appeared thrice. Each case contained information on the three factors and QoL at baseline and 6 months later. Therefore, for the QoL at 6 months, the QoL and three factors at baseline were jointly entered as independent variables. For the QoL at 12 months, the QoL and three factors at 6 months were entered into the model.

Standardised estimates were reported and compared for the RI-CLPM analysis. The significance level was set to 0.05. A full information maximum likelihood estimation was adopted to handle missing data under the assumption of 'missing at random'.<sup>43</sup> Both RI-CLPM and multilevel modelling analyses were performed using Mplus version 8.10.

## 3 | RESULTS

### 3.1 | Characteristics of care receivers

Participant characteristics are listed in Table 1. From the full ( $N = 13,149$ ) cohort, cases with completely missing data for all relevant variables were removed, resulting in the final sample of  $N = 11,582$ . Differences between the included and excluded cases are presented in Supplementary Tables S1 and S2. Included cases were less likely to be older and have self-reported dementia than excluded cases for missing follow-up assessments and those for missing values of all three factors.

Distributions of subjective cognitive impairment, pain and depressive symptoms are presented in Table 2. Thirty percent of participants reported some problems in subjective cognitive impairment across three times of assessment. More than half of participants (53%–54%) reported moderate pain. On average, they reported almost never depressive symptoms and middle level of QoL. The overall distribution was stable across three time points (Table 2). The Pearson's pairwise correlation coefficients across subjective cognitive impairment, depressive symptoms and pain ranged 0.12–0.31 at each time of assessment.

	T0	T1	T2
Subjective cognitive impairment, <i>n</i> (%)	<i>N</i> = 11,480	<i>N</i> = 11,458	<i>N</i> = 11,476
No problems	7981 (69.5)	8005(69.9)	7930 (69.1)
Some problems	3338 (29.1)	3287 (28.7)	3340 (29.1)
Serious problems	161 (1.4)	166 (1.4)	206 (1.8)
Missing values	102	124	98
Pain, <i>n</i> (%)	<i>N</i> = 11,456	<i>N</i> = 11,452	<i>N</i> = 11,427
No	4658 (40.7)	4794 (41.9)	4705 (41.2)
Moderate	6169 (53.8)	6032 (52.7)	6046 (52.9)
Extreme	629 (5.5)	626 (5.5)	676 (5.9)
Missing values	126	130	155
Depressive symptoms, range: 0–100, mean (SD)	<i>N</i> = 11,297	<i>N</i> = 11,495	<i>N</i> = 11,250
	23.5 (21.6)	24.0 (21.6)	24.8 (21.6)
Missing values	285	87	332
Quality of life, range: 0–4, mean (SD)	<i>N</i> = 10,953	<i>N</i> = 11,131	<i>N</i> = 10,963
	2.2 (0.9)	2.2 (0.9)	2.1 (0.9)
Missing values	629	451	619

Note: Subjective cognitive impairment was assessed using an item about cognitive function in the modified EuroQoL-Five Dimensional instrument (EQ-5D)+C. Pain was measured using an item about pain/discomfort in the EQ-5D+C. Depressive symptoms were measured using an item, 'down-hearted and blue', in the RAND-36 mental health sub-scale. QoL was evaluated from a five-level response option ranging from 'poor = 1' to excellent = 5'.

Abbreviation: QoL, quality of life.

### 3.2 | Validity of subjective cognitive impairment and depressive symptoms

The  $\chi^2$  test, performed to assess the validity of subjective cognitive impairment and depressive symptoms, showed that participants who reported having dementia had significantly higher scores of subjective cognitive impairment than those who did not report a diagnosis of dementia (Supplementary Table S3). Similarly, participants who reported having depression in the last 12 months had significantly more severe depressive symptoms than those who did not report depression (Supplementary Table S4).

### 3.3 | Association between the three factors

Trivariate RI-CLPM analyses revealed that individuals who experienced pain at 6 months exhibited an increased likelihood of reporting more severe depressive symptoms at 12 months ( $\beta = 0.04$ ,  $p = 0.024$ ). Depressive symptoms at 6 months demonstrated a borderline within-person prospective association with pain at 12 months ( $\beta = 0.03$ ,  $p = 0.051$ ). The prospective association from depressive symptoms to subjective cognitive impairment was not significant ( $\beta =$  from  $-0.03$  to  $0.03$ , all  $p > 0.05$ ). Subjective cognitive impairment did not show any significant within-person prospective associations with either depressive symptoms ( $\beta =$  from  $-0.02$  to

$-0.001$ , all  $p > 0.05$ ) or pain ( $\beta =$  from  $-0.03$  to  $0.02$ , all  $p > 0.05$ ), respectively. Parameter estimates are presented in Figure 2 and Supplementary Table S5.

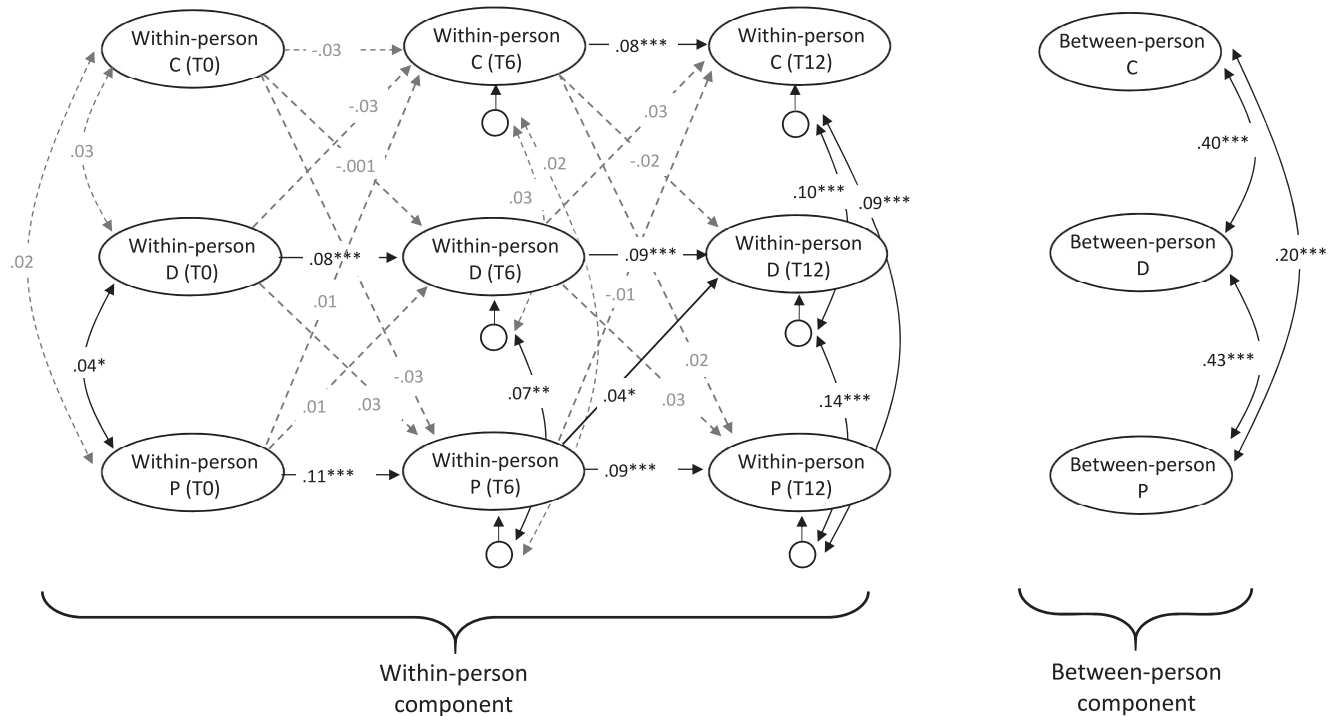
Auto-regressive effects for depressive symptoms and pain were significant at both baseline–6 months ( $\beta = 0.08$ ,  $p < 0.001$  and  $\beta = 0.11$ ,  $p < 0.001$ , respectively) and 6–12 months ( $\beta = 0.08$ ,  $p < 0.001$  and  $\beta = 0.09$ ,  $p < 0.001$ , respectively), suggesting that both factors were prospectively associated with themselves at all time points. In contrast, subjective cognitive impairment at baseline was not associated with itself at 6 months ( $\beta = -0.03$ ,  $p = 0.159$ ), which, however, did predict subjective cognitive impairment at 12 months ( $\beta = 0.08$ ,  $p < 0.001$ ). At the between-person level, the random intercepts of subjective cognitive impairment, depressive symptoms and pain were significantly correlated ( $\beta =$  from  $0.20$  to  $0.43$ , all  $p < 0.001$ ).

Model fit indices included  $\chi^2/df(1) = 6.429$  ( $p = 0.093$ ), CFI: 1.000, RMSEA: 0.010 [90% CI: 0.000–0.021], and SRMR: 0.003. All indices except for  $\chi^2/df$  matched the conventional thresholds,<sup>42,43</sup> suggesting a moderate fit of the built model to data.

### 3.4 | Associations between the three factors and QoL

Longitudinal multilevel linear regression analyses of QoL after adjusting for baseline QoL, subjective cognitive impairment,

TABLE 2 Distribution of subjective cognitive impairment, depressive symptoms and pain.



**FIGURE 2** Simplified representation of the trivariate Random Intercept Cross-Lagged Panel Model analysis of the reciprocal effects of subject cognitive impairment, depressive symptoms and pain at T0, T6 and T12 as a time-varying covariate. Home-dwelling older adults are included in the analysis ( $N = 11,582$ ). Solid black arrows represent significant regression weights (single-headed) or correlations (double-headed); a significant cross-lagged effect between (P) and (D) is in boldface. Standardised estimates are reported. Dashed arrows denote non-significant parameters ( $p > 0.05$ ). Model  $\chi^2/df(3): 6.429$  ( $p = 0.093$ ), CFI: 1.000, RMSEA: 0.010 [90% CI: 0.000–0.021], SRMR: 0.003. \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ . (C), subjective cognitive impairment; (D), depressive symptoms; (P), pain; CFI, comparative fit index; RMSEA, root mean square error of approximation; SRMR, standardised root-mean-square residual; T0, baseline; T6, 6 months follow-up; T12, 12 months follow-up.

depressive symptoms and pain were significantly associated with subsequent poor QoL. Parameter estimates are listed in Table 3.

## 4 | DISCUSSION

The within-person analyses showed an evident directional relationship from pain to depressive symptoms. Home-dwelling care recipients who reported pain had an increased risk of subsequent depressive symptoms. The reverse association, from depressive symptoms to an increased risk of subsequent pain, was observed with a borderline significance ( $p = 0.051$ ). Any other directional relationships were not significant ( $p > 0.05$ ) either between depressive symptoms and subjective cognitive impairment or pain and subjective cognitive impairment. All three factors were significantly associated with later QoL.

The RI-CLPM enabled us to elucidate the directionality and specificity of the association between pain and depressive symptoms. A recent longitudinal study among nursing home residents with dementia reported that reduced pain was followed by less depressive symptoms.<sup>44</sup> Our findings support the longitudinal associations reported in the previous study and indicate the need for prioritising pain reduction. As the reverse association from depressive symptoms to pain was likely to exist at the same period, pain reduction would

also be helpful to prevent worsening of pain along with depressive symptoms. Moreover, the integration of pain management has a potential benefit in interventions to optimising the QoL, as our study found that pain had an impact on later QoL as well. Pain assessment is crucial among older adults with subjective cognitive impairment. Our results revealed that subjective cognitive impairment and pain were likely to co-exist in the same person, although a directional relationship was not found between these factors. Pain is common in people with clinically diagnosed dementia,<sup>16–18</sup> and they are at increased risk of having pain underassessed and undertreated<sup>45,46</sup> because of challenges in orientation and alerting attention, which could interfere with responses to psychosocial interventions. Therefore, interprofessional collaboration is needed to improve pain assessment and management in people with dementia.<sup>47</sup>

The absence of a relationship between subjective cognitive impairment and depressive symptoms and pain in our study is inconsistent with those reported in previous studies which suggest a directional relationship from cognitive impairment (based on clinical history and observational rating) to depressive symptoms<sup>48</sup> and from pain to probable dementia (based on objective probability scores).<sup>32</sup> The difference in definition, information source and range of cognitive impairment could have led to divergent findings. In contrast to other studies that included persons with objective cognitive

	Coefficient (95%CI)	p value
Within-person level		
QoL, range: 1–5	–0.36*** (–0.38 to –0.34)	<0.001
Subjective cognitive impairment, range: 1–3	–0.17*** (–0.19 to –0.15)	<0.001
Depressive symptoms, range: 0–100	–0.01*** (–0.01 to –0.01)	<0.001
Pain, range: 1–3	–0.21*** (–0.23 to –0.19)	<0.001
Time of assessment, 12 months	–0.08*** (–0.09 to –0.06)	<0.001
Between-person level		
Variances	0.43*** (0.42 to 0.45)	<0.001
Residual variances	0.26*** (0.25 to 0.27)	<0.001

Note: Linear multilevel modelling in a two-level random intercept model was used to estimate coefficients of the three factors at the within-person level. Full information maximum likelihood method was used to handle missing data. For QoL at 6 months, QoL and subjective cognitive impairment, depressive symptoms, and pain at baseline were entered as independent variables. For QoL at 12 months, QoL and the three factors at 6 months were entered as independent variables. Subjective cognitive impairment was assessed using an item about cognitive function in the modified EuroQoL-Five Dimensional instrument (EQ-5D)+C. Pain was measured using an item about pain/discomfort in the EQ-5D+C. Depressive symptoms were measured using an item, 'down-hearted and blue', in the RAND-36 mental health sub-scale. QoL was evaluated from a five-level response option ranging from 'poor = 1' to 'excellent = 5'.

Abbreviations: CI, confidence interval; QoL, quality of life.

\*\*\* $p < 0.001$ .

impairment, in our study, older adults who reported cognitive problems may not yet have the dementia diagnosis. While subjective cognitive impairment is often an early marker of future objective impairment,<sup>49</sup> it can reflect psychological distress rather than actual impairment.<sup>50</sup> However, the validity of subjective cognitive impairment was partially confirmed by its significant association with diagnosed dementia. Another possible explanation for the dissimilar results is that prevalence and change in subjective cognitive impairment, depressive symptoms and pain could be less frequently observed compared to in nursing home residents assessed in previous studies.<sup>32,48</sup> Nursing home residents are supposed to have a high prevalence of dementia (60% in the Netherlands).<sup>51</sup> Yet, the prevalence of symptoms in our participants appeared to be similar with that in general older adult population regarding objective mild cognitive impairment (22%)<sup>52,53</sup> and depression (13%–32%),<sup>54–56</sup> except for pain (12%–28%).<sup>57,58</sup> Since the majority of studies sampled in TOPICS-MDS were from primary care settings,<sup>35</sup> highly prevalent pain in our participants could have reflected some physical complications that necessitate outpatient care.

#### 4.1 | Strengths and limitations

The main strength of our study lies in the analytic approach, the RI-CLPM, which allowed us to detect within-person effects over time. Furthermore, the use of longitudinal data of a large cohort ensured that the assessment of subjective cognitive impairment, pain and depressive symptoms were the same with regard to instrument at

every time point, which facilitated the comparative analysis across time. The statistical approach using RI-CLPM allowed us to examine changes over time also on a within-individual level.

Our study has some limitations. First, selection bias could have affected the results owing to the exclusion of participants without complete follow-up assessment of all relevant variables. These participants more often self-reported dementia. Therefore, the variability in subjective cognitive impairment over time may have been reduced, which may have led to underestimated impact of cognitive impairment on depressive symptoms and pain. The association between depressive symptoms and QoL could be overrated, as the assessment was conducted using questions from one validated instrument (RAND-36) that are thus already parts of the same concept. Second, subjective cognitive impairment could have been under-reported as it was based on self-reported symptoms. All measures used in the model were assessed by a single question some with only a few response options, which may have limited the variability as well. Especially, subjective cognitive impairment and pain were rated based on three categories, which could reduce the detection of time-varying symptoms. Third, since TOPICS-MDS comprised data from diverse research projects with different inclusion criteria, the frailest home-dwelling older persons may have been less often included. Future longitudinal studies with uniform inclusion criteria and longer duration of observation may provide insights into the trajectory of the development of age-related cognitive impairment, pain and depressive symptoms. The depth understanding of the cycle will guide professional caregivers to prevent and mitigate these symptoms. Fourth, outcomes of family caregivers should be included in the

TABLE 3 Longitudinal associations between subjective cognitive impairment, depressive symptoms, pain and quality of life among home-dwelling older adults.



analysis of depressive symptoms and QoL, as dyadic studies have indicated an interdependent association of the outcomes between patients with chronic illnesses and their caregivers.<sup>59–61</sup>

## 5 | CONCLUSION

In this study, we used RI-CLPM to understand the interrelation between subjective cognitive impairment, pain and depressive symptoms over time (at baseline, 6 and 12 months), although the relationship was neither strong nor consistent over time. This study highlights the fact that pre-existing pain was associated with worsened depressive symptoms and reduced QoL. Therefore, the integration of pain reduction measures may be beneficial for health and social care workers in interventions to prevent subsequent depressive symptoms and poor QoL.

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## CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest to report.

## DATA AVAILABILITY STATEMENT

TOPICS-MDS has been archived as a thematic data repository by the TOPICS-MDS Project Group in DANS, the Dutch institute for permanent access to digital research resources ([doi.org/10.17026/dans-xvh-dbbf](https://doi.org/10.17026/dans-xvh-dbbf)). TOPICS-MDS encompasses three different datasets: (1) care receiver, (2) care giver, and (3) care receiver – care giver dyads. The data used for this study originated from the first data set ([doi.org/10.17026/dans-xwf-g759](https://doi.org/10.17026/dans-xwf-g759)). The data are available with restricted access after approval of the TOPICS-MDS Project Group. All other documents (background information on TOPICS-MDS, questionnaires, codebooks, SPSS syntax, and metadata) have open access.

## ETHICS STATEMENT

Since the data are de-identified, studies using TOPICS-MDS are not within the ambit of the Dutch Medical Research Involving Human Subjects Act (WMO). Hence, no ethical review was needed for this study.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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