



# BMJ Open Association between severity of depressive symptoms and chronic knee pain in Korean adults aged over 50 years: a cross-sectional study using nationally representative data

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## ABSTRACT

**Objectives** To identify the association between the presence and severity of depressive symptoms and those of chronic knee pain.

**Design** A retrospective cross-sectional study.

**Participants** We used data from the sixth Korea National Health and Nutrition Examination Survey (KNHANES VI-2) performed in 2014. Overall, 7550 patients were included in the KNHANES VI-2.

**Outcome measures** Participants were asked whether they had chronic knee pain, and each answer was either 'yes' or 'no'. Patient Health Questionnaire-9 (PHQ-9) was used as a screening tool for depressive symptoms, and PHQ-9 scores of 10 or higher was classified as the depressed group. In total, 527 patients reported that they had pain in their knee, of whom 91 also had depressive symptoms.

**Results** The prevalence of chronic knee pain in the Korean population aged over 50 years was 19.8%. Multiple logistic regression was conducted after adjustment for sex, age, smoking, alcohol drinking, education level, household income, physical activity, sleep duration and comorbidity. The analysis revealed a significant association between depressive symptoms and chronic knee pain (adjusted OR=2.333,  $p<0.001$ ). In contrast, the severity of depressive symptoms was linearly correlated with the intensity of chronic knee pain ( $p$  for trend  $<0.001$ ). In participants with no chronic knee pain (Numerical Rating Scale; NRS=0) or mild chronic knee pain (NRS=1–4), the prevalence of moderate and severe depressive symptoms was 3.4% and 0.6%, respectively. However, in those with severe chronic knee pain (NRS=8–10), there was a higher prevalence of moderate and severe depressive symptoms (10.1% and 5.8%, respectively) ( $p<0.001$ ).

**Conclusions** A strong association was observed between the presence and severity of depressive symptoms and the presence of chronic knee pain. The association became stronger with higher levels of depressive symptoms, indicating a positive correlation between depressive symptoms severity and chronic knee pain.

## INTRODUCTION

Depressive symptoms are one of the most common mental illnesses. An earlier

## Strengths and limitations of this study

- This study is based on highly reliable data from the national survey using the Korean population-based questionnaire.
- We found a strong association between the severity of depressive symptoms and the presence and intensity of chronic knee pain.
- Because the questionnaire regarding chronic knee pain was only asked to a population aged over 50 years, the younger population with chronic knee pain was excluded in the analysis.
- As this was a retrospective cross-sectional study, it assessed depressive symptoms and chronic knee pain using ORs without analysing the cause–effect relationship between the variables.
- Response biases cannot be ruled out because self-report questionnaires, Numerical Rating Scale and Patient Health Questionnaire-9, were used to assess chronic knee pain and depressive symptoms, respectively.

systematic review and meta-analysis reported that a lifetime prevalence of psychotic depressive symptoms ranges from 0.35% to 1% and that the rates of psychotic depressive symptoms increase with age.<sup>1</sup> According to a Chinese systematic review, a lifetime prevalence of major depressive disorder (MDD) varies between 1.1% and 3.3%.<sup>2</sup> However, the prevalence of major depressive episode (MDE), which indicates the relatively mild symptoms of depression, is markedly higher. A cohort study using a sample of 29 621 people representing the general US population found that the 3-year prevalence rate was 8% for MDE.<sup>3</sup> Additionally, a Canadian longitudinal study reported that the prevalence of depressive episode at baseline was 7.5%.<sup>4</sup> Based on World Mental Health Survey data, a cross-sectional study identified diabetes, arthritis, asthma, chronic pulmonary disease,

angina symptoms, stroke, advanced age, women, underweight and lower levels of income and education as risk factors related to depressive symptoms.<sup>5</sup>

The prevalence of knee pain is one of the most common symptoms in the ageing population around the world. According to the sixth National Health and Nutrition Survey (KNHANES VI, 2013–2015), 20.8% of Korean population aged over 50 years reported chronic knee pain.<sup>6</sup> In an Italian cross-sectional study, 22.4% of the population aged over 65 years complained about pain in the knee.<sup>7</sup> In a study involving the British population aged over 65 years, 32.6% of participants reported knee pain.<sup>8</sup> As risk factors for chronic knee pain, advanced age, low education and high BMI have a cause–effect relationship with chronic knee pain.<sup>9</sup>

Emotional distress is also known to worsen physical pain, and many studies are underway in this context. The patients with temporomandibular disorders who have anxiety and depressive symptoms are more likely to develop migraine and primary headache.<sup>10</sup> According to a systematic review, depressive symptoms and anxiety symptoms are associated with high morbidity neck pain.<sup>11</sup>

The relationship between depressive symptoms and chronic knee pain has been investigated in previous literature.<sup>12</sup> A systematic review revealed strong evidence supporting such a relationship between depressive symptoms and chronic knee pain, with reference to five high-quality studies.<sup>13</sup> A cohort study involving the Japanese population aged over 65 years found that the development of depressive symptoms was associated with the presence of chronic knee pain.<sup>14</sup> Among previous studies, a cross-sectional study described the relationship between depressive symptoms and severity of chronic knee pain assessed by the Numerical Rating Scale (NRS) and the Kellgren-Lawrence Scale.<sup>15</sup> Moreover, a recent study revealed a relationship between depressive symptom subtypes and risk for symptomatic knee pain.<sup>16</sup>

However, few studies have been conducted to identify the association between the severity of depressive symptoms and the presence and intensity of knee pain. Recently, one study revealed that participants with physical pain

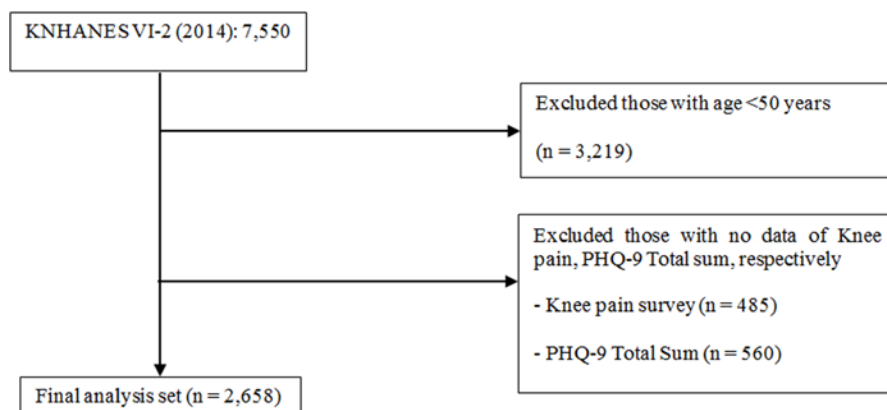
were significantly associated with depressive symptoms severity. According to this study, participants with pain showed higher scores of Montgomery-Asberg depressive symptoms rating scales. However, results of these studies are limited to showing the mean of depressive symptom severity score depending on the presence of pain symptoms.<sup>17</sup> Moreover, a longitudinal analysis revealed that pain severity was a strong predictor of subsequent depressive symptom severity, and conversely, depressive symptom severity was a strong predictor of subsequent pain severity.<sup>18</sup>

In addition to previous studies regarding depressive symptoms and chronic knee pain, this study aimed to identify the association between the presence and severity of depressive symptoms and those of chronic knee pain. To our knowledge, our study is the first to explore both aspects of the severity of depressive symptoms and severity of chronic knee pain measured by Patient Health Questionnaire-9 (PHQ-9) and NRS.

## METHODS

### Study population

This study was based on the results of the nationally representative survey, the sixth Korea National Health and Nutrition Examination Survey (KNHANES VI-2), which was first launched in 1998 and conducted every year with population-based random samples using standardised questionnaires. This survey is intended to identify sociodemographic characteristics and health and nutritional status of the general Korean population and households, and survey responses are not tracked when the survey is completed each year. KNHANES VI-2 used the PHQ-9 as a screening instrument to diagnose depressive disorder. This questionnaire was provided to 7550 respondents. Of those administered questionnaires, 2658 questionnaires completed by Korean adults aged over 50 years were analysed with respect to the relationship between depressive symptoms and chronic knee pain (figure 1).



**Figure 1** Flow chart diagram of inclusion and exclusion of participants from the 2014 Korea National Health and Nutrition Examination Surveys (KNHANES). PHQ-9, Patient Health Questionnaire-9.

### Definition of depressive symptoms and chronic knee pain

A total score of 10 or higher on the PHQ-9 was used to define the presence of depressive symptoms.<sup>19</sup> In previous studies, the PHQ-9 questionnaire was often used to monitor depressive symptoms in patients with chronic pain.<sup>20–21</sup> The PHQ-9 items are based on the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders and designed to ask about symptoms that relate to depression over the last 2 weeks. Each item is scored from 0 (not at all) to 3 (nearly every day). The PHQ-9, consisting of nine questions, is a reliable and valid depressive symptoms scale. As a severity measure, its score ranges from 0 to 27, with higher scores indicating higher severity of depressive symptoms.<sup>22–23</sup>

In previous studies, a PHQ-9 score  $\geq 10$  was used to determine the presence of depressive symptoms, and the reliability of this questionnaire has been proven. In this study, a PHQ-9 score  $\geq 10$  was also used to indicate the presence of depressive symptoms. The severity of depressive symptoms was divided into not depressed (0–4 scores), mild (5–9 scores), moderate (10–14), moderately severe (15–19) and severe (20–27), according to previous studies.<sup>22–24</sup>

The questionnaire used to identify the presence of chronic knee pain in the respondents aged over 50 years included the question 'Have you had knee pain for at least 30 days during the last 3 months? Those who answered 'yes' to this question were classified as the chronic knee pain group, and their knee pain intensity was assessed using the NRS. Because the questionnaire regarding chronic knee pain was only asked to respondents aged over 50 years in KNHANES VI-2, the analysed data were limited to a population aged over 50 years.

### Description of demographic and characteristics of the study population

Patient information, including demographic characteristics, socioeconomic background, medical history and life habits, was analysed. Body mass index (BMI) was calculated by dividing body weight in kilograms by the square of height in metres and categorised into three groups: underweight ( $<18.5 \text{ kg/m}^2$ ), normal weight ( $18.5\text{--}24.9 \text{ kg/m}^2$ ) and overweight ( $\geq 25.0 \text{ kg/m}^2$ ). Smoking status was classified into non-smoker, ex-smoker and current smoker. The frequency of alcohol consumption was grouped into none, once a month or less, two drinks/month to three drinks/week and more than four times a month. Occupation was classified into four groups: unemployed (student, housewife, etc); office work/sales and services; agriculture, forestry and fishery; and machine fitting and simple labour. Household income was classified into quartiles: low, low-moderate and moderate-high/high. Education level was also categorised into three groups:  $\leq 6$  years, 7–9 years and  $\geq 10$  years. Physical activity was categorised into three groups: moderate activity at least 2 hours and 30 min a week, vigorous activity at least 1 hour and 15 min a week and combination of moderate and vigorous activity for longer hours (1 min vigorous activity

was considered equal to 2 min moderate activity). This study also investigated the presence of comorbidities, such as hypertension, dyslipidaemia, stroke, myocardial infarction, angina, arthritis, asthma and diabetes mellitus.

### Statistical analysis

The KNHANES is a survey of nationwide sample of Koreans selected through stratified clustered sampling, and sampling weights are used for survey data. Accordingly, complex sample survey data were analysed using parameters for strata, clusters and weights, which comprise the sample design. SAS V.9.4 (SAS Institute, Cary, North Carolina, USA) was used for statistical analysis, and  $p < 0.05$  was used as the threshold for statistical significance. Continuous variables are presented as mean and SD, and categorical variables are presented as frequency and percentage. The Rao-Scott  $\chi^2$  test or t-test was performed to determine differences between groups with/without chronic knee pain. To assess the effects of depressive symptoms on chronic knee pain, logistic regression analysis with complex sampling design was performed by adjusting for covariates. As a result, ORs, as well as 95% CIs for the ORs, were generated. Additionally, this study investigated if there was an underlying trend from different levels of depressive symptoms in each model (P for trend). To verify a linear relationship between the intensity of chronic knee pain and depressive symptoms, we used the Cochran-Armitage trend test and complex samples logistic regression.

### Patient and public involvement

We did not involve patients or the public in our work.

## RESULTS

### Characteristics of the study population according to chronic knee pain

This study found that the overall prevalence of chronic knee pain in the Korean population aged over 50 years was 19.8%. Of those, women (77.8%) far outpaced men (22.2%). The presence of depressive symptoms, determined by PHQ-9 score  $\geq 10$ , was significantly higher in the participants with chronic knee pain (17.3%), compared with those without chronic knee pain (5.2%) ( $p < 0.001$ , table 1). When compared with the participants without chronic knee pain, those with chronic knee pain showed greater frequency of depressive symptoms, higher percentages of older women and unemployment, lower household income, lower levels of education and physical activity, more comorbidities (hypertension, dyslipidaemia, stroke, arthritis, asthma) and shorter sleep duration (table 1).

### Clinical characteristics of participants with chronic knee pain according to the presence of depressive symptoms

When compared with non-depressed patients with chronic knee pain, depressed patients with chronic knee pain had lower household income, lower levels of education and aerobic physical activity, and shorter sleep duration.

**Table 1** Characteristics of the study population according to chronic knee pain

Variable	Without chronic knee pain (n=2131)	Chronic knee pain (n=527)	P value
<b>PHQ-9, n (%)</b>			
<10	2021 (94.8)	436 (82.7)	<0.0001
≥10	110 (5.2)	91 (17.3)	
<b>Levels of depressive symptom, n (%)</b>			
None (PHQ-9 ≤4)	1780 (83.5)	303 (57.5)	<0.0001
Mild (5–9)	241 (11.3)	133 (25.2)	
Moderate (10–14)	66 (3.1)	51 (9.7)	
Moderately severe (15–19)	33 (1.6)	28 (5.3)	
Severe (≥20)	11 (0.5)	12 (2.3)	
Age, years (mean±SD)	61.2±8.6	66.1±9.1	<0.0001
<b>Age, n (%)</b>			
50–59 years	845 (39.7)	111 (21.1)	<0.0001
60–69 years	698 (32.8)	182 (34.5)	
≥80 years	588 (27.6)	234 (44.4)	
<b>Sex, n (%)</b>			
Male	1002 (47)	117 (22.2)	<0.0001
Female	1129 (53)	410 (77.8)	
BMI, kg/m <sup>2</sup> (mean±SD)	23.9±3.1	24.3±3.3	0.0533
<b>Obesity, n (%)</b>			
Underweight (≤18.5 kg/m <sup>2</sup> )	55 (2.6)	13 (2.5)	0.2473
Normal (18.5–24.9 kg/m <sup>2</sup> )	1365 (64.1)	300 (57)	
Obese (≥25 kg/m <sup>2</sup> )	711 (33.4)	213 (40.5)	
<b>Smoking status, n (%)</b>			
Non-smoker	1265 (60.4)	383 (75)	<0.0001
Ex-smoker	496 (23.7)	78 (15.3)	
Current smoker	334 (15.9)	50 (9.8)	
<b>Alcohol consumption, n (%)</b>			
None	805 (38.4)	235 (45.7)	<0.0001
One drink/month or less	516 (24.6)	156 (30.4)	
Two drinks/ month to three drinks/ week	585 (27.9)	93 (18.1)	
Four drinks/ week or more	193 (9.2)	30 (5.8)	
<b>Occupation, n (%)</b>			
Unemployed (student, housewife, etc)	1003 (47.1)	328 (62.2)	<0.0001
Office work/sales and services	463 (21.8)	53 (10.1)	
Agriculture, forestry and fishery	186 (8.7)	50 (9.5)	
Machine fitting and simple labour	477 (22.4)	96 (18.2)	
<b>Household income, n (%)</b>			
Low	546 (25.7)	232 (44.3)	<0.0001
Low–moderate	589 (27.7)	136 (26)	
Moderate–high/high	989 (46.6)	156 (29.8)	
<b>Educational level, n (%)</b>			
≤6 years	805 (37.8)	345 (65.5)	<0.0001
7–9 years	396 (18.6)	73 (13.9)	

Continued

**Table 1** Continued

Variable	Without chronic knee pain (n=2131)	Chronic knee pain (n=527)	P value
≥10 years	928 (43.6)	109 (20.7)	
Aerobic physical activity, n (%)			
No	1100 (52.0)	313 (60.5)	0.0005
Yes	1016 (48.0)	204 (39.5)	
Duration of sleep, hours	6.7±1.4	6.4±1.7	0.0026
Comorbidities, n (%)			
Hypertension	765 (35.9)	262 (49.7)	<0.0001
Dyslipidaemia	413 (19.4)	145 (27.5)	0.0002
Stroke	77 (3.6)	38 (7.2)	0.0002
Myocardial infarction	31 (1.5)	13 (2.5)	0.2165
Angina	64 (3)	17 (3.2)	0.698
Arthritis	252 (11.8)	285 (54.1)	<0.0001
Asthma	56 (2.6)	33 (6.3)	<0.0001
Diabetes mellitus	304 (14.3)	86 (16.3)	0.7091

The Rao-Scott  $\chi^2$  test or t-test was performed to determine differences between groups with/without chronic knee pain. Missing values/non-responses were excluded from analysis. Individuals with PHQ-9 scores >10 were considered to have depressive symptoms. Levels of depressive symptom were divided into five quartiles: none (0–4), mild (5–9), moderate (10–14), moderately severe (15–19) and severe (20–27) according to the PHQ-9 score. Continuous variables are presented as mean and SD, and categorical variables are presented as frequency and percentage.

BMI, body mass index; PHQ-9, Patient Health Questionnaire-9.

However, no difference between the two groups was found with respect to age, sex, BMI, obesity, alcohol consumption and occupation. In case of smoking status, the percentage of non-smokers was high in the group with coexisting depressive symptoms and chronic knee pain (table 2).

### Associations between depressive symptoms and chronic knee pain

Multiple logistic regression models were used to analyse the effects of depressive symptoms on chronic knee pain. Univariate analyses revealed a strong association between depressive symptoms and chronic knee pain (model 1, OR=3.553, 95% CI 2.558 to 4.935,  $p<0.0001$ ). After adjusting for sex and age, a clear association between depressive symptoms and chronic knee pain was present (model 2, OR=2.722, 95% CI 1.844 to 4.017,  $p<0.0001$ ). After adjusting for sex, age, smoking status, alcohol use, education level, household income, physical activity, sleep duration and comorbidities, there was still a clear association between depressive symptoms and chronic knee pain (model 3, OR=2.333, 95% CI 1.605 to 3.391,  $p<0.0001$ ). The OR of depressive symptom levels also indicated an association between the severity of depressive symptoms and chronic knee pain. When compared with the absence of depressive symptoms, the probability of having chronic knee pain increased with the severity of depressive symptoms: mild (OR=3.715, 95% CI 2.687 to 5.138,  $p<0.0001$ ), moderate (OR=4.525, 95% CI 2.964 to 6.909,  $p<0.0001$ ), moderately severe (OR=4.124, 95% CI 2.256 to 7.539,  $p=0.0002$ ) and severe depressive symptoms (model 1, OR=6.93, 95% CI 2.519 to 19.068,  $p$  for trend  $<0.0001$ ). In the fully adjusted logistic regression

model (model 3), the association between severe depressive symptom and chronic knee pain was strongly significant. When compared with the absence of depressive symptoms, the probability of having chronic knee pain increased with depressive symptom severity showing mild depressive symptoms (OR=2.944, 95% CI 2.112 to 4.103,  $p<0.0001$ ) and severe depressive symptoms (OR=4.552, model 3, 95% CI 1.489 to 13.92,  $p$  for trend  $<0.0001$ ; table 3). Driven by the Cochran-Armitage trend test and complex samples logistic regression, a linear relationship was found between chronic knee pain and depressive symptoms (online supplementary table 1, figures 1 and 2).

### Association between depressive symptom state and chronic knee pain intensity

The comparison between severity of depressive symptoms and intensity of chronic knee pain, measured by NRS, showed a positive linear association. When the chronic knee pain NRS score ranged from 0 to 4, the prevalence of moderate depressive symptom was 3.4%, and the prevalence of severe depressive symptoms was 0.6%. In the presence of severe chronic knee pain (NRS=8–10), the prevalence of moderate and severe depressive symptoms was high (10.1% and 5.6%, respectively) ( $p<0.001$ ; table 4, figure 2).

## DISCUSSION

This study analysed the association between the severity of depressive symptoms and chronic knee pain by examining a sample of 7550 Koreans

**Table 2** Characteristics of chronic knee pain population according to presence of depressive symptoms

Variables	Non-depressive (n=436)	Depressive (n=91)	P value
Age, years (mean±SD)	65.9±9.2	67±8.8	0.4956
Age, n (%)			
50–59 years	94 (21.6)	17 (18.7)	0.8051
60–69 years	152 (34.9)	30 (33)	
≥70 years	190 (43.6)	44 (48.4)	
Sex, n (%)			
Male	104 (23.9)	13 (14.3)	0.1181
Female	332 (76.2)	78 (85.7)	
BMI, kg/m <sup>2</sup> , (mean±SD)	24.4±3.3	23.8±3.1	0.1927
Obesity, n (%)			
Underweight (<18.5 kg/m <sup>2</sup> )	9 (2.1)	4 (4.4)	0.1711
Normal (18.5–24.9 kg/m <sup>2</sup> )	246 (56.4)	54 (60)	
Obese (≥25 kg/m <sup>2</sup> )	181 (41.5)	32 (35.6)	
Smoking status, n (%)			
Non-smoker	312 (73.8)	71 (80.7)	0.0372
Ex-smoker	71 (16.8)	7 (8)	
Current smoker	40 (9.5)	10 (11.4)	
Alcohol consumption, n (%)			
None	183 (43)	52 (59.1)	0.2782
One drink/month or less	136 (31.9)	20 (22.7)	
Two drinks/month to three drinks/week	83 (19.5)	10 (11.4)	
Four drinks/week or more	24 (5.6)	6 (6.8)	
Occupation, n (%)			
Unemployed (student, housewife, etc)	262 (60.1)	66 (72.5)	0.0561
Office work/sales and services	48 (11)	5 (5.5)	
Agriculture, forestry and fishery	42 (9.6)	8 (8.8)	
Machine fitting and simple labour	84 (19.3)	12 (13.2)	
Household income, n (%)			
Low	171 (39.5)	61 (67)	<0.0001
Low–moderate	112 (25.9)	24 (26.4)	
Moderate–high/high	150 (34.6)	6 (6.6)	
Educational level, n (%)			
≤6 years	278 (63.8)	67 (73.6)	0.0076
7–9 years	58 (13.3)	15 (16.5)	
≥10 years	100 (22.9)	9 (9.9)	
Aerobic physical activity, n (%)			
No	254 (59.1)	59 (67.8)	0.0162
Yes	176 (40.9)	28 (32.2)	
Duration of sleep, hours (mean)	6.5±1.7	5.9±1.9	0.0325

The Rao-Scott  $\chi^2$  test or t-test was performed to determine differences between groups with/without depressive symptoms. Missing values/non-responses were excluded from analysis. Individuals with PHQ-9 scores >10 were considered to have depressive symptoms. Levels of depressive symptoms were divided into five quartiles: none (0–4), mild (5–9), moderate (10–14), moderately severe (15–19) and severe (20–27) according to the PHQ-9 score.

BMI, body mass index; PHQ-9, Patient Health Questionnaire-9.

representing the general population from the reliable nationwide survey data. All the participants selected for this study were aged 50 years or older

and shared information about their chronic knee pain, for which NRS was used to measure the pain intensity.

**Table 3** Association between severity of depressive symptoms and chronic knee pain

	Model 1		Model 2		Model 3	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
<b>Diagnosis of depressive symptoms</b>						
No	1		1		1	
Yes	3.553 (2.558 to 4.935)	<0.0001	2.722 (1.844 to 4.017)	<0.0001	2.333 (1.605 to 3.391)	<0.0001
<b>Levels of depressive symptom</b>						
None (0–4)	1		1		1	
Mild (5–9)	3.715 (2.687 to 5.138)	<0.0001	3.266 (2.35 to 4.541)	<0.0001	2.944 (2.112 to 4.103)	<0.0001
Moderate (10–14)	4.525 (2.964 to 6.909)	<0.0001	3.619 (2.233 to 5.865)	<0.0001	3.211 (1.977 to 5.217)	<0.0001
Moderately severe (15–19)	4.124 (2.256 to 7.539)	<0.0001	2.805 (1.553 to 5.066)	0.0007	2.43 (1.355 to 4.359)	0.0031
Severe (20–27)	6.93 (2.519 to 19.068)	0.0002	5.109 (1.606 to 16.257)	0.006	4.552 (1.489 to 13.92)	0.0082
P value for trend		<0.0001		<0.0001		<0.0001

Logistic regression analysis with complex sampling design was performed by adjusting for covariates. Individuals with PHQ-9 scores >10 were considered to have depressive symptoms. Levels of depressive symptom were divided into five quartiles: none (0–4), mild (5–9), moderate (10–14), moderately severe (15–19) and severe (20–27) according to the PHQ-9 score. Model 1 was unadjusted ORs. Model 2 was adjusted by age and sex. Model 3 was fully adjusted by age, sex and other environmental factors, such as smoking, alcohol consumption, educational level, household income, physical activity, duration of sleep and comorbidities. PHQ-9, Patient Health Questionnaire-9.

The association between depressive symptoms and pain is well established by previous studies.<sup>13–15</sup> Moreover, a study indicated that persistent depressive symptoms was significantly associated with worsening of osteoarthritis (OA) knee pain.<sup>25</sup> Another previous study also demonstrated that physical pain symptoms were significantly associated with the mean score of depressive symptoms severity.<sup>17</sup> Furthermore, a longitudinal analysis revealed that pain severity was a strong predictor of subsequent depressive symptom severity, and conversely, depressive symptom severity was a strong predictor of subsequent pain severity.<sup>18</sup> Further to this, our report is a cross-sectional study which explores the association between severity of depressive symptoms and intensity of chronic knee pain.

In our study, the positive association became stronger in the group with severe depressive symptoms, when compared with that of those having the symptoms of mild to moderate depressive symptoms. The strong linear correlation between depressive symptoms and chronic

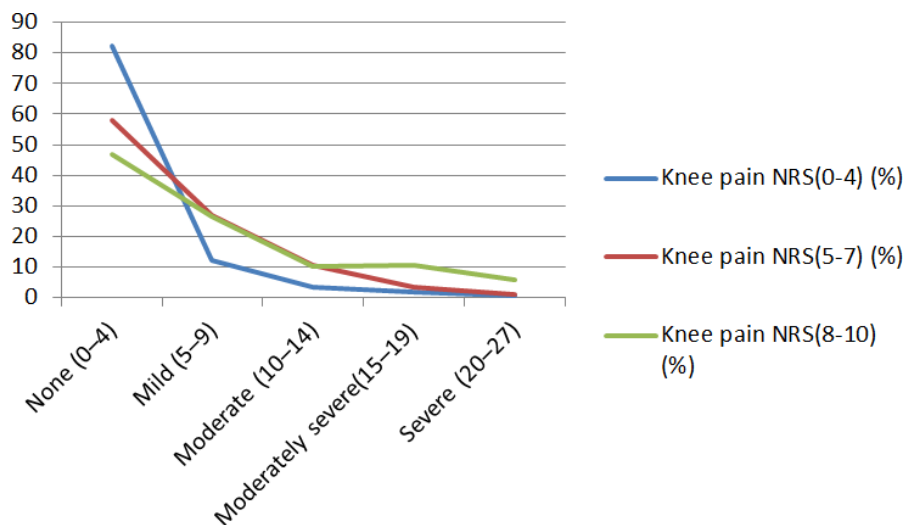
knee pain was still present after adjusting for variables, such as socioeconomic indicators and comorbidity. In the PHQ-9 survey, a significantly strong association was observed in the severely depressed group, identified with PHQ-9 score of 20 or above. Such a highly significant association persisted even after adjusting for variables, such as sex, age, socioeconomic indicators, smoking status and alcohol use. Although a previous study using KNHANES revealed a relationship between self-reported depressive symptoms and Kellgren-Lawrence knee OA grade, our study is the first to demonstrate the association between depressive symptoms and chronic knee pain using PHQ-9 and NRS in the Korean population.<sup>15</sup>

In our study, a positive linear relationship existed between intensity of chronic knee pain and severity of depressive symptoms as shown in table 4. We divided severity of depressive symptoms as not depressed (0–4 scores), mild (5–9 scores), moderate (10–14), moderately severe (15–19) and severe (20–27), and divided severity of chronic knee pain as light (0–4), moderate (5–7) and

**Table 4** Association between severity of chronic knee pain NRS and severity of depressive symptoms

Chronic knee pain NRS	Depressive symptoms					P value
	None (0–4)	Mild (5–9)	Moderate (10–14)	Moderately severe (15–19)	Severe (20–27)	
NRS (0–4) (%)	1872 (82.4)	272 (12)	77 (3.4)	38 (1.7)	13 (0.6)	<0.0001
NRS (5–7) (%)	136 (58.1)	63 (26.9)	25 (10.7)	8 (3.4)	2 (0.9)	
NRS (8–10) (%)	65 (46.8)	37 (26.6)	14 (10.1)	15 (10.8)	8 (5.8)	

The Rao-Scott  $\chi^2$  test was performed to compare severity of depressive symptoms according to chronic knee pain NRS. Individuals without knee pain were regarded as NRS 0. NRS, Numerical Rating Scale.



**Figure 2** Severity of depressive symptoms according to chronic knee pain NRS. Individuals without knee pain were regarded as NRS 0. Severity of depressive symptoms according to PHQ-9 score: none (0–4), mild (5–9), moderate (10–14), moderately severe (15–19) and severe (20–27). Individuals without knee pain were regarded as NRS 0. NRS, Numerical Rating Scale.

intense (8–10). In the participants with no chronic knee pain or light pain (NRS=0–4), the prevalence of severe depressive symptoms was 0.6. However, it increased to 5.8% in the participants with more intense chronic knee pain (NRS=8–10). To our knowledge, our study is the first to divide and compare both aspects of severity of depressive symptoms and intensity of chronic knee pain. As a result, we found a strong association between severity of depressive symptoms and intensity of chronic knee pain. It is a cross-sectional proof of a previous longitudinal study that suggested severe pain and severe depressive symptoms can be a predictor of each other.<sup>18</sup>

Although there is no clear evidence that depressive symptoms can cause chronic knee pain, many potential hypotheses have been suggested. Depressive symptom can interfere with the mechanism of inflammatory cytokines and the regulation of autonomic nervous system. Moreover, it can also destabilise the hypothalamic–pituitary–adrenal axis.<sup>26–28</sup> Depressive symptom-induced pathological conditions act as the catalyst for chronic pain syndrome.<sup>29–30</sup> Furthermore, neurotransmitters of norepinephrine and serotonin are associated with the pathological mechanism of depressive symptom. These neurotransmitters also play an important role in pain inhibitory pathways.<sup>31–33</sup> The association between depressive symptoms and chronic knee pain can also be explained by reduced physical activity, which may be associated with depressive symptoms, consequently decreasing muscle strength and joint stability, whereby negative outcomes, such as OA, can be induced.<sup>34–35</sup> Taken together, these findings suggest the effects of depressive symptoms on the pathogenic mechanism of chronic pain.

### Strength and limitations

This study has the following strengths. First, this study was based on highly reliable data from the national survey using the Korean population-based questionnaire.

Second, to our knowledge, this is the first study to describe the correlation between the severity of depressive symptoms and the intensity of chronic knee pain.

However, this study had certain limitations. First, this study was a cross-sectional study. Therefore, it assessed depressive symptoms and chronic knee pain using ORs without the analysis of the cause–effect relationship between the variables. Second, because the questionnaire regarding chronic knee pain was only asked to a population aged over 50 years, the younger population with chronic knee pain was excluded in the analysis. Third, self-reporting questionnaires were used to assess the NRS and PHQ-9 scores for chronic knee pain and depressive symptoms, respectively. Therefore, response biases cannot be ruled out.

### CONCLUSIONS

This study identified a strong association between the presence and severity of depressive symptoms and the presence and intensity of chronic knee pain. Furthermore, the association became stronger with higher levels of depressive symptoms, demonstrating greater NRS scores for chronic knee pain. This study suggests depressive symptoms as an independent risk factor when screening for chronic knee pain.

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consent was obtained from all participants when the surveys were conducted. The approval of IRB was not required because the study did not deal with any sensitive information, but rather accessed only publicly available data from the KNHANES (JASENG IRB File No: 2018-11-017).

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