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## Association between changes in handgrip strength and depression in Korean adults: a longitudinal panel study

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Depression in older adults is a global socioeconomic burden. Identifying factors, such as physical activity or exercise that can help prevent depression is important. We aimed to investigate the relationship between changes in handgrip strength and the presence of depression using longitudinal, nationwide data of older Korean adults. Data from the Korean Longitudinal Study of Aging were used in this study. A total of 6783 participants who had undergone a handgrip strength test and completed the short-form Center for Epidemiologic Studies Depression Scale (CESD-10-D) questionnaire from 2006 to 2018 were included. General estimating equations were used to assess the temporal effect of the changes in handgrip strength on depression. A decrease in handgrip strength was associated with high CESD-10-D scores ( $\beta = 0.1889$  in men,  $\beta = 0.1552$  in women). As a continuous variable, handgrip strength was negatively correlated with CESD-10-D scores ( $\beta = -0.0166$  in men,  $\beta = -0.0196$  in women). Changes in the handgrip strength were associated with depressive symptoms in our longitudinal study. Those who experienced a decrease in handgrip strength had severe depressive symptoms compared to those with unchanged or increased handgrip strength. These findings can be used to guide general health policies for the prevention of depression.

Globally, depression is a major health problem and a leading cause of socioeconomic burden due to its growing prevalence and associated high suicide rate<sup>1–5</sup>. In particular, South Korea has been struggling with a higher prevalence of suicidality than other countries of the Organization for Economic Co-operation and Development and thus has focused on mitigating the associated risks for the last few decades<sup>6,7</sup>. To address this problem, previous studies in South Korea have mainly focused on biological and psychological treatment methods for depression, such as medications and cognitive or behavioral psychotherapy<sup>8–10</sup>. However, it is important to find methods that involve lifestyle changes, such as eating habits, nutrition, exercise, and sleep pattern, to reduce the prevalence of depression. Among studies on the methods for modifying lifestyle, a previous study suggested that increased levels of exercise can help prevent depression<sup>11</sup>.

Patients with depression exhibit various symptoms, including reduced physical activity, with some patients showing an extreme form of inactivity because of catatonia. Researchers and clinicians have focused on the symptom-reducing function of physical activity or exercise among depressive patients. In fact, previous studies showed that exercise led to a reduction in depressive symptoms and that cognitive behavior therapy combined with exercise led to favorable outcomes<sup>12–15</sup>. These studies prompted many countries, including South Korea, to include exercise in their depression treatment guidelines<sup>16,17</sup>.

While the therapeutic potential of exercise in alleviating depression has been established, its efficacy as a depression prevention measure remains unclear. Previous studies found an association between initial physical activity and reduced depression<sup>18</sup> and between handgrip strength asymmetry and depression<sup>19</sup>. However, very few studies have investigated the association between exercise and the prevalence of depression using a longitudinal study design. Moreover, previous studies did not use methods that allowed for instant measurement of the exercise status of the participants, thus limiting the utilization of the results in clinical settings. Therefore, this

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study used handgrip strength, which can be measured instantly and easily, as a proxy for the muscle power status of a participant<sup>20</sup>. Further, changes in handgrip strength can also be measured regularly to determine the exercise status of participants in a given period<sup>21–23</sup>. This study aimed to investigate the relationship between changes in handgrip strength and depressive symptoms in a Korean adult population cohort selected from a panel study.

## Methods

**Study population and data.** The data analyzed in this study were extracted from the Korean Longitudinal Study of Aging database (KLoSA). The KLoSA is a longitudinal panel survey of national representative samples of community-dwelling adults aged above 45 years and has been conducted every two years since 2006<sup>24</sup>. The baseline data were gathered in 2006, where 10,254 Korean adults were interviewed by trained interviewers. The survey collected information on family background, demographics, family, health, employment status, income, and assets and included questionnaires on subjective expectations and subjective quality of life. In 2018, the seventh wave was conducted, and the effective sample number was 6,136 from the original panels and 804 from the newly included panels. In this study, we used biannual survey data from 2006 to 2018, resulting in seven rounds of data. After removing data with missing values for the study variables, 6,793 participants (3,052 men and 3,731 women) were included in this study. The baseline characteristics of the included and excluded individuals are shown in Table S1. For statistical analysis, each change in handgrip strength from 2006 to 2018, rather than each participant, was treated as an individual case.

**Measures.** The short-form Center for Epidemiologic Studies Depression Scale (CESD-10-D) was used for measuring depressive symptoms. The validity of the Korean version of CESD-10-D for screening of depression is well established<sup>25,26</sup>. The participants were asked to answer 10 questions about their depressive condition using a binomial scoring system. The KLoSA provides a raw score by adding the scores of all the answers, and this score ranges from 0 to 10, with high scores indicating high severity of depression. We used a CESD-10-D cut-off score of 3 to determine the association between the change in handgrip strength and the presence of depressive symptoms.

**Handgrip strength.** Handgrip strength was measured in kilograms using a handgrip dynamometer (Hand Grip Meter 6103, Tanita, Tokyo, Japan). The participants were asked to squeeze the dynamometer twice with each hand, and the highest value among the four trials was used in this study. The participants who refused to perform the test due to physical problems were excluded from the data analysis. To analyze the relationship between the change in handgrip strength and the presence of depressive symptoms, the changes in both domains over the previous year were recorded. The continuous variable of handgrip strength was categorized into two groups: (1) decreased and (2) same or increased; the analyses were conducted assuming the presence of continuous changes in the recorded values across the two groups.

**Covariates.** Demographic and health-related factors were included as covariates in the analysis. The following demographic characteristics were included: age, educational level, dwelling region, working status, household income, participation in social activities, and the number of cohabiting generations<sup>27</sup>. The following health-related factors were included: smoking/alcohol use status, number of chronic medical conditions, body mass index (BMI), and perceived health status. All the covariates were measured using survey questionnaires. The KLoSA provides the number of chronic medical conditions for each participant, including hypertension, diabetes, cancers, chronic lung diseases, liver disease, cardiac disease, cerebrovascular diseases, psychiatric disease, arthritis, prostate disease, dementia, and other chronic diseases. All multivariable models were controlled for all of the covariates unless stated otherwise.

**Statistical analysis.** All statistical analyses were performed separately for men and women to rule out the effect of sex on depression. Analysis of variance was used to compare the general characteristics of the groups<sup>27</sup>. A generalized estimating equation (GEE) model was used for regression analysis of CESD-10 scores, change in handgrip strength, and other covariates. CESD-10 score was included as the outcome variable, and other variables in Table 1 were included in the GEE model. We used normal distribution with the identity link function for continuous variables and binomial distribution and logit link function for binary outcome variables. The temporal variable was the wave, i.e., every 2 years, and person ID was used to identify repeated subjects using the unstructured working correlation matrix for the GEE model. The analysis was conducted twice: first, after dividing the change in handgrip strength into two groups, and second, after setting the change in handgrip strength as a continuous variable. The results are presented as regression coefficients ( $\beta$ ) and standard errors.

Subgroup analyses were performed to assess the interaction between handgrip strength change and other variables that were associated with the CESD-10 score further. We conducted subgroup analyses for age, working status, participation in social activities, number of chronic medical conditions, and perceived health status. All analyses were carried out using SAS software version 9.4 (SAS Institute, Cary, North Carolina, USA), and the results were considered statistically significant if the p-value was < 0.05 and very highly significant if the p-value was < 0.001.

**Ethical considerations.** The KLoSA study was approved by Statistics Korea of the Korean Government (Approval number: 33602 and the Institutional Review Board of Korea National Institute for Ethics Policy (P01-201909-22-002)). The survey was conducted after acquiring written informed consent of the participants by the trained study interviewer of KLoSA survey. This study was approved as exempt by the Institutional Review

	Men (n = 3052)					Women (n = 3731)						
	Participants		CESD-10-D			Participants		CESD-10-D				
	N	%	Mean	SD	p-value	N	%	Mean	SD	p-value		
<b>Changes in handgrip strength</b>						0.8602						0.7542
Same or Increased	1213	39.7	3.042	2.756		1691	45.3	3.793	2.883			
Decreased	1839	60.3	3.058	2.698		2040	54.7	3.820	2.891			
<b>Age, years</b>						<0.0001						<0.0001
45–54	845	27.7	2.512	2.445		1150	30.8	2.925	2.569			
55–64	954	31.3	2.698	2.585		1083	29.0	3.547	2.849			
65–74	890	29.2	3.430	2.826		1002	26.9	4.515	2.898			
≥75	363	11.9	4.309	2.884		496	13.3	4.994	2.897			
<b>Education level</b>						<0.0001						<0.0001
Elementary school or less	924	30.3	3.868	2.913		2018	54.1	4.466	2.930			
Middle school	529	17.3	3.149	2.805		642	17.2	3.402	2.735			
High school	1085	35.6	2.690	2.568		897	24.0	2.858	2.566			
University or beyond	514	16.8	2.247	2.146		174	4.7	2.557	2.427			
<b>Region</b>						<0.0001						0.0003
Metropolitan	1266	41.5	2.694	2.539		1589	42.6	3.497	2.821			
Small or medium cities	1009	33.1	3.105	2.804		1226	32.9	3.879	2.962			
Rural	777	25.5	3.566	2.812		916	24.6	4.250	2.838			
<b>Working status</b>						<0.0001						<0.0001
Working	1937	63.5	2.590	2.519		1230	33.0	3.221	2.660			
Non-working	1115	36.5	3.854	2.870		2501	67.0	4.096	2.951			
<b>Household income</b>						<0.0001						<0.0001
Quartile 1 (low)	609	20.0	4.118	2.866		988	26.5	4.968	2.947			
Quartile 2	825	27.0	3.238	2.775		997	26.7	3.876	2.839			
Quartile 3	865	28.3	2.690	2.576		910	24.4	3.313	2.737			
Quartile 4 (high)	753	24.7	2.401	2.409		836	22.4	2.894	2.549			
<b>Participation in social activities</b>						<0.0001						<0.0001
No	538	17.6	4.126	3.002		819	22.0	4.722	2.988			
Yes	2514	82.4	2.822	2.600		2912	78.0	3.550	2.805			
<b>Smoking</b>						0.0776						<0.0001
Current	1188	38.9	3.115	2.748		109	2.9	5.459	3.114			
Former	789	25.9	3.118	2.673		38	1.0	4.605	3.150			
Never	1075	35.2	2.933	2.724		3584	96.1	3.749	2.862			
<b>Alcohol intake</b>						0.4527						0.4280
Yes	1926	63.1	2.911	2.659		715	19.2	3.418	2.774			
No	1126	36.9	3.292	2.809		3016	80.8	3.900	2.906			
<b>Number of chronic medical conditions</b>						<0.0001						0.5450
None	175	51.6	2.639	2.558		1697	45.5	3.11	2.68			
1	905	29.7	3.190	2.737		1143	30.6	3.90	2.90			
≥2	572	18.7	3.970	2.884		891	23.9	5.00	2.86			
<b>Number of cohabiting generations</b>						0.4463						0.0791
Couple	1424	46.7	3.270	2.786		1790	48.0	4.085	2.949			
Two generation	1287	42.2	2.810	2.602		1436	38.5	3.498	2.812			
Over two generation	341	11.2	3.053	2.814		505	13.5	3.705	2.782			
<b>BMI</b>						0.0005						0.0494
Underweight	92	3.0	4.000	3.045		113	3.0	4.301	3.062			
Normal weight	1341	43.9	3.293	2.787		1647	44.1	3.760	2.878			
Overweight	1027	33.7	2.888	2.627		1039	27.8	3.774	2.831			
Obesity	559	18.3	2.615	2.579		820	22.0	3.883	2.913			
Severe obesity	33	1.1	3.091	2.788		112	3.0	3.768	3.148			
<b>Perceived health status</b>						<0.0001						<0.0001
Continued												

	Men (n = 3052)					Women (n = 3731)				
	Participants		CESD-10-D			Participants		CESD-10-D		
	N	%	Mean	SD	p-value	N	%	Mean	SD	p-value
Healthy	1787	58.6	2.357	2.383		1707	45.8	2.755	2.527	
Average	865	28.3	3.527	2.747		1231	33.0	4.017	2.716	
Unhealthy	400	13.1	5.128	2.809		793	21.3	5.749	2.795	

**Table 1.** Baseline characteristics of the study population according to the short-form Center for Epidemiologic Studies Depression Scale (CESD-10-D) scores. Underweight: BMI < 18.5; normal weight: 18.5 ≤ BMI < 23; overweight: 23 ≤ BMI < 25; obesity: 25 ≤ BMI < 30; severe obesity: 30 ≤ BMI. BMI body mass index, SD standard deviation, CESD-10-D Shorter form of the Center for Epidemiologic Studies Depression Scale.

Board of Yonsei University's Health System (4-2021-0307). This study adhered to the principles of the Declaration of Helsinki.

## Results

The baseline characteristics of the study population, stratified by sex, are presented in Table 1. A total of 6,793 participants (3,052 men and 3,731 women) were included in the analysis. Of the participants, 39.7% of the men and 45.3% of the women showed either no changes in handgrip in the first two waves or an increase in the second wave. In the unadjusted analysis, we found no significant difference in CESD-10-D scores between the two handgrip strength groups in both sexes. However, the other covariates such as age, educational level, region, working status, household income, participation in social activities, number of chronic medical conditions, BMI, and perceived health status significantly differed in CESD-10-D scores for both sexes.

Table 2 shows the multiple regression analysis results for the CESD-10-D score and groups of change in handgrip after adjusting for the covariates. Compared to the same or increased handgrip strength group, the decreased handgrip strength group showed regression coefficients of 0.1889 in men and 0.1552 in women, which were highly significant at  $p < 0.0001$ . A decrease in handgrip strength was associated with an increase in CESD-10-D scores in both sexes. The results of the other covariates are shown in Table 2. Table 3 shows the results of multiple regression analysis between CESD-10-D score and handgrip strength change as continuous values using the same covariates from Table 2. The regression coefficients were  $-0.0166$  in men and  $-0.0196$  in women, with a high significance level of  $p < 0.0001$ . These results suggest that the change in handgrip strength was negatively associated with the CESD-10-D total score in both sexes. Table 4 shows that the decreased handgrip strength group showed a higher odds ratio (OR) for depression (OR = 1.18, 95% confidence interval [CI] 1.10–1.27 in men, OR = 1.09, 95% CI 1.02–1.16 in women) after dividing the participants into two groups using the CESD-10-D cut-off score of 3.

The results of the subgroup analysis are shown in Table S2. When we grouped the data by age, all age groups showed high CESD-10 scores when their handgrip strength had decreased, except the oldest male and female groups, which showed no significant relationship between handgrip change and depression.

## Discussions

We found that a decrease in handgrip strength during the previous 2 years was associated with depressive symptoms in Korean adults. The participants whose handgrip strength decreased had reported higher CESD-10-D scores than those whose handgrip strength had remained the same or increased in the same period. Furthermore, we found that handgrip strength was negatively correlated with the CESD-10-D score in our study population.

The results of the present study are generally consistent with those of previous studies, namely that handgrip strength was associated with a high prevalence of depression or an increase in depressive symptoms. For example, one study found that weak handgrip strength was associated with a high odds ratio for depression in low- and middle-income countries. Although it was a cross-sectional study, the odds ratio of depression was 1.45 in the weak hand strength group, suggesting that handgrip strength was directly related to depressive symptomatology<sup>28</sup>. Furthermore, a cross-sectional study involving community-dwelling adults in the USA also found that sarcopenia, denoted by decreased handgrip strength, was associated with the presence of depression<sup>29</sup>. Another cohort study conducted in Japan by Fukumori et al. reported that low baseline handgrip strength was associated with depressive symptoms<sup>30</sup>. Reduced handgrip strength was also associated with the development of depression after 1 year in a longitudinal analysis; this study suggested that a higher handgrip strength might prevent depression.

The mechanism underlying the association between handgrip strength and the presence of depressive symptoms has not yet been established. However, several hypotheses have suggested that exercise has antidepressant effects, giving us a clue about the association between muscle strength, a result of exercise, and depressive symptoms. One hypothesis is that exercise relieves depressive symptoms by reversing depression-induced atrophy of brain structures. Atrophy of brain structures such as the hippocampus, anterior cingulate cortex, and prefrontal cortex has been reported in patients with depression<sup>31</sup>. Importantly, several studies have shown that exercise increases the volume of the hippocampus, anterior accumbens, and prefrontal cortex, thus providing antidepressant effects<sup>32–34</sup>. Activated muscle or increased muscle mass might produce antidepressant effects by elevating the level of serotonin in the brain. In fact, since muscles consume branched-chain amino acids as their metabolism substrates, the serum concentration of single amino acids such as tryptophan increases. High levels

	Men			Women		
	$\beta$	S.E.	p-value	$\beta$	S.E.	p-value
<b>Changes in handgrip strength</b>						
Same or increased	Ref			Ref		
Decreased	0.1889	0.0417	<0.0001	0.1552	0.0390	<0.0001
<b>Age, years</b>						
45–54	Ref			Ref		
55–64	–0.1467	0.0704	0.0372	–0.1234	0.0656	0.0598
65–74	–0.1658	0.0939	0.0774	–0.1689	0.0893	0.0586
$\geq 75$	–0.0880	0.1174	0.4535	–0.1139	0.1089	0.2955
<b>Education level</b>						
Elementary school or less	0.7297	0.1101	<0.0001	0.7245	0.1454	<0.0001
Middle school	0.4702	0.1148	<0.0001	0.3180	0.1492	0.0331
High school	0.3426	0.0920	0.0002	0.0770	0.1386	0.5788
University or beyond	Ref			Ref		
<b>Region</b>						
Metropolitan	Ref			Ref		
Small or medium cities	0.2786	0.0794	0.0005	0.3028	0.0722	<0.0001
Rural	0.1342	0.0850	0.1143	0.1490	0.0782	0.0568
<b>Working status</b>						
Working	Ref			Ref		
Non-working	0.5319	0.0668	<0.0001	0.3145	0.0580	<0.0001
<b>Household income</b>						
Quartile 1 (low)	0.2382	0.0998	0.0171	0.5562	0.0873	<0.0001
Quartile 2	0.1686	0.0817	0.0390	0.3516	0.0766	<0.0001
Quartile 3	0.0526	0.0682	0.4405	0.1007	0.0698	0.1490
Quartile 4 (high)	Ref			Ref		
<b>Participation in social activities</b>						
No	0.4939	0.0746	<0.0001	0.2227	0.0632	0.0004
Yes	Ref			Ref		
<b>Smoking</b>						
Current	0.0747	0.0821	0.3628	0.6841	0.1953	0.0005
Former	–0.1596	0.0798	0.0456	0.4384	0.2427	0.0709
Never	Ref			Ref		
<b>Alcohol intake</b>						
Yes	–0.0860	0.0639	0.1782	–0.1416	0.0740	0.0557
No	Ref			Ref		
<b>Number of chronic medical conditions</b>						
None	Ref			Ref		
1	–0.0047	0.0701	0.9461	0.1335	0.0689	0.0526
$\geq 2$	–0.0410	0.0861	0.6341	0.3419	0.0813	<0.0001
<b>Number of cohabiting generations</b>						
Couple	0.0141	0.1078	0.8961	–0.1809	0.0944	0.0552
Two generation	0.1243	0.1033	0.2289	0.0291	0.0933	0.7548
Over two generation	Ref			Ref		
<b>BMI</b>						
Underweight	0.1099	0.1603	0.4932	0.1297	0.1492	0.3847
Normal weight	Ref			Ref		
Overweight	–0.1384	0.0624	0.0265	–0.0192	0.0584	0.7426
Obesity	–0.2770	0.0787	0.0004	–0.1326	0.0690	0.0547
Severe obesity	–0.5115	0.2828	0.0704	–0.2835	0.1855	0.1264
<b>Perceived health status</b>						
Healthy	Ref			Ref		
Average	0.3562	0.0546	<0.0001	0.3485	0.0503	<0.0001
Unhealthy	1.6343	0.0893	<0.0001	1.5368	0.0744	<0.0001

**Table 2.** Results of the generalized estimating equation analysis of handgrip strength change in the two groups and short-form Center for Epidemiologic Studies Depression Scale scores. Underweight: BMI < 18.5; normal weight: 18.5  $\leq$  BMI < 23; overweight: 23  $\leq$  BMI < 25; obesity: 25  $\leq$  BMI < 30; severe obesity: 30  $\leq$  BMI. BMI body mass index, S.E. standard error.

	Men			Women		
	$\beta$	S.E.	p-value	$\beta$	S.E.	p-value
Handgrip strength change (kg)	- 0.0166	0.0030	<0.0001	- 0.0196	0.0039	<0.0001

**Table 3.** Results of the generalized estimating equation analysis of handgrip strength change as a continuous variable and short-form Center for Epidemiologic Studies Depression Scale scores. All covariates in Table 2 were included in this analysis. S.E. standard error.

	Depression(3 ≤ CESD-10-D)			
	Men		Women	
	Adjusted OR	95% CI	Adjusted OR	95% CI
<b>Changes in Handgrip strength</b>				
Same or increased	Ref		Ref	
Decreased	1.18	(1.10–1.27)	1.09	(1.02–1.16)

**Table 4.** Results of the GEE analysis of handgrip strength change and depression. All variables in Table 2 were included in the GEE model.

of tryptophan in the serum and cerebrospinal fluid lead to increased levels of serotonin and dopamine, resulting in a reduction in depression<sup>35,36</sup>. Exercise has also been found to increase the levels of brain-derived neurotrophic factor (BDNF), which is known to regenerate as well as enhance the function of the hippocampus. Given that decreased levels of BDNF have been found to be related to depression in older patients, exercise may not only reverse but also prevent depressive symptoms by increasing BDNF levels<sup>37</sup>. These previous studies suggest that exercise might prevent depression, and since we can measure the exercise status via handgrip strength, it might be associated with depression in individuals.

This study had some limitations. First, we used survey-based data and excluded non-responders; thus, the results might have been affected by this bias. Individuals with severe depression or severe sarcopenia might not have accurately responded to the survey or may not have been included; thus, our results might have been underestimated. Second, we could not determine the biological risk factors for depression since we used only a survey-based database. As several biological factors have been established as risk factors for depression in adults, future studies should analyze them in regression models<sup>38</sup>. Third, causation could not be determined because of the lack of a prospective design. We used the change in handgrip strength between two waves and analyzed its association with depressive symptoms in the subsequent wave to minimize the risk of reciprocal causation. However, depressive symptoms in the previous waves could have caused a decrease in handgrip strength. Thus, future studies using a prospective design including interventions of strengthening exercises are needed to establish the causal relationship between changes in handgrip strength and depressive symptomology.

Despite these limitations, our study has many strengths. We conducted the analysis with a relatively large sample size that represented the general adult population of South Korea and used a longitudinal design. These results can be applied to the general Korean population to establish health care policies or conduct future studies. Second, we used standardized tools to measure muscle strength. Handgrip strength is easily measurable and can be standardized across different groups and studies. Third, we used the change in handgrip strength rather than baseline strength; thus, the results could be analyzed as the exercise or physical activity status of the previous period. Finally, our results suggest that increasing handgrip strength by modifying lifestyle habits is a useful strategy for preventing depressive symptoms in adults.

In conclusion, this longitudinal, large-sized study showed that change in handgrip strength was associated with depressive symptoms in South Korea. A decrease in handgrip strength was associated with severe depressive symptoms compared to no change or increased handgrip strength. Future studies exploring the underlying mechanisms of this association as well as the preventive effects of increasing handgrip strength on depressive symptoms may provide valuable strategies for treating and preventing depressive symptoms.

### Data availability

The datasets analyzed during the current study are available in the KLoSA repository, <https://survey.keis.or.kr/eng/klosa/databoard/List.jsp>.

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### Author contributions

H.K. and W.J. had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: H.K., S.I.J.; data acquisition, analysis, and interpretation of data: H.K., Y.S.P.; drafting of the manuscript: H.K., S.H.K.; critical revision of the manuscript for important intellectual content: Y.K., E.C.P., S.I.J.; statistical analysis: H.K., S.H.K.; supervision: E.C.P.

### Competing interests

The authors declare no competing interests.

### Additional information

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