

1 *Association between muscle strength and depression in a cohort of young adults*

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19 **Abstract**

20 *Background:* The study investigated the association between knee joint muscle strength and the
21 prevalence of depression in a cohort of young adults. *Methods:* The observational, population-
22 based study was performed with 909 participants (29.02 ± 2.03 years; 48.73% male) from the
23 Central European Longitudinal Studies of Parents and Children: Young Adults (CELSPAC:
24 YA), who were retained to analysis. Quadriceps and hamstring knee muscle strength were
25 assessed by isokinetic dynamometry, and depression by Beck's Depression Inventory (BDI-II).
26 Statistical comparisons (Mann-Whitney and Chi-squared test) and effect size analyses (Eta-
27 Squared, and Odds Ratio) were conducted. *Results:* The main findings revealed an inverse
28 association between knee joint muscle strength and depression, with individuals who had low
29 muscle strength having 3.15 (95% CI = 2.74–3.62) times higher odds of experiencing
30 depression. Specifically, participants with low extensor strength had 4.63 (95% CI = 2.20–9.74)
31 times higher odds, and those with low flexor strength had 2.68 (95% CI = 1.47–4.89) times
32 higher odds of experiencing depression compared to those individuals with high muscle
33 strength. Furthermore, gender-specific analyses revealed that males with low muscle strength
34 had 2.51 (95% CI = 1.53–4.14) times higher odds, while females had 3.46 (95% CI = 2.93–
35 4.08) times higher odds of experiencing depression compared to individuals with high muscle
36 strength. *Conclusions:* Strong knee muscles seems to be a key factor in preventing depression,
37 specially in female young adults. The results support the importance of promoting an increase
38 in muscle strength through physical activity as a preventive strategy against depression in this
39 population.

40

41 **Keywords:** Muscle strength; Mental disorders; Mental health; Muscle strength dynamometer;
42 Depressive disorders; Exercise; Sedentary lifestyle.

43 **Introduction**

44 The positive impact of high levels of physical activity on depression in the adult population
45 is well-documented (1). Consequently, due to physical activity being a modifiable factor related
46 to muscular strength, recent studies have focused on evaluating the connection between muscle
47 strength and the prevalence of depression (2).

48 Depression is one of the most prevalent and personally debilitating mental health
49 disorders, posing a significant public health issue in contemporary times. Nowadays, it affects
50 more than 280 million people, and its prevalence is still significantly increasing (3). Inseparably
51 linked with poor health (4), including an increased risk of cardiovascular diseases (4) and type 2
52 diabetes (5), as well as being a leading cause of suicide (6).

53 Within the workforce, depression stands out as a substantial contributor to absenteeism
54 and disability (7). Furthermore, the total costs of mental health problems are estimated to be
55 more than 4% of the total gross domestic product (more than EUR 600 billion) across the 27
56 European countries and the United Kingdom (8). The prevalence of depression is nearly twice
57 as high in females compared to males across all ages, and both genders experience a peak in
58 prevalence during their second and third decades of life (9,10). Currently, medication and
59 psychotherapy, are the main treatments for depression. However, drug treatments are hindered
60 by side effects, addiction, high prices, and poor patient compliance, resulting in an overall
61 unsatisfactory and seriously affected quality of life for patients. (11). Moreover, psychotherapy
62 can be expensive and inaccessible, and its overall effects can be overestimated (12). Given the
63 breadth of depressive disorders, strategies that may reduce the onset of depression are urgently
64 needed.

65 Exercise interventions demonstrate promise as viable treatments for depressive
66 symptoms, presenting benefits in comparison to antidepressant medications and psychotherapy
67 due to their minimal adverse effects and reduced expenses. Furthermore, current studies are

68 focused on how muscle strength can be perceived as a modifiable factor related to lower levels
69 of depression prevalence. Recently, a 7-year follow-up study with 5,228 participants
70 demonstrated that higher relative handgrip strength was a protective factor against depression
71 in the adult population (13). While the handgrip strength test has commonly been utilized as a
72 parameter of muscle strength in populational studies due to its non-invasiveness, low cost, and
73 practicality, it is worth noting that the activation of muscle groups during this test is limited and
74 may have lower applicability when considering daily physical activities. Therefore, it seems
75 reasonable to investigate muscle strength by focusing on major muscle groups.

76 Methods such as walking pace (14,15) and the Sit to Stand Test (13) have been recently
77 used in examining the association between lower limb strength and depression, particularly in
78 the elderly population. Considering that the young adult population is more sensitive to
79 depression (16), it is necessary to investigate the possible association between depression and
80 low limb muscle strength using a gold-standard method.

81 Therefore, the main aim of the study is to examine whether there is an association
82 between high levels of low limb muscle strength and depression in the young adult population.
83 For this purpose, the study will use the gold-standard method for muscle strength testing,
84 isokinetic dynamometry, to measure the strength of the knee extensor and flexor muscles. The
85 study will also investigate associations between depression and knee joint muscle strength in
86 both males and females. We hypothesized that a higher level of muscular strength in the lower
87 limbs will be associated with lower scores with depressive symptoms, with a stronger
88 association in females compared to males.

89

90 **Materials and Methods**

91 **Study design, setting and sample**

92 This observational population-based study originates from the Central European
93 Longitudinal Studies of Parents and Children: Young Adults (CELSPAC: YA). Young Adults
94 cohort is an on-going follow-up study of the Czech part of the ELSPAC birth cohort (European
95 Longitudinal Study of Pregnancy and Childhood) that was initiated in 1991–1992 in the Czech
96 Republic, in Brno and Znojmo region. Detailed information about the ELSPAC-CZ study is
97 provided elsewhere (17). For the current research goal, data from participants in the CELSPAC:
98 YA cohort were collected between March 1, 2019, and February 1, 2023. The data were
99 accessed for research purposes on February 15, 2023. Authors had access to information that
100 could identify individual participants after data collection. The CELSPAC: YA study was
101 approved by the ELSPAC Ethics Committee (Ref. No: ELSPAC/EK/2/2019), and all
102 participants of this study provided written informed consent.

103 To examine the relationship between muscle strength and the incidence of depression,
104 the variables were selected by using isokinetic muscle strength testing and questionnaires.
105 Questionnaires including both the health condition and the health history were filled by the
106 participants with health practitioner assistance. The depressive symptoms assessment and
107 alcohol compulsion were filled out by the participants themselves. Participants who did not
108 provide information regarding these variables were excluded. The study included participants
109 who took part in the surveys and were evaluated for isokinetic knee muscle strength.

110 The following exclusion criteria were applied: participants with physical disabilities
111 (such as chronic lower extremity pain, acute injuries, or injuries related to the knee joint) that
112 could affect muscle strength measurements were not included in the study. Additionally,
113 participants with previously diagnosed psychiatric disorders including schizophrenia, bipolar

114 disorder, or substance abuse were also excluded from the analysis. From a total of 967
115 participants, 909 young adult participants meet the inclusion criteria and were retained and
116 analyzed in this study. The participants descriptive statistics are presented in Table 1. A priori
117 Power analysis for the Proportion test was conducted utilizing G*Power (3.1.9.6) software. For
118 total of 909 participants the Power (1-b) exceeds 0.91 (with medium effect, α of 0.05 and
119 allocation ratio of 0.957).

120

121 **Muscle strength measurement**

122 To assess knee muscle strength, a calibrated isokinetic dynamometer (Humac Norm,
123 Computer Sports Medicine, Inc., Stoughton, MA, USA) was used. Recent research by (18) has
124 demonstrated the excellent reliability of the Humac Norm isokinetic dynamometer for testing
125 knee joint muscle strength. For the evaluation of muscle strength, we conducted a similar testing
126 protocol as described in the study by (19). Briefly, participants were seated in the isokinetic
127 dynamometer chair with the back support set at an angle of 85°. The pad of the dynamometer
128 was positioned approximately 3 cm above the lateral malleolus. The knee joint axis was
129 carefully aligned with the mechanical axis of the dynamometer. The testing protocol began by
130 evaluating the dominant limb first. To warm up and familiarize themselves with the movements,
131 participants performed five non-maximal trials on the dynamometer for each movement.
132 Following a thirty-second pause, the concentric isokinetic knee flexion and extension
133 movements were assessed at an angular velocity of 60 degrees per second ($60^\circ/\text{s}^{-1}$). Each
134 movement consisted of five maximal repetitions over a range of motion of 90 degrees, from 0°
135 (full knee extension) to 90° of knee flexion. The maximal knee extensor and flexor strengths
136 were assessed by measuring the peak torque (in Newton meters, Nm) during the isokinetic
137 concentric contraction. During the tests, the investigator provided verbal encouragement to help
138 participants achieve their maximal strength. Participants were not permitted to view the screen

139 during testing. Prior to each test, gravity correction was obtained to ensure accurate
140 measurements.

141

142 **Depression assessment**

143 The severity of depression was assessed using the second edition of the Beck Depression
144 Inventory (BDI-II) questionnaire. The validity and reliability of the BDI-II for screening of
145 depression is well established (20). The BDI-II is a self-report questionnaire that assesses
146 symptoms of depression and has a strong correlation with clinical diagnosis of depression (21).
147 The BDI-II consists of 21 items, and participants rate each item on a Likert scale ranging from
148 0 to 3. Higher scores on the questionnaire indicate more severe depressive symptoms. Total
149 scores on the BDI-II questionnaire can range from 0 to 63. The classification of depression
150 severity is as follows: scores between 0 and 13 are classified as no depression, scores between
151 14 and 19 are classified as mild depression, scores between 20 and 28 are classified as moderate
152 depression, and scores between 29 and 63 are classified as severe depression (22). For this study,
153 the BDI-II questionnaire has been translated and standardized into the Czech language.

154

155 **Sociodemographic and lifestyle characteristics**

156 Supplementary variables were determined at baseline. The sociodemographic
157 characteristics included age, sex, height, and weight. Lifestyle factors included alcohol
158 consumption. The anthropometric characteristics of participants were measured using a digital
159 scale, (Seca 285, Hamburg, Germany). Standing height (cm) and weight (kg) were measured.
160 The body mass index body mass index (BMI; $\text{weight}/\text{height}^2$) was used to classify participants
161 as underweight ($<18.5 \text{ kg}/\text{m}^2$), normal weight ($18.5\text{--}24.9 \text{ kg}/\text{m}^2$), overweight ($25.0\text{--}29.9$
162 kg/m^2), and obese ($\geq 30 \text{ kg}/\text{m}^2$).

163 The lifestyle about participants' alcohol consumption habits were self-reported using
164 survey questionnaires. Alcohol consumption was classified as follows: never (never to 3 times
165 a month), moderate (1-4 times a week), and heavy (5-7 times a week).

166

167 **Statistical analysis**

168 A Mann-Whitney *U* test was used for continuous data, while a Chi-squared test of
169 independence (χ^2) was employed for categorical data in order to assess differences between the
170 researched groups in terms of baseline characteristics. An effect size test was also conducted
171 for both tests, specifically using Cramer's *V* (V , $df_{\min} = 1$) for the Chi-squared test and Eta-
172 Squared (h^2) for the Mann-Whitney *U* test. The effect size results were interpreted as small (V
173 $= 0.10$; $\eta^2 = 0.01$), medium ($V = 0.30$; $\eta^2 = 0.06$) or large ($V = 0.50$; $\eta^2 = 0.14$) effect (23). The
174 distribution of participants with and without depression, as well as the tertiles (T1 – T3) of
175 relative muscular strength (Nm/Kg), was calculated using Chi-square goodness of fit test,
176 assuming equal expected frequencies (24). The adjustment estimation for the random-effects
177 model utilized the log Odds Ratio (OR) for binary outcomes in a 2 by 2 table to quantify the
178 odds of participants with lower muscle strength having depression compared to participants
179 without depression. To determine if the effect size was consistent across and between the
180 investigated variables (movements), a test of homogeneity (Q statistic) was performed. The
181 significance level was set at $p = .05$. The analysis was conducted using IBM SPSS Statistics for
182 Windows version 29.0.0 software (IBM Corp. Armonk, NY, USA).

183 **Results**

184 A total of 909 participants were included in the study, with an average age of 29.02 ± 2.03
185 years and 48.73% of them being male. Table 1 provides additional details on the anthropometric
186 characteristics of the participants. Table 2 presents the characteristics of the participants and the

187 prevalence of depression. Individuals with depression were more likely to be female ($p = .031$)
 188 and have normal weight ($p = .045$) in comparison to individuals without depression.

189

190 **Table 1. Basic descriptive statistics of the study participants.**

Variable	Age (yrs)	Weight (kg)	Height (cm)	BMI (kg/m ²)
Total	29.02 (2.03)	74.65 (16.02)	174.94 (9.62)	24.27 (4.21)
Sex				
- Male	29.17 (2.01)	83.56 (14.48)	182.12 (6.72)	25.17 (4.02)
- Female	28.87 (2.04)	66.18 (12.41)	168.11 (6.48)	23.42 (4.21)

191 BMI, Body Mass Index.

192 **Table 2. Participants characteristics and depression prevalence.**

Variable	Depressed ($n=150/16.50\%$)	Not depressed ($n=759/83.50\%$)	Total ($n=909/100\%$)	<i>P</i>	ES
Weight, kg	75.26±17.44)	74.53±15.74	909	.816	<0.001
Height, cm	174.06±9.08	175.11±9.73	909	.243	0.001
Sex, <i>n</i> (%)					
- Male	61 (40.67)	382 (50.33)	443 (48.73)	.031	0.072
- Female	89 (59.33)	377 (49.67)	466 (51.27)		
BMI, <i>n</i> (%)					
- Underweight	9 (6.00)	24 (3.16)	33 (3.63)	.045	0.094
- Normal Weight	80 (53.33)	474 (62.45)	554 (60.95)		
- Overweight	42 (28.00)	202 (26.61)	244 (26.84)		
- Obese	19 (12.67)	59 (7.77)	78 (8.58)		
Alcohol intake, <i>n</i> (%)					
- Never	56 (37.33)	285 (37.55)	341 (37.51)	.988	0.005
- Moderate	83 (55.33)	421 (55.47)	504 (55.45)		
- Heavy	11 (7.33)	53 (6.98)	64 (7.04)		

193 *p*-value was calculated using Mann-Whitney U test for continuous data and Chi-squared test

194 of Independence (χ^2) for categorical data; ES χ^2 for continuous data and Cramer's V for

195 categorical data.

196

197 The relative isokinetic muscle strength of various muscle groups of the knee joint ($n=8$)

198 was separated into tertiles (T1 – T3) based on z-scores. T1 corresponded to low muscle strength

199 (z-score < 1), T2 corresponded to average muscle strength (z-score \pm 1), and T3 corresponded

200 to high muscle strength (z-score > 1). In order to focus on extreme outcomes (T1 and T3),

201 participants with average muscle strength (T2) were excluded from the study. The low muscular
 202 strength group consisted of 131 to 149 participants, while the high muscular strength group
 203 consisted of 127 to 152 participants, as shown in Table 3.

204

205 **Table 3. Participants relative muscle strength according to z-score.**

Variable	n	Relative muscular strength (Nm/kg)			p
		T1 Low (z< 1SD)	T2 Average (z±1SD)	T3 High (z>1SD)	
EXT_R	908	149 (16.59%)	622 (69.27%)	137 (14.14%)	<.001
EXT_L	909	131 (14.41%)	651 (71.62%)	127 (13.97%)	<.001
FLEX_L	909	148 (16.28%)	609 (67.00%)	152 (16.72%)	<.001
FLEX_R	908	141 (15.53%)	617 (67.95%)	150 (16.52%)	<.001
FLEX+EXT_L	909	132 (14.52%)	645 (70.96%)	132 (14.52%)	<.001
FLEX+EXT_R	908	135 (14.87%)	638 (70.26%)	135 (14.87%)	<.001
EXT_R+L	909	139 (15.29%)	637 (70.08%)	133 (14.63%)	<.001
FLEX_R+L	909	145 (15.95%)	616 (67.77%)	148 (16.28%)	<.001

206 EXT_R, muscle strength right knee extensors; FLEX_L, muscle strength left knee flexors;
 207 FLEX_R, muscle strength right knee flexors; EXT_L, muscle strength left knee extensors;
 208 FLEX+EXT_L, muscle strength thigh muscles left leg; FLEX+EXT_R, muscle strength thigh
 209 muscles right leg; EXT_R+L, muscle strength right and left extensors; FLEX_R+L, muscle
 210 strength right and left flexors; p-value was calculated using chi-square goodness of fit test with
 211 equal expected distribution (33.3%).

212 Table 4 presents the results observed in all participants using dichotomized outcomes
 213 for muscle strength (low vs. high) and depression (no depression vs. depression). An inverse
 214 association between the muscle strength of the knee joint and depression were found,
 215 demonstrating that individuals with low muscle strength of the knee joint having 3.15 times
 216 higher odds of having depression (95% CI = 2.74–3.62) compared to those with high muscle
 217 strength. Specifically, participants with low extensor strength had 4.63 (95% CI = 2.20–9.74)
 218 times higher odds, while those with low flexor strength had 2.68 (95% CI = 1.47–4.89) times
 219 higher odds of experiencing depression when compared to individuals with high muscle
 220 strength. Considering limb preference, the odds of experiencing depression in participants with
 221 low muscle strength were more pronounced in the extensors and flexors of the right limb (OR

222 = 3.64, 95% CI = 1.87–7.08) compared to the left limb (OR = 2.92, 95% CI = 1.51–5.66), when
 223 compared to individuals with high muscle strength.

224

225 **Table 4. Overview of effect size results from participants muscle groups and depression.**

Variable	OR	95% CI	<i>p</i>	Weight	Weight (%)
EXT_R	3.01	[1.55, 5.84]	.001	8.70	2.85
FLEX_L	2.76	[1.50, 5.08]	.001	10.28	3.37
FLEX_R	3.09	[1.63, 5.85]	<.001	9.44	3.09
EXT_L	3.30	[1.69, 6.45]	<.001	8.52	2.79
FLEX+EXT_L	2.92	[1.51, 5.66]	.001	8.82	2.89
FLEX+EXT_R	3.64	[1.87, 7.08]	<.001	8.68	2.84
EXT_R+L	4.63	[2.20, 9.74]	<.001	6.93	2.27
FLEX_R+L	2.68	[1.47, 4.89]	.001	10.59	3.47
Overall effect	3.15	[2.74, 3.62]	.001		

226 *p*-value was calculated using Odds ratio test (OR); CI, confidence interval.

227 Due to evidence of interactions between depression and sex, separate analyses were
 228 conducted for males and females. In brief, knee muscle strength was found to be inversely
 229 associated with depression in both genders, except for knee flexors in males. Males with low
 230 muscle strength have 2.51 (95% CI = 1.53–4.14) times higher odds of experiencing depression
 231 compared to males with high muscle strength. Females with low muscle strength had 3.46 (95%
 232 CI = 2.93–4.08) times higher odds of experiencing depression compared to females with high
 233 muscle strength, as shown in Table 5 and Figure 1.

234

235 **Table 5. Overview of effect size results from muscle strength and depression according**
 236 **to sex.**

Subgroup	Variable	OR	95% CI	<i>p</i>	Weight	Weight (%)
Male	EXT_R	4.16	[1.28, 13.47]	.018	2.80	0.9
	FLEX_L	1.63	[0.61, 4.37]	.333	3.94	1.30
	FLEX_R	0.89	[0.28, 2.84]	.846	2.87	0.90
	EXT_L	4.45	[1.52, 13.05]	.006	3.32	1.10
	FLEX+EXT_L	3.79	[1.29, 11.12]	.015	3.31	1.10
	FLEX+EXT_R	3.93	[1.19, 13.01]	.025	2.69	0.90
	EXT_R+L	3.21	[1.15, 8.99]	.026	3.63	1.20
	FLEX_R+L	1.44	[1.53, 3.91]	.476	3.84	1.30
Subgroup overall		2.51	[1.53, 4.14]	.001		
Female	EXT_R	3.06	[1.28, 7.32]	.012	5.05	1.70
	FLEX_L	3.05	[1.13, 8.23]	.028	3.9	1.30
	FLEX_R	2.85	[1.25, 6.50]	.013	5.67	1.90
	EXT_L	3.18	[1.29, 7.84]	.012	4.73	1.50
	FLEX+EXT_L	3.12	[1.22, 7.95]	.017	4.38	1.40
	FLEX+EXT_R	5.00	[1.98, 12.65]	<.001	4.47	1.50
	EXT_R+L	3.89	[1.53, 9.92]	.004	4.39	1.40
	FLEX_R+L	4.25	[1.61, 11.21]	.003	4.09	1.30
Subgroup overall		3.46	[2.93, 4.08]	.001		

237 *p*-value was calculated using Odds ratio test (OR); CI, confidence interval.

238

239 Figure 1. Overview of effect size results according to sex.

240 **Discussion**

241 The study aimed to investigate the association between isokinetic muscle strength of the
242 knee joint and depression. The results confirmed the hypothesis, indicating that young adults
243 with low muscle strength were at 3.15 times higher odds of experiencing depression compared
244 to those with high muscle strength. Additionally, the study found that individuals with a low
245 level of extensor strength had 4.63 times higher odds of experiencing depression, while those
246 with a low level of flexor strength had 2.68 times higher odds of depression compared to
247 individuals with a high level of muscle strength. Furthermore, the study revealed that the
248 isokinetic muscle strength of the knee joint was inversely associated with depressive symptoms
249 in both sexes, however, a higher prevalence of depression was found in females. Specifically,
250 females with low muscle strength had 3.46 times higher odds of experiencing depression
251 compared to females with high muscle strength. Similarly, males with low muscle strength had
252 2.51 times higher odds of depression compared to males with high knee muscle strength.

253 The findings of our study align with previous research that has reported a causal
254 relationship between depressive symptoms and low muscle strength in the lower limbs. For
255 example, the study by (13) that utilized the five-repetitions sit-to-stand test (FRSTST) to
256 examine the incidence of depression disorders during a seven-year follow-up in middle-aged
257 and older adults, identified a hazard ratio of 1.32 (95% CI = 1.08–1.62) for the lowest quartile
258 compared to the highest quartile of muscle strength ($p = 0.007$). In a recent meta-analysis, (25),
259 concluded that adults aged 44 to 74 years who demonstrated slow gait speed had a pooled OR
260 from 11 studies of 1.93 (95% CI = 1.54–2.42). Similarly, (15) revealed that senior participants
261 who performed significantly poorer in physical performance tests such as the 4-meter walking
262 speed test, FRSTST, isometric leg strength, handgrip strength, and 6-minute walk test exhibited
263 an elevated risk of developing depression over the 4-year follow-up period.

264 Besides the association between low muscle strength and risk of depression were similar
265 with the aforementioned articles, it is possible to noticed that the young adults in the present
266 study presented a higher odd (OR= 3.15) compared to studies with older adults and predictive
267 tests (OR= 1.32 – 1.93). It can be speculated that either the young adult population present a
268 higher odds of low muscle strength and risk of depression compared to older population, and
269 also that the indirect measures can underestimate the results compared to the direct measure of
270 low limb muscle strength. It is worth noting that previous studies often relied on predictive
271 methods to assess lower limb muscle strength, whereas our study utilized a gold-standard
272 method. Nonetheless, the use of predictive methods can increase the error by underestimating
273 or overestimating the actual result. This strengthens the validity of our findings and provides
274 more robust evidence for the association between depressive symptoms and lower limb muscle
275 strength.

276 Regarding the different lower limb muscle strengths assessed, our study presented a
277 stronger inverse association between muscle strength and depression in the extensor muscles
278 compared to the flexor muscles. These findings reported that participants with low extensor
279 muscle strength of the right and left limbs have 4.63 (95% CI = 2.20-9.74) higher odds of
280 developing depression compared to participants with high muscle strength. It can be explained
281 by the fact that knee extensor muscles are more involved in walking, and could be supported
282 by previous results that used walking tests and FRSTST which are widely recognized as indirect
283 tests for assessing lower limb muscle strength, particularly knee extensor muscles (26,27).

284 As expected, our study confirmed that young adult females exhibited a higher
285 prevalence of depression compared to males. These findings align with previous research
286 evidence, which also indicated a greater prevalence of depression among females than in males
287 (28), and also with the WHO report, which estimated the prevalence of depression in the

288 population to be higher among females (5.1%) than among males (3.6%) (10). The increased
289 prevalence of depression among females may be associated with hormonal changes.

290 Additionally, our study also revealed that participants with depression have a healthy
291 weight compared to those without depression, which corresponds with the findings of (29), who
292 also found that individuals with depression have lower BMI values. This association can be
293 attributed to the fact that participants with normal weight have had the highest representation
294 in our research group.

295 The physiological mechanisms related to higher level of muscle strength and anti-
296 depressant effects remain hypothetical, despite its robust clinical effect. Several physiological
297 theories have been proposed to clarify the anti-depressive effects of exercise affecting muscle
298 strength, but the serotonin theory may be of particular significance.

299 The relationship between strength training and increasing of serotonin level can be
300 explained by theory of (30), who suggested that strength training can increase the amount of
301 free fatty acids and thus increase the levels of free tryptophan (TRP) in the bloodstream,
302 influencing the availability and synthesis of serotonin (5-HT) in the Central Nervous System
303 (CNS). It has been highlighted that any increase in the peripheral supply of TRP to the brain
304 leads to an increased synthesis of 5-HT (31), thus the decreased peripheral 5-HT levels may
305 reflect an increased transport of TRP into the CNS that would ultimately result in increased
306 central 5-HT levels (32). Furthermore, in the CNS, 5-HT modulates a broad spectrum of
307 functions, including mood, cognition, anxiety, learning, memory, reward processing, and sleep
308 (33), which can be associated with antidepressant effect.

309 Consistent with previous research, we have demonstrated that higher levels of muscle
310 strength exert a beneficial effect on depression. Our study is the first to report the relationship
311 between depressive disorders and knee muscle strength by using the gold-standard method.

312 The limitations of the study must be mentioned. Firstly, the nature of this study does not
313 allow us to establish causal influences, highlighting the need for future well-designed
314 longitudinal studies to clarify causality. Secondly, it is important to acknowledge that data
315 collection for our study was conducted during the Covid-19 pandemic, which could have
316 potentially influenced participants' perception of depression and led to reduced strength due to
317 restrictions on physical activity. Additionally, our study did not focus on the influence of
318 lifestyle characteristics, such as marital status, education level, and multi-comorbidity, on
319 depression related to participants' age, as these characteristics may be incomplete. We also did
320 not report the smoking status variables due to the various possible mechanisms of nicotine
321 intake, such as cigarette smoking, e-cigarette use, vaping, waterpipe use, and smokeless tobacco
322 products, where the nicotine dosage can vary. The influence of various types of nicotine intake
323 on depression was reported elsewhere (34). Regarding the sample, it is important to note that
324 our study focused exclusively on young adult participants. As a result, caution should be
325 exercised when generalizing the results to the broader population.

326 Despite the mentioned limitations, we firmly believe that our study holds significant
327 implications for both research and clinical practice. Specifically, the increase in muscle strength
328 through regular physical activity can be utilized as an effective tool to prevent and treat
329 depressive disorders in the young adults' population. Furthermore, we highly recommend the
330 aerobic and anaerobic interventions activities for both the prevention and additional treatment
331 of depressive disorders. Further research involving different populations is warranted in future
332 studies to enhance the external validity of our findings.

333 **Conclusions**

334 The study demonstrated that strong knee muscles seems to be a key factor in preventing
335 depression, especially in Czech female young adults. To the best of our knowledge, this is the

336 first population-based study that investigates the associations between knee joint muscle
337 strength, assessed using the gold-standard method, and depressive symptoms in the young adult
338 population. The current findings demonstrate that participants with low knee muscle strength
339 have three times more chance to have depression compared to those with high muscle strength.
340 Regarding the muscle groups, we found almost twice stronger inverse association between
341 muscle strength and depression in the extensor muscles than in flexor muscles. Additionally,
342 we observed a higher association between low muscle strength and depression in females than
343 in males.

344 **Acknowledgments**

345 We thank all collaborating participants who invested their time and provided
346 information for this study.

347

348 **Data Availability Statement**

349

350 Data are available on reasonable request. All data relevant to the study are included in
351 the article. Anonymized data can be made available from the study management
352 (info@celspac.cz). Release of data is a subject of approval of the Ethical and Scientific boards.

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