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1 Association between Muscular Strength and Depressive Symptoms among
2 Chinese Nursing Freshmen—A Cross-Sectional Study

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22 Keywords: Depressive symptoms; Muscular strength; College freshman; Chinese; Handgrip strength

23 Abstract

24 Increased physical activity level is related to lower risk of depressive symptoms, and an inverse
25 association between muscular strength and risk of depressive symptoms among the elderly
26 population. However, the association among younger adults is unclear. The aim of this study was to
27 examine the association between muscle strength, using handgrip strength as a representative of
28 skeletal muscle strength, and the risk of depressive symptoms among Chinese female college
29 freshman. A cross-sectional study was conducted among 867 participants aged between 16-23 years.
30 Handgrip strength was measured with a handheld digital Smedley dynamometer, and depressive
31 symptoms were evaluated using the 20-item Zung self-rating depression scale (SDS) with 3 cut-off
32 points to indicate elevated depressive symptoms. We found that 10.7% of participants (17.2% or
33 29.2%) were classified as having moderate to severe depressive symptoms using 50 as the cut-off
34 point. After adjusting for these potential confounders, the adjusted odds ratios for moderate-to-severe
35 depressive symptoms across tertile of relative handgrip strength were 1.00 (reference) for tertile 1,

36 0.61 (95% CI: 0.35, 1.04) for tertile 2, and 0.53 (95% CI: 0.39, 0.94) for tertile 3 (P for trend: 0.024).
37 The significant associations remained when other cut-off points (SDS 48 or 45) were used.
38 Interactions between the handgrip strength and potential confounders for depressive symptoms in the
39 final models were insignificant. This study showed that handgrip strength is inversely and
40 independently related to the risk of depressive symptoms among Chinese female college freshman.
41 These results can help with the development of an effective intervention strategy against depression.
42 For future research, it is important to explore the causality of the effects of handgrip strength on the
43 depressive symptoms by intervention study.

44

45 1 Introduction

46 For college students, attending university for the first time is an important stage of life. The
47 unfamiliarity of university life requires students to accomplish academic tasks and negotiate a new
48 social world. Meanwhile, to facilitate their transition and adjustment to college life, many college
49 freshmen may have to face academic and life stresses in today's competitive world. In this context,
50 many college students experience psychological disturbances such as depression. Indeed, the
51 National College Health Assessment in the United States found that approximately 53% of freshmen
52 reported having experienced depression since beginning college (1). In Japan, 20%-30% of college
53 freshmen reported having major depression (2). Similarly, the prevalence of depression or depressive
54 symptoms among first-year university students in mainland China and Hong Kong was 24.8% and
55 43.9, respectively (3). Although the prevalence of depressive symptoms among college freshmen in
56 these studies differ from that of the general population (37.9% for depressive symptoms) (4), which
57 may be due to the use of different measurement tools, different methodologies, and different
58 appraisal standards, previous studies have also found a general increase in mental health problems in
59 college students (5). Furthermore, it is well known that depression contributes to the onset of cancer
60 (6), diabetes mellitus (7), coronary heart disease (7), stroke (8), and metabolic syndrome (9). At its worst,
61 it can lead to suicide (10). Thus, the identification of potentially modifiable risk factors associated
62 with the risk of depression is imperative to the development of an effective preventive strategy.

63 Although increasing levels of physical activity (PA) could protect against developing depression (11),
64 only a few studies have examined objective measurements of physical fitness in relation to
65 depression. Physical fitness (which includes both cardiorespiratory fitness and muscular strength) (12)
66 may be a more objective risk factor, because improved physical fitness represents adaptation to
67 regular PA (13). So far, an inverse association between cardiorespiratory fitness and risk of depression
68 have been well-established among young (14) and middle-aged adults (15:16). Similarly, previous
69 studies also reported an association between muscular strength and depression risk among the elderly
70 population (17-19). However, to our knowledge, there have been no reports yet on whether muscle
71 strength has a significant association with depression at younger ages. Elucidation of muscular
72 strength at younger ages may help facilitate earlier and more effective preventive interventions.

73 Because handgrip strength is a simple, accurate and quick measurement of muscle strength, it can be
74 a subrogation of general muscle strength (20). Moreover, handgrip strength is predictive of validity
75 for mortality in older populations (21). To investigate the association between relative handgrip
76 strength and the risk of depressive symptoms among the younger population, we designed a cross-
77 sectional study in Chinese female college freshman.

78

79 2 Materials and Methods

80 2.1 Design and samples

81 The Chongqing Nursing Vocational College Physical Fitness and Health study is a prospective
82 ongoing cohort study to assess the association between physical fitness and the health status of
83 college students in Chongqing, China. Chongqing is the largest municipality of approximately 30.75
84 million inhabitants, located in the Southwest China.

85 Ethics approval was obtained from the ethical committee of the College of Physical Education of
86 Southwest University (SWU20190101). A cross-sectional study was conducted to explore the
87 association between muscular strength and depressive symptoms among Chinese nursing freshmen.
88 In the period between October - December 2018 (baseline period), we recruited 1094 college
89 freshmen at Chongqing Nursing Vocational College, who each participated in the annual physical
90 fitness and completed a self-administered questionnaire. This provided information about
91 demographics, anthropometrics, lifestyle factors, and depressive status for data analysis. Written
92 informed consent was obtained from all the participants or their parents or legal guardians for
93 participants under the age of 16. We excluded participants who did not complete the handgrip
94 strength assessment (n=59), as well as participants with missing information on age, height and/or
95 body weight measurements, and PA (n=62). Because of gender differences in handgrip strength, we
96 found that the number of male participants (n=106) were too small to perform a multiple logistic
97 regression analysis and were therefore excluded. After the exclusions, the final sample of this study
98 included 867 female participants between the age range of 16~23 years (mean 18.7, SD 1.0).

99 2.2 Assessment of handgrip strength

100 Assessment of handgrip strength was obtained using a dynamometer (EH101; CAMRY, Guangdong,
101 China). All participants were told to adjust the dynamometer width for optimal hand comfort, and to
102 relax their arm in a standing and stationary position. Each participant made four attempts using each
103 hand with a brief interval between trials. The highest weight in kilograms of all handgrip strength
104 measurements was used as a representative value of muscle strength. Handgrip strength relative to
105 body weight (kg/kg) was calculated and examined as categorical variables in tertiles (low [0.32-
106 0.50], medium [0.51-0.58], and high [0.59-0.94]).

107 2.3 Assessment of depressive symptoms

108 The Zung self-rating depression scale (SDS) was used to examine depression severity (22). It
109 comprises of 20 items, and each item score ranges from 1 to 4, with a sum score between 20 to 80.
110 Higher scores represent a more severe depressive state. In order to increase the sensitivity of the
111 detection and distinguish the severity of depressive symptoms, scores higher than these cut-off points
112 (45, 48, and 50) reflect moderate or severe depressive symptoms (23;24). The reliability and validity
113 of the Chinese version of SDS have been described in previous studies (25). In the present study, the
114 Cronbach's α coefficient for the scale was 0.788, which indicates that the Chinese version of the SDS
115 in this study has a strong internal consistency.

116 2.4 Relevant covariates

117 The anthropometric variables (height and body weight) were measured using a standard protocol.
118 Body mass index (BMI) was calculated as weight (kg)/height² (m²). Demographic variables included:
119 age (continuous variable), only child (yes or no), race (Han nationality, Tujia nationality, Miao

120 nationality or other), father's educational level (senior high school or below, college or postgraduate),
121 mother's educational level (senior high school or below, college or postgraduate), and parent's
122 marital status (married, widowed or divorced). Lifestyle factors included: smoking status (never,
123 occasionally or regularly), drinking status (never, occasionally or regularly), sleep duration (6-8
124 hour/d or less), and sleep quality (good or not) were assessed via a self-administered questionnaire.
125 Levels of PA were assessed by the International Physical Activity Questionnaire (IPAQ) (short
126 version) (26). Total weekly PA was calculated by metabolic equivalents \times hour/week (26).

127 2.5 Data analysis

128 All continuous and categorical variables were presented as geometric least square mean (95%
129 confidence interval) or proportions, and non-normal continuous variables were log-transformed for
130 multivariate statistical analyses. For subject's characteristics, continuous variables were compared
131 using analysis of variance (ANOVA), and categorical variables were compared by using chi-square
132 tests.

133 Depressive symptoms were used as dependent variables and the tertiles of relative handgrip strength
134 was used as independent variables. Multiple logistic regression analysis was also used to examine the
135 relationship between tertiles of relative handgrip strength and depressive symptoms. Model 1 was a
136 crude univariate model, while model 2 was adjusted for the relevant covariates. Interactions between
137 handgrip strength levels and confounders of depressive symptoms were tested by the addition of
138 cross-product terms to the regression model. P-values <0.05 were considered statistically significant
139 for all two-sided tests. All tests were performed using the IBM SPSS Statistics 24.0 software (IBM
140 SPSS Inc., Chicago, IL, USA).

141

142 3 Results

143 3.1. Participants' characteristics according to tertiles of relative handgrip strength

144 The subject's characteristics according to the tertile of relative handgrip strength are presented in
145 Table 1. Compared to participants in the lowest tertile of relative handgrip strength, a lower
146 proportion of participants in the upper two tertiles were obese (≥ 30 kg/m²) or overweight (≥ 25 kg/m²
147 and <30 kg/m²) (P for all trends < 0.05). Excluding this, no significant difference was observed
148 across the tertile of relative handgrip strength.

149 3.2 Crude and adjusted associations of relative handgrip strength with depressive symptoms

150 We analyzed the crude and adjusted relationship between the tertile of relative handgrip strength and
151 total score for depressive symptoms. The total score for depressive symptoms differed significantly
152 among tertiles of relative handgrip strength after adjustment for potential confounders. The mean
153 (95% CIs) for the low, middle, and high groups were 40.9 (40.1-41.7), 40.2 (39.4-41.0), and 39.4
154 (38.6-40.2), respectively (P for trend: 0.011) (Figure 1).

155 3.3 Adjusted odds ratios (OR) (95% confidence interval) of associations of relative handgrip strength 156 with depressive symptoms

157 We also found that 10.7% (17.2% or 29.2%) of freshmen were classified as having moderate to
158 severe depressive symptoms using 50 (48 or 45) as the cut-off point. Figure 2-4 shows the crude and

159 adjusted significant relationship between the tertile of relative handgrip strength, and the risk of
160 moderate-to-severe depressive symptoms. Using the 50 cut-off point in the final model, the adjusted
161 ORs for moderate-to-severe depressive symptoms across tertiles of relative handgrip strength was
162 1.00 (reference) for tertile 1, 0.61 (95% CI: 0.35, 1.04) for tertile 2, and 0.53 (95% CI: 0.39, 0.94) for
163 tertile 3 (P for trend: 0.024). Similar relationships were observed when using 48 or 45 as the cut-off
164 point (Figure 4). Tests conducted to identify interactions between the tertile of relative handgrip
165 strength and these potential confounders for depressive symptoms in the final models were not found
166 to be significant.

167

168 4 Discussion

169 A cross-sectional study was conducted among Chinese female college freshman to assess the
170 relationship between handgrip strength and depressive symptoms. Multivariate logistic analyses have
171 shown that higher handgrip strength level was significantly and independently associated with a
172 lower risk of depressive symptoms after adjustment for potential confounders.

173 Currently, the relationship between higher handgrip strength (indicator of overall muscle strength),
174 and lower risk of depressive symptoms is already widely accepted (17-19). However, this relationship
175 had not been previously confirmed among younger adults. Our study expands on previous findings
176 demonstrating that increased handgrip strength could be independently related to lows risk of
177 depressive symptoms among college freshmen.

178 Although depressive symptoms are chronic and debilitating mood disorders, the exact etiology for
179 depressive symptoms is unknown. We considered several plausible mechanisms. First, PA levels
180 could mediate the inverse association between handgrip strength and depressive symptoms by
181 lowering hypothalamic-pituitary-adrenocortical axis (HPA) reactivity to psychosocial stress, thus
182 relieving depressive symptoms (27). In addition, physical activity may also reduce urine cortisol and
183 epinephrine secretions (an indicator of sympathetic nerve activity in for psychophysical stress and
184 depression) (28). In addition to physiological state, physical activity is also beneficial to one's
185 psychological status. Regularly participating in physical activity can usually distract individuals from
186 a negative or depressive mood to help cope with depression (29). Furthermore, perceived self-efficacy
187 of physical activity may also play an important role in depressive moods. A randomized controlled
188 trial-based meta-analysis demonstrated that physical activity is an effective method for improving
189 perceived self-efficacy (30). The theory of self-efficacy highlights the importance of self-regulation
190 wherein higher level of perceived self-efficacy makes an individual more likely to initiate and
191 maintain the behavior (31). In summary, regular physical activity could have a positive impact on
192 depressive symptoms via physiological and psychological mechanisms. Although the significant
193 relationship between handgrip strength and depressive symptoms remained after adjustment for PA
194 level analyzed by the short version of IPAQ, other confounding PA types could still be associated
195 with handgrip strength and depressive symptoms (26;32).

196 Second, Agudelo and colleagues found that depressive symptoms are related to elevated kynurenine
197 levels, a tryptophan metabolite generated under stress (33). Activation of the skeletal muscle increases
198 peroxisome proliferator-activated receptor-gamma co-activator-1 alpha 1 overexpression, promoting
199 kynurenine aminotransferase expression, which likely prevents kynurenine from crossing the blood
200 brain barrier to disrupt neural plasticity (34). Thus, improvement or maintenance of muscle strength
201 may have a preventive effect against the risk of depressive symptoms.

202 Third, inflammatory biomarkers may also mediate the relationship between handgrip strength and
203 risk of depressive symptoms. An adolescent-based study demonstrated that inflammatory proteins
204 (C-reactive protein and IL-6) are inversely related to muscle strength (35). Inflammatory cytokines
205 inhibit the production of insulin-like growth factor-1 by the liver, which is an important anabolic
206 stimulus for muscle (36). However, a positive relationship between inflammatory cytokine levels and
207 depressive symptoms has also been shown (37). Studies have shown that a) activation of the
208 inflammatory cytokine in depression can induce HPA-hyperactivity; b) cell-mediated immune
209 activation may also contribute to disturbances of 5-hydroxytryptamine. Unfortunately, we were
210 unable to provide evidence for kynurenine levels and inflammatory proteins. Future studies need to
211 confirm whether kynurenine levels and inflammatory proteins mediate this relationship between
212 handgrip strength and risk of depressive symptoms.

213 Furthermore, in this population-based study, we adjusted for a considerable number of confounding
214 factors, which is especially important considering the complex etiology of depressive symptoms.
215 Firstly, it is well known that the incidence of depressive symptoms and decline in skeletal muscle
216 strength is increasing among Chinese college students (38;39). However, the association between
217 handgrip strength and depressive symptoms remained, even after adjusting for age. It was reported
218 that there was no significant association of depressive symptom with race (40), father's educational
219 level (41), mother's educational level (41), parent's marital status (41), and being the only child (42).
220 However, the adjustment of these socio-demographic variables did not have an effect on the
221 significant association between handgrip strength and depressive symptoms. Second, greater muscle
222 strength represents adaptation to regular physical activity, and physical activity may predict onset of
223 depressive symptoms (11). Therefore, physical activity may play an intermediate role in the
224 association between handgrip strength and depressive symptoms. However, additional adjustments
225 for physical activity in our analysis did not alter our findings. Finally, adjusting the effect of weight
226 (43), smoking (44), drinking (45) sleep duration (46), and sleep quality (47) on muscle strength did not
227 change the significant association between handgrip strength and depressive symptoms. This
228 suggests that handgrip strength is independently associated with depressive symptoms.

229 4.1 Implications

230 Previous studies investigating the association between muscle strength and the risk of depressive
231 symptoms are widely based on epidemiologic studies, and the mechanism underlying this association
232 is uncertain. The primary purpose of these studies were to provide specific exercise recommendations
233 to prevent the development of depressive symptoms for improving public health. The current study
234 further strengthens the evidence that greater muscle strength could be associated with a lower risk of
235 depressive symptoms among the younger population, e.g., college students. Since each physical
236 fitness component represents adaptation to regular physical activity, further prospective or
237 intervention studies should identify whether each physical fitness component has a positive influence
238 on depressive symptoms. These studies will provide insight regarding exercise recommendations that
239 can be used by physicians and patients with depression, as well as provide information about the kind
240 of sport activities that could help lower the risk of recurrent depression. The present study suggests
241 that greater muscle strength is also associated with lower risk of depressive symptoms among
242 younger population.

243 4.2 Limitations

244 There are several limitations to our study. Firstly, since our study design was a population-based
245 cross-sectional study, the causation between handgrip strength and depressive symptoms could be not

246 established. Secondly, although three cut-off points (SDS score: 45, 48 and 50) were used to define
247 having moderate-to-severe depressive symptoms, we were unable to conduct a clinical diagnosis to
248 determine the exact morbidity of depression. Thirdly, in the current study, the participants were all
249 female freshmen. A meta-analysis including 39 studies and 32,694 Chinese college students showed
250 no gender difference in prevalence of depressive symptoms (38). In addition, muscular strength is
251 strongly associated with cardiorespiratory fitness (48), and there was an inverse association between
252 cardiorespiratory fitness level and the risk of depressive symptoms (14). Inverse association similar to
253 that in the current study seems validated. Nevertheless, further studies with a larger sample size of
254 male college freshmen is necessary to confirm an association between muscle strength and the risk of
255 depressive symptoms. Fourth, a longitudinal studies-based review showed that baseline depression
256 may be a significant risk factor for the development of sedentary lifestyle or decreased level of
257 physical activity (49). Thus, both bidirectional associations between muscle strength and depressive
258 symptoms may exist. Further studies should take the causality and mechanism between the two into
259 consideration. Finally, the results may not be representative of the Chinese general college freshman;
260 therefore, further investigations with a larger sample size are needed to confirm our findings.

261

262 5 Conclusions

263 Our cross-sectional study assessed the relationship between handgrip strength and depressive
264 symptoms in Chinese female college freshman. Increased physical activity level is an important
265 factors to prevent the development of depressive symptoms, and measuring handgrip strength can be
266 an indicator of muscle strength adaptation to regular physical activity. We demonstrated that an
267 increased handgrip strength was significantly and independently related to lower risk of depressive
268 symptoms. This can help with the development of an effective intervention strategy against
269 depression. In future research, it is necessary to explore the causality between the effects of handgrip
270 strength and depressive symptoms using intervention studies.

271

272 6 Conflict of Interest

273 All the authors have no conflicts of interest exists to disclose.

274

275 7 Author Contributions

276 Conceived and designed the experiments: ZR LP CC. Performed the experiments: JC YL PC BL ZH
277 HY DS. Analyzed the data: LG JC CC. Contributed reagents/materials/analysis tools: PC ZR. Wrote
278 the paper: LG JC. Data collection: JC YL PC BL ZH HY DS.

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281

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285

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290

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292

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Figures

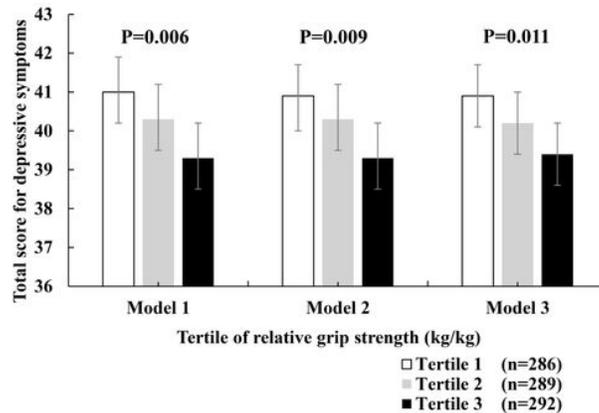


Figure 1. Crude and adjusted associations of relative handgrip strength with depressive symptoms among Chinese female college students. Model 1 are a crude univariate model; Model 2 adjusted for age (continuous variable) and BMI ($\geq 30\text{kg/m}^2$, $\geq 25\text{kg/m}^2$ and $<30\text{kg/m}^2$, or $<25\text{kg/m}^2$); Model 3 additionally adjusted for race (han nationality, tujia nationality, miao nationality and other nationality), only one child (yes or no), father education (senior high school or less, college and postgraduate), mother education (senior high school or less, college and postgraduate), smoking status (never smoker, former smoker and current smoker), drinking status (never drinker, former drinker and current drinker), physical activity level (low, middle, and high), sleep quality (good or not), sleep duration (6-8hour or not) and parent's marital status (married, widowed and divorced). Data are shown as means (total score for depressive symptoms) and 95% confidence intervals.

Figure 1

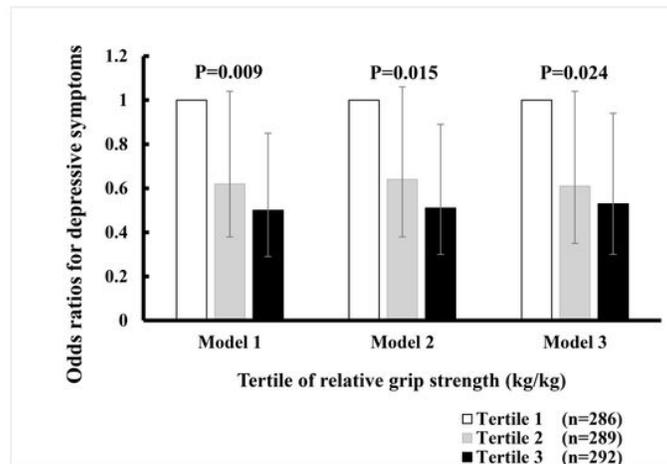


Figure 2. Adjusted odds ratios (95% confidence interval) of associations of relative handgrip strength with depressive symptoms (SDS ≥ 50) among Chinese female college students. Model 1 are a crude univariate model; Model 2 adjusted for age (continuous variable) and BMI ($\geq 30\text{kg/m}^2$, $\geq 25\text{kg/m}^2$ and $<30\text{kg/m}^2$, or $<25\text{kg/m}^2$); Model 3 additionally adjusted for race (han nationality, tujia nationality, miao nationality and other nationality), only one child (yes or no), father education (senior high school or less, college and postgraduate), mother education (senior high school or less, college and postgraduate), smoking status (never smoker, former smoker and current smoker), drinking status (never drinker, former drinker and current drinker), physical activity level (low, middle, and high), sleep quality (good or not), sleep duration (6-8hour or not) and parent's marital status (married, widowed and divorced)

Figure 2

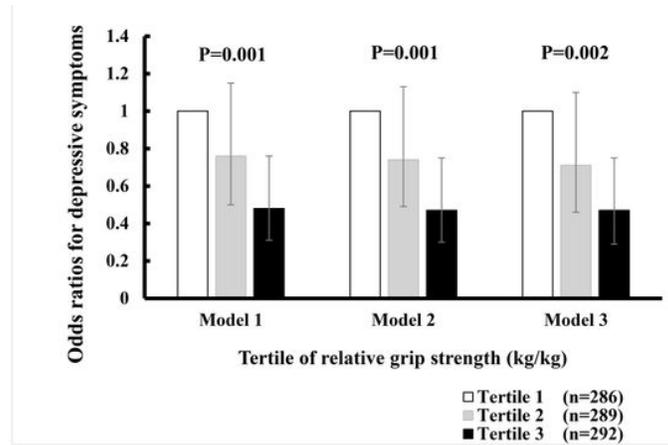


Figure 3. Adjusted odds ratios (95% confidence interval) of associations of relative handgrip strength with depressive symptoms (SDS ≥ 48) among Chinese female college students. Model 1 are a crude univariate model; Model 2 adjusted for age (continuous variable) and BMI ($\geq 30\text{kg/m}^2$, $\geq 25\text{kg/m}^2$ and $<30\text{kg/m}^2$, or $<25\text{ kg/m}^2$); Model 3 additionally adjusted for race (han nationality, tujia nationality, miao nationality and other nationality), only one child (yes or no), father education (senior high school or less, college and postgraduate), mother education (senior high school or less, college and postgraduate), smoking status (never smoker, former smoker and current smoker), drinking status (never drinker, former drinker and current drinker), physical activity level (low, middle, and high), sleep quality (good or not), sleep duration (6-8hour or not) and parent's marital status (married, widowed and divorced)

Figure 3

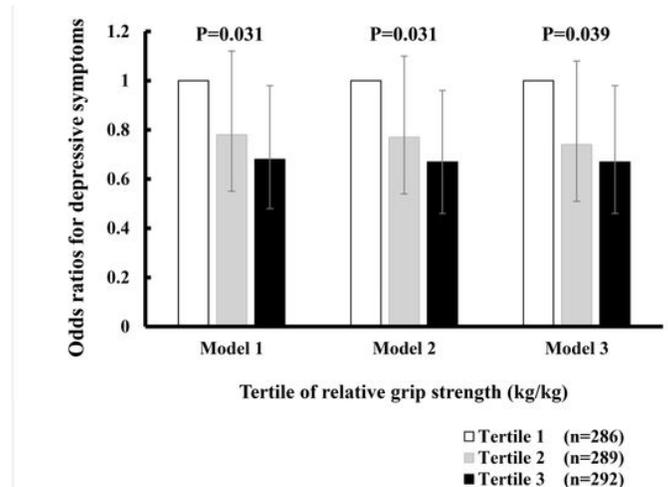


Figure 4. Adjusted odds ratios (95% confidence interval) of associations of relative handgrip strength with depressive symptoms (SDS ≥ 45) among Chinese female college students. Model 1 are a crude univariate model; Model 2 adjusted for age (continuous variable) and BMI ($\geq 30\text{kg/m}^2$, $\geq 25\text{kg/m}^2$ and $<30\text{kg/m}^2$, or $<25\text{ kg/m}^2$); Model 3 additionally adjusted for race (han nationality, tujia nationality, miao nationality and other nationality), only one child (yes or no), father education (senior high school or less, college and postgraduate), mother education (senior high school or less, college and postgraduate), smoking status (never smoker, former smoker and current smoker), drinking status (never drinker, former drinker and current drinker), physical activity level (low, middle, and high), sleep quality (good or not), sleep duration (6-8hour or not) and parent's marital status (married, widowed and divorced)

Figure 4