Handgrip Strength Deviation of Weakness and Asymmetry on the Risk of Depression among Middle Aged and Older Adults

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Abstract: This study aims to explore the interaction between all characteristics of handgrip (HGS) decline and gender on the risk of depression. Use Wave 2 and Wave 3 of the National Health and Retirement Longitudinal Study (CHARLS) for a two-year follow-up. 4,002 middle elderly individuals aged 45 and above, were selected from CHARLS, spanning from 2013 (Wave 2) to 2015 (Wave 3). After two years follow up, the HGS of 49.6% participants exhibited variations. HGS deviation of weakness and asymmetry is highly correlated with depression risk, and there is a trend of escalating risk for depression correlating with diminished HGS, with women exhibiting a more pronounced trend compared to men (Log rank test: Chi square = 82.502, p < 0.01). The combined effects of weakness and asymmetryis can be utilized to assess how varying levels of HGS influence depression differently based on gender factors.

Keywords: HGS Deviation; Weak; Asymmetry; Risk of Depression

1. Introduction

Handgrip strength (HGS), often measured using a dynamometer, is a clinically significant indicator of overall physical health and functionality [1-2]. Research has shown that lower HGS is associated with various health conditions, including cardiovascular disease, diabetes, and chronic pain [3-5]. In addition to these physical health outcomes, HGS has also been linked to mental health conditions such as depression [3,5]. Depression is a common mental health disorder characterized by persistent feelings of sadness, loss of interest or pleasure in activities, and a range of other symptoms [3]. While the exact cause of depression is complex and multifactorial, it is well-documented that physical health plays a significant role in its development and severity [3]. Several studies have investigated the interaction between HGS and depression. These studies have found that individuals with lower HGS are more likely to experience symptoms of depression [3]. This association is thought to be due to several factors: Physical Activity Levels: Lower HGS may indicate poorer physical functioning, which can limit an individual's ability to engage in regular physical activity. Physical activity is known to improve mood and reduce symptoms of depression [6]. Therefore, the lack of physical activity associated with lower HGS may contribute to the development or worsening of depression [7]. Chronic Disease Risk: Lower HGS is often a marker of increased risk for chronic diseases such as cardiovascular disease and diabetes [8]. These conditions are known to be associated with depression, further reinforcing the link between HGS and mental health Inflammation. Lower HGS has been linked to increased levels of inflammation in the body and it is thought to play a role in the development of depression, as it can affect brain function and neurotransmitter levels [9]. The neurodegenerative disorders is a major problem in the body that plays a role in regulating stress responses and inflammation. Lower HGS has been associated with impaired vagus nerve function, which may contribute to the development of depression [10]. Despite these findings, it is important to note that the interaction between HGS and depression is complex and not necessarily causal. Other factors such as age, sex, socioeconomic status, and genetics may also influence both HGS and depression risk. While there is evidence to suggest that lower HGS is associated with an increased risk of depression, additional research is needed to fully understand the mechanisms underlying this interaction. Nonetheless,

maintaining good physical health through regular exercise and healthy lifestyle choices may help reduce the risk of both physical and mental health conditions.

The interaction between gender and depression is a complex and multifaceted topic that has been the subject of extensive research. Gender differences in depression can be observed in various aspects, including prevalence rates, symptom expression, and treatment response. Prevalence rates of depression vary significantly between men and women. Studies have shown that women are more likely to experience depression compared to men. This disparity may be attributed to biological, psychological, and social factors. Biologically, hormonal changes during puberty, menstruation, pregnancy, and menopause can affect mood and increase the risk of depression in women. Psychologically, women may be more likely to experience stressors such as societal pressures, gender roles, and interpersonal interactions that contribute to depression. Socially, women may face unique challenges such as sexual abuse, domestic violence, and discrimination, which can also increase the risk of depression. Symptom expression of depression also varies between men and women. Women are more likely to report symptoms such as sadness, anxiety, and guilt, while men are more likely to exhibit symptoms such as irritability, anger, and aggression. These differences in symptom expression can lead to misdiagnosis and inadequate treatment for men who may not receive the same level of attention and care as women. Treatment response for depression also varies between men and women. Antidepressants are commonly prescribed to treat depression, but studies have shown that women may be more sensitive to the side effects of these medications than men. Additionally, women may be more likely to experience relapse or recurrence of depression after treatment compared to men. These differences in treatment response highlight the need for personalized approaches to treating depression that take into account gender-specific factors. Gender differences in depression are evident in prevalence rates, symptom expression, and treatment response. Understanding these differences is crucial for developing effective interventions that address the specific needs of men and women who experience depression. Researchers continue to explore the underlying mechanisms that contribute to these differences and work towards developing more effective treatments that can improve the quality of life for individuals affected by depression.

Numerous studies have already proven that HGS is associated with various adverse health outcomes. The strong correlation between HGS and the risk of depression has also been widely validated. Additionally, it has been verified that women are at a high risk of depression. However, the classification of HGS as an independent variable in previous studies is not yet comprehensive enough, which leads to the loss of information about HGS. Moreover, so far, previous research still lacks studies on the impact of the interaction between HGS and gender on depression. This study, operating under the assumption that both HGS influences depression and gender differences play a role in its manifestation, seeks to ascertain whether the interplay between HGS and gender exerts an effect on depression. A longitudinal design is put to use by a choice of a two-year follow-up period.

2. Methods

2.1 Study Population

This study involved 4,002 middle elderly individuals aged 45 and above, who were selected from the China Health and Retirement Longitudinal Study (CHARLS) data survey, spanning from 2013 (Wave 2) to 2015 (Wave 3). The CHARLS survey has been granted approval by the Biomedical Ethics Committee of Peking University for each cycle. The fieldwork plan for this phase of the family questionnaire survey has been approved and is endorsed with the approval number: IRB00001052-11015. During the field survey, every individual who agreed to participate in the study was required to sign two copies of the informed consent form. One copy was retained by the participant, while the other was kept on file at the CHARLS office and archived as a PDF scan. This research was conducted in adherence to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

2.2 Assessing Depressive Symptoms

In Wave 3, depressive symptoms were assessed using the CES-D short form, a widely utilized self-report tool for evaluating depressive symptoms in population-based research and

various application contexts. The CES-D short form comprises 10 items: I. Things bothered me; II. I had trouble keeping my mind on what I was doing; III. I felt depressed; IV. I felt that everything I did was an effort; V. I felt hopeful about the future; VI. I was afraid; VII. My sleep was restless; VIII. I was happy; IX. I felt lonely; X. I could not get going. Depressive symptoms over the past week were measured on a scale from 1 (rarely or none of the time [less than 1 day]) to 4 (most or all of the time [5-7 days]). Before calculating the total scores, it was necessary to reverse score items 5 and 8. The total score of the CES-D ranges from 0 to 30, with higher scores indicating a greater number of depressive symptoms. The CES-D short form exhibits excellent psychometric properties within the elderly population in China. A total score of 12 or above is utilized as a threshold to identify the exacerbation of depressive symptoms.

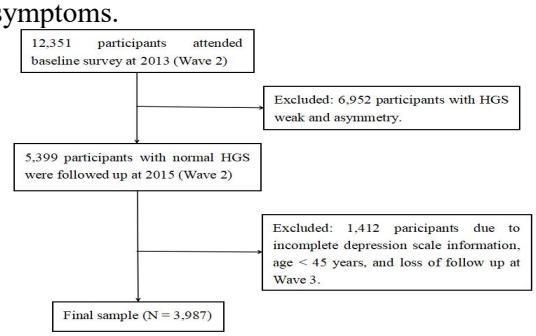

Figure 1. Flow Chart of Participants Selection.

2.3 HGS assessment

HGS was measured using a hydraulic hand dynamometer following standardized procedures at baseline. Participants were requested to squeeze as hard as possible with their hands. The mean of two maximal strength attempts on each hand, measured in absolute units (kilograms), was applied in our study. To examine the joint effect of hand HGS weakness and asymmetry, abnormal HGS was classified into categories based on the degree of hand HGS decrease and the hand HGS asymmetry (Table 1.). HGS weakness was defined as the HGS of either hand being lower than 28kg for males or 18kg for females. HGS asymmetry was defined as the ratio of HGS_{max} (right or left) to HGS_{mix} (left or right) being less than 10%.

2.4 Covariates

The data on socio-demographic status and health-related factors were collected, encompassing age, gender, residence, and marital status. Marital status was classified into two categories: Group 1 comprised of "Married and living with spouse" and "Married but temporarily not living with spouse due to work or other reasons", while Group 2 included other marital statuses ("Separated, not living together as spouses", "Divorced", "Widowed", and "Never married"). Residence was further categorized into three groups: Group 1 denoted "Downtown or town center", Group 2 referred to "Suburban/rural area or town area", and Group 3 included "Village" or "Special area". Received Amount of Income: by Month (0-1000RMB) was further categorized into two groups: Group 1 = 0-1000 RMB. Variables of health status and functionality included Purpose for physical activity, smoking, drinking, nighttime sleep duration, disabilities, non-communicable chronic diseases, and social activity participation.

2.5 Statistic Analysis

Use Stata 18 and SPSS 25 for overall data statistics. Record data using mean ± standard deviation (SD) and express frequencies and percentages. For data comparison, employ one-way ANOVA and chi-square analysis. Utilize the Kaplan-Meier method in survival analysis to analyze the development of data trends. The interaction between HGS and gender on depression was analyzed using a binary logistic regression model. All missing data were considered invalid data in the follow-up. The robustness test of this study is completed by the independent variable and dependent variable interchange detection.

3. Results

This study first selected 12,351 participants from the CHARLS database (2013, Wave 2). Participants with weak grip strength and asymmetry were then excluded, leaving 5,399 participants with normal grip strength levels (2013, Wave 3). On this basis, 1,412 subjects were further excluded due to lacking depression scale information, being under 45 years old, or being lost to follow-up. Finally, 3,987 subjects were determined to meet the requirements of this study (Figure 1).

The study included a total of 3,987 individuals aged 45 and above. Following a two-year period of observation, the HGS of 1,977 (49.6%) participants exhibited variations. HGS weakness was systematically categorized into three groups:

the bilateral non-weak group ((1): n = 3,263, 81.8%), the unilateral weak group ((2): n = 369, 9.3%), and the bilateral weak group ((3): n = 355, 8.9%). Subsequently, HGS deviation was further subgrouped based on the HGS weakness classification with symmetry (I (2010,61.6 %), III (45,12.2 %),V (188,53.0 %)) and asymmetry (II (1253, 38.4 %), IV (324, 87.8 %),VI (167, 47.0 %)) (Table 1.).

One-way ANOVA reveals a significant disparity in depression scores among the normal HGS group and those with unilateral and bilateral weak HGS (Table 1). Furthermore, subsequent subgroup analysis also indicates notable differences.

The Kaplan-Meier survival analysis reveals (refer to Figures 2 and 3) a trend of escalating risk for depression correlating with diminished HGS, with women exhibiting a more pronounced trend compared to men (Log rank test: Chi square = 82.502, $p < 0.01$). Comparable outcomes were noted in the subgroup analysis focusing on asymmetrical HGS (Log rank test: Chi square = 63.605, $p < 0.01$).

Table 1. Characteristics of participants by HGS Stepped stratification (N = 3,987, %)

Variables	(1): No weak on Bilateral (3,263, 81.8)		(2): Weak on Unilateral (369, 9.3)		(3) Weak on Bilateral (355, 8.9)		p
	I: Symmetric (2010, 61.6)	II: Asymmetric (1253, 38.4)	III: Symmetric (45, 12.2)	IV: Asymmetric (324, 87.8)	V: Symmetric (188, 53.0)	VI: Asymmetric (167, 47)	
Age	59.26±8.06		64.82±8.40*		66.43±10.24*		--
	59.32±8.08	59.16±8.03	65.33±7.34****	64.75±8.54****	66.45±9.93****	66.40±10.62****	--
Gender (1)	1593 (48.8)		193(52.3)		172 (48.5)		0.43
	1405 (52.0)	548 (43.7)	30 (66.7)	163 (50.3)	97 (51.6)	75 (44.9)	0.00
Residence (urban)	386 (11.8)		32 (8.7)		21(5.9)		0.00
	240(11.9)	146 (11.7)	3 (6.7)	29 (9.0)	12 (6.4)	9 (5.4)	0.05
Matrial (no)	298 (9.1)		58 (15.7)		72 (20.3)		0.00
	180 (9.0)	118 (9.4)	5 (11.1)	53 (16.4)	39 (20.7)	33 (19.9)	
Self health	194 (6.0)		12 (3.3)		9 (2.5)		0.00
	120 (6.0)	74 (5.9)	0 (0)	12 (3.7)	3 (1.6)	6 (3.6)	0.03
Health childhood	1323 (40.6)		119 (32.3)		142 (40.1)		0.08
	835 (41.6)	488 (39.0)	16 (35.6)	103 (31.9)	70 (37.2)	72 (43.4)	0.00
Smoking (yes)	73 (2.2)		4 (1.1)		8 (2.3)		0.34
	38 (1.9)	35 (2.8)	0 (0)	4 (1.1)	5 (2.7)	3 (1.8)	0.33
Drinking (yes)	1195 (36.6)		128 (34.7)		106 (29.9)		0.04
	742 (36.9)	453 (36.2)	18 (40)	110 (34.0)	58 (28.2)	58 (31,7)	0.16
Social interaction (yes)	1247 (38.3)		113 (30.7)		108 (30.5)		0.00
	754 (37.5)	493 (39.4)	9 (20)	104 (32.2)	59 (31.4)	49 (29.5)	0.00
Sleeping (1)	408 (12.5)		63 (17.1)		61 (17.2)		0.00
	251 (12.5)	157 (12.5)	6 (13.3)	57 (17.6)	31 (16.5)	30 (18.0)	0.00
BMI	3263(24.14±3.76)		369(23.61±4.06)**		355(22.8±4.01)**		--
	2010(24.05±3.60)	1253(24.30±4.00)	45(22.97±3.45)**	324(23.12±4.12)****	188(22.91±4.11)****	167(22.83±3.90)****	--
Purpose for PA (1)	536 (16.4)		49 (13.3)		65 (18.3)		0.34
	324 (16.1)	212 (16.9)	9 (20)	40 (12.3)	34 (18.1)	31 (18.6)	0.43
PEF	319.53±119.51		262.58±114.71**		243.37±120.87****		--
	323.12±118.80	314.82±120.53	237.33±115.43****	266.09±114.34****	251.40±109.79****	234.33±131.99****	--
HGS_{max}	33.24±8.41		25.78±5.93**		19.17±5.82****		--
	32.93±8.40	33.74±8.40*	25.11±5.04**	25.87±6.04**	19.50±5.78**	18.80±5.88**	--
DS	7.30±5.88		9.06±6.30*		9.60±6.94*		--
	7.18±5.78	7.50±6.04	8.98±5.94*	9.07±6.62**	10.00±7.73**	9.15±5.93**	--
CCD (yes)	1214 (37.2)		179 (48.5)		186 (52.4)		0.00
	738 (36.7)	476(38.0)	24 (53.3)	155 (47.8)	102 (54.3)	84 (50.3)	0.00
Pain (yes)	818 (25.1)		137 (37.2)		131 (37.0)		0.00
	489 (24.4)	329 (26.3)	13 (28.9)	124 (38.4)	69 (36.7)	62 (37.3）	0.00
Income<1000	1837 (56.3)		238 (64.5)		256(72.1)		0.00
	1126(56.0)	771(56.7)	26 (57.8)	212 (65.4)	126 (67.0)	130 (77.8)	0.00

*p<0.05, **p<0.01: Significantly different from (1); *p<0.05,**p<0.01: Significantly different from (2).Abbreviation: PA, physical acticvity; PEF, peak expiratory flow; BMI, body mass index; DS, depressive symptoms; HGS, handHGS; CCD, comorbid chronic diseases.

As can be seen from Figure 3 this study formed a clear gradient and differentiation for the division of grip weakness and asymmetry, forming a gradual deterioration trend, and this

trend was highly correlated with the probability of depression trend.

Based on the known significant impact of HGS deviation and gender factors on depression, the interaction effects of HGS deviation and gender on depression are explored (Table 2.). The multiplicative interactions in Model 1 are as follows: Gender × HGS deviation of weak, OR = 1.24 (95% CI: 1.16-1.33), $p < 0.01$; Gender × HGS deviation, OR = 1.11 (95% CI: 1.07-1.14), $p < 0.01$. The multiplicative interactions in Model 2 are: Gender × HGS deviation of weak, OR = 1.51 (95% CI: 1.37-1.68), $p < 0.01$; Gender × HGS deviation, OR = 1.24 (95% CI: 1.17-1.32), $p < 0.01$. The addictive interaction in modle 1 are as follows: Gender + HGS deviation of weak, OR = 1.48 (95% CI: 1.33-1.66), $p < 0.01$; Gender + HGS deviation, OR = 1.20 (95% CI: 1.14-1.26), $p < 0.01$. The addictive interaction in modle 2 are as follows: Gender + HGS deviation of weak, OR = 2.06 (95% CI: 1.77-2.40), $p < 0.01$; Gender + HGS deviation, OR = 2.05 (95% CI: 1.76-2.39), $p < 0.01$.

4. Discussion

This study investigated the interaction between HGS weakness, deviation, and gender in relation to depression among middle-aged and elderly individuals, employing data from the CHARLS public health platform, via cross-sectional surveys and longitudinal follow-ups. This research, which confirmed that both gender and HGS individually influence depression, examined the impact of the interplay between HGS and gender on depressive symptoms. There have been many systematic studies on the relationship between grip strength and depression, but a common flaw in these studies is the lack of rigor in grouping grip strength levels, which can obscure many research factors and is not conducive to verifying the authenticity of events.

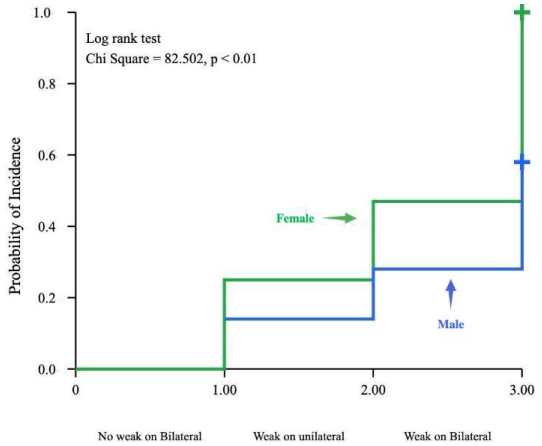

Figure 2. The Probability Trends of Incidence of Depressive Symptoms at Different Levels of HGS Weakness between Male and Female

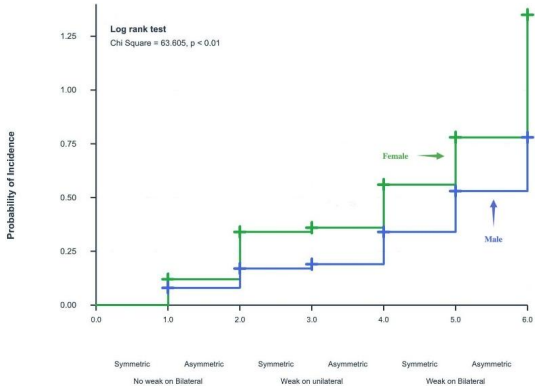

Figure 3. The Probability Trends of Incidence of Depressive Symptoms at Different Levels of HGS deviation between Male and Female

Table 2. Interaction Analysis between HGS and Gender on the Risk of Depression

Variables	Model 1			Model 2		
	OR	95.0 % CI for OR		OR	95.0 % CI for OR	
		LL	UL		LL	UL
Multiplicative interaction						
Gender × HGS weakness	1.24**	1.16	1.33	1.51**	1.37	1.68
Gender × HGS deviation	1.11**	1.07	1.14	1.24**	1.17	1.32
Addictive interaction						
Gender + HGS weakness	1.48**	1.33	1.66	2.06**	1.77	2.40
Gender + HGS deviation	1.20**	1.14	1.26	2.05**	1.76	2.39

HGS deviation of weak: No weak on bilateral > Weak on unilateral > Weak on bilateral.
HGS deviation of weak and asymmetry: No weak on bilateral (Symmetric > Asymmetric) > Weak on unilateral (Symmetric > Asymmetric) > Weak on bilateral (Symmetric > Asymetric).
Model 1: Adjusting for gender. Model 2: Adjusting for HGS deviation of weak, or HGS deviation of weak and asymmetry.
Abbreviation: HGS, handHGS; OR, odds ratio; CI, confidence interval; LL, lower limitation; UL, upper limitation.
**: $p < 0.01$.

The interaction between HGS and gender in their relationship with depression is a topic of growing interest among researchers. HGS, often measured as the force exerted by the hand when squeezing a dynamometer, has been found to be a predictor of various health outcomes, including cardiovascular health, cognitive function, and overall physical fitness. Similarly, depression is a complex mental health condition that affects millions of people worldwide. While the causes of depression are multifaceted and can include genetic, environmental, and biological factors, there is increasing evidence to suggest that physical health, including HGS, may play a role in its development and severity. HGS is often found to be lower in individuals with depression compared to those without. This may be due to a number of factors, including reduced physical activity, poor nutrition, and chronic inflammation. Additionally, depression itself can lead to muscle atrophy and decreased physical function, further weakening HGS. The interaction between HGS and gender is also an important consideration. Women tend to have weaker HGS than men, which may be due to differences in muscle mass, bone density, and hormonal factors. However, this does not necessarily mean that women are more susceptible to depression or that their depression is more severe. Instead, it suggests that gender differences in HGS may influence the way in which depression manifests and is experienced by individuals. In terms of interventions, improving HGS through physical activity and exercise may be a promising strategy for reducing the risk of depression. By increasing muscle strength and endurance, individuals may be able to improve their overall physical health and reduce the risk of developing depression. Overall, the interaction between HGS and gender in their interaction with depression is complex and multifaceted. While more research is needed to fully understand these interactions, it is clear that improving physical health through physical activity and exercise may be an important strategy for reducing the risk of depression in both men and women.

Interaction between HGS and gender on depression among middle aged and elderly can be understood in terms of their combined effect on an outcome, and this interaction can either be additive or multiplicative. In additive interaction, the combined effect of HGS and gender on an outcome is equal to the sum of their individual effects. This means that the factors act independently of each other, and the total impact on the outcome is simply the arithmetic sum of the impacts of each factor when considered separately. For example, if Factor HGS increases the risk of a depression by a %, and Factor gender increases the risk by b%, then in the presence of both factors together, the total increase in risk would be a+b % (assuming no overlap in the mechanisms through which they increase risk of depression). Mathematically, if $E(Y \mid A)$ represents the expected outcome given factor HGS, $E(Y \mid B)$ represents the expected outcome given Factor gender, and $E(Y \mid A \cap B)$ represents the expected outcome given both factors, then for additive interaction: $E(Y \mid A \cap B) = E(Y \mid A) + E(Y \mid B) - E(Y)$. Where $E(Y)$ is the expected outcome without any factors. The subtraction of $E(Y)$ accounts for the baseline risk. In multiplicative interaction, also known as synergistic or supra-additive interaction, the combined effect of HGS and gender on risk of depression is greater than the product of their individual effects. This indicates that the factors interact in such a way that their joint effect is more than what would be expected based on their separate effects. For instance, if Factor HGS doubles the risk of depression and Factor gender triples the risk, then in the presence of both factors, the risk might increase by sixfold or more, indicating a synergistic interaction. Mathematically, for multiplicative interaction: $E(Y \mid A \cap B) > E(Y \mid A) \times E(Y \mid B)$. This inequality shows that the joint effect of factors HGS and gender is greater than the product of their individual effects. It's important to note that these interactions can also be negative, meaning that the combined effect of the factors could be less than the sum or product of their individual effects, indicating antagonistic or sub-additive/sub-multiplicative interactions, respectively. Understanding whether an interaction is additive or multiplicative is crucial in fields like epidemiology, biology, sociology, and many others, as it helps in understanding the underlying mechanisms and predicting outcomes more accurately. In this study of two-factor interactions, the additive effect is greater than the multiplicative effect. This phenomenon can be explained as follows: Nature of Interaction: When two factors interact, their combined effect on a dependent variable may not simply be the

product of their individual effects. Instead, the interaction might produce an effect that is greater than the sum of the individual effects. This is because the factors may influence each other in a way that amplifies their impact when they are present together. Non-linear Relationships: The relationship between the factors and the outcome may not be linear. In non-linear relationships, the effect of one factor can change depending on the level of the other factor. This means that the total effect of both factors together can be more than what would be expected from their individual effects alone. Synergistic Effects: In this study, the combination of two factors can lead to synergistic effects, where the total effect is greater than the sum of the individual effects. This occurs when the factors work together in a way that enhances each other's impact. Contextual Dependence: The effect of an interaction can depend on the context in which it occurs. For example, the presence of a moderating variable can change the nature of the interaction, potentially leading to an additive effect that is greater than the multiplicative effect. Statistical Modeling: The choice of statistical model can also influence how interactions are interpreted. Some models may better capture the complexity of interactions, revealing additive effects that are larger than those predicted by simpler models that assume multiplicative effects. Data Variability: The variability in the data can also play a role. If the data points are more spread out or if there are extreme values, the additive effect might appear larger because it takes into account the full range of possible outcomes. In this study, the reason why the additive effect is greater than the multiplicative effect in the interaction of two factors lies in the complex nature of interactions, which can include non-linear relationships, synergistic effects, contextual dependencies, and the influence of statistical modeling and data variability. It is worth mentioning that this study innovatively employs Cox regression analysis, replacing the time-series variables with grip strength weakness level variables, which effectively explains the correlation between grip strength asymmetry and depression.

This study has limitations that cannot be ignored. The loss of follow-up in longitudinal data will undoubtedly undermine the credibility of the results. Further research should be conducted in more rigorous community experiments with appropriately stable samples.

5. Conclusion

An interaction between HGS deviation and gender has been observed, indicating an increased risk of depression among middle-aged and elderly Chinese individuals. The findings of this study may serve as a reference indicating that individuals with HGS deviation should pay attention to the potential onset of depression, and that the combination of HGS deviation with gender may subject them to an elevated risk of depression.

Acknowledgments

Funding: This work was supported by Scientific Research Foundation of Education Department of Anhui Province of China (Grant No. 2023AH051509).

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