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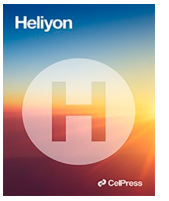

Research article

Effects of educational attainment on comorbidity of pain and depression in Chinese older adults

Haiyan Zhu [a], Yang Xiao [b], Tongjin Xie [b], Mohan Yang [b], Xun Zhou [b], Biao Xiao [b], Jingxuan Peng [c], Jianfu Yang [b,*]

[a] Department of Anesthesiology, The Third Xiangya Hospital, Central South University, 138 Tongzipo Road, Changsha, Hunan, China
[b] Department of Urology, The Third Xiangya Hospital, Central South University, 138 Tongzipo Road, Changsha, Hunan, China
[c] Department of Urology, Xiangya Hospital, Central South University, 87 Xiangya Road, Changsha, Hunan, China

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ABSTRACT

Pain and depression comorbidity (PD) among older adults in China is common and significantly affects their physical and mental health. The psychosocial factors may affect people's feelings, understanding and expression of pain and depression, leading to inaccurate assessment of this condition. Educational attainment is thought to be associated with either pain or depression. However, we do not yet know the relationship between educational attainment and PD. Using data from the 2018 China Health and Retirement Longitudinal Study in 2018, we analyzed various variables in 7742 individuals aged 60 years and older. Our results indicate significant differences between the PD and non-PD populations in terms of social, lifestyle, and behavioral factors. We observed a significant decrease in the incidence of PD among older adults with higher levels of education ($p < 0.001$). This association appears to be partially mediated by cognitive ability, suggesting that educational attainment may mitigate the risk of PD through cognitive enhancement. In addition, our analysis shows that the effect of educational attainment on PD is moderated by additional psychosocial factors, including living environment and alcohol consumption patterns. Older adults with higher levels of education tend to live in urban areas and have better control over alcohol consumption, which may contribute to a lower incidence of PD. Therefore, interventions aimed at enhancing cognitive abilities, improving living environments, and promoting healthier lifestyles and habits among older adults could potentially reduce their burden of PD.

1. Introduction

Over the past decade, with the aging of the global population, the comorbidity of pain and depression (PD) has increased rapidly in older adults and has become a major problem that seriously affects their health and quality of life [1]. Studies have reported that the incidence of PD ranges from 30 % to 60 %, highlighting that pain and depression may share common neurological changes [2]. There are important neurophysiological overlaps between pain and depression [3], as well as psychosocial overlaps, such as cognitive, emotional and behavioral factors which are thought to be involved in comorbid pain and depression [4]. Although pain and depression may share common biological pathways, the underlying mechanism of comorbidity of pain and depression is still unknown [5], and

* Corresponding author.
E-mail address: jeffxy3yy@csu.edu.cn (J. Yang).

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the treatment strategy for this condition has not been determined. Comorbid pain and depression is still a serious clinical, social and economic problem challenging us. Therefore, an in-depth exploration of the social and psychological factors influencing the comorbidity of pain and depression will help us to better understand this complex disease and pave the way for more effective interventions.

Years of research have led to an understanding that lower levels of education are associated with poor health outcomes [6,7]. Low level of education, along with other socioeconomic and demographic indicators, including separation or divorce and low income, are associated with an increased risk of depression [8,9]. Some other studies suggest that lower education level is also associated with more severe pain [10,11]. However, some interesting phenomena were found in a large survey from the United States (U.S.). Of more than 70,000 adults aged 30–49 who participated in this survey, more than 50 % reported different types of pain. Overall, Americans with more education reported less pain than those with less education. But the story was different for people with a high-school equivalency diploma or some college education, who reported more pain than other groups [12]. This suggests that although education level affects pain, the psychosocial factors and mechanisms involved may be complex. Given that pain and depression are often comorbid, it is necessary to investigate the possible influence of education level on this condition.

Due to the complex relationship between psychosocial environment and pain perception or depression experience [13], there may be some psychosocial factors that affect older adults' subjective perception of their pain and/or depressive symptoms, and may even interfere with the accurate expression of their experiences. We speculate that educational attainment may be an important factor affecting older adults' pain perception and depression experience (Fig. 1). Therefore, we searched the China Health and Retirement Longitudinal Study (CHARLS) database and collected comprehensive epidemiologic data on older adults aged over 60 years, covering individual, family, social, economic and psychological factors to explore the relationship between educational attainment and comorbidity of pain and depression, as well as the factors that may influence their relationship.

2. Methods

2.1. Study design and participants

The China Health and Retirement Longitudinal Study (CHARLS) is a longitudinal survey that investigates the socioeconomic and health status of Chinese residents aged 45 and older. It is a nationally representative random sample survey covering all county-level units in China. The samples include 28 provinces, 150 counties/districts, and 450 villages/urban communities across the country. One person per household aged 45 years or older and their spouses, a total of 17,708 individuals from 10,257 households participated in the CHARLS's baseline survey in 2011–2012 [14]. Since then, the study has conducted three waves of follow-up surveys in 2013, 2015 and 2018. We selected data from the most recent survey (2018), which included 19744 individuals, each of whom received a face-to-face computer-assisted personal interview with two trained investigators. 8650 participants aged <60 years and 317 with unknown age were excluded. After 3035 participants with missing data were also excluded, 7742 participants were enrolled into the final study (Fig. 2). Ethical approval for CHARLS was granted by the Institutional Review Board (IRB) of Peking University. The IRB approval number for the study is IRB00001052-11015, and all the participants gave informed consent to participate in the study.

2.2. Data collection and definitions

All the participants were interviewed in their homes by two trained researchers. The aim was to obtain as much detailed information as possible, with the help of computer-assisted technology. It included questions on demographics, family structure and changes, health status and functioning, general health, physician-diagnosed chronic illnesses, lifestyle and health-related behaviors (smoking, drinking, physical activities), activities of daily living, health care and insurance, work, retirement and pension, income and consumption, and assets.

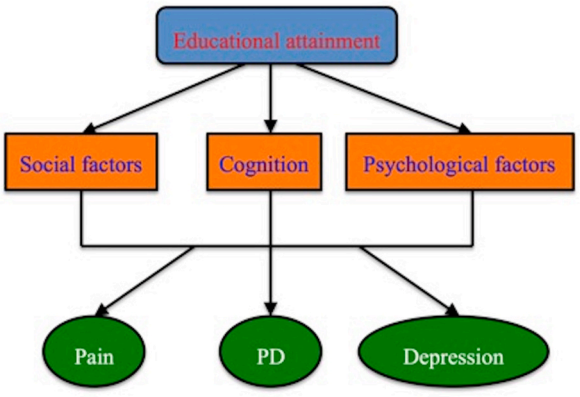

Fig. 1. Educationa attainment may have impact on pain, depression and PD through cognition, social and psychological factors. PD, comorbidity of pain and depression.

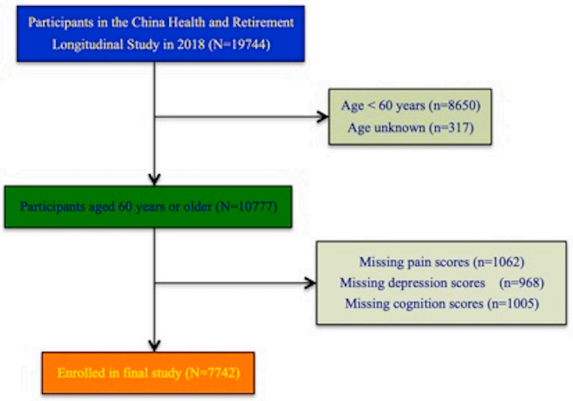

Fig. 2. Flowchart of screening participants for study.

2.3. Cognitive ability

The cognitive ability of the subjects was evaluated using the Mini Mental State Exam (MMSE), a widely utilized instrument in medical settings for assessing cognitive function and its changes in patients [15]. The Chinese MMSE has been validated and demonstrated to be reliable among Chinese older adults [16]. The MMSE score is categorized into four levels of cognitive function, ranging from 0 to 30. A score of 24–30 indicates normal cognition, 19–23 indicates mild cognitive impairment (MCI); 10–18 suggests moderate cognitive impairment, and 0–9 implies severe cognitive impairment.

2.4. Depression

The 10-item version of Center for Epidemiological Studies Depression Scale (CESD) was employed to assess the participants' depression symptoms. The 10-item CESD has been validated as a reliable measure of depression in individuals [17], and the reliability and validity of the Chinese CESD-10 have been verified among Chinese middle-aged and older populations [18]. The CESD-10 scores range from 0 to 30, representing different mental states. A score of 0–9 indicates no or doubtful depression, while a score of 10–30 means depressive symptoms.

2.5. Pain

The intensity of pain experienced by participants was quantified through self-report, with responses categorized into five levels: (I) no pain at all; (II) a little pain; (III) somewhat pain; (IV) quite a bit pain; and (V) very painful.

2.6. Self-reported health status

The subjects were requested to assess their physical condition based on their subjective feelings over the past few years. The subjects' health status was classified into five categories: 1) very good, 2) good, 3) fair, 4) poor, and 5) very poor.

2.7. Statistical analysis

The data were extracted from the database of the CHARLS (wave 2018) using RStudio version 1.2.1335 (RStudio Inc). The statistical analyses of the extracted data were conducted using the R statistical programming language version 4.2.0. Descriptive analyses were employed to summarize the data characteristics. The results were expressed as the mean ± standard deviation or number (percentage) when appropriate. Kruskal-Wallis test was used for comparison among groups. A pairwise comparison of multiple sample ratios was conducted using the Bofferni method. The bruceR package was employed to analyze the mediating and moderating effects. The threshold for statistical significance was set at $p < 0.05$.

3. Results

3.1. Descriptive analysis

A total of 7742 Chinese older adults over the age of 60 were enrolled into this study, including 3702 males with a mean age of 67.91 ± 5.93 and 4040 females with a mean age of 68.27 ± 6.20. The participants were classified into four groups based on their pain and CESD-10 scores: no pain and depression (NPD), pain without depression (PWD), depression without pain (DWP) and comorbidity of pain and depression (PD) as shown in Table 1. The incidence of PD was 29.32 %, close to that of NPD (30.38 %) and PWD (32.07 %)

groups. In contrast, the incidence of DWP (8.33 %) was significantly lower than that of the other three groups ($p < 0.001$, Table 1). There was no significant difference in age among the four groups of older adults ($p > 0.05$). The incidence of PD in older men was significantly higher than that in older women (37.79 % vs. 21.56 %, $p < 0.001$). There was no significant difference between men and women in the PWD group (33.04 % vs. 31.19 %, $p > 0.05$). However, the proportion of older female participants in the DWP was higher than that of older male participants (9.01 % vs. 7.59 %, $p < 0.05$).

3.1.1. Marriage

A comparison of the incidence of PD between those who had been widowed, divorced, or never married and those who were married and living with their spouses revealed a significantly lower incidence among the latter group (27.49 % vs. 37.83 %, $p < 0.001$). There was no significant difference in the prevalence of DWP among married subjects (8.23 % vs. 8.82 %, $p > 0.05$). However, the incidence of PWD in the married older adults was significantly higher than that in those without spouses (33.01 % vs. 27.70 %, $p < 0.001$).

3.1.2. Living environment

A higher prevalence of PD was observed among older individuals residing in rural areas (32.64 % vs. 21.31 %, $p < 0.001$). Individuals residing in rural areas exhibited a higher prevalence of depressive symptoms than those in urban areas among DWP participants (8.86 % vs. 7.05 %, $p < 0.01$). Conversely, those residing in urban areas were more likely to have PWD than those residing in rural areas (34.04 % vs. 31.26 %, $p < 0.05$).

3.1.3. Individual income

The NPD group exhibited the highest average personal income, which was significantly higher than that of the other three groups ($p < 0.001$). The income of the PWD population was found to be significantly higher than that of the DWP and PD populations ($p < 0.001$). The statistical analysis revealed that individuals with DWP earned slightly less than those with PD ($p < 0.05$). The findings

Table 1
Descriptive characteristics of older adults in China.

	NPD	PWD	DWP	PD	*P*
Number (%)	2344 (30.38)	2483 (32.07)	645 (8.33)	2270 (29.32)	<0.001
Age (years)	68.07 ± 6.13	67.95 ± 6.02	68.28 ± 6.28	68.24 ± 6.02	0.205
Gender					<0.001
Male (%)	799 (21.58)	1223 (33.04)	281 (7.59)	1399 (37.79)	
Female (%)	1545 (38.24)	1260 (31.19)	364 (9.01)	871 (21.56)	
CESD-10 score	3.79 ± 2.79	4.81 ± 2.77	14.67 ± 4.30	16.10 ± 4.78	<0.001
Marriage status					<0.001
Married and live with spouse present (%)	1992 (31.27)	2103 (33.01)	524 (8.23)	1751 (27.49)	
Divorced, widowed or never married (%)	352 (25.66)	380 (27.70)	121 (8.82)	519 (37.83)	
Living environment					<0.001
Urban (%)	854 (37.60)	773 (34.04)	160 (7.05)	484 (21.31)	
Rural (%)	1490 (27.23)	1710 (31.26)	485 (8.86)	1786 (32.64)	
Individual income (RMB)	25333.14 ± 13194.4	16790.72 ± 10128.52	13513.01 ± 7015.42	14511.63 ± 5752.25	<0.001
Frequency of social activities					<0.001
Almost daily (%)	1363 (28.21)	1502 (31.09)	420 (8.69)	1546 (32.00)	
Almost every week (%)	757 (35.74)	718 (33.90)	158 (7.46)	485 (22.90)	
Not regularly (%)	224 (28.25)	263 (33.17)	67 (8.45)	239 (30.14)	
Smoking					<0.001
Still smoking or have quitted (%)	1287 (35.62)	1126 (31.17)	311 (8.61)	889 (24.61)	
Never smoke (%)	1057 (25.60)	1357 (32.87)	334 (8.09)	1381 (33.45)	
Frequency of Alcohol drinking					<0.001
More than once a month (%)	812 (39.19)	655 (31.61)	168 (8.11)	437 (21.09)	
Drink but less than once a month (%)	164 (29.03)	202 (35.75)	44 (7.79)	155 (27.43)	
Never drink (%)	1367 (26.78)	1626 (31.86)	433 (8.48)	1678 (32.88)	
MMSE score	22.35 ± 4.93	21.97 ± 5.10	20.37 ± 5.08	19.56 ± 5.31	<0.001
Sleep duration (hours)	6.69 ± 1.75	6.26 ± 1.84	6.09 ± 2.02	5.39 ± 2.22	<0.001
Physical activity					<0.001
No physical activity (%)	833 (29.09)	836 (29.19)	285 (9.95)	910 (31.77)	
Light physical activity (%)	857 (32.77)	814 (31.13)	206 (7.88)	738 (28.22)	
Moderate physical activity (%)	530 (29.43)	681 (37.81)	113 (6.27)	477 (26.49)	
Intensive physical activity (%)	124 (26.84)	152 (32.90)	41 (8.87)	145 (31.39)	
Self-reported health status	2.48 ± 0.95	3.06 ± 0.89	3.07 ± 1.01	3.57 ± 0.89	<0.001
Education level					<0.001
Illiterate (%)	395 (21.76)	546 (30.08)	156 (8.60)	718 (39.56)	
Elementary school (%)	1023 (28.35)	1142 (31.65)	334 (9.26)	1109 (30.74)	
Junior high school (%)	543 (37.84)	486 (33.87)	95 (6.62)	311 (21.67)	
High school or above (%)	383 (43.33)	309 (34.95)	60 (6.79)	132 (14.93)	

Data presented as mean ± SD or numbers (%). Abbreviations: NPD, no pain and depression; PWD, pain without depression; DWP, depression without pain; PD, comorbidity of pain and depression; SD, standard deviation.

indicated that older individuals with depressive symptoms exhibited a lower income.

3.1.4. Social behavior

The prevalence of PD in older adults who engaged in weekly social activities was significantly lower than that in those who engaged in social activities less or more frequently ($P < 0.001$). This may indicate that appropriate social activities can help reduce the incidence of PD. Conversely, excessive or inadequate social interaction is not conducive to the well-being of older adults. Nevertheless, no significant difference was observed in the proportion of older adults with different social frequencies in the PWD or DWP populations ($p > 0.05$).

3.1.5. Smoking

There was no significant difference in the prevalence of PWD (31.17 % vs. 32.87 %) and DWP (8.61 % vs. 8.09 %) between the older adults who were still smoking or had quit smoking and those who had never smoked ($p > 0.05$). Nevertheless, the incidence of PD was higher among non-smokers than among those who were still smoking or had ever smoked (33.45 % vs. 24.61 %, $P < 0.001$).

3.1.6. Alcohol drinking

The prevalence of PD was found to be significantly lower among older adults who consumed alcohol at least once a month (21.09

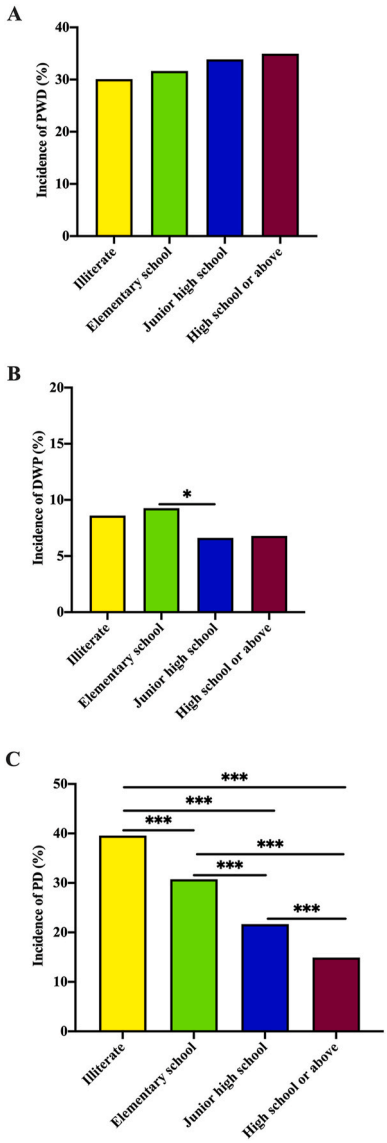

Fig. 3. Prevalence of PWD (A), DWP (B), and PD (C) in the older adults with different education levels. Abbreviations: PWD, pain without depression; DWP, depression without pain; PD, comorbidity of pain and depression. ***, $p < 0.001$; *, $p < 0.05$.

%) compared to those who drank less than once a month (27.43 %) or never drank (32.88 %, $p < 0.01$). This disparity was not observed in the populations of people with PWD or with DWP ($p > 0.05$).

3.1.7. Physical activity

The results indicated that regular light to moderate intensity exercise each week was more beneficial for older adults. The incidence of PD in older adults who engaged in light to moderate intensity exercise each week was significantly lower than that in those who engaged in little exercise ($P < 0.01$). Too much or too little physical activity seems to be of little benefit to the older adults ($p > 0.05$). Similar results were found in the DWP population, where those with moderate physical activity exhibited the lowest incidence of depression ($P < 0.001$). In the PWD population, the incidence of pain in the older adults with moderate physical activity (37.81 %) was the highest, while the lowest incidence occurred in those who had little physical activity (29.19 %, $P < 0.05$).

3.1.8. Sleep duration

Among the four populations, the NPD individuals exhibited the longest sleep duration (6.69 ± 1.75 h) per day, while those with PD exhibited the shortest daily sleep duration (5.39 ± 2.22 h, $p < 0.001$). The sleep durations of the PWD and DWP populations were longer than that of the PD population ($p < 0.001$). However, no significant difference was observed between the PWD and DWP groups ($p > 0.05$).

3.1.9. Self-reported health status

In our study, the highest average score (3.57 ± 0.89) was observed in PD population, while the lowest score (2.48 ± 0.95) was in NPD people. Compared to NPD people, either pain or depression could increase the score (3.06 ± 0.89 for PWD and 3.07 ± 1.01 for DWP, $P < 0.001$). Since there was no significant difference in self-reported health status between the PWD and DWP older people ($p > 0.05$), it was not possible to determine whether either of these two symptoms had a greater impact on their health. However, when pain and depression co-occurred in the older person, his or her health was found to be significantly worse than that of the other three groups' people ($p < 0.001$).

3.1.10. Cognitive ability

The mean MMSE score for the NPD older adults was the highest among the four populations (22.35 ± 4.93), while that of the PD population was the lowest (19.56 ± 5.31). The results did not indicate a statistically significant difference between the NPD and PWD populations ($p > 0.05$). However, the MMSE score of DWP older people was found to be significantly lower than that of NPD or PWD people ($p < 0.01$), indicating that depression may impair the older adults' cognitive ability. It can be posited that pain may exacerbate the impairment effect of depression on cognitive function. However, it should be noted that pain alone is not sufficient to significantly affect cognitive ability.

3.1.11. Educational attainment

The multiple comparisons of the incidence of PWD did not reveal any significant differences among individuals with varying educational levels ($p > 0.05$, Table 1 and Fig. 3A).

Among the DWP population, the prevalence of depression in older adults with junior high school education was found to be lower than that in those with primary school education ($p < 0.05$). Nevertheless, no statistically significant differences were observed between the other groups ($p > 0.05$, Table 1 and Fig. 3B).

A notable disparity was observed in the distribution of PD among older adults with varying educational backgrounds. The incidence of PD was found to be inversely proportional to the educational attainment of older adults, with a statistically significant gradient difference observed ($p < 0.001$). This relationship is illustrated in Table 1 and Fig. 3C.

3.2. Mediating effect of cognitive ability on the relationship between educational attainment and PWD, DWP or PD

Recent studies have demonstrated that pain is common in older adults and is associated with cognitive impairment [19,20].

Table 2
Mediation effects of cognitive ability on the relationship between educational attainment and PWD, DWP or PD.

		Effect	S.E.	z	*p*	95 % CI
Educational attainment → PWD	Indirect	−0.099	0.009	−11.681	<0.001	−0.116, −0.082
	Direct	−0.092	0.017	−5.555	<0.001	−0.122, −0.058
	Total	−0.191	0.015	−13.037	<0.001	−0.219, −0.160
Educational attainment → DWP	Indirect	−0.099	0.009	−11.681	<0.001	−0.116, −0.082
	Direct	−0.092	0.017	−5.555	<0.001	−0.122, −0.058
	Total	−0.191	0.015	−13.037	<0.001	−0.219, −0.160
Educational attainment → PD	Indirect	−0.099	0.009	−11.681	<0.001	−0.116, −0.082
	Direct	−0.092	0.017	−5.555	<0.001	−0.122, −0.058
	Total	−0.191	0.015	−13.037	<0.001	−0.219, −0.160

Abbreviations: S.E., standard error; z, value for Sobel test; CI, confidence interval. PWD, pain without depression; DWP, depression without pain; PD, comorbidity of pain and depression.

Similarly, cognitive impairment and depression often co-occur in older people, and it is postulated that their depression is related to cognitive decline [21,22]. Consequently, there is a compelling rationale to hypothesize that there is an important link between cognition and PD. Given the close relationship between educational attainment and cognitive ability [23,24], it can be reasonably assumed that cognitive ability plays an important role in the relationship between educational attainment and PWD, DWP or PD. We constructed mediating models for education level and PWD, DWP and PD, respectively, and demonstrated that cognitive ability partially mediated the relationship between education level and PWD, DWP or PD ($p < 001$, Table 2).

The mediating effects of cognitive ability on the relationship between education level and DWP or PD accounted for more than half of the total effect (60.90 % for DWP and 51.83 % for PD), whereas the portion mediated by cognitive ability in the relationship between educational attainment and PWD was 35.43 %. In other words, cognitive ability plays a more significant role in the relationship between educational attainment and depression or depression-related illnesses.

In these three paths, the values of total effect, indirect effect, and direct effect were all negative ($p < 0.001$), indicating that, regardless of the mediating effects of cognitive ability, education level has a negative impact on its targets (PWD, DWP, and PD).

3.3. Moderators in the relationship between educational attainment and PD

Education level may affect health in a number of ways [25]. Some factors may be involved in and moderate these processes. Therefore, our study incorporated a multitude of social, behavioral and environmental variables, including marital status, living environment, tobacco and alcohol consumption, personal income, sleep patterns, and physical exercise habits, etc. (Table 1). Significant differences were observed in these factors between the PD and non-PD populations. However, it was not yet determined whether these factors were involved in the effect of educational attainment on PD. Thus, we incorporated these variables into the moderation model examining the association between educational attainment and PD. Our findings indicated that living environment and alcohol consumption (Table 3, $p < 0.05$) may act as moderators in this relationship, whereas the other variables did not appear to significantly influence the association between educational attainment and PD ($p > 0.05$).

The coefficient of the main effect, education level, was negative, and that of the moderating factor, living environment (urban area), was positive. In contrast, the coefficient of the interaction between educational attainment and living environment was negative (Table 3). These findings indicated that although the interaction between the living environment and educational attainment had a negative impact on PD, the living environment actually mitigated the inhibitory effect of educational attainment on PD.

Our previous analysis indicated that a higher frequency of alcohol consumption was associated with a lower incidence of PD in older adults. However, in the moderating model, the difference in drinking frequency among older people with different educational levels did not demonstrate a dose-effect relationship with the incidence of PD. After adjusting for educational attainment, light drinking (less than once a month) was associated with a reduced incidence of PD ($p < 0.01$ for the interaction between educational attainment and alcohol drinking less than once a month), while more frequent drinking had no additional benefits ($p > 0.05$ for the interaction between educational attainment and alcohol drinking more than once a month, Table 3).

4. Discussion

Low reporting rates of chronic pain and low prevalence of depression and anxiety are frequently reported among Chinese and Chinese immigrants in other countries. However, these findings may be partially explained by the limitations of standard diagnostic tools, which may not adequately detect differences in pain perception and communication within the context of Chinese and culture [26]. Therefore, a more precise comprehension of the prevalence of pain and depression among older adults in China, along with the

Table 3
Moderating effects of living environment and alcohol consumption on the relationship between educational attainment and PD.

	Model for living environment		Model for alcohol drinking		
	1	2	1	2	
Educational attainment	−0.252 ***	−0.225 ***	−0.253 ***	−0.200 ***	
	(0.014)	(0.015)	(0.014)	(0.028)	
Moderating effect		0.219 ***		Drink less than once a month	0.281 ***
					(0.057)
		(0.032)		Drink more than once a month	0.298 ***
					(0.031)
Interaction		−0.077 *		Educational attainment: drink less than once a month	−0.158 **
					(0.059)
		(0.032)		Educational attainment: drink more than once a month	−0.031
					(0.034)
R^2	0.038	0.044	0.038	0.050	
Adjusted R^2	0.038	0.043	0.038	0.049	
p value for interaction		0.015		0.026	

In model for living environment, living in rural area served as the baseline for comparison. In model for alcohol drinking, never drinking was used as the baseline for comparison. Model 1 is the effect of educational attainment, the main effect on PD when the moderating effect is not introduced into the model. Model 2 is the influence of the main effect, moderating effect and their interaction on PD after the moderating effect have been introduced. ***, $p < 0.001$; **, $p < 0.01$; *, $p < 0.05$. Numbers in brackets are the standard errors of the corresponding numbers before them.

underlying interconnections and mechanisms, will facilitate more accurate diagnoses and treatments of this prevalent condition. The study found that education in early life could affect the comorbidity of pain and depression in late life through cognition. Individuals with higher levels of education are more likely to demonstrate enhanced cognitive abilities, which may significantly reduce the risk of developing PD compared to those with lower levels of education. This suggests that educational attainment may act as a protective factor against PD in late life. Furthermore, individuals with higher levels of education tend to reside in more favorable living environments and engage in healthier habits, which may help to mitigate the challenges associated with PD.

Pain is an unpleasant sensation and emotional experience related to actual or potential tissue damage, or similar experiences [27]. It is a subjective experience, and is influenced to varying degrees by many factors including biology, psychology and social environment [28]. Pain is usually an adaptive and protective feeling, but it can also adversely affect physical, mental and social functioning. On the other hand, mental state can affect the perception of pain, and then be influenced by pain [29]. The brain of patients with chronic pain can continuously receive and processes background pain by integrating information from different brain regions related to sensory, cognitive and emotional functions [30]. This mechanism of signal connection and integration allows pain, emotion, and cognitive function to communicate with each other. Therefore, pain actually includes three components: sensory discrimination that reflects the physical properties of noxious stimuli, emotional motivational components (disgust, fear, and avoidance motivation) caused by noxious stimuli, and cognitive evaluation component [31]. This helps us to better understand the high comorbidity of pain and depression.

Chronic pain and depression have complex and bidirectional relationships: depression is a risk factor for chronic pain, and chronic pain is a risk factor for depression [32]. Another important fact is that chronic pain is usually associated with not only emotional but also cognitive deficits [33]. We found that the MMSE score of older adults with PD was significantly lower than that of the non-PD population, even in depressed people without pain, suggesting that pain and depression may impair the cognitive ability of older adults. In our study, depression was more destructive to cognitive ability, and pain alone did not seem to significantly affect cognitive ability. Although some literature suggests that persistent pain is associated with cognitive decline [34], our results are not consistent with them, because we cannot rule out that cognitive impairment may limit the ability to report pain and depressive symptoms, leading to a lack of pain awareness among respondents [35].

There may be a bidirectional association between depression and cognition. A large representative sample study in the U.S. suggested that cognition among older adults may be altered by late-life depression, and older adults with depression may also be affected by cognition, particularly in those with both depression and diabetes [36]. Another study showed that cognitive performance was significantly inversely associated with clinically significant depressive symptoms among older adults in the United States after controlling for multistage sampling, sociodemographic, and medical history covariates [37]. Depression may lead to cognitive impairment [38], and conversely, cognitive decline may increase the risk of depression [39], suggesting that they have a negative impact on each other. Although we don't completely understand the impact of cognition on comorbid pain and depression, the interaction between cognition and depression may play an important role in their relationship.

Many studies figure out that the educational attainment of individuals is closely related to their cognitive ability [40]. Educational attainment has been regarded as an important proxy of cognitive ability in genetic research [41]. An analysis of large nationally representative sample study in the U.S. revealed that subjective cognitive decline, low income, low educational attainment, and poor self-reported health, were independently associated with cognitive decline [42]. With the elevation of education level, cognitive impairment gradually decreased [43], and engagement in mental stimulation activities or high education level can buffer the negative impact of abnormal brain lesions on cognitive function [44], suggesting that educational attainment may be a protective factor of cognitive function. Moreover, in late-life cognitive impairment, tasks that require higher mental effort, particularly executive, computational, or processing functions, are more affected than relatively simple cognitive functions such as memory or rehearsal [36]. These advanced cognitive functions are often associated with early life education, which may influence the resulting cognitive reserve in late life [45]. Less education may reduce cognitive ability through low cognitive reserve in late life, which in turn promotes depression. Our study also confirmed that older adults with higher education level had higher MMSE scores than those with lower education level. In the mediation models, education level affected PWD, DWP and PD through the partial mediation of cognitive ability. Depression may be more affected by the brain regions associated with cognitive and emotional functions, whereas pain may be more affected by the brain regions associated with sensory and cognitive functions. Therefore, cognitive function is likely to link pain and depression together as a hub in the process of pain and depression comorbidity. Higher educational attainment may make older adults have a clearer understanding of pain and depression by better cognition, thus reducing the incidence of pain and depression comorbidity.

Previous studies suggested that people with low education level had more depressive symptoms than people with high education level [9,46]. However, this may not be true in all countries or regions. A cross-sectional study from 18 countries found no evidence that the difference in the incidence of depression among older adults in Japan was due to educational inequality, while in the United States, people with low education had more depressive symptoms than those with high education [9]. In our study, the statistically significant difference of the incidence of depression in older adults was found only between those with junior high school and those with primary school. Although we do not yet know the cause of this difference, it may be due to derive from the differences in politics, economy, culture, education, ideology, customs and external environment and resources among different countries.

We know that comorbidity is not a simple combination of several diseases, as there is some intrinsic association between them. Education level is associated with both pain and depression, suggesting that it may influence the onset and progression of pain and depression comorbidity through related psychosocial and environmental factors.

In China, regional disparities and developmental imbalances lead to large differences between urban and rural areas. In most parts of China, more educated or trained people usually choose to work in cities, especially in big cities. Urban facilities are relatively

complete, concentrated, and have a perfect service system and well-developed transportation, making it convenient for individuals and families to live, study, receive medical treatment, etc. These location advantages are not available in most of China's rural areas. In particular, rural areas lack good health conditions and high-level doctors, which significantly reduces the quality of medical care. These insurmountable disadvantages in a short period of time will certainly affect the quality of life and health of older adults. A report from the United States shows that the prevalence of depression in rural areas is slightly higher than in urban areas, but the suicide rate is significantly higher [47]. It is unclear whether depression among rural Americans is related to rural residence itself, or to the health and resource disparities common in rural areas [48]. In our moderation model, the interaction coefficient between living environment and education level was statistically significant, while that between self-reported health status and education level was not significant, suggesting that living environment may moderate the relationship between education level and PD through the external environment and resources.

In fact, China's urban-rural disparity and the uneven distribution of the older population partially mask the dampening effect of educational attainment on PD. More of older adults with higher education level lived in urban areas, while the education levels of such living in rural areas were generally lower than those in urban areas. This uneven regional distribution of the population made the impact of educational attainment on PD less significant than that before the living environment was introduced into the model.

Drinking habits, which is thought to relieve anxiety, stress, pain and similar problems, may lead to the formation of addiction [49]. It is believed that chronic pain may increase the tendency to drink alcohol [50]. Many people turn to alcohol as a "self-medication" for pain relief when they suffer from chronic pain [51]. Our survey also seems to support this view that the higher the frequency of drinking, the less prone to PD. However, we found that the truth is not so simple after examining the moderating role of drinking frequency in the relationship between education level and PD. Among older adults with different educational levels, the effect of drinking on PD is not dose dependent. Low frequency drinking should be better controlled to reduce the incidence of PD, and more drinking does not benefit the PD population.

Additionally, more education can significantly reduce the risk of alcohol dependence [52]. Studies have shown that alcohol consumption varies with people's education level: people with higher education levels prefer drinking, but they are not greedy for alcohol, and they know more about quitting, while alcohol abuse is more common in less educated communities [53]. That is to say, people with higher education are more likely to control their own behavior and thoughts. For them, enjoying a drink doesn't mean drinking too much. To date, the protective effect of moderate alcohol consumption remains controversial. However, in some cases, moderate drinking can protect against cardiovascular disease, diabetes and major depression [54], suggesting that the influence of lifestyle and behavioral habits on disease is significant.

Most Chinese people retire around the age of 60, and the transition from work to retirement may lead to their physical, social and psychological changes. In this process, psychological adjustment is very important, resulting in changes in behavior and lifestyle. Cognitive resilience provides the basis for psychological adjustment during this period, i.e., more flexible coping strategies, more multifaceted understanding and cognition, and better mental feedback may enable older adults to experience this particular period more smoothly. Higher educational attainment is often associated with better cognitive resilience [55], which helps older adults to better adapt to retirement life and reduce the related discomforts and illnesses. Even in the process of aging, cognitive resilience and reserve are also beneficial to slow cognitive decline and reduce or alleviate depressive symptoms. In our study, older adults with high educational attainment have better cognitive ability, are more likely to live in the city, and have better control of alcohol consumption, so their incidence of PD is lower than those with low educational attainment.

Several brain regions are involved in depression and pain [56]. Especially for long-lasting pain, signals from brain regions encoding emotion-motivation processes rather than from sensory brain regions dominate pain processing and perception [57], suggesting that long-term stimulation and memory involve more brain regions in related activities. This may suggest that the comorbidity of pain and depression may be long-term influnced by social, psychological, behavioral, and other factors that change the activity of brain regions.

There are some limitations in our study: (1) The relationship between educational attainment and PD may be more complex than what we understand based on interviews and observations. Responses or self-reports from respondents may be biased or inaccurate, which is a limitation of our study, although a large-scale survey can reduce these biases. (2) The mechanism by which education affects cognitive function in the context of comorbid pain and depression deserves further exploration. Therefore, we need to conduct more detailed qualitative research in the future to enrich our results.

In conclusion, the impact of educational attainment on pain and depression comorbidity may involve multiple psychosocial and environmental factors. High educational attainment can reduce the comorbidity of pain and depression among older adults by improving their cognitive ability, and alleviate their suffering from PD by moderating and adapting to the environment and lifestyle. Therefore, our focus on older adults with comorbid pain and depression should not be limited to the disease itself, but should also address related psychosocial issues. In addition to appropriate medical treatment and care, the living environment and lifestyle of older adults also need to be improved.

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Ethics declarations

This study was reviewed and approved by the Institutional Review Board (IRB) at Peking University, with the approval number:

IRB00001052-11015. All participants provided informed consent to participate in the study, and they also provided informed consent for the publication of their anonymised case details.

Data availability statement

All data collected in the China Health and Retirement Longitudinal (CHARLS) are maintained at the Institute of Social Science Survey of Peking University, Beijing, China. The first three waves of CHARLS data plus the Life History wave have all been released publicly, on the CHARLS website (http://www.charls.pku.edu.cn/en). The data have been deposited at "2018 CHARLS Wave 4" (https://charls.charlsdata.com/pages/Data/2018-charls-wave4/en.html) with accession number (SHA1: 42F3E6BF26CEA8072D9FA9F6050F413556D20A69).

CRediT authorship contribution statement

Haiyan Zhu: Writing – original draft, Visualization, Resources, Investigation, Formal analysis, Data curation. **Yang Xiao:** Investigation, Formal analysis. **Tongjin Xie:** Investigation, Formal analysis. **Mohan Yang:** Formal analysis. **Xun Zhou:** Formal analysis. **Biao Xiao:** Data curation. **Jingxuan Peng:** Data curation. **Jianfu Yang:** Writing – review & editing, Supervision, Project administration, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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