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Association between Earthquake and Depression 37 Years after the Tangshan Earthquake: a Community-based Study

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ABSTRACT

Objective To investigate the association between a major earthquake, the Tangshan earthquake, and the risk of depression over 37 years.

Design and setting Prospective, population-based cohort study conducted in Tangshan from 2013 to 2014.

Participants This general community sample included 5024 participants who were born before July 28, 1976, when the Tangshan earthquake occurred, with available data on their earthquake experiences and depression 37 years after the earthquake.

Outcomes and variables ORs for having earthquake experience with or without bereavement (relative to no earthquake experience) obtained by multinomial logistic regression, adjusted for gender, age during the earthquake, marital status, smoking, drinking, education, income, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidemia.

Results Of the 5024 participants, 641 experienced the Tangshan earthquake, and 98 experienced bereavement. Participants who experienced the earthquake (with or without bereavement) were 83% (odds ratios (OR) 1.83, 95% confidence interval (CI) 1.02-3.29) more likely to develop depression after 37 years. Those who lost relatives after the earthquake were nearly 3 times (OR 2.82, 95% CI 1.24-6.39) as likely to develop depression as those who did not experience the earthquake. The association was more pronounced for women: women who experienced the earthquake with or without bereavement were more than 3 times as likely to develop depression, whereas no significant association was found for men (interaction by gender p=0.02).

Conclusions The Tangshan earthquake is associated with an increased long-term risk of depression in survivors who experienced bereavement, particularly women. Our findings suggest a need for long-term surveillance of depression and early intervention among survivors of major earthquakes.

Strengths and limitations of this study

- This is the first study to show long-term risk of depression 37 years following an earthquake.
- Participants are stratified by gender and age at the earthquake. which is necessary for clinicians and policymakers to identify high-risk populations for long-term prevention of depression after an earthquake.
- We were unable to control for every event or factor during the follow-up.
- Whether the subjects were taking antidepressants was unknown.
- Depression was assessed only once during the study.

INTRODUCTION

The prevalence of depression is increasing worldwide[1]. According to the World Health Organization, depression will be a major reason for disability around the world by 2030[2]. Therefore, it is critical to identify populations at high risk of depression.

In recent years, an increasing number of studies have suggested that earthquakes are closely related to the development of mental illnesses, including post-traumatic stress disorder (PTSD), depression and anxiety[3-6]. In particular, several studies have indicated an increased prevalence of depression among individuals who survived a major earthquake[7, 8]. Moreover, survivors who lost relatives and vulnerable individuals, such as women and the elderly, during the earthquake were particularly affected[9, 10]. However, these studies mainly examined the effects of earthquakes on depression in the short-term. It was unclear whether the increased risk of depression persisted over a long period following the earthquakes. Depression is chronic and debilitating[11], and the long-term effects of an earthquake on depression may result in chronic psychological disorders[12, 13]. The likelihood of developing a long-term psychiatric disorder may be reduced if effective treatment can be implemented among the population that needs it most before the disorder becomes entrenched[14].

These long-term effects are difficult to establish due to the scarcity of information concerning the present health status of survivors, which is due to the high cost and difficulty of tracking individuals over time[15]. In China, the Jidong Cohort, located in Tangshan, provides a suitable setting for studying the long-term effect of an earthquake on depression. The Tangshan earthquake, which

occurred in 1976, had a magnitude of 7.8 on the Richter scale[16]. Over the past 37 years, numerous studies have examined the effects of the Tangshan earthquake on physical health outcomes. These studies suggested an increased risk of diabetes, cardiovascular disease, and elevated levels of uric acid among survivors of the Tangshan earthquake even more than 30 years later[17-19]. However, no study to date has examined the long-term effect of Tangshan earthquake on the risk of depression. Given the high morbidity and additional complications of depression, it is important to identify the high-risk group to provide evidence for psychological intervention in the vulnerable group.

The present study aimed to examine whether the Tangshan earthquake increased the rate of depression 37 years later and to study whether those who lost relatives during the earthquake were particularly affected. We also examined whether the association between the earthquake and depression varies by gender and age at the time of the earthquake.

MATERIALS AND METHODS

Study participants

We used data obtained from the Jidong Cohort, an ongoing community-based study[20]. Jidong is located in the Caofeidian district of Tangshan City, which is 60 km from the epicenter of the Tangshan earthquake. From July 2013 to August 2014, a total of 9078 residents of Jidong were recruited for the study, completed a standardized questionnaire, and underwent physical examinations and laboratory assessments. We included 5024 participants from the Jidong Cohort; all were born before July 28, 1976, when the earthquake occurred, and provided baseline information on their experiences with the

earthquake. This study was conducted in accordance with the guidelines in the Helsinki Declaration and approved by the Ethics Committee of Jidong Oilfield Staff Hospital. All participants provided written informed consent.

Assessment of the earthquake experience

During the baseline visit, participants reported their earthquake experience and related bereavement using a standardized questionnaire. Participants were asked "Were you in the Tangshan earthquake area in 1976?" and "Did you lose any relatives in the earthquake?". Participants who confirmed that they had experienced the earthquake were placed into one of 3 groups: no earthquake experience; earthquake experience without bereavement; and earthquake experience with bereavement.

Assessment of depression

Depressive symptoms were assessed using the Center for Epidemiological Studies Depression Scale (CES-D), which was initially developed by the United States National Institute of Mental Health in 1977[21]. The Chinese version of the CES-D was translated by two psychiatrists on the basis of the international standard version of the CES-D questionnaire in 1985[22] and was specifically designed to screen for depression[23]. All investigators attended a 3-day training course and were licensed before conducting CES-D interviews. The highest possible score on the CES-D scale was 60, and a score of 16 or higher was used to define clinically meaningful depressive symptoms.

Assessment of potential covariates

All demographic and behavioral variables were collected using questionnaires, which were

administered by well-trained research nurses. Potential confounding variables included gender, age at time of earthquake, smoking, drinking, education, income, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidemia. Age at the time of the earthquake was defined as a continuous variable. The average monthly income of each family member was categorized as "<¥3000", "¥3000–5000" or ">¥5,000". Educational level was categorized as "illiterate or primary school," "middle school or high school," and "university or above." Possible responses to questions on smoking status, drinking status were "yes" and "no." Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured twice with the subject in a seated position using a mercury sphygmomanometer. If the difference between the two measurements exceeded 5 mm Hg, an additional reading was taken, and the average of the three readings was used. Hypertension was defined as having a history of hypertension, exhibiting an SBP ≥140 mm Hg or a DPB ≥90 mm Hg, or using antihypertensive medications. Diabetes mellitus was defined as a fasting glucose level ≥7.0 mmol/l (126 mg/dl), any use of glucose-lowing drugs, or any self-reported history of diabetes mellitus. Hyperlipidemia was defined as having a history of hyperlipidemia, total blood cholesterol levels ≥220 mg/dl, triglyceride levels≥ 150 mg/dl, or using anti-hyperlipidemic medications.

Patients and public involvement

Patients and public did not involve in the design of the study. However, Participants signed written informed consent. They actively cooperated with the researcher to complete the collection of questionnaire information and were willing to provide support for further use of data.

Statistical analysis

We first compared the baseline characteristics of individuals according to their earthquake and bereavement experiences (no earthquake experience, earthquake experience without bereavement, and earthquake experience with bereavement) using the chi-square test for categorical variables and one-way ANOVA or the Kruskal Wallis test for continuous variables.

We used logistic regression to examine the association between earthquake experience and depression and obtained odds ratios of the development of clinically meaningful depressive symptoms with "no earthquake experience" as the reference group. We adjusted for a number of potential confounders, including gender, age during the earthquake, smoking, drinking, education, income, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidemia. To determine whether the association between earthquake and depression varied by gender and age during the earthquake, we also performed a subgroup analysis using these variables and tested for significance of the interaction terms.

All statistical tests were 2-sided, and results with a P-value<0.05 was considered statistically significant. Analyses were implemented in SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Baseline characteristics

Baseline characteristics of earthquake and bereavement experiences are shown in Table 1. In total, 543 (10.8%) out of 5024 individuals experienced the earthquake without bereavement, and 98 (2.0%)

participants lost relatives. Individuals who experienced earthquakes, with or without bereavement, were younger (14.8±9.2, 13.1±9.1 vs. 14.8±9.2) and were more likely to have lived in Tangshan 1-2 years after the earthquake (86.7%, 79.4% vs. 1%) than those who had not experienced earthquakes. There was no difference in gender, smoking, drinking, education, income, hypertension, diabetes or dyslipidemia. Compared to those without earthquake experience, there was a higher incidence of depression in the bereaved and non-bereaved groups (12.2% (39/543) and 7.2% (12/98)) (Figure 1).

Association of earthquake experience with depression

Odds ratios (ORs) with 95% confidence intervals (CIs) between earthquake experience and depression are presented in Table 2. Earthquake experience was significantly associated with depression. The adjusted OR of the group that had earthquake experience was 1.83 (OR, 1.83; 95% CI, 1.02-3.29) with respect to that of the group with no earthquake experience. However, when the group with earthquake experience was divided into bereaved and non-bereaved subgroups, a higher risk of depression was found only in the bereaved subgroup. As shown in Table 2, the risk of depression in the bereaved subgroup was 2.82 times (OR, 2.82; 95% CI, 1.24-6.39) that in the group with no earthquake experience.

Subgroup analysis by gender and age during the earthquake

In models stratified by gender, both the bereaved (OR, 3.07; 95% CI, 1.44-6.56) and non-bereaved (OR, 3.51; 95% CI, 1.21-10.16) subgroups were associated with increased risk of depression in female subjects. There were significant associations between the earthquake and depression in females but not

in males (P for interaction=0.02). In models stratified by age at the time of the earthquake, we did not identify any significant interaction between age during the earthquake and depression (*P* for interaction=0.51) (Figure 2).

Discussion

To our knowledge, this is the first study to prove that earthquake survivors have a higher risk of developing depressive symptoms than those who did not experience an earthquake, even 37 years later.

These findings extend the current literature, which largely focuses on short-term follow-up with earthquake survivors. The short-term effects of a disaster on mental health are believed to result from acute stressors, such as frightening and terrible conditions in the immediate aftermath of traumatic exposure[7, 24]. In contrast to short-term effects, the long-term effects following different pathogeneses are referred to as chronic stressors. In most cases, an acute stressor increases the adverse psychological reaction in the short term but abates in the ensuring period, whereas a chronic stressor might result in long-standing psychological disorders[24, 25].

Our study observed the long-term effects of an earthquake on depression among individuals who experienced bereavement, suggesting that a loss of family during the earthquake could lead to chronic stress. Our findings were similar to those obtained in a longitudinal study of an earthquake in Italy with a 7-year follow-up period, which reported that survivors who were exposed to loss and damage had an increased risk of negative psychological consequences than those who merely lived in the

earthquake zone[26]. These findings demonstrated that the adverse consequences induced by an earthquake are long-term risk factors that increase the prevalence of mental disorders.

Many studies have also assessed specific population groups, particularly women and youth, who are more vulnerable to earthquakes. Several studies of earthquakes have shown that these vulnerable populations might be at higher risk of depression[10, 27-29]. Similar results were obtained in the subgroup analysis of gender in our study, which found that female survivors with or without bereavement were more affected by an earthquake even 37 years later. However, in the subgroup analysis of age, the interaction between age during the earthquake and depression was not significant in the current study, which was probably due to the small size of the subgroups.

The results of our study are very relevant to future research on depression in earthquake survivors. For instance, survivors of earthquakes in Japan, Haiti, and China were all affected by high rates of depression in the short term. Although these studies varied in ethnicity, severity of earthquake exposure, consequent degree of damage and demographic characteristics, they had similar general characteristics and traumatic experiences, which could have contributed to long-lasting adverse psychological outcomes.

Our study had a few limitations. First, the study was conducted over a long period, and we were unable to control for every event or factor during the follow-up. For example, we did not consider other traumatic events, such as traffic accidents, economic crises or floods, which might also result in

depression. Additionally, whether the subjects were taking antidepressants was unknown. Finally, depression was assessed only once during the study, and therefore, we could not exclude the possibility of reverse causality. However, it was unlikely that people who experienced an earthquake were more likely to be depressed prior to the earthquake.

This study suggests that the effect of an earthquake on depression remains for 37 years and helps identify individuals who are prone to depression. It should be noted that depression can cause a series of physiological disorders, exacerbate diseases and disabilities, and even result in suicide[11, 30, 31]. Therefore, long-term depression could result in higher prevalence of physical morbidity and mortality. Clinicians and policymakers in public health should pay more attention to survivors who are likely to develop long-term depression because they may obtain benefit from early intervention policies and strategies.

Conclusions

In summary, having experienced an earthquake increases the risk of depression and has long-lasting effects on depression in bereaved survivors, particularly women, after the earthquake. Future studies are required to examine the underlying mechanisms of the association between an earthquake and development of depression in the long term. Survivors of major earthquakes need to be monitored carefully and continuously for mental health symptoms. Early intervention should be considered to prevent the development of depression in these populations.

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Contributors All authors have been involved from the beginning in all phase of the study. XG, YZ and HPH designed the study. XG and YL analyzed the data and prepared the manuscript. JCY, QHC and BG critiqued the manuscript for important intellectual content. XG and YCG conducted the statistical analysis. All authors have read and approved the final version of this manuscript.

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Competing interests None declared.

Patient consent Obtained

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Data sharing statement The data used or analyzed during the current study are available from the corresponding author on reasonable request.

TABLE 1 Baseline characteristics according to earthquake experience

Characteristic	Overall	No experience (n=4383)	Experience without bereavement (n= 543)	Experience with bereavement (n= 98)	*P Value*
Men, No. (%)	2524(50.2)	2210(50.4)	276(50.8)	38(38.8)	.07
Age at the time of the earthquake, mean (SD), y	14.6(9.2)	14.8(9.2)	13.1(9.1)	12.1(9.0)	<.001
Smoking, No. (%)	1286(25.6)	1136(25.9)	132(24.3)	18(18.4)	.18
Drinking, No. (%)	1578(31.4)	1364(31.1)	186(34.3)	28(28.6)	.28
Education, No. (%)					.69
Illiterate/primary school	318(6.3)	279(6.4)	31(5.7)	8(8.2)	
Middle/high school	2704(53.8)	2370(54.1)	282(51.9)	52(53.1)	
University or above	2002(39.9)	1734(39.6)	230(42.4)	38(38.8)	
Income, No. (%)					.13
<=3000	2415(48.1)	2087(47.6)	270(49.7)	58(59.2)	
3001-5000	2278(45.3)	2002(45.7)	243(44.8)	33(33.7)	
>5000	331(6.6)	294(6.7)	30(5.5)	7(7.1)	
Characteristic	**Overall**	**No experience**	**Experience without**	**Experience with**	***P Value***

		(n=4383)	bereavement (n= 543)	bereavement (n= 98)	
Residence in Tangshan 1-2 years after the earthquake, No. (%)	561(11.2)	45(1.0)	431(79.4)	85(86.7)	<.001
Hypertension, No. (%)	2158(43.0)	1872(42.7)	237(43.7)	45(45.9)	.46
Diabetes, No. (%)	550(11.0)	497(11.3)	43(7.9)	10(10.2)	.05
Dyslipidemia, No. (%)	3102(61.7)	2696(61.5)	343(63.2)	63(64.3)	.66
Depression, No. (%)	266(5.3)	215(4.9)	39(7.2)	12(12.2)	<.001

Table 2. Association of Earthquake Experience with Depression

Characteristic	Odds Ratio (95% CI)			
	No experience (n= 4383)	No bereavement (n=543)	Bereavement (n=98)	Experience (n=641)
n (%)	87.2	10.8	2.0	12.8
Unadjusted Models	1	1.42(0.99-2.20)	2.46(1.32-4.59)	1.58(1.14-2.17)
Adjusted Models*	1	1.69(0.93-3.08)	2.82(1.24-6.39)	1.83(1.02-3.29)

* Adjusted ORs are adjusted for gender, age during the earthquake, smoking, drinking, education, income, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidemia

Figure 1. Depression rates for four categories of earthquake experience

Figure 2. Adjusted ORs of earthquake experience for depression stratified by gender and age during the Tangshan earthquake (adjusted for gender, age during the earthquake, marital status, smoking, drinking, education, income, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidemia).

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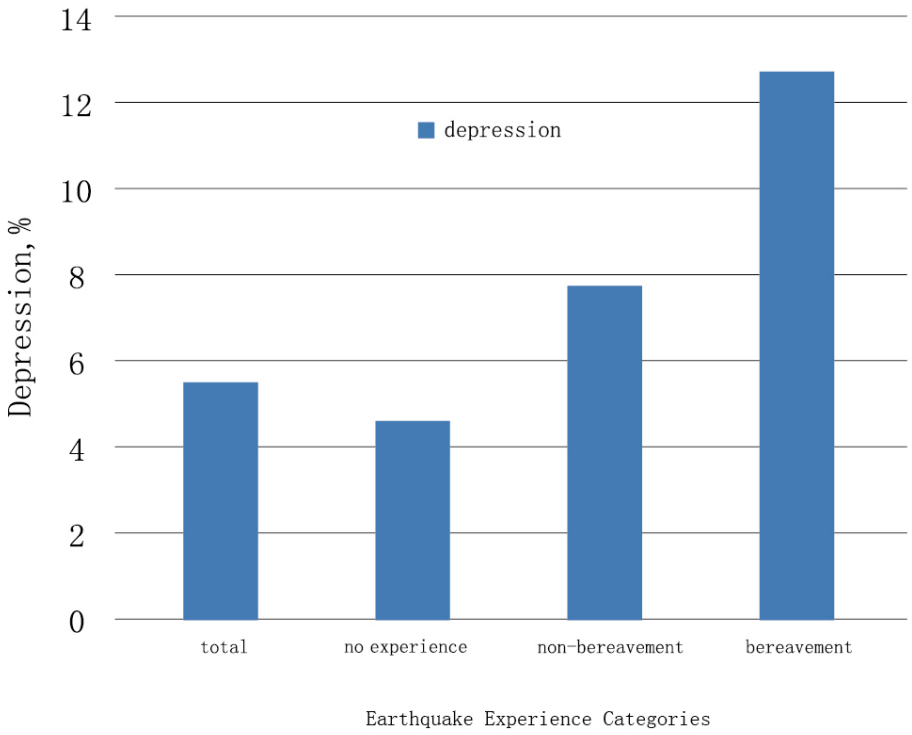

Depression rates for four categories of earthquake experience

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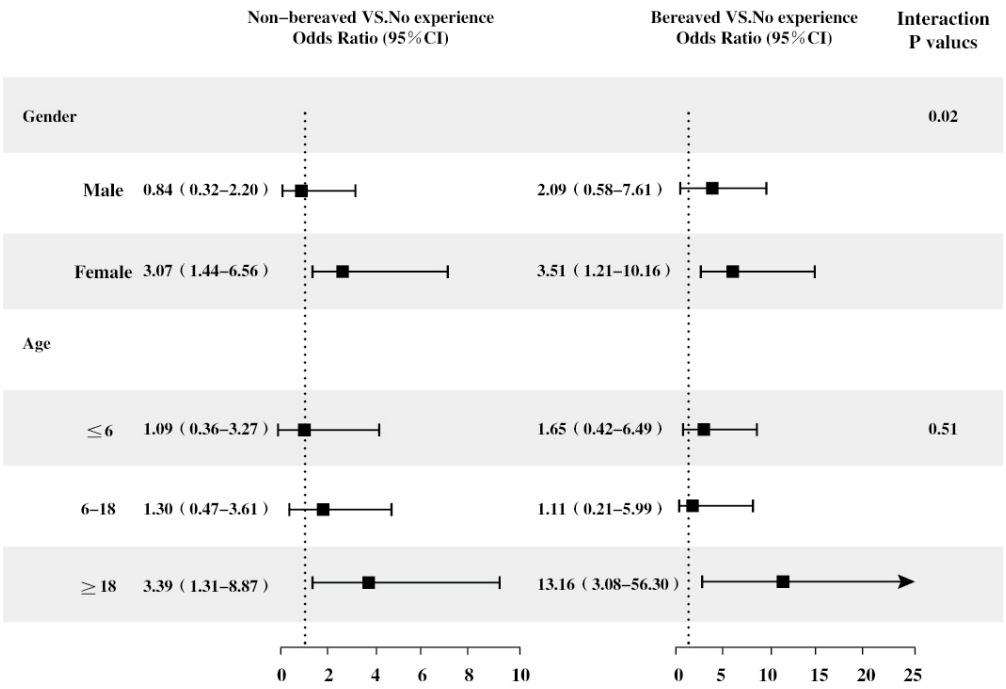

Adjusted ORs of earthquake experience for depression stratified by gender and age during the Tangshan earthquake

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ABSTRACT

Objective To investigate the association between the Tangshan earthquake and the risk of depression after 37 years.

Design and setting A cross-sectional study conducted in Tangshan from 2013 to 2014.

Participants The sample included 5024 participants born before July 28, 1976, when the Tangshan earthquake occurred, with available data on their earthquake experiences and depression 37 years after the earthquake.

Outcomes and variables The outcome was depression measured using the Center for Epidemiological Study and Depression Scale (CES-D). The independent variable was earthquake experience, with 3 groups: no earthquake experience, earthquake experience without bereavement, and earthquake experience with bereavement. Multivariable logistic analysis was used to evaluate the association between earthquake experience and depression after adjusting for gender, age at the time of the earthquake, smoking status, drinking status, education, income, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidemia.

Results Of the 5024 participants, 641 experienced the Tangshan earthquake, and 98 experienced bereavement. Participants who experienced the earthquake (with or without bereavement) had higher prevalence of depression than those without earthquake experience (12.2%, 7.2% vs. 4.9%, respectively), 37 years after the earthquake. Survivors who lost relatives during the earthquake were nearly 3-times (OR 2.82, 95% CI 1.24-6.39) as likely to have depression as those who did not experience the earthquake. A statistically significant association between the earthquake and depression was found in women, but not in men, and in individuals over 18 years of age.

Conclusions Earthquake experience had long-lasting effects on depression among bereaved survivors, women and individuals over 18 years old 37 years later.

Word count: 260

Strengths and limitations of this study

- The study investigated the long-term risk of depression as long as 37 years after a major earthquake.
- Participants were stratified by gender and age at the time of the earthquake.
- We were unable to control for every event or factor, such as adverse childhood experiences, other bereavement or current psychological stressors.
- Individuals who experienced the Tangshan earthquake did not include those who died.

INTRODUCTION

Depression is predicted to be a major reason for disability around the world by 2030 according to the World Health Organization[1]. In addition, the chronic and debilitating nature of depression complicates the prognosis of chronic diseases, aggravates diseases and even leads to suicide[2-4]. Evidence shows that depression is related to demographic characteristics, living habits, education, income, and health status[5-7]. Participants exposed to disasters at early life stage are of higher risk of depression, independent to age, gender, income, education and other confounders in the short term (1-4 years)[8-10]. Meanwhile, studies report that some survivors have psychological problems in the immediate aftermath of disaster trauma, most of these reactions abate over time, and only a minority of survivors develop a long-standing disorder[11 12]. Therefore, long-term evidence is essential to evaluate the effects of disaster on depression.

Findings regarding the long-term impact of disasters on mental health have been mixed. Several studies have reported no differences[13 14], but others have revealed more psychological problems in exposed individuals compared with non-exposed individuals for more than a decade after disasters[10 15 16]. Moreover, evidences show that such effects are increased if survivors suffer from bereavement[10 12] . Overall levels of psychological symptoms may be associated with different age stages[17 18], and women show more psychological symptoms than men[13 19]. However, in these studies, the samples were relative small and not representative of the affected population. One study with a sample of 529 people followed the childhood survivors of natural disasters for 20 years, while depression was not investigated[14].

Our study provides a suitable setting for investigating the long-term effect of disasters on depression. The Tangshan earthquake, which occurred in 1976, had a

magnitude of 7.8 on the Richter scale[20]. The earthquake caused 242,769 deaths and left 164,851 people severely injured, representing the most deadly and the strongest natural disaster in the twentieth century[20]. Over the past 37 years, numerous studies have examined the effects of the Tangshan earthquake on physical health outcomes. These studies report increased risks of diabetes, cardiovascular disease, and elevated levels of uric acid among survivors of the Tangshan earthquake even more than 30 years later[21-23]. However, no study to date has examined the long-term effect of the Tangshan earthquake on the risk of depression.

The aim of our study was to examine the long-term effect of disaster on depression 37 years later. We hypothesized that the earthquake-exposed group would be more likely to exhibit depression. Furthermore, we expected that bereaved survivors would be more likely to experience depression than the non-bereaved. Considering that age and gender may confound the association between earthquake experience and depression, we also performed an analysis stratified by age and gender.

METHODS

Study participants

The participants were selected from the Jidong Cohort, an ongoing community-based prospective study on Chinese adults[24]. In brief, the Jidong community is located in the Caofeidian district of Tangshan City, which is approximately 60 km from the epicenter of the Tangshan earthquake. A clustering sample method was used to select participants. From July 2013 to August 2014, a total of 9078 residents in Jidong community were recruited to participate in the cohort. This cohort has prospectively collected data regarding demographic and behavioral characteristics, insomnia, cognition, depression, and biochemical indicators at annual follow-ups since 2013[25-

[27]. These data were collected using a set of combined self-administered questionnaires (including the Center for Epidemiological Study and Depression Scale (CES-D)) with assistance of well-trained research nurses during face-to-face interviews. Biomedical variables were collected by physical examinations and laboratory assessments. The research field of this cohort has gradually expanded from the initial sub-health to depression, cardiovascular and cerebrovascular and other fields [25-28].

In the current study, we excluded 4054 subjects from the 9078 participants according to the following standards: (1) born after July 28th, 1976 (n=4053), (2) incomplete information on relevant earthquake experience (n=1), and (3) missing values in the surveys for the CES-D measurement scale (n=0). Missing data for confounding variables (60 income variables) were imputed with their mean values among these participants. Finally, a total of 5024 individuals were included in this cross-sectional study. The response rate was 99.99% (5024/5025).

This study was performed according to guidelines from the Helsinki Declaration and approved by the Ethics Committee of Jidong Oilfield Staff Hospital. All participants provided written informed consent.

Assessment of the earthquake experience

The exposure variable of interest was earthquake experience. Earthquake experience and related bereavement were collected from a structured questionnaire. These factors were obtained using the question “Were you in the Tangshan earthquake area in 1976?” and “Did you lose any relatives in the earthquake?”[23] According to the answers to these questions, subjects were classified into 3 groups: no earthquake experience, earthquake experience without bereavement, and earthquake experience with bereavement.

Assessment of current depression

Depressive symptoms were assessed using CES-D, which was initially developed by the United States National Institute of Mental Health in 1977[29]. The Chinese version of the CES-D was translated by two psychiatrists on the basis of the international standard version of the CES-D questionnaire in 1985 and was specifically designed to screen for depression[30]. The CES-D measures the frequency of common depressive symptoms over the past week, which are surveyed through the questionnaire. Each item in the depression assessment section of the questionnaire is scored from 0 (rarely or none of the time, less than one day) to 3 (all of the time, 5–7 days). The four positive statement items (item 4, I felt that I was just as good as other people; item 8, I felt hopeful about the future; item 12, I was happy; item 16, I enjoyed life) are reverse-coded to calculate the total score, which ranges from 0 to 60. The cut-off value of ≥16 has been widely used to define clinically meaningful depressive symptoms[31-33]. All investigators attended a 3-day training course and were licensed before conducting the CES-D interviews.

Assessment of potential covariates

The selected covariates included factors known to be predictive of depression and/or potentially correlated with earthquake exposure, including age at the time of the earthquake, gender, education, income, smoking, drinking, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidemia.

Age at the time of the earthquake was defined as a continuous variable and a categorical variable ("<=6 years", "6-18 years", or ">=18 years"). The average monthly income of each family member was categorized as "<¥3000", "¥3000–5000" or ">¥5,000". Educational level was classified into three categories: "illiterate or

primary school," "middle school or high school," and "university or above." Smoking status was classified as "yes" (current smoker or quit <12 months ago) and "no" (nonsmoker or quit >12 months ago)." Drinking status was divided into "yes" (<1 standard servings/day, <2 standard servings/day, 2-4 standard servings/day, >=5 standard servings/day) and "no" (never drink). A standard serving was 15 g of ethanol. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured twice with the subject in a seated position using a mercury sphygmomanometer. If the difference between the two measurements exceeded 5 mm Hg, an additional reading was taken, and the average of the three readings was used. Hypertension was defined as having a history of hypertension, exhibiting an SBP ≥140 mm Hg or a DPB ≥90 mm Hg, or using antihypertensive medications. The definition of diabetes mellitus was a fasting glucose level ≥7.0 mmol/l (126 mg/dl), current treatment with insulin/oral hypoglycemic agents or a history of diabetes mellitus. Dyslipidemia was defined as having a history of hyperlipidemia, total blood cholesterol levels ≥220 mg/dl, triglyceride levels ≥150 mg/dl, or using anti-hyperlipidemic medications. All measures were current in this cross-sectional study.

Statistical analysis

We first compared the characteristics of individuals according to their earthquake and bereavement experiences (no earthquake experience, earthquake experience without bereavement, and earthquake experience with bereavement) using the chi-square test for categorical variables and one-way ANOVA or the Kruskal–Wallis test for continuous variables.

We used logistic regression to examine the association between earthquake experience and current depression, with "no earthquake experience" as the reference

group. Four multivariate models were fitted as follows: Model 1 was the unadjusted model. Model 2 was adjusted for age at the time of the earthquake and gender. Model 3 was further adjusted for smoking status, drinking status, education, income, residence in Tangshan 1-2 years after the earthquake. Model 4 was further adjusted for hypertension, diabetes, and dyslipidemia.

We also used multiple logistic regression to examine the association stratified by gender and age at the time of the earthquake. To evaluate whether effect of the earthquake on depression would be modified by gender and age at the time of the earthquake, we tested the statistical significance of earthquake × gender and earthquake × age at the time of the earthquake in a multiple-adjustment logistic model by a post-estimation Wald test to obtain an omnibus P-value for the interactions between earthquake categories and depression.

All statistical tests were 2-sided, and results with a P-value <0.05 were considered statistically significant. The analyses were performed in SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Patient and public involvement

Patients and the public were not involved in development of the research question or outcome measures, study design, or recruitment to and conduct of this study. Results will be disseminated to study participants through annual information events.

RESULTS

Characteristics of the study participants

The characteristics of the participants according to earthquake and bereavement experiences are shown in Table 1. In total, 5024 participants were included in this

study, with 50.2% male participants and current ages ranging from 37 to 82 years. Among all participants, 543 (10.8%) individuals experienced the earthquake without bereavement, and 98 (2.0%) participants lost relatives. The individuals who experienced the earthquake with or without bereavement were younger (12.1±9.0, 13.1±9.1 vs. 14.8±9.2 years, respectively) and were more likely to have lived in Tangshan 1-2 years after the earthquake (86.7%, 79.4% vs. 1%, respectively) than those who had not experienced the earthquake. No differences were found in gender, smoking status, drinking status, education, income, hypertension, diabetes or dyslipidemia. A higher incidence of depression was observed in the bereaved and non-bereaved groups (12.2% (39/543) and 7.2% (12/98), respectively) than in those without earthquake experience (4.9% (215/4383)).

Association of earthquake experience with depression

Odds ratios (ORs) with 95% confidence intervals (CIs) for the association between earthquake experience and depression are presented in Table 2. The risk of depression in the bereaved subgroup was 2.82-times (OR, 2.82; 95% CI, 1.24-6.39) higher than that in the group with no earthquake experience, after adjusting for gender, age at the time of the earthquake, smoking status, drinking status, education, income, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidemia. However, no statistically significant association was found in the non-bereaved group.

Subgroup analysis by gender and age during the earthquake

In the models stratified by gender, the female subjects in both the bereaved (OR, 3.07; 95% CI, 1.44-6.56) and non-bereaved (OR, 3.51; 95% CI, 1.21-10.16) subgroups had an increased risk of depression. In the models stratified by age at the time of the

earthquake, we found a statistically significant association in individuals over 18 years with bereavement (OR, 13.16; 95% CI, 3.08-56.3) or without bereavement (OR, 3.39; 95% CI, 1.31-8.87). We also found a statistically significant interaction between gender and depression (*P* for interaction= 0.02), but not significant between age at the time of the earthquake and depression (*P* for interaction= 0.51) (Figure 1).

DISCUSSION

In the community-based study, we observed that earthquake survivors had a higher risk of depression than those who did not experience an earthquake even 37 years later. In addition, long-term effects of an earthquake on depression were found among survivors with bereavement, women and individuals over 18 years. This is the first study to investigate the association between earthquake experience and depression as long as 37 years after an earthquake.

Consistent with our findings, a longitudinal study on the Alexander Kiedand oil platform collapse shows that survivors have a higher risk of depression than non-exposed individuals 27 years after the disaster[15]. Similar results are observed in another longitudinal study with 10 years of follow-up, which indicates that survivors of the Piper Alpha oil platform disaster show continued problems of mental health compared with non-exposed individuals[16]. In contrast, some previous studies report no significant differences between exposed population and non-exposed population in mental health[13 14]. The inconsistent results may be explained by 3 reasons. First, subclinical psychotic experiences (SPE) and depression reflect different aspects of psychological problems. SPE is defined as symptoms or experiences of or experiences resembling hallucinations, delusions or both[34], whereas depressive disorder is characterized by sadness or irritability[35]. Differences in symptoms may explain why

our findings differ from the results of the 20-year follow-up study of Australian bush fires. Second, psychological problems may depend on the severity of a trauma. For example, Galletly C et al reported that the risk of psychological disorder is associated with multiple traumas rather than a single major trauma[14]. Third, the trauma experiences of the participants in these studies are different. In the study on Buffalo Creek survivors, few survivors suffer from bereavement[13], which is different from the survivors in our study. Different characteristics of trauma experiences between the two studies may account for the discrepancy.

The long-term effect of disaster on depression seems to depend on traumatic experience. In our study, a statistically significant association between earthquake experience and depression was observed in bereaved survivors but not in non-bereaved survivors 37 years after the earthquake. The finding was consistent with a longitudinal study carried out in Italian, which shows that exposure to loss and damage during the earthquake is of higher risk of negative psychological consequences than these merely live in the earthquake zone[10]. Similarly, a longitudinal study on MS Estonia Disaster indicates that psychological disorders can persist in bereaved survivors but not in non-bereaved survivors 14 years after the disaster[12]. Traumatic bereavement may be associated with more severe long-term posttraumatic stress reactions after disasters[36], which is considered to be involved in the onset of depression[4].

Several plausible explanations may link earthquake exposure to the prevalence of depressive symptoms. Earthquakes can cause tremendous, immediate damage to the environment and even lead to adverse life events such as the death of a family member and related events, thus exerting negative effects on individuals' emotions and resulting in long-term posttraumatic stress reactions after the disaster[4 12]. Long-

term posttraumatic stress reactions may affect neurobiological adjustments, which have been linked to several brain areas (the frontolimbic and striatal areas) [36 37]. These areas and the functional connectivities located within the fronto-striato-thalamic and default-mode networks have been found to be correlated with progression of depressive symptom and may play important roles in adaptation to trauma[4 38].

Gender, age at the time of the earthquake, education, income, smoking, drinking, living in the affected area after a disaster, hypertension, diabetes and dyslipdemia were controlled in the multiple variable analysis. To avoid over-adjustment, four models were used to adjust confounding variables step by step. The resulting ORs reflected minor changes in the 4 models, suggesting that earthquake experience may be an independent risk factor for the occurrence of depression.

Evidence shows that trauma experience in childhood and adolescence may have a determining effect on brain structural development, sympathetic nervous system responsivity, and the hypothalamic pituitary adrenal axis, especially in younger children (preschool) and school-age children (late childhood and early adolescence), resulting in a large stress response and some psychological problems[18]. Therefore, we classified age into 0-6, 6-18 and older than 18 years to investigate the long-term impact of disaster on mental health at different age stages. However, statistically significant associations were found only in individuals over 18 years. One possible explanation is that perception of disaster-related stressors in the <=6 and 6-18 years age groups is different from that in the >18 years age group. Disaster trauma as a stressor is not sufficient to promote mental illness among individuals at the ages of 0-6 and 6-18 years. A preschool child has less specific cognitive awareness of the nature and meaning of disaster trauma[39]. Although a school-age child has a more mature cognitive understanding of the nature of a trauma situation and may respond with

symptoms related to depression, parental care and family play important roles in determining the risk of psychological disorder among school-age children[40]. We also found a long-term effect of earthquake experience on depression in women. Similar results have been found in several previous studies of disaster, indicating that women may be at a higher risk of depression than men[13 19].

Our study had a few limitations. First, substantial time has passed since the earthquake occurred, and we were unable to control for every event or factor. For example, we did not consider other traumatic events, such as traffic accidents, adverse childhood experiences, other bereavement or current psychological stressors, which could have confounded the observed associations. Additionally, the sample was not representative of all survivors of the Tangshan earthquake. We did not include survivors who had died in the past 37 years. Premature death may be related to depression and disease. Meanwhile, in our sample, nearly 20% of the survivors did not live in the earthquake zone 1-2 years after the earthquake. These people left the painful environment and may have attended school or worked in another place for several years, which may have largely relieved psychological stress and alleviated the symptoms of depression. Therefore, the potential impacts of the earthquake on depression may have been underestimated. Third, whether the subjects were taking antidepressants was unknown. Fourth, this is a cross-sectional study, which precludes causal inferences. However, since the earthquake is immutable, the earthquake is likely to be the cause of depression. Finally, depression was assessed only once during the study; therefore, we could not exclude the possibility of reverse causality.

The results of our study are very relevant to future research on depression among disaster survivors. For instance, survivors of earthquakes in Japan, Haiti, and China were all affected by high rates of depression in the short term[41-44]. Although the time

and severity of a disaster, the ethnicity of the affected population, and the growing environment are different, the stressors caused by disasters ar similar. Intervention is highly effective in facilitating recovery from disaster trauma[45 46] . Clinicians and policymakers in public health should direct more attention toward high-risk survivors of disasters, which may reduce the incidence of mental health problems, including depression, in disaster zones[47], even if the disaster has passed for a long time.

CONCLUSIONS

Earthquake experience had long-lasting effects on depression among bereaved survivors, women and individuals over 18 years 37 years later. Our study provides evidence supporting the hypothesis that the effect of an earthquake on depression persists for 37 years.

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Contributors All authors have been involved from the beginning in all phases of the study. XG, YZ and HPH designed the study. XG and YL analyzed the data and prepared the manuscript. JCY, QHC and BG critiqued the manuscript for important intellectual content. XG and YCG conducted the statistical analysis. All authors have read and approved the final version of this manuscript.

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Competing interests None declared.

Ethics approval The research was approved by the Ethics Committee of Jidong Oilfield Staff Hospital.

Data sharing statement The data used or analyzed during the current study are available from the corresponding author upon reasonable request.

Table 1 Population characteristics according to earthquake experience

Characteristics	Overall	No experience (n=4383)	Experience without bereavement (n=543)	Experience with loss of family (n=98)	*P-value*
Men, n (%)	2524 (50.2)	2210 (50.4)	276 (50.8)	38 (38.8)	0.07
Age at the time of the earthquake, mean (SD)	14.6±9.2	14.8±9.2	13.1±9.1	12.1±9.0	<0.0001
=<6	1063 (21.2)	880 (20.08)	146 (26.89)	37 (37.76)	<.0001
6-18	2053 (40.9)	1796 (40.98)	226 (41.62)	31 (31.63)	
>=18	1908 (38.0)	1707 (38.95)	171 (31.49)	30 (30.61)	
Smoking, n (%)	1286 (25.6)	1136 (25.9)	132 (24.3)	18 (18.4)	0.18
Drinking, n (%)	1578 (31.4)	1364 (31.1)	186 (34.3)	28 (28.6)	0.28
Education, n (%)					0.69
Illiteracy/primary	318 (6.3)	279 (6.4)	31 (5.7)	8 (8.2)	

Middle school/High school	2704 (53.8)	2370 (54.1)	282 (51.9)	52 (53.1)	
University or above	2002 (39.9)	1734 (39.6)	230 (42.4)	38 (38.8)	
Income, n (%)					0.13
<=3000	2415 (48.1)	2087 (47.6)	270 (49.7)	58 (59.2)	
3001-5000	2278 (45.3)	2002 (45.7)	243 (44.8)	33 (33.7)	
>5000	331 (6.6)	294 (6.7)	30 (5.5)	7 (7.1)	
Residence in Tangshan 1-2 years after the earthquake, n (%)	561 (11.2)	45 (1.0)	431 (79.4)	85 (86.7)	<0.0001
Hypertension, n (%)	2158 (43.0)	1872 (42.7)	237 (43.7)	45 (45.9)	0.46
Diabetes, n (%)	550 (11.0)	497 (11.3)	43 (7.9)	10 (10.2)	0.05
Dyslipidemia, n (%)	3102 (61.7)	2696 (61.5)	343 (63.2)	63 (64.3)	0.66
Depression, n (%)	266 (5.3)	215 (4.9)	39 (7.2)	12 (12.2)	0.0007

Table 2. Odds ratios for the association between earthquake experience and depression

	no earthquake experience (n=4383, 87.2%)	experience without bereavement (n=543, 10.8%)	experience with bereavement (n=98, 2.0%)
Model 1	1	1.42 (0.99-2.20)	2.46 (1.32-4.59)
Model 2	1	1.43 (1.01-2.04)	2.50 (1.34-4.68)
Model 3	1	1.61 (0.88 -2.95)	2.88 (1.26 -6.57)
Model 4	1	1.69 (0.93 -3.08)	2.82 (1.24 -6.39)

Model 1 refers to the unadjusted model.

Model 2 refers to the model adjusted for gender and age at the time of the earthquake.

Model 3 refers to the model adjusted for gender, age at the time of the earthquake, smoking status, drinking status, education, income, and residence in Tangshan 1-2 years after the earthquake.

Model 4 refers to the model adjusted for gender, age at the time of the earthquake, smoking status, drinking status, education, income, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidemia.

Figure 1 Odds Ratio of earthquake experience for depression stratified by gender and age at the time of the earthquake.

Adjusted for gender, age at the time of the earthquake, smoking status, drinking status, education, income, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidemia.

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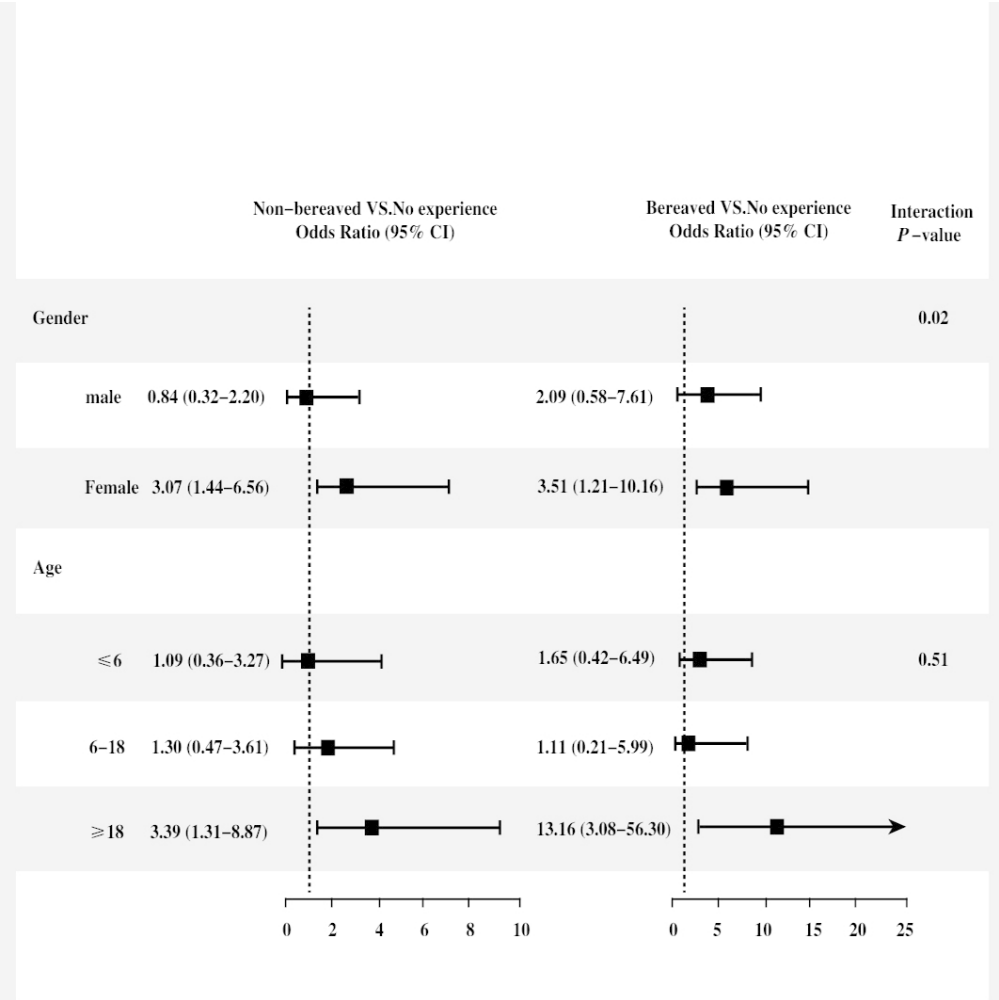

Figure 1 Odds Ratio of earthquake experience for depression stratified by gender and age at the time of the earthquake.
Adjusted for gender, age at the time of the earthquake, smoking status, drinking status, education, income, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidemia.

90x90mm (300 x 300 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1	Line 1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3-4	Line 44-69
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6-7	Line 81-112
Objectives	3	State specific objectives, including any prespecified hypotheses	7	Line 113-118
Methods				
Study design	4	Present key elements of study design early in the paper	8	Line 141-142
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-8	Line 122-135
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	8	Line 136-142
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-10	Line 148-195
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8-9	Line 148-169
Bias	9	Describe any efforts to address potential sources of bias	11	Line 203-209
Study size	10	Explain how the study size was arrived at	8	Line 136-142

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10	Line 198-202
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10-11	Line 198-219
		(*b*) Describe any methods used to examine subgroups and interactions	11	Line 210-216
		(*c*) Explain how missing data were addressed	8	Line 137-141
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	7	Line 125-126
		(*e*) Describe any sensitivity analyses		NA
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11-12	Line 229-232
		(b) Give reasons for non-participation at each stage	8	Line 136-142
		(c) Consider use of a flow diagram		NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11-12	Line 228-240,Table 1
		(b) Indicate number of participants with missing data for each variable of interest	8	Line 137-141
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)		NA
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time		
		Case-control study—Report numbers in each exposure category, or summary measures of exposure		
		Cross-sectional study—Report numbers of outcome events or summary measures	12	Line 238-240
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12-13	Line 243-249, Table 2
		(*b*) Report category boundaries when continuous variables were categorized	9	Line 176-179, Table 1
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period		NA

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12-13	Line 252-259
Discussion				
Key results	18	Summarise key results with reference to study objectives	13	Line 262-267
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16	Line 335-351
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-17	Line 268-360
Generalisability	21	Discuss the generalisability (external validity) of the study results	16	Line 339-347
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	18	Line 377-380

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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The Association between Earthquake Experience and Depression 37 Years after the Tangshan Earthquake: A Cross-sectional Study

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The Association between Earthquake Experience and Depression 37 Years after the Tangshan Earthquake: A Cross-sectional Study

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Word count: 3611

ABSTRACT

Objective To investigate the association between the Tangshan earthquake and the risk of depression after 37 years.

Design and setting A cross-sectional study conducted in Tangshan from 2013 to 2014.

Participants The sample included 5024 participants born before July 28, 1976, the date of the Tangshan earthquake, with available data on their earthquake experiences and depression 37 years after the earthquake.

Outcomes and variables The outcome was depression measured using the Center for Epidemiological Study and Depression Scale (CES-D). The independent variable was earthquake experience, which was classified into 3 groups: no earthquake experience, earthquake experience without bereavement, and earthquake experience with bereavement. Multivariable logistic regression analysis was used to evaluate the association between earthquake experience and depression after adjusting for gender, age at the time of the earthquake, smoking status, drinking status, education, income, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidaemia.

Results Of the 5024 participants, 641 had experienced the Tangshan earthquake, and 98 had experienced bereavement due to the earthquake. As of 37 years after the earthquake, participants who had experienced the earthquake (with or without bereavement) had a higher prevalence of depression than those without earthquake experience (12.2%, 7.2% vs. 4.9%, respectively). Survivors who had lost relatives during the earthquake were nearly 3 times (odds ratio 2.82, 95% confidence interval 1.24-6.39) as likely to have depression as those who had not experienced the earthquake. A statistically significant association between the earthquake and

depression was found in women but not men and in individuals who were over 18 years of age at the time of the earthquake.

Conclusions Thirty-seven years after the Tangshan earthquake, earthquake experience was associated with depression among bereaved survivors, women and individuals over 18 years old at the time.

Word count:290

Strengths and limitations of this study

- The study investigated the long-term risk of depression 37 years after a major earthquake.
- Participants were stratified by gender and age at the time of the earthquake.
- We were unable to control for every event or factor, such as adverse childhood experiences, other bereavement or current psychological stressors.
- Only participants who were still alive 37 years after the earthquake were able to participate in the study.

INTRODUCTION

Depression is predicted to be a major reason for disability around the world by 2030, according to the World Health Organization[1]. In addition, the chronic and debilitating nature of depression complicates the prognosis of chronic diseases, aggravates various diseases and may lead to suicide[2-4]. Evidence shows that depression is related to demographic characteristics, living habits, education, income, and health status[5-7]. Participants exposed to disasters at an early life stage are at an increased risk of depression in the short term (1-4 years), independent of age, gender, income, education and other confounders[8-10]. Additionally, studies report that some survivors have psychological problems in the immediate aftermath of disaster trauma; most of these reactions abate over time, and only a minority of survivors develop a long-standing disorder[11 12]. Therefore, long-term evidence is essential to evaluate the effects of disaster on depression.

Findings regarding the long-term impact of disasters on mental health have been mixed. Several studies have reported no significant differences[13 14], but others have revealed more psychological problems in exposed individuals than in non-exposed individuals for more than a decade after disasters[10 15 16]. Moreover, evidence shows that such effects are increased if survivors suffer from bereavement[10 12]. Additionally, the association between earthquakes and depression may vary according to age or gender. Studies indicate that overall levels of psychological symptoms may vary among children, adolescents, and adults due to differences in physiology and cognition[17 18].In response to disaster, women appear develop more intense and longer-lasting psychological symptoms than men[13 19]. However, very few of these studies investigated the long-term effect of earthquakes on depression risk in the Chinese population.

Our study provides a suitable setting for investigating the long-term impact of earthquakes on depression in the Chinese population. The Tangshan earthquake, which occurred in 1976, had a magnitude of 7.8 on the Richter scale[20]. The earthquake caused 242,769 deaths and left 164,851 people severely injured, representing the strongest and deadliest natural disaster in the twentieth century[20].Since the earthquake, numerous studies have examined the effects of the event on physical health outcomes. These studies report increased risks of diabetes, cardiovascular disease, and elevated levels of uric acid among survivors of the Tangshan earthquake even at timepoints more than 30 years later[21-23]. However, no study to date has examined the long-term effect of the Tangshan earthquake on the risk of depression.

The aim of our study was to examine the long-term effect of disaster on depression 37 years later. We hypothesized that the earthquake-exposed group would be more likely than the non-exposed group to exhibit depression. Furthermore, we expected that bereaved survivors would be more likely to experience depression than non-bereaved survivors. Considering that age and gender may confound the association between earthquake experience and depression, we also performed an analysis stratified by age and gender.

METHODS

Study participants

The participants were selected from the Jidong Cohort, an ongoing community-based prospective study in Chinese adults[24]. The Jidong community is located in the Caofeidian district of Tangshan City, which is approximately 60 km from the epicentre of the Tangshan earthquake. Cluster sampling was used to select

participants. From July 2013 to August 2014, a total of 9078 residents in the Jidong community were recruited to participate in the cohort. Data regarding demographic and behavioural characteristics, insomnia, cognition, depression, and biochemical indicators have been collected from this cohort at annual follow-ups since 2013[25-27].These data were collected using a set of self-administered questionnaires (including the Center for Epidemiological Study and Depression Scale (CES-D)) with the assistance of well-trained research nurses during face-to-face interviews. Biomedical variables were collected by physical examinations and laboratory assessments. Research on this cohort originally examined sub-health and later expanded to examine depression, cardiovascular health, cerebrovascular health and other areas[25-28].

In the current study, we excluded 4054 of the 9078 candidate participants according to the following standards: (1) birth date after July 28th, 1976 (n=4053); (2) incomplete information on relevant earthquake experience (n=1);and (3) missing values in the surveys for the CES-D measurement scale (n=0). Missing data for confounding variables (60 income variables) were imputed with their mean values among these participants. Ultimately, a total of 5024 individuals were included in this cross-sectional study. The participants in the Jidong Cohort are subjected to a physical examination annually, which is paid for by the community. Therefore, the response rate was almost 100%(5024/5025).

This study was performed according to guidelines from the Declaration of Helsinki and approved by the Ethics Committee of Jidong Oilfield Staff Hospital. All participants provided written informed consent.

Assessment of earthquake experience

The exposure variable of interest was experience with the earthquake. Earthquake experience and related bereavement were collected through a structured questionnaire. These factors were obtained using the following questions: "Were you in the Tangshan earthquake area in 1976?" and "Did you lose any relatives in the earthquake?"[23]According to the answers to these questions, subjects were classified into 3 groups: no earthquake experience, earthquake experience without bereavement, and earthquake experience with bereavement.

Assessment of current depression

Depressive symptoms were assessed using the CES-D, which was initially developed by the United States National Institute of Mental Health in 1977[29]. The Chinese version of the CES-D was translated from the international standard version of the CES-D questionnaire in 1985 by two psychiatrists and was specifically designed to screen for depression[30].The CES-D questionnaire surveys the frequency of common depressive symptoms over the past week. Each item in the depression assessment section of the questionnaire is scored from 0 (rarely or none of the time, less than one day) to 3 (all of the time, 5–7 days). The four positive statement items (item 4, I felt that I was just as good as other people; item 8, I felt hopeful about the future; item 12, I was happy; item 16, I enjoyed life) are reverse coded to calculate the total score, which ranges from 0 to 60. A cut-off value of ≥16 has been widely used to define clinically meaningful depressive symptoms[31-33]. All investigators attended a 3-day training course and were licensed before conducting the CES-D interviews.

Assessment of potential covariates

The selected covariates included factors known to be predictive of depression and/or

potentially correlated with earthquake exposure, including age at the time of the earthquake, gender, education, income, smoking status, drinking status, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidaemia. Age at the time of the earthquake was defined as a continuous variable and then a categorical variable ("≤6 years", "6-18 years", or "≥18 years"). The average monthly income of each family member was categorized as "<¥3000", "¥3000–5000" or ">¥5,000". Educational level was classified into three categories: "illiteracy or primary school," "middle school or high school," and "university or above." Residence in Tangshan 1-2 years after the earthquake was classified as "yes" and "no". Smoking status was classified as "yes" (current smoker or quit<12 months ago) and "no" (nonsmoker or quit>12 months ago)." Drinking status was divided into "yes" (current drinking <1 standard servings/day, <2 standard servings/day, 2-4 standard servings/day, ≥5 standard servings/day) and "no" (never drank, drank in the past).A standard serving was defined as15 g of ethanol. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured twice using a mercury sphygmomanometer with the subject in a seated position. If the difference between the two measurements exceeded 5 mm Hg, an additional reading was taken, and the average of the three readings was used. Hypertension was defined as having a history of hypertension, exhibiting an SBP ≥140 mm Hg or a DBP≥90 mm Hg, or using antihypertensive medications. The definition of diabetes mellitus was a fasting glucose level ≥7.0 mmol/l (126 mg/dl), current treatment with insulin/oral hypoglycaemic agents or a history of diabetes mellitus. Dyslipidaemia was defined as a history of hyperlipidaemia, a total blood cholesterol level ≥220 mg/dl, a triglyceride level≥150 mg/dl, or use of anti-hyperlipidaemic medications. All measures in this cross-sectional study reflected the current values as of data collection.

Statistical analysis

We first compared the characteristics of individuals according to their earthquake and bereavement experiences (no earthquake experience, earthquake experience without bereavement, and earthquake experience with bereavement) using the chi-squared test for categorical variables and one-way ANOVA or the Kruskal–Wallis test for continuous variables.

We used logistic regression to examine the association between earthquake experience and current depression, with "no earthquake experience" as the reference group. Four multivariate models were fitted as follows: Model 1 was the unadjusted model. Model 2 was adjusted for age at the time of the earthquake and gender. Model 3 was further adjusted for smoking status, drinking status, education, income, and residence in Tangshan 1-2 years after the earthquake. Model 4 was further adjusted for hypertension, diabetes, and dyslipidaemia.

We also used multiple logistic regression to examine the association stratified by gender and age at the time of the earthquake. To evaluate whether the effect of the earthquake on depression would be modified by gender and/or age at the time of the earthquake, we tested the statistical significance of earthquake × gender and earthquake × age at the time of the earthquake as interaction effects in a multiple-adjustment logistic model by applying a post-estimation Wald test to obtain an omnibus P-value for the interactions between earthquake categories and depression.

All statistical tests were 2-sided, and results with a P-value<0.05 were considered statistically significant. The analyses were performed in SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Patient and public involvement

Patients and the public were not involved in the development of the research question or outcome measures, study design, recruitment, or conduct of the study. The results will be disseminated to study participants through annual information events.

RESULTS

Characteristics of the study participants

The characteristics of the participants according to earthquake and bereavement experiences are shown in Table 1. In total, 5024 participants were included in this study; the participants were 50.2% male and ranged in age from 37 to 82 years at the time of data collection. Among all participants, 543 (10.8%) individuals experienced the earthquake without bereavement, and 98 (2.0%) participants lost relatives. The individuals who experienced the earthquake with or without bereavement were younger and were more likely to have lived in Tangshan 1-2 years after the earthquake than those who had not experienced the earthquake(12.1±9.0, 13.1±9.1,and 14.8±9.2 years, respectively, for age;86.7%, 79.4%, and 1%, respectively, for residence). No differences were found in gender, smoking status, drinking status, education, income, hypertension, diabetes or dyslipidaemia. A higher incidence of depression was observed in the bereaved and non-bereaved earthquake survivors(12.2% (39/543) and 7.2% (12/98), respectively) than in those without earthquake experience (4.9% (215/4383)).

Association between earthquake experience and depression

Odds ratios (ORs) and 95% confidence intervals (CIs) for the association between earthquake experience and depression are presented in Table 2.The risk of depression

in the bereaved subgroup was 2.82 times (OR, 2.82; 95% CI, 1.24-6.39) higher than that in the group with no earthquake experience after adjusting for gender, age at the time of the earthquake, smoking status, drinking status, education, income, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidaemia. However, no statistically significant association was found in the non-bereaved group.

Subgroup analysis by gender and age as of the earthquake

In the models stratified by gender, the female subjects in both the bereaved (OR, 3.51; 95% CI, 1.21-10.16) and non-bereaved (OR, 3.07; 95% CI, 1.44-6.56) subgroups had an increased risk of depression. In contrast, no significant association was found between earthquake experience and the risk of depression among male subjects in either the bereaved (OR, 2.09; 95% CI, 0.58-7.61) or the non-bereaved (OR, 0.84; 95% CI, 0.32-2.20) subgroup. In the models stratified by age at the time of the earthquake, we found a statistically significant association in individuals over 18 years old whether they had lost relatives in the earthquake (OR, 13.16; 95% CI, 3.08-56.3) or not (OR, 3.39; 95% CI, 1.31-8.87).No statistically significant association was found in survivors under 6 years old whether they had been bereaved (OR, 1.65; 95% CI, 0.42-6.49) or not (OR, 1.09; 95% CI, 0.36-3.27), and there was also no significant association in survivors aged between 6 and 18 years whether they had lost relatives (OR, 1.11; 95% CI, 0.21-5.99) or not (OR, 1.30; 95% CI, 0.47-3.61). In addition, we found a statistically significant interaction between gender and depression *(P* for interaction= 0.02) but no significant interaction between age at the time of the earthquake and depression (*P* for interaction= 0.51) (Figure 1).

DISCUSSION

In this community-based study, we observed that, even after 37 years, earthquake survivors had a higher risk of depression than those who had not experienced the earthquake. In addition, long-term effects of the earthquake on depression were found among bereaved survivors, women and individuals over 18 years old. This study is the first to investigate the association between earthquake experience and depression 37 years after an earthquake.

Evidence shows that traumatic experiences in childhood and adolescence may have a determining effect on brain structural development, sympathetic nervous system responsivity, and the hypothalamic–pituitary–adrenal axis, especially in younger children (preschool) and school-age children (late childhood and early adolescence), resulting in a large stress response and some psychological problems[18]. Therefore, we classified the participants into age categories of 0-6, 6-18 and older than 18 years to investigate the long-term impact of disaster on mental health during different stages of life. However, statistically significant associations were found only in individuals over 18 years of age. One explanation is that different ages have different needs for social networks. Social networking is associated with the onset of depression[34]. Children's and adolescents' social needs are met by parental care and family[35]. Adults, in contrast, need support from social interaction in the neighbourhood, the communities, and the work place in addition to family support [36]. The advent of the earthquake destroyed the previously stable social networks and economic foundation of the community. Social-network destruction may lead to some mental health disorders. Additionally, survivors under 18 years old recover from disaster more easily than older survivors do. Insensitivity to the nature and meaning of disaster trauma[37]and access to mental health intervention in the early postdisaster stages[38] may

contribute to recovery from psychological problems among child and adolescent survivors.

With regard to gender, we found a significant association between earthquake experience and depression in females but not in males. Similar results have been found in several previous studies of disaster, indicating that women may be at a higher risk of depression than men[13 19].One explanation of this gender difference is that men tend to externalize stress, while women tend to internalize it[39]. Thus, of the two genders, women have higher rates of anxiety and depression (internalizing disorders), and men have higher rates of substance abuse (externalizing disorders)[40]. Additionally, difference may be related to the culturally taught goals and roles of men and women in society and the family. Men are required to have innate masculinity and strength, while women are required to show empathy and tender-mindedness[41 42]. Consequently, in the face of disasters, men are more stress-resistant than women and recover more quickly. Women are more likely than men to be sentimental than men[43 44]. Once women fall into deep emotional pain, it is difficult for them to extricate themselves[45]. We also found that, in female, the risk of depression was 3 times higher in the group with earthquake experience group than in the group without. One interpretation of this finding is that there are some components of earthquake-related aftermath that weaken women's psychological defence mechanisms. Evidence show that women are more likely than men to carry out rumination[46],which is characterized by continuous and repetitive thinking about painful memories[47]. When fear memories of earthquake-related morbidity, mortality, and destruction constantly resurface, women who have experienced earthquake face long-lasting emotional pain that can lead to depression.

Consistent with our findings, a longitudinal study on the Alexander Kielland oil platform collapse shows that survivors have a higher risk of depression than non-exposed individuals 27 years after the disaster[15]. Similar results are observed in another longitudinal study with 10 years of follow-up, which indicates that survivors of the Piper Alpha oil platform disaster show a long-lasting increase in mental health problems compared with non-exposed individuals[16]. In contrast, two studies indicate that disaster has little long-term effect on depression[13 14]. The inconsistency of the results may be explained by the severity of the disaster. The Tangshan earthquake caused more damage than the Buffalo Creek dam collapse or the Australian bushfire disaster. The earthquake reduced Tangshan to ruins in a few minutes, with approximately 85% of the buildings collapsed and at least 400,000 casualties[20 48]. The earthquake afflicted the survivors with not only the loss of their homes but also, more importantly, the tension and fear brought by the disaster itself, the loss of loved ones, the complete destruction of social networks and a sense of despair [49 50]. During the long-term urban reconstruction process, all these effects of the disaster might lead to long-term adverse psychological effects on the survivors. In addition, the Tangshan earthquake broke out at the end of the decade of the Cultural Revolution. The consequences of the Cultural Revolution, which include a fragile economic foundation, low economic compensation, lack of societal acknowledgement, and destruction of the health care service network, may have delayed recovery.

The long-term effect of disaster on depression seems to depend on traumatic experience. In our study, a statistically significant association between earthquake experience and depression was observed in bereaved survivors but not in non-bereaved survivors 37 years after the earthquake. This finding was consistent with a longitudinal study carried out in Italy showing that exposure to loss and

damage during an earthquake confers an additional risk of negative psychological consequences above and beyond living in the earthquake zone[10]. Similarly, a longitudinal study 14 years after MS Estonia Disaster indicated that non-bereaved survivors recovered from their posttraumatic stress reactions, while little change was found over that period in the reaction of the bereaved[12].Traumatic bereavement may be associated with increased severity of long-term posttraumatic stress reactions after disasters[51], which is considered to be involved in the onset of depression[4].

Several plausible explanations may link earthquake exposure to the prevalence of depressive symptoms. Earthquakes can cause tremendous, immediate damage to the environment and even lead to adverse life events such as the death of a family member and related events, thus exerting negative effects on individuals' emotions and resulting in posttraumatic stress disorder (PTSD) after the disaster[4 12]. PTSD, as a frequent comorbidity of depression[52 53], may persist for decades following disaster[54-56]. These findings suggest that traumatic bereavement might be a common mediating mechanism of both depression and PTSD. The pain of loss in survivors may have neurobiological effects on several brain areas (the frontolimbic and striatalareas)[51 57]. These areas and the functional connectivity within the fronto-striato-thalamic and default-mode networks have been found to be correlated with the progression of mental health problems and may play important roles in adaptation to trauma[4 58]. The trauma caused by disasters has a variety of mechanisms. Whether PTSD symptoms further transform into depression or other mental illnesses in the long term will require further exploration.

Gender, age at the time of the earthquake, education, income, smoking, drinking, living in the affected area after a disaster, hypertension, diabetes and dyslipidaemia were controlled in the multiple variable analysis. To avoid overfitting, we used four

models to adjust confounding variables step by step. The resulting ORs reflected minor changes in the 4 models, suggesting that earthquake experience may be an independent risk factor for the occurrence of depression.

Our study has a few limitations. First, substantial time has passed since the earthquake occurred, and we were unable to control for every event or factor. For example, we did not consider other traumatic events, such as traffic accidents, adverse childhood experiences, other bereavement or current psychological stressors, which could have confounded the observed associations. Additionally, the sample was not representative of all survivors of the Tangshan earthquake. We did not include survivors who had died in the past 37 years. Premature death may be related to depression and disease. Meanwhile, in our sample, nearly 20% of the survivors did not live in the earthquake zone 1-2 years after the earthquake. These people left the painful environment and may have worked or attended school elsewhere for several years, which may have largely relieved psychological stress and alleviated the symptoms of depression. Therefore, the potential impacts of the earthquake on depression may have been underestimated. Third, whether the subjects were taking antidepressants was unknown. Fourth, the cross-sectional design of this study precludes causal inferences. Finally, depression was assessed only once during the study; therefore, we could not exclude the possibility of reverse causality.

The results of our study are very relevant to future research on depression among disaster survivors. For instance, survivors of earthquakes in Japan, Haiti, and China were all affected by high rates of depression in the short term[59-62]. Although the timing and severity of the disasters, the ethnicity of the affected population, and the living environment of the survivors are different, the stressors caused by disasters are similar. Strengthening community social cohesion can facilitate recovery from

disaster trauma[63 64].Clinicians and policymakers in public health should direct additional early social support towards high-risk survivors of disasters, a measure that may reduce the incidence of mental health problems, including depression, in disaster zones[65], even long after the disaster has passed.

CONCLUSIONS

Thirty-seven years after the disasters, earthquake experience was associated with depression among bereaved survivors, women and individuals over 18 years old at the time. Our study provides evidence supporting the hypothesis that the effect of an earthquake on depression persists for at least 37 years.

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Contributors All authors were involved from the beginning in all phases of the study. XG, YZ and HPH designed the study. XG and YL analysed the data and prepared the manuscript. JCY, QHC and BG critiqued the manuscript for important intellectual content. XG and YCG conducted the statistical analysis. All authors have read and approved the final version of this manuscript.

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Table 1 Population characteristics according to earthquake experience

Characteristics	Overall	No experience (n=4383)	Experience without bereavement (n=543)	Experience with Bereavement (n=98)	*P-value*
Men, n (%)	2524(50.2)	2210(50.4)	276(50.8)	38(38.8)	0.071
Age at the time of the earthquake, mean (SD)	14.6±9.2	14.8±9.2	13.1±9.1	12.1±9.0	<0.001
≤6	1063(21.2)	880(20.08)	146(26.89)	37(37.76)	<0.001
6-18	2053(40.9)	1796(40.98)	226(41.62)	31(31.63)	
≥18	1908(38.0)	1707(38.95)	171(31.49)	30(30.61)	
Smoking, n (%)	1286(25.6)	1136(25.9)	132(24.3)	18(18.4)	0.182
Drinking, n (%)	1578(31.4)	1364(31.1)	186(34.3)	28(28.6)	0.276
Education, n (%)					0.689
Illiteracy/primary	318(6.3)	279(6.4)	31(5.7)	8(8.2)	

Middle school/high school	2704(53.8)	2370(54.1)	282(51.9)	52(53.1)	
University or above	2002(39.9)	1734(39.6)	230(42.4)	38(38.8)	
Income, n (%)					0.127
≤3000	2415(48.1)	2087(47.6)	270(49.7)	58(59.2)	
3001-5000	2278(45.3)	2002(45.7)	243(44.8)	33(33.7)	
>5000	331(6.6)	294(6.7)	30(5.5)	7(7.1)	
Residence in Tangshan 1-2 years after the earthquake, n (%)	561(11.2)	45(1.0)	431(79.4)	85(86.7)	<0.001
Hypertension, n (%)	2158(43.0)	1872(42.7)	237(43.7)	45(45.9)	0.463
Diabetes, n (%)	550(11.0)	497(11.3)	43(7.9)	10(10.2)	0.054
Dyslipidaemia, n (%)	3102(61.7)	2696(61.5)	343(63.2)	63(64.3)	0.659
Depression, n (%)	266(5.3)	215(4.9)	39(7.2)	12(12.2)	0.001

Table 2. Odds ratios for the association between earthquake experience and depression

	No earthquake experience (n=4383, 87.2%)	Experience without bereavement (n=543, 10.8%)	Experience with bereavement (n=98, 2.0%)
Model 1	1	1.42(0.99-2.20)	2.46(1.32-4.59)
Model 2	1	1.43(1.01-2.04)	2.50(1.34-4.68)
Model 3	1	1.61 (0.88-2.95)	2.88 (1.26-6.57)
Model 4	1	1.69(0.93-3.08)	2.82(1.24-6.39)

Model 1 refers to the unadjusted model.

Model 2 refers to the model adjusted for gender and age at the time of the earthquake.

Model 3 refers to the model adjusted for gender, age at the time of the earthquake, smoking status, drinking status, education, income, and residence in Tangshan 1-2 years after the earthquake.

Model 4 refers to the model adjusted for gender, age at the time of the earthquake, smoking status, drinking status, education, income, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidaemia.

Figure 1 Odds ratio of depression given earthquake experience, stratified by gender and age at the time of the earthquake.

Groups stratified by gender, adjusted for age at the time of the earthquake, smoking status, drinking status, education, income, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidaemia. Groups stratified by age at the time of the earthquake, adjusted for gender, smoking status, drinking status, education, income, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidaemia.

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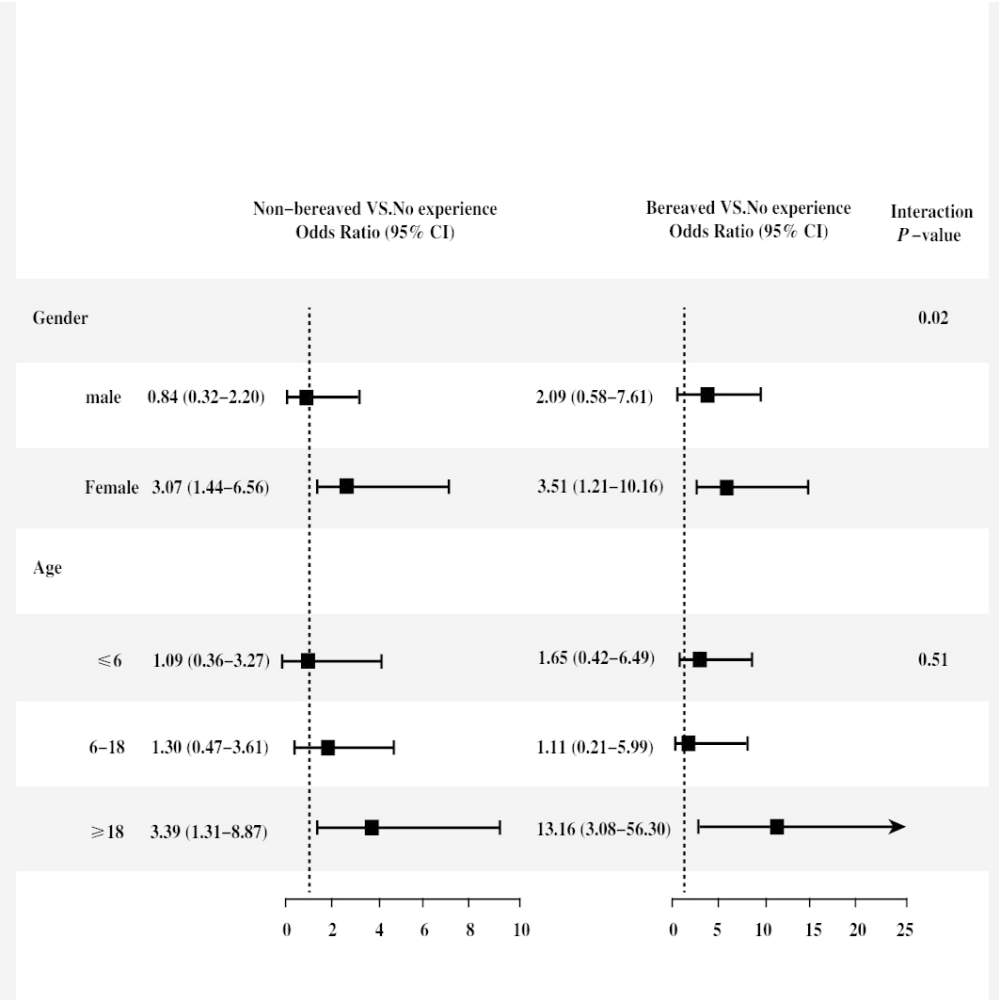

Figure 1 Odds ratio of depression given earthquake experience, stratified by gender and age at the time of the earthquake.
Groups stratified by gender, adjusted for age at the time of the earthquake, smoking status, drinking status, education, income, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidaemia. Groups stratified by age at the time of the earthquake, adjusted for gender, smoking status, drinking status, education, income, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidaemia.

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The Association between Earthquake Experience and Depression 37 Years after the Tangshan Earthquake: A Cross-sectional Study

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The Association between Earthquake Experience and Depression 37 Years after the Tangshan Earthquake: A Cross-sectional Study

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ABSTRACT

Objective To investigate the association between the Tangshan earthquake and depression after 37 years.

Design and setting A cross-sectional study conducted in Tangshan from 2013 to 2014.

Participants The sample included 5024 participants born before July 28, 1976, the date of the Tangshan earthquake, with available data on their earthquake experiences and depression 37 years post-earthquake.

Outcomes and variables The outcome was depression measured using the CES-D. The independent variable was earthquake experience, which was classified into 3 groups: no earthquake experience, earthquake experience without bereavement, and earthquake experience with bereavement. Multivariable logistic regression analysis was used to evaluate the association between earthquake experience and depression after adjusting for gender, age at the time of the earthquake, smoking status, drinking status, education, income, residence in Tangshan 1-2 years post-earthquake, hypertension, diabetes, and dyslipidaemia.

Results Of the 5024 participants, 641 experienced the Tangshan earthquake, and 98 experienced bereavement due to the earthquake. Thirty-seven years after the earthquake, survivors who had lost relatives during the earthquake were nearly 3 times (OR 2.82, 95% CI 1.24-6.39) as likely to have depression as those who had not experienced the earthquake, while those who had not lost relatives were 1.69 times as likely (OR 1.69, 95% CI 0.93-3.08). Stratified analyses showed that earthquake was significantly associated with depression in women with (OR 3.51, 95% CI 1.21-10.16) or without bereavement (OR 3.07, 95% CI 1.44-6.56) but not in men; this association was also significant in individuals over 18 years old at the time of the earthquake with

(OR 13.16, 95% CI 3.08-56.3) or without bereavement (OR 3.39, 95% CI 1.31-8.87) but not in individuals less than 18 years old.

Conclusions Thirty-seven years after the Tangshan earthquake, earthquake experience was associated with depression among bereaved survivors, women and individuals over 18 years old at the time.

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Strengths and limitations of this study

- The study investigated the long-term risk of depression 37 years after a major earthquake.
- Participants were stratified by gender and age at the time of the earthquake.
- We were unable to control for every event or factor, such as adverse childhood experiences, other bereavement or current psychological stressors.
- Only participants who were still alive 37 years after the earthquake were able to participate in the study.

INTRODUCTION

Depression is predicted to be a major reason for disability around the world by 2030, according to the World Health Organization[1]. In addition, the chronic and debilitating nature of depression complicates the prognosis of chronic diseases, aggravates various diseases and may lead to suicide[2-4]. Evidence shows that depression is related to demographic characteristics, living habits, education, income, and health status[5-7]. Participants exposed to disasters at an early life stage are at an increased risk of depression in the short term (1-4 years), independent of age, gender, income, education and other confounders[8-10]. Additionally, studies report that some survivors have psychological problems in the immediate aftermath of disaster trauma; most of these reactions abate over time, and only a minority of survivors develop a long-standing disorder[11 12]. Therefore, long-term evidence is essential to evaluate the effects of disaster on depression.

Findings regarding the long-term impact of disasters on mental health have been mixed. Several studies have reported no significant differences[13 14], but others have revealed more psychological problems in exposed individuals than in non-exposed individuals for more than a decade after disasters[10 15 16]. Moreover, evidence shows that such effects are increased if survivors suffer from bereavement[10 12]. Additionally, the association between earthquakes and depression may vary according to age or gender. Studies indicate that overall levels of psychological symptoms may vary among children, adolescents, and adults due to differences in physiology and cognition[17 18]. In response to disaster, women appear develop more intense and longer-lasting psychological symptoms than men[13 19]. However, very few of these studies investigated the long-term effect of earthquakes on depression risk in the Chinese population.

Our study provides a suitable setting for investigating the long-term impact of earthquakes on depression in the Chinese population. The Tangshan earthquake, which occurred in 1976, had a magnitude of 7.8 on the Richter scale[20]. The earthquake caused 242,769 deaths and left 164,851 people severely injured, representing the strongest and deadliest natural disaster in the twentieth century[20]. Since the earthquake, numerous studies have examined the effects of the event on physical health outcomes. These studies report increased risks of diabetes, cardiovascular disease, and elevated levels of uric acid among survivors of the Tangshan earthquake even at time points more than 30 years later[21-23]. However, no study to date has examined the long-term effect of the Tangshan earthquake on the risk of depression.

The aim of our study was to examine the long-term effect of disaster on depression 37 years later. We hypothesized that the earthquake-exposed group would be more likely than the non-exposed group to exhibit depression. Furthermore, we expected that bereaved survivors would be more likely to experience depression than non-bereaved survivors. Considering that age and gender may confound the association between earthquake experience and depression, we also performed an analysis stratified by age and gender.

METHODS

Study participants

The participants were selected from the Jidong Cohort, an ongoing community-based prospective study in Chinese adults[24]. The Jidong community is located in the Caofeidian district of Tangshan City, which is approximately 60 km from the epicentre of the Tangshan earthquake. Cluster sampling was used to select

participants. From July 2013 to August 2014, a total of 9078 residents in the Jidong community were recruited to participate in the cohort. Data regarding demographic and behavioural characteristics, insomnia, cognition, depression, and biochemical indicators have been collected from this cohort at annual follow-ups since 2013[25-27]. These data were collected using a set of self-administered questionnaires (including the Center for Epidemiological Study and Depression Scale (CES-D)) with the assistance of well-trained research nurses during face-to-face interviews. Biomedical variables were collected by physical examinations and laboratory assessments. Research on this cohort originally examined sub-health and later expanded to examine depression, cardiovascular health, cerebrovascular health and other areas[25-28].

In the current study, we excluded 4054 of the 9078 candidate participants according to the following standards: (1) birth date after July 28th, 1976 (n=4053); (2) incomplete information on relevant earthquake experience (n=1); and(3) missing values in the surveys for the CES-D measurement scale (n=0). Missing data for confounding variables (60 income variables) were imputed with their mean values among these participants. Ultimately, a total of 5024 individuals were included in this cross-sectional study. The participants in the Jidong Cohort are subjected to a physical examination annually, which is paid for by the community. Therefore, the response rate was almost 100%(5024/5025).

This study was performed according to guidelines from the Declaration of Helsinki and approved by the Ethics Committee of Jidong Oilfield Staff Hospital. All participants provided written informed consent.

Assessment of earthquake experience

The exposure variable of interest was experience with the earthquake. Earthquake experience and related bereavement were collected through a structured questionnaire. These factors were obtained using the following questions: "Were you in the Tangshan earthquake area in 1976?" and "Did you lose any relatives in the earthquake?"[23] According to the answers to these questions, subjects were classified into 3 groups: no earthquake experience, earthquake experience without bereavement, and earthquake experience with bereavement.

Assessment of current depression

Depressive symptoms were assessed using the CES-D, which was initially developed by the United States National Institute of Mental Health in 1977[29]. The Chinese version of the CES-D was translated from the international standard version of the CES-D questionnaire in 1985 by two psychiatrists and was specifically designed to screen for depression[30]. The CES-D questionnaire surveys the frequency of common depressive symptoms over the past week. Each item in the depression assessment section of the questionnaire is scored from 0 (rarely or none of the time, less than one day) to 3 (all of the time, 5–7 days). The four positive statement items (item 4, I felt that I was just as good as other people; item 8, I felt hopeful about the future; item 12, I was happy; item 16, I enjoyed life) are reverse coded to calculate the total score, which ranges from 0 to 60. A cut-off value of ≥16 has been widely used to define clinically meaningful depressive symptoms[31-33]. All investigators attended a 3-day training course and were licensed before conducting the CES-D interviews.

Assessment of potential covariates

The selected covariates included factors known to be predictive of depression and/or

potentially correlated with earthquake exposure, including age at the time of the earthquake, gender, education, income, smoking status, drinking status, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidaemia. Age at the time of the earthquake was defined as a continuous variable and then a categorical variable ("≤6 years", "6-18 years", or "≥18 years"). The average monthly income of each family member was categorized as "<¥3000", "¥3000–5000" or ">¥5,000". Educational level was classified into three categories: "illiteracy or primary school," "middle school or high school," and "university or above." Residence in Tangshan 1-2 years after the earthquake was classified as "yes" and "no". Smoking status was classified as "yes" (current smoker or quit<12 months ago) and "no" (non-smoker or quit>12 months ago)." Drinking status was divided into "yes" (current drinking <1 standard servings/day, <2 standard servings/day, 2-4 standard servings/day, ≥5 standard servings/day) and "no" (never drank, drank in the past).A standard serving was defined as 15 g of ethanol. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured twice using a mercury sphygmomanometer with the subject in a seated position. If the difference between the two measurements exceeded 5 mm Hg, an additional reading was taken, and the average of the three readings was used. Hypertension was defined as having a history of hypertension, exhibiting an SBP ≥140 mm Hg or a DBP ≥90 mm Hg, or using antihypertensive medications. The definition of diabetes mellitus was a fasting glucose level ≥7.0 mmol/l (126 mg/dl), current treatment with insulin/oral hypoglycaemic agents or a history of diabetes mellitus. Dyslipidaemia was defined as a history of hyperlipidaemia, a total blood cholesterol level ≥220 mg/dl, a triglyceride level≥ 150 mg/dl, or use of anti-hyperlipidaemic medications. All measures in this cross-sectional study reflected the current values as of data collection.

Statistical analysis

We first compared the characteristics of individuals according to their earthquake and bereavement experiences (no earthquake experience, earthquake experience without bereavement, and earthquake experience with bereavement) using the chi-squared test for categorical variables and one-way ANOVA or the Kruskal–Wallis test for continuous variables.

We used logistic regression to examine the association between earthquake experience and current depression, with "no earthquake experience" as the reference group. Four multivariate models were fitted as follows: Model 1 was the unadjusted model. Model 2 was adjusted for age at the time of the earthquake and gender. Model 3 was further adjusted for smoking status, drinking status, education, income, and residence in Tangshan 1-2 years after the earthquake. Model 4 was further adjusted for hypertension, diabetes, and dyslipidaemia.

We also used multiple logistic regression to examine the association stratified by gender and age at the time of the earthquake. To evaluate whether the effect of the earthquake on depression would be modified by gender and/or age at the time of the earthquake, we tested the statistical significance of earthquake × gender and earthquake × age at the time of the earthquake as interaction effects in a multiple-adjustment logistic model by applying a post-estimation Wald test to obtain an omnibus P-value for the interactions between earthquake categories and depression.

All statistical tests were 2-sided, and results with a P-value<0.05 were considered statistically significant. The analyses were performed in SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Patient and public involvement

Patients and the public were not involved in the development of the research question or outcome measures, study design, recruitment, or conduct of the study. The results will be disseminated to study participants through annual information events.

RESULTS

Characteristics of the study participants

The characteristics of the participants according to earthquake and bereavement experiences are shown in Table 1. In total, 5024 participants were included in this study; the participants were 50.2% male and ranged in age from 37 to 82 years at the time of data collection. Among all participants, 543 (10.8%) individuals experienced the earthquake without bereavement, and 98 (2.0%) participants lost relatives. The individuals who experienced the earthquake with or without bereavement were younger and were more likely to have lived in Tangshan 1-2 years after the earthquake than those who had not experienced the earthquake (12.1±9.0, 13.1±9.1, and 14.8±9.2 years, respectively, for age; 86.7%, 79.4%, and 1%, respectively, for residence). No differences were found in gender, smoking status, drinking status, education, income, hypertension, diabetes or dyslipidaemia. A higher incidence of depression was observed in the bereaved and non-bereaved earthquake survivors (12.2% (12/98) and 7.2% (39/543), respectively) than in those without earthquake experience (4.9% (215/4383)).

Association between earthquake experience and depression

Odds ratios (ORs) and 95% confidence intervals (CIs) for the association between earthquake experience and depression are presented in Table 2. The risk of depression

in the bereaved subgroup was 2.82 times (OR, 2.82; 95% CI, 1.24-6.39) higher than that in the group with no earthquake experience after adjusting for gender, age at the time of the earthquake, smoking status, drinking status, education, income, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidaemia. However, no statistically significant association was found in the non-bereaved group.

Subgroup analysis by gender and age as of the earthquake

In the models stratified by gender, the female subjects in both the bereaved (OR, 3.51; 95% CI, 1.21-10.16) and non-bereaved (OR, 3.07; 95% CI, 1.44-6.56) subgroups had an increased risk of depression. In contrast, no significant association was found between earthquake experience and the risk of depression among male subjects in either the bereaved (OR, 2.09; 95% CI, 0.58-7.61) or the non-bereaved (OR, 0.84; 95% CI, 0.32-2.20) subgroup. In the models stratified by age at the time of the earthquake, we found a statistically significant association in individuals over 18 years old whether they had lost relatives in the earthquake (OR, 13.16; 95% CI, 3.08-56.3) or not (OR, 3.39; 95% CI, 1.31-8.87).No statistically significant association was found in survivors under 6 years old whether they had been bereaved (OR, 1.65; 95% CI, 0.42-6.49) or not (OR, 1.09; 95% CI, 0.36-3.27), and there was also no significant association in survivors aged between 6 and 18 years whether they had lost relatives (OR, 1.11; 95% CI, 0.21-5.99) or not (OR, 1.30; 95% CI, 0.47-3.61).In addition, we found a statistically significant interaction between gender and depression *(P* for interaction= 0.02) but no significant interaction between age at the time of the earthquake and depression (*P* for interaction= 0.51) (Figure 1).

DISCUSSION

In this community-based study, we observed that, even after 37 years, earthquake survivors had a higher risk of depression than those who had not experienced the earthquake. In addition, long-term effects of the earthquake on depression were found among bereaved survivors, women and individuals over 18 years old. This study is the first to investigate the association between earthquake experience and depression 37 years after an earthquake.

Evidence shows that traumatic experiences in childhood and adolescence may have a determining effect on brain structural development, sympathetic nervous system responsivity, and the hypothalamic–pituitary–adrenal axis, especially in younger children (preschool) and school-age children (late childhood and early adolescence), resulting in a large stress response and some psychological problems[18]. Therefore, we classified the participants into age categories of 0-6, 6-18 and older than 18 years to investigate the long-term impact of disaster on mental health during different stages of life. However, statistically significant associations were found only in individuals over 18 years of age. One explanation is that different ages have different needs for social networks. Social networking is associated with the onset of depression[34]. Children's and adolescents' social needs are met by parental care and family[35]. Adults, in contrast, need support from social interaction in the neighbourhood, the communities, and the work place in addition to family support[36]. The advent of the earthquake destroyed the previously stable social networks and economic foundation of the community. Social-network destruction may lead to some mental health disorders. Additionally, survivors under 18 years old recover from disaster more easily than older survivors do. Insensitivity to the nature and meaning of disaster trauma[37] and access to mental health intervention in the early post-disaster stages[38]

may contribute to recovery from psychological problems among child and adolescent survivors.

With regard to gender, we found a significant association between earthquake experience and depression in women but not in men. Similar results have been found in several previous studies of disaster, indicating that women may be at a higher risk of depression than men when they experienced disasters including large earthquake [13 19]. Differences in physiology, personality, social role and rumination between women and men might result in this gender difference in the association between depression and disaster[39-43]. The exact causal factors leading to gender differences in long-term effects of earthquakes remains a big challenge for future researches.

Consistent with our findings, a longitudinal study on the Alexander Kielland oil platform collapse shows that survivors have a higher risk of depression than non-exposed individuals 27 years after the disaster[15]. Similar results are observed in another longitudinal study with 10 years of follow-up, which indicates that survivors of the Piper Alpha oil platform disaster show a long-lasting increase in mental health problems compared with non-exposed individuals[16]. In contrast, two studies indicate that disaster has little long-term effect on depression[13 14]. The inconsistency of the results may be explained by the severity of the disaster. The Tangshan earthquake caused more damage than the Buffalo Creek dam collapse or the Australian bushfire disaster. The earthquake reduced Tangshan to ruins in a few minutes, with approximately 85% of the buildings collapsed and at least 400,000 casualties[20 44]. The earthquake afflicted the survivors with not only the loss of their homes but also, more importantly, the tension and fear brought by the disaster itself, the loss of loved ones, the complete destruction of social networks and a sense of despair [45 46]. During the long-term urban reconstruction process, all these effects of the disaster might lead to

long-term adverse psychological effects on the survivors. In addition, the Tangshan earthquake broke out at the end of the decade of the Cultural Revolution. The consequences of the Cultural Revolution, which include a fragile economic foundation, low economic compensation, lack of societal acknowledgement, and destruction of the health care service network, may have delayed recovery.

The long-term effect of disaster on depression seems to depend on traumatic experience. In our study, a statistically significant association between earthquake experience and depression was observed in bereaved survivors but not in non-bereaved survivors 37 years after the earthquake. This finding was consistent with a longitudinal study carried out in Italy showing that exposure to loss and damage during an earthquake confers an additional risk of negative psychological consequences above and beyond living in the earthquake zone[10]. Similarly, a longitudinal study 14 years after MS Estonia Disaster indicated that non-bereaved survivors recovered from their posttraumatic stress reactions, while little change was found over that period in the reaction of the bereaved[12]. Traumatic bereavement may be associated with increased severity of long-term posttraumatic stress reactions after disasters[47], which is considered to be involved in the onset of depression[4].

Several plausible explanations may link earthquake exposure to the prevalence of depressive symptoms. Earthquakes can cause tremendous, immediate damage to the environment and even lead to adverse life events such as the death of a family member and related events, thus exerting negative effects on individuals' emotions and resulting in posttraumatic stress disorder (PTSD) after the disaster[4 12]. PTSD, as a frequent comorbidity of depression[48 49], may persist for decades following disaster[50-52]. These findings suggest that traumatic bereavement might be a common mediating mechanism of both depression and PTSD. The pain of loss in survivors may have

neurobiological effects on several brain areas (the frontolimbic and striatal areas)[47 53]. These areas and the functional connectivity within the fronto-striato-thalamic and default-mode networks have been found to be correlated with the progression of mental health problems and may play important roles in adaptation to trauma[4 54]. The trauma caused by disasters has a variety of mechanisms. Whether PTSD symptoms further transform into depression or other mental illnesses in the long term will require further exploration.

Gender, age at the time of the earthquake, education, income, smoking, drinking, living in the affected area after a disaster, hypertension, diabetes and dyslipidaemia were controlled in the multiple variable analysis. To avoid over fitting, we used four models to adjust confounding variables step by step. The resulting ORs reflected minor changes in the 4 models, suggesting that earthquake experience may be an independent risk factor for the occurrence of depression.

Our study has a few limitations. First, substantial time has passed since the earthquake occurred, and we were unable to control for every event or factor. For example, we did not consider other traumatic events, such as traffic accidents, adverse childhood experiences, other bereavement or current psychological stressors, which could have confounded the observed associations. Additionally, the sample was not representative of all survivors of the Tangshan earthquake. We did not include survivors who had died in the past 37 years. Premature death may be related to depression and disease. Meanwhile, in our sample, nearly 20% of the survivors did not live in the earthquake zone 1-2 years after the earthquake. These people left the painful environment and may have worked or attended school elsewhere for several years, which may have largely relieved psychological stress and alleviated the symptoms of depression. Therefore, the potential impacts of the earthquake on

depression may have been underestimated. Third, whether the subjects were taking antidepressants was unknown. Fourth, the cross-sectional design of this study precludes causal inferences. Finally, depression was assessed only once during the study; therefore, we could not exclude the possibility of reverse causality.

The results of our study are very relevant to future research on depression among disaster survivors. For instance, survivors of earthquakes in Japan, Haiti, and China were all affected by high rates of depression in the short term[55-58]. Although the timing and severity of the disasters, the ethnicity of the affected population, and the living environment of the survivors are different, the stressors caused by disasters are similar. Strengthening community social cohesion can facilitate recovery from disaster trauma[59 60]. Clinicians and policymakers in public health should direct additional early social support towards high-risk survivors of disasters, a measure that may reduce the incidence of mental health problems, including depression, in disaster zones[61], even long after the disaster has passed.

CONCLUSIONS

Thirty-seven years after the disasters, earthquake experience was associated with depression among bereaved survivors, women and individuals over 18 years old at the time. Our study provides evidence supporting the hypothesis that the effect of an earthquake on depression persists for at least 37 years.

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Contributors All authors were involved from the beginning in all phases of the study. XG, YZ and HPH designed the study. XG and YL analysed the data and prepared the manuscript. JCY, QHC and BG critiqued the manuscript for important intellectual content. XG and YCG conducted the statistical analysis. All authors have read and approved the final version of this manuscript.

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Competing interests None declared.

Ethics approval The research was approved by the Ethics Committee of Jidong Oilfield Staff Hospital.

Data sharing statement All data used or analysed in the current study are available from the corresponding author upon reasonable request.

Table 1 Population characteristics according to earthquake experience

Characteristics	Overall	No experience (n=4383)	Experience without bereavement (n=543)	Experience with bereavement (n=98)	*P-value*
Men, n (%)	2524(50.2)	2210(50.4)	276(50.8)	38(38.8)	0.071
Age at the time of the earthquake, mean (SD)	14.6±9.2	14.8±9.2	13.1±9.1	12.1±9.0	<0.001
≤6	1063(21.2)	880(20.08)	146(26.89)	37(37.76)	<0.001
6-18	2053(40.9)	1796(40.98)	226(41.62)	31(31.63)	
≥18	1908(38.0)	1707(38.95)	171(31.49)	30(30.61)	
Smoking, n (%)	1286(25.6)	1136(25.9)	132(24.3)	18(18.4)	0.182
Drinking, n (%)	1578(31.4)	1364(31.1)	186(34.3)	28(28.6)	0.276
Education, n (%)					0.689
Illiteracy/primary	318(6.3)	279(6.4)	31(5.7)	8(8.2)	

Middle school/high school	2704(53.8)	2370(54.1)	282(51.9)	52(53.1)	
University or above	2002(39.9)	1734(39.6)	230(42.4)	38(38.8)	
Income, n (%)					0.127
≤3000	2415(48.1)	2087(47.6)	270(49.7)	58(59.2)	
3001-5000	2278(45.3)	2002(45.7)	243(44.8)	33(33.7)	
>5000	331(6.6)	294(6.7)	30(5.5)	7(7.1)	
Residence in Tangshan 1-2 years after the earthquake, n (%)	561(11.2)	45(1.0)	431(79.4)	85(86.7)	<0.001
Hypertension, n (%)	2158(43.0)	1872(42.7)	237(43.7)	45(45.9)	0.463
Diabetes, n (%)	550(11.0)	497(11.3)	43(7.9)	10(10.2)	0.054
Dyslipidaemia, n (%)	3102(61.7)	2696(61.5)	343(63.2)	63(64.3)	0.659
Depression, n (%)	266(5.3)	215(4.9)	39(7.2)	12(12.2)	0.001

Table 2. Odds ratios for the association between earthquake experience and depression

	No earthquake experience (n=4383, 87.2%)	Experience without bereavement (n=543, 10.8%)	Experience with bereavement (n=98, 2.0%)
Model 1	1	1.42(0.99-2.20)	2.46(1.32-4.59)
Model 2	1	1.43(1.01-2.04)	2.50(1.34-4.68)
Model 3	1	1.61 (0.88-2.95)	2.88 (1.26-6.57)
Model 4	1	1.69(0.93-3.08)	2.82(1.24-6.39)

Model 1 refers to the unadjusted model.

Model 2 refers to the model adjusted for gender and age at the time of the earthquake.

Model 3 refers to the model adjusted for gender, age at the time of the earthquake, smoking status, drinking status, education, income, and residence in Tangshan 1-2 years after the earthquake.

Model 4 refers to the model adjusted for gender, age at the time of the earthquake, smoking status, drinking status, education, income, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidaemia.

Figure 1 Odds ratio of depression given earthquake experience, stratified by gender and age at the time of the earthquake.

Groups stratified by gender, adjusted for age at the time of the earthquake, smoking status, drinking status, education, income, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidaemia. Groups stratified by age at the time of the earthquake, adjusted for gender, smoking status, drinking status, education, income, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidaemia.

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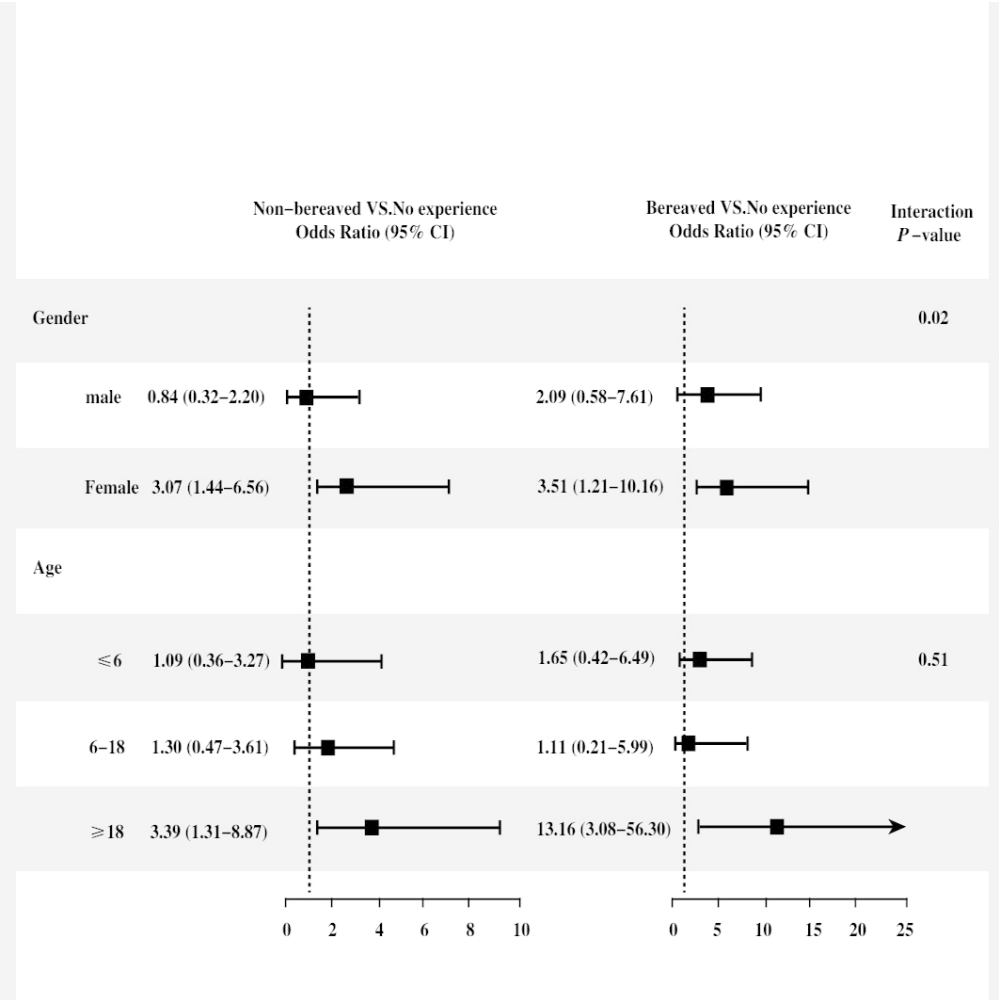

Figure 1 Odds ratio of depression given earthquake experience, stratified by gender and age at the time of the earthquake.
Groups stratified by gender, adjusted for age at the time of the earthquake, smoking status, drinking status, education, income, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidaemia. Groups stratified by age at the time of the earthquake, adjusted for gender, smoking status, drinking status, education, income, residence in Tangshan 1-2 years after the earthquake, hypertension, diabetes, and dyslipidaemia.

90x90mm (300 x 300 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1	Line 1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3-4	Line 36-65
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6-7	Line 77-111
Objectives	3	State specific objectives, including any prespecified hypotheses	7	Line 112-118
Methods				
Study design	4	Present key elements of study design early in the paper	8	Line 142
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-8	Line 122-135
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	8	Line 137-144
		(*b*)*Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-10	Line 150-199
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8-9	Line150-171
Bias	9	Describe any efforts to address potential sources of bias	11	Line 206-212
Study size	10	Explain how the study size was arrived at	8	Line 137-144

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	11	Line 204-205
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	11	Line 201-223
		(*b*) Describe any methods used to examine subgroups and interactions	11	Line 213-220
		(*c*) Explain how missing data were addressed	8	Line 139-142
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	7-8	Line 125-126
		(*e*) Describe any sensitivity analyses		NA
				Results
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	12	Line 233-236
		(b) Give reasons for non-participation at each stage	8	Line 137-141
		(c) Consider use of a flow diagram		NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	12	Line 232-245,Table 1
		(b) Indicate number of participants with missing data for each variable of interest	8	Line 139-142
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)		NA
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time		
		Case-control study—Report numbers in each exposure category, or summary measures of exposure		
		Cross-sectional study—Report numbers of outcome events or summary measures	12	Line 242-245
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12-13	Line 248-254,Table 2
		(*b*) Report category boundaries when continuous variables were categorized	10	Line179-181,Table 1
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period		NA

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	13	Line 257-272
Discussion				
Key results	18	Summarise key results with reference to study objectives	14	Line 275-280
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	17	Line 362-377
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-18	Line 281-387
Generalisability	21	Discuss the generalisability (external validity) of the study results	17-18	Line 366-374
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19	Line 404-407

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.