

# Association between Exposure to Earthquake in Early Life and Risk of Diabetes Mellitus in Adulthood: Results from the Kailuan Study

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# Abstract

## Background

Investigations on the potential effects of earthquake exposure in early life are limited. Furthermore, no study has explored specific earthquake exposure windows for early life. This study evaluated the associations between earthquake exposure in early life and the incidence of adulthood diabetes mellitus (DM) and explored critical specific earthquake exposure windows, using the Tangshan Earthquake in 1976 as a natural exposure.

## Methods

We analyzed 7,568 participants born around the time of the Tangshan earthquake and free of diabetes at baseline within the Kailuan study based in Tangshan, Hebei, China. Participants born from 28 Jun 1974 to 04 May 1977 were divided into the exposed group, and participants born from 04 May 1977 to 04 May 1979 were divided into nonexposed group. The exposed group was further stratified to fetal, infant, and early childhood exposed group. Cox proportional hazards model was used to examine the association between earthquake exposure in early life and incident risk of DM in adulthood.

## Results

During a median follow-up of 5.8 years, compared with nonexposed participants, the exposed participants had increased risk of DM, with multivariate-adjusted hazard ratios (HRs) (95% confidence intervals [CI]) of 1.47 (1.19-1.82). Furthermore, the HRs of DM were 1.68 (1.30-2.19) and 1.44 (1.08-1.91) for infant exposed group and early childhood exposed group, respectively, compared with the nonexposed participants. A significant interaction has been detected between early life earthquake exposure and alcohol consumptions on DM developing in adulthood ( $P$  for interaction = 0.03).

## Conclusions

The increased risk of DM in adulthood was associated with earthquake exposure in early life. Our findings suggest that infant and early childhood are critical time windows of DM development among earthquake survivors, therefore, preventions of metabolic diseases and risk factors deserve more attentions among adults who experienced disasters in their early lives.

## 1. Introduction

Diabetes mellitus (DM) is a common kind of metabolic disease globally with an estimation of 425 million afflicted individuals in 2017, and the global prevalence of DM is increasing and expected to reach to 522 million by 2030 (1). As a metabolic disease, the origin of DM is complicated and human genetic and lifestyle factors act to promote DM in adulthood (2). Previous studies have identified over 100 genetic loci variant associated with DM (3), and lifestyle factors, such as diet dysregulation (2) and cigarette smoking

(4) were significantly associated with increasing risk of DM. In addition, the environment factors, including pollutants (5) and adverse experience exposure (6) were also identified as risk factors of DM.

Emerging evidence suggests exposure to environment factors in utero and early life is a major determinant of adult health. One study conducted in Lanzhou, China, reported that maternal exposure to particulate matter could increase the risk of infant's metabolic disorder, cancer and cardiovascular disease in later life (7). And the positive associations observed between persistent organic pollutants (POPs) or heavy metals (8) and DM reflecting the impact of early life exposure on the development of adult diseases. Besides pollutants exposure, study on the Ukraine famine of 1932-1933 also indicated a dose-response relation between famine severity during prenatal development and odds of DM in later life (9). Indeed, the pathways from exposure factors affecting early life to outcomes in adult life are far from clear due to the lack of longitudinal cohort study. The "Developmental Origins of Health and Disease" (DOHaD) hypothesis provide a potential link through biological reactions to early life exposure that are posited to predispose individuals to metabolic diseases (10). However, most studies have focused on the chronic exposure rather than acute exposure, such as disaster events, mainly because of the comprehensive cohort study is limited, and data collection is hard to implement after disaster events happened.

Earthquake is a kind of severe natural catastrophic event that can cause adverse physiological and mental responses by fractures, crush injuries, and the severe damages of their properties and loss of their relatives (11) Studies on earthquake experience confirmed that earthquake trauma could increase the risk of DM. Three months after the Great East Japan Earthquake, the worsening of glycemic control was observed in a study of 497 DM patients, which suggested the endogenous insulin secretion caused by hyperactivity of sympathetic nerve in a relatively short term (12). A study of Kumamoto Earthquake revealed that the glycemic deterioration after earthquake could be explained by increased production of cortisol and/or catecholamine (13). However, little longitudinal cohort studies have examined the DM risk in adults who have experienced earthquake during early life.

Thus, we use the Great Tangshan Earthquake as a nature exposure, which happened in Hebei, China, with an epicenter at Tangshan city on July 28 in 1976, a magnitude level of 7.8 on the Richter scale. The survey data were collected from the Kailuan Study, a community-based cohort in Tangshan, we aimed to examine the association between exposure to the Great Tangshan Earthquake during the early life and the incidence of diabetes, and explore the sensitive window stratified by different exposure periods.

## **2. Materials And Methods**

### **2.1 Study population**

The Kailuan study is an ongoing prospective cohort (trial registration number: ChiCTR-TNC-11001489) study in Tangshan, China (14,15). In 2006 to 2007, a total of 101,510 participants ( $\geq 18$  years, including retired individuals) from Kailuan community received questionnaires and the first survey at Kailuan General Hospital and 10 affiliated hospitals. Following surveys were provided every 2 years since 2006.

In this study, we included participants who participated in at least one survey from 2006 to 2017 and were born in the destructive zone of the Great Tangshan earthquake between 28 July 1974 and 4 May 1979. Criteria for birth dates was based on the Tangshan earthquake date (i.e., July 28, 1976) and gestation period of 280 days. According to the date of the Tangshan earthquake and birth date of each participant, participants born between 04 May 1977 and 04 May 1979 were defined as nonexposed group, and participants born between 28 July 1974 and 04 May 1977 were defined as exposed group. Meanwhile, exposed group were further divided into fetal exposed group with participants born between 28 July 1976 and 04 May 1977, infant exposed group with participants born between 28 July 1975 and 28 July 1976, and early childhood exposed group with participants born between 28 July 1974 and 28 July 1975.

Meanwhile, we excluded participants who were not born in the destructive zone of the Great Tangshan earthquake; without location of birth; or with DM at the baseline.

Ultimately, a total of 7,568 eligible participants were included in this study. The study followed the Declaration of Helsinki and was approved by the Ethics Committee of the Kailuan Medical Group. All participants gave their written informed consent.

## **2.2 Earthquake exposure**

The Tangshan earthquake was a natural disaster resulting from a magnitude 7.6 earthquake that hit the region around Tangshan, Hebei, People's Republic of China on 28 July 1976. The magnitude of the Tangshan earthquake is indicated by the extent of felt zones: up to 1,100 km away, across most of northeastern China, and even in Mongolia and Korea (16). In and around Beijing, 140 kilometers from the epicenter, the shaking reached an intensity of VI on the Chinese intensity scale (16). It is a kind of severe natural catastrophic event that can cause adverse physiological and mental responses. There is no definite conclusion about the mechanism of the Tangshan earthquake, the predominant mechanism is the plate movement. Tangshan lies at the intersection of the Bohai-Zhangjiakou Fault Zone (BZfz) and the Tangshan-Cixian-Ninghe Fault Zone, which is the most important intraplate seismic belt within the Huabei Basin. In the northern Huabei Basin, the Yanliao epsilon-shaped structure is composed of the Huairou-Sanhe-Tangshan-Jinzhou-Xialiaohe arcuate structure belt and the NS-trending Tangshan-Fengnan uplift. The backbone of Tangshan-Fengnan uplift pushed southward and made the compressive stress concentrate at the apex of the arcuate structure belt (17). The stress would be released when it exceeded the limiting value and caused the Tangshan earthquake.

In this study, earthquake exposure was defined by the date of the Tangshan earthquake and birth date of each participant. Earthquake severity was measured by seismic intensity according to the New Chinese Seismic Intensity Scale in 1957 (18, 11), and varied from I (not felt) to XI (disastrous). The category of the seismic intensity in prefecture level were divided into three groups: destructive, felt and not felt. Destructive zones comprised prefectures where the intensity was destructive to disastrous (V–XI) (11). We selected individuals who were born in the Tangshan earthquake destructive zones, and had similar

characteristics of socio-economic status, living habits. Moreover, we defined the place of birth of participants based on individual identity card information in questionnaire.

### **2.3 Health data collection**

DM was defined as either a self-reported physician diagnosis, or taking antidiabetic medication, or fasting blood glucose (FBG)  $\geq 7.0$  mmol/L in physical examination (19). Self-report of a physician diagnosis and an antidiabetic medication were collected by questionnaires provided by the survey among Kailuan General Hospital and 10 affiliated hospitals participants. Fasting blood glucose was measured using the hexokinase/glucose-6-phosphate dehydrogenase method (Mind Bioengineering Co Ltd, Shanghai, China) (20).

Data on birth date, gender, education level, physical exercise, smoking status, alcohol consumption were collected using a self-reported questionnaire, as detailed previously (18, 14, 15). Higher education level was defined as high school and above. Regular physical activity was defined as exercise  $\geq 3$  times/week for a duration of  $\geq 30$ min each (21). Current smoker was defined as smoking at least one cigarette on average in a recent year (19). Drinking status was defined according to average alcohol consumption in the past year, as detailed elsewhere (19).

Blood pressure was measured by physical examination in the morning and prohibited coffee, tea, or physical exercise within 30 minutes before measurement. Measurement of blood pressure was repeated for 3 times, with each measurement interval of 1 to 2 minutes, and the mean value was taken. Height and weight were measured by trained nurses, and body mass index (BMI) was calculated as weight (kg)/height<sup>2</sup> (m<sup>2</sup>). Biochemical evaluation used the same fasting blood sample taken in the morning. Concentrations of low-density lipoprotein cholesterol, high-density lipoprotein cholesterol and triglycerides were measured at Kailuan General Hospital and 10 affiliated hospitals using an autoanalyzer (Hitachi 747; Hitachi, Tokyo, Japan).

### **2.4 Statistical Analyses**

For baseline characteristics of the study participants' description, mean standard deviation (SD) was used for normally distributed variables. Number and percentage (%) were used to describe categorical variables. Pearson  $\chi^2$  test for categorical variables and Student t test or Mann-Whitney U test for continuous variables were used to compare the characteristics of the participants across baseline groups. The follow-up period was defined from the baseline survey to the onset of DM or the last visit on December 31, 2017. Incidence density of DM was calculated during the follow-up.

Multivariate cox regression model was used to compare the risk of incident DM with earthquake exposure. Hazard ratios (HRs) with 95% CIs were calculated, with nonexposed individuals as the reference category. Model 1 adjusted for gender (male or female). Model 2 additionally adjusted for body mass index ( $\geq 24$  kg/m<sup>2</sup> or  $< 24$  kg/m<sup>2</sup>), smoking status (smoker or non-smoker), alcohol consumption (drinker or non-drinker), physical exercise (yes or no), and high education level (below high school or high

school or above). Model 3 included model 2 and additionally adjusted for systolic pressure (continuous variables), triglycerides (continuous variables), high-density lipoprotein (continuous variables), and low-density lipoprotein (continuous variables).

We further compared the risk of incident DM with stratification of earthquake exposure (fetal exposure, infant exposure, and age exposed group of 1-2 year), with the nonexposed group as the reference category. To demonstrate the possible interaction of earthquake exposure in the development of DM, we generated interaction terms using the cross products of earthquake exposure with baseline BMI, smoking status, alcohol consumption and regular physical exercise into multivariate cox regression model, respectively. The *P* for interaction was calculated based on the number of exposure groups (nonexposed and exposed) and the number of subgroups for each modifier in the subgroup analysis. Additionally, we assumed that the missing data were random and used multiple imputations by chained equations to impute each missing data (22).

All analyses were conducted using SAS (Version 9.4; SAS Institute, Cary, NC), and a two-tailed *P*<0.05 was considered as statistically significant.

### 3. Results

Among 169,548 individuals participated Kailuan physical examinations between 2006 and 2016, 9,520 participants were born between 28 July 1974 and 4 May 1979. After excluding participants who had missing information of birth places (n=1449), were not born in earthquake destructive zone (n=309) and had DM at the baseline (n=194), 7,568 participants were included in this study (**Figure 1**). Among them, 6,111 (80.75%) were males, and the mean age was  $33.5 \pm 4.0$  years. As shown in **Table 1**, compared with participants in the nonexposed group, participants in the exposed group were slightly older, and had higher average diastolic blood pressure. In addition, the baseline characteristics were almost comparable between participants included and those excluded due to missing birth places information, except that participants without birth places information had a lower proportion of males (**Table S1**).

365 (4.82%) DM cases were identified during a median 5.8 years of follow-up. As shown in **Table 2**, the incidence density of DM was 6.59/1000 person-years and 9.91/1000 person-years for the nonexposed and exposed groups, respectively. Compared with the nonexposed participants, the exposed participants had increased risks of DM in adulthood with HR of 1.47 (95%CI, 1.19-1.82) after multivariable adjustment in Model 3.

The incidence density of DM was 8.76/1000 person-years, 11.29/1000 person-years and 9.37 person-years for the fetal, infant and early childhood, respectively. Compared with nonexposed participants, infant and early childhood had increased risks of DM in adulthood with HR of 1.69 (95%CI, 1.30-2.19) and 1.44 (95%CI, 1.08-1.91) after multivariable adjustment in Model 3 (**Table 3**).

In the predefined subgroup analyses, the positive associations between earthquake exposure and risk of DM were still observed across most of subgroups, although the results were not significant among non-

drinkers and people with regular physical exercise (**Table 4**). Furthermore, the estimation for the association of the Tangshan earthquake exposed with DM was stronger in drinkers than non-drinkers with a significant interaction obtained ( $P=0.03$ ).

## 4. Discussion

To the best of our knowledge, this is the first study investigated associations between earthquake exposure in early life and risk of DM in adulthood. Moreover, this study indicated that the infant and early childhood were specific susceptible earthquake exposure windows of DM development. Furthermore, an interaction was detected between alcohol consumption and early life earthquake exposure on risk of DM in adulthood.

Our results showed a 1.47-fold increase in developing DM in adulthood among participants who exposed to earthquake in early life. Interestingly, some studies linking exposure to disaster events in early life to metabolic disorders in adulthood provided strong support to our findings. Lumey et al. showed that fetuses and children exposed to the Ukraine famine of 1932-33 was associated with an increased risk of DM in adulthood, with an odds ratio of 1.47 (95% CI 1.37-1.58) and 1.26 (95% CI 1.14-1.39) in extreme famine regions and severe famine regions (9). Dongfeng-Tongji cohort adequately demonstrated that the exposure to the Chinese famine (1959-1961) was associated with DM in adulthood during the 5 years follow-up period (23). In addition, early life adverse experiences such as emotional and physical neglect, and household dysfunction (e.g., substance abuse, mental illness) were also shown to be related to the increasing incidence of adulthood metabolic diseases (24), especially DM (25, 26). However, limited studies investigated the association between earthquake exposure in early life and DM in adulthood partially due to the lack of longitudinal cohort study and hard data collection. In present study, data collected from a comprehensive cohort study in Tangshan, the Kailuan study, were used to analyze the impact of the great Tangshan Earthquake on the incidence of DM in adults. The exposure group was stratified to fetal exposed group, infant exposed group and early childhood exposed group. The findings showed that infant and early childhood exposed group appeared to have significant increased risk of DM, compared with nonexposed individuals. The association between fetal earthquake exposure and risk of DM in adulthood was positive but not significant, which might be due to the inadequate sample size. The findings need independent validation based on other epidemiological and biomechanical researches.

The mechanisms underlying the observed association between earthquake exposure in early life and DM in adulthood is difficult to determine and should be explored further. Evidence suggests that physiological stress response due to exposure to adversity in early life may be associated with concomitant activations of stress-related biological pathways (27-29). Although stress-related biological pathways (e.g. oxidative stress and inflammation) have been implicated in the development of diabetes and metabolic disorders (30, 31), the activation process of this system is not clear. This is likely to occur through dialogue with dysfunction of the The hypothalamic-pituitary-adrenal (HPA) axis (32-36). Specifically, activation of the HPA axis by stress should normally lead to an increase in glucocorticoid sensitivity, enabling cortisol to inhibit and thus regulate inflammatory responses (35). Inflammation may promote the secretion of

cortisol through compensatory mechanisms, and the basal secretion capacity of  $\beta$  cells and high density lipoprotein cholesterol (HDL-C) may regulate the secretion of basal cortisol through negative feedback and lead to the onset and development of DM (32, 34). Nelson et al. showed 6-12 months is specific time to developmental domains for HPA axis and this specific time is a critical period for the development of chronic metabolic diseases (29). Moreover, Shonkoff et al. showed children response to adverse events, which called the “toxic stress response”, prolonged activation of the stress response systems that directly lead to dysregulation of the HPA axis and associated neuro-endocrine-immune as well as epigenetic effects (37). Another behavioral risk factor surveillance system data in U.S showed children exposed to high psychological stress have higher cortisol levels and greater risk of common diseases (28). Our findings showed that infant and early childhood earthquake exposed group appeared to have significant increased risk of DM, which were consistent with previous studies (38, 28).

In addition, the study examined potential interaction roles of lifestyle factors and exposure to earthquake in early life and the risk of adulthood DM. Interestingly, we found that the increased risk of DM due to earthquake exposure might be modified by alcohol consumption with a higher risk among drinkers. Recent studies likewise implied the adverse health effect of disaster exposure in early life might be strengthened by unhealthy life habit such as alcohol drinking (39). Orui et.al identified 37,867 individuals who did not drink prior to the Japan triple disaster on March 11, 2011, 9.6% reported drinking in 2012, and 53.8% reported continued drinking in 2013 (39). Although non-significant interaction was detected in BMI and smoking strata and earthquake exposure on risk of DM, a higher risk was found in BMI < 24kg/m<sup>2</sup> and non-smokers compared with BMI  $\geq$  24kg/m<sup>2</sup> and smokers, respectively. This is inconsistent with a previous study which reported that the risk of DM increased among exposed participants with smokers, however, there was no statistical significance in either strata of BMI (40). To be the best of our knowledge, obesity is the most prominent risk factor, which is more common in females (41). However, 82.07% participants of our participants were males, which may contribute to the discordant results. It is notable that smoking is another certain risk factor of DM (42). The inconsistency of our results might be due to the association modified by smoking. The adverse impact of smoking dominated the main effect on DM events, and the effect of exposure to earthquake in early life was underestimated.

## 5. Strength And Limitation

The large community-based cohort in northern China covers data on medical examinations, histories of disease, lifestyle factors, and the information about individual birth date. The medical examinations and the histories of disease which were retrieved by electronic health record systems empowered us to collect the data on the diagnosis time of DM, and the information on lifestyle factors enable us to adjust potential confounding factors at individual level. The availability of participants' birth dates allows us to separate exposure periods. Additionally, the ages of eligible participants exposure to the Tangshan earthquake have been limited from fetal to 2 years old, which minimized the impact of aging on elevated risks of DM outcomes. Furthermore, one previous publication on the association between earthquake

exposure and DM did not stratify participants by age at earthquake exposure using a cross-sectional analysis without follow-up data (43), while this study fills the gap for the long-term effect of earthquake in early life on adulthood glucose metabolism.

Several limitations need addressed in our study. First, in Kailuan study, the diagnosis of DM was based on a single measurement of FBG rather than oral glucose tolerance testing or the measurement of hemoglobin A1c, and therefore, the incidence of type 2 diabetes mellitus (T2DM) might have been underestimated. Second, we did not distinguish between type 1 diabetes mellitus (T1DM) and T2DM in our study. According to the Clinical Guideline for Prevention and Treatment of T2DM in China, T2DM represents 95% of all cases of DM. Third, all participants were employees and retirees of the Kailuan Group, and 82.07% of participants were males, and we did not further stratify the analysis by gender. In addition, the territoriality of our northern occupational population is a restriction. The generalizability of the results is relatively limited.

## 6. Conclusion

In conclusion, the cohort study among Chinese populations suggests that exposure to earthquake in early life associated with DM in adulthood. The significant associations were observed in infant and early childhood exposed group, which might be the sensitive windows of exposure period. These findings provide evidence on the adverse experience in early life linked to DM in adults and emphasize the importance to enhance health education and practices among earthquake survivors to prevent chronic metabolic disorders at early stage.

## Abbreviations

DM Diabetes mellitus

POPs Persistent organic pollutants

DOHaD Developmental Origins of Health and Disease

HRs Hazard ratios

CIs Confidence intervals

BZfZ Bohai-Zhangjiakou Fault Zone

FBG Fasting blood glucose

BMI Body mass index

SD Standard deviation

HPA Hypothalamic-pituitary-adrenal

HDL\_C High density liprotein cholesterol

T1DM Type 1 diabetes mellitus

T2DM Type 2 diabetes mellitus

## Declarations

### Ethics approval and consent to participate

Not applicable.

### Consent for publication

The authors give their consent for publication.

### Availability of data and materials

Not applicable.

### Competing interests

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

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### Authors' contribution

**Xinying Shui:** Conceptualization, Methodology, Data curation, Formal analysis, Original draft preparation, Writing-Reviewing and Editing. **Lei Zhao:** Conceptualization, Methodology, Visualization, Writing-Reviewing and Editing, Funding acquisition. **Wenli Li:** Methodology, Writing-Reviewing and Editing, **Yanling Jia:** Methodology, Data curation. **Ziquan Liu:** Reviewing and Editing, Funding acquisition. **Chen Li:** Data curation, Methodology. **Xueli Yang:** Conceptualization, Methodology, Reviewing and Editing. **Shouling Wu:** Data curation, Investigation, Methodology. **Shuohua Chen:** Data curation, Investigation. **Jingli Gao:** Methodology, Investigation, Reviewing and Editing. **Xiaolan Li:** Investigation, Reviewing and Editing. **Aitian Wang:** Methodology, Investigation, **Liqiong Guo:** Conceptualization, Methodology, Supervision, Reviewing and Editing Funding acquisition. **Shike Hou:** Methodology, Supervision, Reviewing and Editing.

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## Tables

**Table 1. Baseline characteristics by different earthquake exposure groups.**

	Earthquake nonexposed	Earthquake exposed
Date of birth	05/04/1977-05/04/1979	07/28/1974-05/04/1977
Participates, n (%)	3634 (48.02)	3934 (51.98)
Age at survey ( $\pm$ s, year)	32.3 $\pm$ 3.9	34.7 $\pm$ 4.0
Male, n (%)	2957 (81.37)	3154 (80.17)
Smoking (%)	1485 (40.86)	1516 (38.54)
Drinking (%)	1996 (54.93)	2179 (55.39)
Regular physical exercise, n (%)	444 (12.22)	447 (11.36)
High education level, n (%)	1914 (52.67)	1895 (48.17)
Body mass index ( $\pm$ s, kg/m <sup>2</sup> )	24.6 $\pm$ 3.8	24.7 $\pm$ 3.6
Systolic blood pressure ( $\pm$ s, mmHg)	121.1 $\pm$ 15.4	122.1 $\pm$ 15.5
Diastolic blood pressure ( $\pm$ s, mmHg)	79.1 $\pm$ 10.0	80.1 $\pm$ 10.2
Total cholesterol ( $\pm$ s, mmol/L)	4.7 $\pm$ 1.1	4.7 $\pm$ 1.1
Triglycerides (IQR, mmol/L) <sup>†</sup>	1.2 (0.8,1.9)	1.2 (0.8,1.9)
Low-density lipoprotein ( $\pm$ s, mmol/L)	2.5 $\pm$ 0.8	2.5 $\pm$ 0.8
High-density lipoprotein ( $\pm$ s, mmol/L)	1.5 $\pm$ 0.4	1.5 $\pm$ 0.4
*Data are presented as mean $\pm$ SD or percentage.		
<sup>†</sup> IQR denotes interquartile range.		

**Table 2. Association between earthquake exposure and risk of DM in adulthood.**

Model	Nonexposed	Exposed
Case subjects/total number	140/3634	225/3934
Incidence	6.59	9.91
Crude Model	1.000	1.50 (1.22-1.85)
Adjusted Model 1	1.000	1.53 (1.24-1.89)
Adjusted Model 2	1.000	1.48 (1.19-1.82)
Adjusted Model 3	1.000	1.47 (1.19-1.82)
Adjusted model 1 was adjusted for gender (male or female).		
Adjusted model 2 included adjusted model 1 plus body mass index ( $\geq 24$ kg/m <sup>2</sup> or $< 24$ kg/m <sup>2</sup> ), smoking status (smoker or non-smoker), alcohol consumption (drinker or non-drinker), physical exercise (yes or no), high education level (less than high school or high school or above).		
Adjusted model 3 included adjusted model 2 plus systolic blood pressure (continuous variables), triglycerides (continuous variables), high-density lipoprotein (continuous variables), low-density lipoprotein (continuous variables).		

**Table 3. Association between stratification of earthquake exposure and risk of DM in adulthood.**

Model	Nonexposed	Fetal	Infant	Early childhood
Case (subjects/total) number	140/3634	57/1135	95/1458	73/1341
Incidence	6.59	8.76	11.29	9.37
Crude Model	1.000	1.31 (0.96-1.78)	1.74 (1.34-2.25)	1.42 (1.07-1.88)
Adjusted Model 1	1.000	1.30 (0.95-1.76)	1.77 (1.37-2.30)	1.48 (1.12-1.97)
Adjusted Model 2	1.000	1.25 (0.92-1.70)	1.69 (1.30-2.20)	1.44 (1.09-1.92)
Adjusted Model 3	1.000	1.25 (0.92-1.70)	1.69 (1.30-2.19)	1.44 (1.08-1.91)
Adjusted model 1 was adjusted for gender (male or female).				
Adjusted model 2 included adjusted model 1 plus body mass index ( $\geq 24$ kg/m <sup>2</sup> or $< 24$ kg/m <sup>2</sup> ), smoking status (smoker or non-smoker), alcohol consumption (drinker or non-drinker), physical exercise (yes or no), high education level (less than high school or high school or above).				
Adjusted model 3 included adjusted model 2 plus systolic blood pressure (continuous variables), triglycerides (continuous variables), high-density lipoprotein (continuous variables), low-density lipoprotein (continuous variables).				

**Table 4. Multivariable-adjusted HRs (95% CIs) for association between earthquake exposure in early life and DM according to subgroup analysis among participants.**

	Case subjects/n	Nonexposed	Exposed	<i>P</i> -interaction
BMI				0.21
< 24.0	89/3482	1.00	1.88 (1.21-2.93)	
≥24.0	276/4086	1.00	1.37 (1.07-1.74)	
Smoking status				0.52
Non-smokers	195/4567	1.00	1.60(1.19-2.14)	
Smokers	170/3001	1.00	1.38 (1.02-1.88)	
Alcohol consumption				0.03
Non-drinkers	150/3393	1.00	1.12 (0.81-1.56)	
Drinkers	215/4175	1.00	1.81 (1.36-2.40)	
Physical exercise				0.42
No	327/6677	1.00	1.52 (1.21-1.90)	
Yes	38/891	1.00	1.20 (0.62-2.29)	

## Figures

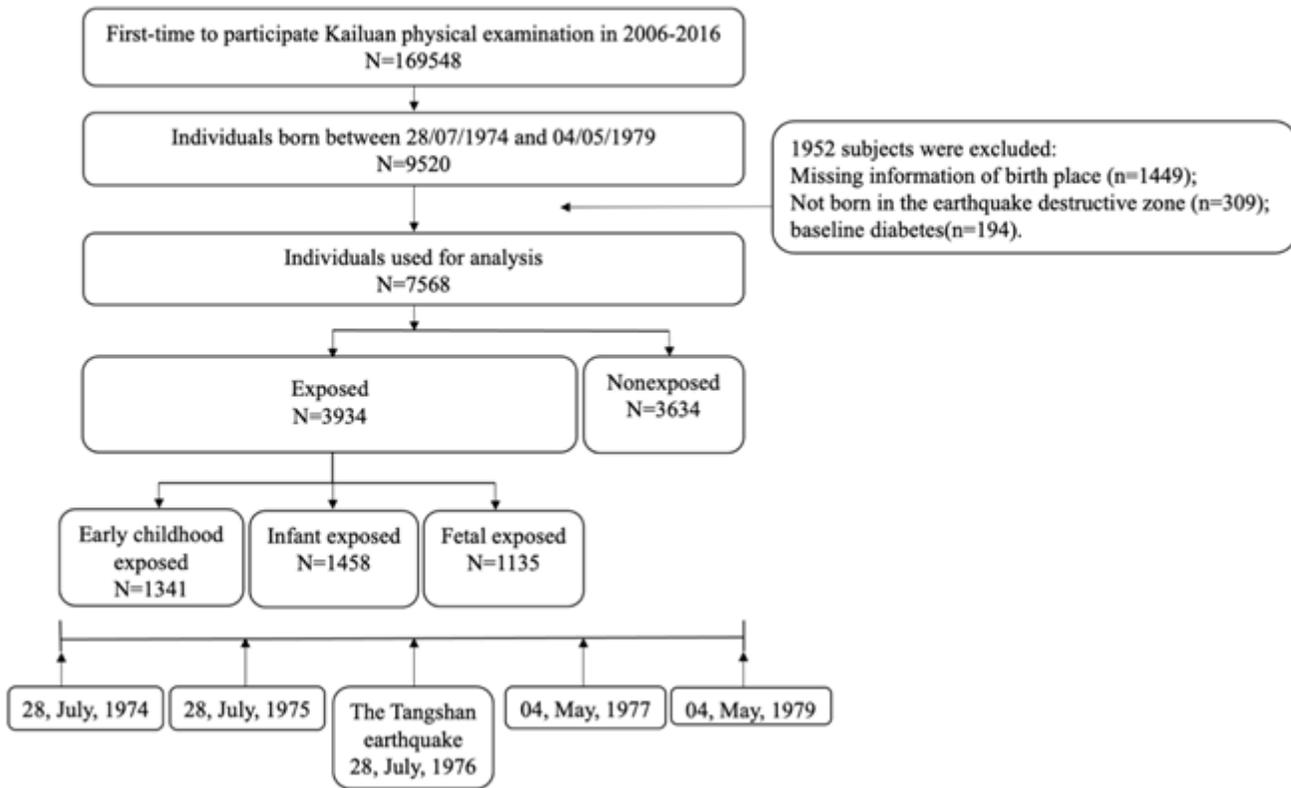


Figure 1

Flowchart of samples collection.

## Supplementary Files

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