Leisure-time physical activity and milk intake synergistically reduce the risk of pathoglycemia: a cross-sectional study in adults in Beijing, China

Running title: LTPA and milk associate with pathoglycemia

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ABSTRACT

Background and Objectives: To evaluate the synergistic and individual associations of leisure-time physical activity (LTPA) intensity and the frequency of milk intake in adulthood with newly diagnosed pathoglycemia. Pathoglycemia comprised impaired fasting glucose (IFG) and type 2 diabetes mellitus (T2DM). **Methods and Study Design:** This cross-sectional study of 3977 adults was conducted in Mentougou District, Beijing, China. After excluding ineligible individuals or those with missing data, 2977 participants were included in the final analysis. Data on LTPA, milk intake, and other demographic characteristics were obtained through previously designed questionnaires. Newly diagnosed pathoglycemia was determined based on fasting plasma glucose (FPG) concentration. **Results:** Among all participants, 21.4% had newly diagnosed pathoglycemia, 9.9% engaged in moderate to vigorous leisure-time physical activity (MVLTPA), and 63.7% drank milk more than once weekly. Relative to those who engaged in low-intensity LTPA and drank milk less than once weekly, those who engaged in MVLTPA (OR: 0.584, 95%CI: 0.410-0.810) and drank milk more than once weekly (OR: 0.734, 95% CI: 0.614-0.878) had a lower risk of pathoglycemia; this association was greater when both variables interacted (OR: 0.446, 95% CI: 0.287-0.669). **Conclusions:** MVLTPA and enough frequency of milk intake synergistically decreased the risk of pathoglycemia. A future interventional study including both factors should be performed.

Key Words: synergistic associations, leisure-time physical activity, the frequency of milk intake, pathoglycemia, impaired fasting glucose

INTRODUCTION

Diabetes mellitus (DM) has become a global public health problem. In 2017, globally, 451 million people were living with DM, and the cost of DM reached $727,000 million annually.[1] And in 2017 in China, 114 million people had DM, with a prevalence of 10.9%. It has been estimated that in 2045 in China, 119 million people will develop DM, with a prevalence of 11.6%.[1] Type 2 diabetes mellitus (T2DM) accounts for 85%–95% of all cases of diabetes.[1] Furthermore, studies have demonstrated that most individuals with impaired fasting glucose (IFG) may develop T2DM eventually.[2] Recent studies have also revealed that psychological pressure and several aspects of personal behavior, such as physical activity (PA) and diet, are associated with a rapid increase in the prevalence of IFG and T2DM.[3-5] Previous research has focused on the influence of total energy consumption to improve health. However, recent

studies have focused more on leisure-time physical activity (LTPA), because among the types of PA, LTPA contributes the most to improving health.[6,7] Recent evidence has indicated that moderate to vigorous leisure-time physical activity (MVLTPA) and milk intake are associated with a decreased prevalence of IFG and T2DM.[3,8,9] Therefore, the synergistic associations of LTPA and milk intake with IFG and T2DM must be examined. Several studies have examined the individual associations of either MVLTPA or dietary factors with IFG and T2DM independently, and very few of them have analyzed the synergistic associations of MVLTPA and milk intake with IFG and T2DM. Therefore, in this study, we assessed the synergistic and the individual effects of MVLTPA and milk intake on IFG and T2DM.

MATERIALS AND METHODS

Ethical consideration

This study was approved by the Peking University Biomedical Ethics Committee. The approval conforms to the provisions of the 1995 Declaration of Helsinki in (revised in Edinburgh in 2000), and the approval number is IRB00001052. Survey respondents provided their written informed consent prior to the conduct of the survey.

Study population

This cross-sectional study was conducted in Mentougou District in Beijing, China, based on the survey Adult Chronic Diseases and Prevalence Factors Monitoring in Mentougou District from October 2016 to November 2016. People in 9 towns and 4 streets were sampled. Those aged ≥18 years who had lived in their locale for 6 months or more in the past 1 year were potential participants. Stratified multistage probability proportional to size sampling was performed in this study. In the first stage, people in administrative villages and neighborhood committees were randomly sampled. In the second stage, those in natural villages or residents' groups of each administrative village or neighborhood committees were randomly sampled. In the third stage, to determine which person will be a potential respondent among their family members, each household was randomly sampled through random sampling.

In this study, we excluded people with missing data, specifically data on fasting plasma glucose (FPG) concentrations, the frequency of milk intake, LTPA, and other important covariates, such as gender, age, marital status, education, personal annual income, occupation, BMI (body mass index), smoking status, drinking status, and the consumption of cereals, tubers, vegetables, and fruit. Among the 3977 initially recruited, we excluded 311 people who self-reported to have beendiagnosed as having DM by a doctor in a community hospital or

above, because the diagnosis of DM could lead to behavioral and psychological changes. Finally, 689 people were excluded because the requisite set of questionnaires, physical examinations, and laboratory measurements had not been completed. The remaining 2977 participants who were eligible and had complete data were included in this study (Figure 1).

This study is a cross-sectional survey in respondents aged ≥18 years. The formula for calculating the minimum sample size was as follows: $N=(z_\alpha^2*p*(1-p))/d^2$. For our study, p = 35.7% (this was the estimated prevalence of pathoglycemia according to a nationally representative cross-sectional survey in 2013 in mainland China),[10] confidence level (bilateral) α = 0.05, d (the allowable error) = 0.1 × p, design effect = 1.5, and nonresponse rate = 10%. With these parameters, the minimum sample size was estimated as 1154, and our included study population of 2977 satisfy the demand of the minimum sample size.

Data collection

In this study, face-to-face interviews, laboratory measurements, and physical examinations were performed locally by trained surveyors. The questionnaires previously designed were used to obtain basic respondent information, including information on their demographic characteristics, personal behavior, dietary consumption, and history of DM. Demographic characteristics included gender, age, marital status, education, personal annual income, occupation, aspects of personal behaviour-including BMI, smoking status, drinking status and the consumption of cereals, tubers, vegetables, and fruit. LTPA intensity was measured using the long volume of International Physical Activity Questionnaire (IPAQ), an effective and widely used questionnaire for examining the PA intensity in adults. Dietary consumption was measured using the food frequency questionnaire (FFQ), which identified the frequency of food (never, monthly, weekly, daily) and the quality each time during the past 1 month. In our research, milk was defined as liquid milk. The frequency of milk intake was determined using FFQ. Although there may be certain differences between the information of milk intake over the past month and the actual situation, the trends are mostly consistent. Furthermore, the recall bias of FFQ in our study was less than that of a survey on milk consumption over the past year. Data on history of DM were obtained from answers to the question "Have you ever been diagnosed as having DM by a doctor in a community hospital or above?"

Physical examinations and laboratory measurements were conducted to obtain data on physiological indexes. Weights and heights were measured with participants wearing light clothing and no shoes. FPG concentrations were measured by a trained surveyor from 7 am to 9 pm using a professional-grade glucometer provided locally. Participants were required to

fast for 8–12 h and abstain from both exercise and hypoglycemic drugs before the measurement of their FPG concentration.

Definition and groups

In this study, newly diagnosed IFG and T2DM were determined by examining FPG concentration. Specifically, newly diagnosed T2DM was defined as FPG concentration ≥7.0 mmol/L and was not diagnosed as having DM by a doctor in a community hospital or above before by self-reported, and newly diagnosed IFG was defined as FPG concentration ≥6.1 mmol/L and <7.0 mmol/L and was not diagnosed by a doctor in a community hospital and above before by self-reported.[11] However, because these new diagnoses were based only on FPG concentrations in the absence of an oral glucose tolerance test, T2DM may be misdiagnosed as FPG in some patients. Thus, we grouped these cases of newly diagnosed IFG and T2DM into a joint category of newly diagnosed pathoglycemia. Thus, newly diagnosed pathoglycemia was defined as FPG concentration ≥6.1 mmol/L and was not diagnosed by a doctor in a community hospital and above before by self-reported.

In this study, LTPA intensity was classified according to the IPAQ criteria,[12] that is, LTPA intensity was divided into 3 intensities of low, moderate, and vigorous. Some researchers have shown that moderate or vigorous LTPA was potentially associated with a decreased risk of chronic diseases. For example, in a landmark study in a large cohort of people of Chinese ancestry, MVLTPA was determined to reduce the risk of diabetes-related outcomes.[13] Furthermore, in a study in large cohorts of people with cardiometabolic multimorbidity from the United Kingdom, moderate LTPA for 150 min was associated with a longer life expectancy.[14] In addition, according to the guidelines on physical activity for adults in China,[15] blood glucose is potentially reduced by moderate LTPA for more than 150 min weekly or vigorous LTPA for more than 75 min weekly-both are collectively defined as MVLTPA in this study, and LTPA that less intense than MVLTPA was defined as low-intensity leisure-time physical activity (LILTPA).

The correlation between the frequency of milk and the development of chronic diseases has been investigated,[16] where the frequency of milk intake was measured using FFQ. To ensure the uniformity of units of frequency, our study adopted the unit that is the number weekly of milk consumption.

Socioeconomic status was indicated by education and personal annual income, which is a comprehensive index that has been used in previous research.[17] Education was categorized into 2 levels; middle school education or below was coded as 0, and high school education or

above was coded as 1. Personal annual income was also categorized into 2 levels; incomes <RMB30000 and ≥RMB30000 were coded as 0 and 1, respectively. Socioeconomic status was then determined by adding both education and income scores and was segmented into 3 levels (low, middle, and high). BMI was calculated as the weight (kg) divided by square of height (m^2). Based on the physiological characteristics and dietary habits of Chinese people, BMI thresholds suitable for the Chinese population were determined in 2004.[18] Specifically, a normal BMI is 18.5–23.9 kg/m^2; a BMI value above this range indicates overweight or obesity; and we adopted this definition for overweight and obesity. The threshold for the quality of intake of cereals, tubers, vegetables, and fruit was determined by the mean quality of intake of them daily.

Statistical analysis

Binary logistic regression was used to estimate the synergistic and individual effects of LTPA intensity and the frequency of milk intake on newly diagnosed pathoglycemia. The regression model included LTPA intensity × frequency of weekly milk intake as a variable for estimating the synergistic effects, with the group with both LILTPA and a frequency of weekly milk intake ≤1 was the reference group; 95% confidence intervals (CI) were calculated for the associations.

Binary logistic regression was conducted with an unadjusted model and 2 adjusted models. In the unadjusted model, we did not adjust for potential confounders; in the 2 adjusted models, we adjusted for potential confounders. Model 1 was adjusted for gender (male or female), age (<50 or ≥50 years), marital status (married or living with others, single or living apart, or divorced or widowed), socioeconomic status (low, middle, or high), and occupation (manual worker or service staff, manager or technician, unemployed or retired, or others). Model 2 was adjusted for BMI (<24 kg/m^2 or ≥24 kg/m^2), smoking status (less or more than once a daily), drinking status (less or more than once monthly), and the total daily intake quality of cereals, tubers, vegetables, and fruit based on Model 1.

In accordance with the STROBE guideline,[19] a sensitivity analysis for the stratification of newly diagnosed IFG and newly diagnosed T2DM was conductedin each regression model, and checked for differences in the results between them and newly diagnosed pathoglycemia. In this study, statistical significance was indicated by *p*<0.05 (two-tailed). Microsoft Excel 2016 was used for data entry and verification, SPSS (version 25.0) was used for statistical analysis, and Microsoft Excel 2019 was used to draw the figure of synergistic association of pathoglycemia with LTPA intensity and the frequency of milk intake.

RESULTS

Participant characteristics

In this study, 2977 participants had an average age of 49.22±14.21 years; 44.3% and 55.7% were men and women, respectively. The average ages for male and female participants were 47.61±14.59 and 50.51±13.78 years, respectively.

Among all participants, 78.6% (2339) were healthy, with the remaining 21.4% (638) having newly diagnosed pathoglycemia. In particular, 12.2% (364) had IFG, and 9.2% (274) had T2DM.

Of the 2977 participants, 9.9% (294) and 90.1% (2683) were engaged in MVLTPA and LILTPA, respectively. The proportion of those with a frequency of weekly milk intake = 1 was in the low tertile; 36.3% (1080) of the total participants drank milk at a frequency less than or equal to once weekly, and 63.7% (1897) of the total participants drank milk more than once weekly. Table 1 presents the general characteristics of the participants.

Association of LTPA intensity and the frequency of milk intake with pathoglycemia

In this study, 14.3% and 22.2% of participants who engaged in MVLTPA and LILTPA had newly diagnosed pathoglycemia, respectively (χ^2=9.43, p<0.002). Relative to those with a lower frequency, participants with the frequency of weekly milk intake >1 had a lower prevalence of newly diagnosed pathoglycemia (χ^2=11.2, p<0.001).The results of logistic regression shows, in the unadjusted models, relative to those who engaged in LILTPA and drank milk at a lower frequency, participants who engaged in MVLTPA and drank milk more than once weekly had a significantly decreased prevalence of newly diagnosed pathoglycemia (OR: 0.584, 95% CI: 0.410-0.810; OR: 0.734, 95% CI: 0.614-0.878). After sociodemographic characteristics were adjusted for (Model 1), including gender, age, marital status, occupation, and socioeconomic status, the significant association between pathoglycemia and LTPA intensity was still significant (OR: 0.663, 95% CI: 0.461-0.934). After full adjustment (Model 2), engagement in MVLTPA was still associated with a decreased prevalence of pathoglycemia (OR: 0681, 95% CI: 0.473-0.960). The results are detailed in Table 2.

Synergistic associations of LTPA intensity and the frequency of milk intake with newly diagnosed pathoglycemia

In all models, LTPA intensity and the frequency of milk intake had significant synergistic associations with newly diagnosed pathoglycemia. Relative to those who engaged in LILTPA and drank milk at a lower frequency, those who engaged in MVLTPA and had a frequency of

weekly milk intake >1 had a significantly lower prevalence of newly diagnosed pathoglycemia. Table 3 details the results of synergistic associations in the unadjusted and 2 adjusted models. Specifically, after adjusting for potential confounders, relative to those who engaged in LILTPA and drank milk at a lower frequency, participants who engaged in MVLTPA and drank milk more than once weekly were 63.1% less likely to develop newly diagnosed pathoglycemia (OR: 0.631; 95% CI: 0.403-0.982). The results of trends and statistical significance of synergistic associations after full adjustment are shown in Figure 2.

Sensitivity analysis

Sensitivity analysis for the stratification of IFG and T2DM indicated that the synergistic and individual associations of LTPA intensity and the frequency of milk intake with IFG or T2DM showed the same trends as those of pathoglycemia. However, no significant results were obtained in several adjusted models. This may be attributable to the small numbers of participants having newly diagnosed IFG and T2DM, which decreases the statistical power of the analysis. The results of sensitivity analysis are presented in Supplementary Material 1.

DISCUSSION

This study has 2 main findings. First, LTPA intensity and the frequency of milk intake were significantly associated with a lower risk of pathoglycemia. This significant association was still present after adjusting for potential confounders, including gender, age, marital status, education, personal annual income, occupation, BMI, smoking status, drinking status, and the consumption of cereals, tubers, vegetables, and fruit. Second, LTPA intensity and the frequency of milk intake were synergistically associated with the prevalence of newly diagnosed pathoglycemia, consistent with the findings of the previous studies[8,20-22] as well as with public health recommendations.[23]

Many studies have explored the factors affecting newly diagnosed pathoglycemia, such as PA and diet-related factors. However, because the effective relief of pathoglycemia requires overall behavioral changes, most recent interventions have focused on changing multiple aspects, rather than a single aspect of behavior.[24] Furthermore, consistent with our results, several randomized controlled trials have demonstrated that the combination of PA and dietary factors potentially reduces the prevalence of pathoglycemia.[24-26]

Previous reviews have noted the association of PA with a reduction in HBA1c; this decrease in HBA1c can reduce the risk of pathoglycemia, but only when combined with diet-related factors.[27,28] Furthermore, recent studies have partially uncovered the biological

mechanism of milk intake to pathoglycemia. Some components of milk, such as calcium, protein, vitamin, and phosphorus, may benefit to decrease the risk of pathoglycemia. This benefit is partially attributable to significant improvements *in vivo* insulin sensitivity, FPG concentration, and insulin response from drinking milk more frequently.[8] However, the fat content of milk may affect the prevalence of pathoglycemia. Specifically, low-fat and high-fat milk potentially lower and increase the risk of pathoglycemia, respectively.

The major strength of our study is the analysis of synergistic associations of LTPA intensity and the frequency of milk intake with newly diagnosed pathoglycemia. By contrast, previous studies have analyzed only the individual associations of dietary factors and PA with pathoglycemia, rather than the synergistic associations of PA and the frequency of milk intake. To the best of our knowledge, this study is the first to address the synergistic associations of LTPA intensity and the frequency of milk intake with pathoglycemia.

However, the study has several limitations. First, data on PA and the frequency of milk intake were self-reported by respondents. Because self-reports are potentially erroneous, such errors would have partially influenced our results. Second, except for LTPA intensity, we did not analyze the associations between the prevalence of pathoglycemia and other types of PA, including work-related PA, housework-related PA, and transportation-related PA. Third, types of milk, such as milk with different fat content, were not considered in our analysis. A future analysis that distinguishes types of milk may yield different results. Fourth, because our research design was cross-sectional, data on the incidence of pathoglycemia could not be obtained. Specifically, although our study focused on participants with newly diagnosed pathoglycemia, people who had developed pathoglycemia might have changed their behavior upon feeling discomfort from pathoglycemia. Such behavioral changes include increasing LTPA intensity and eating healthier food, which may result in an underestimation of the effect of LTPA intensity and the frequency of milk intake. Therefore, future interventional studies should be conducted to address this concern.

Conclusion

In summary, we determined that both MVLTPA and an enough frequency of milk intake were associated with a significantly lower risk of newly diagnosed pathoglycemia. This reduction in risk was greater when both MVLTPA and an enough frequency of milk intake occurred jointly. Therefore, an intervention study including the 2 factors should be performed.

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CONFLICT OF INTEREST AND FUNDING DISCLOSURE

REFERENCES

1. IDF. International Diabetes Federation diabetes atlas - 8th edition 3/27 [cited: 2019/05/30]; Available from: http://www.diabetesatlas.org/.

2. Shaw JE, Zimmet PZ, de Courten M, Dowse GK, Chitson P, Gareeboo H et al. Impaired fasting glucose or impaired glucose tolerance. What best predicts future diabetes in Mauritius? Diabetes Care. 1999;22:399-402. doi: 10.2337/diacare.22.3.399.

3. Ezzati M, Riboli E. Behavioral and dietary risk factors for noncommunicable diseases. N Engl J Med. 2013;369:954-64. doi: 10.1056/NEJMra1203528.

4. Hemmingsen B, Gimenez-Perez G, Mauricio D, Roque IFM, Metzendorf MI, Richter B. Diet, physical activity or both for prevention or delay of type 2 diabetes mellitus and its associated complications in people at increased risk of developing type 2 diabetes mellitus. Cochrane Database Syst Rev. 2017;4:CD003054. doi: 10.1002/14651858.CD003054.pub4.

5. Shan Z, Li Y, Zong G, Guo Y, Li J, Manson JE et al. Rotating night shift work and adherence to unhealthy lifestyle in predicting risk of type 2 diabetes: results from two large US cohorts of female nurses. BMJ. 2018;363:k4641. doi: 10.1136/bmj.k4641.

6. Levine JA WR, Chevassus S, Martinez CD, Burlingame B, Coward WA. The Work Burden of Women. Science. 2001;294:812. doi: 10.1126/science.1064627.

7. Liu Y, Wen W, Gao YT, Li HL, Yang G, Xiang YB, Shu XO, Zheng W. Level of moderate-intensity leisure-time physical activity and reduced mortality in middle-aged and elderly Chinese. J Epidemiol Community Health. 2018;72:13-20. doi: 10.1136/jech-2017-209903.

8. Moslehi N, Shab-Bidar S, Mirmiran P, Sadeghi M, Azizi F. Associations between dairy products consumption and risk of type 2 diabetes: Tehran lipid and glucose study. Int J Food Sci Nutr. 2015;66:692-9. doi: 10.3109/09637486.2015.1034249.

9. Vissers LET, Sluijs I, van der Schouw YT, Forouhi NG, Imamura F, Burgess S et al. Dairy Product Intake and Risk of Type 2 Diabetes in EPIC-InterAct: A Mendelian Randomization Study. Diabetes Care. 2019;42:568-75. doi: 10.2337/dc18-2034.

10. Wang L, Gao P, Zhang M, Huang Z, Zhang D, Deng Q et al. Prevalence and Ethnic Pattern of Diabetes and Prediabetes in China in 2013. JAMA. 2017;317:2515-23. doi: 10.1001/jama.2017.7596.

11. Weng J, Ji L, Jia W, Lu J, Zhou Z, Zou D et al. Standards of care for type 2 diabetes in China. Diabetes Metab Res Rev. 2016;32:442-58. doi: 10.1002/dmrr.2827.

12. Fan M, Lyu J, He P. Chinese guidelines for data processing and analysis concerning the International Physical Activity Questionnaire. Chinese Journal of Epidemiology. 2014;35:961-4. doi: 10.1260/1750-9548.6.4.365.

13. Wen CP, Wai JP, Tsai MK, Yang YC, Cheng TY, Lee MC et al. Minimum amount of physical activity for reduced mortality and extended life expectancy: a prospective cohort study. Lancet. 2011;378:1244-53. doi: 10.1016/s0140-6736(11)60749-6.

14. Chudasama YV, Zaccardi F, Gillies CL, Dhalwani NN, Yates T, Rowlands AV, Davies MJ, Khunti KK. Leisure-time Physical Activity and Life Expectancy in people with Cardiometabolic Multimorbidity and Depression. J Intern Med. 2019. doi: 10.1111/joim.12987.

15. MOH.PRC. Guideline on physical activity for adults in China: People's Medical Publishing House; 2011.

16. Talaei M, Hosseini N, van Dam RM, Sadeghi M, Oveisgharan S, Dianatkhah M, Sarrafzadegan N. Whole milk consumption and risk of cardiovascular disease and mortality: Isfahan Cohort Study. Eur J Nutr. 2019;58:163-71. doi: 10.1007/s00394-017-1581-1.

17. Wang X, Zhang T, Wu J, Yin S, Nan X, Du M, Liu A, Wang P. The Association between Socioeconomic Status, Smoking, and Chronic Disease in Inner Mongolia in Northern China. Int J Environ Res Public Health. 2019;16:169-80. doi: 10.3390/ijerph16020169.

18. Chen C, Lu FC. The guidelines for prevention and control of overweight and obesity in Chinese adults. Biomed Environ Sci. 2004;17:1-36. doi: 10.1111/j.1365-2028.2008.00991.x.

19. Elm Ev, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. BMJ. 2007;335:806-8. doi: 10.1136/bmj.39335.541782.AD.

20. Brouwer-Brolsma EM, Sluik D, Singh-Povel CM, Feskens EJM. Dairy product consumption is associated with pre-diabetes and newly diagnosed type 2 diabetes in the Lifelines Cohort Study. Br J Nutr. 2018;119:442-55. doi: 10.1017/S0007114517003762.

21. Medina C, Janssen I, Barquera S, Bautista-Arredondo S, Gonzalez ME, Gonzalez C. Occupational and leisure time physical inactivity and the risk of type II diabetes and hypertension among Mexican adults: A prospective cohort study. Sci Rep. 2018;8:5399-405. doi: 10.1038/s41598-018-23553-6.

22. Tian Y, Jiang C, Wang M, Cai R, Zhang Y, He Z et al. BMI, leisure-time physical activity, and physical fitness in adults in China: results from a series of national surveys, 2000–14. The Lancet Diabetes & Endocrinology. 2016;4:487-97. doi: 10.1016/s2213-8587(16)00081-4.

23. WHO. Prevention of noncommunicable diseases 3/27 [cited: 2019/5/30]; Available from: https://www.who.int/activities/preventing-noncommunicable-diseases/.

24. Hyman DJ, Pavlik VN, Taylor WC, Goodrick GK, Moye L. Simultaneous vs sequential counseling for multiple behavior change. Arch Intern Med. 2007;167:1152-8. doi: 10.1001/archinte.167.11.1152.

25. Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002;346:393-403. doi: 10.1056/NEJMoa012512.

26. Tuomilehto J, Lindström J, Eriksson JG, Valle TT, Hämäläinen H, Ilanne-Parikka P et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med. 2001;344:1343-50. doi: 10.1056/nejm200105033441801.

27. Greaves CJ, Sheppard KE, Abraham C, Hardeman W, Roden M, Evans PH, Schwarz P. Systematic review of reviews of intervention components associated with increased effectiveness in dietary and physical activity interventions. BMC Public Health. 2011;11:119-30. doi: 10.1186/1471-2458-11-119.

28. Umpierre D, Ribeiro PA, Kramer CK, Leitao CB, Zucatti AT, Azevedo MJ, Gross JL, Ribeiro JP, Schaan BD. Physical activity advice only or structured exercise training and association with HbA1c levels in type 2 diabetes: a systematic review and meta-analysis. JAMA. 2011;305:1790-9. doi: 10.1001/jama.2011.576.

Table 1. General characteristics of LTPA intensity and the frequency of milk intake in the study population (n/%)

Item	N	LTPA intensity				The frequency of milk intake			
		MVLTPA	LILTPA	χ^2	$p^\dagger$	>once/week	≤once/week	χ^2	$p^\dagger$
Gender									
male	1320	159 (12.0%)	1161 (88.0%)	12.1	<0.001	745 (56.4%)	575 (43.6%)	53.8	<0.001
female	1657	263 (15.0%)	1493 (85.0%)			1152 (69.5%)	505 (30.5%)		
Age (years)									
≤50	1458	176 (12.1%)	1282 (87.9%)	15.0	<0.001	937 (64.3%)	521 (35.7%)	0.3	0.571
≥50	1519	118 (7.8%)	1401 (92.2%)			960 (63.2%)	559 (36.8%)		
Marital status									
married or living with others	2570	214 (8.3%)	2356 (91.7%)	80.4	<0.001	1618 (63.0%)	952 (37.0%)	7.10	0.029
single or living apart	255	66 (25.9%)	189 (74.1%)			182 (71.4%)	73 (28.6%)		
Divorced or widowed	152	14 (9.2%)	138 (90.8%)			97 (63.8%)	55 (36.2%)		
Socioeconomic status									
low	1017	65 (6.4%)	952（93.6%）	21.2	<0.001	566 (55.7%)	451 (44.3%)	63.0	<0.001
middle	791	90 (11.4%)	701（88.6%）			491 (62.1%)	300 (37.9%)		
high	1169	139 (11.9%)	1030（88.1%）			840 (71.9%)	329 (28.1%)		
Occupation									
manual worker or service staff	809	53 (6.6%)	756 (93.4%)	60.6	<0.001	471 (58.2%)	338 (41.8%)	28.4	<0.001
managers or technician	881	86 (9.8%)	795 (90.2%)			620 (70.4%)	261 (29.6%)		
unemployment or retired	921	79 (8.6%)	842 (91.4%)			581 (63.1%)	340 (36.9%)		
others	366	76 (20.8%)	290 (79.2%)			225 (61.5%)	141 (38.5%)		
BMI									
<24	1135	129 (11.4%)	1006 (88.6%)	4.6	0.032	777 (68.5%)	358 (31.5%)	17.5	<0.001
≥24	1842	165 (9.0%)	1677 (91.0%)			1120 (60.8%)	722 (66.9%)		
Smoking (times/day)									
<1	2213	217 (9.8%)	1996 (90.2%)	0.02	0.883	1522 (68.8%)	691 (31.2%)	94.4	<0.001
≥1	764	77 (10.1%)	687 (89.9%)			375 (49.1%)	389 (50.9%)		
Alcohol (times/ day)									
<1	2085	213 (10.2%)	1872 (89.8%)	0.8	0.377	1429 (68.5%)	656 (31.5%)	69.1	<0.001
≥1	892	81 (9.1%)	811 (90.9%)			468 (52.5%)	424 (47.5%)		
Total mass of cereals, tubers, vegetables and fruit (g)									
<800	1515	118 (7.8%)	1397 (92.2%)	15.1	<0.001	916 (60.5%)	599 (39.5%)	13.9	<0.001
≥800	1462	176 (12.0%)	1286 (88.0%)			981 (67.1%)	481 (32.9%)		

LTPA: leisure-time physical activity; MVLTPA: moderate and vigorous leisure-time physical activity; LILTPA: low intensity of leisure-time physical activity; OR, odds rate.
†*p*-value is the result of a simple Chi-square test to examine whether association between sociodemographic information and leisure- time physical activity intensity, the frequency of milk intake respectively was statistically significant.
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Table 2. Association of LTPA intensity and the frequency of milk intake with newly diagnosed pathoglycemia

Item	N	Newly diagnosed pathoglycemia	Unadjusted		Model 1[†]		Model 2[‡]	
			p	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)
LTPA intensity								
MVLTPA	294	42 (14.3%)	0.002	0.584 (0.410-0.810)	0.022	0.663 (0.461-0.934)	0.033	0.681 (0.473-0.960)
LILTPA	2683	596 (22.2%)		1.000 (reference)		1.000 (reference)		1.000 (reference)
The frequency of milk intake								
>once/week	1897	370 (19.5%)	0.001	0.734 (0.614-0.878)	0.102	0.855 (0.708-1.032)	0.252	0.895 (0.739-1.083)
≤once/week	1080	201 (24.8%)		1.000 (reference)		1.000 (reference)		1.000 (reference)

LTPA: leisure-time physical activity; MVLTPA: moderate and vigorous leisure-time physical activity; LILTPA: low intensity of leisure-time physical activity; CI: confidence interval; OR: odds rate.
[†]Model 1 adjusted for age, gender, marital status, occupation and socioeconomic status.
[‡]Model 2 adjusted for family history of BMI, smoking status, drinking status and total mass of cereals, tubers, vegetables and fruit based on Model 1.

Table 3. Synergistic associations of LTPA intensity and the frequency of milk intake with newly diagnosed pathoglycemia

LTPA intensity	The frequency of milk intake	N	Newly diagnosed pathoglycemia	Unadjusted		Model 1[†]		Model 2[‡]	
				p	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)
LILTPA	≤once/week	998	254(25.5%)		1.000 (reference)		1.000 (reference)		1.000 (reference)
	>once/week	1685	342(20.3%)	0.002	0.746(0.620- 0.898)	0.135	0.856 (0.705-1.042)	0.264	0.893(0.732-1.090)
MVLTPA	≤once/week	82	14(17.1%)	0.094	0.603(0.321- 1.058)	0.120	0.630(0.331-1.1222)	0.138	0.638(0.330-1.128)
	>once/week	212	28(13.2%)	<0.001	0.446(0.287-0.669)	0.020	0.593 (0.375- 0.908)	0.048	0.631(0.403-0.982)

LTPA: leisure-time physical activity; MVLTPA: moderate and vigorous leisure-time physical activity; LILTPA: low intensity of leisure-time physical activity; CI: confidence interval; OR: odds rate.
[†]Model 1 adjusted for age, gender, marital status, occupation and socioeconomic status.
[‡]Model 2 adjusted for family history of BMI, smoking status, drinking status and total mass of cereals, tubers, vegetables and fruit based on model 1
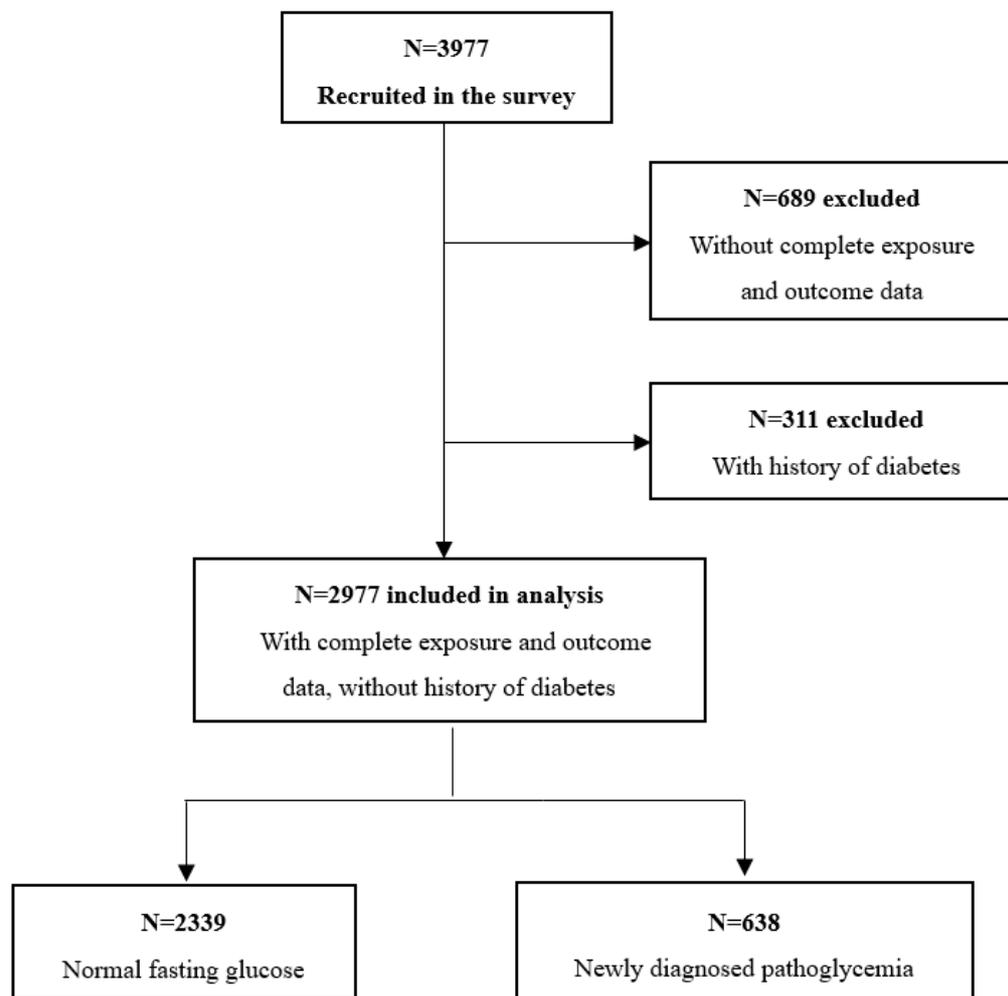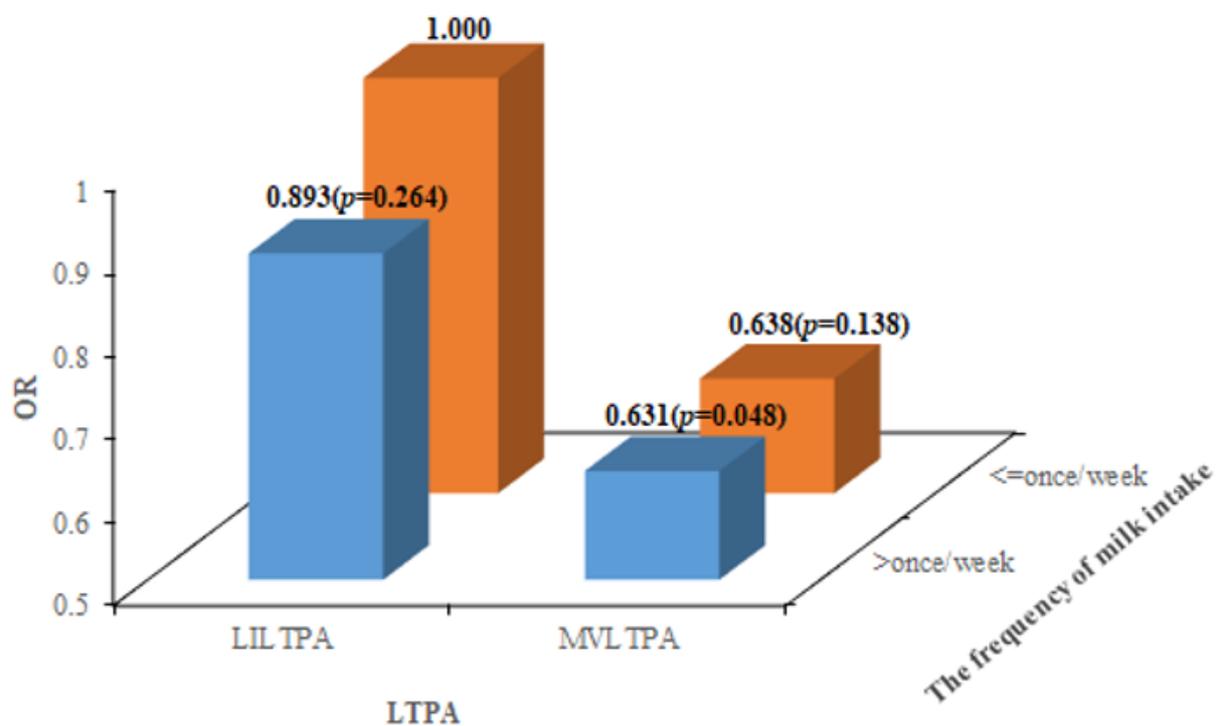
Figure 1. Study design figure.

Figure 2. Synergistic associations of LTPA intensity and the frequency of milk intake with pathoglycemia. OR was calculated to estimate the synergistic associations in binary logistic regression after adjusting gender, age, marital status, socioeconomic status, occupation, BMI, smoking status, drinking status, the total quality intake of cereals, tubers, vegetables, and fruit per day, with the LILTPA and frequency of milk intake ≤once/week group as the reference group. LTPA: leisure-time physical activity; MVLTPA: moderate and vigorous leisure-time physical activity; LILTPA: low intensity of leisure-time physical activity; OR: odds rate.

Supplementary table 1. Association of LTPA intensity and the frequency of milk intake with newly diagnosed IFG and T2DM

Item	IFG				T2DM			
	N (%)	Unadjusted OR	Model 1[†] OR	Model 2[‡] OR	N (%)	Unadjusted OR	Model 1[†] OR	Model 2[‡] OR
LTPA intensity								
MVLTPA	23 (8.36)	0.559 (0.350-0.850)**	0.631 (0.391-0.975)*	0.650 (0.402-1.006)	19 (7.01)	0.617 (0.368-0.975)	0.712 (0.419-1.146)	0.729 (0.429-1.174)
LILTPA	341 (14.04)	1.000 (reference)	1.000 (reference)	1.000 (reference)	255 (10.89)	1.000 (reference)	1.000 (reference)	1.000 (reference)
The frequency of milk intake								
>once/week	212 (12.19)	0.742 (0.593-0.930)**	0.864 (0.685-1.094)	0.904 (0.714-1.147)	158 (9.38)	0.724 (0.117-0.172)*	0.881 (0.675-1.151)	0.910 (0.696-1.194)
≤once/week	152 (15.78)	1.000 (reference)	1.000 (reference)	1.000 (reference)	116 (12.50)	1.000 (reference)	1.000 (reference)	1.000 (reference)

LTPA: leisure-time physical activity; MVLTPA: moderate and vigorous leisure-time physical activity; LILTPA: low intensity of leisure-time physical activity; CI: confidence interval; OR: odds rate.
[†]Model 1 adjusted for age, gender, marital status, occupation and socioeconomic status.
[‡]Model 2 adjusted for family history of BMI, smoking status, drinking status and total mass of cereals, tubers, vegetables and fruit based on model 1.
*$p<0.05$, **$p<0.01$.

Supplementary table 2. Synergistic associations of LTPA intensity and the frequency of milk intake with newly diagnosed IFG and T2DM

LTPA intensity	The frequency of milk intake	IFG				T2DM			
		N (%)	Unadjusted OR	Model 1[†] OR	Model 2[‡] OR	N	Unadjusted OR	Model 1[†] OR	Model 2[‡] OR
LILTPA	≤once/week	144 (16.2)	1.000 (reference)	1.000 (reference)	1.000 (reference)	110 (12.9)	1.000 (reference)	1.000 (reference)	1.000 (reference)
	>once/week	197 (12.8)	0.758 (0.601-0.958)*	0.869 (0.682-1.108)	0.904 (0.780-1.157)	145 (9.7)	0.730 (0.562-0.952)*	0.875 (0.665-1.154)	0.904 (0.780-1.157)
MVLTPA	≤once/week	8 (10.5)	0.608 (0.265-1.220)	0.622 (0.269-1.264)	0.623 (0.268-1.271)	6 (8.1)	0.597 (0.227-1.302)	0.633 (0.238-1.404)	0.623 (0.268-1.271)
	>once/week	15 (7.5)	0.421 (0.232-0.712)*	0.559 (0.303-0.967)*	0.606 (0.328-1.050)	13 (6.6)	0.478 (0.251-0.838)*	0.671 (0.345-1.212)	0.606 (0.328-1.050)

LTPA: leisure-time physical activity; MVLTPA: moderate and vigorous leisure-time physical activity; LILTPA: low intensity of leisure-time physical activity; CI: confidence interval; OR: odds rate.
[†]Model 1 adjusted for age, gender, marital status, occupation and socioeconomic status.
[‡]Model 2 adjusted for family history of BMI, smoking status, drinking status and total mass of cereals, tubers, vegetables and fruit based on model 1.
*$p<0.05$.