

# Rethinking Diabetes Risk in Perimenopause: Beyond BMI, the Dynamic Role of Weight Change over Time

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## Research Article

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# Abstract

## Background

The association between BMI and the risk of T2DM in perimenopausal women remains insufficient. This study aims to systematically explore the prospective relationship between BMI, its changes, and the incidence of T2DM in a Chinese cohort of perimenopausal women.

## Methods

The study based on the CHARLS, enrolled diabetes-free perimenopausal women across five survey waves (2011–2020). The outcome was new-onset T2DM during follow-up. The exposure variables included baseline BMI status, its change patterns and relative BMI changes during the perimenopausal period. Cox proportional hazards regression model were used to analyze the association of both continuous BMI and its dynamic changes with T2DM risk, and the accelerated failure time (AFT) model was used to analyze the impact of BMI categories on the onset time. All models incorporated sequential adjustment for covariates including demographics, socioeconomic status, behaviors, and depressive symptoms.

## Results

A total of 1325 perimenopausal women were included and 150 of them developed new-onset diabetes. Cox regression analysis revealed that each 1 kg/m<sup>2</sup> increase in BMI was associated with an 11.6% increased risk of T2DM ( $HR = 1.116$ , 95%  $CI$ : 1.073 to 1.161), with restricted cubic spline analysis confirming a continuous dose-response relationship ( $P < 0.001$ ). Meanwhile, the AFT model showed that diabetes onset was 45.2% and 66.6% earlier in the overweight and obese groups than in the underweight/normal weight group, respectively. Among 579 women with repeated BMI assessments, maintaining normal weight during perimenopause was associated with a 69% lower risk of diabetes ( $HR = 0.31$ , 95%  $CI$ : 0.13 to 0.73) relative to persistent obesity. However, no significant association was found between relative BMI change with a threshold of  $\pm 3\%$ ,  $\pm 5\%$  and the risk of diabetes.

## Conclusion

In perimenopausal women, higher BMI is an independent risk factor for T2DM and accelerates the onset of T2DM. Maintaining a normal weight throughout this stage significantly reduces future diabetes risk, underscoring the critical importance of long - term weight management during perimenopause for diabetes prevention in this population.

## Background

Type 2 Diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by dysregulation of insulin metabolism and is widely recognized as one of the major global public health challenges[1]. Epidemiological data indicate that the prevalence of diabetes among the global population aged 20–79 years is approximately 9.09%[2], with a higher prevalence observed in women (10.5%)[3]. While prior research has predominantly focused on classical metabolic mechanisms such as insulin resistance, increasing attention has been directed toward the association between female-specific reproductive endocrine features and metabolic health.

Perimenopause represents a critical transitional phase from reproductive to non-reproductive status in women. During this period, declining estrogen levels trigger significant metabolic remodeling, including alterations in body fat distribution, activation of inflammatory factors, lipid metabolism disorders, and reduced insulin sensitivity – collectively forming a key pathological basis for the development of T2DM[4]. Compared with other physiological stages, perimenopausal women exhibit an elevated risk of T2DM[5, 6], a phenomenon closely linked to hormone-driven increases in metabolic syndrome susceptibility[4]. Furthermore, epidemiological evidence demonstrates that abnormal age at menopause (whether premature or delayed) is significantly associated with T2DM risk, suggesting a potential interrelationship between reproductive endocrine changes and glucose metabolism dysregulation[7].

Much of the excess T2DM risk associated with these perimenopausal metabolic changes is mediated by or reflected in changes in body weight and fat distribution. Consequently, Body Mass Index (BMI), as a core metric for assessing obesity, is closely associated with the risk of incident T2DM in this population. Dynamic BMI changes during the perimenopausal period exhibit stage-specific patterns[8, 9], with elevated BMI serves as a critical biomarker reflecting adipose tissue accumulation and its disruptive impact on metabolic homeostasis[10]. Notably, long-term patterns of BMI change can more accurately reflect the cumulative metabolic risk burden compared with single-timepoint BMI measurements[11, 12].

In longitudinal BMI studies, existing literature shows methodological divergence in characterizing dynamic weight changes: some studies focus on BMI status temporal evolution patterns[13–16] or transitions between BMI categories[17] to reveal individual phenotypic trajectory heterogeneity, while others emphasize quantifying weight change magnitude to clarify associations between change extent and health outcomes[18–20]. Notably, these two approaches have been predominantly applied separately without systematic integration. This study innovatively synthesizes both perspectives to comprehensively delineate BMI dynamics in perimenopausal women: (1) capturing directional patterns of weight change through transitions in BMI categories over time, and (2) defining relative BMI change to reflect the magnitude of BMI fluctuation.

Given the rising prevalence of diabetes and the unique metabolic vulnerability of perimenopausal women, existing evidence exhibits notable limitations. Most longitudinal studies have predominantly focused on middle-aged or the elderly[15, 21] or broadly defined populations[22], thereby failing to systematically elucidate the associations between BMI – including its baseline status, dynamic patterns,

and relative BMI changes – and T2DM risk specifically within the perimenopausal physiological transition period.

To address this gap, concentrating on perimenopausal women to comprehensively investigate the temporal relationships between BMI characteristics and T2DM incidence is essential. Identifying clinically meaningful weight-change thresholds would not only facilitate the identification of high-risk individuals and refinement of risk prediction tools but also provide evidence-based foundations for precise interventions during this critical window, ultimately holding substantial public health significance for mitigating the lifelong metabolic disease burden in women.

## Methods

### Data Source

The China Health and Retirement Longitudinal Study (CHARLS) is a nationally representative prospective cohort study targeting Chinese adults aged  $\geq 45$  years from 150 counties across 28 provinces. Data were collected through face-to-face household interviews, covering demographics, socioeconomic status, family structure, and health-related variables. The baseline survey was initiated in 2011, with follow-up surveys conducted biennially through 2020 (in 2013, 2015, 2018, and 2020). The present analysis utilized longitudinal data spanning all five survey waves.

### Study design and participants

This study focused on perimenopausal women. Based on previous research, perimenopause is defined as the reproductive aging stage that begins with the menopausal transition (typically lasting 2 to 8 years, averaging approximately 4 years) and continues until 12 months after the final menstrual period[23] (Figure S1). In the CHARLS dataset, perimenopausal status was ascertained using two survey items: “DA027. Have you started menopause?” and “DA028\_1. In which year did your menopause begin?” Women who reported not having reached menopause in an earlier wave but subsequently reported menopause onset in a later wave were classified as perimenopausal at the time of the prior survey based on their responses to DA027. Additionally, women whose self-reported year of menopause onset (from DA028\_1) matched the calendar year of the survey were designated as perimenopausal during that wave. The operational definition and detailed screening process is presented in Fig. 1.

From this cohort, participants were excluded if they met any of the following criteria at Wave 1 (T1): age  $< 30$  or  $> 60$  years, missing BMI data, self-reported diagnosis of T2DM, or loss to follow-up after T1. This resulted in a final analytical sample of 1325 women, with T1 serving as the baseline for examining the association between baseline BMI and incident T2DM risk. These participants were followed until their last survey participation.

Subsequently, within this subset, further exclusions were applied for missing BMI data, self-reported T2DM at Wave 2 (T2), or loss to follow-up after T2. Ultimately, 579 women remained, with T2 redefined as the new baseline, to investigate the association between BMI changes during the perimenopause and subsequent incident T2DM risk. The participant flow is summarized in Fig. 2.

## Outcome variables

The study outcome was incident type 2 diabetes mellitus (T2DM). Diabetes status was ascertained using self-reported data from CHARLS, applying the following criteria: prior clinical diagnosis of T2DM by a healthcare institution, current regular use of oral hypoglycemic agents, or current insulin therapy. Participants meeting any one of these criterion were classified as having T2DM. For incident case identification, the time of T2DM onset was estimated as the midpoint between the last survey wave reporting absence of diabetes and the first wave reporting diabetes diagnosis or treatment initiation. Survival time (time-to-event) was calculated as the interval (in years) from baseline assessment to the estimated onset data. For participants remaining diabetes-free throughout follow-up, survival time was right-censored at the date of their last valid follow-up survey.

## Exposure assessment

BMI and its change patterns were the primary exposures in this study. BMI was calculated by standard formula:  $BMI = \text{weight (kg)} / [\text{height (m)}]^2$ , expressed in  $\text{kg/m}^2$ . BMI classification adhered to the criteria for Chinese adults established by the China Working Group on Obesity[24], dividing individuals into four groups: underweight group ( $BMI < 18.5\text{kg/m}^2$ ), normal weight group ( $18.5 \leq BMI < 24.0\text{kg/m}^2$ ), overweight group ( $24.0 \leq BMI < 28.0\text{kg/m}^2$ ), and obese group ( $BMI \geq 28.0\text{kg/m}^2$ ). In our study, underweight participants were merged with the normal weight group due to their low prevalence of 2.6%. Developed based on Chinese-specific body composition and metabolic risk profiles, this classification is widely used in epidemiological studies of chronic disease risk in Chinese cohorts[24, 25].

Based on BMI data from two time points and consistent with prior research, we defined the following BMI change patterns[17]: (1) stable normal weight (maintained underweight or normal weight at both time points), (2) maximal overweight (overweight at one time point and non-obese at the other), (3) obese to non-obese (obese at the first time point and non-obese at the second), (4) non-obese to obese (non-obese at the first time point and obese at the second), and (5) stable obese (persistently obese at both time points). Additionally, we calculates relative BMI change using BMI data from two time points:  $BMI \text{ change (\%)} = (BMI_2 - BMI_1) / BMI_1 \times 100\%$ . Relative BMI changes were categorized into five groups[18, 26]: significant decrease ( $\text{change} \leq -5\%$ ), moderate decrease ( $-5\% < \text{change} \leq -3\%$ ), stable (absolute change  $< 3\%$ ), moderate increase ( $3\% \leq \text{change} < 5\%$ ), and significant increase ( $\text{change} \geq 5\%$ ).

## Covariates

Based on literature review and causal inference framework, we constructed a directed acyclic graph (DAG) using DAGitty software to identify the minimally sufficient adjustment set (MSA) for controlling confounding bias[27]. The MSA, validated by the back-door criterion, includes sociodemographic variables (age, ethnicity, economic status, educational level, marital status, and residence type), behavioral and lifestyle factors (smoking status, drinking status, physical activity, and sleep duration), and health indicators (depressive symptoms), as showed in Figure S3

Age was treated as a continuous variable, whereas all other variables were analyzed as categorical. Ethnicity was categorized as Han Chinese or ethnic minority. Educational attainment was classified into four levels: illiterate, primary school or below, junior high school, and senior high school or above. Marital status was classified as married or cohabiting versus other statuses including separated, divorced, widowed, or never married. Residence type was defined as urban or rural. Economic status was evaluated based on household consumption expenditure and stratified into four quartiles: low, lower-middle, upper-middle, and high economic status. Smoking status was categorized as never smoked versus ever/current smoker. Drinking status was categorized as never drank versus ever/current drinker. Physical activity was defined as active if participants engaged in at least one session of moderate- or vigorous-intensity activity per month, otherwise, they were classified as inactive[28]. Sleep duration was categorized into three groups based on criteria widely adopted in epidemiological and large cohort studies: short (< 7 hours), normal (7–8 hours), and long (> 8 hours) night-time sleep duration[29]. Depressive symptoms were assessed using the 10-item Center for Epidemiologic Studies Depression Scale (CESD-10), which evaluates the frequency of depressive symptoms experienced over the past week across 10 items. Total scores range from 0 to 30, with a score of  $\geq 10$  indicating the presence of depressive symptoms and < 10 indicating absence.

Missing covariates were handled using multiple imputation (MI)[30, 31]. The imputation procedure was configured to generate five complete datasets ( $m = 5$ ) with the number of iterations set to 10 ( $\text{maxit} = 10$ ). Finally, parameter estimates and standard errors were pooled according to Rubin's rules. The proportions of missing values for each variable are summarized in Table S1 and Table S3.

## Statistical analysis

Baseline continuous variables were summarized as mean $\pm$ standard deviation (SD) and compared between groups using independent samples t-test. Categorical variables were presented as frequency (percentage), with group differences assessed by chi-square test for unordered categories and Mann-Whitney U test for ordinal variables.

Associations of baseline BMI and BMI change patterns with T2DM risk were evaluated using Cox proportional hazards regression, reporting results as hazard ratios (HRs) with 95% confidence intervals (95% CIs). The restricted cubic spline (RCS) model with knots at standard BMI cut-offs for normal weight, overweight, and obesity was used to assess dose-response relationships. Both overall and non-linearity p-values are reported. Kaplan-Meier curves for categorical BMI groups crossed, and Schoenfeld residual

testing confirmed violation of the proportional hazards (PH) assumption for categorical BMI, ethnicity, and smoking status ( $P < 0.05$ , Supplementary Figs. 7). Consequently, the Accelerated Failure Time (AFT) model was used to estimate the association between baseline categorical BMI and T2DM risk.

Because the missing data proportion of the physical activity variable exceeded 30%[32], and following methodological recommendations cautious handling of variables with substantial missingness, this variable was excluded from subsequent sensitivity analyses to evaluate the robustness of the primary findings under scenarios excluding extreme missingness. Additionally, underweight individuals were excluded for sensitivity analysis.

Four sequential models were fitted. Model 1 was unadjusted. Model 2 adjusted for sociodemographic variables (age, ethnicity, economic level, education level, marital status, and residence type). Model 3 further adjusted for behavioral and lifestyle factors (smoking status, drinking status, physical activity and sleep duration). Model 4 additionally adjusted for depressive symptoms. The PH assumption was evaluated using the Schoenfeld residuals test. For variables violating it, stratified Cox regression was performed. All statistical analyses were conducted using R software (v4.5.1), and two-sided  $P < 0.05$  considered significant.

## Results

### Baseline Characteristics of the Study Population

A total of 1325 perimenopausal women were included in analysis 1. During the follow-up period, 150 (11.32%) women developed incident T2DM, whereas 1,175 remained diabetes-free. The mean age was  $50.6 \pm 3.5$  years in the T2DM group and  $50.0 \pm 3.4$  years in the non-T2DM group, and this difference was statistically significant ( $P < 0.001$ ). The incidence of T2DM in overweight and obese individuals was significantly higher than that in underweight or normal weight individuals, with rates of 40.67% in the overweight group, 33.33% in the obese group, and 26.00% in the underweight/normal weight group ( $P < 0.001$ ), refer to Table 1 for details.

Table 1  
Demographic characteristics of participants

| Characteristics                 | Total<br>(n = 1325) | non-T2DM<br>(n = 1175) | T2DM<br>(n = 150) | <i>P value</i> |
|---------------------------------|---------------------|------------------------|-------------------|----------------|
| <b>BMI</b>                      | 24.7 ± 3.7          | 24.5 ± 3.6             | 26.3 ± 3.8        | < 0.001        |
| <b>BMI_C</b>                    |                     |                        |                   | < 0.001        |
| underweight/normal weight group | 579(43.70%)         | 540(45.96%)            | 39(26.00%)        |                |
| overweight group                | 512(38.64%)         | 451(38.38%)            | 61(40.67%)        |                |
| obese group                     | 234(17.66%)         | 184(15.66%)            | 50(33.33%)        |                |
| <b>age (years)</b>              | 50.0 ± 3.4          | 50.0 ± 3.4             | 50.6 ± 3.5        | 0.036          |
| <b>ethnicity</b>                |                     |                        |                   | 0.377          |
| Han Chinese                     | 1237(93.36%)        | 1100(93.62%)           | 137(91.33%)       |                |
| ethnic minorities               | 88(6.64%)           | 75(6.38%)              | 13(8.67%)         |                |
| <b>economic</b>                 |                     |                        |                   | 0.511          |
| low economic status             | 260(25.05%)         | 226(24.54%)            | 34(29.06%)        |                |
| lower-middle economic status    | 259(24.95%)         | 235(25.52%)            | 24(20.51%)        |                |
| upper-middle economic status    | 259(24.94%)         | 226(24.54%)            | 33(28.21%)        |                |
| high economic status            | 260(25.05%)         | 234(25.41%)            | 26(22.22%)        |                |
| <b>education</b>                |                     |                        |                   | 0.792          |
| illiterate                      | 295(22.26%)         | 253(21.53%)            | 42(28.00%)        |                |
| primary or below                | 523(39.47%)         | 478(40.68%)            | 45(30.00%)        |                |
| junior high                     | 339(25.58%)         | 295(25.11%)            | 44(29.33%)        |                |
| senior high or above            | 168(12.68%)         | 149(12.68%)            | 19(12.67%)        |                |
| <b>marital status</b>           |                     |                        |                   |                |
| married/cohabiting              | 1268(95.70%)        | 1129(96.09%)           | 139(92.67%)       | 0.084          |
| other situations                | 57(4.30%)           | 46(3.91%)              | 11(7.33%)         |                |
| <b>residence type</b>           |                     |                        |                   | > 0.999        |
| urban                           | 479(36.15%)         | 425(36.17%)            | 54(36.00%)        |                |
| rural                           | 846(63.85%)         | 750(63.83%)            | 96(64.00%)        |                |
| <b>smoking status</b>           |                     |                        |                   | 0.200          |

| Characteristics            | Total<br>(n = 1325) | non-T2DM<br>(n = 1175) | T2DM<br>(n = 150) | <i>P</i> value |
|----------------------------|---------------------|------------------------|-------------------|----------------|
| never                      | 1253(94.57%)        | 1115(94.89%)           | 138(92.00%)       |                |
| ever/current               | 72(5.43%)           | 60(5.11%)              | 12(8.00%)         |                |
| <b>drinking status</b>     |                     |                        |                   | 0.390          |
| never                      | 1065(80.38%)        | 940(80.00%)            | 125(83.33%)       |                |
| ever/current               | 260(19.62%)         | 235(20.00%)            | 25(16.67%)        |                |
| <b>physical activity</b>   |                     |                        |                   | 0.426          |
| active                     | 481(76.59%)         | 444(77.08%)            | 37(71.15%)        |                |
| inactive                   | 147(23.41%)         | 132(22.92%)            | 15(28.85%)        |                |
| <b>sleep duration</b>      |                     |                        |                   | 0.448          |
| <7h                        | 547(41.82%)         | 492(42.34%)            | 55(37.67%)        |                |
| 7 ~ 8h                     | 661(50.54%)         | 580(49.91%)            | 81(55.48%)        |                |
| >8h                        | 100(7.65%)          | 90(7.75%)              | 10(6.85%)         |                |
| <b>Depressive symptoms</b> |                     |                        |                   | 0.703          |
| No                         | 789(59.77%)         | 702(60.00%)            | 87(58.00%)        |                |
| Yes                        | 531(40.23%)         | 468(40.00%)            | 63(42.00%)        |                |

## Continuous BMI and the risk of T2DM

The restricted cubic spline (RCS) analysis depicted a continuous, positive dose-response relationship between BMI and the risk of incident T2DM ( $P_{\text{overall}} < 0.001$ ,  $P_{\text{non-linear}} > 0.05$ , Figure S6), confirming that T2DM risk rises progressively with increasing BMI without evidence of threshold effects or curvature. Cox proportional hazards regression (Fig. 3) consistently demonstrated hazard ratios ( $HR > 1$ ,  $P < 0.001$ ) across all four sequentially adjusted models, reinforcing that higher BMI is independently associated with elevated risk of incident T2DM. In the fully adjusted Model 4, each 1 kg/m<sup>2</sup> increment in BMI was associated with an 11.6% higher risk of developing T2DM ( $HR = 1.116$ , 95%CI: 1.073 to 1.161,  $P < 0.001$ ).

## Categorical BMI and the risk of T2DM

Analysis using AFT model confirmed that overweight and obesity are independent risk factors for T2DM incidence. After adjusting for potential confounders (Model 4) and using the underweight/normal weight group as the reference, the time ratio (TR) for the obese group was 0.334 (95%CI: 0.234 to 0.476,  $P < 0.001$ ). This indicates that the onset time of diabetes among obese individuals is advanced by approximately 66.6% compared to the reference group. For the overweight group, the TR was 0.548

(95%CI: 0.395 to 0.763,  $P < 0.001$ ), signifying a reduction in time to onset to 54.8% of the reference group (Table 2). The results are consistent with the K-M survival analyses (Figure S8).

Table 2  
Accelerated failure time model results for time to T2DM (Log-normal distribution)

| Model   | BMI<br>ref: underweight/normal weight | TR (95% CI)         | P value |
|---------|---------------------------------------|---------------------|---------|
| Model 1 | overweight                            | 0.557 (0.402–0.771) | < 0.001 |
|         | obeses                                | 0.338 (0.231–0.495) | < 0.001 |
| Model 2 | overweight                            | 0.546 (0.393–0.760) | < 0.001 |
|         | obeses                                | 0.327 (0.222–0.481) | < 0.001 |
| Model 3 | overweight                            | 0.549 (0.395–0.762) | < 0.001 |
|         | obeses                                | 0.333 (0.227–0.490) | < 0.001 |
| Model 4 | overweight                            | 0.548 (0.394–0.763) | < 0.001 |
|         | obeses                                | 0.334 (0.234–0.476) | < 0.001 |

Notes. Abbreviations: BMI, Body Mass Index; TR, Time Ratio; CI, confidence interval. Model 1 represented the crude model without adjustment for any variables. Model 2 adjusted sociodemographic factors, including age, ethnicity, economic level, education level, marital status, and residence type. Model 3 further adjusted for behavioral and lifestyle factors—specifically smoking status, drinking status, physical activity and sleep duration. Model 4 further incorporated depressive symptoms.

## BMI change patterns and the risk of T2DM

In analysis 2, among 579 perimenopausal women, 59 incident cases of T2DM were identified (10.23%). The distribution of T2DM cases differed significantly across BMI change groups ( $P = 0.007$ ): maximal overweight ( $n = 22$ , 37.3%), stable underweight/normal weight ( $n = 14$ , 23.7%), stable obese ( $n = 13$ , 22.0%), non-obese to obese group ( $n = 6$ , 10.2%), and obese to non-obese group ( $n = 4$ , 6.8%).

Cox regression analyses consistently demonstrated that women maintaining stable underweight/normal weight exhibited a significantly lower risk of T2DM compared to those with stable obesity (Fig. 4). In Model 4, the hazard ratio was 0.31 (95%CI: 0.13 to 0.72,  $P = 0.009$ ), indicating a 69% reduction in T2DM incidence. This underscores the protective role of sustained normal-weight status during the perimenopausal transition against T2DM development.

## Relative BMI Change and the risk of T2DM

Relative BMI change was categorized into significant decrease, moderate decrease, stable, moderate increase, and significant increase. In Model 4, compared with stable group, none of other groups showed a statistically significant association with incident diabetes (Figure S14). These findings indicate that

relative BMI changes (by 3% and 5% thresholds) in either direction conferred no significant alteration in diabetes risk.

## Sensitivity Analysis

Sensitivity analyses excluding underweight individuals and omitting physical activity adjustment corroborated primary findings: overweight and obesity are significantly associated with earlier T2D onset. Sustaining normal weight during perimenopause holds notable clinical and public health significance for T2D prevention (Figure S16-S23, Table S4-S5).

## Discussion

This study examined the associations of BMI, BMI change patterns, and relative BMI change with incident T2DM risk during perimenopause. Analyses revealed a continuous, positive dose-response relationship between BMI and T2DM risk, without no threshold effect. Compared with the underweight/normal weight group, overweight and obese groups showed earlier T2DM onset, with median diagnosis age reduced by 45.2% and 66.6%, respectively. Furthermore, maintaining normal BMI during perimenopause was associated with a 69% lower T2DM risk, indicating a potentially protective association.

In overweight and obese perimenopausal women, accelerated diabetes onset aligns with stage-specific metabolic changes. Declining estrogen promotes adiposity and insulin resistance, elevating T2DM risk[4]. The perimenopause is a critical window for accelerated cardiometabolic risk, with diabetes prevalence converging with or exceeding other groups[3]. The graded association between body weight and diabetes risk is consistent with evidence from Cox proportional hazards models[18, 33].

This study demonstrates that sustained normal BMI during perimenopause reduces T2DM risk by 69% versus persistent obesity, corroborated by multiple cohorts. Among women with prior gestational diabetes mellitus[34], "persistently high" or "inverted U-shaped" postpartum BMI trajectory were linked to elevated T2DM risk, underscoring the benefit of maintaining a normal BMI as early as possible. Another cohort study[35] indicated that long-term maintenance of target BMI also lowered T2DM incidence in the general middle-aged/older population, with pronounced protection in women and those < 60 years. These findings highlight that weight stability is as crucial as achieving target thresholds.

Notably, however, we found no significant association between two-years BMI increase (3% and 5% ) and diabetes risk in perimenopausal women, diverging from prior literature. Studies by Kagisaki et al.[18] and Asgari et al[19]. reported greater weight increase corresponded to progressively elevated T2D risk. This discrepancy may arise because perimenopausal hormonal fluctuations substantially alter adiposity dynamics, rendering a short-term BMI assessment insufficient to capture long-term metabolic trajectories. Larger longitudinal studies are warranted to clarify the weight change–T2D risk relationship in this population and identify critical thresholds.

Despite the prospective perimenopausal cohort design and multivariable adjustment for confounders, several key limitations persist. First, data constraints precluded the inclusion of critical biomarkers such as glycemic parameters and sex hormone levels, which may result in residual confounding. Second, the ascertainment of T2D relied on self-reported diagnosis or antidiabetic medication use without biochemical verification, potentially introducing bias into outcome classification and exposure–outcome estimates. Third, discrete BMI measurements obtained within a narrow temporal window preclude robust characterization of long-term weight trajectories. Fourth, perimenopause—a dynamic physiological transition—was assessed using periodic questionnaires rather than standardized reproductive staging or serial hormone monitoring, weakening the validity of causal inferences. Future research should integrate longitudinal BMI trajectory modeling, serial hormonal profiling, and genetic analysis to clarify the mechanisms underlying weight dynamics and metabolic risk. Such efforts would inform precision prevention strategies targeting high-risk weight trajectories to reduce the risk of T2D in perimenopausal women.

## Conclusion

In conclusion, this study clarifies a dose-response relationship between BMI and T2DM incidence in perimenopausal women, confirming that overweight and obesity expedite its onset. Longitudinal analysis further identifies sustained normal weight during this transition as a critical protective factor against T2DM.

## Abbreviations

CHARLS

China Health and Retirement Longitudinal Study

BMI

Body mass index

DAGs

Directed acyclic graphs

RCS

Restricted cubic spline

AFT

accelerated failure time model

HR

Hazard ratio

CI

Confidence interval

SD

Standard deviation

# Declarations

## Data availability

The data supporting this study are available on the China Health and Retirement Longitudinal Study (CHARLS) website at <http://charls.pku.edu.cn/>.

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Not applicable.

## Author Contributions

Jing Qi: Data curation and analysis, methodology, and writing original draft. Linyang Song: Methodology and revision of the manuscript. Chuiran Kong, Zhujun Zhong: Manuscript table creation and revision. Yang Wan: Validation and writing-review & editing. All authors read and approved the final manuscript.

## Ethics declarations

### Ethics approval and consent to participate

The original CHARLS data collection was approved by the Institutional Review Board of Peking University (IRB00001052-11015) and conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent before enrollment. This secondary analysis of de-identified public data did not require additional ethical approval.

### Consent for publication

Not applicable.

### Competing interests

The authors declare no competing interests.

# References

1. Pagidipati NJ, Deedwania P. A Comprehensive Cardiovascular-Renal-Metabolic Risk Reduction Approach to Patients with Type 2 Diabetes Mellitus. *Am J Med.* 2021;134(9):1076–84.
2. Ravi H, Das S, Devi Rajeswari V, Venkatraman G, Choudhury AA, Chakraborty S, et al. Hormonal regulation in diabetes: Special emphasis on sex hormones and metabolic traits. *Adv Protein Chem*

Struct Biol. 2024;142:257–91.

3. Lim BSY, Chen M, Li HY, Li LJ. Metformin use in prediabetes: A review of evidence and a focus on metabolic features among peri-menopausal women. *Diabetes Obes Metab*. 2025;27(Suppl 3):3–15.
4. Lambrinoudaki I, Paschou SA, Armeni E, Goulis DG. The interplay between diabetes mellitus and menopause: clinical implications. *Nat Reviews Endocrinol*. 2022;18(10):608–22.
5. Munshi A, Garg R. Diabetes and Menopause: An Intricate Interplay. *J Midlife Health*. 2025;16(3):231–4.
6. Meegaswatte H, McKune AJ, Panagiotakos DB, Osiriphun S, Leksawasdi N, Rachtanapun P et al. The Association Between the American Heart Association Life's Essential 8 and Metabolic Syndrome Among Postmenopausal Women: Findings from NHANES 2011–2020. *Nutrients*. 2025;17(10).
7. Ko BJ, Jung JH, Han K, Nam GE. Age at Menopause and Development of Type 2 Diabetes in Korea. *JAMA Netw Open*. 2025;8(1):e2455388.
8. Abelman RA, Nguyen TTJ, Ma Y, Bacchetti P, Messerlian G, French AL, et al. Body Composition Changes Over the Menopausal Transition in Women With and Without Human Immunodeficiency Virus. *Clin Infect Dis*. 2023;77(2):265–71.
9. Leitão M, Pérez-López FR, Marôco J, Pimenta F. Exploring weight management beliefs during the menopausal transition (ME-WEL project): A qualitative comparative study based on Health Belief Model. *Br J Health Psychol*. 2025;30(1):e12779.
10. Athar F, Gregory S, Houston EJ, Templeman NM. Insulin levels early in perimenopause inform vasomotor symptom incidence across the menopausal transition. *J Clin Endocrinol Metab*. 2026.
11. Krüger A, van Willems K, van Heemst D, Noordam R. Long-term body mass index trajectories and the risk of type 2 diabetes mellitus and atherosclerotic cardiovascular disease using healthcare data from UK Biobank participants. *Atherosclerosis*. 2025;403:119135.
12. Kan Y, Liu L, Li X, Pang J, Bi Y, Zhang L, et al. Association between distinct body mass index trajectories according to the group-based trajectory modeling and the risk of incident diabetes: A systematic review. *Obes Rev*. 2022;23(12):e13508.
13. Lv L, Long L, Zheng Y, Yang N, Xiao J, Ma T, et al. A U-shaped relationship between body mass index and the risk of elevated liver stiffness in older people: evidence from the 5-year retrospective cohort study. *Int J Obes (Lond)*. 2025;49(10):2110–6.
14. Ma F, Zhang R, Geng W, Gao Z, Li C, Liu J, et al. Association between body roundness index trajectories and the incidence of diabetes mellitus: a perspective from the China health and retirement longitudinal study. *Lipids Health Dis*. 2025;25(1):32.
15. Luo J, Hodge A, Hendryx M, Byles JE. BMI trajectory and subsequent risk of type 2 diabetes among middle-aged women. *Nutr Metab Cardiovasc Dis*. 2021;31(4):1063–70.
16. Owora AH, Allison DB, Zhang X, Gletsu-Miller N, Gadde KM. Risk of Type 2 Diabetes Among Individuals with Excess Weight: Weight Trajectory Effects. *Curr Diab Rep*. 2022;22(9):471–9.

17. Cao X, Yang G, Li X, Fu J, Mohedaner M, Danzengzhuoga, et al. Weight change across adulthood and accelerated biological aging in middle-aged and older adults. *Am J Clin Nutr.* 2023;117(1):1–11.
18. Kagisaki T, Baden MY, Oyama A, Noguchi M, Iso H, Shimomura I. Effect of Weight Change on Type 2 Diabetes Risk: A Prospective Study in a Japanese Population. *J Clin Endocrinol Metab.* 2026;111(4):e1107–15.
19. Asgari S, Khalili D, Azizi F, Hadaegh F. Weight change and risk of incident type 2 diabetes: short, medium and long-term follow-up in tehran lipid and glucose study. *Cardiovasc Diabetol.* 2024;23(1):207.
20. Wang J, Zheng Y, Wang Y, Zhang C, Jiang Y, Suo C, et al. BMI trajectory of rapid and excessive weight gain during adulthood is associated with bone loss: a cross-sectional study from NHANES 2005–2018. *J Transl Med.* 2023;21(1):536.
21. Li S, Yang B, Shang S, Jiang W. Associations of BMI, sleep quality, and sleep duration trajectories with new-onset diabetes mellitus in the elderly. *Obes (Silver Spring).* 2025;33(8):1595–605.
22. Zhao Y, Han M, Qie R, Zhang Y, Wu Y, Fu X, et al. Associations of body mass index trajectory, waist circumference trajectory, or both with type 2 diabetes mellitus risk in Chinese adults: The China-PAR project. *Diabetes Obes Metab.* 2024;26(5):1919–28.
23. Davis SR, Pinkerton J, Santoro N, Simoncini T. Menopause—Biology, consequences, supportive care, and therapeutic options. *Cell.* 2023;186(19):4038–58.
24. Fan H, Kouvari M, Guo C, Liu Z, Zhang X, Wang H, et al. A comprehensive comparison of two commonly used BMI thresholds for non-communicable diseases and multimorbidity in the Chinese population. *Clin Nutr.* 2025;48:70–9.
25. Pang D, Chen M, Xiao C, Zhuang R, Kong C, Xiao M. Comparative analysis of three BMI cutoffs for five metabolic abnormalities in the population of Western Guangdong, China. *Front Nutr.* 2025;12:1732345.
26. Beeri MS, Tirosh A, Lin HM, Golan S, Boccara E, Sano M, et al. Stability in BMI over time is associated with a better cognitive trajectory in older adults. *Alzheimers Dement.* 2022;18(11):2131–9.
27. Ferguson KD, McCann M, Katikireddi SV, Thomson H, Green MJ, Smith DJ, et al. Evidence synthesis for constructing directed acyclic graphs (ESC-DAGs): a novel and systematic method for building directed acyclic graphs. *Int J Epidemiol.* 2020;49(1):322–9.
28. Zhou Y, Kivimäki M, Holt-Lunstad J, Yan LL, Zhang Y, Wang H, et al. Stressful life events in childhood and adulthood and risk of physical, psychological and cognitive multimorbidities: a multicohort study. *EClinicalMedicine.* 2025;83:103225.
29. Ungvari Z, Fekete M, Varga P, Fekete JT, Lehoczki A, Buda A, et al. Imbalanced sleep increases mortality risk by 14–34%: a meta-analysis. *Geroscience.* 2025;47(3):4545–66.
30. Kim RK, Kim YM, Lee WJ, Im J, Lee J, Bang YJ, et al. Data integration of National Dose Registry and survey data using multivariate imputation by chained equations. *PLoS ONE.* 2022;17(6):e0261534.
31. Zhang Z. Multiple imputation with multivariate imputation by chained equation (MICE) package. *Ann Transl Med.* 2016;4(2):30.

32. Taherkhani N, Sepehri MM, Khasha R, Shafaghi S. Determining the Level of Importance of Variables in Predicting Kidney Transplant Survival Based on a Novel Ranking Method. Transplantation. 2021;105(10):2307–15.

33. Egan AM, Wood-Wentz CM, Mohan S, Bailey KR, Vella A. Baseline Fasting Glucose Level, Age, Sex, and Body Mass Index and the Development of Diabetes in US Adults. JAMA Netw Open. 2025;8(1):e2456067.

34. Zhang L, Shen Y, Liu H, Li W, Wang L, Zhang S, et al. Body mass index trajectories and time in target range after delivery and long-term type 2 diabetes risk in women with a history of gestational diabetes mellitus. Diabetes Obes Metab. 2025;27(1):320–7.

35. Chu C, Zhang Y, Deng F, Zhang L. Long-term time in target range for body mass index (BMI) and diabetes incidence: insights from CHARLS. Nutr Diabetes. 2025;15(1):46.

## Figures

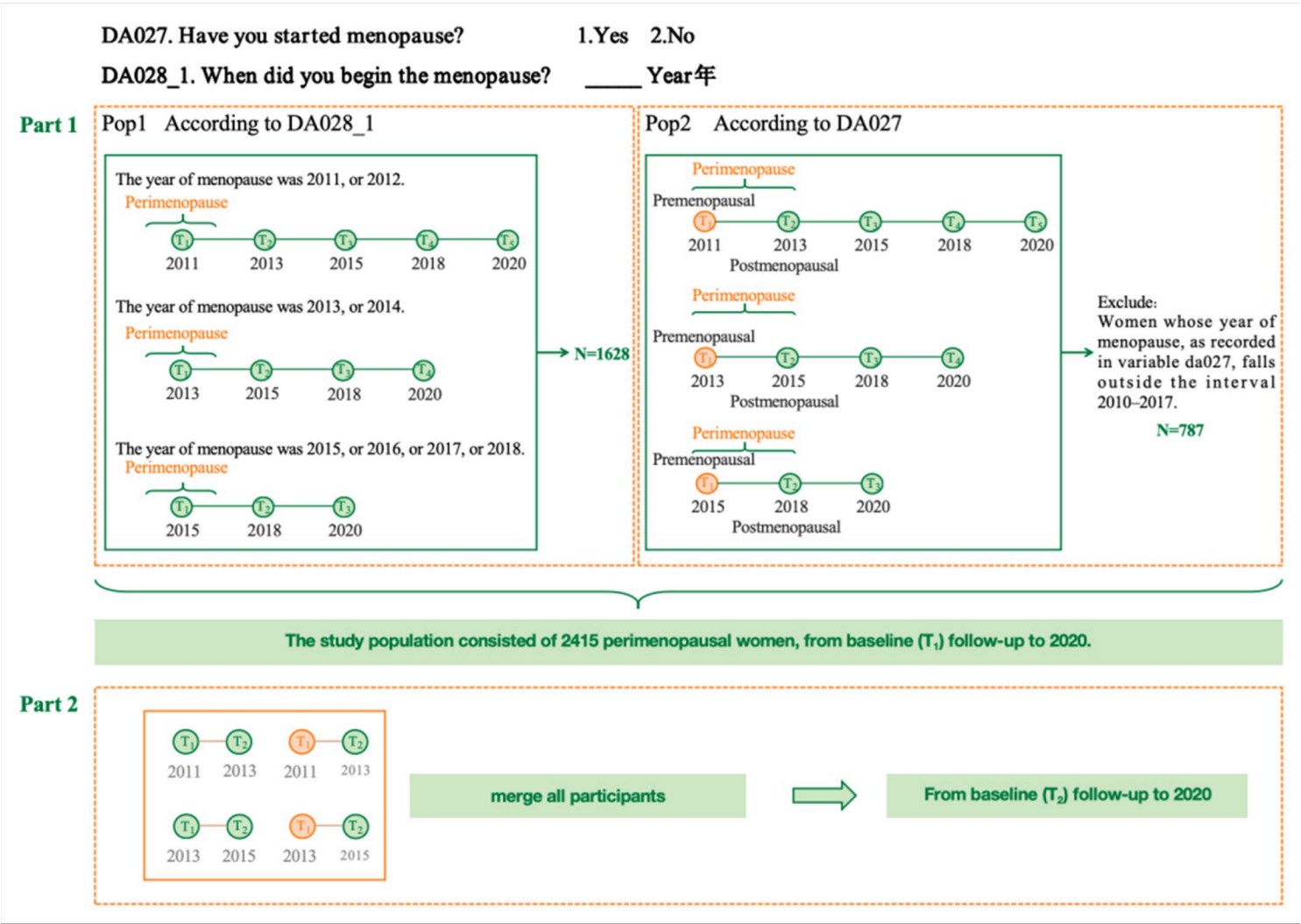


Figure 1

Operational definition and identification criteria for perimenopausal women in the CHARLS

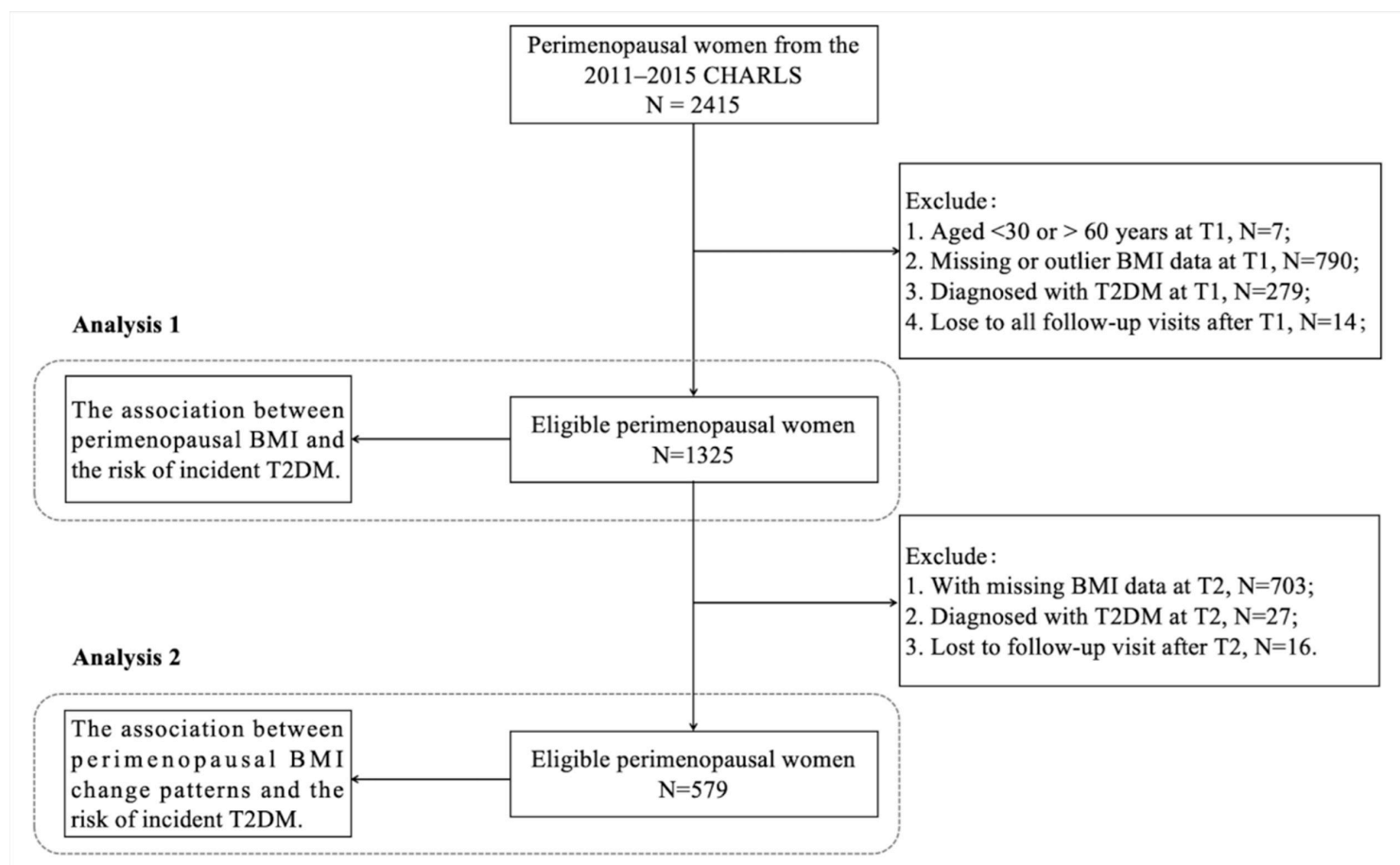


**Figure 2**

Selection process of the study population for analyses

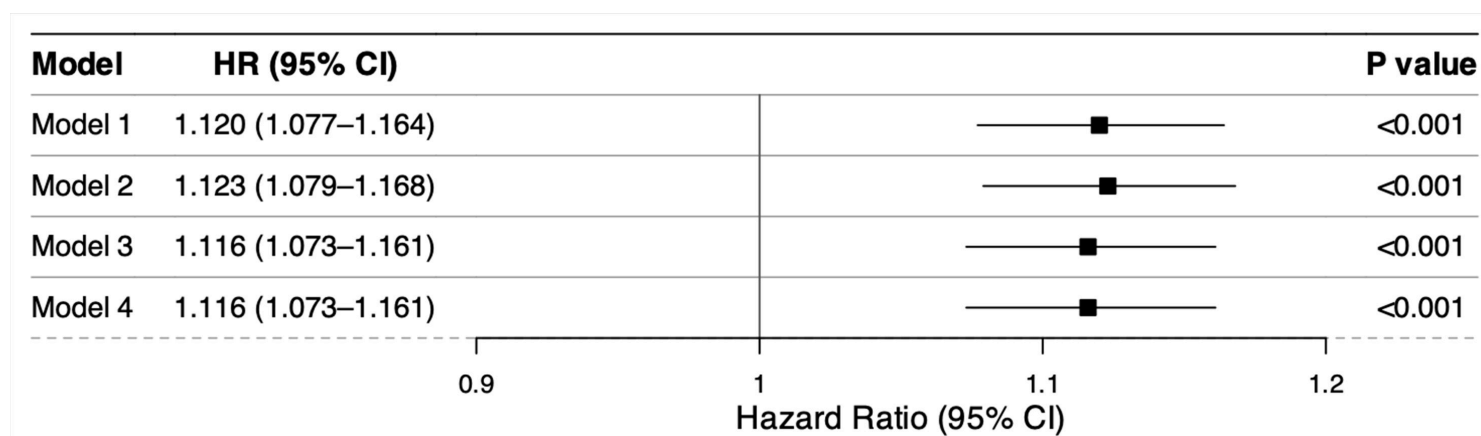


**Figure 3**

Cox association between continuous BMI and T2DM. Notes. Abbreviations: CI, confidence interval; HR, hazard ratio. Model 1 represented the crude model without adjustment for any variables. Model 2 adjusted sociodemographic factors, including age, ethnicity, economic level, education level, marital status, and residence type. Model 3 further adjusted for behavioral and lifestyle factors—specifically

smoking status, drinking status, physical activity and sleep duration. Model 4 further incorporated depressive symptoms.

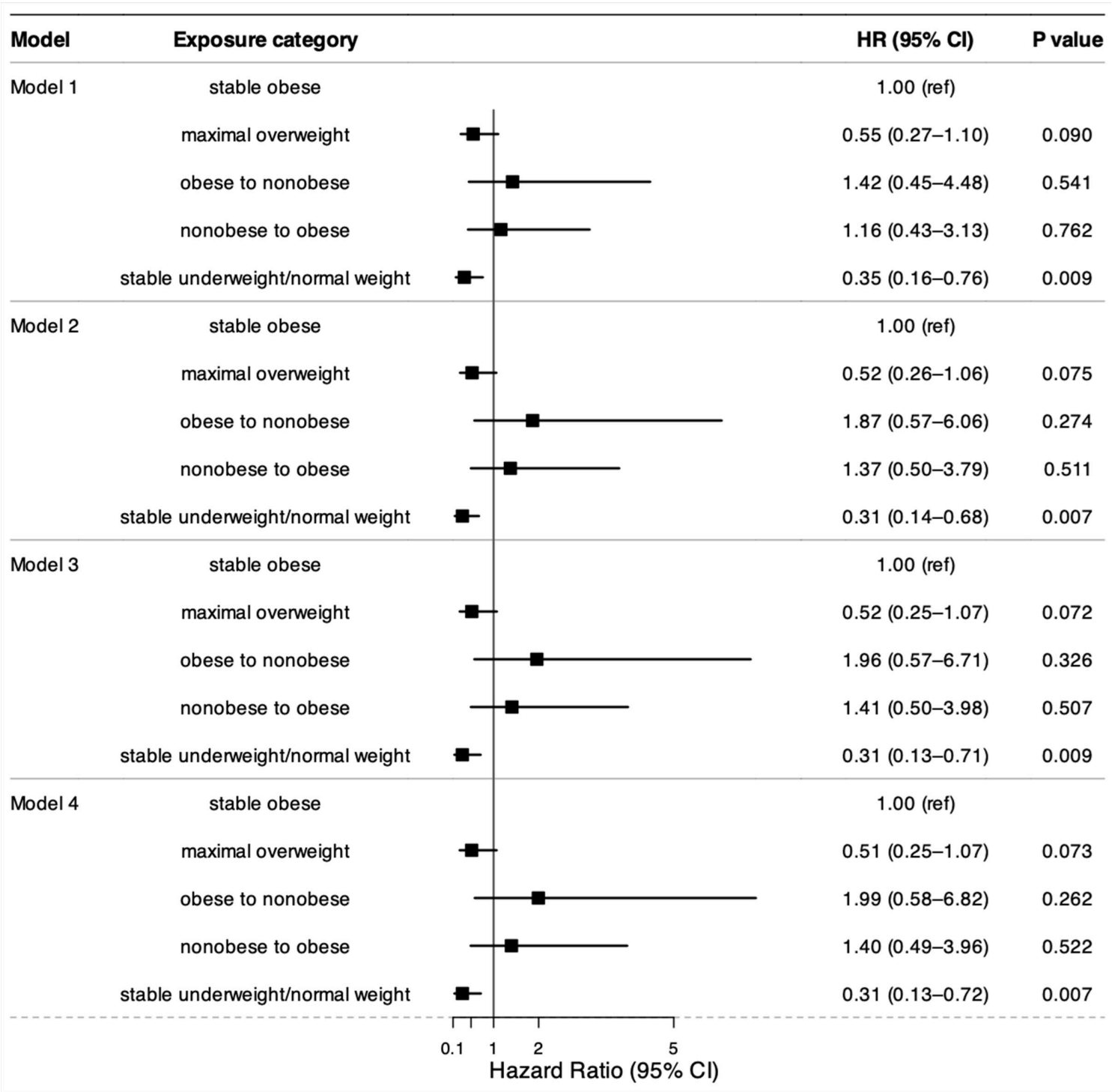


Figure 4

The association between BMI change patterns and T2DM. Notes. Abbreviations: HR, Hazard ratio; CI, confidence interval. Model 1 represented the crude model without adjustment for any variables. Model 2 adjusted sociodemographic factors, including age, ethnicity, economic level, education level, marital status, and residence type. Model 3 further adjusted for behavioral and lifestyle factors—specifically

smoking status, drinking status, physical activity and sleep duration. Model 4 further incorporated depressive symptoms

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