Associations of percentage body cell mass with insulin resistance and type 2 diabetes: mediation effect of body mass index

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ABSTRACT

Background and Objectives: Type 2 diabetes (T2D) stems from metabolic dysregulation, and body cell mass (BCM) comprises the principal physiological substrate of basal metabolic rate (BMR); however, the association between BCM and diabetes is still unclear. This study examined the relationship of percentage body cell mass (PBCM) with insulin resistance (IR) and T2D, and evaluated the mediators of this association. **Methods and Study Design:** This study utilized data from U.S. adults in the National Health and Nutrition Survey (1999–2004). Weighted multivariate regression, restricted cubic spline analysis, subgroup analyses, and sensitivity analysis were employed to investigate the relationship of PBCM with T2D risk biomarkers, IR and T2D. The potential mediating role of body mass index (BMI) was explored. **Results:** A total of 2,923 participants aged 18 years or older were included. Preliminary analysis demonstrated an inverse association between PBCM and biomarkers of T2D risk. Further analyses revealed that higher PBCM was associated with lower odds of IR (OR = 0.91, 95% CI: 0.88–0.94, p <0.001) and T2D (OR = 0.89, 95% CI: 0.84–0.94, p <0.001) in the fully adjusted model. Mediation analysis indicated that BMI mediated 70.6% (95% CI: 55.1%–88.9%, p <0.001) of the total effect of PBCM on IR, and 29.9% (95% CI: 14.2%–65.9%, p <0.001) of that on T2D, respectively. **Conclusions:** PBCM was negatively associated with the prevalence of IR and T2D. Mediation analyses demonstrated a mediating effect of BMI, suggesting that PBCM might be related to IR and T2D, potentially mediated by BMI.

Key Words: body mass index, insulin resistance, mediation analysis, percentage body cell mass, type 2 diabetes

INTRODUCTION

Type 2 diabetes (T2D), a chronic metabolic disorder, has evolved into an increasingly severe global health crisis. Insulin resistance (IR) is one of the most important pathophysiological factors driving disease progression and complications in T2D.[1,2] Identifying modifiable factors associated with IR and T2D is therefore crucial for prevention strategies. The most prominent risk factor for IR and T2D is obesity.[3,4] Body mass index (BMI) serves as a commonly employed diagnostic tool for overweight and obesity, with relevant research demonstrating its significant correlation with T2D onset and progression.[5,6] However, BMI is a crude proxy that fails to capture detailed body composition or fat distribution.[7,8]

Imaging techniques, such as computed tomography (CT) and dual-energy X-ray absorptiometry (DXA), can provide precise body composition assessment. However, their high cost, risk of ionizing radiation exposure, and lack of feasibility limit their use in large-scale epidemiological

studies.[9] In recent years, bioelectrical impedance analysis (BIA) has gained increasing attention due to its simple operation, high safety, non-invasiveness, and low cost, making it applicable to both clinical practice and large-scale epidemiological investigations.[10] BIA employs various parameters, including body cell mass (BCM), total body water (TBW), extracellular water (ECW), intracellular fluid (ICF), fat-free mass (FFM), and fat mass (FM) (Figure 1). In BIA parameters, both FFM and FM were associated with T2D, with low FFM and excess FM, particularly visceral adiposity, most frequently regarded as risk factors for IR and T2D.[4,8,11,12] BCM, comprising all metabolically active tissues within the organism, the sum of intracellular water and protein, has been proposed as a comprehensive marker of muscle quantity, quality, and nutritional status. BCM was a strong and independent risk factor for mortality, BCM assessment might provide more useful prognostic information for clinicians.[13] Percentage body cell mass (PBCM), defined as BCM relative to body weight, could more accurately reflect the bioactive components in the body.[14] However, there are relatively few studies on the association between PBCM and IR or T2D.

Therefore, utilizing the nationally representative, large-scale National Health and Nutrition Examination Survey (NHANES) dataset, the objective of this study was to investigate the associations of PBCM with IR and T2D. We hypothesized that PBCM may be inversely associated with IR and T2D. Furthermore, the study examined the mediating role of BMI in these associations.

MATERIALS AND METHODS

Data sources

Data were collected from publicly available datasets spanning three consecutive NHANES cycles between 1999 and 2004. The NHANES is a continuous cross-sectional observational study designed to gather health data from a nationally representative sample of the non-institutionalized U.S. population. The survey employs a complex, multi-stage probability cluster sampling design to ensure comprehensive and reliable data collection. The NHANES study protocol (#98-12) was approved by the National Center for Health Statistics (NCHS) Institutional Review Board (IRB), with written informed consent obtained from all participants. Our secondary analysis adhered to STROBE guidelines and did not require additional IRB approval. Detailed methodological and ethical documentation regarding NHANES is accessible through the Centers for Disease Control and Prevention (CDC) and NCHS websites (https://www.cdc.gov/nchs/nhanes/about/erb.html). All participant data were accessed for research purposes from 1 December 2025 to 27 February 2026. We had access to information that did not identify individual participants during or after data collection.

Study design and population

Among 31,126 participants, we excluded minors aged <18 years (n=14,065), pregnant individuals (n=927), participants with missing data on T2D diagnosis (n=2), fasting plasma glucose (FPG) (n=9,197), glycohemoglobin (HbA1c) (n=6), fasting serum insulin (FSI) (n=120), body composition (n=3,843), body weight (n=1), or dietary sample weights data (n=42). Finally, 2,923 participants were included in this study (Figure 2).

Exposure, outcome, and mediator

PBCM (%) was calculated as BCM (kg) divided by body weight (kg) and multiplied by 100, representing the percentage of body cell mass relative to total body weight.[14] BCM was calculated as ICF (L) / 0.70 (L/kg), where 0.70 is the mean hydration of BCM.[15] ICF was measured using the Hydra ECF/ICF Bioimpedance Spectroscopy Analyzer (Model 4200; Xitron Technologies, San Diego, CA, USA). Measurements were performed by trained medical technicians in accordance with the operational guidelines stipulated in the NHANES Body Composition Procedures Manual. This multi-frequency analyzer employs 12-bit digital signal processing to measure impedance at 50 logarithmically spaced frequency points ranging from 5 kHz to 1 MHz. The raw spectral data were fitted to the Cole biophysical model using non-linear least-squares curve fitting. Subsequently, ICF volume was predicted using the RE and RI parameters derived from the Cole model, in conjunction with equations based on the Hanai mixture theory. Body weight was measured at the Mobile Examination Center (MEC).

Outcome variables comprised the prevalence of IR and T2D, along with T2D risk markers including FPG (mmol/L), HbA1c (%), FSI (pmol/L), and homeostasis model assessment of insulin resistance (HOMA-IR). FPG, HbA1c, and FSI data were obtained from laboratory test results. HOMA-IR was calculated as (FPG [mmol/L] × FSI [μU/mL]) / 22.5.[16,17] Based on prior research, a HOMA-IR value exceeding 2.6 defines IR in the US general population, which was adopted as the diagnostic criterion in our study.[17,18] Individuals were considered to have T2D if they met one or more of the following criteria: (1) FPG ≥7.0 mmol/L; (2) HbA1c ≥6.5%; (3) taking diabetic pills or insulin; and (4) self-reported physician diagnosis of T2D.[19-21]

BMI (kg/m²) was calculated as weight (kg) divided by the square of height (m). Body weight and height were measured at MECs.

Covariates

The selection of covariates was based on established clinical relevance and prior research findings.[17,20,22] Age, gender, race, educational level, marital status, family poverty-income ratio (PIR), smoking status, drinking status, physical activity, hypertension, coronary heart disease,

stroke, and kidney disease were obtained from demographic data and questionnaires in the NHANES survey.[23,24] Race was categorized as non-Hispanic white, non-Hispanic black, Mexican American, and others. Education level was categorized as <9 years, 9-12 years, and >12 years. Marital status was classified as married or cohabiting, and solitary living. Family PIR was categorized as <1.3, 1.3-3.5, and >3.5. Smoking status was categorized as never (< 100 cigarettes smoked in a lifetime), former (quit smoking after smoking ≥100 cigarettes), and current (smoking ≥100 cigarettes and smoking some days or every day now). Drinking status was defined by consuming ≥12 alcoholic drinks in any given year. Physical activity was categorized as sedentary, moderate (≥10 minutes of light to moderate exercise in the past 30 days), and vigorous (≥10 minutes of heavy exercise in the past 30 days). Waist circumference was measured at MECs. ECF was measured by BIA, TBW was calculated as ECW + ICF, and percent body fat (PFAT) was calculated using the hybrid model. Energy, carbohydrate, protein, and total fat intakes were obtained through 24-hour dietary recall interviews.[23] Hypertension, coronary heart disease, stroke, and kidney disease were identified based on self-reported prior clinical diagnoses. Triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), alanine aminotransferase (ALT), creatinine (Cr), and uric acid (UA) were obtained from laboratory test results.[24] Dyslipidemia was defined as having any one of the following: TG ≥3.89 mmol/L, TC ≥5.18 mmol/L, LDL-c ≥3.37 mmol/L, or HDL-c <1.04 mmol/L (males) or 1.30 mmol/L (females).[25]

Statistical analysis

Dietary sampling weights were applied to account for the complex survey design, as recommended in NHANES guidelines, to generate nationally representative estimates. The weighting procedure was as follows: 1999–2002 data were weighted at two-thirds of the four-year dietary sampling weights, and 2003–2004 data at one-third of the two-year dietary sampling weights. Baseline characteristics for categorical variables are presented as unweighted counts and weighted percentages, while continuous variables are summarized as means with standard deviations (SD) or medians with interquartile ranges (IQR). To analyze differences in continuous variables, weighted regression models were employed, whereas differences in categorical variables were assessed using weighted chi-square tests. Potential multicollinearity among covariates was evaluated using the variance inflation factor (VIF); a VIF ≥ 5 was considered indicative of significant multicollinearity. Missing values in covariates were handled using multiple imputation by chained equations (MICE) using the R mice package, generating five multiply imputed datasets to maximize statistical efficiency and minimize bias.

According to the STROBE statement,[26] unadjusted, minimally adjusted, and fully adjusted models were employed in this study. Model 1 was unadjusted for covariates; model 2 was adjusted for age, gender, race, and NHANES cycle; model 3 was additionally adjusted for physical activity, smoking status, drinking status, energy intakes, hypertension, and dyslipidemia. To evaluate the association of PBCM with T2D risk markers, IR, and T2D, we applied weighted multivariable linear or logistic regression models and computed β values or odds ratios (ORs) with corresponding 95% confidence intervals (CIs) across three models. Additionally, we employed complex sampling-weighted restricted cubic spline (RCS) analysis to examine potential non-linear associations between them. Then, sensitivity analyses were conducted to verify the stability of the results after excluding participants with missing covariate data. Furthermore, mediation analyses were performed using the Sobel test, bootstrap resampling, and the quasi-Bayesian Monte Carlo method with 1,000 simulations based on the normal approximation. Subsequently, stratified analyses were conducted to test for interaction while accounting for potential confounders across predefined subgroups, including age (<35 and ≥35), gender, physical activity, smoking status, drinking status, hypertension, and dyslipidemia. Weighted multivariable logistic regression was employed in the stratified analyses. If the *p*-value for interaction was not statistically significant, the results across different strata were considered robust; otherwise, potential heterogeneity may exist in specific subpopulations.

Data analysis was performed using R software (version 4.2.1; https://www.r-project.org/) and Free Statistics software (version 2.3; Beijing Free Clinical Medical Technology Co., Ltd.). Statistical significance was defined as a two-tailed *p*-value < 0.05.

RESULTS

Characteristics of the population

The baseline characteristics of enrolled participants grouped by PBCM are presented in Table 1. Among 2,923 participants (weighted sample size of 42,885,440), the mean (SD) age was 31.5 (10.1) years; 1,544 (52.4%) were men; 1,462 (44.8%) had insulin resistance; and 115 (3.4%) had diabetes. Compared with the individuals in the lower PBCM group, those in the higher PBCM group tended to be younger, men, solitary living, drinkers, and taller, engage in vigorous physical activity, have higher TBW, ICF, and ECW, have higher nutrient intakes (energy, carbohydrate, protein, and total fat), and have higher levels of Cr and UA, whereas PFAT, HbA1c, FSI, and HOMA-IR were lower (all p <0.05). Notably, participants with higher PBCM levels exhibited significantly lower BMI, prevalence of IR and T2D (all p <0.001).

Association of PBCM with T2D risk markers

In fully adjusted multivariate linear regression models, statistically significant inverse associations were observed between PBCM and FPG (β = -0.02, 95% CI: -0.03 – -0.01, p <0.001), HbA1c (β = -0.01, 95% CI: -0.02 – -0.00, p = 0.002), FSI (β = -1.87, 95% CI: -2.62 – -1.13, p <0.001), and HOMA-IR (β = -0.09, 95% CI: -0.13 – -0.06, p <0.001). A statistically significant trend across PBCM quartiles persisted. Compared with the lowest quartile, participants in the second, third, and fourth PBCM quartiles demonstrated progressively lower levels of FPG, HbA1c, FSI, and HOMA-IR (p for trend <0.001, = 0.009, <0.001, and <0.001, respectively) (Supplementary Table 1).

Association between PBCM and IR

As shown in Table 2, an elevated PBCM level was associated with decreased odds of IR across all multivariate logistic regression models (model 1: OR = 0.96, 95% CI: 0.95 – 0.98, p <0.001; model 2: OR = 0.90, 95% CI: 0.87 – 0.93, p <0.001; model 3: OR = 0.91, 95% CI: 0.88 – 0.94, p <0.001). Full adjustment for potential confounders (model 3) revealed that every one-unit increase in PBCM was associated with a 9% decrease in the odds of IR. Furthermore, this trend maintained statistical significance when analyzed as a categorical variable (quartiles): higher PBCM quartiles exhibited progressively decreased odds of IR compared with the lowest quartile (p for trend <0.001). This inverse association was found in both men and women (Supplementary Table 2).

To investigate potential non-linear association between PBCM and IR, we performed RCS analysis. The statistical analysis revealed a significant overall relationship (p <0.001) and a non-linear trend (p = 0.017), suggesting a non-linear association between PBCM and IR (Figure 3a). In subsequent threshold (two-piecewise) analyses, when PBCM was <41%, the OR for IR was 0.87 (95% CI: 0.82 – 0.92, p <0.001), whereas when PBCM was ≥41%, the OR was 0.95 (95% CI: 0.91 – 0.99, p = 0.010) (Supplementary Table 4). In gender-stratified analyses, a non-linear association between PBCM and IR was observed in men (p for non-linearity = 0.022; p for overall <0.001). When PBCM was <48%, the OR for IR was 0.84 (95% CI: 0.76–0.92, p <0.001), indicating that the odds of IR were 16% lower for every one-unit increase in PBCM. However, no significant association was observed between PBCM and IR in participants with PBCM values ≥48% (Supplementary Figure 1a and Table 5). No evidence of a non-linear association between PBCM and IR was found in women (Supplementary Figure 1b).

Across multiple subgroups, stratified analyses were performed to assess potential effect modification of the relationship between PBCM and IR. After stratifying by age, gender, physical activity, smoking status, drinking status, hypertension, and dyslipidemia, no significant

interactions were observed across all subgroups (all p >0.05), suggesting that the inverse association between PBCM and IR remained consistent across these factors (Figure 4a).

Association between PBCM and T2D

As indicated in Table 3, regardless of adjustment for confounding variables, PBCM remained negatively associated with T2D prevalence in all multivariate logistic regression models (model 1: OR = 0.93, 95% CI: 0.91 – 0.96, p <0.001; model 2: OR = 0.88, 95% CI: 0.84 – 0.93, p <0.001; model 3: OR = 0.89, 95% CI: 0.84 – 0.94, p <0.001). Notably, after fully adjusting for potential confounders (model 3), every one-unit increase in PBCM was associated with an 11% decrease in the odds of T2D. Furthermore, when PBCM was treated as a categorical variable, this trend remained statistically significant. In the fully adjusted multivariable logistic regression model, higher quartiles of PBCM were associated with progressively lower odds of T2D compared with the lowest quartile group (p for trend = 0.006). The gender-stratified analyses showed that the association between PBCM and T2D remained statistically significant in men but not in women (Supplementary Table 3). Moreover, RCS analysis was employed to examine potential non-linear association between PBCM and T2D, and no evidence of non-linearity was observed (p for non-linearity = 0.444) (Figure 3b). In the gender-stratified analysis, no evidence of non-linearity was found either in men or women (Supplementary Figure 2).

In subgroup analyses stratified by age, gender, physical activity, smoking status, drinking status, hypertension, and dyslipidemia, no significant interactions were observed in any subgroups. Although p-values for interaction with physical activity and hypertension were < 0.05, the findings may not have reached clinical significance given the consistency in the direction of association and the potential influence of multiple testing (Figure 4b).

Mediation analysis

Mediation analysis indicated the potential mediating role of BMI in the relationship of PBCM with IR and T2D (Figure 5). PBCM was inversely related to BMI (β = -0.33, 95% CI: -0.38 – -0.27, p <0.001), and BMI was positively associated with odds of IR (OR = 1.24, 95%CI: 1.21–1.28, p <0.001) and T2D (OR = 1.13, 95%CI: 1.08–1.18, p <0.001). Significant mediating effects of BMI in the relationships of PBCM with IR (proportion of mediated: 70.6%, 95%CI: 55.1%–88.9%, p <0.001) and T2D (proportion of mediated: 29.9%, 95%CI: 14.2%–65.9%, p <0.001) were observed.

Sensitivity and additional analysis

After excluding participants with missing covariate data, 2,172 individuals remained. The associations of PBCM with IR and T2D remained robust. Specifically, PBCM was inversely associated with the odds of IR (fully adjusted OR = 0.91, 95% CI: 0.89 – 0.94, p <0.001), with higher quartiles showing progressively lower odds (p for trend <0.001). Likewise, PBCM was inversely associated with T2D (fully adjusted OR = 0.89, 95% CI: 0.84 – 0.94, p <0.001), and higher quartiles were associated with lower prevalence compared with the lowest quartile (p for trend = 0.021) (Supplementary Table 6).

DISCUSSION

In this study, we found that PBCM was significantly and negatively associated with the prevalence of IR and T2D. Furthermore, mediating effects of BMI in the relationships between PBCM and both IR and T2D was observed. Sensitivity analyses supported the robustness of these associations.

Our results corroborate and extend previous research. A systematic review and meta-analysis by Gupta et al. included 20 observational studies, indicating that increasing FFM may contribute to reduced T2D risk.[27] In a 6-year prospective cohort study among Hispanic/Latino adults in the U.S., LeCroy et al. found that attenuating FFM loss during adulthood may lower prediabetes risk primarily through improving insulin resistance, suggesting that maintenance of muscle mass holds significant implications for preventing glucose metabolism disorders.[11] Kahn et al. proposed in their review article that obesity increases the risk of IR and T2D, providing a comprehensive mechanistic framework linking obesity to IR and T2D.[4] As BCM is the metabolically active compartment of FFM, reflecting the cellular components (living cells) of the body involved in resting metabolism, oxygen consumption, and carbon dioxide production,[28,29] we provide a more physiologically precise measure. In this study, PBCM was inversely associated with IR and T2D, a finding consistent with its relevance to metabolic health. Notably, our study further indicated that BMI mediated the associations between PBCM and both IR and T2D.

The observed inverse associations of PBCM with IR and T2D are biologically plausible. Physiological modeling of body composition at the cellular level can be categorized into functionally distinct compartments: energy storage in FM, energy expenditure and metabolism by BCM, exchanges in ECW, and support by mineral mass (Figure 1).[28] FFM, approximately 50% composed of which is skeletal muscle (SM), serves as the primary site for insulin-mediated glucose disposal.[30,31] SM, as a critical insulin-sensitive tissue, is involved in glucose metabolism;[32,33] its mass reduction may directly contribute to the functional impairment of glucose metabolic capacity.[34] While excess FM, particularly visceral adiposity, is strongly

associated with IR and T2D,[8,35] lower FFM has been linked to impaired glucose metabolism and heightened T2D risk.[11,36] BCM, a key indicator of cellular mass and metabolic activity, is the major determinant of basal metabolic rate (BMR) and energy expenditure, contains all the metabolically active tissues (living cell protein mass) of the body and ICF (water inside living cells). ICF constitutes a principal component of BCM and is widely used to estimate BCM.[37-39] BCM represents a more precise physiological measure than FFM, as it excludes ECW and mineral mass.

While preserving BCM, reduction of FM and ECW may confer favorable effects on glucose metabolism; enhancing the proportion of metabolically active tissue may be beneficial even in the presence of elevated FM. This is particularly relevant to conditions such as sarcopenic obesity, wherein diminished muscle mass (and presumably reduced BCM) coexists with excess adiposity, constituting a high-risk metabolic phenotype.[36,40] Higher or preserved BCM, such as through resistance exercise training combined with adequate protein intake, may be associated with greater insulin sensitivity and lower odds of T2D.[41-43]

Additionally, in the gender-stratified analysis, we observed an inverse association between PBCM and IR in both men and women; a non-linear association was observed in men but not in women. The inverse association between PBCM and T2D was significant in men but not in women; no evidence of non-linearity was found in either gender. These disparities may be attributable to differences in sex hormones, adipose tissue distribution, or skeletal muscle metabolism.

This study has several strengths, including its nationally representative sample, the analysis of associations with multiple T2D risk markers, mediation analysis, and rigorous adjustment for various confounders. Nevertheless, it should be acknowledged that certain limitations exist. First, although we employed multivariable regression and conducted extensive subgroup and sensitivity analyses, residual confounding cannot be entirely ruled out. Second, the cross-sectional design precludes determination of a causal relationship between PBCM and IR or T2D. Our conclusions describe observed associations rather than definitive causal relationships. Mediation analyses using cross-sectional data can yield unstable or misleading results. Any detected mediation should be interpreted as an association consistent with a proposed causal framework, not as proof of causality. The observed patterns may reflect statistical mediation, but only within the constraints of the study design. Prospective longitudinal studies or randomized controlled trials are required to establish causality. Third, PBCM and BMI both incorporate body weight, and that some degree of structural dependency between these variables cannot be completely excluded. Although no significant multicollinearity was detected, the observed associations should be interpreted with caution. Lastly, this study was conducted in a U.S. population. Given established variations in

diabetes phenotypes across ethnic groups and regional healthcare disparities, extrapolation to non-U.S. populations requires caution. Validation in other populations is warranted to assess the generalizability of these findings.

Conclusion

This study observed inverse associations of PBCM with IR and T2D among U.S. adults. Furthermore, BMI mediated the associations between PBCM and both IR and T2D. These findings provide novel insights for the prevention and management of insulin resistance and type 2 diabetes. Prospective longitudinal studies are needed to clarify causal relationships and underlying mechanisms.

Ethics Approval and Informed Consent:

The survey protocol was approved by National Center for Health Statistics Ethics Review Board of the Centers for Disease Control and Prevention (Protocol #98-12, https://www.cdc.gov/nchs/nhanes/about/erb.html). Written informed consent was obtained from all participants.

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CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors declare no conflicts of interest.

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Table 1. Characteristics of the study population

Characteristics	PBCM (%)					
	Total	**Q1 (<36)**	**Q2 (36-41)**	**Q3 (41-48)**	**Q4 (≥48)**	***p* Value**
Unweighted sample size, n	2923	731	730	731	731	
Weighted sample size, n (%)	42,885,440	10,738,476	11,046,147	11,569,195	9,531,622	
Age, Mean (SD)	31.5 (10.1)	33.0 (10.2)	32.2 (10.2)	31.9 (9.9)	28.8 (9.6)	<0.001
Gender, n (%)						<0.001
Men	1544 (52.4)	27 (3.2)	217 (31.9)	592 (81.1)	708 (96.9)	
Women	1379 (47.6)	704 (96.8)	513 (68.1)	139 (18.9)	23 (3.1)	
Race						0.011
Non-Hispanic white	1193 (68.7)	278 (67.2)	324 (71.0)	313 (69.8)	278 (66.2)	
Non-Hispanic black	678 (12.6)	197 (16.9)	156 (11.1)	144 (10.2)	181 (12.2)	
Mexican American	802 (9.1)	205 (9.0)	187 (7.9)	211 (9.7)	199 (10.0)	
Others	250 (9.6)	51 (6.9)	63 (9.9)	63 (10.3)	73 (11.6)	
Education level, n (%)						0.034
<9	227 (4.8)	50 (3.2)	61 (5.5)	63 (4.8)	53 (5.7)	
9-12	971 (39.7)	239 (40.3)	234 (35.6)	250 (39.4)	248 (44.2)	
>12	1146 (55.6)	326 (56.5)	302 (58.9)	289 (55.8)	229 (50.1)	
Marital status, n (%)						<0.001
Married or cohabiting	1420 (57.2)	377 (63.8)	388 (62.3)	370 (53.8)	285 (48.0)	
Solitary living	1416 (42.8)	327 (36.2)	318 (37.7)	341 (46.2)	430 (52.0)	
Family PIR, n (%)						0.489
<1.3	834 (23.2)	219 (26.0)	205 (21.8)	221 (23.6)	189 (21.3)	
1.3-3.5	1011 (34.6)	248 (36.5)	251 (32.8)	243 (35.2)	269 (33.6)	
>3.5	859 (42.2)	205 (37.5)	222 (45.3)	213 (41.2)	219 (45.1)	
Physical activity, n (%)						<0.001
Sedentary	972 (30.4)	283 (36.2)	256 (30.7)	238 (30.2)	195 (23.6)	
Moderate	640 (24.7)	196 (29.1)	178 (28.6)	157 (24.6)	109 (15.3)	
Vigorous	1308 (44.9)	252 (34.7)	294 (40.7)	335 (45.2)	427 (61.0)	
Smoking status, n (%)						0.001
Never	1316 (54.6)	384 (61.1)	343 (53.3)	309 (51.0)	280 (52.8)	
Former	359 (16.8)	89 (17.5)	84 (17.0)	107 (16.5)	79 (16.0)	
Current	672 (28.6)	143 (21.3)	169 (29.7)	186 (32.4)	174 (31.2)	
Drinking status, n (%)	1666 (76.4)	353 (64.6)	390 (72.9)	479 (82.7)	444 (86.2)	<0.001
BMI (kg/m2), Mean ± SD	27.3 (6.0)	30.5 (7.3)	27.0 (5.7)	26.6 (4.9)	25.0 (4.2)	<0.001
Weight (kg), Mean (SD)	78.2 (18.5)	81.5 (20.7)	75.4 (19.5)	79.7 (17.8)	76.2 (14.7)	<0.001
Height (cm), Mean (SD)	169.2 (10.0)	163.3 (7.3)	166.6 (10.0)	172.7 (9.6)	174.3 (8.4)	<0.001
Waist circumference (cm), Mean (SD)	91.9 (14.8)	97.2 (16.4)	91.3 (15.0)	92.5 (13.7)	86.6 (11.6)	<0.001
TBW (L), Mean (SD)	39.7 (9.9)	33.4 (7.4)	36.0 (8.9)	42.9 (9.1)	46.5 (8.3)	<0.001
ECW (L), Mean (SD)	16.7 (3.6)	15.1 (3.1)	15.6 (3.6)	17.8 (3.6)	18.2 (3.0)	<0.001
ICF (L), Mean (SD)	23.0 (6.6)	18.3 (4.4)	20.4 (5.4)	25.1 (5.7)	28.3 (5.6)	<0.001
BCM (kg), Mean (SD)	32.9 (9.4)	26.2 (6.4)	29.1 (7.7)	35.8 (8.1)	40.4 (8.0)	<0.001
PFAT (%), Mean (SD)	31.2 (11.1)	44.8 (4.2)	35.8 (3.0)	27.3 (3.3)	16.9 (5.1)	<0.001
Energy intakes (kcal/d), Mean (SD)	2419.(1103)	1990 (856)	2228 (1007)	2646 (1105)	2812 (1216)	<0.001
Carbohydrate intakes (g/d), Mean (SD)	304 (146)	254 (116)	282 (135)	327 (147)	352 (160)	<0.001
Protein intakes (g/d), Mean (SD)	87.4 (46.7)	71.6 (36.0)	78.5 (39.9)	97.0 (46.5)	103 (54.8)	<0.001
Total fat intakes (g/d), Mean (SD)	88.5 (49.3)	75.1 (41.0)	83.0 (46.7)	95.8 (49.1)	100 (55.2)	<0.001
Hypertension, n (%)	261 (10.6)	85 (12.9)	77 (13.2)	70 (9.7)	29 (6.2)	<0.001
Coronary heart disease, n (%)	8 (0.5)	2 (0.2)	4 (1.3)	2 (0.3)	0 (0.0)	0.32
Stroke, n (%)	10 (0.5)	4 (1.2)	4 (0.7)	2 (0.2)	0 (0.0)	0.239
Kidney disease, n (%)	33 (1.1)	14 (2.1)	9 (1.1)	7 (0.5)	3 (0.8)	0.095
Dyslipidemia, n (%)	1781 (63.3)	495 (64.1)	477 (64.8)	459 (66.4)	350 (56.6)	<0.001
FPG (mmol/L), Mean (SD)	5.3 (1.5)	5.4 (1.5)	5.3 (1.5)	5.4 (1.7)	5.3 (1.2)	0.207
HbA1c (%), Mean (SD)	5.3 (0.7)	5.3 (0.8)	5.3 (0.8)	5.3 (0.7)	5.2 (0.5)	0.012

ALT, alanine aminotransferase; BCM, body cell mass; Cr, creatinine; ECW, extracellular water; FPG, fasting plasma glucose; FSI, fasting serum insulin; HbA1c, glycated hemoglobin; HDL-c, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; ICF, intracellular fluid; IR, insulin resistance; LDL-c, low-density lipoprotein cholesterol; PBCM, percentage body cell mass; PFAT, percent body fat; T2D, type 2 diabetes; TBW, total body water; TC, total cholesterol; TG, triglycerides; UA, uric acid.

[†]Data were presented as unweighted number (weighted percentage) for categorical variables, mean (SD, standard deviation) or median (IQR, interquartile range) for continuous variables. Differences in baseline characteristics were compared using the χ^2 test for categorical variables and the t-test or Wilcoxon rank-sum test for continuous variables.

Table 1. Characteristics of the study population (cont.)

Characteristics	PBCM (%)					
	Total	**Q1 (<36)**	**Q2 (36-41)**	**Q3 (41-48)**	**Q4 (≥48)**	***p* Value**
FSI (pmol/L), Median (IQR)	55.4 (37.6, 85.2)	64.6 (44.6, 103)	58.3 (38.9, 86.3)	54.5 (37.2, 83.6)	46.3 (32.5, 69.5)	<0.001
HOMA-IR, Median (IQR)	2.1 (1.4, 3.4)	2.5 (1.6, 4.1)	2.2 (1.4, 3.5)	2.1 (1.4, 3.4)	1.8 (1.2, 2.8)	<0.001
TG (mmol/L), Median (IQR)	1.0 (0.7, 1.6)	1.0 (0.7, 1.5)	1.0 (0.7, 1.6)	1.0 (0.7, 1.6)	1.0 (0.7, 1.5)	0.062
TC (mmol/L), Mean (SD)	4.9 (1.0)	4.9 (1.0)	4.9 (1.0)	5.0 (1.1)	4.7 (1.1)	<0.001
HDL-c (mmol/L), Mean (SD)	1.3 (0.4)	1.4 (0.4)	1.3 (0.4)	1.3 (0.4)	1.3 (0.3)	<0.001
LDL-c (mmol/L), Mean (SD)	2.9 (0.9)	2.9 (0.8)	2.9 (0.9)	3.0 (0.9)	2.9 (1.0)	0.005
ALT (U/L), Median (IQR)	21.0 (16.0, 30.0)	18.0 (14.0, 24.0)	19.0 (14.0, 28.0)	24.0 (17.0, 34.0)	23.0 (18.0, 32.0)	<0.001
Cr (umol/L), Mean (SD)	71.5 (24.2)	58.6 (12.9)	66.7 (19.7)	77.7 (34.5)	83.0 (15.6)	<0.001
UA (umol/L), Mean (SD)	316 (81.1)	279 (69.8)	292 (81.2)	341 (80.1)	351 (68.4)	<0.001
IR, n (%)	1462 (44.8)	446 (54.2)	378 (44.9)	360 (42.8)	278 (36.4)	<0.001
T2D, n (%)	115 (3.4)	42 (5.4)	34 (3.8)	28 (2.7)	11 (1.7)	<0.001

ALT, alanine aminotransferase; BCM, body cell mass; Cr, creatinine; ECW, extracellular water; FPG, fasting plasma glucose; FSI, fasting serum insulin; HbA1c, glycated hemoglobin; HDL-c, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; ICF, intracellular fluid; IR, insulin resistance; LDL-c, low-density lipoprotein cholesterol; PBCM, percentage body cell mass; PFAT, percent body fat; T2D, type 2 diabetes; TBW, total body water; TC, total cholesterol; TG, triglycerides; UA, uric acid.
[†]Data were presented as unweighted number (weighted percentage) for categorical variables, mean (SD, standard deviation) or median (IQR, interquartile range) for continuous variables. Differences in baseline characteristics were compared using the χ^2 test for categorical variables and the t-test or Wilcoxon rank-sum test for continuous variables.

Table 2. Association between PBCM and IR

Variable	Total	Event (%)	Model 1		Model 2		Model 3	
			OR (95%CI)	*p* Value	OR (95%CI)	*p* Value	OR (95%CI)	*p* Value
PBCM (%)	2923	1462 (44.8)	0.96 (0.95, 0.98)	<0.001	0.90 (0.87, 0.93)	<0.001	0.91 (0.88, 0.94)	<0.001
PBCM (Quartiles)								
Q1 (< 36)	731	446 (54.2)	1 (Ref)		1 (Ref)		1 (Ref)	
Q2 (36-41)	730	378 (44.9)	0.69 (0.51, 0.94)	0.019	0.48 (0.34, 0.68)	<0.001	0.48 (0.34, 0.69)	<0.001
Q3 (41-48)	731	360 (42.8)	0.63 (0.48, 0.83)	0.001	0.23 (0.15, 0.34)	<0.001	0.25 (0.16, 0.38)	<0.001
Q4 (≥48)	731	278 (36.4)	0.48 (0.35, 0.67)	<0.001	0.14 (0.09, 0.23)	<0.001	0.17 (0.11, 0.28)	<0.001
p for trend				<0.001		<0.001		<0.001

IR, insulin resistance; NHANES, National Health and Nutrition Examination Survey; PBCM, percentage body cell mass.
[†]Model 1 was unadjusted for covariates.
[‡]Model 2 was adjusted for age, gender, race, and NHANES cycle.
[§]Model 3 was additionally adjusted for physical activity, smoking status, drinking status, energy intakes, hypertension, and dyslipidemia.

Table 3. Association between PBCM and T2D

Variable	Total	Event (%)	Model 1		Model 2		Model 3	
			OR (95%CI)	*p* Value	OR (95%CI)	*p* Value	OR (95%CI)	*p* Value
PBCM (%)	2923	115 (3.4)	0.93 (0.91, 0.96)	<0.001	0.88 (0.84, 0.93)	<0.001	0.89 (0.84, 0.94)	<0.001
PBCM (Quartiles)								
Q1 (< 36)	731	42 (5.4)	1 (Ref)		1 (Ref)		1 (Ref)	
Q2 (36-41)	730	34 (3.8)	0.69 (0.36, 1.32)	0.260	0.54 (0.23, 1.26)	0.150	0.53 (0.21, 1.33)	0.169
Q3 (41-48)	731	28 (2.7)	0.48 (0.23, 0.98)	0.045	0.28 (0.09, 0.92)	0.037	0.28 (0.08, 0.96)	0.043
Q4 (≥48)	731	11 (1.7)	0.29 (0.14, 0.60)	0.001	0.18 (0.06, 0.56)	0.004	0.18 (0.05, 0.58)	0.006
p for trend				<0.001		0.005		0.006

NHANES, National Health and Nutrition Examination Survey; PBCM, percentage body cell mass; T2D, type 2 diabetes.
[†]Model 1 was unadjusted for covariates.
[‡]Model 2 was adjusted for age, gender, race, and NHANES cycle.
[§]Model 3 was additionally adjusted for physical activity, smoking status, drinking status, energy intakes, hypertension, and dyslipidemia.

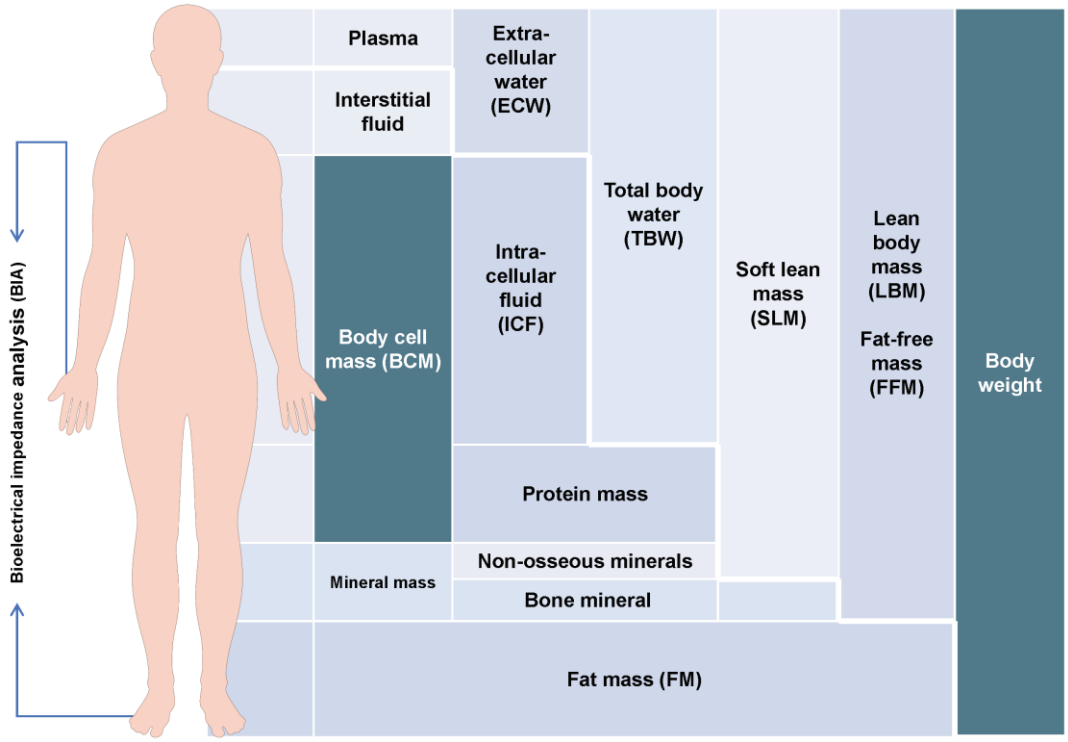


Figure 1. Bioelectrical impedance analysis (BIA) for measuring body composition

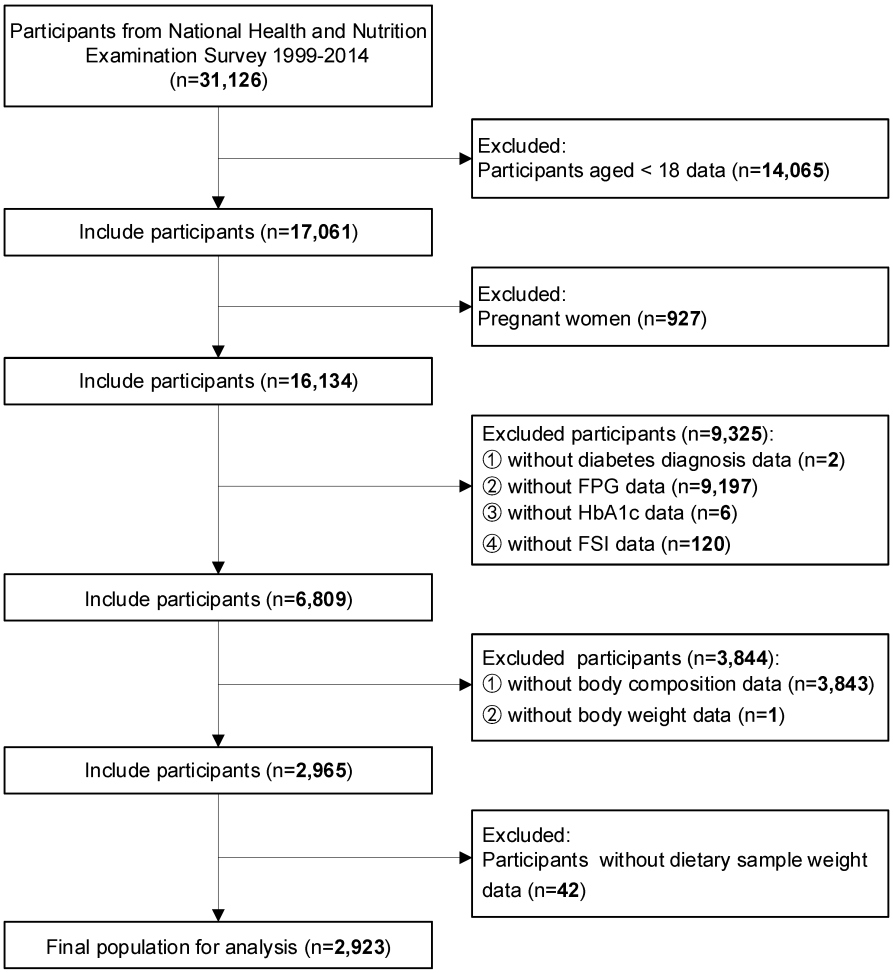


Figure 2. Flow chart of participants selection

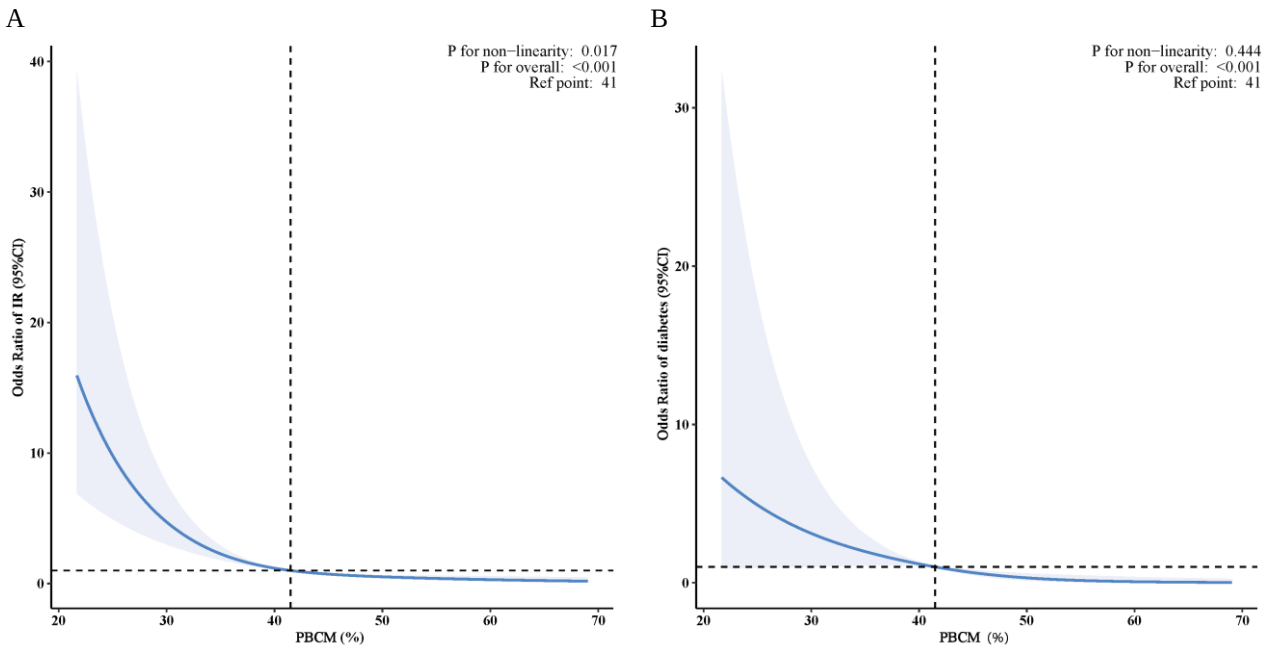
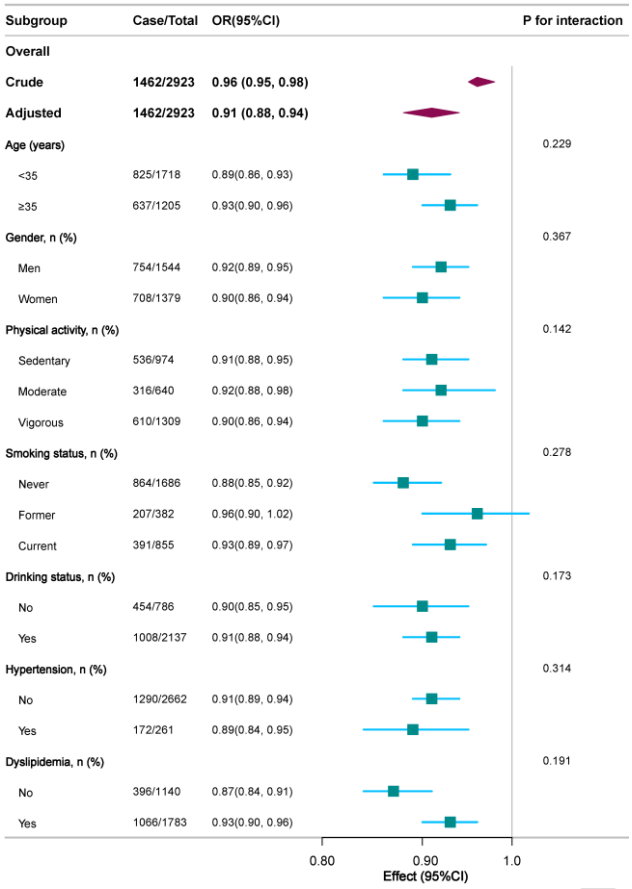


Figure 3. The complex sampling-weighted RCS analysis of PBCM with (A) IR and (B) T2D. The solid curved line represents the estimates for the association of PBCM with IR and T2D, and shading, the 95% CI. IR, insulin resistance; PBCM, percentage body cell mass; T2D, type 2 diabetes

A



B

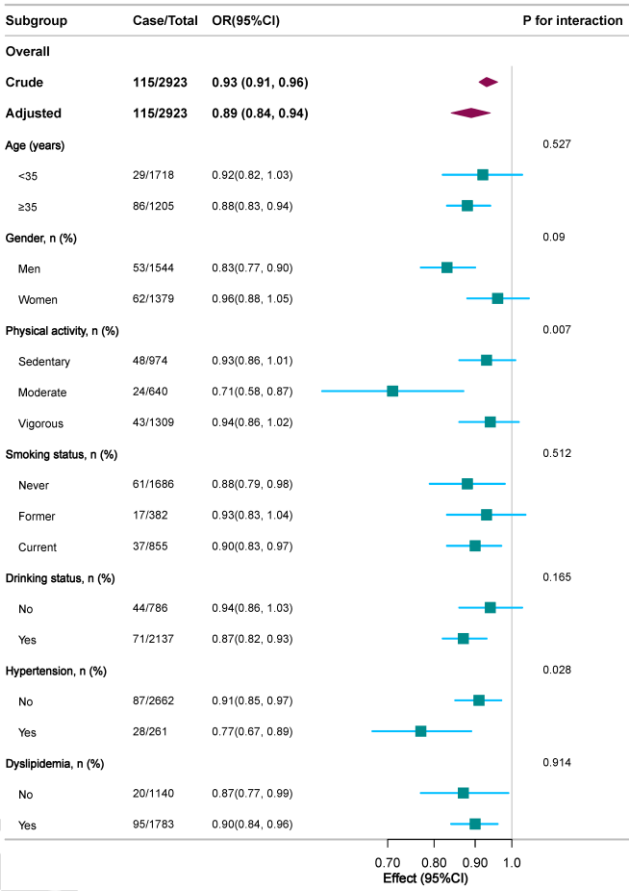


Figure 4. Association of PBCM with (A) IR and (B) T2D according to basic features. Note: Except for the stratification component itself, each stratification factor was adjusted for all other variables, including age, gender, race, physical activity, smoking status, drinking status, energy intakes, hypertension, dyslipidemia, and NHANES cycle. IR, insulin resistance; PBCM, percentage body cell mass; T2D, type 2 diabetes

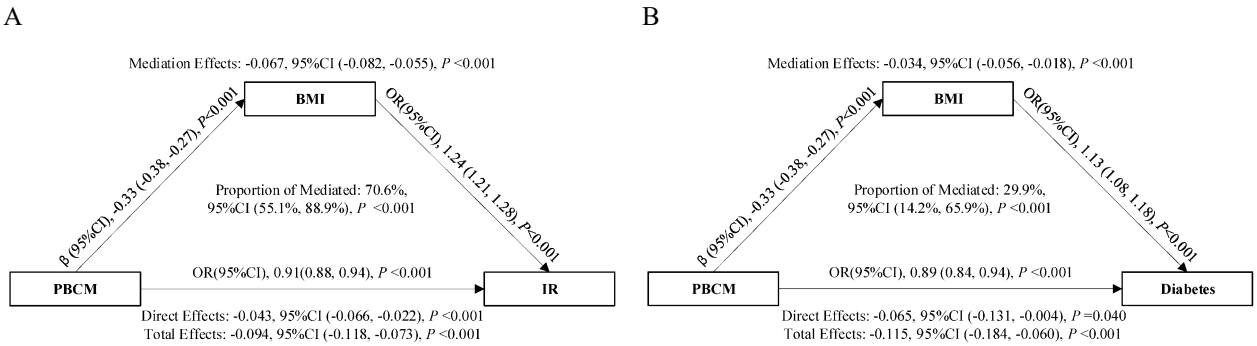


Figure 5. Mediation analysis of BMI in the associations of PBCM with IR (A) and T2D (B). ORs in logistic regression are non-collapsible. Therefore, the total effect (c) does not necessarily equal the sum of direct (c') and mediation effects (a×b) when mediators are added to the model. This is a well-established property of mediation analysis with binary outcomes (VanderWeele, 2010).
BMI, body mass index; IR, insulin resistance; PBCM, percentage body cell mass; T2D, type 2 diabetes