

Associations of parental pre-pregnancy BMI with cardiometabolic risk in offspring conceived via assisted reproductive technology: a retrospective cohort study

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Abstract

Background

Parental pre-pregnancy adiposity may influence offspring cardiometabolic health, but the independent and joint contributions of maternal and paternal body mass index (BMI) remain uncertain, particularly among children conceived through assisted reproductive technology (ART). We examined sex-specific associations of parental pre-pregnancy BMI with cardiometabolic profiles in ART-conceived children.

Methods

This retrospective cohort study included 2,989 singleton children conceived through ART and assessed at 3–6 years of age. Parental pre-pregnancy BMI was obtained from prospectively recorded clinical records. Offspring outcomes included BMI, blood pressure, fasting glucose, lipid profiles, the triglyceride-glucose body mass index (TyG-BMI), and the metabolic score for insulin resistance (METS-IR). Linear and logistic regression models, sex-stratified analyses, parental overweight/obesity combination analyses, and mediation analyses were performed.

Results

Higher maternal and paternal pre-pregnancy BMI were each associated with higher offspring BMI and insulin resistance indices. Maternal BMI showed stronger associations with offspring BMI than paternal BMI in boys ($\beta = 0.121$ vs 0.055) and girls ($\beta = 0.090$ vs 0.056 ; all $P < 0.001$). Compared with children whose parents were not overweight/obese, the largest increases in TyG-BMI were observed when both parents had overweight/obesity: 5.918 (95% CI 2.820 – 9.016) in girls and 8.805 (95% CI 5.840 – 11.770) in boys (both $P < 0.001$). Similar patterns were observed for METS-IR, with corresponding increases of 1.081 (95% CI 0.513 – 1.648) in girls and 1.609 (95% CI 1.077 – 2.141) in boys. Mediation analyses indicated that child BMI accounted for most of the mediated association between parental BMI and offspring insulin resistance indices, whereas birthweight contributed less.

Conclusions

Both maternal and paternal pre-pregnancy BMI were associated with cardiometabolic profiles in ART-conceived children, and children with overweight/obesity in both parents showed the greatest elevations in insulin resistance indices. These findings support preconception weight management for both parents and early monitoring of offspring weight as potential targets for cardiometabolic risk reduction.

Background

Assisted reproductive technology (ART) has resulted in approximately 8 million births worldwide, with numbers continuing to rise¹. However, concerns regarding the long-term health outcomes of children conceived through ART persist². Previous studies have highlighted the critical role of parental pre-pregnancy health in shaping offspring outcomes, potentially through effects on gametes and the intrauterine environment, as described within the Developmental Origins of Health and Disease (DOHaD) framework³. In light of this concept, the pre-ART management of infertile couples emerges as a crucial factor in mitigating potential health risks for their future offspring^{4, 5}.

In 2021, approximately 1.00 billion adult men and 1.11 billion adult women worldwide were living with overweight or obesity. By 2050, the prevalence of overweight or obesity is projected to reach approximately 57.4% in men and 60.3% in women⁶. While paternal pre-pregnancy BMI (pBMI) is an important pre-pregnancy exposure^{7–16}, limited research has simultaneously examined maternal and paternal pBMI in relation to offspring cardiovascular risk within the same cohort^{8, 14}. The ART population is characterized by considerable specificity and heterogeneity, and the effects of parental pBMI on cardiometabolic health for offspring via ART remain unclear^{17, 18}. Due to obesity-related infertility, ART patients have a higher prevalence of obesity^{19–21}. Prior studies suggest that ART may impact offspring's cardiometabolic health, possibly via epigenetic modifications^{22–26}. However, evidence on the joint associations of maternal and paternal pBMI with cardiometabolic health in ART-conceived offspring remains limited. Addressing this gap is important for pre-ART management.

This study aimed to investigate the independent and joint associations of maternal and paternal pBMI with cardiometabolic health in ART-conceived offspring during early childhood. Given sex-specific differences in cardiometabolic profiles, analyses were stratified by offspring sex. We also evaluated the potential mediating roles of birthweight and child BMI.

Methods

Setting and participants

We conducted a secondary analysis of parents and their offspring aged 3–6 years enrolled in the ART Offspring Follow-Up Study (n = 3227) from September 2009 to April 2023 at the university-affiliated Reproductive Center of Women's Hospital, School of Medicine, Zhejiang University. This cohort was established to investigate ART offspring health, as previously described²⁷. The analysis in this study focused on associations between parental pBMI and offspring cardiometabolic risk. Individuals with missing data on key variables were excluded such as paternal pBMI (n = 192), parental education (n = 19), birthweight (n = 10), and child weight (n = 17). Ultimately, 2989 singletons conceived through IVF or ICSI were included. Of these, 2950 singletons completed blood pressure assessments, and 2841 singletons provided blood samples for glucose and lipid biochemical measurements (**Figure S1**).

Ethics approval

The study was approved by the Ethics Committee of the Women's Hospital, School of Medicine, Zhejiang University (IRB-20250104-R) and registered with the Chinese Clinical Trial Registry (ChiCTR2500104140). Written informed consent was obtained from the parents or legal guardians of all participating children after written and oral study information was provided.

Offspring and parent follow-up

Families were first contacted by phone, then followed up at the ART Offspring Health Monitoring Center when children were aged 3–6 years. The follow-up included: (1) physical examinations conducted by trained pediatric physicians and nurses, (2) assessments of cardiometabolic profiles, and (3) parent-completed questionnaires. The median follow-up duration for the cohort was 4.7 years, with an interquartile range of 4.5 months, spanning from 3 to 6 years.

Parental exposures and covariables

Parental characteristics, ART parameters, and neonatal data were collected from prospectively recorded medical records. Baseline characteristics included parental age, pBMI, education level, smoking exposure (maternal, paternal, or primary caregiver self-reported), parity, gravidity, residence (rural or urban), factors contributing to infertility, fertilization method (IVF or ICSI), embryo transfer method (fresh-ET or FET), gestational diabetes mellitus (GDM), hypertensive disorders of pregnancy (HDP), birthweight, and age at visit. Parental education level was categorized as junior high school and below, senior high school and college or above. Low birthweight was defined as a birth weight of less than 2500 g; macrosomia was defined as a birth weight greater than 4000 g²⁸.

Parental pBMI was classified as obesity (BMI ≥ 28 kg/m²), overweight (24–27.9 kg/m²), normal weight (18.5–23.9 kg/m²), and underweight (< 18.5 kg/m²), according to the criteria for adults in China²⁹. BMI was calculated as weight (kg)/height (m²).

Cardiometabolic profiling outcomes

The primary outcomes were offspring cardiometabolic profiles. Height and weight were measured in light clothing on two separate occasions, and the average recorded. Overweight and obesity were defined by age- and sex-specific BMI percentiles for Chinese children³⁰. Blood pressure was measured on the right arm while the child was seated. Three readings were taken. The average of the last two readings was used. Blood samples were collected after overnight fasting to assess triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and glucose levels. Samples were processed following standard procedures. Non-high-density lipoprotein cholesterol (non-HDL-C) was calculated as TC minus HDL-C. The triglyceride-glucose (TyG)

index was calculated as $\ln [\text{fasting TG (mg/dL)} \times \text{fasting glucose (mg/dL)} / 2]$. The triglyceride-glucose body mass index (TyG-BMI) was calculated as $\text{TyG index} \times \text{BMI (kg/m}^2\text{)}^{31}$. Metabolic score for insulin resistance (METS-IR) index was calculated as $\ln [2 \times \text{fasting glucose (mg/dL)} + \text{fasting TG (mg/dL)}] \times \text{BMI (kg/m}^2\text{)} / \ln [\text{HDL-C (mg/dL)}]^{32}$. Dyslipidemia was defined as values above the 95th percentile according to pediatric guidelines, corresponding to $\text{TC} \geq 5.2 \text{ mmol/L}$, $\text{LDL-C} \geq 3.4 \text{ mmol/L}$, $\text{TG} \geq 1.1 \text{ mmol/L}$ (0–9 years) or $\geq 1.5 \text{ mmol/L}$ (10–19 years) or $\text{HDL-C} < 1.0 \text{ mmol/L}^{33}$.

Mediation analyses

Mediation analysis was conducted using the R package mediation to evaluate potential mediation by birthweight and offspring BMI. Models were adjusted for parental age, educational level, smoking, residence, gravidity, parity, fertilization method, and embryo transfer mode. Maternal pBMI was included as a covariate in analyses of paternal pBMI, and paternal pBMI was included in analyses of maternal pBMI. Within a counterfactual framework, the total association of parental pBMI with each outcome was decomposed into direct and indirect components through the specified mediator.

Statistical analysis

Data were analyzed using SPSS version 26.0 and R. Normality of distributions of all characteristics was visually assessed. Normally distributed continuous variables are presented as mean $\pm$ SD, with group comparisons made using the independent-samples t test. Non-normally distributed variables are presented as median (interquartile range, IQR), with group comparisons conducted using the Mann-Whitney U test. Categorical variables are reported as proportions, with comparisons using the chi-square or Fisher's exact test, as appropriate. Odds ratios for binary outcomes were estimated using logistic regression, and linear regression was used for continuous outcomes. Multivariable linear regression models were used to examine associations between parental pBMI combinations and offspring cardiometabolic profiles. Parental pBMI was categorized into four groups, with the "normal pBMI" group as reference.

Crude associations were estimated first, followed by adjusted models. Covariates considered in the adjusted models included paternal age, maternal age, parental educational level, smoking, offspring sex, residence, gravidity, parity, fertilization method, embryo transfer mode, GDM, hypertensive disorders of pregnancy, and birthweight. Given known differences in cardiometabolic profiles between boys and girls, analyses were stratified by offspring sex. A P value < 0.05 was considered statistically significant, and results are presented with 95% confidence intervals (CIs).

Missing data were observed for residence (n = 162), gravidity (n = 6), parity (n = 6), smoking exposure (n = 12), GDM (n = 20), and hypertensive disorders of pregnancy (n = 19). To address this, multiple imputation using chained equations was performed.

Results

Baseline and Perinatal Characteristics

A total of 2989 mother-father-offspring trios were enrolled in the study, including 1417 girls and 1572 boys. Maternal and paternal demographics, ART parameters, pregnancy and offspring characteristics were shown in **Table 1**. Most characteristics were comparable between parents of girls and boys, whereas higher maternal pBMI was observed among mothers of girls. Boys had higher birthweight and rates of macrosomia than girls. The children's age was comparable at the time of assessment (**Table 1**).

Parental pBMI and offspring cardiometabolic risk

The associations between maternal and paternal pBMI and cardiometabolic components of the offspring by sex in unadjusted models were shown in **Tables S1 and S2**. The linear regression analyses and logistic regression analyses after adjusting for confounders by sex were performed. Mother-offspring and father-offspring associations with pBMI and cardiometabolic components are presented by sex in **Figure 1A**.

Maternal pBMI was positively associated with their son's BMI at age 3-6 years (adjusted $\beta = 0.121$, 95%CI 0.093-0.149, adjusted $P < 0.001$). A similar, but weaker, relationship was also observed between paternal pBMI and their son's BMI (adjusted $\beta = 0.055$, 95%CI 0.031-0.079, adjusted $P < 0.001$). Similarly, for daughters, both maternal pBMI (adjusted $\beta = 0.090$, 95%CI 0.061-0.118, adjusted $P < 0.001$) and paternal pBMI (adjusted $\beta = 0.056$, 95%CI 0.032-0.081, adjusted $P < 0.001$) was positively associated with offspring BMI at age 3-6 years (**Figure 1A**).

Although weak relationships were observed between maternal pBMI and some lipids (TC and HDL-C in boys, non-HDL-C in girls), dyslipidemia was not associated with either maternal or paternal pBMI in boys and girls. No associations were found between maternal or paternal pBMI and offspring blood pressure or fasting glucose in boys and girls. The only cardiometabolic parameters for which there were associations between paternal pBMI and offspring measurements were TyG-BMI index and METS-IR index, both in boys (TyG-BMI index: adjusted $\beta = 0.493$, 95%CI 0.279-0.706, adjusted $P < 0.001$; METS-IR index: adjusted $\beta = 0.090$, 95%CI 0.051-0.129, adjusted $P < 0.001$) and girls (TyG-BMI index: adjusted $\beta = 0.468$, 95%CI 0.239-0.697, adjusted $P < 0.001$; METS-IR index: adjusted $\beta = 0.091$, 95%CI 0.048-0.135, adjusted $P < 0.001$). Similar and stronger associations were observed for maternal pBMI-offspring in TyG-BMI index (boys: adjusted $\beta = 1.045$, 95%CI 0.791-1.299, adjusted $P < 0.001$; girls: adjusted $\beta = 0.730$, 95%CI 0.472-0.988, adjusted $P < 0.001$) and METS-IR index (boys: adjusted $\beta = 0.200$, 95%CI 0.154-0.247, adjusted $P < 0.001$; girls: adjusted $\beta = 0.117$, 95%CI 0.068-0.165, adjusted $P < 0.001$) (**Figure 1A**).

We further evaluated how different combinations of parental overweight/obesity ($\text{pBMI} \geq 24 \text{ kg/m}^2$) influenced children's insulin resistance markers, with the results revealing a clear sex-specific dose-response relationship (**Figure 1B**).

Regarding the TyG-BMI index, significant positive associations were observed across all parental categories. In girls, maternal-only overweight/obesity and paternal-only overweight/obesity were

associated with increases in the TyG-BMI index of 3.321 (95% CI 0.851 - 5.791, adjusted $P=0.009$) and 1.900 (95%CI 0.247 -3.554, adjusted $P=0.024$), respectively. The largest association in girls was observed when both parents had overweight/obesity, with a β of 5.918 (95%CI 2.820-9.016, adjusted $P<0.001$). Similarly, in boys, significant associations were identified for maternal-only overweight/obesity ($\beta= 5.040$, 95% CI 2.615-7.465, adjusted $P<0.001$) and paternal-only overweight/obesity ($\beta= 3.080$, 95%CI 1.432-4.729, adjusted $P<0.001$). The largest association was observed when both parents had overweight/obesity with the TyG-BMI index increasing by 8.805 (95%CI 5.840-11.770, adjusted $P< 0.001$) (**Figure 1B**).

Among girls, maternal-only overweight/obesity was not significantly associated with the METS-IR index ($\beta= 0.339$, 95%CI -0.121-0.799, adjusted $P=0.149$), whereas paternal-only overweight/obesity showed a significant positive association ($\beta= 0.360$, 95% CI 0.052-0.669, adjusted $P=0.022$). The strongest association in girls was observed when both parents were overweight/obese, with a β of 1.081 (95% CI 0.513-1.648, adjusted $P<0.001$). In boys, all three parental categories were significantly associated with an increased METS-IR index: the β values were 0.713 (95% CI 0.263-1.163, adjusted $P=0.002$) for maternal-only overweight/obesity, 0.466 (95% CI 0.166-0.766, adjusted $P=0.002$) for paternal-only overweight/obesity, and reached a maximum of 1.609 (95% CI 1.077-2.141, adjusted $P<0.001$) when both parents had overweight/obesity (**Figure 1B**). Collectively, these findings indicate that the largest elevations in offspring insulin resistance markers were observed when both parents had overweight/obesity.

Mediation analyses

The association between maternal pBMI and child BMI in childhood was partly mediated by the offspring's birthweight both in girls (8.34%, $P<0.001$) and boys (3.29%, $P=0.004$), while the mediation of birthweight between paternal pBMI and child BMI was only shown in girls (5.54%, $P=0.048$)(**Table S3**).

We then investigated potential mediation by the birthweight and child BMI on association between maternal pBMI, paternal pBMI and METS-IR index, TyG-BMI index (**Figure 2**). In girls, almost all the effects of maternal pBMI and paternal pBMI on METS-IR index and TyG-BMI index were mediated by child BMI, and partly mediated by birthweight. In boys, both maternal and paternal pBMI were associated with the METS-IR index and TyG-BMI index, with child BMI as a key mediator; however, birthweight mediated only maternal associations, not paternal ones (**Table S4**).

Discussion

Principal findings

In this cohort of ART-conceived offspring, higher maternal and paternal pBMI were associated with higher childhood BMI and insulin resistance indices at ages 3–6 years. Maternal pBMI generally showed stronger associations than paternal pBMI. Children with overweight/obesity in both parents had the

largest elevations in TyG-BMI and METS-IR. Mediation analyses suggested that child BMI contributed more strongly than birthweight to the observed associations.

Strengths and limitations

First, the strengths of this study include its large sample size, detailed data collection in parental pre-pregnancy characteristics and ART treatment, offspring growth and cardiometabolic outcomes. Second, this study thoroughly examines both the independent and joint associations of maternal and paternal pBMI on offspring cardiometabolic risk, which is particularly important given that offspring conceived through ART may be more susceptible to metabolic disorders compared to those conceived naturally^{34, 35}. However, our study also has several limitations. We lack data on offspring fasting insulin levels and HOMA-IR, a commonly used indicator for quantifying insulin resistance. Instead, we used the METS-IR index and TyG-BMI index as alternative indicators. Additionally, residual confounding from missing data on gestational weight gain and nutrition intake may have introduced residual confounding and biased the effect estimates.

Interpretation

Both maternal and paternal pBMI were independently associated with offspring outcomes, setting the stage for comparing their relative contributions.

Offspring birthweight and childhood BMI were more strongly associated with maternal preconception BMI than paternal BMI, consistent with previous reports on maternal influence^{8, 36}, although other studies found comparable maternal and paternal associations with child BMI throughout childhood, adolescence, and adulthood^{36,37,38}.

Insulin resistance, an early sign of childhood metabolic abnormalities, is closely linked to cardiovascular events³⁹. Recently, sensitive insulin resistance markers such as the TyG-BMI and METS-IR index have gained attention due to their reported associations with cardiometabolic risk^{40, 41}. In our study, maternal pBMI showed a stronger association with offspring insulin resistance indices than paternal pBMI. Previous research also demonstrates a strong maternal association with offspring insulin resistance^{7,8,42}. However, evidence on paternal associations remains mixed: one study reported no association between paternal pBMI and offspring insulin resistance⁸, while another study found comparable effects from both parents⁴².

To our knowledge, this is the first study to investigate the joint associations of maternal and paternal preconception BMI on cardiometabolic health in ART-conceived offspring. Previous studies that included both parents have largely assessed maternal and paternal BMI in isolation rather than examining their joint associations^{8, 14}. In our analyses, maternal and paternal overweight/obesity were independently associated with elevated insulin resistance in ART offspring. Notably, children with overweight/obesity in both parents had larger elevations in METS-IR and TyG-BMI than children with overweight/obesity in only

one parent. Because formal additive interaction estimates were not reported, this pattern should be interpreted as a joint association rather than evidence of statistical synergy.

Maternal and paternal obesity may influence offspring metabolism through partly distinct pathways (Fig. 3). Maternal obesity may adversely affect offspring cardiometabolic health through mechanisms such as epigenetic alterations, metabolic and inflammatory pathways, and direct structural effects, all of which are established during fetal development and shaped by the intrauterine environment⁴³. Paternal obesity may influence offspring partly through sperm epigenetic alterations, such as disrupted DNA methylation and histone modifications^{44, 45}. Our findings support the preconception period as an important window for risk assessment and prevention. Preconception weight optimization should be considered for both parents before ART treatment as part of efforts to reduce offspring cardiometabolic risk. The stronger maternal associations are compatible with a contribution from intrauterine mechanisms beyond shared familial, lifestyle, or genetic influences, which are established as early as the embryonic stage^{46–49}.

Postnatally, shared familial, lifestyle, and genetic factors from both parents continue to shape offspring growth. Child BMI mediated the relationship between parental pBMI and offspring insulin resistance, indicating a modifiable target. This aligns with prior studies in which adjustment for child BMI attenuated parental–offspring cardiometabolic associations^{37, 50}. Family-based lifestyle interventions, including promoting physical activity and maintaining healthy weight in early life, may therefore be essential to mitigate long-term cardiometabolic risk^{51, 52}. Because childhood adiposity is potentially modifiable and cardiometabolic abnormalities may persist into adulthood, early family-based prevention may have long-term relevance^{53–56}.

Conclusions

In conclusion, both maternal and paternal pre-pregnancy BMI were independently associated with offspring growth and cardiometabolic profiles, with generally stronger maternal associations. Children with overweight/obesity in both parents showed the greatest elevations in insulin resistance indices. Mediation analyses suggested that child BMI accounted for a substantial proportion of the association between parental BMI and offspring insulin resistance. These findings support weight optimization for both parents before ART and early monitoring of offspring BMI as potential strategies for reducing later cardiometabolic risk.

Abbreviations

ART
assisted reproductive technology
BMI
body mass index
CI

confidence interval
DOHaD
Developmental Origins of Health and Disease
FET
frozen embryo transfer
GDM
gestational diabetes mellitus
HDL-C
high-density lipoprotein cholesterol
HDP
hypertensive disorders of pregnancy
ICSI
intracytoplasmic sperm injection
IQR
interquartile range
IVF
in vitro fertilization
LDL-C
low-density lipoprotein cholesterol
METS-IR
metabolic score for insulin resistance
non-HDL-C
non-high-density lipoprotein cholesterol
pBMI
pre-pregnancy body mass index
TC
total cholesterol
TG
triglyceride
TyG
triglyceride-glucose index
TyG-BMI
triglyceride-glucose body mass index.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Women's Hospital, School of Medicine, Zhejiang University (IRB-20250104-R). Written informed consent was obtained from the parents or legal guardians of all participating children. Clinical trial number: ChiCTR2500104140; date of registration: 11 June 2025.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Authors' information

Not applicable.

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Author Contribution

Minyue Tang: conceptualization, data curation, formal analysis, funding acquisition, methodology, project administration, resources, supervision, writing– original draft, and writing – review and editing. Xinyue Wu: conceptualization, data curation, formal analysis, methodology, writing– original draft, and writing – review and editing. Zhekun Zhao: methodology, and writing – review and editing. Shuangying Liu: methodology, and writing – review and editing. Yingzhi Yang: methodology, and writing – review and editing. Yimin Zhu: conceptualization, data curation, funding acquisition, project administration, resources, supervision, and writing – review and editing.

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Not applicable.

Data Availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request. Requests should include a description of the study objectives and a statistical analysis plan and will be evaluated in accordance with applicable institutional and ethical requirements.

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Table 1

Table 1. Characteristics of the study population by offspring sex

	All	Girls	Boys	P value
N	2989	1417	1572	
Parental characteristics				
Maternal age (years)	30 (5)	30 (5)	30 (5)	0.367
Paternal age (years)	32 (6)	32 (5)	32 (6)	0.762
Maternal BMI (kg/m ²)	21.50 (3.59)	21.67 (3.70)	21.48 (3.50)	0.034
Underweight	244 (8.2%)	103 (7.3%)	141 (9.0%)	
Normal	2105 (70.4%)	994 (70.1%)	1111 (70.7%)	
Overweight	537 (18.0%)	270 (19.1%)	267 (17.0%)	
Obese	103 (3.4%)	50 (3.5%)	53 (3.4%)	
Paternal BMI (kg/m ²)	23.51 (4.36)	23.44 (4.26)	23.64 (4.46)	0.484
Underweight	90 (3.0%)	42 (3.0%)	48 (3.1%)	
Normal	1593 (53.3%)	776 (54.8%)	817 (52.0%)	
Overweight	1036 (34.7%)	470 (33.2%)	566 (36.0%)	
Obese	270 (9.0%)	129 (9.1%)	141 (9.0%)	
Gravidity	2 (2)	2 (2)	2 (2)	0.014
Parity	1 (0)	1 (0)	1 (0)	0.119
Smoking exposure	925 (30.9%)	443 (31.3%)	482 (30.7%)	0.722
Maternal education level				0.315
Junior high school and below	921 (30.8%)	453 (32.0%)	468 (29.8%)	
Senior high school	1318 (44.1%)	623 (44.0%)	695 (44.2%)	
College or above	750 (25.1%)	341 (24.1%)	409 (26.0%)	
Paternal education level				0.789
Junior high school and below	834 (27.9%)	389 (27.5%)	445 (28.3%)	
Senior high school	1289 (43.1%)	620 (43.8%)	669 (42.6%)	
College or above	866 (29.0%)	408 (28.8%)	458 (29.1%)	
Residence				0.199
Rural	1467 (49.1%)	713 (50.3%)	754 (48.0%)	
Urban	1522 (50.9%)	704 (49.7%)	818 (52.0%)	

	All	Girls	Boys	P value
ART characteristics				
Factors causing infertility				0.915
Tube factor	1467 (49.1%)	700 (49.4%)	767 (48.8%)	
Ovulation disorder	200 (6.7%)	95 (6.7%)	105 (6.7%)	
Endometriosis or uterine factor	190 (6.4%)	86 (6.1%)	104 (6.6%)	
Male	514 (17.2%)	252 (17.8%)	262 (16.7%)	
Combined	332 (11.1%)	152 (10.7%)	180 (11.5%)	
Unknown	286 (9.6%)	132 (9.3%)	154 (9.8%)	
ART therapy				
IVF	2260 (75.6%)	1077 (76.0%)	1183 (75.3%)	0.633
ICSI	729 (24.4%)	340 (24.0%)	389 (24.7%)	
FET	1191 (39.8%)	565 (39.9%)	626 (39.8%)	0.977
Fresh-ET	1798 (60.2%)	852 (60.1%)	946 (60.2%)	
Pregnancy and offspring characteristics				
Gestational diabetes mellitus	330 (11.0%)	157 (11.1%)	173 (11.0%)	0.948
Hypertensive disease of pregnancy	173 (5.8%)	88 (6.2%)	85 (5.4%)	0.348
Birthweight	3.35 (0.60)	3.30 (0.55)	3.40 (0.64)	<0.001
Low birthweight	19 (0.6%)	13 (0.9%)	6 (0.4%)	0.066
Macrosomia	182 (6.1%)	61 (4.3%)	121 (7.7%)	<0.001
Age at assessment (months)	56.50 (4.50)	56.50(4.45)	56.60 (4.50)	0.971

Data are presented as Median (IQR) or n (%).

Abbreviations: BMI, body mass index; ART, assisted reproductive technology; IVF, in-vitro fertilization; ICSI, intracytoplasmic sperm injection; FET, frozen-embryo transfer; fresh-ET, fresh-embryo transfer.

Figures

A

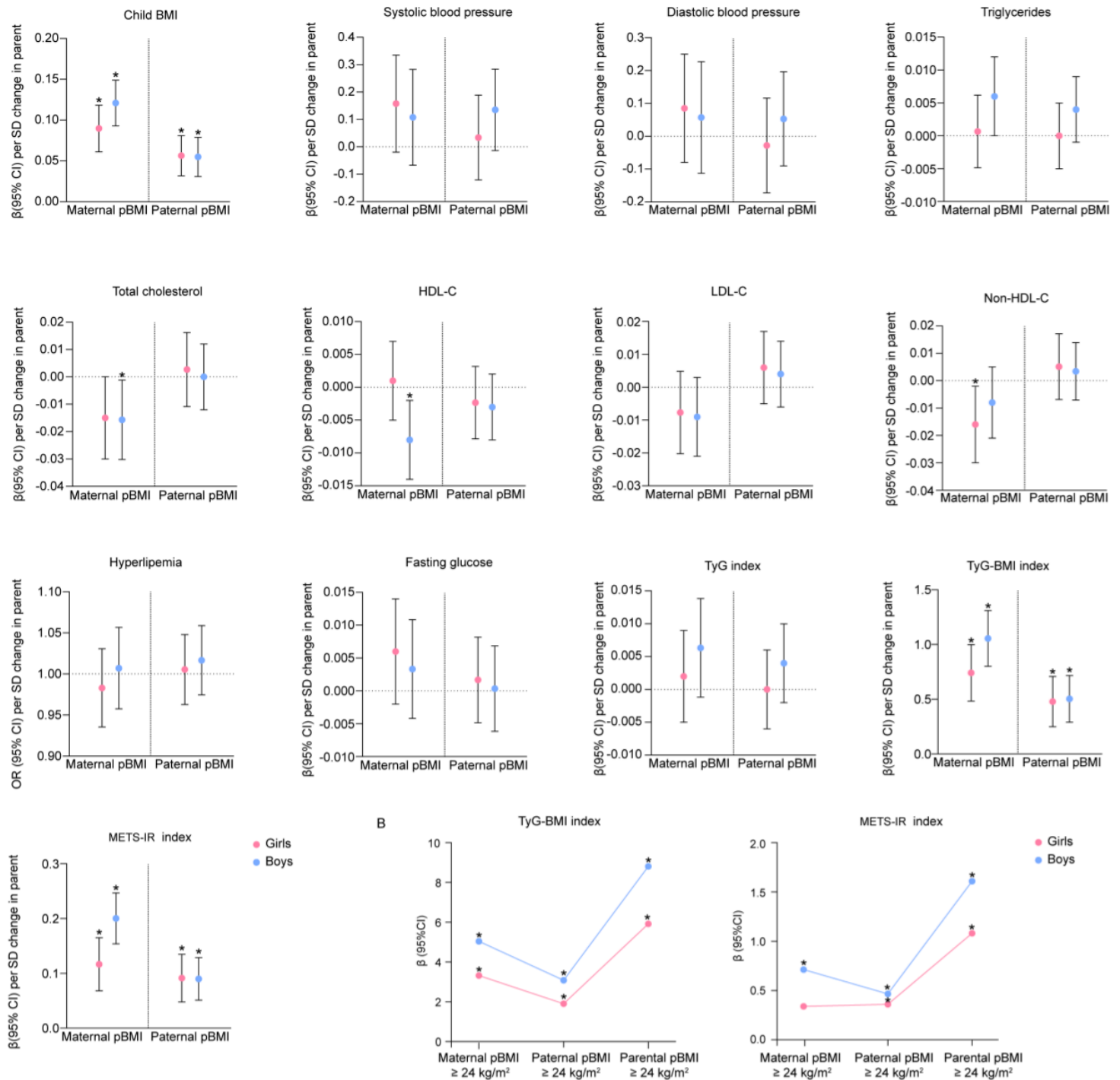


Figure 1

Associations of parental pre-pregnancy BMI with offspring cardiometabolic outcomes.

A. Sex-stratified associations between parental pBMI and offspring cardiometabolic markers.

B. Comparison of TyG-BMI and METS-IR indices across different parental pBMI groups. The groups are categorized based on parental overweight/obesity status (pBMI ≥ 24 kg/m²).

Outcomes are presented in mean estimated differences with a 95% CI. *P < 0.05 was considered to be a statistically significant difference.

Abbreviations: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; non-HDL-C, non-high density lipoprotein cholesterol; METS-IR, metabolic score for insulin resistance; TyG index, triglyceride and glucose index; TyG-BMI index, triglyceride-glucose-body mass index.

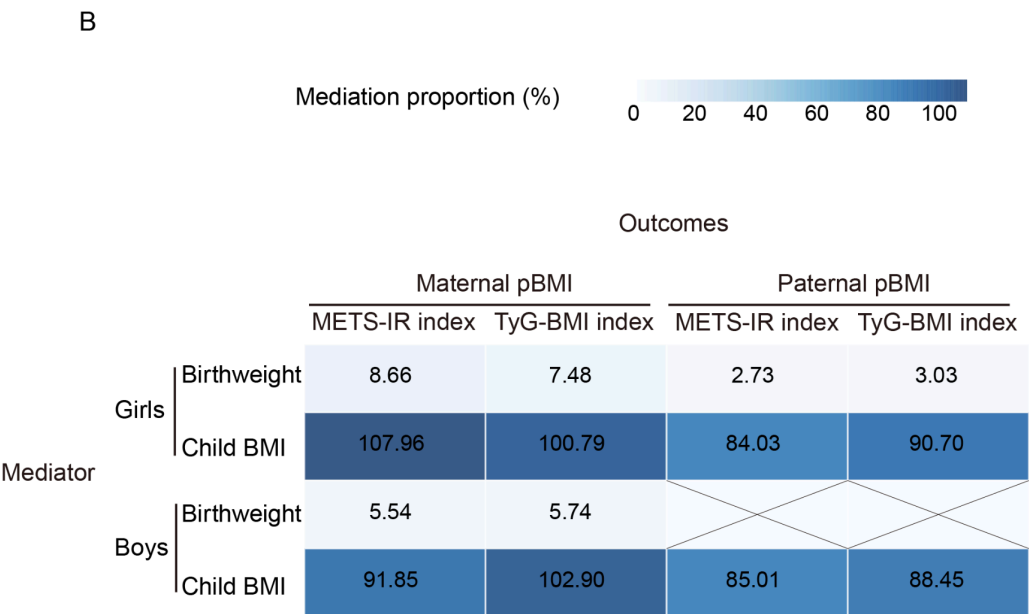
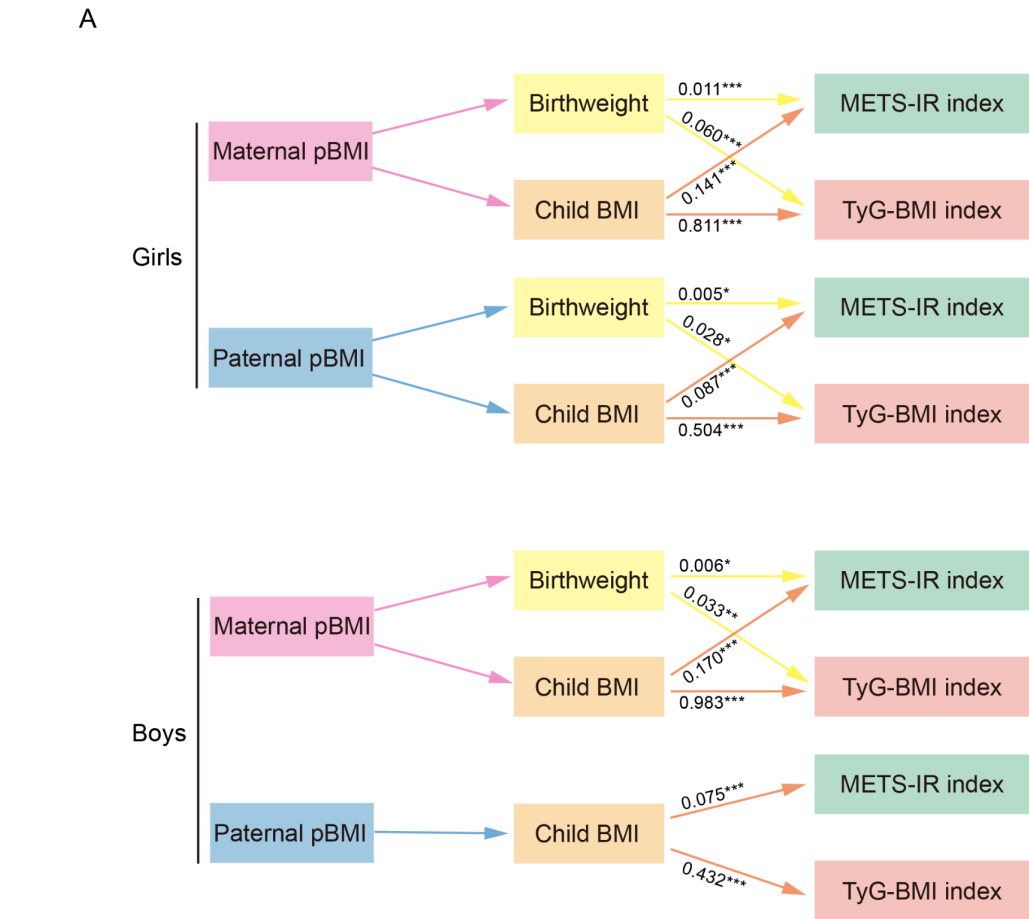


Figure 2

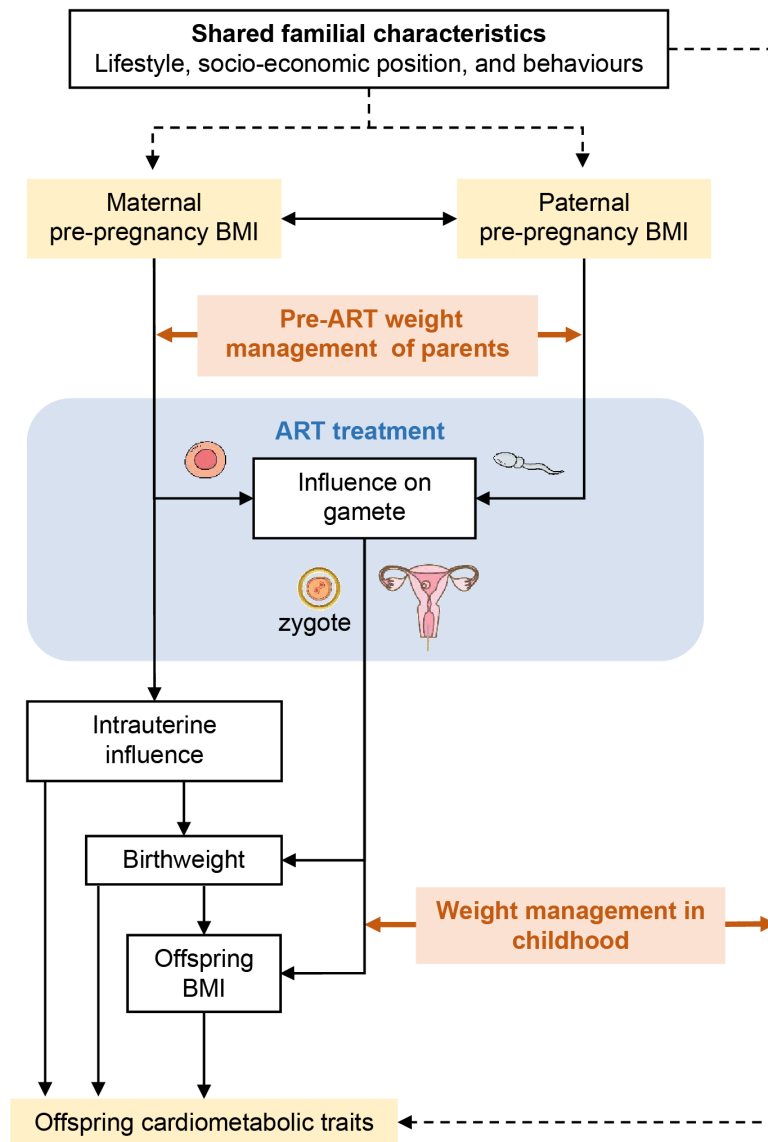
Mediation of parental pre-pregnancy BMI associations with offspring insulin resistance indices.

A. Mediation models for associations of maternal and paternal pBMI with METS-IR and TyG-BMI indices through birthweight and child BMI. The numbers on the arrows represent the β values and P value (*P < 0.05, **P < 0.01, ***P < 0.001).

B. The mediation proportions (%) for maternal and paternal pBMI on the METS-IR index and TyG-BMI index in girls and boys, highlighting the contribution of child BMI and birthweight as mediators.

*P < 0.05 was considered to be a statistically significant difference.

Abbreviations: BMI, body mass index; METS-IR, metabolic score for insulin resistance; TyG-BMI index, triglyceride-glucose-body mass index.



Maternal pre-pregnancy BMI could affect offspring cardiometabolic traits via 3 Key mechanism:

- Influence on gamete
- Intrauterine influence
- confounding by shared familial characteristics

Paternal pre-pregnancy BMI could affect offspring cardiometabolic traits via 2 Key mechanism:

- Influence on gamete
- confounding by shared familial characteristics

Figure 3

Hypothesized pathways linking parental pre-pregnancy BMI to offspring cardiometabolic traits.

Supplementary Files

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