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Key Words:	birth weight, body mass index, twins

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Abstract

Background: There is evidence that birth weight is positively associated with body mass index (BMI) in later life, but it remains unclear whether this is explained by genetic factors or the intrauterine environment. We analyzed the association between birth weight and BMI from infancy to adulthood within twin pairs, which provides insights into the role of genetic and environmental individual-specific factors.

Methods: This study is based on the data from 27 twin cohorts in 17 countries. The pooled data included 78,642 twin individuals (20,635 monozygotic and 18,686 same-sex dizygotic twin pairs) with information on birth weight and a total of 214,930 BMI measurements at ages ranging from 1 to 49 years. The association between birth weight and BMI was analyzed at both the individual and within-pair level using linear regression analyses.

Results: When twins were treated as individuals, a 1-kg increase in birth weight was linearly associated with up to 0.9 kg/m^2 higher BMI ($p<0.001$). Within twin pairs, regression coefficients were generally greater (up to 1.2 kg/m^2 per kg birth weight, $p<0.001$) than those from the individual level analyses. Intra-pair associations between birth weight and later BMI were similar in both zygosity groups and sexes, and tended to be attenuated in adulthood.

Conclusions: These findings suggest that environmental factors unique to each individual have an important role in the positive association between birth weight and later BMI, at least until young adulthood.

Keywords

birth weight, body mass index, twins

Key messages

Birth weight is positively and linearly associated with later BMI.

This association is similar in males and females and tends to be attenuated in adulthood.

Environmental factors unique to each individual have an important role in the positive association between birth weight and later BMI.

Introduction

The increasing prevalence of overweight and obesity over the last decades has grown into a global epidemic that currently affects a large part of the world's population[1]. The interest in the role of gestational factors behind adult health outcomes[2] has resulted in a number of epidemiological studies analyzing the association between birth weight and later body mass index (BMI). Several very large and well-conducted studies have shown a positive association of birth weight with BMI and overweight/obesity in children, adolescents and adults[3-9], but J- or U-shaped associations have also been reported[10,11]. The mechanisms underlying this association are, however, still poorly understood. It has been suggested that the fetal period may be critical for the development of obesity[10,12], but it is unclear how far the associations between birth weight and subsequent BMI reflect early developmental factors in the intrauterine environment or whether they are explained by common genetic factors affecting body size from fetal life until adulthood.

Twins create a natural experiment and offer an opportunity to shed light into the mechanisms underlying the association between birth and later BMI[13,14]. Twins come from the same family, share the same maternal environment, have the same gestational age, and in the case of monozygotic (MZ) twins are genetically identical. However, each fetus has its own fetoplacental environmental conditions, such as supply of nutrients and oxygen, which may differ substantially from that of its co-twin[15]. The association between the intra-pair differences in birth weight and later BMI cannot be explained by shared family factors, such as maternal nutrition, parental education or socio-economic status. Further, differences within MZ pairs cannot be explained by preconceptional parental influences or genetic factors. The comparison of intra-pair associations in MZ and dizygotic (DZ) twins is thus a strong design to explore within family effects. A stronger association in DZ than in MZ twins is taken as evidence that the relationship between birth weight and later BMI is explained by genetic factors. Differences in birth weight and later BMI within MZ pairs can only be influenced by environmental factors that are unique to individuals (i.e. the intrauterine environment), while differences within DZ pairs can also be influenced by genetic factors[13,14].

A few twin studies have performed pair-wise analyses between birth weight and BMI in late adolescence and adulthood, but the results have been somewhat conflicting. Intra-pair differences in birth weight were not related with intra-pair differences in BMI in adults from Minnesota and the United Kingdom[16,17]. In young adult Belgian MZ twins, only when the birth weight difference between the twins exceeded 15%, the heavier twin at birth showed a trend toward a higher BMI[18,19]. A positive and significant association was observed in Swedish young adult MZ males[20], and in Finnish MZ and DZ twins of both sexes (aged 16-18.5 years)[21]. This suggests that intrauterine environment may play a role in later BMI, but this is far from settled. Moreover, it is not known whether the effects vary in their importance by age, particularly in childhood. To address this question, we analyzed the association between birth weight and later BMI from infancy to adulthood in MZ and DZ twins of both sexes in multinational twin data from 27 cohorts in 17 countries.

Material and methods

Sample

This study is based on the data from the COllaborative project of Development of Anthropometrical measures in Twins (CODATwins), which was intended to pool data from all twin projects in the world having information on height and weight[22]. Information on birth weight was available in 27 cohorts; birth length and gestational age were available in 14 and 17 of these cohorts, respectively. The participating twin cohorts are identified in Table 1 (footnote) and were previously described in detail[22].

In the original database, there were 122,582 twin individuals with information on birth weight. We excluded 81 individuals with birth weight <0.5 or >5 kg. The remaining 122,501 individuals presented a total of 355,650 height and weight measurements at later ages. Age was classified to single-year age groups from age 1 to 19 years (e.g. age 1 refers to 0.5-1.5 years range) and three adult age groups (20-29, 30-39 and 40-49 years). Measurements at ages ≤0.5 and > 49.5 years (which is a proxy for menopausal status in women) were excluded because the sample sizes were too small. BMI was calculated as weight (kg)/square of height (m^2). Impossible values and outliers were checked by visual inspection of histograms for each age and sex group and were removed (<0.3 % of the measurements) allowing the distribution of BMI data to be positively skewed, resulting in 344,104 measurements. After restricting the analyses to one BMI measure per individual in each age group by keeping the measurement at the youngest age (6% of the measurements were removed), we had 324,968 observations from 119,323 individuals.

We next excluded unmatched pairs (without data on their co-twins) resulting in 149,435 paired observations. Furthermore, because of the effects of sex differences within a pair on both birth weight and BMI especially during and after puberty, opposite-sex dizygotic twin pairs were excluded (41,733 paired observations). Intra-pair differences in birth weight and later BMI were checked by visual inspection of histograms. We removed birth weight differences greater than ±1.7 kg (72 paired observations) and outliers for the within-pair BMI difference in each age group (125 paired observations). Together we had 214,930 observations (107,465 paired observations), 55% MZ and 45% same- sex DZ, from 78,642 twin individuals (39,321 complete twin pairs). In summary, excluding opposite-sex dizygotic twin pairs, the study database (39,321 twin pairs) is 95% of the eligible sample (41,599 twin pairs).

For secondary analyses, we additionally calculated birth weight standardized by gestational age and ponderal index at birth. Birth weight was expressed as SD scores of the respective means/weeks of gestation (z-scores; i.e., mean = 0 and SD = 1) to estimate the relative position of birth weight for a given gestational age. Individuals without data on gestational age, gestational age <25 or >45 weeks or with discordant information on gestational age within pairs were excluded. Unrealistic birth weight values for a given gestation were checked by visual inspection of histograms for each gestational week and removed (<0.2% of the observations). After these exclusions, we had 84,357 paired observations. For the calculation of ponderal index at birth (PI=weight (kg)/height (m^3)), we removed those cases without information on birth length, birth length <25 or >60 cm, PI<12 or >38, or intra-pair difference in PI >15 kg/ m^3 (from the 107,465 paired observations in the primary analyses), resulting in 68,954 paired observations.

All participants were volunteers and gave their informed consent when participating in their original studies. Only a limited set of observational variables and anonymized data were delivered to the data management center at University of Helsinki. The pooled analysis was approved by the ethical committee of Department of Public Health, University of Helsinki, and the methods were carried out in accordance with the approved guidelines.

Statistical analyses

Statistical analyses were conducted using the Stata statistical software package (version 12.0; StataCorp, College Station, Texas, USA). First, all BMI measurements were adjusted for exact age within each age and sex group using linear regression (BMI was used as dependent variable and age as continuous independent variable) and the resulting residuals were used as input variables for the following analyses.

In primary analyses, we studied the association between birth weight and later BMI at both the individual and within-pair level. At the individual level, we performed linear regression analysis adjusted for birth year and twin cohort separately by sex, zygosity and age group. BMI was used as the dependent variable and birth weight as the independent variable. The non-independence within twin pairs was taken into account by using the "cluster" option available in Stata. Since regression analyses with log-transformed BMI and untransformed BMI provided very similar results, we used raw BMI data in order to make these results comparable with those from the pair-wise analyses. In the within-pair analyses, intra-pair differences with both positive and negative values were created by randomly subtracting the co-twin with the lowest birth weight from the co-twin with the highest birth weight or vice versa. As in individual level analyses, linear regression analysis adjusted for birth year and twin cohort separately by sex, zygosity and age group was carried out (intra-pair BMI difference was used as the dependent variable and intra-pair birth weight difference as the independent variable). Next, we ensured that the regression lines passed through the origin by checking that the intercept was not significantly different from zero.

An interaction analysis was performed to investigate whether zygosity influenced the associations between birth weight and BMI by introducing a product term of zygosity and birth weight into the regression model. At the individual level, we used linear regression analysis, with BMI as dependent variable and birth weight as independent variable, adjusted for zygosity, the product term of zygosity and birth weight, birth year and twin cohort separately by age and sex. At the within-pair level, we used linear regression analysis with intra-pair BMI difference as dependent variable and intra-pair birth weight difference as independent variable, adjusted for zygosity, the product term of zygosity and intra-pair birth weight differences, birth year and twin cohort separately by age and sex. There was no interaction effects between zygosity and birth weight in individual level analyses (only 2 of 44 tests had p-value < 0.05 and none of them had p-value <0.0011 that would correspond to p-value <0.05 after Bonferroni correction of multiple testing); similar findings were observed between zygosity and intra-pair birth weight differences in pair-wise analyses (Appendix Table 1). The quadratic effect of birth weight was investigated by introducing the term in the regression models of the primary analyses, that is, by introducing the quadratic term of birth weight in the individual level analyses and the quadratic term of intra-pair birth weight differences in the pair-wise analyses. No quadratic effect of birth weight or intra-pair birth weight differences was found (Appendix Table 2).

In secondary analyses, we used the regression models described in the primary analyses. We analyzed the association between gestational age standardized birth weight (independent variable) and later BMI (dependent variable) at the individual level. Finally, we analyzed the association between PI at birth (independent variable) and later BMI (dependent variable) at the individual level, and between intra-pair PI differences (independent variable) and intra-pair BMI differences (dependent variable) at the within-pair level.

Results

Table 1 provides descriptive statistics for birth weight and BMI by zygosity, age and sex. Mean birth weight was slightly greater in males than in females and in DZ than in MZ twins; the same pattern was observed for the SD of birth weight. Regarding BMI, sample size for each zygosity, age, and sex group ranged between 530 and 6176 measurements. The 6, 19 and 40-49 years age groups had the smallest sample sizes. Mean BMI declined from the age of 1 to 5 years and then started to increase; these mean values were higher in males than in females from age 1 to 6 years and from the age of 17 years onwards. The SD of BMI generally increased with age. Despite similar values in early childhood, DZ twins had slightly higher mean BMI and greater SD than MZ twins at most ages.

When twins were treated as individuals, birth weight was generally positively associated with later BMI; however, no evidence of association was observed for some age-zygosity groups in adolescence and adulthood (Table 2). The magnitude of the associations was roughly similar and did not present any specific pattern across age, zygosity and sex groups. Regression coefficients showed that a 1-kg increase in birth weight was associated with up to 0.9 kg/m^2 higher BMI, ranging between 0.3 and 0.6 kg/m^2 at most ages. When birth weight was expressed as a z-score for gestational age, the associations generally slightly increased in childhood and early adolescence, but from middle adolescence onwards the pattern was not clear (Appendix Table 3).

Within MZ twin pairs, greater birth weight was also associated with higher BMI at most ages (Table 3). Regression coefficients generally ranged from 0.6 to 1.0 kg/m^2 per kg birth weight (up to 1.2 kg/m^2), were similar in males and females and somewhat greater in childhood than in late adolescence and adulthood; no association was observed at 30-39 for men or at 40-49 years. Supported by the lack of interaction between zygosity and intra-pair birth weight differences, the magnitude of the associations in DZ twins was similar to that of MZ twins; when different, they were generally greater in MZ twins (except at 9 and 19 years in males). A positive association was also observed between PI at birth and later BMI (Figure 1 and Appendix Table 4). A MZ intra-pair difference of a 1- kg/m^3 increase in PI generally resulted in a BMI difference of 0.03-0.08 kg/m^2, but the effects were somewhat greater in DZ twins at some ages.

Discussion

The present study, based on a multinational database of 27 twin cohorts with 107,465 paired observations, showed that birth weight is associated with later BMI within male and female MZ pairs from infancy onwards, but the association tends to be attenuated in adulthood. Our results thus support the role of environmental factors unique to each individual in the associations and refine previous findings by considering, in addition to adult age, childhood and adolescence using one-year age groups from 1 to 19 years.

When twins were treated as individuals, the increase in BMI associated with a 1 kg increase in birth weight (0.3-0.6 kg/m^2 at most ages) was in the range of other twin and singletons studies in late adolescence and young adulthood[4,9,18]. The quadratic effects of birth weight were independently tested in each age, zygosity and sex groups, and there was no evidence of non-linearity between birth weight and later BMI. Further, since smallness for gestational age, rather than smallness due to prematurity, has shown to be an indicator for shortness and lightness in early childhood[23], we standardized birth weight for gestational age. The magnitude of the associations slightly increased until early adolescence, suggesting that the effect of gestational age on the association between birth weight and BMI remains important, at least until this period.

The pair-wise analysis of MZ twins showed that environmental individual-specific factors are important in the association between birth weight and later BMI, suggesting the role of the intrauterine environment. The magnitude of these individual-specific factors tended to persist during childhood but decreased from late adolescence. For example, the effects at ages 20-29 years (0.41 kg/m^2 and 0.68 kg/m^2 per kg in males in females, respectively) were comparable with those reported in other studies[18,19,20,21]; however, none of them analyzed the relationship in childhood. These intra-pair associations between birth weight and later BMI observed in different populations suggest that a causal relation is biologically plausible. The number of fat cells (adipocytes) has shown to be a major determinant of fat mass in adults[24]. Spalding et al[24] found that the adipocyte number is set during childhood and adolescence and, although there is a high turnover (10% annually), stays constant during adulthood. Further, there is evidence that the number of muscle cells in the body is determined before birth[25]. Since intra-pair differences in birth weight have shown a positive association with intra-pair differences in both total lean mass and total fat mass[26], one possible explanation is that higher birth weight implies a greater number of cells in both adipose and non-adipose tissues, and this cell number difference remains in later life. The decreasing association between birth weight and BMI across adulthood might be explained by changes in BMI independent of the number of fat or muscle cells, but also by a lower accuracy of birth weight measurements in individuals born earlier (69 % of the individuals with BMI measurements at 40-49 years born before 1950).

There is also evidence that environmental exposures during early life can induce persistent alterations in the epigenome, which may lead to an increased risk of obesity later in life[27]. For example, a recent study suggested that both maternal obesity and, to a larger degree, underweight affect the neonatal epigenome via an intrauterine mechanism[28]. DNA methylation patterns in cord blood showed some association with altered gene expression, body size and composition in childhood, but the authors found no association between methylation status and birth weight[29]. A twin study using gene expression discordance as a proxy measure of epigenetic discordance in MZ twins at birth reported some association between birth weight and expression of genes involved in metabolism and cardiovascular function[30]. However, there is no evidence, to our knowledge, of epigenetic mechanisms explaining the positive association between birth weight and later BMI. It is noteworthy that overall epigenetic changes are weakly associated with BMI and are more prominent only when metabolic complications of obesity arise[31].

Although the findings from previous studies are contrasting[18,20,21], our data revealed that the magnitude of the associations in DZ pairs was generally similar to that in MZ pairs and thus suggest that genetic factors are not importantly involved in the relationship between birth weight and later BMI. However, in the absence of data on chorionicity, a possible genetic influence cannot be fully excluded. Approximately two thirds of MZ twins are monochorionic and thus share the same placenta; an unequal placental sharing is a major cause of fetal growth discordance in MZ twins[32]. Therefore, intrauterine factors that could potentially account for our findings are placental differences between MZ and DZ twins and between monochorionic and dichorionic MZ twins[32,33]. It has been reported that monochorionic MZ twins are more discordant than dichorionic MZ twins for BMI throughout childhood and adolescence[32]. Therefore, it could be argued that besides genetic factors, these placental differences may increase the intra-pair associations in MZ pairs, making them thus more similar to those in DZ pairs.

Birth weight may not be the ideal measurement of body composition in newborns since it does not discriminate between those infants of different sizes or body shapes. Thus we repeated the analyses for PI, a measure of relative weight at birth. The effects were greater in DZ twins at some ages, suggesting that genetic factors may play a role in the association, which is agreement with the findings in Finnish twins[21]. After standardization, the units of weight and PI at birth became comparable (results not shown). It was then evident that intra-pair differences in BMI were more strongly associated with birth weight than with PI in most zygosity, age and sex groups. However, neither PI nor BMI determine fat mass per se. BMI is generally used as a proxy for body fat in epidemiologic studies, but it does not allow the drawing of conclusions about body composition[34]. As reviewed by Rogers[10], birth weight is usually positively associated with lean body mass and negatively associated with relative adiposity, suggesting that the association between birth weight and BMI/overweight does not necessarily reflect increased adiposity at higher birth weights.

The main strength of the present study is the large sample size of our multinational database of twin cohorts with information on size at birth and height and weight measures from infancy to adulthood. We performed an individual based pooled analysis to provide results for this sample including the large majority of existing twin cohorts. Generalization for the global population is, however, not possible because countries or regions are not equally represented and the database is heavily weighted towards Caucasian populations following Westernized lifestyle. Another limitation of the data is that most of the measures were parentally reported (birth measures) and self-reported or parental-reported (later measures)[22]. However, the accuracy between maternal recall and medical records of birth weights (in singletons) have reached a kappa value of 0.89[35], and the correlations between measured and self-reported heights and weights have commonly been over 0.90[36,37]. Finally, it has been questioned whether differences in birth size in twins are a suitable model for differences in birth weight in general, because intrauterine growth in twins is different from that in singletons and fetal growth may be particularly compromised in MZ twins[38]. However, the magnitude of the relationship between birth weight and BMI in twins was at the same level to that reported in singletons[4]. As concluded by Morley[38], there is no reason to suggest that data from twins cannot be used to shed light on causal pathways underlying the association between birth weight and cardiovascular risk factors.

In conclusion, our findings showed that environmental factors unique to each individual are important in the association between birth weight and later BMI, and thus support the role of the intrauterine environment in the development of later BMI. The association of birth weight with later BMI persists across ages but is attenuated in adulthood. Identifying intrauterine environmental factors affecting later BMI may thus be important when trying to understand the development of obesity across the life-span.

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Aline Jelenkovic will act as guarantor for the paper.

Table 1. Descriptive statistics of birth weight and BMI by zygosity, age and sex

	Males						Females					
	MZ			DZ			MZ			DZ		
	N	Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD
Birth weight (kg)	19864	2.52	0.55	19208	2.60	0.57	21406	2.41	0.52	18164	2.50	0.54
BMI (kg/m^2)												
Age 1	5572	17.15	1.41	5070	17.11	1.35	5966	16.78	1.41	4692	16.71	1.34
Age 2	4448	16.54	1.39	4212	16.53	1.43	4540	16.09	1.37	3666	16.15	1.36
Age 3	5490	15.94	1.37	5298	15.96	1.50	6176	15.61	1.43	4968	15.68	1.54
Age 4	3042	15.85	1.75	2950	15.93	1.86	3152	15.65	1.95	2750	15.69	1.87
Age 5	2488	15.25	1.52	2342	15.29	1.61	2678	15.06	1.60	2078	15.18	1.72
Age 6	1058	15.43	1.73	660	15.47	1.89	922	15.18	1.68	530	15.32	2.22
Age 7	4536	15.34	1.68	3954	15.43	1.89	5018	15.36	1.90	3826	15.46	2.01
Age 8	2066	15.57	1.64	1494	15.72	2.01	2078	15.55	1.90	1264	15.79	2.09
Age 9	1982	16.24	2.07	1466	16.52	2.48	2008	16.24	2.33	1290	16.50	2.66
Age 10	3776	16.56	2.21	3184	16.59	2.32	4074	16.59	2.40	2892	16.79	2.56
Age 11	2992	17.21	2.49	2366	17.45	2.65	3162	17.38	2.79	2052	17.70	3.05
Age 12	3934	17.70	2.62	3062	17.90	2.88	4108	17.83	2.80	2980	17.98	2.97
Age 13	1198	18.41	2.94	1002	18.60	3.22	1124	18.85	3.23	834	18.91	3.19
Age 14	2072	19.16	2.73	1848	19.45	3.11	2410	19.47	3.00	1890	19.66	3.17
Age 15	1228	19.98	3.16	1094	20.20	3.17	1164	20.37	3.44	992	20.81	3.75
Age 16	1614	20.59	2.88	1550	20.78	2.97	1996	20.55	2.87	1700	20.80	3.11
Age 17	1824	21.11	2.80	1910	21.46	3.02	2464	20.69	2.87	1988	20.95	3.00
Age 18	2028	21.35	2.55	1694	21.89	2.92	1378	21.29	3.18	1140	21.44	3.32
Age 19	814	21.57	2.49	784	21.82	2.46	998	21.04	3.01	734	21.49	3.17
Age 20-29	2786	23.19	3.03	2290	23.45	2.96	2804	22.12	3.73	2118	22.15	3.51
Age 30-39	1242	24.78	3.34	1066	25.20	3.62	2114	22.94	4.05	1686	22.82	3.99
Age 40-49	670	26.11	3.48	492	26.54	3.95	1096	24.15	4.80	782	23.86	4.39

Names list of the participating twin cohorts in this study: Australian Twin Registry, Boston University Twin Project, Carolina African American Twin Study of Aging, Colorado Twin Registry, East Flanders Prospective Twin Survey, Finntwin12, Finntwin16, Gemini Study, Guinea-Bissau Twin Study, Hungarian Twin Registry, Italian Twin Registry, Japanese Twin Cohort, Longitudinal Israeli Study of Twins, Michigan Twins Study, Minnesota Twin Family Study, Minnesota Twin Registry, Mongolian Twin Registry, Murcia Twin Registry, Norwegian Twin Registry, Peri/Postnatal Epigenetic Twins Study, Qingdao Twin Registry of Children, Quebec Newborn Twin Study, Swedish Young Male Twins Study of Adults, Swedish Young Male Twins Study of Children, Twins Early Developmental Study, West Japan Twins and Higher Order Multiple Births Registry and Young Netherlands Twin Registry.

Names list of the participating countries (Number of twin cohorts per country, % of the total sample): Australia (2, 0.51%), Belgium (1, 0.31%), Canada (1, 1.63%), China (1, 0.32%), Finland (2, 10.88%), Guinea Bissau (1, 0.08%), Hungary (1, 0.06%), Israel (1, 0.29%), Italy, (1, 0.59%), Japan (2, 12.19%), Mongolia (1, 0.04%), Netherlands (1, 35.28%), Norway (1, 1.99%), Spain (1, 0.06%), Sweden (2, 4.60%), United Kingdom (2, 20.47%), United States of America (6, 10.69%).

Table 2. Regression coefficients for the association between birth weight and BMI (BMI units per kg birth weight), with monozygotic (MZ) and dizygotic (DZ) twins treated as individuals

	Males								Females							
	MZ				DZ				MZ				DZ			
	B	p-value	95% CIs		B	p-value	95% CIs		B	p-value	95% CIs		B	p-value	95% CIs	
Age 1	0.52	<0.001	0.43	0.61	0.40	<0.001	0.32	0.48	0.43	<0.001	0.34	0.53	0.52	<0.001	0.43	0.61
Age 2	0.55	<0.001	0.46	0.65	0.50	<0.001	0.41	0.59	0.49	<0.001	0.39	0.60	0.56	<0.001	0.47	0.66
Age 3	0.53	<0.001	0.44	0.63	0.45	<0.001	0.36	0.53	0.45	<0.001	0.36	0.54	0.43	<0.001	0.33	0.53
Age 4	0.55	<0.001	0.40	0.69	0.42	<0.001	0.27	0.57	0.50	<0.001	0.34	0.67	0.51	<0.001	0.36	0.67
Age 5	0.56	<0.001	0.41	0.71	0.39	<0.001	0.24	0.53	0.49	<0.001	0.35	0.64	0.49	<0.001	0.34	0.65
Age 6	0.46	0.002	0.16	0.76	0.39	0.015	0.08	0.70	0.34	0.021	0.05	0.64	0.67	0.003	0.23	1.11
Age 7	0.32	<0.001	0.20	0.44	0.41	<0.001	0.29	0.54	0.45	<0.001	0.31	0.59	0.39	<0.001	0.25	0.54
Age 8	0.67	<0.001	0.52	0.83	0.40	<0.001	0.20	0.60	0.44	<0.001	0.23	0.64	0.63	<0.001	0.38	0.88
Age 9	0.40	0.001	0.17	0.63	0.61	<0.001	0.34	0.88	0.57	<0.001	0.33	0.81	0.55	0.002	0.21	0.90
Age 10	0.39	<0.001	0.22	0.56	0.40	<0.001	0.22	0.58	0.40	<0.001	0.21	0.59	0.37	<0.001	0.17	0.56
Age 11	0.55	<0.001	0.33	0.77	0.44	<0.001	0.20	0.69	0.41	0.002	0.15	0.66	0.54	0.001	0.24	0.85
Age 12	0.50	<0.001	0.30	0.70	0.51	<0.001	0.30	0.73	0.35	0.002	0.13	0.56	0.37	0.003	0.13	0.62
Age 13	0.19	0.358	-0.22	0.60	0.21	0.364	-0.24	0.66	0.16	0.480	-0.28	0.59	-0.19	0.448	-0.67	0.30
Age 14	0.36	0.012	0.08	0.65	0.30	0.065	-0.02	0.62	0.17	0.255	-0.12	0.46	0.13	0.395	-0.17	0.44
Age 15	0.20	0.329	-0.20	0.59	0.48	0.009	0.12	0.84	0.64	0.007	0.18	1.09	0.03	0.922	-0.48	0.53
Age 16	0.52	0.001	0.20	0.83	0.66	<0.001	0.29	1.03	0.62	<0.001	0.30	0.95	0.45	0.005	0.13	0.77
Age 17	0.33	0.030	0.03	0.62	0.71	<0.001	0.43	0.98	0.35	0.015	0.07	0.64	0.37	0.008	0.10	0.64
Age 18	0.28	0.046	0.00	0.55	0.02	0.911	-0.30	0.33	0.42	0.048	0.00	0.83	0.20	0.409	-0.28	0.68
Age 19	0.66	0.010	0.16	1.15	0.86	<0.001	0.52	1.20	0.86	0.001	0.33	1.38	0.38	0.141	-0.13	0.88
Age 20-29	0.41	0.003	0.14	0.69	0.48	<0.001	0.22	0.73	-0.07	0.687	-0.42	0.28	0.32	0.035	0.02	0.63
Age 30-39	0.55	0.005	0.17	0.94	0.93	<0.001	0.50	1.35	0.32	0.086	-0.05	0.69	-0.12	0.533	-0.49	0.26
Age 40-49	-0.08	0.745	-0.58	0.41	0.77	0.013	0.16	1.38	-0.06	0.837	-0.58	0.47	0.04	0.872	-0.49	0.57

B, regression coefficient; 95% CIs, 95% confidence intervals

Table 3. Regression coefficients for the association between intra-pair differences in birth weight and BMI (BMI units per kg birth weight) in monozygotic (MZ) and dizygotic (DZ) twins

	Males								Females							
	MZ				DZ				MZ				DZ			
	B	p-value	95% CIs		B	p-value	95% CIs		B	p-value	95% CIs		B	p-value	95% CIs	
Age 1	0.92	<0.001	0.84	0.99	0.88	<0.001	0.77	1.00	1.05	<0.001	0.98	1.13	0.97	<0.001	0.84	1.09
Age 2	0.84	<0.001	0.76	0.93	0.97	<0.001	0.84	1.09	0.97	<0.001	0.90	1.05	0.83	<0.001	0.69	0.96
Age 3	0.76	<0.001	0.69	0.83	0.78	<0.001	0.66	0.89	0.89	<0.001	0.82	0.97	0.80	<0.001	0.68	0.92
Age 4	0.71	<0.001	0.60	0.83	0.78	<0.001	0.61	0.96	0.87	<0.001	0.74	1.00	0.73	<0.001	0.53	0.94
Age 5	0.81	<0.001	0.69	0.92	0.91	<0.001	0.73	1.09	0.80	<0.001	0.69	0.92	0.90	<0.001	0.67	1.12
Age 6	0.79	<0.001	0.61	0.98	0.58	0.002	0.21	0.95	0.97	<0.001	0.74	1.20	1.01	<0.001	0.51	1.51
Age 7	0.70	<0.001	0.60	0.80	0.65	<0.001	0.48	0.83	0.98	<0.001	0.89	1.08	0.54	<0.001	0.35	0.73
Age 8	0.80	<0.001	0.66	0.94	0.89	<0.001	0.60	1.18	0.95	<0.001	0.81	1.09	1.07	<0.001	0.72	1.43
Age 9	0.72	<0.001	0.52	0.91	1.24	<0.001	0.83	1.65	1.08	<0.001	0.91	1.25	0.69	0.003	0.24	1.14
Age 10	0.83	<0.001	0.69	0.96	0.62	<0.001	0.36	0.88	1.06	<0.001	0.94	1.19	0.90	<0.001	0.60	1.21
Age 11	0.98	<0.001	0.80	1.15	0.79	<0.001	0.45	1.14	1.10	<0.001	0.94	1.26	0.98	<0.001	0.54	1.41
Age 12	0.83	<0.001	0.68	0.98	0.75	<0.001	0.44	1.06	0.97	<0.001	0.81	1.12	0.57	0.002	0.21	0.93
Age 13	1.05	<0.001	0.71	1.38	1.03	0.001	0.43	1.63	0.89	<0.001	0.53	1.25	0.63	0.087	-0.09	1.34
Age 14	0.87	<0.001	0.61	1.12	0.84	<0.001	0.39	1.29	0.71	<0.001	0.47	0.96	0.80	0.001	0.32	1.27
Age 15	0.78	<0.001	0.48	1.08	0.35	0.226	-0.22	0.92	1.05	<0.001	0.68	1.41	0.47	0.209	-0.27	1.21
Age 16	0.85	<0.001	0.53	1.16	1.05	<0.001	0.52	1.58	0.73	<0.001	0.46	0.99	0.86	0.002	0.33	1.39
Age 17	0.48	0.001	0.20	0.76	0.54	0.027	0.06	1.02	0.64	<0.001	0.37	0.90	0.75	0.002	0.27	1.22
Age 18	0.60	<0.001	0.37	0.83	0.22	0.367	-0.26	0.71	0.96	<0.001	0.60	1.33	0.88	0.011	0.20	1.55
Age 19	0.17	0.447	-0.27	0.61	0.84	0.012	0.18	1.50	0.75	<0.001	0.36	1.15	0.96	0.018	0.17	1.75
Age 20-29	0.41	0.002	0.16	0.67	0.38	0.079	-0.04	0.80	0.68	<0.001	0.35	1.02	0.48	0.071	-0.04	0.99
Age 30-39	0.27	0.239	-0.18	0.72	0.73	0.041	0.03	1.44	0.50	0.018	0.09	0.92	0.51	0.139	-0.17	1.20
Age 40-49	-0.15	0.615	-0.73	0.43	-0.20	0.740	-1.40	1.00	0.11	0.739	-0.54	0.76	-1.10	0.044	-2.18	-0.03

B, regression coefficient; 95% CIs, 95% confidence intervals

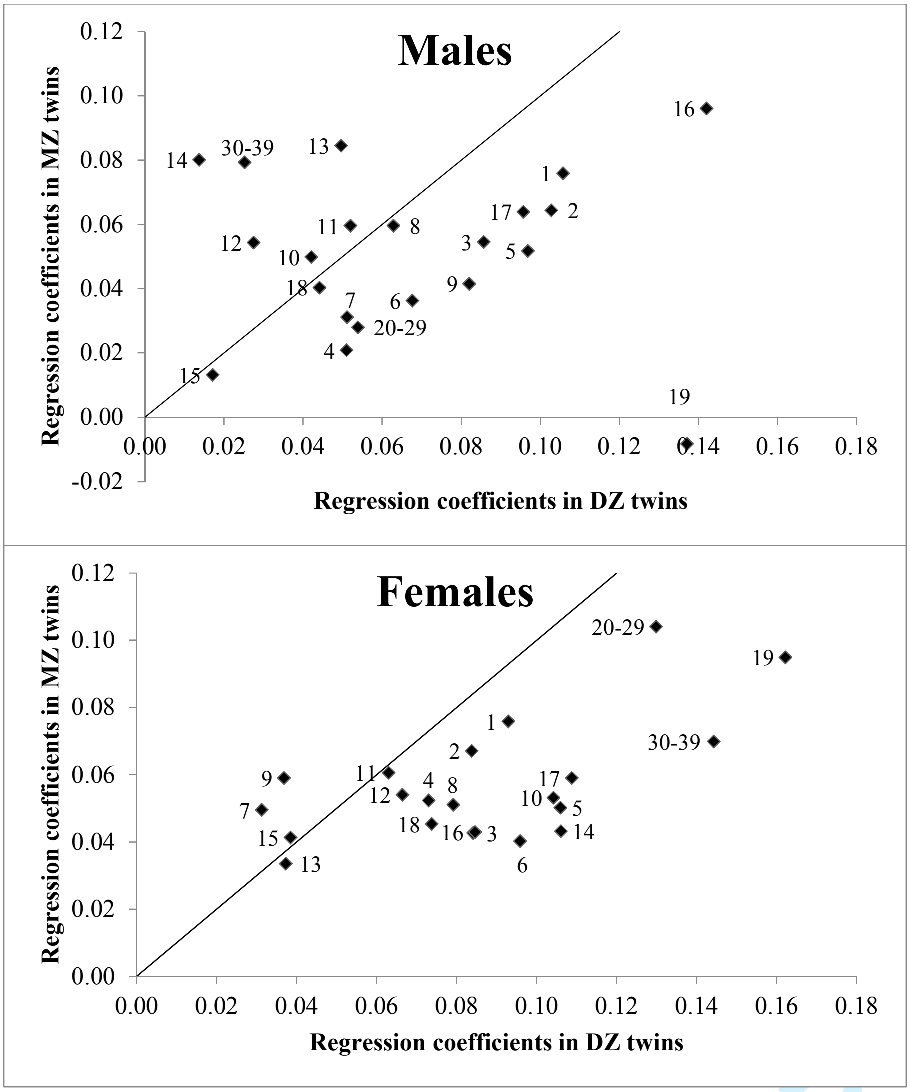

Figure 1- Scatter plots of the regression coefficients for the intra-pair differences in PI at birth and later BMI (BMI units per PI unit) in monozygotic (MZ) vs. dizygotic (DZ) twins. Plot labels indicate the specific age (years at BMI measurements) at which the associations were analyzed.