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Twin's birth-order differences in height and body mass index from birth to old age: a pooled study of 26 twin cohorts participated in the CODATwins project

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Abstract

We analyzed birth order differences in means and variances of height and body mass index (BMI) in monozygotic (MZ) and dizygotic (DZ) twins from infancy to old age. The data were derived from the international CODATwins database. The total number of height and BMI measures from 0.5 to 79.5 years of age was 397,466. As expected, first-born twins had greater birth weight than second-born twins. With respect to height, first-born twins were slightly taller than second-born twins in childhood. After adjusting the results for birth weight, the birth order differences decreased and were not statistically significant anymore. First-born twins had greater BMI than the second-born twins over childhood and adolescence. After adjusting the results for birth weight, birth order was still associated with BMI until 12 years of age. No interaction effect between birth order and zygosity was found. Only limited evidence was found that birth order influenced variances of height or BMI. The results were similar among boys and girls and also in MZ and DZ twins. Overall, the differences in height and BMI between first and second born twins were modest even in early childhood, while adjustment for birth weight reduced the birth order differences but did not remove them for BMI.

Keywords

birth order; BMI; height; zygosity

It is well known that growth patterns of twins during the third trimester of pregnancy differ from those of singletons. In addition to having two fetuses in *utero*, there are twin-specific factors, such as birth order (Glinianaia et al., 2000; Gielen, et al., 2007), zygosity (Loos, et al., 2005; Daw, et al., 1975; Buckler & Green, 2008) and chorionicity (Gruenwald, 1970; Ananth, et al., 1998; Naeye, et al., 1966; Bleker, et al., 1979; Gielen M, et al., 2009; van Beijsterveldt et al. 2015), which are associated with intrauterine twin growth. Previous studies of twins have reported that the second-born twin is, on average, lighter than the firstborn twin at birth (Glinianaia et al., 2000; Gielen, et al., 2007; van Baal and Boomsma, 1998). The factors determining birth order have a greater influence on birth weight than zygosity or chorionicity (Gielen, et al., 2007; Sheay, et al., 2004).

The lower birth weight for second-born twins could be due to the fact that first-born twins have higher placental weights and have more often a central insertion of the umbilical cord,

which are both positively correlated with birth weight. Possibly, first-born twins are also more optimally positioned with respect to nutrients intake (Gielen et al., 2006; Heinonen, et al, 1996). In addition, previous studies have shown that first-born twins are, on average, taller and heavier than second-born twins until adolescence (Silventoinen et al., 2007; Pietiläinen et al., 2002). Second-born twins have also higher morbidity and mortality (Armson, et al., 2006; Smith, et al., 2007; Shinwell et al., 2004; Luo, et al., 2014).

The persistence of the birth-order association suggests that prenatal factors can have longlasting effects on body size. However, it is not known how these associations may change over the life course. Studies on age-dependent birth order differences in height and body mass index (BMI) are scarce, and small sample sizes make comparisons of the existing results difficult. Further, it is not known whether the factors behind birth order differences in height and BMI also induce variance differences. In this study, we aim to analyze birth-order differences in means and variances of height and BMI among MZ and DZ twins from infancy to old age and to test whether they can be explained by differences in birth weight. The data were derived from the large international CODATwins database, which was intended to collect together height and weight measurements from all twin cohorts in the world.

Data and methods

In the CODATwins database (Silventoinen, et al., 2015), there are 960,859 height and weight measures from twins at ages ranging from 0.5 to 103 years. Information on birth order, height and weight measures were self-reported (67%), parentally reported (19%), or based on measures by nurses and clinicians (14%). In this study, we included the following cohorts with information on birth order: Australian Twin Registry, Boston University Twin Project, Carolina African American Twin Study of Aging, FinnTwin12, FinnTwin16, Gemini Study, Guangzhou Twin Eye Study, Guinea-Bissau Twin Study, Hungarian Twin Registry, Japanese Twin Cohort, Korean Twin-Family Register, Longitudinal Israeli Study of Twins, Michigan Twins Study, Murcia Twin Registry, Norwegian Twin Registry, Peri/Postnatal Epigenetic Twins Study, Qingdao Twin Registry of Children, Quebec Newborn Twin Study, Queensland Twin Register, Swedish Young Male Twins Study of Adults, Swedish Young Male Twins Study of Children, South Korea Twin Registry, Swedish Twin Cohorts, Twins Early Developmental Study, West Japan Twins and Higher Order Multiple Births Registry and Young Netherlands Twin Registry. Height and weight measurement protocols, sample frames and other basic information of these cohorts have been described elsewhere (Silventoinen, et al., 2015). Age was classified to 1-year age groups from age 1 to 19 years (e.g., age 1 refers to 0.5–1.5 years range), and 10-year age groups from age 20 to 79 years (e.g., 20–29, ..., and age 70–79 years). Since the number of twin participants at 80 years of age or older was small, this group was excluded from the analyses.

In total, we had 429,587 height and BMI measurements at ages 0.5–79.5 years with information on birth order. Additionally we had information on birth weight from 107,782 and birth length from 54,941 twin individuals. BMI was calculated as weight (kg)/square of height (m²). Outliers were checked by visual inspection of histograms for each age and sex group. They were removed to obtain an approximately normal distribution of height,

whereas the distribution of BMI was allowed to be positively skewed. The number of observations removed (n=1134) represented less than 0.3% of the whole database. We also excluded extreme birth length (<25cm or >65 cm) or birth weight (<500g or >6000g) values. For the purpose of this study, we restricted the analyses to one observation per individual in each age group. The total number of height and BMI measures in this study was 397,466; in 307,606 of these cases we had information also on birth weight.

Equality of mean values between first- and second- born twins by zygosity, age group and sex was tested using fixed effects regression analysis corrected for clustering of twin pairs. Equality of variances was tested using the Levene's clustered test based on the 10% trimmed mean (Iachine et al. 2010). This clustered version of the Levene's test is robust under the non-normality of outcomes. The interaction effects between zygosity and birth order were tested using Bonferroni correction of multiple testing with alpha level 0.0005 (0.05/100 tests). Percentage difference (%) between first- and second-born twins in mean values [(first born mean-second born mean) / second born mean] * 100 and standard deviations (SD) [(first born SD-second born SD) / second born SD] * 100 of height and BMI were calculated by sex. We also tested how the adjustment for birth weight affected the birth order difference on height and BMI in the cohorts having this information available using the fixed effects multiple regression model in each age groups. Statistical analyses were conducted using the Stata statistical software package (version 12.0; StataCorp, College Station, Texas, USA).

The pooled analysis was approved by the ethical board of the Department of Public Health, University of Helsinki. The data collections procedures of participating twin cohorts were approved by local ethical boards following the regulation in each country. Only anonymized data were delivered to the data management center at University of Helsinki.

Results

Table 1 provides the mean birth length and birth weight according to birth order, sex and zygosity. In MZ twins, the first-born male twins had greater length than the second-born male twins. However, in DZ twins, average birth length was not significantly different between the first-born and the second-born twins. In MZ and DZ twins, the first-born twins had greater birth weight than the second-born twins. The SDs of birth weight in the first-born and the second-born twins were significantly different except in MZ boys.

Descriptive statistics by birth order, age, and sex in MZ and DZ twins are presented in Table 2 and 3 for height, respectively. Sample size for each birth order, age, and sex group ranged between 421 and 5,407 individuals from age 1 through 19 years, and between 117 and 4,398 individuals in adulthood (20 years). The 6 and 70-year age groups in MZ twins had the smallest sample sizes. In MZ twins, significantly taller height in the first-born than in the second-born twins were observed at the age of one, three, five, eight and 10 years in men and from the age of one to three, seven and 12 years in women (Table 2). However, in DZ twins, average height was not significantly different between the first-born and the second-born twins (Table 3). The SDs of height in the first-born and the second-born twins in MZ

and DZ twin were not significantly different in the majority of age groups. Results were similar in men and women.

Table 4 and 5 shows the respective results for BMI. The sample sizes are same as for height. In MZ twins, the first-born twins had greater BMI than the second-born twins except the 18 and 50-year age groups in men, and the 40–49 year age group in women. Statistical significance was attained in the majority of age groups until 12 years age groups (Table 4). In DZ twins, first-borns had greater BMI than the second-born twins except the 14 and 60–69 years old men. The differences were also statistically significant particularly until 5 years of age. The SDs of BMI in the first-born and the second-born twins in MZ twins were not significantly different. However, the SDs of BMI in the first-born and the second-born twins in DZ twins were significantly different at the age of one, three, 10, 15, 17, and 18 years in men, and the age of 16, 18, and 20–29 years in women (Table 5).

Because the interaction effects between birth order and zygosity were not statistically significant after Bonferroni correction for height or BMI (nominal p-values 0.047–0.008), data from MZ and DZ twins were combined in the further analyses. Figure 1 illustrates the percentage difference (%) in the mean and SD of height between the first-born and the second-born twins in men and women in the pooled data of MZ and DZ twins. Figure 2 presents the same results for BMI. Both for height and BMI, the first-born twins showed almost always higher mean values than the second-born twins. The mean differences in height between the first-born and the second-born twins ranged from -0.1% to 0.3% in men (at the age of 15 years) and from -0.3% to 0.4% in women (at the 15 and 70-year age groups). The first-born male twins presented up to 1.4% greater BMI than the second-born male twins until 17 years of age and decreased with age in adulthood. The mean differences between the first-born and the second-born twins ranged from 0.2% to 1.4% in women (at the age of 15 years and 15 years and 18 years). For SD the differences were small and did not show any systematic pattern varying from negative to positive.

Table 6 shows the results of fixed effects regression analysis of height and BMI at each age in the sub-cohort with information on birth weight. Adjustment for birth weight decreased the birth order differences in height and BMI. After adjusting for birth weight, birth order was associated with height at the age of one, three, five, seven and 10 years in men, whereas birth order was not associated with height in women. Moreover, as adjusting for birth weight, birth order was associated with BMI from the age of one to five, seven, 10, 11 and 12 years in men, and from the age of one to five, seven, 10 and 12 years in women.

Discussion

The CODATwins study established database with data on body size from twin cohorts in different countries from infancy to old age. Previous studies in twins have reported that the second-born twin was lighter than the first-born twin at birth (Glinianaia et al., 2000; Gielen M, et al., 2007) and our results from this very large international database are consistent with these studies. First-born twins were slightly taller than second-born twins in MZ pairs at some ages until 12 years of age. After adjustment for birth weight, birth order was associated with height in males only at some ages until 10 years of age. We did not find any

strong evidence that birth order differences varied according to zygosity since the interaction effects between zygosity and birth order were not statistically significant after Bonferroni correction. These results suggest that birth order has a slight influence on height in twins during childhood mainly explained by birth weight.

Meanwhile, the current study revealed birth order differences in mean BMI until 12 years of age in MZ pairs, and in mean values of BMI until 5 years of age in DZ twin pairs. These birth order differences in mean values of BMI were generally modest but still statistically significant. Adjustment for birth weight reduced these differences, but a significant association of birth order with BMI remained until 12 years of age. Jelenkovic et al. (2015) reported that DZ twins are consistently taller than MZ twins, but mean BMI is not significantly different between MZ and DZ twins at young ages. Based on our study, birth order difference seems to associate more strongly with BMI than zygosity difference. For SDs of height and BMI the results were not statistically significant and did not show any systematic pattern either. Thus, it seems that the factors behind the mean differences between first-born and second-born twins were not associated with variances.

According to the Developmental Origins of Health and Disease hypothesis, birth weight is associated with disease risk later in life and is a determinant of adult health (Barker, 1998; Brodsky and Christou, 2004). This appears more salient for twins, who are born earlier and weigh less as compared to singletons (Loos, et al., 2005). However, it is indicated that growth of twins is not equal to growth of singletons after 29 weeks of gestation (Loos, et al., 2005), and the optimal intrauterine growth and lowest morbidity is achieved earlier in gestation for twins than for singletons (Luke, et al., 1993; Soucie, et al., 2006). In addition, previous studies in twins have reported that the second-born twin was lighter than the firstborn twin at birth (Glinianaia et al., 2000; Gielen M, et al., 2007). Moreover, low birth weight predicts lower adult BMI in twins (Johansson & Rasmussen, 2001; Pietiläinen et al., 2001). Whitfield et al. (2001) reported that the correlation between birth weight and BMI in adulthood was positive, and the correlation is due to genetic factors and non-shared environmental factors. Gielen et al. (2007) indicated that the factors determining birth order, which is one of twin-specific factors, have a greater influence on birth weight than zygosity, chorionicity and fusion of the placentas. However it was not known how the birth order differences change over the life course. We found residual differences in BMI between the first-born and the second-born twins until 12 years of age in boys and girls after adjusting for birth weight. Our findings are in accordance with a previous Dutch study showing that the first-born twins were slightly heavier form three to 12 years of age (Silventoinen et al., 2007).

The reasons for the birth order difference in BMI in twins are not clear. It is possible that vascular and placental circumstances are important. Twins offer an opportunity to distinguish between maternal factors (smoking, alcohol, and total placental weight) affecting both twins and factors unique to each twin, such as individual placental weight and site of the insertion of the umbilical cord. Gielen et al. (2007) reported that the individual placental weight has a stronger association with birth weight than the total placental weight. This suggests that the unique factors are more important than the maternal factors. While placental factors appear to be important, consideration of chorionicity is also necessary.

There are three types of MZ twins based on chorionicity. MZ twins can either share one chorion and one amnion, each twin can have own amnion, or MZ twins can, like all DZ twins, each have their own chorion and amnion. Sharing the same chorion could create either a more similar or a more dissimilar prenatal environment (van Beijsterveldt et al. 2015). Kent et al. (2011) reported that monochorionic twins had higher rates of marginal and velamentous placental cord insertion, and noncentral cord insertion contributed to birth weight discordance in monochorionic twin pregnancies. Antoniou et al. (2011), who examine the genetic and environmental etiology of the umbilical cord in a large population of twins, indicated that partly genetic and unique environmental factors influence a number of the morphological characteristics of the overall umbilical cord development. Thus, even in the very early stages of life, twins can experience unique environmental influences (Antoniou et al., 2011). Unfortunately, our database does not have information on chorionicity, which is gathered reliably in few cohorts.

The birth order of twins is determined in early pregnancy, and the first twin at the beginning of pregnancy intrinsically remains in this position (Bronshtein et al., 1998). However, the relationship between the amniotic sac and the cervix, which remains relatively constant throughout gestation, may change near term or during labor in about 10% of twin pairs discordant for sex leading to a change in the anticipated twin order (Bronshtein et al., 1998). Since we did not find the interaction effects between birth order and zygosity, potential prenatal environmental differences between MZ and DZ twins do not seem to modify the birth order differences in BMI or height. However, we observed that birth order effects on BMI appear to last longer in MZ twins than in DZ twins, which may reflect the differences in chorionicity. The differences of intrauterine environment between the first-born and the second-born twins need more detailed research.

Birth order differences have been analyzed previously for perinatal and neonatal outcomes. Previous studies (Smith, et al., 2002; Sheay, et al., 2004; Smith, et al., 2005; Armson, et al., 2006; Smith, et al., 2007) have reported an increased risk of perinatal death of second-born compared with first-born twins. It has been proposed that this may be mainly a problem of more stillbirths in the second twins (Smith, et al., 2002). Luo et al. (2014) reported that perinatal mortality risk differences in second vs first twins depended on their relative birth size, and vaginal delivery at term was associated with a substantially greater risk of perinatal mortality in second twins. These early deaths would have resulted in such pairs not being included in our database.

With regard to neonatal morbidity, the studies of Hacking et al. (2001) and Donovan et al. (1998) both found that second-born twins have increased risk for respiratory distress syndrome. Shinwell et al. (2004) reported that very low birthweight (< 1500g) second twins were at increased risk for acute and chronic lung disease and neonatal mortality, irrespective of mode of delivery. Moreover, Marttila et al. (2004), who analyzed respiratory distress syndrome by gestational age in singletons, first-born and second-born twins, indicated that first-born twins had a significantly lower incidence of respiratory distress syndrome compared with second-born twins and singletons, except at less than 28 weeks of gestation. By being delivered by the same mother at the same time and gestational age, these factors cannot influence postnatal difference in growth, perinatal mortality, and neonatal morbidity

risk between the second-born and the first-born twins. So, any such differences are likely to be attributable to birthweight, fetal growth, and intrauterine environment. Our study suggests that the impact of early morbidity, to the degree that it is indexed by birth order, is limited in time to early childhood, and more so on BMI than height.

The major strength of the present study is the large sample size of our international database of twin cohorts with height and weight measures covering almost the whole lifespan. However, a limitation is that countries or geographical regions are not equally represented, and the database is heavily weighted toward Caucasian populations. Accordingly, we could not study in detail possible ethnic differences in birth order differences. In addition, the number of twin participants in the oldest age groups is small. Multiple testing may have resulted in false-positive differences between the first-born and the second-born twins. However, mean values showed a consistent pattern across age and sex groups in both MZ and DZ twins, which provides considerable robustness to the results. Finally a large majority of height, weight and birth order measures are self- or maternally reported. This probably increases random error which lead to decreasing effect sizes. Our results may thus be underestimations of the real birth order differences.

In conclusion, the first-born twins had greater BMI and are slightly taller than the secondborn twins. Birth order showed a significant association with BMI before 12 year of age. However, in generally, the differences in BMI and height between first-born and secondborn twins were very modest even in early childhood. Adjustment for birth weight reduced the birth order differences but did not fully remove them for BMI. Evidence that birth order affects variances of height and BMI was limited.

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Figure 1.

Mean and standard deviation differences (%) in height between first- and second- born twins across ages.



Figure 2.

Mean and standard deviation differences (%) in BMI between first- and second- born twins across ages.

Number of twin individuals, mean and standard deviation of birth length (cm) and birth weight (kg) by birth order, sex and zygosity

					DUYS					GITIS		
		Birth order	Z	Mean	p value ^a	SD	<i>p</i> value ^b	Z	Mean	p value ^a	SD	<i>p</i> value ^b
	- H 1	1	5304	47.0	0000	3.58	100 0	5101	46.3		3.58	0.005
	n lengun	2	5293	46.8	700.0	3.69	100.0	5070	46.2	761.0	3.64	cøn.n
INIONOZYGOUIC IWINS	(1	9617	2.54	100.01	0.56		10383	2.43	100.01	0.54	100.00
	n weigni (kg)	2	9524	2.51	100.0>	0.57	/00/0	10330	2.39	100.0>	0.55	100.0>
	- 	1	9160	47.4		3.55	00000	7967	46.8	101.0	3.60	0100
	n lengu	2	8914	47.4	107.0	3.65	600.0	8132	46.7	161.0	3.64	0.010
Dizygouc twins		1	17468	2.63		0.57	2000	16562	2.53		0.55	100.0
	n weigni (kg)	2	17098	2.58	100.0>	0.58	c00.0	16800	2.47	100.0>	0.56	100.0

p value^{a_i}. p value for equality of means, p value^b: p value for equality of variances, SD: standard deviation.

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Table 2

Number of twin individuals, mean and standard deviation of height (cm) by birth order, age and sex in monozygotic twins

				Men					Women		
	Birth order	Z	Mean	<i>p</i> value ^a	SD	<i>p</i> value ^b	N	Mean	<i>p</i> value ^a	SD	<i>p</i> value ^b
-	1	2843	73.6	0000	4.54		2994	72.4	100	4.55	
Age I	2	2838	73.5	670.0	4.59	0/1/0	2991	72.3	0.014	4.55	0.207
	1	2310	86.5		4.41	100	2339	85.4	0000	4.42	
Age 2	2	2293	86.4	171.0	4.46	0.047	2323	85.3	070.0	4.44	/06.0
с •	1	2830	95.8	7700	4.45	1200	3140	94.9	0000	4.39	0.775
Age 3	2	2834	95.7	0.044	4.47	0.204	3125	94.8	0.002	4.38	
	1	1600	102.1	101.0	5.17	0.015	1594	101.0		5.13	0110
Age 4	2	1588	101.9	181.0	5.33	C+0.0	1595	100.9	0110	5.29	0.110
	1	1272	110.8	9100	5.91		1341	110.2	0000	6.16	1070
C age	2	1266	110.7	\$10°0	5.93	0/70	1328	110.1	667.0	6.06	0.490
	1	528	114.1		6.45	1000	427	112.9	1000	5.66	0100
Age 0	2	512	113.7	617.0	6.40	000.0	421	112.9	0.834	5.88	0.180
	1	2345	123.6	2100	6.62	1010	2540	122.9		6.49	6 E O O
Age /	2	2330	123.5	0.210	6.72	461.0	2536	122.8	070.0	6.53	c/6.0
0 4	1	1057	127.6	0.016	6.35		1020	127.0		6.42	0000
Ageo	2	1042	127.4	010.0	6.23	776.0	1021	126.8	0.0.0	6.56	607.0
0	1	1042	133.0	C7 - C	6.97	0 500	1005	132.0	0 133	6.93	0 500
Age 7	2	<i>L</i> 66	132.8	0.140	7.04	600.0	986	131.8	767.0	6.92	060.0
	1	1988	140.0	1100	7.18		2088	139.8	211.0	7.41	0 100
Age 10	2	1924	139.9	0.044	7.19	161.0	2048	139.7	C11.0	7.47	661.0
A == 11	1	1530	143.4		7.15	0200	1588	144.2	0.100	7.30	0.002
Age 11	2	1470	143.3	0.470	7.12	606.0	1530	144.0	0.180	7.48	c00.0
	1	2032	151.4	1010	8.30	100 0	2127	152.3	2000	8.01	0.000
Age 12	2	1955	151.3	404.0	8.24	0.004	2053	152.1	000.0	8.18	060.0
	1	692	157.9	202.0	9.30		642	157.3	0,000	7.40	0.404
CI age	2	620	157.6	C60.0	9.39	100.0	591	157.2	607.0	7.54	0.494
Age 14	1	1328	165.4	0.815	8.95	0.808	1497	161.8	0.441	6.68	0.066

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	Birth order	Z	Mean	<i>p</i> value ^a	SD	<i>p</i> value ^b	Z	Mean	<i>p</i> value ^a	SD	<i>p</i> value ^b
	2	1280	165.4		9.09		1468	161.8		6.85	
2 T - T	1	658	171.5	<i>cc1</i> 0	8.68	870.0	639	164.5	2120	7.32	00000
ci əğr	2	639	171.7	0.450	8.70	0.908	606	165.1	C10.U	7.00	670.0
21 V	1	1074	175.5		7.61	0 516	1311	164.4	0000	6.56	
Age 10	2	1028	175.5	16/.0	7.56	040.0	1257	164.5	066.0	6.34	/00/0
	1	1100	177.7	210.0	7.29	0,00	1411	165.6		6.62	102.0
Age 1/	2	1074	177.8	C15.0	7.47	0.008	1388	165.8	0./10	6.59	100.0
A 10	1	1253	178.9		7.05	200.0	826	166.1	0.450	6.48	0.405
Age 10	2	1253	178.9	0.201	6.89	C00.0	812	166.1	0.4.00	6.64	0.44.0
01 V	1	639	179.2	2720	7.04	0200	717	166.1	0.055	6.98	0200
Age 19	2	607	179.3	C+C.U	6.85	007.0	702	165.9	CC7.0	6.83	617.0
	1	2890	179.2		6.90		3488	164.5	100 0	6.50	0000
Age 20–29	2	2878	179.0	/11.0	6.98	0.412	3478	164.6	0.881	6.47	668.0
A 20. 20	1	2305	178.1	0360	7.04	1010	3378	164.0	660 V	6.67	0 551
Age JU-29	2	2290	177.9	000.0	6.92	0.494	3349	164.0	CC7.U	6.62	400.0
A 40 40	1	1420	177.2	200.0	7.04	0200	1886	163.2	1000	6.65	2010
Age 40-49	2	1355	177.1	C67.0	7.03	0/6-0	1844	163.1	0.924	6.58	004.0
A ED ED	1	1038	176.4	2000	7.02	191.0	1601	162.5	612.0	6.50	
Age-uc age	2	1029	176.3	CU0.U	7.22	101.0	1609	162.4	C10.0	6.70	0.047
	1	506	174.9	786.0	6.40	200.0	880	161.7	022.0	6.30	
Age 00-09	2	494	174.4	0.380	6.99	0.000	878	161.9	0.000	6.47	167.0
	1	126	173.7	C17 0	7.09	0100	273	161.3	0100	6.91	
Age /0-19	2	117	173.1	0.412	7.48	661.0	268	160.8	0/5.0	6.61	0.102
<i>p</i> value ^a : <i>p</i> val	lue for equality c	of means	s, <i>p</i> value ^l	b: <i>p</i> value fo	or equali	ity of varianc	ces, SD:	standard	deviation.		

Table 3

Number of twin individuals, mean and standard deviation of height (cm) by birth order, age and sex in dizygotic twins

				Men					Women		
	Birth order	N	Mean	p value ^a	SD	<i>p</i> value ^b	N	Mean	<i>p</i> value ^a	SD	<i>p</i> value ^b
, i i	1	5088	74.8	0.051	4.11	102.0	4759	73.4	C O	4.06	0.750
Age I	2	4962	74.6	100.0	4.11	166.0	4821	73.2	c11.0	4.14	600.U
	1	4184	87.4	0100	4.22	370.0	3815	86.3	171 0	4.34	0100
Age 2	2	4102	87.2	0.040.0	4.28	C07.U	3871	86.1	0.141	4.27	0.109
	1	5407	96.6	1000	4.43		5085	92.6	0150	4.55	
Age 5	2	5266	96.4	0.0/4	4.42	0.822	5208	95.4	661.0	4.62	107.0
	1	2993	102.4	CE0 0	5.27		2818	101.3	14 17 0	5.21	0110
Age 4	2	2954	102.5	c/0.0	5.31	0.8/2	2848	101.1	0./40	5.25	611.0
	1	2349	112.0		6.07	000	2099	111.1	C7 - C	6.37	
Age J	2	2259	111.5	0.120	6.13	0.478	2189	110.7	0.140	6.41	700.0
	1	583	114.5	0100	6.88		455	114.2		7.55	0100
Age o	2	552	114.8	0.819	7.15	116.0	469	113.6	107.0	7.39	0.180
	1	3986	124.8		6.59	2200	3877	123.8	0200	6.71	0.120
Age /	2	3981	124.5	767.0	6.72	0.200	3864	123.8	600.0	6.65	662.0
0 v	1	1478	129.2	0 500	6.42	0 154	1279	128.3	010	6.82	102.0
Age o	2	1433	128.9	ccc.0	6.65	401.0	1318	127.9	761.0	6.87	0.721
0 4	1	1445	134.5	0 664	7.30	120.0	1354	133.9	100.0	7.25	000
Age 9	2	1449	134.2	0.004	7.14	0.2/1	1316	133.9	0.994	7.38	000.0
01 <u>00</u> 4	1	3171	141.8	200.0	7.02		2994	141.2	0230	7.35	0 5 2 0
Age 10	2	3148	141.4	160.0	7.21	077.0	2973	141.0	0/0.0	7.39	666.0
A 11	1	2385	145.2	001.0	7.23	0 505	2146	145.1	0.401	TT.T	0200
Age 11	2	2288	144.6	061.0	7.41	c0c.0	2153	145.4	160.0	7.92	617.0
C1 V	1	3152	152.5	0.045	7.82	L17 0	3031	153.3	0.012	8.36	777 0
Age 12	2	3021	152.3	0.74.0	7.92	/10.0	3048	153.3	C10.0	8.24	0.444
C1 V	1	1035	158.8	200 0	8.77	0.051	868	158.4	0000	7.80	1000
CI age	2	965	158.7	0.00/	9.36	100.0	896	158.7	006.0	7.98	0.904
Age 14	1	2353	165.6	0.888	8.94	0.031	2332	162.8	0.358	6.74	0.529

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Women

Men

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	Birth order	Z	Mean	<i>p</i> value ^a	SD	<i>p</i> value ^b	Z	Mean	<i>p</i> value ^a	SD	<i>p</i> value ^b
	2	2266	165.8		8.62		2370	162.5		6.87	
4 - 1 - 1	1	1143	172.2	010.0	8.84	0022 0	1042	165.4		7.18	0 7 5 0
ci əğr	2	1078	172.3	0.0/0	8.87	671.0	1013	165.7	140.0	7.03	000.0
21 V	1	1990	176.0	0.055	7.52		2086	165.4	0.050	6.61	5010
Age 10	2	1940	175.8	CC0.0	7.46	170.0	2090	165.5	706.0	6.43	0.1/4
	1	2159	178.5		7.30	211 0	2230	166.4	0 7 5 0	6.32	2000
Age 1/	2	2092	178.0	0.317	7.16	C14.0	2224	166.4	80/.0	6.70	C5U.U
A 10	1	1680	179.4	777 O	6.95	0 572	1281	166.8	1010	6.77	
Age 10	2	1614	179.2	0.444	6.91	c/c.n	1320	166.3	0.404	6.49	07.0
01 V	1	1044	180.4		6.72	0200	1099	167.2	0000	6.60	101.0
Age 19	2	1049	179.8	C/6.0	6.86	200.0	1047	167.3	700.0	6.47	/01.0
	1	4036	179.9	101.0	6.69		4398	165.8	2200	6.56	
Age 20–29	2	4121	179.4	161.0	6.74	0.024	4270	165.5	CC7.0	6.50	/01.0
A 20. 20	1	3221	179.2	7270	6.82	00000	4120	165.2	0 504	6.58	0200
Age JU-JY	2	3351	178.9	0.0/4	6.64	607.0	3887	165.0	460.0	6.43	600.0
A 40 40	1	2403	178.9		6.69		2877	164.6	2000	6.36	120.0
Age 40-49	2	2411	178.9	16/.0	6.70	<i>C11.</i> 0	2775	164.9	000.0	6.33	106.0
A ED ED	1	2678	178.0	0 500	6.73	190.0	3261	164.1	000 0	6.20	190.0
ec-uc age	2	2634	177.7	760.0	6.56	107.0	3086	164.3	0.696	6.05	10.00
	1	1265	175.9		6.73		1560	162.9	C10 0	6.13	0000
Age 00-09	2	1276	175.8	176.0	6.85	/ 00.0	1532	162.9	C10.U	6.27	0.200
	1	310	175.3	2020	6.53		435	162.1	0 512	6.78	1200
Age 10-19	2	329	175.0	000.0	6.82	107.0	390	161.4	C+C.D	6.05	0.004
<i>p</i> value ^a : <i>p</i> val	lue for equality o	of means	s, <i>p</i> value ^l	: <i>p</i> value fo	r equali	ity of varian	ces, SD:	standard	deviation.		

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Table 4

Number of twin individuals, mean and standard deviation of birth weight (kg) and BMI (kg/m²) by birth order, age and sex in monozygotic twins

				Men					Women		
	Birth order	Z	Mean	p value ^a	SD	<i>p</i> value ^b	Z	Mean	<i>p</i> value ^a	SD	<i>p</i> value ^b
-	1	2843	17.21	100 0	1.41	001.0	2994	16.84	100 01	1.42	u U U U
Age I	2	2838	17.11	100.0>	1.42	0.798	2991	16.74	100.0>	1.42	cc/.0
	1	2310	16.62	100.01	1.40	100.0	2339	16.17	100.02	1.38	0.015
Age 2	2	2293	16.51	100.0>	1.39	176.0	2323	16.04	100.0>	1.38	C16.0
C V	1	2830	16.02	100.07	1.41		3140	15.68	100.02	1.50	L100
Age J	2	2834	15.88	100.0>	1.39	0/7.0	3125	15.58	100.0>	1.47	0.217
	1	1600	15.90	<i></i> 0	1.78	2020	1594	15.71	100.0	2.01	0.755
Age 4	2	1588	15.84	CZU.U	1.81	000.0	1595	15.59	100.0	1.98	ccc.0
2 V	1	1272	15.34	100.01	1.54	122 0	1341	15.13	100.02	1.64	0200
Age J	2	1266	15.20	100.0>	1.51	1/0.0	1328	15.01	100.0>	1.64	000.0
A 200 K	1	528	15.54	2700	1.77	301.0	427	15.25	100.0	1.76	301.0
Age 0	2	512	15.48	C07.U	1.77	cc/.0	421	15.14	0.084	1.74	cc/.0
	1	2345	15.40		1.69	0110	2540	15.44	100.02	1.93	100
Age /	2	2330	15.31	700.0	1.71	0.419	2536	15.31	100.0>	1.93	410.0
0 00 V	1	1057	15.64	2000	1.72	0.321	1020	15.65	100.0/	1.97	0100
Age o	2	1042	15.54	070.0	1.67	100.0	1021	15.50	100.0>	1.93	0.240
0 V	1	1042	16.29	L20 0	2.10	0100	1005	16.33	0.150	2.38	0 556
Age 9	2	7997	16.23	100.0	2.17	010.0	986	16.22	761.0	2.39	0000
A 20 10	1	1988	16.64	2000	2.30	CF0 0	2088	16.67	100.02	2.45	0 500
Age 10	2	1924	16.54	c00.0	2.17	0.042	2048	16.56	100.0>	2.40	700.0
۸ ۵۰۰ 11	1	1530	17.32	100.07	2.56	100.0	1588	17.37	2000	2.72	7200
Age 11	2	1470	17.10		2.44	0.004	1530	17.30	CC0.0	2.80	+/c.0
CT ~~ A	1	2032	17.87	100.07	2.72	201.0	2127	17.92	100.02	2.74	0000
Age 12	2	1955	17.72	100.0>	2.67	161.0	2053	17.77	100.0>	2.71	666.0
C1 V	1	692	18.45		2.89	0.051	642	18.94	100.0	3.19	0000
CI 284	2	620	18.30	760.0	2.79	100.0	591	18.82	0.094	3.27	coc.0
Age 14	1	1328	19.28	0.132	2.86	0.422	1497	19.67	0.007	3.02	0.956

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Women

Men

Author Manuscript

	Birth order	N	Mean	<i>p</i> value ^a	SD	<i>p</i> value ^b	Z	Mean	<i>p</i> value ^a	SD	<i>p</i> value ^b
	2	1280	19.23		2.82		1468	19.59		3.01	
21 - V	1	658	19.64	101.0	2.92	217 0	639	19.95	010	3.20	0 500
ci əğr	2	639	19.59	0.194	2.93	0.410	606	19.80	0.108	3.15	cuc.u
21 V	1	1074	20.68	961.0	2.99	201.0	1311	20.64	0000	2.98	
Age 10	2	1028	20.55	861.0	2.87	0.100	1257	20.57	860.0	2.95	7/1.0
	1	1100	20.94		2.72	0.950	1411	20.73		2.87	
Age 1/	2	1074	20.88	100.0	2.68	000.0	1388	20.60	0.112	2.85	786.0
A 10	1	1253	21.32	027.0	2.57	0000	826	21.00	2000	2.82	021.0
Age 10	2	1253	21.33	0.479	2.49	060.0	812	20.81	0.200	2.74	0/1/0
01 V	1	639	21.66	0 512	2.51	0000	717	21.00		2.76	00000
Age 19	2	607	21.59	c1c.0	2.59	006.0	702	20.95	760.0	2.83	000-0
	1	2890	23.09	0100	2.96	100	3488	21.85	0100	3.69	0100
Age 20–29	2	2878	22.94	010.0	2.97	400.0	3478	21.73	010.0	3.57	0.240
A 20. 20	1	2305	24.65	0.461	3.39	2100	3378	22.86		4.03	
Age Juc age	2	2290	24.52	0.401	3.30	C17.0	3349	22.85	0./12	4.07	600.0
V 10 10	1	1420	25.44		3.59	CF0 0	1886	23.75		4.20	007 0
Age 40-49	2	1355	25.25	/61.0	3.33	0.042	1844	23.77	0/0/0	4.33	0.420
V ~~ EV EV	1	1038	25.43	0770	3.21	0 577	1601	24.65	FOC O	4.30	0700
ec-uc age	2	1029	25.56	0.000	3.18	C7C.U	1609	24.55	400.0	4.13	000.0
	1	506	25.59	0.960	3.20	7700	880	25.24	010	4.26	0100
Age 00-09	2	494	25.73	700.0	3.28	0.204	878	25.02	0.108	4.17	210.0
	1	126	24.74	2000	3.20	0 537	273	24.95	2120	4.30	0.112
Age 10-19	2	117	24.90	C76.0	3.27	766.0	268	24.58	C/0.0	3.71	C17.0
<i>p</i> value ^a : <i>p</i> val	lue for equality o	of means	s, <i>p</i> value ^l	: <i>p</i> value fo	r equali	ty of varianc	ces, SD:	standard	deviation.		

Table 5

Number of twin individuals, mean and standard deviation of birth weight (kg) and BMI (kg/m²) by birth order, age and sex in dizygotic twins

Yokoyama et al.

				Men					Women		
	Birth order	Z	Mean	<i>p</i> value ^a	SD	<i>p</i> value ^b	Z	Mean	<i>p</i> value ^a	SD	<i>p</i> value ^b
	1	5088	17.20	100.02	1.39	2000	4759	16.81	0.001	1.35	0020
Age I	2	4962	17.04	100.0>	1.34	100.0	4821	16.67	0.004	1.35	07/70
	1	4184	16.57	100.02	1.41		3815	16.20	200.0	1.38	CCF 0
Age 2	2	4102	16.40	100.0>	1.40	006.0	3871	16.04	0,000	1.39	0.420
	1	5407	16.03	0000	1.54	0000	5085	15.74	0100	1.53	1120
Age 5	2	5266	15.84	c00.0	1.47	c00.0	5208	15.63	010.0	1.57	410.0
4 	1	2993	16.01	L 0 0	1.87	000 0	2818	15.81	1000	1.89	0.657
Age 4	2	2954	15.82	0.04 /	1.89	0.000	2848	15.68	0.044	1.93	000.0
2000	1	2349	15.33	0000	1.59	200 0	2099	15.24	0,010	1.68	0.105
Age J	2	2259	15.17	070.0	1.60	0.000	2189	15.09	0.049	1.71	C61.0
7 V	1	583	15.65	270 0	2.02	0.152	455	15.65	1510	2.29	7630
Age o	2	552	15.59	0.00/	2.21	cc1.0	469	15.40	0.104	2.22	4/C.U
	1	3986	15.50	0.010	1.85		3877	15.59	0 170	2.09	111
Age /	2	3981	15.35	0.010	1.92	110.0	3864	15.41	0.170	2.03	0.144
0 00 0	1	1478	15.75	200	2.09	5070	1279	15.96	0 104	2.26	0.052
Age o	2	1433	15.63	067.0	2.04	C70.0	1318	15.76	0.194	2.26	<i>ccc</i> .0
A 20 0	1	1445	16.61	0,660	2.61	0 161	1354	16.77	0 101	2.80	292.0
1260 J	2	1449	16.41	0.000	2.49	101.0	1316	16.58	101.0	2.82	001.0
A 10	1	3171	16.70	0.060	2.43		2994	16.98	L01.0	2.58	CCF 0
Age 10	2	3148	16.48	0.000	2.32	700.0	2973	16.77	/01.0	2.68	0.422
11 4	1	2385	17.56		2.77		2146	17.77	0100	3.01	0.465
Age 11	2	2288	17.40	075.0	2.80	766.0	2153	17.65	0./10	3.04	0.402
	1	3152	18.06		2.99	0.050	3031	18.26	100.0	3.05	0.201
Age 12	2	3021	17.89	167.0	2.99	CC0.0	3048	18.02	0.294	3.02	160.0
A 200 12	1	1035	18.59	2000	3.25	0 572	868	18.95	0.052	3.35	7200
A80 13	2	965	18.52	C10.0	3.20	7100	896	18.85	CC0.0	3.35	0.070
Age 14	1	2353	19.58	0.315	3.24	0.741	2332	19.92	0.339	3.16	0.539

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Women

Men

	Birth order	Z	Mean	p value ^a	SD	<i>p</i> value ^b	Z	Mean	<i>p</i> value ^a	SD	<i>p</i> value ^b
	2	2266	19.58		3.16		2370	19.70		3.11	
4 - 1 - 1	1	1143	20.03	201.0	3.28	200.0	1042	20.23	808.0	3.26	1100
ci əğr	2	1078	19.62	0.100	2.90	/00.0	1013	20.24	0.090	3.37	116.0
-	1	1990	20.87	00000	3.03	00000	2086	21.05	001.0	3.34	
Age 10	2	1940	20.77	067.0	3.01	0.800	2090	20.75	01.0	3.11	0.046
	1	2159	21.39		2.85	800.0	2230	21.09	0150	2.98	0 500
Age 17	2	2092	21.30	0.044	3.04	860.0	2224	20.79	QC1.0	2.93	000-0
A 10	1	1680	21.79	202.0	2.86	000	1281	21.29	0110	3.02	1000
Age 10	2	1614	21.83	160.0	3.01	710.0	1320	20.93	0.140	2.76	0.024
01 V	1	1044	21.91	201.0	2.61	0200	1099	21.38		3.05	
Age 19	2	1049	21.83	cø/.0	2.67	606.0	1047	21.12	0.212	2.84	0.082
	1	4036	23.39	00000	3.04	102.0	4398	22.07		3.58	0100
Age 20–29	2	4121	23.37	866.0	3.11	100.0	4270	21.82	1/1.0	3.42	0.040
	1	3221	24.81	C10 0	3.42	L90 0	4120	23.19	012.0	4.30	2010
Age 30-39	2	3351	24.75	618.0	3.41	186.0	3887	23.02	0.019	4.17	C71.0
07 07 TO	1	2403	25.48		3.35	5	2877	24.07	0000	4.23	
Age 40-49	2	2411	25.39	766.0	3.40	ccc.0	2775	23.99	676.0	4.25	C/6.0
A ED ED	1	2678	25.69		3.35	CE2 0	3261	24.75	2020	4.00	0.025
Age-uc age	2	2634	25.63	0/6.0	3.28	C/0.0	3086	24.53	C7C.N	3.89	C00.0
	1	1265	25.49		3.19	0 505	1560	25.15	076.0	4.19	
Age 00-09	2	1276	25.64	160.0	3.29	C6C.0	1532	25.07	607.0	4.09	c/c.U
	1	310	25.34	0000	3.35	0200	435	24.99	0.005	3.86	0.610
Age 10-19	2	329	25.31	606.0	3.20	617.0	390	24.87	CUE.U	4.03	
<i>p</i> value ^a : <i>p</i> val	ue for equality o	of means	, <i>p</i> value ^t	: <i>p</i> value fo	r equali	ty of varianc	ces, SD:	standard	deviation.		

Fixed effects regression coefficients for the association of birth order with height and BMI

			Hei	ight			BI	Ш	
		Model	1	Model	5	Model	1	Model	5
		в	<i>p</i> value	в	<i>p</i> value	в	<i>p</i> value	в	p value
Men	Age 1	-0.14	0.004	-0.02	0.565	-0.15	<0.001	-0.10	<0.001
	Age 2	-0.10	0.120	0.00	0.980	-0.16	<0.001	-0.11	<0.001
	Age 3	-0.18	0.008	-0.09	0.162	-0.15	<0.001	-0.12	<0.001
	Age 4	-0.07	0.510	0.00	0.978	-0.11	0.005	-0.08	0.025
	Age 5	-0.30	0.017	-0.17	0.167	-0.16	<0.001	-0.11	0.005
	Age 6	-0.01	0.952	0.13	0.510	-0.03	0.635	00.0	0.981
	Age 7	-0.20	0.045	-0.12	0.238	-0.13	0.001	-0.10	0.004
	Age 8	-0.21	0.169	-0.11	0.455	-0.10	0.062	-0.06	0.250
	Age 9	-0.10	0.572	-0.03	0.852	-0.07	0.376	-0.04	0.584
	Age 10	-0.36	0.008	-0.24	0.064	-0.16	0.003	-0.13	0.015
	Age 11	-0.29	0.089	-0.19	0.251	-0.17	0.015	-0.14	0.044
	Age 12	-0.07	0.678	0.03	0.839	-0.18	0.004	-0.15	0.020
	Age 13	-0.16	0.658	-0.08	0.813	-0.08	0.498	-0.04	0.708
	Age 14	0.04	0.895	0.11	0.699	-0.08	0.415	-0.05	0.608
	Age 15	0.03	0.932	0.09	0.825	-0.29	0.042	-0.28	0.058
	Age 16	-0.03	0.900	0.05	0.845	-0.16	0.172	-0.13	0.249
	Age 17	-0.28	0.239	-0.19	0.411	-0.05	0.663	-0.04	0.735
	Age 18	-0.29	0.135	-0.10	0.607	-0.07	0.475	-0.04	0.638
	Age 19	-0.21	0.536	-0.02	0.962	-0.11	0.477	-0.09	0.563
	Age 20–29	-0.30	0.068	-0.12	0.447	-0.08	0.341	-0.07	0.445
	Age 30–39	-0.59	0.095	-0.39	0.257	0.06	0.771	0.10	0.616
	Age 40–49	0.17	0.770	0.22	0.697	-0.18	0.646	-0.17	0.660
	Age 50–59	0.10	0.917	0.13	0.886	-0.01	066.0	-0.01	066.0
	Age 60–69	-0.35	0.795	-0.33	0.784	-0.56	0.571	-0.56	0.577
	Age 70–79	-4.00	0.753	-3.88	0.807	1.58	0.691	1.88	0.698
Women	Age 1	-0.13	0.005	0.00	0.970	-0.13	<0.001	-0.07	0.002

BMI

	Model	7
o value	В	<i>p</i> value
<0.001	-0.08	0.002
<0.001	-0.09	<0.001
<0.001	-0.13	0.002
<0.001	-0.11	0.008
0.033	-0.11	0.204
0.001	-0.10	0.006
0.003	-0.11	0.059
0.046	-0.11	0.190
0.001	-0.13	0.016
0.208	-0.07	0.306
0.007	-0.14	0:030
0.344	-0.09	0.504
0.033	-0.18	0.053

-0.13

-0.12-0.180.07 -0.04

> 0.742 0.235

0.031

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p value

p value

p value

0.9590.185 0.618 0.3300.6280.2230.273 0.668 0.729

0.00 -0.08-0.05-0.12

0.015

Age 2 Age 3 Age 4 Age 5 Age 6 Age 7 Age 8

0.007 0.288 0.056 0.1880.048

-0.18-0.11 -0.24-0.35-0.19-0.35 -0.06

Model 1 æ -0.14-0.12-0.15-0.15-0.18-0.13-0.18-0.16-0.18

Model 2 e

Model 1 æ -0.15

Height

Model 1: Unadjusted, Model 2: Adjusted for birth weight B: Unstandardized regression coefficient

0.788

0.921 0.802 0.940

0.8890.833

0.700 0.438 0.736

-0.17 0.40-0.41

0.5640.675

-0.25

Age 50–59

0.790

0.10

0.914

0.04

Age 40–49

0.12

0.09

0.08

0.999

0.00

0.554

-0.73

Age 70–79

0.22

Age 60–69

0.245 0.159 0.565

-0.18

0.180

-0.21

0.728

0.10

-0.24

0.047

-0.16

0.097 0.475 0.778

-0.18

0.647

-0.07-0.01

0.214

-0.20-0.16

Age 20–29

Age 19

-0.090.08 0.04

-0.110.08 0.05

0.953

0.457

Age 30–39

0.071 0.081

-0.17

0.951 0.571

-0.21

-0.24-0.19-0.28

0.697 0.538 0.2260.980

0.588

0.191

-0.25 0.17 -0.08-0.12-0.32 -0.01

Age 14 Age 15 Age 16 Age 17 Age 18

Age 13

0.6300.066

-0.08

0.506 0.036 0.045

-0.11

-0.17-0.12-0.20

0.450 0.833 0.3690.293 0.924

-0.12

0.269

-0.18-0.03

Age 12

0.07 -0.170.32 0.02 -0.01-0.15

0.925

-0.09

0.972

0.01

0.820

-0.04

Age 11

-0.15

Age 10

Age 9