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Published in:
Twin Research and Human Genetics

DOI:
10.1017/thg.2016.11

Publication date:
2016

Document version:
Final published version

Twin Research and Human Genetics
Volume 19 ▮ Number 2 ▮ pp. 112–124 ▮ © The Author(s) 2016 ▮ doi:10.1017/thg.2016.11

Twin's Birth-Order Differences in Height and Body Mass Index From Birth to Old Age: A Pooled Study of 26 Twin Cohorts Participating in the CODATwins Project

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RECEIVED 13 January 2016; ACCEPTED 4 February 2016.

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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 no longer statistically significant. 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 (Gielen et al., 2007; Glinianaia et al., 2000), zygosity (Buckler & Green, 2008; Daw & Walker, 1975; Loos et al., 2005), and chorionicity (Ananth et al., 1998; Bleker et al., 1979; Gielen et al., 2009; Gruenwald, 1970; Naeye et al., 1966; van Beijsterveldt et al., 2015) that are associated with intrauterine twin growth. Previous studies of twins have reported that the second-born twin is, on average, lighter than the first-born twin at birth (Gielen et al., 2007; Glinianaia et al., 2000; van Baal & 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 more often have 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 nutrient 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 (Pietiläinen et al., 2002; Silventoinen et al., 2007). Second-born twins also have higher morbidity and mortality (Armson et al., 2006; Luo et al., 2014; Shinwell et al., 2004; Smith et al., 2007).

The persistence of the birth-order association suggests that prenatal factors can have long-lasting 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 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 into 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 twin individuals and birth length from 54,941 twin individuals. BMI was calculated as weight (kg)/square of height (m^2). 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 (<25 cm or >65 cm) or birth weight (<500 g or >6000 g) 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.

TABLE 1

Number of Twin Individuals, Mean and Standard Deviation of Birth Length (cm) and Birth Weight (kg) by Birth Order, Sex, and Zygosity

			Boys					Girls				
		Birth order	*N*	Mean	*p* value[a]	*SD*	*p* value[b]	*N*	Mean	*p* value[a]	*SD*	*p* value[b]
Monozygotic twins	Birth length	1	5,304	47.0	.002	3.58	.001	5,101	46.3	.132	3.58	.085
		2	5,293	46.8		3.69		5,070	46.2		3.64	
	Birth weight (kg)	1	9,617	2.54	<.001	0.56	.067	10,383	2.43	<.001	0.54	<.001
		2	9,524	2.51		0.57		10,330	2.39		0.55	
Dizygotic twins	Birth length	1	9,160	47.4	.207	3.55	.009	7,967	46.8	.191	3.60	.018
		2	8,914	47.4		3.65		8,132	46.7		3.64	
	Birth weight (kg)	1	17,468	2.63	<.001	0.57	.005	16,562	2.53	<.001	0.55	.001
		2	17,098	2.58		0.58		16,800	2.47		0.56	

Note: *p* value[a] = *p* value for equality of means; *p* value[b] = *p* value for equality of variances; *SD* = standard deviation.

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 standard deviations of birth weight in the first-born and the second-born twins in MZ and DZ twins were significantly different except in MZ boys.

Descriptive statistics by birth order, age, and sex in MZ and DZ twins are presented in Tables 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 1, 2, 5, 8, and 10 years in men and from the age of 1 to 3, 7, 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 standard deviations 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.

Tables 4 and 5 show 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- to 49-year age group in women. Statistical significance was attained in the majority of age groups until the 12 years age groups (Table 4). In DZ twins, first-borns had greater BMI than the second-born twins except the 14- and 60- to 69-years-old men. The differences were also statistically significant particularly until 5 years of age. The standard deviations of BMI in the first-born and the second-born twins in MZ twins were not significantly different. However, the standard deviations of BMI in the first-born and the second-born twins in DZ twins were significantly different at the age of 1, 3, 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 .047–.008), data from MZ and DZ twins were combined in the further analyses. Figure 1 illustrates the percentage difference (%) in the mean and standard deviation 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 almost always showed 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 5 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 18 years). For standard deviation, 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 1, 3, 5, 7, and 10 years in men, whereas birth order was not associated with height in women. Moreover, after adjusting for birth weight, birth order was associated with BMI from the age of 1 to 5, 7, 10, 11, and 12 years in men, and from the age of 1 to 5, 7, 10, and 12 years in women.

Discussion

The CODATwins study established a database with data on body size from twin cohorts in different countries from

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	*N*	Mean	*p* value[a]	*SD*	*p* value[b]	*N*	Mean	*p* value[a]	*SD*	*p* value[b]
Age 1	1	2,843	73.6	.029	4.54	0.176	2,994	72.4	0.014	4.55	.267
	2	2,838	73.5		4.59		2,991	72.3		4.55	
Age 2	1	2,310	86.5	.121	4.41	0.047	2,339	85.4	0.020	4.42	.307
	2	2,293	86.4		4.46		2,323	85.3		4.44	
Age 3	1	2,830	95.8	.044	4.45	0.264	3,140	94.9	0.002	4.39	.775
	2	2,834	95.7		4.47		3,125	94.8		4.38	
Age 4	1	1,600	102.1	.18	5.17	0.045	1,594	101.0	0.116	5.13	.118
	2	1,588	101.9		5.33		1,595	100.9		5.29	
Age 5	1	1,272	110.8	.018	5.91	0.770	1,341	110.2	0.299	6.16	.496
	2	1,266	110.7		5.93		1,328	110.1		6.06	
Age 6	1	528	114.1	.279	6.45	0.856	427	112.9	0.834	5.66	.180
	2	512	113.7		6.40		421	112.9		5.88	
Age 7	1	2,345	123.6	.216	6.62	0.134	2,540	122.9	0.020	6.49	.973
	2	2,330	123.5		6.72		2,536	122.8		6.53	
Age 8	1	1,057	127.6	.016	6.35	0.322	1,020	127.0	0.077	6.42	.209
	2	1,042	127.4		6.23		1,021	126.8		6.56	
Age 9	1	1,042	133.0	.143	6.97	0.509	1,005	132.0	0.232	6.93	.590
	2	997	132.8		7.04		986	131.8		6.92	
Age 10	1	1,988	140.0	.044	7.18	0.737	2,088	139.8	0.115	7.41	.199
	2	1,924	139.9		7.19		2,048	139.7		7.47	
Age 11	1	1,530	143.4	.470	7.15	0.959	1,588	144.2	0.180	7.30	.003
	2	1,470	143.3		7.12		1,530	144.0		7.48	
Age 12	1	2,032	151.4	.434	8.30	0.884	2,127	152.3	0.036	8.01	.030
	2	1,955	151.3		8.24		2,053	152.1		8.18	
Age 13	1	692	157.9	.693	9.30	0.301	642	157.3	0.269	7.40	.494
	2	620	157.6		9.39		591	157.2		7.54	
Age 14	1	1,328	165.4	.815	8.95	0.808	1,497	161.8	0.441	6.68	.066
	2	1,280	165.4		9.09		1,468	161.8		6.85	
Age 15	1	658	171.5	.433	8.68	0.968	639	164.5	0.615	7.32	.029
	2	639	171.7		8.70		606	165.1		7.00	
Age 16	1	1,074	175.5	.731	7.61	0.546	1,311	164.4	0.398	6.56	.067
	2	1,028	175.5		7.56		1,257	164.5		6.34	
Age 17	1	1,100	177.7	.315	7.29	0.608	1,411	165.6	0.710	6.62	.601
	2	1,074	177.8		7.47		1,388	165.8		6.59	
Age 18	1	1,253	178.9	.207	7.05	0.085	826	166.1	0.450	6.48	.495
	2	1,253	178.9		6.89		812	166.1		6.64	
Age 19	1	639	179.2	.345	7.04	0.250	717	166.1	0.255	6.98	.279
	2	607	179.3		6.85		702	165.9		6.83	
Age 20–29	1	2,890	179.2	.117	6.90	0.412	3,488	164.5	0.881	6.50	.839
	2	2,878	179.0		6.98		3,478	164.6		6.47	
Age 30–39	1	2,305	178.1	.360	7.04	0.494	3,378	164.0	0.233	6.67	.554
	2	2,290	177.9		6.92		3,349	164.0		6.62	
Age 40–49	1	1,420	177.2	.295	7.04	0.370	1,886	163.2	0.924	6.65	.436
	2	1,355	177.1		7.03		1,844	163.1		6.58	
Age 50–59	1	1,038	176.4	.805	7.02	0.181	1,601	162.5	0.613	6.50	.047
	2	1,029	176.3		7.22		1,609	162.4		6.70	
Age 60–69	1	506	174.9	.386	6.40	0.006	880	161.7	0.660	6.30	.297
	2	494	174.4		6.99		878	161.9		6.47	
Age 70–79	1	126	173.7	.412	7.09	0.199	273	161.3	0.378	6.91	.162
	2	117	173.1		7.48		268	160.8		6.61	

Note: *p* value[a] = *p* value for equality of means; *p* value[b] = *p* value for equality of variances; *SD* = standard deviation.

infancy to old age. Previous studies in twins have reported that the second-born twin was lighter than the first-born twin at birth (Gielen et al., 2007; Glinianaia et al., 2000) 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

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*	*p* value[b]	*N*	Mean	*p* value[a]	*SD*	*p* value[b]
Age 1	1	5,088	74.8	.051	4.11	.531	4,759	73.4	.113	4.06	.359
	2	4,962	74.6		4.11		4,821	73.2		4.14	
Age 2	1	4,184	87.4	.340	4.22	.265	3,815	86.3	.141	4.34	.189
	2	4,102	87.2		4.28		3,871	86.1		4.27	
Age 3	1	5,407	96.6	.074	4.43	.822	5,085	95.6	.159	4.55	.257
	2	5,266	96.4		4.42		5,208	95.4		4.62	
Age 4	1	2,993	102.4	.873	5.27	.872	2,818	101.3	.745	5.21	.119
	2	2,954	102.5		5.31		2,848	101.1		5.25	
Age 5	1	2,349	112.0	.126	6.07	.478	2,099	111.1	.143	6.37	.602
	2	2,259	111.5		6.13		2,189	110.7		6.41	
Age 6	1	583	114.5	.819	6.88	.311	455	114.2	.261	7.55	.180
	2	552	114.8		7.15		469	113.6		7.39	
Age 7	1	3,986	124.8	.232	6.59	.266	3,877	123.8	.359	6.71	.239
	2	3,981	124.5		6.72		3,864	123.8		6.65	
Age 8	1	1,478	129.2	.533	6.42	.154	1,279	128.3	.192	6.82	.721
	2	1,433	128.9		6.65		1,318	127.9		6.87	
Age 9	1	1,445	134.5	.664	7.30	.271	1,354	133.9	.994	7.25	.830
	2	1,449	134.2		7.14		1,316	133.9		7.38	
Age 10	1	3,171	141.8	.097	7.02	.226	2,994	141.2	.578	7.35	.539
	2	3,148	141.4		7.21		2,973	141.0		7.39	
Age 11	1	2,385	145.2	.130	7.23	.505	2,146	145.1	.691	7.77	.279
	2	2,288	144.6		7.41		2,153	145.4		7.92	
Age 12	1	3,152	152.5	.945	7.82	.617	3,031	153.3	.813	8.36	.444
	2	3,021	152.3		7.92		3,048	153.3		8.24	
Age 13	1	1,035	158.8	.887	8.77	.051	898	158.4	.938	7.80	.964
	2	965	158.7		9.36		896	158.7		7.98	
Age 14	1	2,353	165.6	.888	8.94	.031	2,332	162.8	.358	6.74	.529
	2	2,266	165.8		8.62		2,370	162.5		6.87	
Age 15	1	1,143	172.2	.878	8.84	.729	1,042	165.4	.547	7.18	.358
	2	1,078	172.3		8.87		1,013	165.7		7.03	
Age 16	1	1,990	176.0	.855	7.52	.827	2,086	165.4	.952	6.61	.174
	2	1,940	175.8		7.46		2,090	165.5		6.43	
Age 17	1	2,159	178.5	.317	7.30	.415	2,230	166.4	.758	6.32	.035
	2	2,092	178.0		7.16		2,224	166.4		6.70	
Age 18	1	1,680	179.4	.444	6.95	.573	1,281	166.8	.434	6.77	.267
	2	1,614	179.2		6.91		1,320	166.3		6.49	
Age 19	1	1,044	180.4	.973	6.72	.362	1,099	167.2	.662	6.60	.187
	2	1,049	179.8		6.86		1,047	167.3		6.47	
Age 20–29	1	4,036	179.9	.191	6.69	.624	4,398	165.8	.255	6.56	.167
	2	4,121	179.4		6.74		4,270	165.5		6.50	
Age 30–39	1	3,221	179.2	.674	6.82	.209	4,120	165.2	.594	6.58	.069
	2	3,351	178.9		6.64		3,887	165.0		6.43	
Age 40–49	1	2,403	178.9	.791	6.69	.775	2,877	164.6	.836	6.36	.961
	2	2,411	178.9		6.70		2,775	164.9		6.33	
Age 50–59	1	2,678	178.0	.532	6.73	.281	3,261	164.1	.898	6.20	.081
	2	2,634	177.7		6.56		3,086	164.3		6.05	
Age 60–69	1	1,265	175.9	.927	6.73	.657	1,560	162.9	.813	6.13	.280
	2	1,276	175.8		6.85		1,532	162.9		6.27	
Age 70–79	1	310	175.3	.586	6.53	.287	435	162.1	.543	6.78	.064
	2	329	175.0		6.82		390	161.4		6.05	

Note: *p* value[a] = *p* value for equality of means; *p* value[b] = *p* value for equality of variances; *SD* = standard deviation.

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 standard deviations 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 & 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 has been 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 first-born twin at birth (Gielen et al., 2007; Glinianaia et al., 2000). Moreover, low birth weight predicts lower adult

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	*N*	Mean	*p* value[a]	*SD*	*p* value[b]	*N*	Mean	*p* value[a]	*SD*	*p* value[b]
Age 1	1	2,843	17.21	<.001	1.41	.798	2,994	16.84	<.001	1.42	.755
	2	2,838	17.11		1.42		2,991	16.74		1.42	
Age 2	1	2,310	16.62	<.001	1.40	.921	2,339	16.17	<.001	1.38	.915
	2	2,293	16.51		1.39		2,323	16.04		1.38	
Age 3	1	2,830	16.02	<.001	1.41	.276	3,140	15.68	<.001	1.50	.217
	2	2,834	15.88		1.39		3,125	15.58		1.47	
Age 4	1	1,600	15.90	.023	1.78	.506	1,594	15.71	.001	2.01	.355
	2	1,588	15.84		1.81		1,595	15.59		1.98	
Age 5	1	1,272	15.34	<.001	1.54	.671	1,341	15.13	<.001	1.64	.360
	2	1,266	15.20		1.51		1,328	15.01		1.64	
Age 6	1	528	15.54	.265	1.77	.735	427	15.25	.084	1.76	.735
	2	512	15.48		1.77		421	15.14		1.74	
Age 7	1	2,345	15.40	.002	1.69	.419	2,540	15.44	<.001	1.93	.314
	2	2,330	15.31		1.71		2,536	15.31		1.93	
Age 8	1	1,057	15.64	.026	1.72	.331	1,020	15.65	<.001	1.97	.240
	2	1,042	15.54		1.67		1,021	15.50		1.93	
Age 9	1	1,042	16.29	.057	2.10	.318	1,005	16.33	.152	2.38	.556
	2	997	16.23		2.17		986	16.22		2.39	
Age 10	1	1,988	16.64	.005	2.30	.042	2,088	16.67	<.001	2.45	.502
	2	1,924	16.54		2.17		2,048	16.56		2.40	
Age 11	1	1,530	17.32	<.001	2.56	.004	1,588	17.37	.035	2.72	.374
	2	1,470	17.10		2.44		1,530	17.30		2.80	
Age 12	1	2,032	17.87	<.001	2.72	.197	2,127	17.92	<.001	2.74	.999
	2	1,955	17.72		2.67		2,053	17.77		2.71	
Age 13	1	692	18.45	.092	2.89	.051	642	18.94	.094	3.19	.383
	2	620	18.30		2.79		591	18.82		3.27	
Age 14	1	1,328	19.28	.132	2.86	.422	1,497	19.67	.007	3.02	.956
	2	1,280	19.23		2.82		1,468	19.59		3.01	
Age 15	1	658	19.64	.194	2.92	.416	639	19.95	.168	3.20	.503
	2	639	19.59		2.93		606	19.80		3.15	
Age 16	1	1,074	20.68	.138	2.99	.106	1,311	20.64	.098	2.98	.172
	2	1,028	20.55		2.87		1,257	20.57		2.95	
Age 17	1	1,100	20.94	.387	2.72	.850	1,411	20.73	.112	2.87	.982
	2	1,074	20.88		2.68		1,388	20.60		2.85	
Age 18	1	1,253	21.32	.479	2.57	.098	826	21.00	.286	2.82	.170
	2	1,253	21.33		2.49		812	20.81		2.74	
Age 19	1	639	21.66	.513	2.51	.900	717	21.00	.892	2.76	.300
	2	607	21.59		2.59		702	20.95		2.83	
Age 20–29	1	2,890	23.09	.010	2.96	.554	3,488	21.85	.010	3.69	.340
	2	2,878	22.94		2.97		3,478	21.73		3.57	
Age 30–39	1	2,305	24.65	.461	3.39	.215	3,378	22.86	.712	4.03	.309
	2	2,290	24.52		3.30		3,349	22.85		4.07	
Age 40–49	1	1,420	25.44	.137	3.59	.042	1,886	23.75	.676	4.20	.428
	2	1,355	25.25		3.33		1,844	23.77		4.33	
Age 50–59	1	1,038	25.43	.668	3.21	.523	1,601	24.65	.384	4.30	.368
	2	1,029	25.56		3.18		1,609	24.55		4.13	
Age 60–69	1	506	25.59	.852	3.20	.264	880	25.24	.168	4.26	.312
	2	494	25.73		3.28		878	25.02		4.17	
Age 70–79	1	126	24.74	.925	3.20	.532	273	24.95	.675	4.30	.213
	2	117	24.90		3.27		268	24.58		3.71	

Note: *p* value[a] = *p* value for equality of means; *p* value[b] = *p* value for equality of variances; *SD* = standard deviation.

BMI in twins (Johansson & Rasmussen, 2001; Pietiläinen et al., 2002). 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 from 3 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 (e.g., smoking, alcohol, and total placental weight) affecting both twins and factors unique to each twin, such as individual placental

TABLE 5

Number of Twin Individuals, Mean and Standard Deviation of Birth Weight (kg) and BMI (kg/m^2) by Birth Order, Age, and Sex in Dizygotic Twins

		Men					Women				
	Birth order	*N*	Mean	*p* value[a]	*SD*	*p* value[b]	*N*	Mean	*p* value[a]	*SD*	*p* value[b]
Age 1	1	5,088	17.20	<.001	1.39	.037	4,759	16.81	.004	1.35	.728
	2	4,962	17.04		1.34		4,821	16.67		1.35	
Age 2	1	4,184	16.57	<.001	1.41	.930	3,815	16.20	.006	1.38	.423
	2	4,102	16.40		1.40		3,871	16.04		1.39	
Age 3	1	5,407	16.03	.003	1.54	.003	5,085	15.74	.010	1.53	.314
	2	5,266	15.84		1.47		5,208	15.63		1.57	
Age 4	1	2,993	16.01	.047	1.87	.808	2,818	15.81	.044	1.89	.656
	2	2,954	15.82		1.89		2,848	15.68		1.93	
Age 5	1	2,349	15.33	.020	1.59	.806	2,099	15.24	.049	1.68	.195
	2	2,259	15.17		1.60		2,189	15.09		1.71	
Age 6	1	583	15.65	.867	2.02	.153	455	15.65	.164	2.29	.574
	2	552	15.59		2.21		469	15.40		2.22	
Age 7	1	3,986	15.50	.018	1.85	.077	3,877	15.59	.178	2.09	.144
	2	3,981	15.35		1.92		3,864	15.41		2.03	
Age 8	1	1,478	15.75	.296	2.09	.625	1,279	15.96	.194	2.26	.953
	2	1,433	15.63		2.04		1,318	15.76		2.26	
Age 9	1	1,445	16.61	.660	2.61	.161	1,354	16.77	.181	2.80	.765
	2	1,449	16.41		2.49		1,316	16.58		2.82	
Age 10	1	3,171	16.70	.060	2.43	.002	2,994	16.98	.107	2.58	.422
	2	3,148	16.48		2.32		2,973	16.77		2.68	
Age 11	1	2,385	17.56	.326	2.77	.992	2,146	17.77	.710	3.01	.465
	2	2,288	17.40		2.80		2,153	17.65		3.04	
Age 12	1	3,152	18.06	.237	2.99	.853	3,031	18.26	.294	3.05	.391
	2	3,021	17.89		2.99		3,048	18.02		3.02	
Age 13	1	1,035	18.59	.875	3.25	.572	898	18.95	.853	3.35	.876
	2	965	18.52		3.20		896	18.85		3.35	
Age 14	1	2,353	19.58	.315	3.24	.741	2,332	19.92	.339	3.16	.539
	2	2,266	19.58		3.16		2,370	19.70		3.11	
Age 15	1	1,143	20.03	.106	3.28	.007	1,042	20.23	.898	3.26	.911
	2	1,078	19.62		2.90		1,013	20.24		3.37	
Age 16	1	1,990	20.87	.290	3.03	.800	2,086	21.05	.109	3.34	.046
	2	1,940	20.77		3.01		2,090	20.75		3.11	
Age 17	1	2,159	21.39	.644	2.85	.038	2,230	21.09	.158	2.98	.500
	2	2,092	21.30		3.04		2,224	20.79		2.93	
Age 18	1	1,680	21.79	.597	2.86	.012	1,281	21.29	.148	3.02	.024
	2	1,614	21.83		3.01		1,320	20.93		2.76	
Age 19	1	1,044	21.91	.785	2.61	.969	1,099	21.38	.212	3.05	.082
	2	1,049	21.83		2.67		1,047	21.12		2.84	
Age 20–29	1	4,036	23.39	.398	3.04	.507	4,398	22.07	.171	3.58	.040
	2	4,121	23.37		3.11		4,270	21.82		3.42	
Age 30–39	1	3,221	24.81	.813	3.42	.987	4,120	23.19	.619	4.30	.125
	2	3,351	24.75		3.41		3,887	23.02		4.17	
Age 40–49	1	2,403	25.48	.932	3.35	.553	2,877	24.07	.929	4.23	.975
	2	2,411	25.39		3.40		2,775	23.99		4.25	
Age 50–59	1	2,678	25.69	.970	3.35	.673	3,261	24.75	.525	4.00	.065
	2	2,634	25.63		3.28		3,086	24.53		3.89	
Age 60–69	1	1,265	25.49	.897	3.19	.595	1,560	25.15	.769	4.19	.373
	2	1,276	25.64		3.29		1,532	25.07		4.09	
Age 70–79	1	310	25.34	.909	3.35	.279	435	24.99	.905	3.86	.610
	2	329	25.31		3.20		390	24.87		4.03	

Note: *p* value[a] = *p* value for equality of means; *p* value[b] = *p* value for equality of variances; *SD* = standard deviation.

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 non-central cord insertion contributed to birth weight discordance in monochorionic twin pregnancies. Antoniou et al. (2011), who examined 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

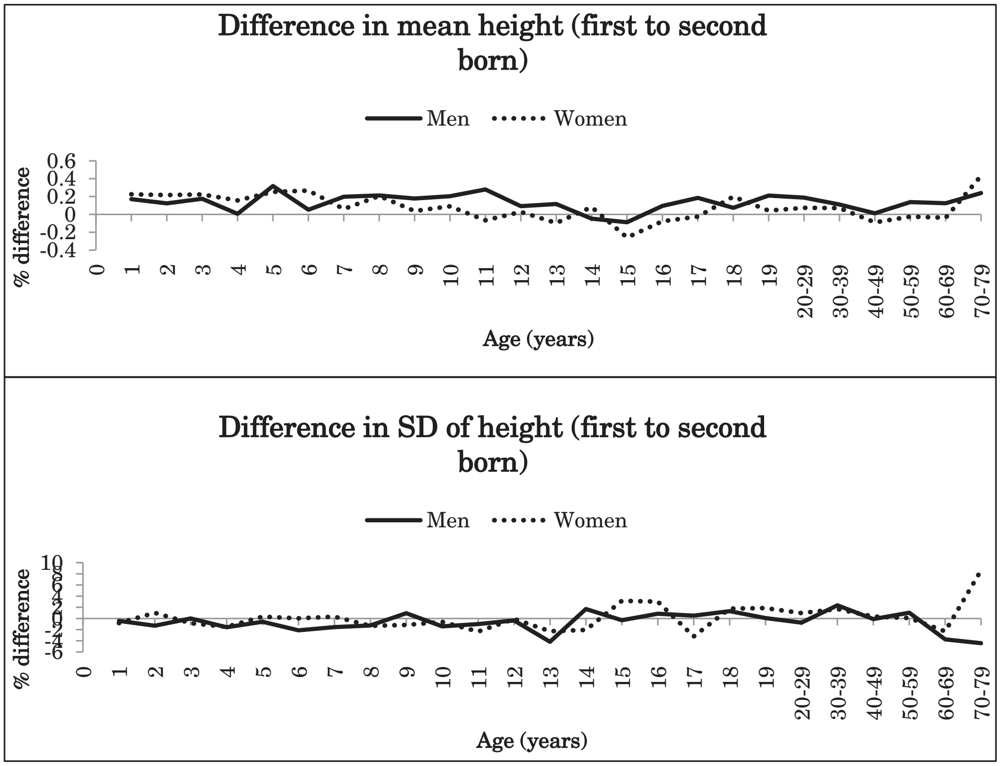

FIGURE 1

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

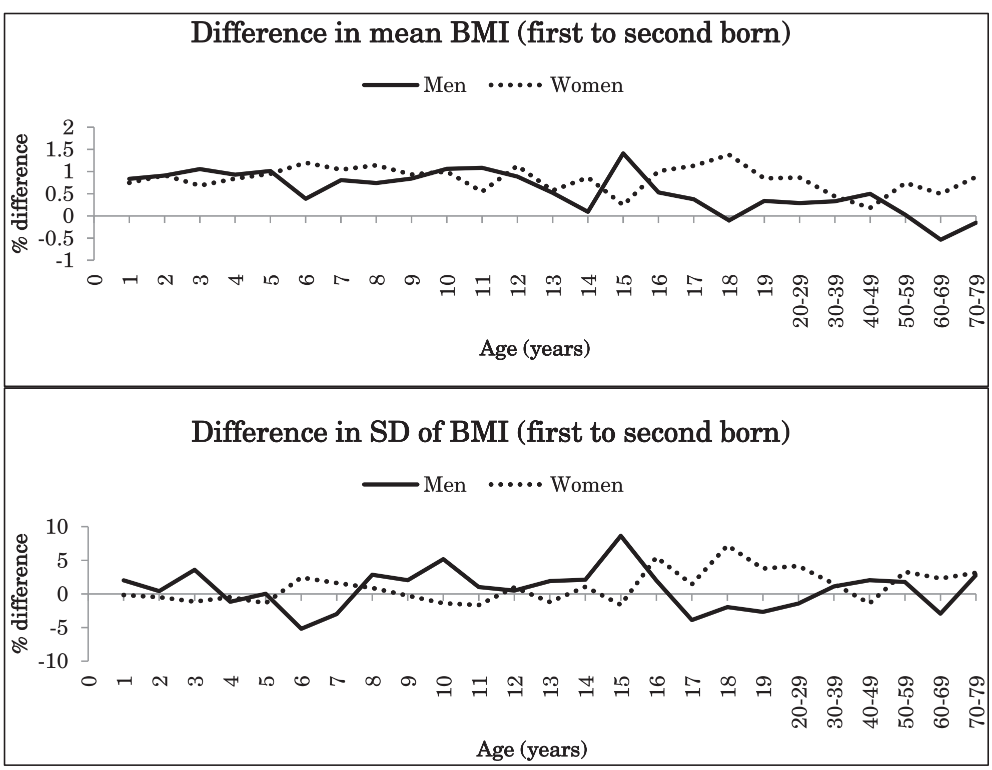

FIGURE 2

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

TABLE 6
Fixed Effects Regression Coefficients for the Association Of Birth Order With Height and BMI

		Height				BMI			
		Model 1		Model 2		Model 1		Model 2	
		B	*p* value	B	*p* value	B	*p* value	B	*p* value
Men	Age 1	-0.14	.004	-0.02	.565	-0.15	<.001	-0.10	<.001
	Age 2	-0.10	.120	0.00	.980	-0.16	<.001	-0.11	<.001
	Age 3	-0.18	.008	-0.09	.162	-0.15	<.001	-0.12	<.001
	Age 4	-0.07	.510	0.00	.978	-0.11	.005	-0.08	.025
	Age 5	-0.30	.017	-0.17	.167	-0.16	<.001	-0.11	.005
	Age 6	-0.01	.952	0.13	.510	-0.03	.635	0.00	.981
	Age 7	-0.20	.045	-0.12	.238	-0.13	.001	-0.10	.004
	Age 8	-0.21	.169	-0.11	.455	-0.10	.062	-0.06	.250
	Age 9	-0.10	.572	-0.03	.852	-0.07	.376	-0.04	.584
	Age 10	-0.36	.008	-0.24	.064	-0.16	.003	-0.13	.015
	Age 11	-0.29	.089	-0.19	.251	-0.17	.015	-0.14	.044
	Age 12	-0.07	.678	0.03	.839	-0.18	.004	-0.15	.020
	Age 13	-0.16	.658	-0.08	.813	-0.08	.498	-0.04	.708
	Age 14	0.04	.895	0.11	.699	-0.08	.415	-0.05	.608
	Age 15	0.03	.932	0.09	.825	-0.29	.042	-0.28	.058
	Age 16	-0.03	.900	0.05	.845	-0.16	.172	-0.13	.249
	Age 17	-0.28	.239	-0.19	.411	-0.05	.663	-0.04	.735
	Age 18	-0.29	.135	-0.10	.607	-0.07	.475	-0.04	.638
	Age 19	-0.21	.536	-0.02	.962	-0.11	.477	-0.09	.563
	Age 20–29	-0.30	.068	-0.12	.447	-0.08	.341	-0.07	.445
	Age 30–39	-0.59	.095	-0.39	.257	0.06	.771	0.10	.616
	Age 40–49	0.17	.770	0.22	.697	-0.18	.646	-0.17	.660
	Age 50–59	0.10	.917	0.13	.886	-0.01	.990	-0.01	.990
	Age 60–69	-0.35	.795	-0.33	.784	-0.56	.571	-0.56	.577
	Age 70–79	-4.00	.753	-3.88	.807	1.58	.691	1.88	.698
Women	Age 1	-0.13	.005	0.00	.970	-0.13	<.001	-0.07	.002
	Age 2	-0.15	.015	0.00	.959	-0.14	<.001	-0.08	.002
	Age 3	-0.18	.007	-0.08	.185	-0.12	<.001	-0.09	<.001
	Age 4	-0.11	.288	-0.05	.618	-0.15	<.001	-0.13	.002
	Age 5	-0.24	.056	-0.12	.330	-0.15	<.001	-0.11	.008
	Age 6	-0.35	.188	-0.13	.628	-0.18	.033	-0.11	.204
	Age 7	-0.19	.048	-0.12	.223	-0.13	.001	-0.10	.006
	Age 8	-0.35	.031	-0.18	.273	-0.18	.003	-0.11	.059
	Age 9	-0.06	.742	0.07	.668	-0.16	.046	-0.11	.190
	Age 10	-0.15	.235	-0.04	.729	-0.18	.001	-0.13	.016
	Age 11	-0.04	.820	0.01	.972	-0.09	.208	-0.07	.306
	Age 12	-0.18	.269	-0.12	.450	-0.17	.007	-0.14	.030
	Age 13	-0.03	.925	0.07	.833	-0.12	.344	-0.09	.504
	Age 14	-0.25	.191	-0.17	.369	-0.20	.033	-0.18	.053
	Age 15	0.17	.588	0.32	.293	-0.11	.506	-0.08	.630
	Age 16	-0.08	.697	0.02	.924	-0.24	.036	-0.21	.066
	Age 17	-0.12	.538	-0.01	.951	-0.19	.045	-0.17	.071
	Age 18	-0.32	.226	-0.15	.571	-0.28	.047	-0.24	.081
	Age 19	-0.01	.980	0.10	.728	-0.21	.180	-0.18	.245
	Age 20–29	-0.20	.214	-0.07	.647	-0.18	.097	-0.16	.159
	Age 30–39	-0.16	.457	-0.01	.953	-0.11	.475	-0.09	.565
	Age 40–49	0.04	.914	0.10	.790	0.08	.778	0.08	.788
	Age 50–59	-0.25	.564	-0.17	.700	0.05	.889	0.04	.921
	Age 60–69	0.22	.675	0.40	.438	0.09	.833	0.12	.802
	Age 70–79	-0.73	.554	-0.41	.736	0.00	.999	0.08	.940

Note: B = Unstandardized regression coefficient; Model 1 = Unadjusted; Model 2 = Adjusted for birth weight.

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 only gathered reliably in a 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 (Armson et al., 2006; Sheay et al., 2004; Smith et al., 2002, 2005, 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-born versus first-born 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 birth weight (<1500 g) second-born 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 birth weight, 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 leads to decreasing effect sizes. Our results may thus be underestimations of the real birth order differences.

In conclusion, the first-born twins had a greater BMI and are slightly taller than the second-born twins. Birth order showed a significant association with BMI before 12 years of age. However, in generally, the differences in BMI and height between first-born and second-born 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.

Acknowledgments

The Australian Twin Registry is supported by a Centre of Research Excellence (grant ID 1079102) from the National Health and Medical Research Council administered by the University of Melbourne. The Boston University Twin Project is funded by grants (#R01 HD068435 #R01 MH062375) from the National Institutes of Health to K. Saudino. The Carolina African American Twin Study of Aging (CAATSA) was funded by a grant from the National Institute on Aging (grant 1RO1-AG13662-01A2) to K. E. Whitfield. Data collection and analyses in Finnish twin cohorts have been supported by ENGAGE — European Network for Genetic and Genomic Epidemiology, FP7-HEALTH-F4-2007, grant agreement number 201413, National Institute of Alcohol Abuse and Alcoholism (grants AA-12502, AA-00145, and AA-09203 to R J Rose, the Academy of Finland Center of Excellence in Complex Disease Genetics (grant numbers: 213506, 129680), and the Academy of Finland (grants 100499, 205585, 118555, 141054, 265240, 263278, and 264146 to J Kaprio). Gemini was supported by a grant from Cancer Research UK (C1418/A7974). Guangzhou Twin Eye Study is supported by National Natural Science Foundation of China (grant #81125007). Anthropometric measurements of the Hungarian twins were supported by Medexpert Ltd., Budapest, Hungary. Korean Twin-Family Register was supported by the Global Research Network Program of the National Research Foundation (NRF 2011-220-E00006). Longitudinal Israeli Study of Twins was funded by the Starting Grant no. 240994 from the European Research Council (ERC) to Ariel Knafo. The Michigan State University Twin Registry has been supported by Michigan State University, as well as grants R01-MH081813, R01-MH0820-54, R01-MH092377-02, R21-MH070542-01, R03-MH63851-01 from the National Institute of Mental Health (NIMH), R01-HD066040 from the Eunice Kennedy Shriver National Institute for Child Health and Human Development (NICHD), and 11-SPG-2518 from the MSU Foundation. The content of this manuscript is solely the responsibility of the authors and does not necessarily represent the official views of the NIMH, the NICHD, or the National Institutes of Health. PETS was supported by grants from the Australian National Health and Medical Research Council (grant numbers 437015 and 607358 to JC, and RS), the Bonnie Babes Foundation (grant number BBF20704 to JMC), the Financial Markets Foundation for Children (grant no. 032–2007 to JMC), and by the Victorian Government's Operational Infrastructure Support Program. The Quebec Newborn Twin Study acknowledges financial support from the Fonds Québécois de la Recherche sur la Société et la Culture, the Fonds de la Recherche en Santé du Québec, the Social Science and Humanities Research Council of Canada, the National Health Research Development Program, the Canadian Institutes for Health Research, Sainte-Justine Hospital's Research Center, and the Canada Research Chair Program (Michel Boivin). South Korea Twin Registry is supported by National Research Foundation of Korea (NRF-371-2011-1 B00047). The Twins Early Development Study (TEDS) is supported by a program grant (G0901245) from the UK Medical Research Council and the work on obesity in TEDS is supported in part by a grant from the UK Biotechnology and Biological Sciences Research Council (31/D19086). The West Japan Twins and Higher Order Multiple Births Registry was supported by Grant-in-Aid for Scientific Research (B) (grant number 15H05105) from the Japan Society for the Promotion of Science. The Murcia Twin Registry is supported by Fundación Séneca, Regional Agency for Science and Technology, Murcia, Spain (08633/PHCS/08, 15302/PHCS/10 & 19479/PI/14) and Ministry of Science and Innovation, Spain (PSI2009-11560 & PSI2014-56680-R). The CODATwins project is supported by Academy of Finland (#266592).

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