Comparison of Obstetric and Birthweight Characteristics Between the Two Largest Databases of Japanese Twins Measured in Childhood

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The purpose of this study is to compare obstetric and birthweight data of twin children from the two largest databases in Japan to estimate the difference between them in sample collection. The first group consisted of 1131 twin-pair school applicants, and the second group consisted of members' children from several maternal associations devoted to twins and included 951 pairs. All data were gathered by questionnaire. The mean birth years of the twins in these two databases were 1979 and 1995 respectively. The percentage of mothers treated with ovulation-stimulating drugs or in-vitro fertilization was markedly higher in the maternal associations group. Gestational age was around 1 week less in the maternal associations group, whereas birthweight according to gestational weeks and intrapair relative birth weight difference as a percentage according to zygosity showed little difference between both groups. We conclude that the obstetric and birthweight feature data from both groups should be considered to construct twin growth charts based on the methods of sample selection.

Many countries including Asian countries are constructing or have constructed large population-based twin registries. No systematic twin registry exists in Japan, however. Three main data sources are used to study the growth and development of multiples in Japan. First, vital statistics can be obtained; however access to individual information is prohibited. Second, data from large hospitals is used in the field of obstetrics, particularly for managing high-risk pregnancies. Twin data collection within this field is relatively easy; however, it has a selection bias towards high-risk infants, for example those with a very low birth weight.

To fill the gap between vital statistics and hospital data, a volunteer-based twin database was set up that is larger and less biased than hospital data and contains more detailed information than vital statistics. In addition, data regarding the condition of twins after birth has been gathered, a difficulty for both vital statistics and hospital data. The database consisted mainly of two independent groups. The purpose of this study is to compare the obstetric and birthweight characteristics of both samples to estimate the effect of different sample collection.

Materials and Methods

Subjects and Data Collection

The present sample consisted of two independent groups. The first group included 1131 mothers and their twin children living in the Tokyo metropolitan area. All of the twins in this group — the school applicant group — had applied between 1981 and 2004 to (though not necessarily enrolled in) the secondary school attached to the Faculty of Education at the University of Tokyo. The second group — the maternal associations group — consisted of 951 mothers from several associations for parents of multiples throughout Japan. The twins' age at data collection was between 11 and 12 years in the school applicant group, and between 0 and 15 years (mean 5.9) in the maternal associations group.

Mailed or hand-delivered questionnaires of nearly the same format were used to collect the data from the two groups. These included questions about family structure; obstetrical findings on the mothers; the twins' physical growth, zygosity, motor, language, and mental development; the twins' and parents' medical histories; and any behavioral problems the twins had had (Ooki & Yokoyama, 2003, 2004). Data on the socioeconomic and educational status of the parents were not obtained because of ethical limi-

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Table 1

Basic Characteristics of Present Database

			School applicants	Maternal associations
N			1131 pairs	951 pairs
Method of data collection			Handed questionnaire and interview	Mailed questionnaire
Year of data collection			1981–2004	2001–2004
District			Tokyo metropolitan area	All around Japan
Birth year of twin pairs		Mean ± *SD* (range)	1979 ± 7 (1968–1992)	1995 ± 4 (1986–2003)
Sex of twin individuals	Male/female		1057/1205	982/920
Zygosity	Monozygotic	MM/FF	336/418	235/210
	Dizygotic	MM/FF/MF/FM	77/69/70/57	95/109/95/113
	Suspended	MM/FF	33/36	46/31
	Insufficient information	MM/FF	19/16	11/6
Age of twin pairs at data collection (years)		Mean ± *SD* (range)	11.9 ± 0.4 (11–12)	5.9 ± 3.8 (0–15)
Maternal age at twins birth (year)[a]		Mean ± *SD* (range)	29.1±3.9 (19–43)	30.7 ± 3.8 (21–41)
Paternal age at twins birth (year)[b]		Mean ± *SD* (range)	31.9 ± 4.7 (19–53)	33.3 ± 4.5 (22–50)
Previous abortion		0	786 (69.5%)	744 (78.2%)
		1	205 (18.1%)	166 (17.5%)
		2–	50 (4.4%)	40 (4.2%)
		Unknown	90 (8.0%)	1 (0.1%)
Treatment of infertility (ovulation stimulating drugs, in-vitro fertilization, and other types of assisted conception)		Yes No Unknown	31 (2.7%) 1015 (89.7%) 85 (7.5%)	292 (30.7%) 640 (67.3%) 19 (2.0%)
Gestation (weeks)[c]		Mean ± SD	37.9 ± 2.2	36.9 ± 2.3
Parity		1	591 (52.3%)	655 (68.9%)
		2	424 (37.5%)	296 (31.1%)[d]
		3–5	115 (10.2%)	
		Unknown	1 (0.1%)	0 (0%)
Neonatal condition (twin individuals)		Healthy	1778 (78.6%)	1491 (78.4%)
		Hyposthenia (not so healthy)	304 (13.4%)	205 (10.8%)
		Neonatal asphyxia	125 (5.5%)	130 (6.8%)
		Unknown	55 (2.4%)	76 (4.0%)

Note: [a] 4 missing values as to school applicants. [b] 14 missing values as to school applicants, and 5 missing values as to maternal associations. [c] 15 missing values as to school applicants, and 14 missing values as to material associations. [d] All multiparity. *SD:* Standard Deviation.

tations and Japanese restrictions on epidemiological data collection.

Obstetric findings were obtained from the *Maternal and Child Health Handbook* (which is presented by the Ministry of Health, Labor and Welfare to all pregnant women and whose format varies depending on the policies of each city). No information on chorionicity was gathered.

The zygosity of the twins was determined primarily by a questionnaire (Ooki & Asaka, 2004) that was completed by the mothers in both groups. Zygosity — monozygotic (MZ), unclassified (UZ) and dizygotic (DZ) — was determined according to similarity scores calculated using five questions about physical similarity and the confusion of identity between the twins. In a previous study in which zygosity determination by DNA/genetic markers was regarded as the gold standard, the accuracy of the zygosity questionnaire was 97.5% (Ooki & Asaka, 2004), although around 10% of pairs were unclassified. A trade-off exists between high accuracy on the one hand and a high percentage of unclassified pairs on the other.

Informed consent regarding the statistical analysis of the school applicant group's data was obtained using written documents as part of the application process. The mothers of the maternal associations group all cooperated voluntarily with the study through the associations or through personal introductions.

Statistical Analysis

The basic characteristics of the samples were summarized, including zygosity, birth year of the twins, maternal and paternal age at the time of the birth of the twins, and gestational age.

Birthweights were then analyzed according to the subject's group and sex. Fiftieth percentiles by gesta-

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Table 2

Birthweight Characteristics of Both Groups According to Sex

	School applicants		Maternal associations	
	Male	Female	Male	Female
N	1053[a]	1200[b]	977[c]	916[d]
Mean (g)	2503	2452	2374	2274
Standard deviation (g)	455	427	445	443
Skewness	–0.03	–0.11	–0.70	–0.40
Kurtosis	0.08	0.28	1.39	0.65
Coefficient of variation	18	17	19	19
Median (g)	2500	2470	2410	2308
Range (g)	2910	3011	2925	2915
Range between 25 and 75 percentiles (g)	585	554	520	556
Fitting of normal distribution[e]	$p < 0.05$	$p < 0.01$	$p < 0.01$	$p < 0.01$
LBW (%)	48.2	52.0	58.7	68.6
VLBW (%)	1.2	1.9	4.1	5.2

Note: [a]4 missing values. [b]5 missing values .[c]5 missing values. [d]4 missing values. [e]Kolmogorov-Smirnov test. LBW: low birth weight < 2500. VLBW: very low birth weight, birthweight < 1500.

tional age were calculated. Smoothing of the growth curves was performed for both groups using a cubic spline function, and the curves compared with the birthweight norms for twins in Japan (Kato, 2004) calculated by using the vital statistics of around 65,000 pairs of twins.

Birthweight discordancy was also analyzed in order to estimate the selection bias through which severely discordant twins are unknowingly excluded from the twin database. For each twin pair, the intrapair relative birthweight difference (RBWD) was calculated as a percentage of the absolute difference of birthweight divided by heavier birthweight (Sadrzadeh et al., 2001), and then compared between the two groups. The mean RBWDs of MZ and DZ same-sex twin pairs within each group were tested using Student's *t* test. The mean RBWDs of twin pairs between groups were also compared to test the selection bias of severely discordant twin pairs. This selection bias was also tested using Student's *t* test.

Statistical analyses were all performed using SAS for Windows (1997). Smoothing of growth curves was performed using the PROC TRANSREG program by specifying the 'pspline' model.

Results

The basic characteristics of the subjects including the obstetric findings of the mothers are summarized in Table 1. The percentage of mothers treated with ovulation-stimulating drugs or in-vitro fertilization was much higher in the maternal associations group. The number of gestational weeks for the maternal associations group was one week less than that of the school applicant group. The mean birth year of the school applicant group was 1979, and 1995 for the maternal association group.

Basic statistics of birthweight are summarized in Table 2. Irrespective of sex, the birthweight of the school applicant group was more than 100g heavier than that of the maternal associations group. For the maternal associations group, twins conceived spontaneously (n = 632 pairs) had shorter gestations, slightly lower birthweights, and higher maternal ages at birth compared with twins conceived with assistance (n = 287 pairs): gestation, 36.8 weeks versus 37.2 weeks ($p < .05$); birthweight, 2306 g versus 2355 g ($p < .05$); maternal age, 30.2 versus 31.7 years

Table 3

Mean and Median Relative Birth Weight Difference in Percentage, Frequencies of Discordant Twins, and Intraclass Correlations According to Zygosity and Sex Combination

	School applicants RBWD						Maternal associations RBWD						Difference of RBWD between Two Groups	
	N	Mean	*SD*	Median	DT (%)	Intraclass correlation	*N*	Mean	*SD*	Median	DT (%)	Intraclass correlation	Variance	*p*
MZ	749	10.53	8.55	8.31	6.9	0.650	442	10.80	8.71	8.87	7.0	0.692	Equal	0.6062
MZM	334	10.44	8.47	8.34	6.6	0.658	234	11.25	8.88	9.35	7.3	0.648	Equal	0.2722
MZF	415	10.61	8.62	8.27	7.2	0.641	208	10.29	8.52	8.71	6.7	0.729	Equal	0.6654
DZSS	145	12.61	10.04	11.19	12.4	0.574	203	13.34	10.85	10.92	11.8	0.572	Equal	0.5269
DZM	77	14.67	10.67	13.21	18.2	0.564	94	13.45	10.95	11.52	11.7	0.556	Equal	0.4625
DZF	68	10.28	8.79	8.81	5.9	0.594	109	13.24	10.82	10.24	11.9	0.571	Equal	0.0591
DZOS	127	12.86	8.30	12.77	10.2	0.485	207	12.15	8.66	10.91	9.7	0.607	Equal	0.4603
SS(all)	997	10.92	8.83	8.81	7.7	0.637	739	11.71	9.50	9.78	8.8	0.652	Unequal	0.0797
SS(MZ + DZ)	894	10.87	8.84	8.68	7.8	0.636	645	11.60	9.50	9.64	8.5	0.652	Unequal	0.1272
SS(unclassified zygosity)	103	11.35	8.84	10.34	6.8	0.631	94	12.44	9.49	11.21	10.6	0.649	Equal	0.4067

Note: RBWD: Relative birth weight difference. DT: Discordant twins (RBWD ≥ 25%). MZM: Monozygotic males. MZF: Monozygotic females. DZM: Dizygotic males. DZF: Dizygotic females. DZSS: Dizygotic same sex. DZOS: Dizygotic opposite sex. SS: Same sex. The difference of mean RBWD between groups were tested using Student's *t* test.

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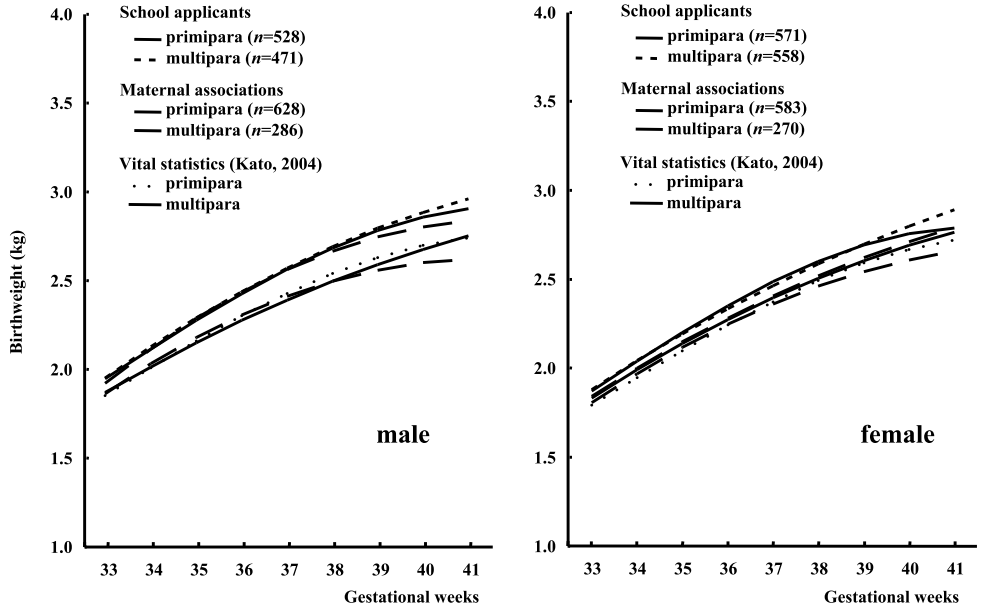

Figure 1

50th percentiles of birthweight according to gestational weeks.

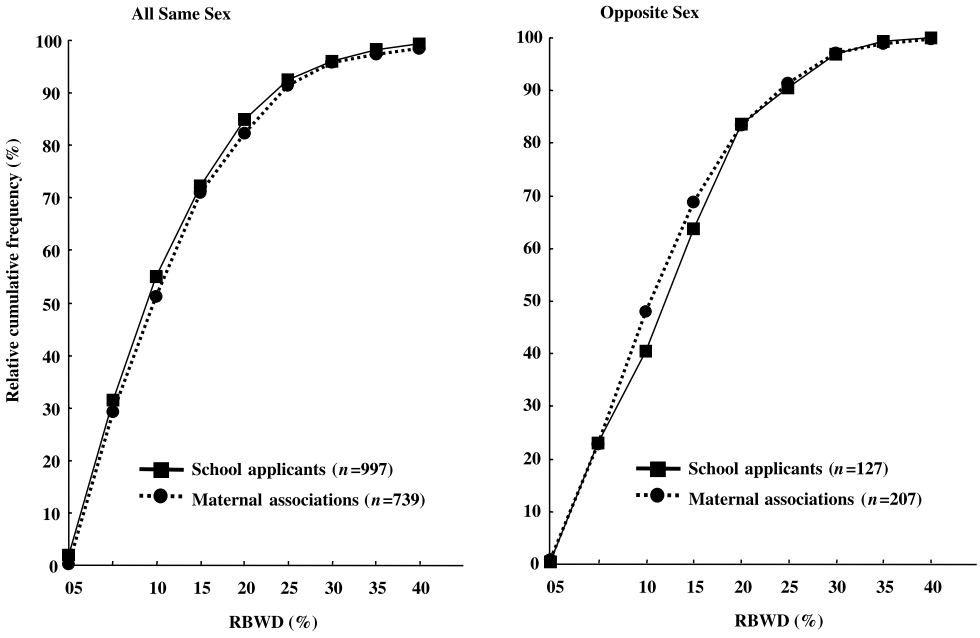

Figure 2

Curve of relative cumulative frequency of RBWD according to sex combination.

Note: RBWD = relative birthweight difference in percentage. All same sex pairs include pairs with unclassified zygosity.

(p < .0001). MZ twins conceived spontaneously were lighter than DZ twins conceived spontaneously in the school applicant group (2469 g vs. 2553 g, p = .0003). This tendency was not observed in the maternal associations group (2305 g vs. 2328 g, *ns*).

The smoothed curves of the birthweight 50th percentile according to gestational weeks separately for sex and parity are shown in Figure 1. Little difference was observed between the school applicant group, the maternal associations group, and the vital statistics.

The curves of the relative cumulative frequency of RBWD according to same-sex pairs and opposite-sex pairs are shown in Figure 2. At the 30% level of RBWD, the relative cumulative frequency of both groups reached between 96% and 97%, irrespective of the sex combination of the pairs. Mean and median

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RBWD in percentage, frequencies of discordant twin pairs and intraclass correlations according to zygosity and sex combination are shown in Table 3. The RBWD of MZ pairs was significantly lower than that of DZ same-sex pairs in both the school applicant group (p = .0206) and the maternal associations group (p = .0037), whereas no significant difference in RBWD was found between the two groups regarding zygosity and sex combinations.

Discussion

Data from the maternal associations and school applicant groups were gathered partly to evaluate the representativeness of the school applicants' data that had already been collected. Features of the school applicant group are as follows: first, both twins were alive and showed no marked growth disturbance at ages 11 and 12 years. Second, the twins lived only in the Tokyo Metropolitan area. Third, all in the group applied to take an entrance examination for a university-affiliated school and appear to have performed well in their schooling up to that point, which could exclude children with disabilities or low birthweight twins. These features may have an advantage regarding intrauterine growth, although the direct effect of these positive selection biases is difficult to specify.

The total MZ/DZ ratio for the school applicant group was 2.76 (754/273), and that of the maternal associations group was 1.08 (445/412). According to Imaizumi and Nonaka (1997), the Japanese MZ/DZ ratio has decreased from 1.90 in 1979 to 1.09 in 1994. The MZ proportion was much higher in the school applicant group, partly reflecting the higher proportion of spontaneous MZ twinning in this period in Japan, but also partly reflecting selection biases based on the sampling process itself whereby MZ pairs are more likely to be applicants.

There was a clear birth year difference between the groups. The mean birth year of the school applicant group was around 16 years earlier than that of the maternal associations group. There was a tendency towards higher maternal and paternal age, higher percentage of primiparity, and considerably higher frequency of treatment using ovulation-stimulating drugs or in-vitro fertilization in the maternal associations group in comparison with the school applicant group. These reflect recent birth trends in Japan including singleton births, reflected in the difference in twins' birth years between the two groups.

The maternal associations group birthweight was lower than that of the school applicant group, as shown in Table 2, partly reflecting the earlier gestational age of the twins in the maternal associations group. This finding may be partly attributed to the recent tendency in Japanese obstetrics to keep maternal body weight gains from becoming too great. Nevertheless, the birthweight of both groups according to gestational weeks was not extremely different to that of the general twin population in Japan (Kato, 2004), as shown in Figure 1.

Many reports have indicated differences between twins conceived spontaneously and those conceived with assistance in maternal and birth characteristics such as socioeconomic and educational status, maternal age, gestation, and birthweight (Helmerhorst, et al., 2004; Zaib-un-Nisa et al., 2003). The maternal associations group clearly reflected some of these differences. Detailed analyses of these characteristics are the next step in the study.

Data on biometrical birth parameters might be influenced by birth year and recruitment methods. According to the results of Sadrzadeh et al. (2001), who analyzed potential biases regarding birthweight in the historical and contemporary twin databases of the Australian Twin Registry (Treloar et al., 2000), the Netherlands Twin Registry (Boomsma, 1998), and the East Flanders Prospective Twin Survey (Loos et al., 1998), each twin registry has its own features represented by birthweight data. MZ twins are subject to negative selection in historical databases through which severely discordant twins are unintentionally excluded, whereas the hypothesis that MZ twins are less discordant for birthweight in a volunteer-based twin registry than in a population-based twin registry had to be rejected.

At the 25%, 30%, 35% and 40% levels of RBWD, the relative cumulative frequency was nearly the same for both groups irrespective of sex combination, as shown in Figure 2. This suggests that there is no fatal selection bias of severely discordant twin pairs in the school applicant group. Some unexpected selection biases may exist, however. We conclude that the obstetric and birthweight features of both groups based on the methods of sample selection should be considered to construct growth charts of twins using this data.

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References

Boomsma, D. I. (1998). Twin registers in Europe: An overview. *Twin Research, 1,* 34–51.

Helmerhorst, F. M., Perquin, D. A. M., Donker, D., & Keirse, M. J. N. (2004). Perinatal outcome of singletons and twins after assisted conception: A systematic

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review of controlled studies. *British Medical Journal, 328,* 261.

Imaizumi, Y., & Nonaka, K. (1997). The twinning rates by zygosity in Japan, 1975–1994. *Acta Geneticae Medicae et Gemellologiae, 46*, 9–22.

Kato, N. (2004). Reference birthweight range for multiple birth neonates in Japan. *BMC Pregnancy and Childbirth*, *4*, 2.

Loos, R., Derom, C., Vlietinck, R., & Derom, R. (1998). The East Flanders Prospective Twin Survey (Belgium): A population-based register. *Twin Research, 1*, 167–175.

Ooki, S., & Asaka, A. (2004). Zygosity diagnosis in young twins by questionnaire for twins' mothers and twins' self-reports. *Twin Research, 7,* 5–12.

Ooki, S., & Yokoyama, Y. (2003). Reference birth weight, length, chest circumference, and head circumference by gestational age in Japanese twins. *Journal of Epidemiology, 13*, 333–341.

Ooki, S., & Yokoyama,Y. (2004). Physical growth charts from birth to six years of age in Japanese twins. *Journal of Epidemiology, 14*, 151–160.

Sadrzadeh, S., Treloar, S. A., Van Baal, G. C., & Lambalk, C. B. (2001). Potential bias regarding birth weight in histrical and contemporary twin data bases. *Twin Research, 4,* 332–336.

SAS. (1997). *SAS/STAT Software: Change and enhancement through Release 6.2*. Carey, NC: SAS Institute, Inc.

Treloar, S. A., Sadrzadeh, S., Do, K. A., Martin, N. G., & Lambalk, C. B. (2000). Birth weight and age at menopause in Australian female twin pairs: Exploration of the fetal origin hypothesis, *Human Reproduction, 15*, 55–59.

Zaib-un-Nisa, S., Ghazal-Aswad, S., & Badrinath, P. (2003). Outcome of twin pregnancies after assisted reproductive techniques: A comparative study. *European Journal of Obstetrics and Gynecology, 109,* 51–54.

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