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Secular Trends in Obesity and Serum Lipid Values among Children in Oita City, Japan, during a 27-Year Period

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Aims: We assessed 27-year trends in obesity and blood lipid levels of 10-year-old children to estimate the risk of metabolic syndrome in adulthood.

Methods: Based on a screening program for lifestyle-related diseases in school children in Oita City, Japan, we evaluated secular trends in height, weight, percentage of overweight (POW), total cholesterol (TC), triglyceride (TG), HDL cholesterol (HDL-C), and non-HDL cholesterol (non-HDL-C) of fifth graders (median age: 10.8 years) in Oita City from 1991 to 2017. We focused on the secular trend in the percentage of children with inappropriate serum levels of each lipid. We also evaluated the long-term trends in the 95th, 50th, and 5th percentiles for each parameter, as dependent variables, with the calendar year as an independent variable. Percentages of children with mild obesity (POW-20), moderate obesity (POW-30), and severe obesity (POW-50) were set as dependent variables.

Results: A total of 58,699 boys and 56,864 girls were evaluated during the study period. The percentage of children with severe obesity (POW-50) consistently increased during these years, and the 95th percentile of degree of obesity significantly increased in both boys and girls. The plot of percentages of children with inappropriate levels of TC, TG, and non-HDL-C showed a mild inverted U shape during the study period. The HDL-C level typically decreased in the study period, and the TC, TG, and non-HDL-C levels were markedly higher while the HDL level was lower in obese children than in non-obese children.

Conclusion: The number of children with severe obesity increased, and obese children had higher percentages of inappropriate lipid levels than non-obese children. The rate of dyslipidemia with low HDL levels gradually increased in all children in Oita City, Japan, over the past 27 years.

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Key words: HDL cholesterol, Non-HDL cholesterol, Children, Percentage of overweight

Introduction

In developed countries, the prevalence of childhood obesity has substantially increased among all age groups since 1988 [1]. Recent studies from the United States demonstrated that obesity in children and adolescents was almost stable or decreased in the early 2000s with social or medical intervention[2, 3]; however, a marked increase in the prevalence of severe obesity was reported, particularly among adolescents and non-Hispanic African American children[4, 5]. A report based on an analysis of 2012–2013 in England also demonstrated a significant increase in severe obesity among children of 2 to 5 years of age[6], and an upward trend continued with a substantial excess of overweight-obesity among South Asian children and Black girls, even with implications for overweight prevention[7].

In Japan, lifestyle-related diseases in adulthood were recognized in the early 1990s to be deeply involved in daily eating and exercise habits[8]. Approximately 8% of Japanese are diagnosed with lifestyle-related diseases or metabolic syndrome in adulthood[9]. Obesity in childhood was also recognized

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in the late 1990s to be associated with susceptibility to metabolic syndrome in adulthood[10]. A longitudinal study based on the data from cross-sectional annual nationwide surveys demonstrated that from 1975 to 2000, the mean (age-adjusted) body mass index (BMI) significantly increased in boys and girls of 6–14 years of age and that the increase in small towns was greater than that in medium-size cities or metropolitan areas (National Nutrition Survey, Japan)[11]. Early prevention of childhood obesity was advocated in 2001, and the diagnostic criteria for pediatric metabolic syndrome were clarified in 2007 by a Ministry of Health, Labor and Welfare research group[12].

Preventive programs for lifestyle-related diseases have been carried out across many municipalities in Japan. Children at school age who are at risk of future lifestyle-related diseases have been screened and medical intervention has been provided. However, the screening strategy, the criteria for determining children who should receive intervention and intervention methods vary greatly among municipalities in Japan. Oita City, the capital of Oita Prefecture in Kyushu Island, Japan, is a mid-sized city in Japan with a population of >470,000 in 2015. The healthy check-up program for fifth graders (10-year-old children) called "screening for lifestyle-related diseases in elementary school children" has been carried out in Oita City since 1991.

We herein report the long-term trends in the 27-year anthropometric indices and serum lipid data of fifth-grade school children from the Oita City program.

Methods and Population

Participants

The municipal government of Oita City in Oita Prefecture started a screening program for the prediction of lifestyle-related diseases in 1979. Blood biochemistry tests were included in the program from 1991. As of 2020, Oita City administers 60 public elementary schools, which have had relatively stable student numbers over the last decade. The screening program was offered to all fifth graders in public elementary schools in the municipality; approximately 85%–95% were enrolled and gave their informed consent. The mean number of fifth graders each year was 2,174 for boys and 2,106 for girls. The anthropometric and blood data were reviewed each year by a committee of pediatric endocrine/metabolic disease experts, personal counseling was provided for participants as needed, and medical information on lifestyle-related diseases was provided to all citizens of Oita. The cumulative data of the medical examinations of 58,699 boys and 56,864 girls were analyzed.

Method of Examination

The screening program was conducted every year from August to December and anthropometric measurements and blood collection were performed at each school by the assigned pediatricians and nurses. The screening parameters included anthropometric measurements (height, weight, percentage of overweight [POW]) and a blood test. The degree of obesity was calculated from the measured height and weight. In Japan, POW is used in children more commonly than the BMI-for-age percentile and is calculated based on the measured weight and standard weight for height as follows: POW (%) = 100 × (measured weight - standard weight for height)/ standard weight for height. The standard weight is the age- and sex-specific weight for height; the coefficients and formula have been described in detail previously. Children with a POW ≥ 20% and <30% (POW-20) are defined as mildly obese, those with POW ≥ 30% and <50% (POW-30) are defined as moderately obese, and those with POW ≥ 50% (POW-50) are defined as severely obese[13]. Blood collection was performed after at least two hours after breakfast but not in a fasting state in the strict sense. The test parameters included total cholesterol (TC), triglyceride (TG), HDL cholesterol (HDL-C), ALT, a complete blood count of the red blood cells, white blood cells, and platelets with the concentration of hemoglobin, and the hematocrit. Non-HDL cholesterol (non-HDL-C) was calculated as TC minus HDL-C. All blood samples were measured in the laboratory at the Oita Prefectural Adult Disease Screening Center. The anthropometric measurements of height, weight, and POW and blood data of TC, TG, HDL-C, and non-HDL-C from 1991 to 2017 were used in the present study and applied in the statistical analysis.

Trends in the Prevalence of Inappropriate Lipid Levels

Based on the cut-off levels for an elevated TC (≥ 220 mg/dl), TG (≥ 140 mg/dl), and non-HDL-C (≥ 150 mg/dl) and reduced HDL-C (<40 mg/dl), defined according to the Japan Atherosclerosis Society Guidelines for Prevention of Atherosclerotic Cardiovascular Diseases 2017[14] and the 2011 Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents[15], the secular trends in the prevalence of children with inappropriate lipid levels are summarized as plots every three years. These data were also separately evaluated and shown in obese and non-obese children.

Geographic features of Oita City

The Oita Prefecture is located on the northeast side of the coastal area of Kyushu Island. Oita City is the capital city of Oita Prefecture, which is located in the center, on the coastal side of the prefecture. The population of Oita City was approximately 470,000 in 2015 and accounted for 40% of the prefecture's population. The population of suburban areas of Oita City has been growing in recent years, accompanied by the development of new towns and shopping centers. Children <15 years of age and elderly individuals >65 years of age account for 13.7% and 27.1% of the population, respectively. The corresponding numbers of the national average in Japan are 12.1% and 27.6%, respectively. Primary, secondary, and tertiary accounted for 1.9%, 22.4%, and 70.5% of industries, respectively. In Japan, the corresponding percentages were 4.0%, 25.0%, and 71.0%, respectively.

Statistical Analyses

The following two methods were used to analyze the secular trends for each parameter: the weighted least-squares method and the quadratic linear weighted least-squares (quadratic) method. The values of Akaike's information criterion (AIC), R-Squared method (R-Squared), mean absolute error (MAE), and likelihood ratio test were referenced to select the most appropriate method; a smaller AIC value, larger R-Squared value, smaller MAE value, and larger likelihood ratio test value were considered to indicate a more appropriate method. The sample size was also included as an independent variable in each analysis model, and the fluctuation of the sample size was taken into consideration each year.

A regression analysis was performed to evaluate the annual trends in height, weight, POW, TC, TG, HDL-C, and non-HDL-C from 1991 to 2017. In all regression models, the calendar year was the independent variable, and the 95th, 50th, and 5th percentiles of the achievement rate were the dependent variables. For a further analysis of obesity, the percentages of children with mild obesity (POW-20), moderate obesity (POW-30), and severe obesity (POW-50) in each year were set as dependent variables. A generalized linear model was created that also included the sample size as an independent variable to account for the varying sample sizes each year. In the weighted non-linear least-squares model, weights were created by regressing the residuals with the fitted values of the un-weighted non-linear regression. Different sets of weights were calculated for each percentile group.

This study was approved by the Ethics Committee of Oita University School of Medicine (Approval number: 1525).

Results

Population Statistics

Table 1 shows the summary of the anthropometric and biochemical data from 1991 to 2017. The plot of the number of fifth-grade students in Oita City followed a U-shape pattern from 1991 to 2017; the number of students were 6235 in 1991, which declined to approximately 4000 and remained stable from 2001 to 2010 and gradually recovered from 2011 to 2017, reaching 4453 in 2017. The percentage of participants among all fifth graders (estimated median age of 10.8 years old) gradually decreased from >98% to approximately 83%, and the rate of participation among boys and girls was almost the same (94.7% vs. 94.9%). The sex distribution remained almost constant over time, with boys accounting for an average of 50.8% of the study population.

Secular Trends in Obesity

The secular trends of the percentages of children with obesity (i.e., mild obesity (POW-20), moderate obesity (POW-30), and severe obesity (POW-50)) are shown in **Fig. 1**. The numbers of children with mild and moderate obesity seemed to slightly fluctuate, whereas those of severe obesity gradually increased during the observed years among both boys and girls.

The annual trend in obesity was statistically evaluated and matched to the quadratic method **(Suppl. Table 1)**. The percentage of children with mild obesity (POW-20) showed weak peaks early in the observation period (in 1994 for boys and 2001 for girls, respectively). The percentages of moderate and severe obesity (POW-30 and POW-50) generally increased, with peaks observed later in the observation period (in 2014 and 2009 for boys, and 2017 and 2016 for girls) **(Suppl. Table 2)**.

Secular Trends in Anthropometric Data

A regression analysis was performed to evaluate the annual trends in height, weight, and POW, with only height ultimately being matched to the quadratic method **(Suppl. Table 3)**; however, the quadratic curves of height seemed very gentle **(Suppl. Fig. 1 A)**. The 95th percentile of height for boys and the 5th, 50th, and 95th percentile of height for girls significantly increased. The body weight was almost consistent,

Table 1A. Secular trend in the percentile values of anthropometric measurements and serum lipid data. (Boys: $n=58699$)

Year	Number	Consultation rate (%)	Height (cm)			Weight (kg)			Percentage of overweight (%)			Total Cholesterol (mg/dL) Percentiles			Triglyceride (mg/dL)			HDL Cholesterol (mg/dL)			Non-HDL Cholesterol (mg/dL)		
			5th	50th	95th	5th	50th	95th	5th	50th	95th	5th	50th	95th	5th	50th	95th	5th	50th	95th	5th	50th	95th
1991	3048	97.9	131	140	151	27	34	51	-19	-3	28	133	170	218	32	58	128	47	65	89	69	104	150
1992	2843	98.5	131	140	150	26	33	49	-18	-2	32	135	172	219	32	60	133	46	65	91	73	105	150
1993	2875	91.0	130	140	150	26	34	50	-16	-2	32	136	173	224	30	58	130	47	65	90	74	107	155
1994	2764	90.2	131	140	151	26	34	51	-18	-2	34	135	173	220	33	61	139	46	66	90	73	105	151
1995	2437	88.4	131	140	151	27	34	51	-17	-1	34	136	174	221	32	60	136	47	69	98	70	103	150
1996	2412	98.4	130	140	152	26	34	52	-19	-2	31	140	177	224	32	64	154	46	65	89	78	110	157
1997	2185	97.9	130	140	151	26	34	52	-19	-4	33	137	175	223	32	63	155	47	69	96	71	105	154
1998	2223	98.1	131	140	152	27	34	53	-20	-4	32	138	176	223	33	66	159	45	67	93	74	107	157
1999	2120	97.7	131	140	152	26	34	52	-20	-5	29	138	175	222	32	64	150	47	67	91	74	106	153
2000	2053	98.7	131	141	152	26	35	54	-20	-3	35	140	178	227	34	66	158	46	68	94	76	108	158
2001	2024	96.6	130	141	152	26	35	53	-18	-3	34	138	176	224	33	66	160	45	66	92	76	108	155
2002	2021	98.4	130	141	152	26	34	53	-21	-5	32	138	177	225	31	62	147	46	66	91	76	109	157
2003	2004	98.8	130	140	151	26	34	52	-20	-4	33	140	176	224	33	67	162	45	65	90	77	110	157
2004	2015	98.3	130	140	151	26	34	53	-19	-4	34	137	174	222	33	64	156	44	61	83	80	111	158
2005	2099	99.0	130	140	151	26	34	52	-20	-4	35	137	175	221	31	63	152	45	65	89	76	109	156
2006	1984	98.6	130	140	151	26	34	53	-20	-4	34	138	178	227	33	64	157	46	65	90	78	111	158
2007	2018	98.3	130	140	152	26	34	53	-19	-3	34	140	178	225	31	64	151	48	67	93	77	108	156
2008	2009	98.6	131	141	152	26	34	52	-18	-3	33	138	178	228	30	61	147	46	66	90	78	110	160
2009	1948	97.7	131	140	152	26	34	51	-18	-3	34	139	176	226	32	60	139	47	66	90	75	108	158
2010	1959	97.5	131	140	151	26	34	52	-19	-3	33	136	176	224	33	63	155	47	67	90	74	108	156
2011	2025	98.6	130	140	151	26	34	51	-18	-2	34	137	174	221	32	65	141	46	66	90	75	107	153
2012	2085	98.5	131	141	152	26	34	51	-17	-1	34	133	170	217	30	61	151	44	61	86	76	107	151
2013	2006	88.1	131	140	152	26	34	51	-17	-1	34	133	170	218	30	59	143	45	63	87	75	105	149
2014	1966	84.6	130	141	152	26	34	52	-19	-3	31	133	170	218	31	58	135	45	64	87	75	106	153
2015	1926	85.9	130	140	151	26	34	52	-19	-3	35	134	172	218	29	60	143	44	63	86	75	107	152
2016	1789	84.5	130	140	152	26	33	52	-19	-3	35	134	172	218	30	58	146	44	63	85	76	107	152
2017	1861	83.0	131	140	152	26	34	52	-19	-2	33	135	172	218	30	61	143	44	63	85	77	106	150

Table 1B. Secular trend in the percentile values of anthropometric measurements and serum lipid data. (Girls: $n=56864$)

Year	Number	Consultation rate (%)	Height (cm)			Weight (kg)			Percentage of overweight (%)			Total Cholesterol (mg/dL) Percentiles			Triglyceride (mg/dL)			HDL Cholesterol (mg/dL)			Non-HDL Cholesterol (mg/dL)		
			5th	50th	95th	5th	50th	95th	5th	50th	95th	5th	50th	95th	5th	50th	95th	5th	50th	95th	5th	50th	95th
1991	2867	91.9	131	142	153	26	35	49	-18	-3	26	130	169	216	37	65	132	46	62	86	72	106	150
1992	2741	96.3	131	142	154	26	35	50	-17	-2	27	133	170	218	36	66	132	46	62	84	74	107	152
1993	2778	91.1	131	142	153	26	34	49	-17	-3	27	135	171	221	35	62	124	45	62	85	76	109	154
1994	2706	91.4	131	142	153	26	34	49	-19	-3	26	134	170	214	38	67	133	45	62	84	75	107	150
1995	2450	91.1	131	142	153	26	34	49	-18	-2	28	137	173	219	37	66	139	45	65	91	74	106	152
1996	2363	98.7	131	142	153	26	35	52	-18	-2	29	138	176	221	37	67	149	45	62	84	79	112	157
1997	2280	98.3	131	142	154	26	35	51	-19	-4	28	137	174	222	38	69	148	46	66	91	73	105	152
1998	2068	98.8	132	142	154	26	35	51	-19	-3	28	138	175	220	37	69	152	47	65	90	76	109	152
1999	2078	98.9	131	142	154	26	35	50	-19	-3	27	136	174	219	37	68	149	46	64	87	76	108	152
2000	2012	98.7	131	143	153	26	35	50	-19	-4	28	137	174	224	37	69	142	47	65	89	75	109	154
2001	1826	95.8	131	143	154	26	35	50	-19	-3	28	139	173	218	38	69	146	45	63	87	78	109	154
2002	1986	99.0	131	142	154	26	35	51	-19	-3	28	135.4	174	221	37	66	144	46	63	85	77	109	154

(Cont. Table 1B)

Year	Number	Consultation rate (%)	Height (cm)			Weight (kg)			Percentage of overweight (%)			Total Cholesterol (mg/dL) Percentiles			Triglyceride (mg/dL)			HDL Cholesterol (mg/dL)			Non-HDL Cholesterol (mg/dL)		
			5th	50th	95th	5th	50th	95th	5th	50th	95th	5th	50th	95th	5th	50th	95th	5th	50th	95th	5th	50th	95th
2003	1953	99.4	131	142	153	26	34	50	-20	-4	30	136	175	220	37	68	154	44	62	83	77	111	156
2004	1842	99.2	131	142	154	26	35	52	-19	-5	27	135	173	220	36	66	149	43	59	79	79	112	158
2005	1997	99.0	131	143	154	26	35	51	-19	-5	27	137	173	222	35	66	140	45	62	84	78	110	155
2006	1909	98.7	131	143	154	26	35	51	-20	-4	30	137	175	225	38	69	149	45	62	84	77	112	157
2007	1927	99.3	131	143	154	26	35	50	-19	-3	28	138	176	226	37	69	147	46	65	88	77	110	157
2008	1926	98.2	132	143	154	27	35	50	-18	-3	28	137	175	225	37	66	145	45	63	85	80	111	158
2009	1937	97.8	131	143	153	26	34	50	-19	-4	27	136	175	227.1	36	66	138	45	63	85	77	111	159
2010	1958	98.7	132	142	153	26	34	49	-18	-3	27	136	174	222	37	68	145	46	64	85	77	109	154
2011	1961	99.3	132	142	154	26	34	50	-17	-2	27	136	173	224	39	70	147	45	63	85	77	109	159
2012	2072	98.9	131	143	154	26	35	50	-18	-2	27	133	169	219	35	64	133	43	60	80	78	109	154
2013	1924	90.6	131	143	154	26	35	50	-17	-2	30	134	171	220	35	65	139	44	61	81	78	108	154
2014	1869	87.2	131	143	153	26	35	50	-19	-3	27	133	170	218	34	64	135	44	61	81	78	108	152
2015	1775	86.3	132	142	154	26	35	50	-17	-2	29	133	171	219	35	64	132	44	61	82	77	109	155
2016	1774	83.4	132	143	154	26	35	50	-17	-2	29	133	171	215	34	63	135	45	60	80	76	109	151
2017	1885	85.3	131	142	154	26	34	50	-18	-3	31	135	171	216	34	64	140	45	61	82	76	108	152

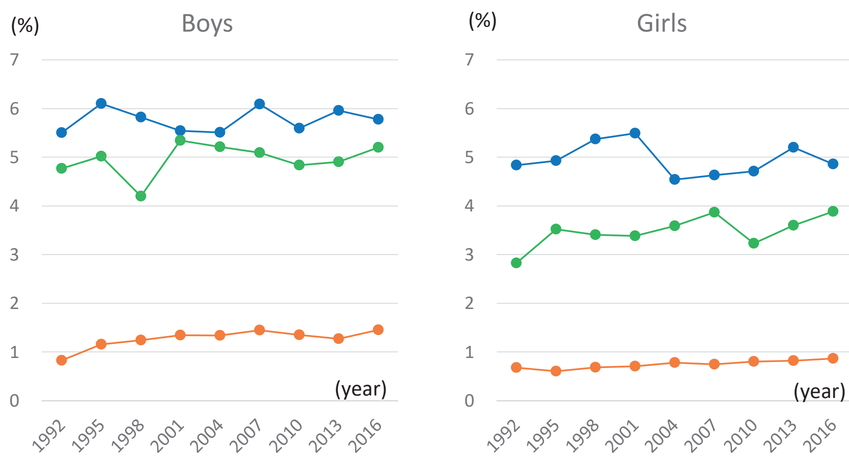

Fig. 1. Secular trends in the percentages of children with obesity

Left side, boys; right side, girls. Data obtained every three years are serially shown. Blue circles, mild obesity (POW-20); green circles, moderate obesity (POW-30); and orange cycles, severe obesity (POW-50).

except for a decrease in the 5th percentile of weight for boys **(Suppl. Fig. 1B)**. The 95th percentile of POW significantly increased for both boys and girls **(Suppl. Fig. 1C, Suppl. Table 4)**.

Secular Trends in Serum Lipid Analytes

Table 1 also shows the long-term trends in serum lipids (TC, TG, HDL-C, and non-HDL-C). A regression analysis was performed to evaluate the annual trends in lipids, which mostly matched the quadratic method **(Suppl. Table 3)**. The 5th, 50th, and 95th percentile values of TC, TG, and non-HDL-C values showed a mild inverted U shape with peaks during the later years of the observation period **(Suppl. Fig. 2 A, B, and D)**. In contrast, the HDL-C level mostly decreased, with modest peaks during the earlier years of the observation period **(Suppl. Fig. 2C and Suppl. Table 5)**.

Trends in Inappropriate Levels of Serum Lipid in Obese and Non-Obese Children

The secular trends in the percentage of children with TC, TG, and non-HDL-C above or HDL-C values below the cut-off levels are shown in **Figure 2A-D**. Inverse U shapes were observed in the percentages of increased TC, TG, and non-HDL-C levels, whereas a gradual increase in children with reduced HDL-C levels was shown. The inappropriate lipid levels in non-obese and obese children were separately evaluated, and the percentages of obese children with inappropriate levels of lipids were markedly higher than among non-obese children **(Fig. 3A-D)**. In particular, the percentage of severely obese children with reduced HDL-C levels gradually increased during the 27-year period **(Fig. 4)**.

Secular trends in lipid levels were separately evaluated and classified by the degree of obesity: mild obese (POW-20), moderate obese (POW-30), severe obese (POW-50), and non-obese **(Suppl. Fig. 3A-D)**. TG and non-HDL-C levels were consistently higher in obese children than in non-obese ones, and HDL-C levels were lower in obese children than in non-obese ones.

Discussion

This study reported the secular trends in overweight children and the blood lipid profiles of fifth-grade elementary school students. The trend in the rate of severe obesity in children in Oita City showed a gradual increase over the 27-year study period. The data seem consistent with the data of the school health statistics reported by the Ministry of Education, Culture, Sports, Science and Technology. The percentage of obese children of 11 years of age in Japan was increased from 6.72% for boys and 6.18% for girls in 1977 to 11.82% for boys and 9.65% for girls in 2006, then gradually decreased to 9.69% for boys and 8.72% for girls in 2017, and then re-increased to 11.11% for boys and 8.84% for girls in 2019 [16]. Kouda *et al.* reported that the prevalence of obesity tended to increase in children in Iwata City from 1997 to 2001 [17], whereas they also reported that the 95th percentile of BMI increased, and that the 5th percentile decreased from 1993 to 2008 [18]. Kouda *et al.* also reported that children in Fukuroi City, adjacent to Iwata City in Shizuoka Prefecture, were almost stable from 2007 to 2017 [19]. In contrast, Shirakawa *et al.* reported that the prevalence of obesity of children in the small town of Ina in Saitama Prefecture, Japan, tended to decrease according to a survey conducted from 2003 to 2012 [20]. Tanaka *et al.* also reported a decreasing trend from 2009 to 2011 and that the rates of moderate or severe obesity remained almost stable thereafter in the Setagaya area in Tokyo, a metropolitan area of Japan [21]. Overall, the obesity of Japanese children tended to increase from the 1980s to 2000, and the increasing trend peaked in the early 2000s and stabilized or generally decreased, especially in large cities or metropolitan areas in comparison to small towns. A further study, however, indicated that the rate of severe obesity in rural areas or small towns continued to increase, as shown in Iwata City by Kouda *et al.*, and in Oita City in the present study. This probably depends on the environmental or cultural aspects of life in each city. In particular, in Oita City, the rates of childhood obesity have long been consistently higher than the national average (fifth graders: 10.3% in 1994, 11.2% in 2000, 10.1% in 2010, and 11.1% in 2018). These results suggest that it would be difficult to change the rate of childhood obesity in municipalities with a high rate of childhood obesity, especially small-size rural cities.

To our knowledge, there have been no reports on the long-term secular trend (>+25 years) of serum lipid values in Japanese children of around 10 years of age. According to reports on the secular trend in serum lipids, there were no significant changes in TC, non-HDL-C, and HDL-C in Iwata City from 1993 to 2008 [18], whereas HDL-C seemed to slightly increase in Fukuroi from 2007 to 2017 [19]; both were adjacent small cities in Shizuoka. In contrast, our longitudinal study of Oita City, a mid-size capital city of Oita Prefecture, from 1991 to 2017 demonstrated a downward trend in HDL-C after the late 1990s and a slight upward trend in TC, TG, and non-HDL-C after the early 2000s. Notably, these trends were remarkable in obese children. These data suggest that the risk of dyslipidemia or cardiovascular disease in adulthood seemed consistent in Oita City, but careful observations are needed, especially concerning the decreasing secular trend in HDL-C, particularly in obese children.

The present study was associated with some limitations. First, since the rate of registration was approximately 80%–90%, the remaining unenrolled children might have had different characteristics (i.e., an underlying selection bias might have affected the results). It has been reported that the rate of severely lean children with psychological disorders, such as anorexia nervosa, has been increasing in Japan; this trend was not observed in the present study. We hypothesize that severely lean children, especially girls, would have avoided enrolling in this health check-up program; this is suggested by the lower enrollment ratios in the later years. Second, the serum HDL-C and LDL-C levels are negatively associated with testosterone or estradiol in boys or girls during puberty; however, we could not evaluate the stage of puberty. Since the height, weight, and obesity index of

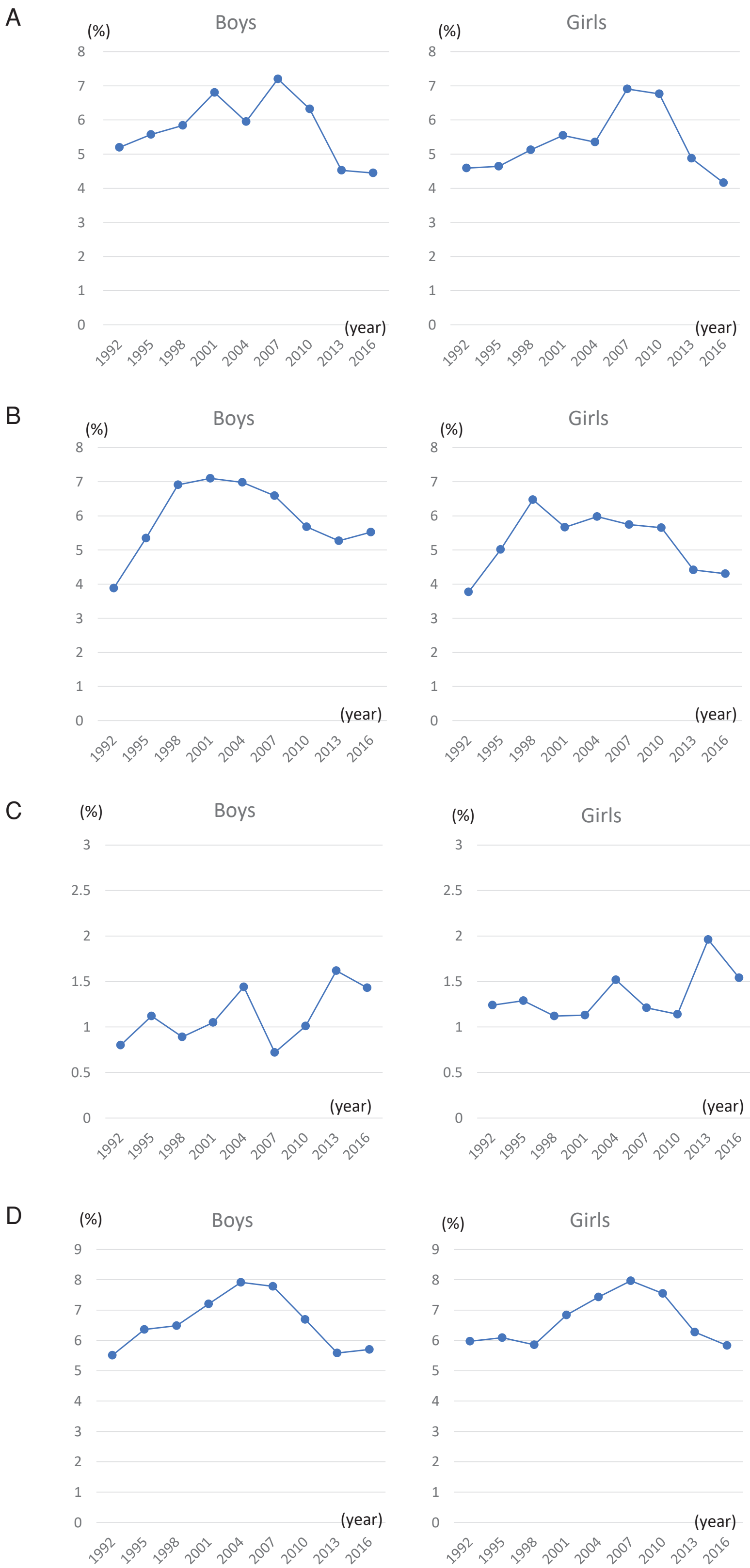

Fig. 2. Secular trends in the percentage of children with inappropriate levels of lipids

A, TC ≥ 220 mg/dl; B, TG ≥ 140 mg/dl; C, HDL-C <40 mg/dl; and D, non-HDL-C ≥ 150 mg/dl. Left side, boys; right side, girls. Data obtained every three years are serially shown.

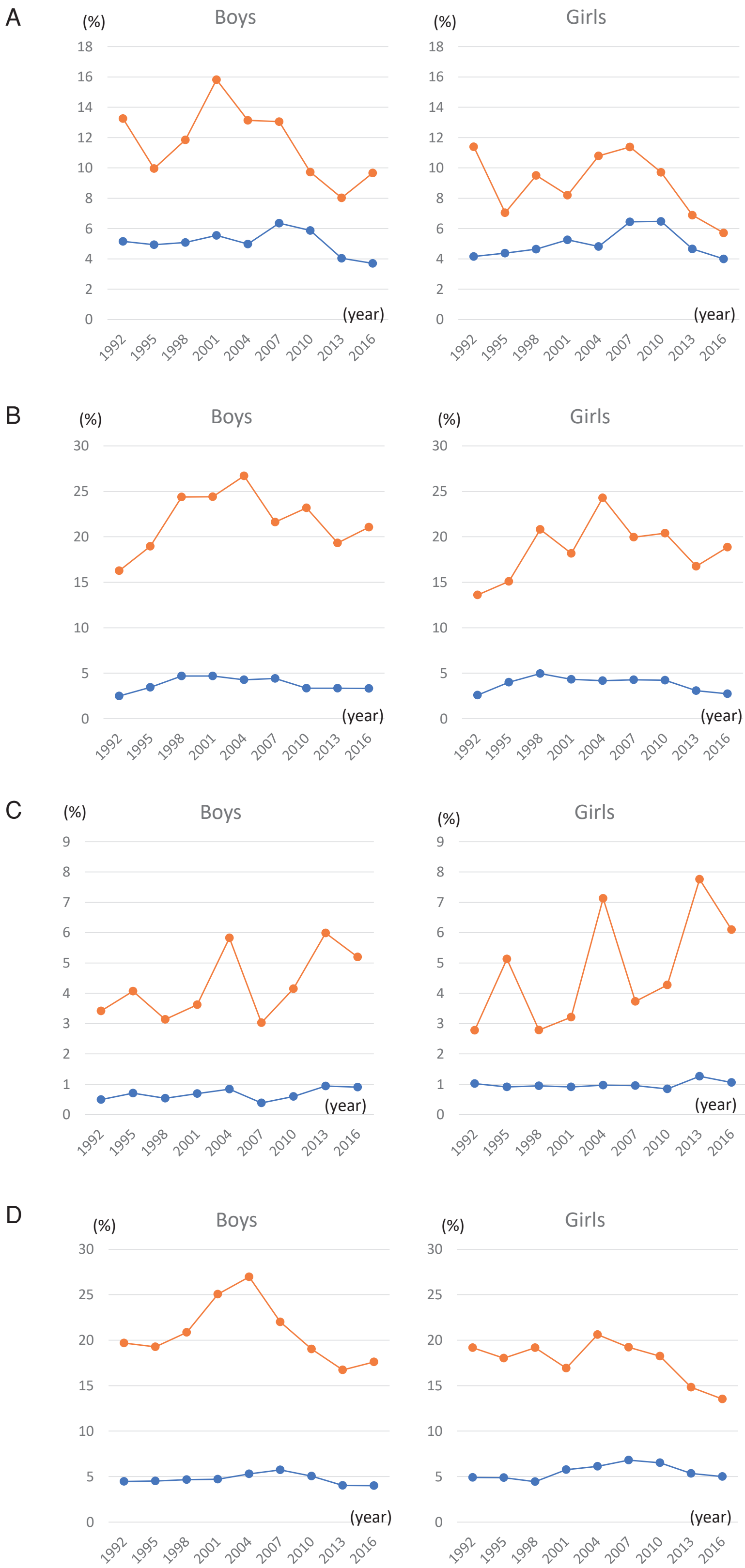

Fig. 3. Secular trends in the percentages of children with inappropriate levels of lipids in non-obese or obese

A, TC ≥ 220 mg/dl; B, TG ≥ 140 mg/dl; C, HDL-C < 40 mg/dl; and D, non-HDL-C ≥ 150 mg/dl. Left side, boys; right side, girls. The dots of three-year data are serially shown. Blue circles, non-obese (POW < 20) and orange circles, obese (POW ≥ 20).

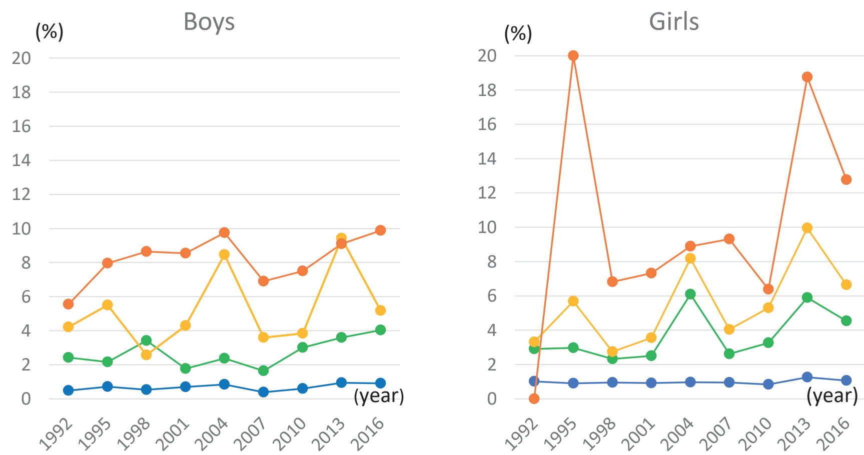

Fig. 4. Comparison of secular trends in the percentages of children with lower HDL-cholesterolemia divided by POWs

Left side, boys; right side, girls. The dots of three-year data are serially shown. Blue circles, non-obese; green cycles, mild obesity (POW-20); yellow cycles, moderate obesity (POW-30); and orange circles, severe obesity (POW-50).

the enrolled children gradually increased during the 27-year period, especially in girls, it might be associated with the trend in the rejuvenation of puberty. This might—at least in part—have influenced the secular trend in serum cholesterol values. Finally, affected individuals with familial hypercholesterolemia (FH) were included in this study although we did not evaluate this point. FH is an autosomal dominant disease caused by abnormalities in the genes that encode low-density lipoprotein (LDL) receptors or related molecules, characterized by hyper-LDL cholesterolemia with an estimated prevalence of approximately 1 in 200–500 in Japan[22). It is estimated that about 10–20 children with FH were included per year, showing very high cholesterolemia without obesity. A further study considering the familial history of FH or medical information of the enrolled children will be important when re-evaluating the findings of the present study.

Conclusion

We reported the analysis of 27 years of anthropometric and blood chemistry data from a children's lifestyle-related disease screening program in Oita City. The obese children had higher percentages of inappropriate lipid levels than non-obese ones. Primary intervention to prevent obesity at earlier school grades would be important for decreasing childhood obesity and for reducing lifestyle-related diseases when these children reach adulthood.

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Conflict of Interest

The authors declare no conflicts of interest in association with the present study.

Ethics

This study was approved by the ethics committee of Oita University Hospital, Oita, Japan (No. 1525). All procedures followed were performed in accordance with the Helsinki Declaration of 1964 and its later amendments.

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Supplementary Table 1. Validation of the regression models by four estimation methods

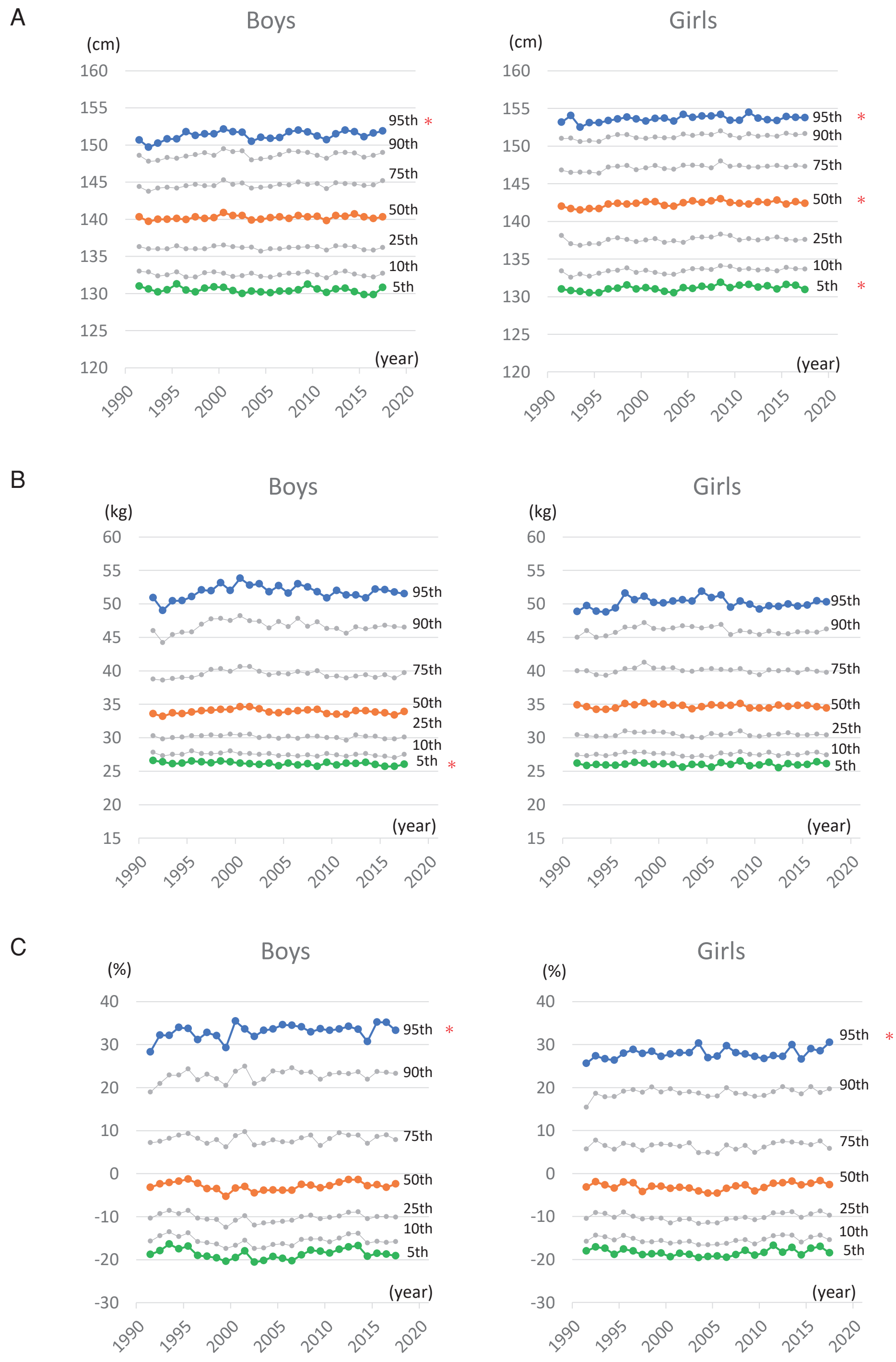
		Percentage of overweight (%)	Regression models	Degree of suitability				Decision
				AIC	R-Squared	MAE	Likelihood Ratio Test	
boys	Prevalence of obesity (%)	20 to <30	WLS	263.9979	0.0848	20.8958	-128.9990	Quadratic
			Quadratic	201.2367	0.8913	6.0901	-95.6180	
		30 to <50	WLS	243.5526	0.0147	13.6816	-118.7760	Quadratic
			Quadratic	207.4312	0.7599	7.4561	-98.7160	
		≥ 50	WLS	192.2043	0.3230	5.6575	-93.1020	Quadratic
			Quadratic	150.4751	0.7482	2.6621	-70.2380	
girls	Prevalence of obesity (%)	20 to <30	WLS	252.7594	0.0914	18.9586	-123.3800	Quadratic
			Quadratic	212.8955	0.7325	8.3577	-101.4500	
		30 to <50	WLS	245.1583	0.0548	18.9712	-119.5790	Quadratic
			Quadratic	194.2519	0.4301	5.9545	-92.1260	
		≥ 50	WLS	138.5724	0.0548	2.2998	-66.2860	Quadratic
			Quadratic	135.7715	0.4301	1.9718	-62.8860	

Supplementary Table 2. The estimated peak years of obesity

Sex	Boys			Girls		
Percentage of overweight(%)	20 to <30	30 to <50	≥ 50	20 to <30	30 to <50	≥ 50
Year	1994	2014	2009	2001	2017	2016
Peak value	6.32	5.03	1.41	5.04	3.74	0.87
P for trend	3.10E-11*	2.61E-07*	4.48E-07*	8.91E-07*	3.71E-07*	4.23E-03*

Supplementary Table 3. Validation of regression models by four estimation methods

	Regression models	Degree of suitability				Decision
		AIC	R-Squared	MAE	Likelihood Ratio Test	
Height	WLS	17.1555	0.9994	0.2537	-5.5778	Quadratic
	Quadratic	18.0632	0.9995	0.2217	-4.0316	
Weight	WLS	72.5468	0.9868	0.7178	-33.2730	WLS
	Quadratic	72.8696	0.9877	0.6807	-32.4350	
Percentage of overweight	WLS	84.4216	0.9607	0.8204	-39.2110	WLS
	Quadratic	86.7339	0.9659	0.8344	-39.3670	
Total Cholesterol	WLS	141.7150	0.9592	2.5360	-67.8580	Quadratic
	Quadratic	135.3710	0.9714	2.1415	-63.6850	
Triglyceride	WLS	195.2624	0.5710	7.1699	94.6310	Quadratic
	Quadratic	161.4676	0.8845	3.5227	76.7340	
HDL cholesterol	WLS	126.3208	0.9325	1.9583	-60.1600	Quadratic
	Quadratic	127.3320	0.9464	1.5778	-59.6660	
Non-HDL cholesterol	WLS	134.4495	0.9579	2.2635	64.2250	Quadratic
	Quadratic	126.8145	0.9702	1.8225	59.4070	

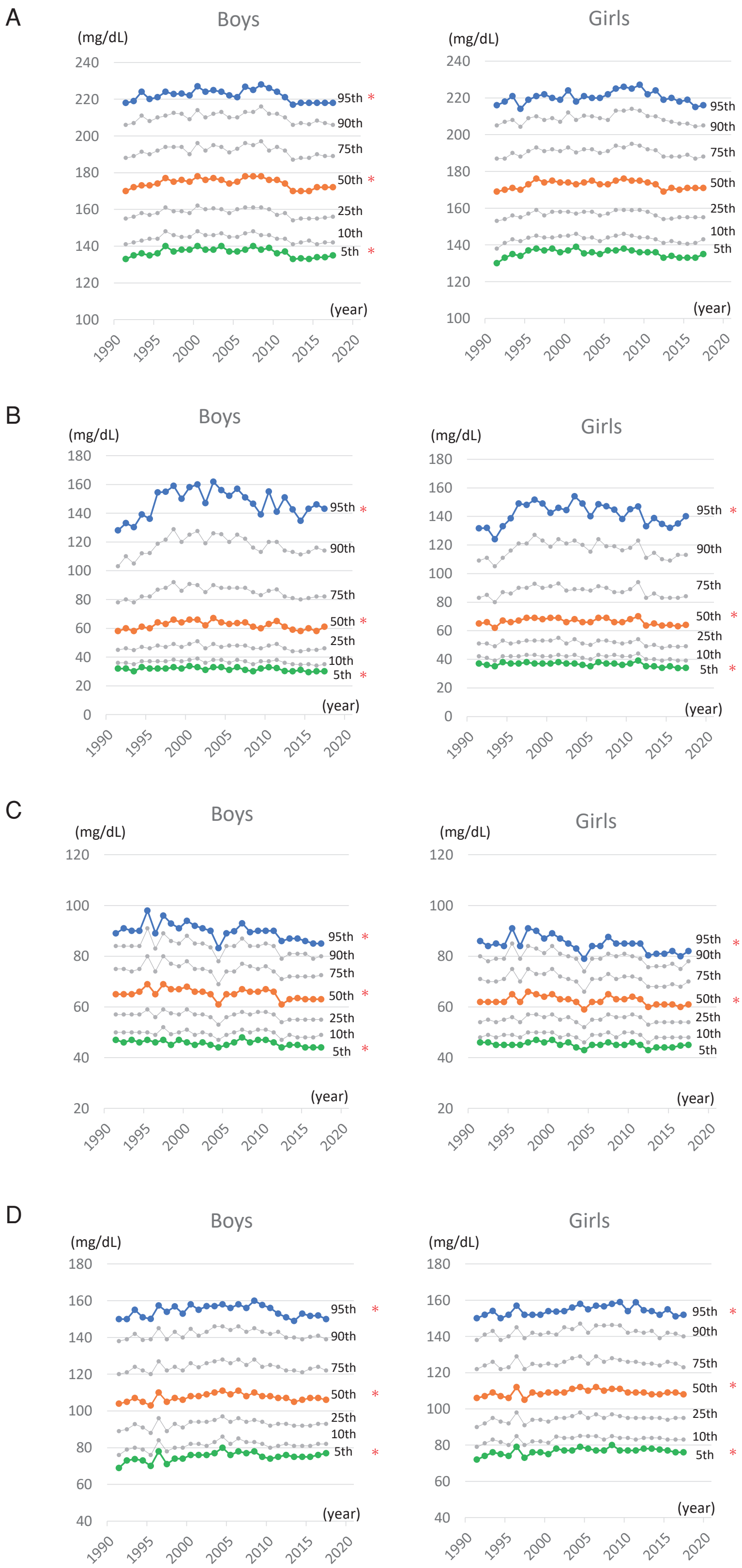


Supplementary Fig. 1. Secular trends in the percentiles of anthropometric parameters

A, Height. B, Weight. C, Percentage of overweight (POW). Blue circles, 95th percentile; orange circles, 50th percentile; and green circles, 5th percentile. Gray circles, 10th, 25th, 75th, and 90th percentiles. Secular trends in the 5th, 50th, and 95th percentiles were statistically analyzed. *P $<$0.05.

Supplementary Table 4. Secular trends in body weight and the percentage of overweight children

	Regression coefficient (95% CI)	
	boys (*n* = 58690)	girls (*n* = 56861)
Body weight (kg)		
95th percentile	-0.005 (-0.049 to 0.039)	-0.006 (-0.042 to 0.031)
50th percentile	-0.010 (-0.026 to 0.007)	-0.006 (-0.02 to 0.007)
5th percentile	-0.021 (-0.031 to -0.011)a	0.001 (-0.011 to 0.012)
Percentage of overweight (%)		
95th percentile	0.081 (0.005 to 0.158)a	0.066 (0.009 to 0.123)a
50th percentile	0.029 (-0.018 to 0.077)	0.024 (-0.019 to 0.066)
5th percentile	0.012 (-0.046 to 0.070)	0.004 (-0.039 to 0.047)



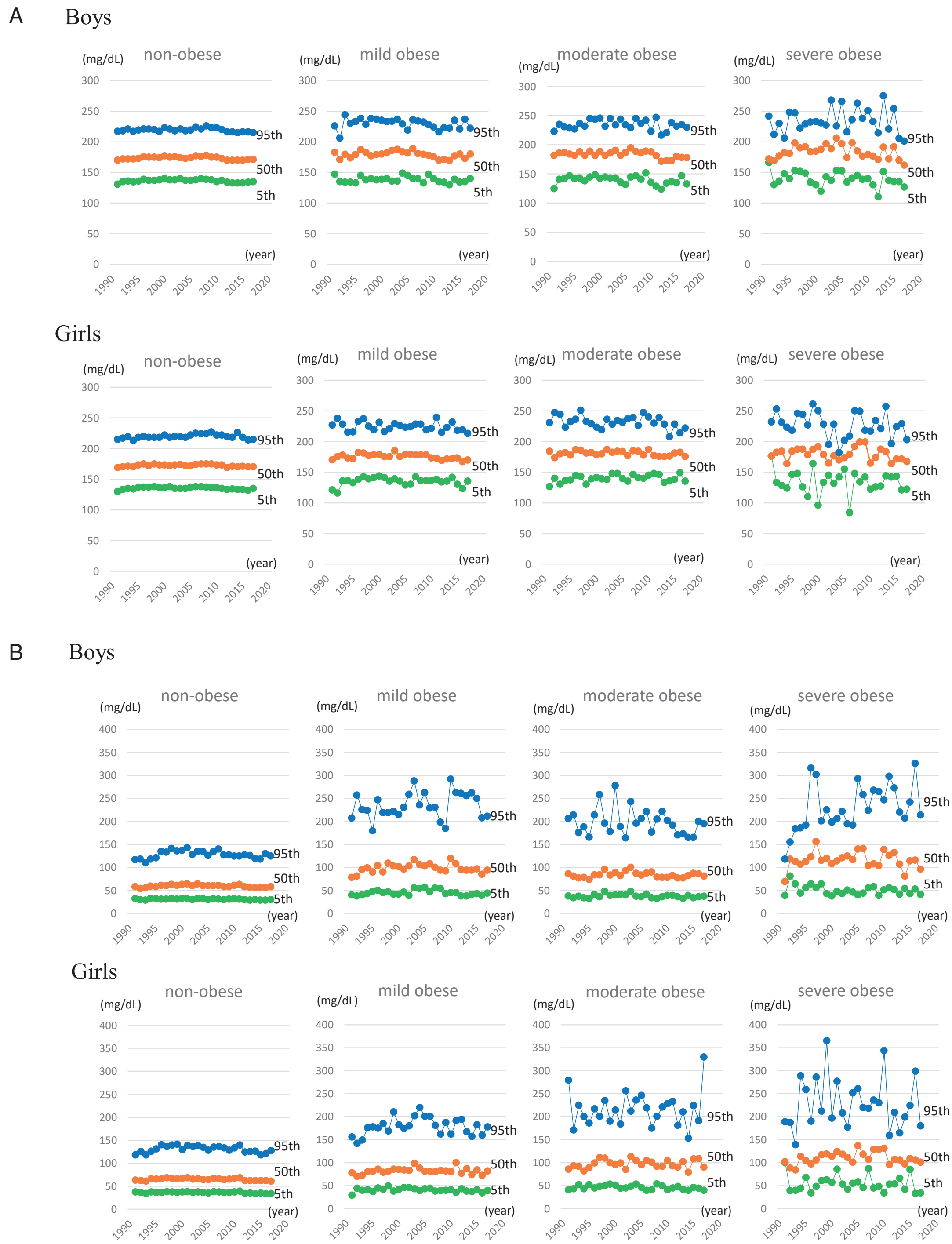
Supplementary Fig. 2. Secular trends in the percentiles of serum lipid levels

A, TC; B, TG; C, HDL-C; and D, non-HDL-C. Blue circles, 95th percentile; orange circles, 50th percentile; and green circles, 5th percentile. Gray circles, 10th, 25th, 75th, and 90th percentiles. The secular trends in the 5th, 50th, and 95th percentiles were statistically analyzed by the quadratic method. *$P<0.05$.

Supplementary Table 5. The estimated peak years of serum lipid levels

Sex	Boys											
	Total cholesterol (mg/dL)			Triglyceride(mg/dL)			HDL cholesterol (mg/dL)			Non-HDL cholesterol (mg/dL)		
Percentiles	5th	50th	95th	5th	50th	95th	5th	50th	95th	5th	50th	95th
Year	2001	2001	2002	2000	2001	2001	1993	1997	1997	2008	2005	2003
Peak value	139	177	225	33	65	157	47	67	93	77	109	157
P for trend	9.20E-06*	1.21E-05*	0.0001*	0.002*	4.46E-05*	5.91E-06*	0.02*	0.004*	0.001*	0.002*	0.001*	9.76E-05*

Sex	Girls											
	Total cholesterol (mg/dL)			Triglyceride(mg/dL)			HDL cholesterol (mg/dL)			Non-HDL cholesterol (mg/dL)		
Percentiles	5th	50th	95th	5th	50th	95th	5th	50th	95th	5th	50th	95th
Year	2005	2001	2001	2002	2001	2001		2001	1998	2008	2005	2005
Peak value	138	175	224	37	69	152		64	87	78	110	156
P for trend	0.0001*	5.26E-05*	0.0003*	0.001*	0.001*	2.51E-05*	0.07	0.04*	0.005*	0.0006*	0.008*	0.0009*



Supplementary Fig. 3. Comparison of a secular trend in lipid levels divided by POWs

Upper panels for boys; lower ones for girls. A, TC; B, TG; C, HDL-C; and D, non-HDL-C. Blue circles, 95th percentile; orange circles, 50th percentile; and green circles, 5th percentile.

(Cont. Supplementary Fig. 3)