*Acta Medica Okayama*

*Volume* 56, *Issue* 3 2002 *Article* 5

JUNE 2002

# Effect of change in body mass index on morbidity in non-obese university graduates.

Kazuo Tobe* Toshio Ogura† Chiaki Tsukamoto‡
Hajime Inoue** Jiro Arata†† Kazuharu Matsuura‡‡

*Okayama University,
†Okayama University,
‡Okayama University,
**Okayama University,
††Okayama University,
‡‡Okayama University,

# Effect of change in body mass index on morbidity in non-obese university graduates.*

Kazuo Tobe, Toshio Ogura, Chiaki Tsukamoto, Hajime Inoue, Jiro Arata, and Kazuharu Matsuura

## Abstract

To establish the actual serial changes in body weight in Japanese people and to elucidate the influence of changes in BMI on morbidity, we conducted a historical cohort study of university graduates from 1955 to 1990 using questionnaires and BMI data. The subjects of this study were 3,675 university graduates aged 26-62 years in whom BMI was determined at the time of enrollment in the university (Pre-BMI), 5 to 40 years earlier. Morbidity (one or more system diseases or obesity-related system diseases) was analyzed according to current age, sex, current BMI, deltaBMI (difference between current BMI and pre-BMI), and various lifestyle variables. The proportion of overweight subjects at enrollment to university was higher in recent male students compared to old students, but not in female graduates, and the BMI in both genders increased progressively after graduation, especially in recent male graduates. Pre-BMI correlated negatively and significantly with deltaBMI. The percentages of obese (BMI > or = 30 kg/m2) males and females were 1.6% and 0.5%, respectively, and high morbidity was observed in 56.1% and 42.2% of males and females, respectively. Stepwise regression analysis showed that in subjects with normal BMI at enrollment, prospective morbidity was dependent on ABMI in addition to age. Our results indicate that in subjects with normal body weight, prospective morbidity is determined by increment of ABMI, and suggest that maintenance of BMI at the late adolescence level is an important factor in preventing future disease.

**KEYWORDS:** body mass index, morbidity, overweight, lifestyle-related diseases, masked obesity, adolescent

*PMID: 12108586 [PubMed - indexed for MEDLINE]

Acta Med. Okayama, 2002
Vol. 56, No. 3, pp. 149-158


Acta Medica Okayama
http://www.lib.okayama-u.ac.jp/www/acta/

*Original Article*

# Effect of Change in Body Mass Index on Morbidity in Non-obese University Graduates

**Kazuo Tobe[a], Toshio Ogura[a*], Chiaki Tsukamoto[a], Hajime Inoue[a,b], Jiro Arata[a,b], and Kazuharu Matsuura[a],**

[a]*Health and Medical Center, Okayama University, Okayama 700-8530, Japan, and*
[b]*Okayama University Hospital, Okayam 700-8558, Japan*

**To establish the actual serial changes in body weight in Japanese people and to elucidate the influence of changes in BMI on morbidity, we conducted a historical cohort study of university graduates from 1955 to 1990 using questionnaires and BMI data. The subjects of this study were 3,675 university graduates aged 26-62 years in whom BMI was determined at the time of enrollment in the university (Pre-BMI), 5 to 40 years earlier. Morbidity (one or more system diseases or obesity-related system diseases) was analyzed according to current age, sex, current BMI, ΔBMI (difference between current BMI and pre-BMI), and various lifestyle variables. The proportion of overweight subjects at enrollment to university was higher in recent male students compared to old students, but not in female graduates, and the BMI in both genders increased progressively after graduation, especially in recent male graduates. Pre-BMI correlated negatively and significantly with ΔBMI. The percentages of obese (BMI $\geq$ 30 kg/m$^2$) males and females were 1.6% and 0.5%, respectively, and high morbidity was observed in 56.1% and 42.2% of males and females, respectively. Stepwise regression analysis showed that in subjects with normal BMI at enrollment, prospective morbidity was dependent on ΔBMI in addition to age. Our results indicate that in subjects with normal body weight, prospective morbidity is determined by increment of ΔBMI, and suggest that maintenance of BMI at the late adolescence level is an important factor in preventing future disease.**

**Key words:** body mass index, morbidity, overweight, lifestyle-related diseases, masked obesity, adolescent

Being overweight or obese in adulthood is considered to be the most critical risk factor for chronic diseases such as heart disease, hypertension, stroke, diabetes mellitus, hyperlipidemia, and hyperuricemia [1-3]. Since the proportion of obese individuals has gradually increased in recent decades in developed as well as in developing countries, the high incidence of obesity is a worldwide public health problem, which has contributed to increased morbidity and mortality [4-7]. Another related issue is the increased number of overweight children and adolescents [8]. Thus, a suitable and concerted effort should be taken to prevent a further rise in the incidence of obesity, and to prevent obesity in both the young and adult population.

The link between childhood and adulthood obesity has been investigated previously by several groups. Saw and Rajan [7] reported that being overweight during childhood or early adolescence frequently leads to obesity in adulthood, and that obese children who become obese adults have more severe obesity than do adults whose

Received October 10, 2001; accepted January 4, 2002.
*Corresponding author. Phone: +81-862-251-7221; Fax: +81-862-251-7222
E-mail: oguogu@cc.okayama-u.ac.jp (T. Ogura)

obesity starts in adulthood. In another study, Guo *et al*. [9] compared the body mass index (BMI) of young subjects (13–18 years) with the BMI of subjects at the age of 35, and concluded that the BMI at the age of 18 was the factor most related to adult obesity. It has also been reported that being overweight in adolescence is a more powerful predictor of morbidity than becoming overweight in adulthood, based on long-term health surveys [10]. These and other previous reports [11–13] suggest that even at a young age, obesity is associated with increased morbidity and mortality. To our knowledge, however, no previous studies have investigated the effect of changes in body weight of non-obese adolescents on risk for diseases in the future. To investigate this issue, we need to perform long-term health surveys from young age to adulthood using an identical mass group.

In the present study we investigated the relationship between changes in BMI and morbidity among a total of 3,675 university graduates at the mean age of $42.8 \pm 11.2$ years (26–62 years) during a period of 40 years on the basis of their health examinations (age, $19.0 \pm 0.1$ years) upon entrance to Okayama University. The aims of our study were to establish the actual serial changes in body weight in Japanese people and to elucidate the influence of these changes in BMI on morbidity, especially that among non-obese adolescents.

## Subjects and Methods

***Subjects.*** The subjects of this study were 8,025 graduates from Okayama University. They were selected from a total of 11,075 graduates (male, 7,771; female, 3,304) in 1955, 1960, 1965, 1970, 1976, 1980, 1985, 1990. In the present study, we used data on the graduates who entered the university in 1976 instead of those who entered in 1975 as subjects, since some health data recorded for the latter could not be retrieved. The inclusion criteria were the availability of health-related data recorded at the entrance health examination, which had been stored in the Health and Medical Center of Okayama University, and the availability of updated and current residential address on the alumnae lists. The study design was ethically approved by the eleven faculty deans of Okayama University.

***Methods.*** An open questionnaire, along with a detailed explanation of the project as described below, was sent to 8,025 graduates on January 14, 1998, using reply-paid envelopes and was to be returned by March 31, 1998. Informed consent was obtained from each graduate. The questionnaires included 5 main items: 1) Present height (cm), body weight (kg) and waist measurement (cm). 2) Body weight (kg) at the ages of 20, 30, 40, 50, and 60 years, according to age of subject. 3) Data related to blood pressure (mmHg), and from recent urine and blood examinations. 4) Any diseases that had been diagnosed previously or recently at a private clinic or hospital. 5) Present and previous lifestyle patterns such as smoking habits, level of alcohol intake, and daily exercise.

The names of diseases identified by the subjects of the present study followed the *International Classification of Diseases, Ninth Revision (ICD-9)* [14], which were finally classified into 17 categories of disease, as follows: cerebral vascular disease, respiratory disease, cardiovascular disease, gastrointestinal disease (excluding liver disease), hypertension, urological disease, liver disease, hyperlipidemia, hyperuricemia, diabetes mellitus, anemia, endocrine disease, malignant disease, psychological disease, gynecological disease, orthopedic disease, and other non-classified diseases. Further, we selected 6 of the above 17 diseases and labeled them as "obesity-related diseases", as follows: cardiovascular disease, hypertension, liver disease, hyperlipidemia, hyperuricemia, and diabetes mellitus. Questionnaire responses about lifestyle were scored as negative or positive with regard to the following items: present or past habitual smoking, present habitual consumption of alcohol, present regular exercise and past exercise suggested by membership of the university sports club. In the present study, we analyzed our data only relative to the frequency of morbidity among the subjects. Since we found only several cases of death, it was suggested that the very small incidence of mortality did not affect the results of our study using the morbidity rate.

Morbidity was classified as none or the presence of at least one of the diseases listed above, diagnosed since graduation from university. Body weight was classified into 5 groups based on $\pm 10$ and $\pm 20\%$ of the standard BMI. A BMI of 21 kg/m$^2$ was regarded as the ideal BMI in this study, since the average BMI of male and female newly-enrolled students in our University from 1955 to 1995 was $20.9 \pm 2.9$ kg/m$^2$ (mean $\pm$ SEM, $n = 7{,}771$) and $20.7 \pm 2.1$ kg/m$^2$ ($n = 3{,}304$), respectively. Subjects were classified into 5 groups according to BMI: lean group, $< 17$ kg/m$^2$; lean-normal group, $\geq 17$ and $< 19$; normal group, $\geq 19$ and $< 23$; normal-overweight group, ≥23 and < 25; and overweight group, ≥25 kg/m². The relationship between morbidity and changes in BMI (ΔBMI), which represented the difference between BMI at the entrance health examination (pre-BMI) and present BMI (post-BMI), was examined using the data of all subjects. To determine the general health outcome of non-obese students, we also divided subjects into 2 groups (pre-BMI < 23 and ≥ 23 kg/m²), and analyzed the relationship between ΔBMI and morbidity.

***Statistical Analysis.*** Data were expressed as mean ± SEM. Differences between groups were analyzed for statistical significance using the Student's *t*-test or analysis of variance when appropriate. Stepwise multiple regression analysis was performed, using morbidity (number of diseases listed above) as the dependent variable. The independent variables considered as risk for morbidity included age, sex, post-BMI, ΔBMI, present waist size, habitual drinking and smoking, present exercise habits. A $P$ value < 0.05 denoted the presence of a statistically significant difference.

## Results

***Reply rate.*** The reply rates are shown in Table 1, stratified according to the graduation year. The reply rate increased with the current age of graduates, and the average reply rate for all graduate groups was 47.2% (3,791/8,025). After excluding questionnaires that were not answered completely, the completed questionnaires of 3,675 subjects (males, 2,348, and females, 1,327; average age, 42.8 ± 11.2, and range, 26–62) were selected for analysis. In the stepwise analysis, we selected the subjects who entered from 1955 to 1980 (average age, 44.9 ± 0.18 years; reply rate, 53.7%), since we intended to obtain more actual results among the high reply rate group.

***Serial changes in BMI between entrance and graduation.*** Pre- and post-BMI of each graduation group are shown in Table 2. The mean age at the entrance health examination of all subjects was 19.0 ± 0.1 years. The mean pre-BMI of all male graduates was similar to that of female graduates. The pre-BMI gradually increased in male graduates from 1955 to 1990, and percent rise during this period was 7.96%. However, BMI was steady in females during the same period (Table 2). On the other hand, the post-BMI was significantly higher than pre-BMI in all male subjects irrespective of the year of enrollment. In females, the post-BMI was significantly higher than pre-BMI in those who enrolled in 1955 to 1970, but was significantly lower than the pre-BMI in graduates of 1985 and 1990 (Table 2).

We also examined the serial changes in body constitution based on pre- and post-BMI from 1955 to 1990. The percentages of overweight and/or normal-overweight males at university entrance steadily increased in progressive enrollment years (or age) in males, which increase was associated with a fall in the percentage of normal males (Fig. 1, left upper panel). Such a tendency was not clearly observed in females. With regard to serial changes in body constitution at survey, the percentages of overweight and/or normal-overweight groups gradually and steadily increased with age (or enrollment year) in both males and females (Fig. 1, lower panels). This was associated with a concomitant fall in the percentages of lean and/or lean-normal groups with age or enrollment year, especially in females. These results indicate an increase in the obese population associated with a fall in the lean population with age in both males and females.

**Table 1** Questionnaire reply rate according to graduate groups

| | 1955* | 1960 | 1965 | 1970 | 1976 | 1980 | 1985 | 1990 | Total |
|---|---|---|---|---|---|---|---|---|---|
| Number of mail outs | 615 | 630 | 746 | 853 | 1,076 | 1,321 | 1,293 | 1,491 | 8,025 |
| Number of replies | 458 | 371 | 414 | 442 | 534 | 593 | 521 | 458 | 3,791 |
| Male | 333 | 276 | 279 | 288 | 329 | 390 | 287 | 243 | 2,425 |
| Female | 125 | 95 | 135 | 154 | 205 | 203 | 234 | 215 | 1,366 |
| Rate of answer (%) | 74.5 | 58.9 | 55.5 | 51.8 | 49.6 | 44.9 | 40.3 | 30.7 | 47.2 |
| Present age (years) † | 61.1 ± 0.04 | 56.3 ± 0.05 | 51.0 ± 0.03 | 46.2 ± 0.04 | 40.2 ± 0.04 | 36.3 ± 0.05 | 31.1 ± 0.05 | 26.1 ± 0.04 | 42.8 ± 11.2 |

*Year represents the year when each group enrolled at Okayama University. Data are mean ± SEM.

Fig. 2 shows representative time-course changes in mean BMI at the ages of 20, 30, 40, 50, and 60 years calculated from questionnaire data of subjects who enrolled at our University in 1955, 1965, 1976, and 1985. The plots show progressive increases in BMI with age in both male and female graduates. Furthermore, there was a steep rise in BMI after graduation in recent male graduates compared with the more gradual rise in older sex-matched graduates. The increment in BMI after graduation in females was not only slow compared with that of male graduates but was also decreased in recent graduates (Fig. 2).

***ΔBMI among BMI-graded groups at University enrollment.*** Fig. 3 shows ΔBMI among

**Table 2** BMI at entrance health examination (pre-BMI) and BMI at survey (post-BMI) in each graduate-group

| group | Males (n = 2,348) | | | | Females (n = 1,327) | | | |
|---|---|---|---|---|---|---|---|---|
| | No. | Age (years) | Pre-BMI (kg/m²) | Post-BMI (kg/m²) | No. | Age (years) | Pre-BMI (kg/m²) | Post-BMI (kg/m²) |
| 1990 | 235 | 26.3 ± 0.06 | 21.7 ± 0.20 | 22.4 ± 0.20* | 210 | 25.9 ± 0.03 | 20.5 ± 0.16 | 19.8 ± 0.13§ |
| 1985 | 277 | 31.3 ± 0.08 | 21.2 ± 0.16 | 22.5 ± 0.17† | 223 | 31.0 ± 0.07 | 20.8 ± 0.13 | 20.3 ± 0.13§ |
| 1980 | 374 | 36.4 ± 0.07 | 21.1 ± 0.12 | 23.0 ± 0.15† | 198 | 36.0 ± 0.07 | 20.2 ± 0.12 | 20.3 ± 0.14 |
| 1976 | 322 | 40.3 ± 0.06 | 20.8 ± 0.11 | 23.2 ± 0.15† | 198 | 40.0 ± 0.03 | 20.6 ± 0.14 | 21.0 ± 0.16 |
| 1970 | 278 | 46.4 ± 0.05 | 20.2 ± 0.12 | 23.2 ± 0.16† | 151 | 45.9 ± 0.05 | 20.6 ± 0.17 | 21.8 ± 0.19† |
| 1965 | 268 | 51.1 ± 0.04 | 20.1 ± 0.11 | 23.1 ± 0.15† | 129 | 50.9 ± 0.04 | 20.5 ± 0.16 | 21.9 ± 0.20† |
| 1960 | 267 | 56.4 ± 0.05 | 20.1 ± 0.11 | 23.4 ± 0.15† | 93 | 55.8 ± 0.06 | 20.6 ± 0.21 | 21.8 ± 0.23§ |
| 1955 | 327 | 61.2 ± 0.05 | 20.1 ± 0.09 | 23.2 ± 0.16† | 125 | 60.9 ± 0.04 | 20.9 ± 0.16 | 22.5 ± 0.27† |
| Average | | 44.1 ± 0.23 | 20.7 ± 0.05 | 23.0 ± 0.06† | | 40.6 ± 0.30 | 20.6 ± 0.06 | 21.0 ± 0.07† |

Year represents the year of enrollment at Okayama University. Age represents current age at the time of the survey. Data represent mean ± SEM. Significant by paired $t$-test, $*P < 0.05$, $§P < 0.01$, and $†P < 0.0001$ *vs*. pre-BMI.

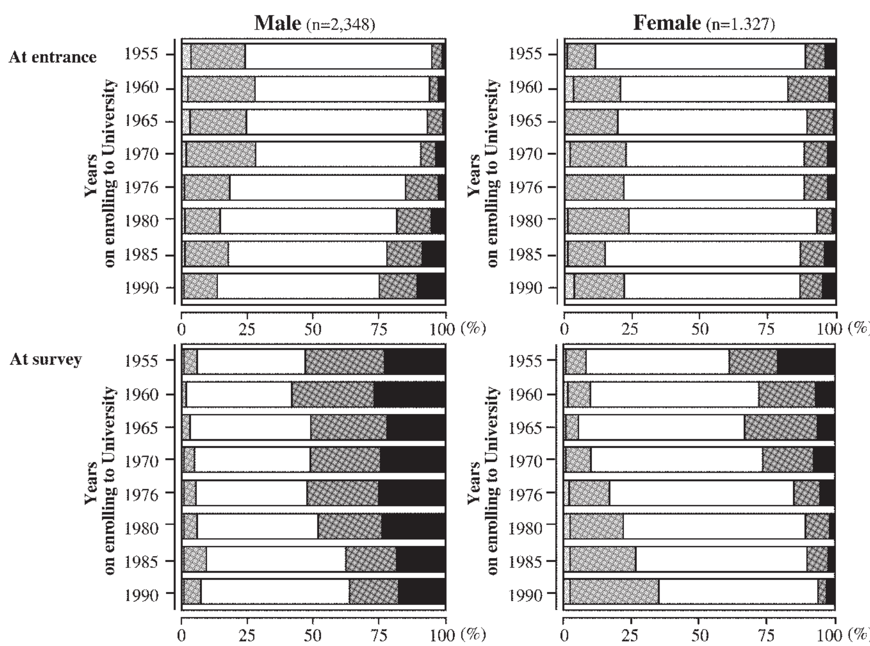


**Fig. 1** Body constitution among graduate-groups according to enrollment year. BMI (kg/m²): ▒: < 17; ░: 17 ≤ and < 19; □: 19 ≤ and < 23; ▓: 23 ≤ and < 25; ■: ≥ 25.

the groups graded according to pre-BMI. ΔBMI was dependent on pre-BMI; namely, the lower the pre-BMI, the higher the increment in ΔBMI, in both male and female graduates. Pre-BMI correlated negatively and significantly with ΔBMI in both males ($r = -0.355$, $P < 0.0001$) and females ($r = -0.345$, $P < 0.0001$).

***Relationship between morbidity and age, post-BMI, and ΔBMI.*** The relationships between morbidity on one hand, and age, post-BMI, and ΔBMI on the other, are shown in Fig. 4 for all subjects. The average morbidity rate was 53.9 and 40.9% in all males and females, respectively. Aging was clearly associated with increased morbidity rate in both genders (Fig. 4A). Although body constitution at enrollment did not affect morbidity (data not shown), morbidity tended to increase with increased post-BMI (Fig. 4B). There was a gradual and progressive increase in morbidity rate with increases in ΔBMI in graduates of both genders (Fig. 4C).

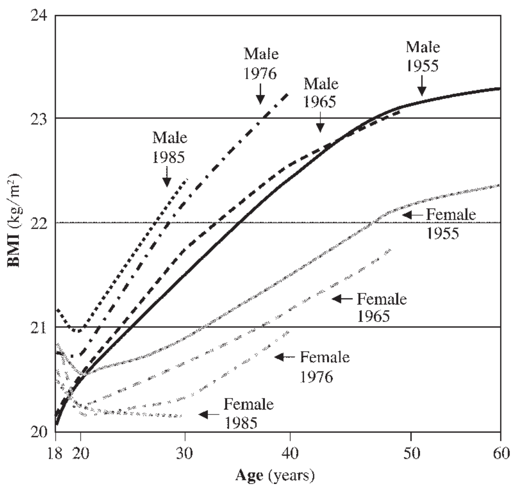


**Fig. 2** Serial changes in BMI among graduate-groups. Representative groups are shown in the figure (subjects enrolled in 1955, 1965, 1976, and 1985). Curves were fitted using the average of BMI at the ages of 18, 20, 30, 40, 50, and 60 years.

***Relationship between ΔBMI and morbidity according to pre-BMI.*** Table 3 compares various parameters (age, pre-BMI, post-BMI, ΔBMI, present waist measurement, and number of diseases) of subjects with pre-BMI $< 23$ kg/m$^2$ (lean + lean-normal and normal BMI groups) and those with $\geq 23$ kg/m$^2$ (normal-overweight + overweight BMI groups). Pre-BMI, post-BMI, and present waist measurement in the $\geq 23$ kg/m$^2$ group were significantly higher than those in the $< 23$ kg/m$^2$ group, although the ΔBMI was significantly higher in the latter than in the former. We also analysed the relationship between ΔBMI and the number of diseases reported by each group (Fig. 5). In males with a pre-BMI of $< 23$ kg/m$^2$, the number of system diseases showed a "J-shape" pattern at the bottom of unchanging ΔBMI ($-2 \leq$ and $< +2$ kg/m$^2$) (Fig. 5Aa), whereas it gradually increased with increased ΔBMI in females (Fig. 5Ab). Further analysis showed that the number of obesity-related diseases gradually increased with increased ΔBMI in both males and females (Fig. 5Ac and d). In the pre-BMI $\geq 23$ kg/m$^2$ group, the ΔBMI tended to be associated with a phase increase in the number of system diseases, but the tendency was not as clear as that observed in subjects with pre-BMI $< 23$ kg/m$^2$ (Fig. 5B). The high increment of ΔBMI was only associated

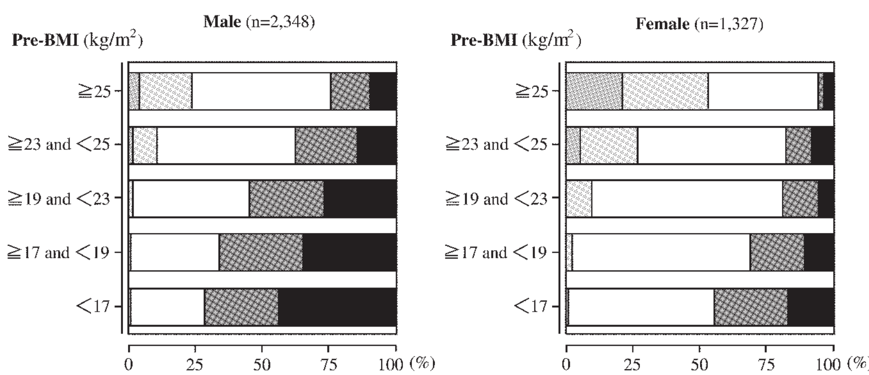


**Fig. 3** Changes in BMI according to pre-BMI. Increment of BMI (kg/m$^2$): ▒: $\leq -4$; ░: $-4 <$ and $< -2$; □: $-2 \leq$ and $\leq +2$; ▒: $+2 <$ and $< +4$; ■: $\geq +4$.

with a significant increase in system diseases and particularly in obesity-related diseases (Fig. 5Ba, b, c, and d).

Finally, stepwise multiple regression analysis was performed using the number of diseases as the dependent variable in both groups (Table 4). Seven independent variables considered as risk factors for morbidity, including age, gender, post-BMI, ΔBMI, present waist measurement, habitual smoking and alcohol drinking, and present exercise level, were entered into the analysis. Age, ΔBMI and gender were significant independent factors for the number of both system diseases and obesity-related diseases in the BMI $< 23\ \mathrm{kg/m^2}$ group. In the BMI $\geq 23\ \mathrm{kg/m^2}$ group, age and ΔBMI or present waist measurement were significant independent factors for the number of both complicating diseases and obesity-related diseases.

## Discussion

In the present study, we investigated the relationship between morbidity and body weight, with a special emphasis on changes in BMI, using a questionnaire survey for university graduates over a period of 5 to 40 years. The purpose of our study was to examine the prognosis of Japanese University students, and to evaluate the services provided through the Health and Medical

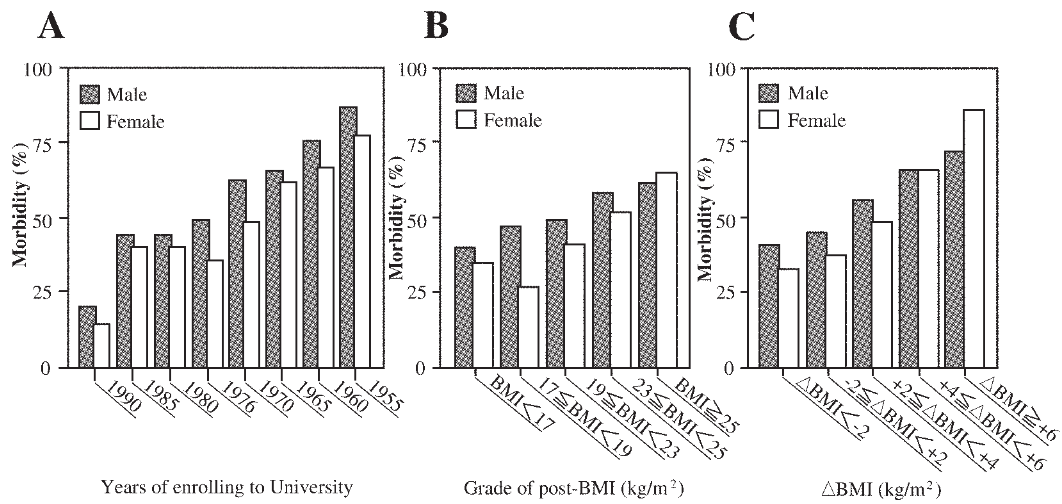


**Fig. 4** Relationships between morbidity and age (**A**), post-BMI (**B**), and ΔBMI (**C**). Morbidity was expressed as the percentage of individuals who had one or more diseases at the time of the survey. (**A**) Morbidity according to the year of enrollment. (**B**) Morbidity according to post-BMI. (**C**) Morbidity according to ΔBMI.

**Table 3** Comparison of parameters between graduates whose BMI was less than 23 kg/m² and over 23 kg/m², respectively, at the entrance health examination

| | Males | | Females | |
|---|---|---|---|---|
| | Pre-BMI $< 23$ kg/m² | Pre-BMI $\geq 23$ kg/m² | Pre-BMI $< 23$ kg/m² | Pre-BMI $\geq 23$ kg/m² |
| n | 2,055 | 293 | 1,186 | 141 |
| Age (years) | 44.7 ± 0.25 | 37.7 ± 0.58† | 40.4 ± 0.32 | 40.7 ± 0.98 |
| Pre-BMI (kg/m²) | 20.1 ± 0.03 | 24.9 ± 0.12† | 20.1 ± 0.04 | 24.4 ± 0.11† |
| Post-BMI (kg/m²) | 22.6 ± 0.06 | 25.6 ± 0.18† | 20.6 ± 0.06 | 23.7 ± 0.23† |
| ΔBMI (kg/m²) | 2.59 ± 0.05 | 0.76 ± 0.16† | 0.52 ± 0.06 | −0.76 ± 0.23† |
| Waist (cm) | 81.6 ± 0.39 | 84.9 ± 0.47§ | 64.5 ± 0.15 | 68.9 ± 0.54† |

Data represent mean ± SEM. Significant by unpaired $t$-test, §$P < 0.01$ and †$P < 0.0001$ *vs*. each sex-matched Pre-BMI < 23 kg/m². ΔBMI, difference between pre- and post-BMI.

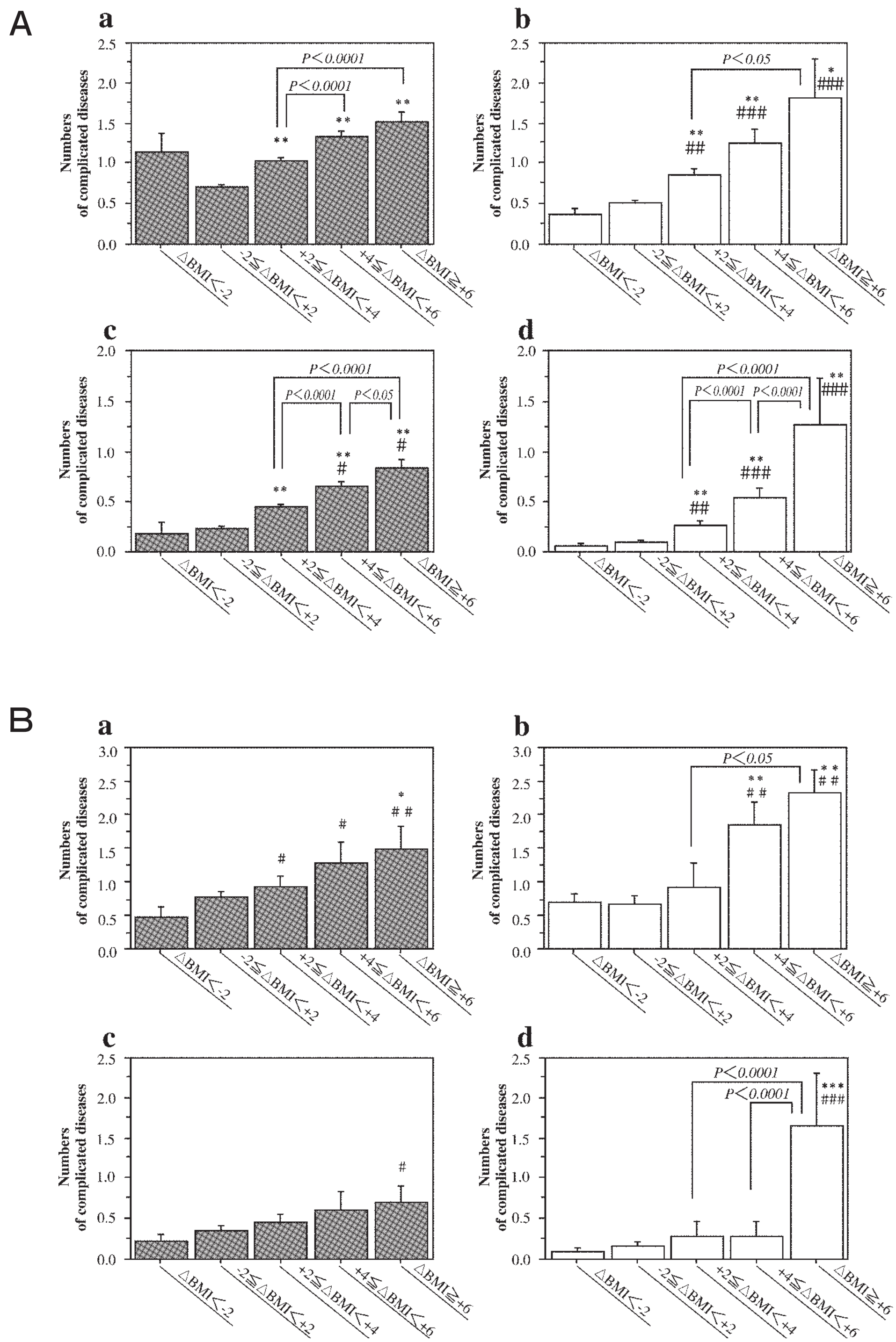


**Fig. 5** Relationship between morbidity and ΔBMI in subjects with BMI $<$ 23 kg/m$^2$ (**A**) and $\geq$ 23 kg/m$^2$ (**B**) at enrollment. The ordinate represents the number of subjects who reported one or more diseases (a and b) or obesity-related diseases (c and d) as described in "Materials and Methods". Closed bars: males, open bars: females. ΔBMI, difference between pre- and post-BMI. Significant by unpaired *t*-test: A, $^{*}P < 0.001$ and $^{**}P < 0.0001$ *vs*. sex matched control (ΔBMI, $\geq -2$ and $< 2$ kg/m$^2$); $^{\#}P < 0.05$, $^{\#\#}P < 0.01$, and $^{\#\#\#}P < 0.0001$ *vs*. the group with ΔBMI $< -2$ kg/m$^2$. B, $^{*}P < 0.05$, $^{**}P < 0.01$, and $^{***}P < 0.0001$ *vs.* sex matched control (ΔBMI, $\geq -2$ and $< 2$ kg/m$^2$); $^{\#}P < 0.05$, $^{\#\#}P < 0.01$, and $^{\#\#\#}P < 0.0001$ *vs*. the group with ΔBMI is $< -2$ kg/m$^2$.

**Table 4** Multivariate stepwise regression analysis using morbidity as the dependent variable using data of 2 groups (Pre-BMI < 23 kg/m$^2$ and Pre-BMI ≥ 23 kg/m$^2$)

| Factor selected | Standardized regression coefficient | Partial correlation coefficient | Multiple correlation coefficient |
|---|---|---|---|
| Pre-BMI < 23 kg/m$^2$ | | | |
| (1) All diseases | | | |
| Age (years) | 0.384† | 0.376 | |
| ΔBMI (kg/m$^2$) | 0.103† | 0.100 | |
| Gender | −0.053** | −0.054 | 0.443† |
| (2) Obesity-related diseases | | | |
| Age (years) | 0.316† | 0.313 | |
| ΔBMI (kg/m$^2$) | 0.108† | 0.065 | |
| Gender | −0.064§ | −0.064 | |
| Post-BMI (kg/m$^2$) | 0.085** | 0.053 | |
| Exercise | −0.036* | −0.040 | 0.431† |
| Pre-BMI ≥ 23 kg/m$^2$ | | | |
| (1) All diseases | | | |
| Age (years) | 0.407† | 0.411 | |
| Waist (cm) | 0.136** | 0.149 | 0.434† |
| (2) Obesity-related diseases | | | |
| Age (years) | 0.319† | 0.337 | |
| Waist (cm) | 0.315† | 0.333 | 0.457† |

Stepwise multiple regression analysis was performed, employing morbidity (all and obesity-related diseases) as the dependent variable. The independent variables considered as risk factors for morbidity included age, gender, post-BMI, ΔBMI, present waist size, habitual drinking and smoking, and previous and present exercise level. *$P < 0.05$, **$P < 0.01$, §$P < 0.001$, and †$P < 0.0001$.

Center (*i.e.*, the management of the overall health of students). The major findings of our study were as follows: 1) prospective morbidity is high in overweight as well as in non-obese adolescents; 2) the lower the BMI at enrollment, the higher the increment of ΔBMI; 3) morbidity is clearly related to ΔBMI in non-obese adolescents. Although our study used a limited sample size (university graduates), we believe that the results represent the true serial changes in ΔBMI and morbidity in Japanese adolescents and adults. Furthermore, although self-reported data from questionnaires were used for the analyses in the study, such surveys are reportedly reliable sources [15].

The BMI (or Quetelet's index) has been generally used as an index of obesity [3-5, 16]. In adults, a BMI cutoff value of 30 kg/m$^2$ has been used to define obesity [5, 16, 17]. The proportion of obese population in Western countries is reported to be 15-25% [5], while it is under 2-3% in Japan [18]. Indeed, the present study showed that the obese population with BMI > 30 kg/m$^2$ formed 1.6% and 0.45% of male and female population samples, respectively. Even when using the recent definition of obesity (BMI > 25 kg/m$^2$) [19], the incidence of obesity in Japanese males and females was only 17.1% and 5.4%, respectively, which is still lower than that reported in Western countries. In spite of these figures, a high morbidity of 53.9% and 40.9% was observed in our male and female subjects, respectively. Although the correlation between obesity and increased mortality and morbidity is well established, our data show a high morbidity among non-obese Japanese individuals. These findings raise several important questions. For example, should we only concentrate on the relationship between obese individuals and morbidity? How does the change in body weight influence morbidity? How do we assess body weight in young (not only overweight but also non-obese) adolescents with respect to future development of various diseases?

In the present study, the size of the obese population sample at enrollment was relatively small (subjects with BMI ≥ 25 kg/m$^2$: 3.7% of males and 2.5% of females), but the incidence of obesity at the time of survey increased to 17.1% and 5.4% in males and females, respectively. Our study indicates that the leaner adolescents tended to show future increases in ΔBMI, while the overweight adolescents tended to maintain a stable body weight over time, resulting in a significant negative correlation between pre-BMI and ΔBMI. These results are clearly different from those in previous reports, which have indicated that being overweight in childhood or adolescence leads to morbid obesity in adulthood [9-13]. It is possible that this difference may be peculiar to Japanese university graduates. A steep rise in ΔBMI after graduation was particularly observed in recent male graduates. We believe that this phenomenon in recent male graduates relates to contemporary trends in the Japanese lifestyle, such as "Westernization of Diet" "Satiation with Food", and "Shortage of Exercise". On the other hand, our results showed that recent female graduates tended to sustain or reduce their BMI with time, probably due to the prevalence of "Yearning for a Slender Body" in young females. These gender differences were also observed in serial changes in body constitution at enrollment (Fig. 1). We recently reported the relationship between serum leptin level and fatty liver in male freshmen [20]. In that study, the proportion of subjects with fatty liver was markedly higher among males (10.2%) than among females (2.4%) at the enrollment health examination, suggesting that accumulation of abdominal fat was markedly higher in males than females.

Several studies have indicated that being overweight in adulthood is an important risk factor for morbidity [1–6], but the significance of changes in body weight for morbidity has not been well discussed. In the present study, we focused on ΔBMI, especially among non-obese adolescents. Our results clearly demonstrated that morbidity never increases independent of BMI, unless ΔBMI is kept under 2 kg/m$^2$ from the basal BMI at 19 years. In other words, our data imply that an increment of only 2 kg/m$^2$ BMI was associated with a significant increase in future morbidity among non-obese adolescents. A change from being of normal weight to being overweight (*i.e.*, "acquired obesity") may be associated with increased mortality and morbidity in adulthood [21]. In particular, a steep rise in body weight is suspected to be associated with accumulation of visceral fat, resulting in the development of associated diseases, such as "Syndrome X" [22] or "Deadly Quartet" [23]. With respect to overweight adolescents, a significant increase in morbidity was only evident when ΔBMI exceeded 6 kg/m$^2$, and especially for obesity-related diseases. This phenomenon was another interesting finding in our study. This peculiar phenomenon might be related to genetic elements (not to acquired obesity).

The relationship between BMI and morbidity, reported to depict a "J- or U-shape" at the bottom of BMI 22 kg/m$^2$, is in accord with the association of the ideal value with the lowest morbidity [24]. However, several studies have examined the ideal BMI values [11, 25–27]. The results of these studies may differ depending on the method of survey, such as scale of study, and the age of subjects or ethnic group, sex, and other risk factors [28]. The level of ideal BMI of young adolescents is also controversial. In our study, the BMI associated with the lowest morbidity was suspected to be less than 22 kg/m$^2$ in both males and females. In addition, our results indicated that ΔBMI is a more important risk factor for morbidity than present BMI in non-obese subjects, even if the most important factor determining morbidity is age. There is a general agreement that the recent increase in the proportion of obese population is mainly due to changes in lifestyle. We suspect that the ideal BMI is that at adolescence, maintained within a ± 2 kg/m$^2$ range of ΔBMI, since each individual may have his/her own ideal BMI depending on genetic elements rather than on environmental factors. In Japan there may exist a large population with normal BMI that acquires lifestyle-related diseases as a result of accumulation of visceral fat due to a high or rapid increment in ΔBMI (so-called "Masked Obesity"). We recently reported a serial change in serum cholesterol levels of new students enrolling at our university from 1989 to 1998, showing that it increased among non-obese students in both sexes during these 10 years [29]. We should consider establishing a set of guidelines emphasizing the importance of maintaining body weight for non-obese adolescents, although it is commonly spread to guide obese people to normal weight.

In conclusion, we have demonstrated in the present study that the increment in ΔBMI during adulthood is an important factor for morbidity, even when the current BMI is not high. We strongly emphasize that maintenance of BMI at the level of adolescence is one of the critical factors for prevention of future obesity and associated diseases.

Acknowledgements. This work was supported in part by a research grant (No. 09670390) from the Japanese Ministry of Education, Science, Sports, Culture and Technology, Japan.

## References

1. Lew EA and Garfinkel L: Variations in mortality by weight among 750,000 men and women. J Chronic Dis (1979) **32**, 563–576.
2. National Institutes of Health Consensus Statement: Health Implications of Obesity. National Institutes of Health Consensus Development Panel on the Health Implications of Obesity. Ann Intern Med (1985) **103**, 1073–1077.
3. Allison DB, Fontaine KR, Manson JE, Stevens J and VanItallie TB: Annual deaths attributable to obesity in the United States. JAMA (1999) **282**, 1530–1538.
4. Kuczmarski RJ, Flegal KM, Campbell SM and Johnson CL: Increasing prevalence of overweight among US adults. The National Health and Nutrition Examination Surveys, 1960–1991. JAMA (1994) **272**, 205–211.
5. Seidell JC: Obesity: A growing problem. Acta Paediatr Suppl (1999) **428**, 46–50.
6. Must A, Spadano J, Coakley EH, Field AE, Colditz G and Dietz WH: The disease burden associated with overweight and obesity. JAMA (1999) **282**, 1523–1529.
7. Saw SM and Rajan U: The epidemiology of obesity: A review. Ann Acad Med Singapore (1997) **26**, 489–493.
8. Power C, Lake JK and Cole TJ: Measurement and long-term health risks of child and adolescent fatness. Int J Obes Relat Metab Disord (1997) **21**, 507–526.
9. Guo SS and Chumlea WC: Tracking of body mass index in children in relation to overweight in adulthood. Am J Clin Nutr (1999) **70** (suppl),

145S–148S.
10. Must A, Jacques PF, Dallal GE, Bajema CJ and Dietz WH: Long-term morbidity and mortality of overweight adolescents. A follow-up of the Harvard Growth Study of 1922 to 1935. N Engl J Med (1992) **327**, 1350–1355.
11. Hoffmans MD, Kromhout D and de Lezenne Coulander C: The impact of body mass index of 78, 612 18-year old Dutch men on 32-year mortality from all causes. J Clin Epidemiol (1988) **41**, 749–756.
12. Rimm IJ and Rimm AA: Association between juvenile obesity and severe adult obesity in 73,532 women. Am J Public Health (1976) **66**, 479–481.
13. DiPietro L, Mossberg H-O and Stunkard AJ: A 40-year history of overweight children in Stockholm: Life-time overweight, morbidity, and mortality. Int J Obes Relat Metab Disord (1994) **18**, 585–590.
14. The International Classification of Diseases, 9th rev. Clinical modification. Ann Arbor Mich (1980) Edwards Brothers.
15. Casey VA, Dwyer JT, Berkey CS, Coleman KA, Gardnet J and Valadian I: Long-term memory of body weight and past weight satisfaction: A longitudinal follow-up study. Am J Clin Nutr (1991) **53**, 1493–1498.
16. Garrow JS and Webster J: Quetelet's index ($W/H^2$) as a measure of fatness. Int J Obes (1985) **9**, 147–153.
17. Bray GA: Complication of obesity. Ann Intern Med (1985) **103**, 1052–1062.
18. Yoshiike N, Matsumura Y, Zaman MM and Yamaguchi M: Descriptive epidemiology of body mass index in Japanese adults in a representative sample from the National Nutrition Survey, 1990–1994. Int J Obes Relat Metab Disord (1998) **22**, 684–687.
19. Report of a WHO study group. Diet, nutrition, and the prevention of chronic diseases. WHO Tec Rep Ser (1990) **797**, 69–74.
20. Tobe K, Ogura T, Tsukamoto C, Imai A, Matsuura K, Iwasaki Y, Shimomura H, Higashi T and Tsuji T: Relationship between serum leptin and fatty liver in Japanese male adolescent university students. Am J Gastroenterol (1999) **94**, 3328–3335.
21. Colditz GA, Willett WC, Stampfer MJ, Manson JE, Hennekens CH, Arky RA and Speizer FE: Weight as a risk factor for clinical diabetes in women. Am J Epidemiol (1990) **132**, 501–513.
22. Reaven GM: Banting lecture 1988. Role of insulin resistance in human disease. Diabetes (1988) **37**, 1595–1607.
23. Kaplan NM: The deadly quartet. Upper-body obesity, glucose intolerance, hypertriglyceridemia, and hypertension. Arch Intern Med (1989) **149**, 1514–1520.
24. Matsuzawa Y, Tokunaga K, Kotani K, Keno Y, Kobayashi T and Tarui S: Simple estimation of ideal body weight from body mass index with the lowest morbidity. Diabetes Res Clin Pract (1990) **10**, S156–164.
25. Grinker JA, Tucker K, Vokonas PS and Rush D: Overweight and leanness in adulthood: Prospective study of male participants in the Normative Aging Study. Int J Obes Relat Metab Disord (1996) **20**, 561–569.
26. Srinivasan SR, Bao W, Wattingney WA and Berenson GS: Adolescent overweight is associated with adult overweight and related multiple cardiovascular risk factors: The Bogalusa Heart Study. Metabolism (1996) **45**, 235–240.
27. Dietz WH and Bellizzi MC: Introduction: The use of body mass index to assess obesity in children. Am J Clin Nutr (1999) **70** (Suppl), 123S–125S.
28. Lee IM, Manson JE, Hennekens CH and Paffenbarger RS Jr: Body weight and mortality. A 27-year follow-up of middle-aged men. JAMA (1993) **270**, 2823–2828.
29. Ogura T, Matsuura K, Suzuki H, Kishida M, Ikeda S, Tsukamoto C, Imai A, Tobe K. Serum total cholesterol of new students enrolled at Okayama University: Trend during 1989–1998. Acta Med Okayama (2001) **55**, 269–276.