

## Relative Weight, Weight Change, and Risk of Coronary Heart Disease in the Honolulu Heart Program

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Risk of coronary heart disease (CHD) among the Honolulu Heart Program participants was examined in relation to body mass index (BMI) at age 25 and two subsequent periods of weight change: age 25 to examination I (1965–1968) and examination I to examination III (1971–1974). During a maximum follow-up period of 17 years after examination III, there were 479 incident cases of CHD among the study sample of 6,176 Japanese-American men. Levels of BMI at age 25 were positively related to CHD incidence after statistical control for age, smoking, and subsequent weight change. Relative risk between the lowest and highest BMI categories was 2.44 (95% confidence interval (CI) 1.61–3.69). Compared with a weight change of less than 2.5 kg between age 25 and examination I, relative risks were 1.41 (95% CI 1.00–1.97) for a weight gain between 2.6 and 5 kg, 1.60 (95% CI 1.22–2.11) for a weight gain between 5.1 and 10 kg, and 1.75 (95% CI 1.32–2.33) for a weight gain of more than 10 kg. During the examination I–III period, in contrast, the highest risk of CHD was found in men who lost the greatest amount of weight; the relative risk of CHD for men who lost more than 2.5 kg was 1.25 (95% CI 0.98–1.60). The authors conclude that levels of relative weight in early adulthood were positively related to risk of CHD occurring much later in the lives of these men. The association between CHD incidence and weight change appeared to be modified by age, with higher risks for earlier weight gain and later weight loss in the lives of these men. *Am J Epidemiol* 1998;147:379–86.

cohort studies; coronary disease; weight gain; weight loss

Despite well-established associations between relative weight and cardiovascular risk factors, epidemiologic studies of relative weight and coronary heart disease (CHD) incidence have provided equivocal results (1–9). This may be due to differences in study duration and size, classification of overweight or obesity, age range and genetic background of study participants, or failure to account for confounders of the relation, such as cigarette smoking (1–4). Regarding study duration, it has been suggested that the putative effects of excess weight or obesity may accumulate over a long period of time (10–13), and some studies

have reported associations between CHD and levels of relative weight in early adulthood (5, 8, 11).

Change in weight would also be expected to be associated with CHD incidence, since CHD risk factor profiles are generally improved by weight loss and worsened by weight gain (14–17). Findings of epidemiologic studies have been contradictory, however, with morbidity and mortality from CHD associated with both weight gain (5, 8, 18, 19) and weight loss (19–21). The period of life during which weight change is measured may be an important consideration. In younger adults, changes in weight primarily reflect changes in body fat, while weight loss in older persons may be due to decreases in fat mass or lean body mass or may indicate underlying disease (5, 22–24).

In this paper, we examine associations between CHD incidence and relative weight and change in weight among the male, Japanese-American participants of the Honolulu Heart Program (HHP). An earlier study indicated that relative weight at age 25 and later weight gain were positively associated with CHD incidence in this cohort (11). We have extended those observations with enhanced analytic techniques, a longer period of follow-up, and examination of two periods of weight change: age 25 to HHP examination I and examination I to examination III.

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Abbreviations: BMI, body mass index; CHD, coronary heart disease; CI, confidence interval; HHP, Honolulu Heart Program.

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## MATERIALS AND METHODS

### Study sample

The HHP began in 1965 as a prospective study of coronary heart disease and stroke among 8,006 men of Japanese ancestry. Sample selection was designed to include all noninstitutionalized, Japanese-American male residents of Oahu, born between 1900 and 1919. Further details of the study and the selection of the cohort are available elsewhere (25, 26). This study uses data from HHP examinations I (1965-1968) and III (1971-1975). Data for examination III were collected from 6,860 of the 7,598 surviving members of the cohort. Examination III nonparticipants were older, had higher body mass index (BMI) levels at age 25, were heavier smokers, and had higher rates of CHD than did the remaining cohort members. For participants included in this study, the average length of time between examinations I and III was 6.1 years (standard deviation, 0.5 years).

### Outcome

CHD was defined as nonfatal myocardial infarction or fatal CHD. During HHP follow-up examinations, prevalence of CHD was established in each participant by clinical history, electrocardiogram, and/or cardiac enzyme measurements, as defined previously (11, 13). Incident cases of CHD were identified via a continuous surveillance system established in 1965. This system consists of regular monitoring of all hospital discharge records, death certificates, local obituary notices, and medical examiner's cases on the island of Oahu (27). All cases are reviewed in a consensus meeting of study physicians. Ascertainment of cases is believed to be complete.

### Risk factor data

At examination I, study participants were asked to recall their weight at age 25. This recalled estimate was found to correlate ( $r = 0.80$ ) with weight provided at the time of draft registration for 1,805 men who were approximately 25 years old at the time of registration (11). The BMI at age 25 was calculated as recalled weight (kg)/height (m)<sup>2</sup> as measured at examination I, assuming no significant change in height. At examinations I and III, weight was measured with a balance scale with the subjects in light clothing and without shoes (28). Weight change was calculated for two periods: examination I weight minus recalled weight at age 25 (early weight change) and examination III weight minus examination I weight (late weight change).

From examination I information, participants were classified as never smokers, former smokers, or cur-

rent smokers of 1-9, 10-19, or 20 or more cigarettes a day. Examination I smoking information was utilized because smoking behavior at this time could have influenced weight change between examinations I and III. Conversely, examination III systolic blood pressure and serum total cholesterol levels were used as covariates in some statistical models, since these measures may have been influenced by previous weight change. Blood pressure was measured three times with a sphygmomanometer and a standard cuff on the left arm of a seated participant, and the average level was used for these analyses. Nonfasting serum cholesterol concentrations were determined in Hawaii by the Autoanalyzer N-24-A method (Technicon Corporation, Tarrytown, New York) (29). The criteria used for diabetes in this paper differ from that recommended by the World Health Organization for epidemiologic studies (30). Participants were classified as diabetic for any of the following conditions at any of the first three HHP examinations: taking diabetic medications, self-reported history of diabetes, or positive urine glucose test. In addition, participants were given a 50-g load of glucose at examination I, in the nonfasted state, and blood glucose in excess of 200 mg/dl after 1 hour was considered to represent diabetes. An additional 43 participants without these conditions but who reported being on a diabetic diet at examination III were classified as diabetic. Occurrence of gastric ulcers and cancer during the HHP examinations were also noted for participants.

### Sample exclusions

A total of 474 men who had prevalent CHD at any of the first three examinations were excluded from these analyses. To minimize the possibility of undiagnosed CHD preceding or accompanying the observed weight change, a further 90 cases of CHD occurring within 3 years of examination III were excluded. A total of 120 men were missing weight or examination I smoking data, making the final sample size 6,176. For analyses incorporating examination III systolic pressure or total cholesterol levels, a further 100 men were excluded for missing information.

### Statistical analysis

Study characteristics were compared between men with and those without incident CHD using *t* tests for continuous variables and chi-square analyses for dichotomous variables. Rates of CHD, adjusted for person-years of follow-up, were calculated across categories of the distributions of BMI at age 25 and early and late weight change. BMI at age 25 was categorized into five groups, using the cutpoints 21.2, 23.0, 24.6,

and 26.2 kg/m<sup>2</sup>. These cutpoints were chosen to correspond to those from an earlier examination of relative weight and CHD in this cohort (11). Men with age 25 BMI estimates of less than 21.2 kg/m<sup>2</sup> formed the reference category in multivariate analyses. Early weight change was categorized by the following cutpoints: -5, -2.5, 2.5, 5, and 10 kg. Participants who gained or lost no more than 2.5 kg between age 25 and examination I constituted a "stable" weight group. Given the shorter duration and lower absolute change between examinations I and III, more narrow cutpoints were used to categorize late weight change: more than 2.5, between 2.5 and 1.1, and  $\pm 1$  kg. The stable weight category for weight change during this period was a gain or loss within 1 kg. The stable categories for both periods of weight change were used as the reference groups in multivariate analyses.

Since follow-up time varied among study participants, proportional hazards analysis was used to determine the relative risks and 95 percent confidence intervals for CHD incidence associated with levels of BMI at age 25 and early and late weight change (31). The base models included adjustment for examination I age level as a continuous variable and dummy terms for the smoking categories described above, with never smokers as the reference. Self-report of parental history of CHD was considered as a covariate, but was not retained, since it was not significantly associated with risk of CHD incidence, and this information was missing for 351 participants.

Additional proportional hazards models included adjustment for examination III levels of systolic pressure and total cholesterol to assess the mediating role of these variables in the weight change and CHD

incidence relation. Since weight loss in the elderly can indicate presence of disease (23, 24), prevalence rates of the above disease conditions were compared between men who lost the greatest amount of weight between examinations I and III and the other participants.

Finally, since the age range of the cohort might have contributed to the misclassification of weight change between "early" and "late" periods of adulthood, the multivariate proportional hazards models were repeated, stratified by the median age of the cohort at examination I (55 years). That is, both periods of weight change may have more accurately coincided with late periods of life among older members of the cohort and early periods of life among younger cohort members. Further justification for these stratified analyses was provided by previous research, which indicated that the association between baseline levels of BMI and CHD in this cohort was modified by age (32). Trend tests were conducted across some of the weight change categories, using the median value of weight change for each category. For all models, the proportional hazards assumption was verified by graphic analyses. All data analyses were carried out using SAS software (SAS Institute, Inc., Cary, North Carolina).

## RESULTS

Descriptive characteristics of the study sample are summarized in table 1, overall and by CHD status. The study sample can be characterized as lean, as assessed by BMI at age 25. On average, participants gained weight between age 25 and examination I, but had a

TABLE 1. Characteristics of the Honolulu Heart Program study sample, according to incidence of coronary heart disease

	Total sample (n = 6,176)		CHD cases (n = 479)		Noncases (n = 5,697)	
	Mean	(SD)†	Mean	(SD)	Mean	(SD)
Age at examination I (years)	54.0	(5.4)	54.9	(5.6)*	53.9	(5.4)
Examination I smoking status (%)						
Nonsmoker	31.9		29.4		32.2	
Former smoker	26.2		25.7		26.2	
Smoker (cigarettes/day)						
1-9	2.5		1.5		2.6	
10-19	7.4		6.1		7.5	
$\geq 20$	32.0		37.4*		31.5	
Body mass index at age 25 (kg/m <sup>2</sup> )	22.0	(2.4)	22.5	(2.6)*	21.9	(2.4)
Weight change (kg)						
Age 25 to examination I	5.0	(7.8)	6.2	(8.1)*	4.9	(7.8)
Examination I to examination III	-0.5	(3.7)	-0.8	(4.0)	-0.5	(3.7)

\* Denotes statistically significant difference ( $p < 0.05$ ) between participants with and those without incident coronary heart disease (CHD). *t* tests were performed for continuous variables and chi-square tests for dichotomous variables.

† SD, standard deviation.

slight loss of weight between examinations I and III. Weight change between the two periods was weakly correlated ( $r = -0.16$ ). Early weight gain and later weight loss were greater among participants with incident CHD over the follow-up period. Men who developed CHD were older and more likely to be heavy smokers than were men who did not develop CHD.

Relative to the thinnest men, risk of incident CHD was significantly elevated in all categories of BMI at age 25 after adjustment for examination I age and smoking status and for early and late weight change categories (table 2, model 1). The heaviest men at age 25 had more than twice the risk of the thinnest men.

Men who gained more than 2.5 kg between age 25 and examination I had a significantly higher risk of incident CHD compared with men in the stable category, and this excess risk increased progressively across the weight gain categories (table 3, model 1). Weight loss over this period was not significantly associated with CHD risk. For the period of later weight change, in contrast, risk of CHD increased progressively with weight loss (table 4, model 1). The excess risk of CHD associated with a weight loss of more than 2.5 kg between examinations I and III was of borderline statistical significance ( $p = 0.07$ ).

Compared with the remaining participants, men who lost more than 2.5 kg between examinations I and III were significantly older than the other participants (54.4 vs. 53.8 years), had higher BMI levels at age 25 (22.2 vs. 21.9 kg/m<sup>2</sup>), and gained more weight between age 25 and examination I (6.8 vs. 4.4 kg) (data not shown). These men also had a significantly higher prevalence of diabetes for the period of examination I through III (39 vs. 29 percent), ulcers (7 vs. 5 percent), and cancer (3 vs. 2 percent) than did the other cohort members. In logistic regression analyses controlled for age, smoking status, BMI at age 25, and early weight change, men who lost more than 2.5 kg between examinations I and III were more likely to be diabetic

(odds ratio = 1.44, 95 percent confidence interval (CI) 1.28–1.63) than were the other men. To explore further the association between CHD incidence and later weight loss of more than 2.5 kg, we repeated the model 1 analyses, stratified by diabetic status. The risk of CHD associated with a later loss of more than 2.5 kg was higher among the diabetics (relative risk = 1.38, 95 percent CI 0.93–2.06) than among the nondiabetics (relative risk = 1.05, 95 percent CI 0.76–1.45).

As expected, addition of systolic pressure and total cholesterol to the proportional hazards models reduced the excess risk associated with higher BMI levels at age 25 and weight gain during the two periods (tables 2–4, model 2). However, the excess risk among those who lost more than 2.5 kg between examinations I and III was further elevated after statistical control for these variables. Later weight change was positively associated with examination III levels of systolic pressure and total cholesterol after adjustment for examination I age, smoking status, BMI at age 25, and early weight change. Across the five categories of later weight change (from weight loss to weight gain), least squares mean estimates of systolic pressure and total cholesterol at examination III varied systematically from 135.2 to 142.4 mmHg and from 5.33 to 5.65 mmol/dl (206.3–218.3 mg/dl), respectively.

Stratified analyses indicated that the association between CHD incidence and weight change was modified by age at examination I (table 5). The risks associated with early weight gain were much higher among the group of men who were less than age 55 years at the time of examination compared with the older group of men (table 5). There was a significant positive trend for CHD across the four categories of the stable and weight gain groups among men younger than 55 years ( $p = 0.0002$ ), but not among the older group ( $p = 0.13$ ). In contrast, weight loss between examinations I and III was more predictive of CHD

TABLE 2. Relative risks and 95% confidence intervals for coronary heart disease, by category of body mass index at age 25 in the Honolulu Heart Program

BMI* category (kg/m <sup>2</sup> )	No.	No. of CHD* cases	CHD rate/1,000 person- years	Model 1†		Model 2‡	
				RR*	95% CI*	RR	95% CI
<21.2	2,408	144	4.24	1.00		1.00	
21.2–22.9	1,985	156	5.62	1.36	1.08–1.71	1.28	1.02–1.61
23.0–24.5	1,044	111	7.61	1.92	1.49–2.47	1.85	1.43–2.39
24.6–26.2	435	37	6.05	1.69	1.17–2.45	1.49	1.02–2.17
>26.2	304	31	7.67	2.44	1.61–3.69	2.01	1.32–3.07

\* BMI, body mass index; CHD, coronary heart disease; RR, relative risk; CI, confidence interval.

† Model 1 adjusted for examination I age and smoking status, weight change between age 25 and examination I, and weight change between examinations I and III ( $n = 6,176$ ).

‡ Model 2 adjusted for model 1 covariates, plus examination III levels of systolic blood pressure and total cholesterol ( $n = 6,076$ ).

**TABLE 3. Relative risks and 95% confidence intervals for coronary heart disease in the Honolulu Heart Program, by category of weight change between age 25 and examination I (early weight change)**

Weight change category	No.	No. of CHD* cases	CHD rate/1,000 person-years	Model 1†		Model 2‡	
				RR*	95% CI*	RR	95% CI
Lost >5 kg	553	35	4.76	0.76	0.51-1.15	0.88	0.58-1.34
Lost 2.6-5 kg	448	31	5.03	0.96	0.64-1.46	1.03	0.68-1.57
Change within $\pm$ 2.5 kg	1,355	83	4.35	1.00		1.00	
Gained 2.6-5 kg	689	58	5.91	1.41	1.00-1.97	1.37	0.98-1.93
Gained 5.1-10 kg	1,612	141	6.18	1.60	1.22-2.11	1.50	1.13-1.98
Gained >10 kg	1,519	131	6.15	1.75	1.32-2.33	1.54	1.16-2.06

\* CHD, coronary heart disease; RR, relative risk; CI, confidence interval.

† Model 1 adjusted for examination I age and smoking status, categories of body mass index at age 25, and weight change between examinations I and III ( $n = 6,176$ ).

‡ Model 2 adjusted for model 1 covariates, plus examination III levels of systolic blood pressure and total cholesterol ( $n = 6,076$ ).

among the older group ( $p = 0.04$  for trend test across the stable and weight loss categories) than among the younger group ( $p = 0.6$ ). Risk of CHD was significantly elevated among men in the older group who lost more than 2.5 kg between examinations I and III compared with the stable group ( $p = 0.05$ ).

## DISCUSSION

Several main findings emerged from this prospective study of weight and weight change and risk of CHD in Japanese-American men. First, levels of relative weight in early adulthood, as indicated by the BMI at age 25, were positively associated with the incidence of CHD in older age, even in this sample of generally lean men. Second, the risk of CHD was further elevated by weight gain between age 25 and examination I, when the sample age range was 45-68 years. Between examinations I and III, however, there was an excess risk of CHD associated with weight loss. Stratified analyses indicated that these relations were modified by age, with higher risks associated with weight gain between ages 25 and 55 and weight

loss after age 55. As far as we are aware, this is the first study to describe the risks of CHD associated with early and late periods of weight change in the same individuals.

Rhoads and Kagan (11) had reported earlier that estimated BMI at age 25 in this cohort was positively associated with CHD occurring within 10 years of examination I, although this relation was not controlled for smoking or unequal length of follow-up. Results of our study show that these early levels of relative weight continue to be strongly associated with risk for CHD over an even longer follow-up period, which began when the median age of the cohort was 62 years (3 years after examination III). Some of the excess risk of CHD in the higher age-25 BMI categories appeared to be mediated through risk factors, although the age-25 BMI terms remained statistically significant predictors. The latter associations (table 2, model 2) may represent residual confounding in measured and unmeasured intermediary variables or, alternatively, a true independent effect of relative weight on CHD risk. Nevertheless, results in this and the Nurses' Health Study (8) support the hypothesis that

**TABLE 4. Relative risks and 95% confidence intervals for coronary heart disease in the Honolulu Heart Program, by category of weight change between examinations I and III (late weight change)**

Weight change category	No.	No. of CHD* cases	CHD rate/1,000 person-years	Model 1†		Model 2‡	
				RR*	95% CI*	RR	95% CI
Lost >2.5 kg	1,595	140	6.49	1.25	0.98-1.60	1.38	1.08-1.78
Lost 1.1-2.5 kg	970	74	5.49	1.14	0.85-1.52	1.15	0.86-1.54
Change within $\pm$ 1 kg	1,781	121	4.75	1.00		1.00	
Gained 1.1-2.5 kg	735	59	5.69	1.24	0.91-1.69	1.20	0.88-1.64
Gained >2.5 kg	1,095	85	5.46	1.10	0.84-1.46	0.97	0.73-1.30

\* CHD, coronary heart disease; RR, relative risk; CI, confidence interval.

† Model 1 adjusted for examination I age and smoking status, categories of body mass index at age 25, and weight change between age 25 and examination I ( $n = 6,176$ ).

‡ Model 2 adjusted for model 1 covariates, plus examination III levels of systolic blood pressure and total cholesterol ( $n = 6,076$ ).

**TABLE 5. Relative risks and 95% confidence intervals for coronary heart disease in the Honolulu Heart Program, by category of body weight change between age 25 and examination I (early weight change) and examinations I and III (late weight change)\***

Weight change category	Examination I (age 45-54 years)			Examination I (≥age 55 years)		
	CHD† cases/total sample	RR†	95% CI†	CHD cases/total sample	RR	95% CI
<b>Age 25 to examination I</b>						
Lost >5 kg	17/228	1.10	0.60-1.99	18/325	0.59	0.34-1.04
Lost 2.6-5 kg	14/221	1.15	0.62-2.14	17/227	0.84	0.48-1.48
Change within ±2.5 kg	38/794	1.00		45/561	1.00	
Gained 2.6-5 kg	36/448	1.79	1.13-2.83	22/241	1.10	0.66-1.84
Gained 5.1-10 kg	72/1,044	1.68	1.13-2.50	69/568	1.60	1.09-2.34
Gained >10 kg	88/1,051	2.19	1.49-3.23	43/468	1.31	0.85-2.02
<b>Examinations I-III</b>						
Lost >2.5 kg	68/931	1.10	0.79-1.55	72/664	1.44	1.00-2.07
Lost 1.1-2.5 kg	42/568	1.14	0.78-1.68	32/402	1.11	0.71-1.72
Change within ±1 kg	70/1,132	1.00		51/649	1.00	
Gained 1.1-2.5 kg	38/470	1.31	0.88-1.95	21/265	1.07	0.65-1.79
Gained >2.5 kg	47/685	1.06	0.73-1.54	38/410	1.17	0.77-1.79

\* Stratification by age at examination I. Adjusted for examination I and smoking status, and categories of body mass index at age 25.

† CHD, coronary heart disease; RR, relative risk; CI, confidence interval.

the effects of excess weight on the development of heart disease may start at an early age and accumulate over a long period of time (1, 12, 13).

Previous studies of weight change and CHD have provided contradictory results. Reports from the Nurses' Health Study described positive associations (8, 18), while weight loss, assessed over two different time periods, was positively associated with CHD among the Framingham cohort (20, 21). A study among Harvard University alumni found significantly higher rates of CHD mortality among both those who lost and those who gained weight (19). In the Health Professionals Follow-up Study, Rimm et al. (5) recently reported that weight gain since age 21 was significantly associated with risk of CHD in men less than age 65 years at the start of follow-up, but not among those over age 65. In discussing the divergent findings between the two age groups, the authors noted that age-related changes in body composition and weight loss due to subclinical disease in the elderly make the interpretation of lifetime weight changes more difficult in this group.

Results of our study underscore the importance of age in the association between weight change and CHD. We found earlier changes in weight to be positively related to CHD incidence and changes that occurred later in life to be negatively related to CHD. The specific age cutpoints and examination intervals used to define life periods in this study were, of course, arbitrary, but the results are consistent with an early weight gain composed primarily of adipose tis-

sue and a later weight loss that may have reflected underlying disease (5, 22-24). It is unlikely that the later weight loss described in this study was voluntary, since only 111 of the men (1.8 percent) reported being on a diet to lose weight at examination III. Men in the highest examination I-III weight loss category had higher rates of certain diseases that affect body weight, and exploratory analyses indicated that the association between weight loss and CHD was stronger among men with diabetes. One plausible interpretation of these observations is that weight gain early in life leads to the development of diabetes, which, in turn, is related both to later wasting (weight loss) (33, 34) and increased risk of CHD (35, 36).

Alternatively, the possibility remains that the observed risks with later weight loss are merely indicative of weight history earlier in life. Later weight loss was associated with higher estimates of BMI at age 25 and larger increases in weight between age 25 and examination I. Even with multivariate analytic techniques, it is not possible to separate completely the effects of early and late changes in weight. Thus, the excess risk associated with later weight loss may be related to residual confounding of weight and weight gain earlier in life or to a history of type II diabetes or to some other morbidity we were not able to adequately describe. There is little reason to believe that weight loss later in life is causally associated with increased risk of CHD. In fact, it is of clinical note that in our study and in the Framingham Study (20), later weight loss was associated with improvements in risk

factors for CHD, even though the actual incidence of CHD was elevated. We found that the risk associated with men losing more than 2.5 kg between examinations I and III was increased after statistical control for systolic pressure and total cholesterol because these men had lower systolic pressure and total cholesterol levels. Thus, weight loss in older age could indicate an increased risk for CHD, although this may not be evident from the risk factor profile, which appears to improve regardless of the cause of the loss in weight.

Prospective studies are subject to survivorship and participation biases, and approximately 14 percent of the original HHP cohort was lost to follow-up by examination III. However, additional analyses indicated that the relations between CHD and age 25 BMI and early weight change were affected little by these types of biases. We were not able to validate directly the recalled weight at age 25 for these men, although other studies have found recalled weight to be accurate (8, 37). In their previous report, Rhoads and Kagan (11) showed a high correlation ( $r = 0.80$ ) between recalled weight at age 25 to measured weight in a subsample of this cohort. If we assume a random error in the recall of weight in this prospective study, this would tend to attenuate the observed relations. Another limitation in this study is the lack of information on weight between age 25 and examination I. We therefore cannot be sure if the reference group for this period was truly weight stable. Body circumference measures were not taken during the first three examinations of HHP, so it was not possible to control for the effects of body fat distribution on risk for CHD (2, 5). We have not controlled for the parameter of weight variability or fluctuation in this study, which has been found to be independently predictive of CHD (21, 38) and cardiovascular disease mortality (39) in other studies. However, in a recent report from HHP (40), an indicator of weight variability was not significantly related to mortality from CHD in this cohort. In preliminary analyses, we found no independent relation between weight variability and the outcome of fatal and nonfatal CHD. Additional limitations of our epidemiologic study include the inability to statistically control for genetic influences and the presence and severity of all the diseases associated with weight change. Finally, we are limited in being able to generalize these results for Japanese-American men to other populations (41), although the consistency of our findings with the literature suggests the biologic effects of weight and weight change to be similar.

These results show that relative weight and weight gain in early adulthood are directly related to later risk of CHD in these Japanese-American men. Conversely, weight loss occurring later in life is associated with

increased risk, although the reasons are unclear. In conclusion, these observations imply a lowered risk of CHD among lean adults who maintain a stable weight over time.

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