15 January 1998 Volume 128 Number 2

Annals of Internal Medicine

Body Weight, Weight Change, and Risk for Hypertension in Women

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Background: Obesity increases the risk for hypertension, but the effects of modest long-term weight changes have not been precisely quantified.

Objective: To investigate body mass index (BMI) and weight change in relation to risk for hypertension.

Design: Cohort study.

Setting: General community.

Participants: Cohort of 82 473 U.S. female nurses 30 to 55 years of age followed every 2 years since 1976. The follow-up rate was 95%.

Measurements: Primary risk factors examined were 1) BMI at age 18 years and midlife and 2) long-term and medium-term weight changes. The outcome was incident cases of hypertension.

Results: By 1992, 16 395 incident cases of hypertension had been diagnosed. After adjustment for multiple covariates, BMI at 18 years of age and midlife were positively associated with occurrence of hypertension (P for trend $<$ 0.001). Long-term weight loss after 18 years of age was related to a significantly lower risk for hypertension, and weight gain dramatically increased the risk for hypertension (compared with weight change $\leq$2 kg, multivariate relative risks were 0.85 for a loss of 5.0 to 9.9 kg, 0.74 for a loss $\geq$10 kg, 1.74 for a gain of 5.0 to 9.9 kg, and 5.21 for a gain $\geq$25.0 kg). Among women in the top tertile of baseline BMI at age 18 years, weight loss had a greater apparent benefit. The association between weight change and risk for hypertension was stronger in younger ($<$45 years of age) than older women ($\geq$55 years of age). Medium-term weight changes after 1976 showed similar relations to risk for hypertension.

Conclusions: Excess weight and even modest adult weight gain substantially increase risk for hypertension. Weight loss reduces the risk for hypertension.

This paper is also available at http://www.acponline.org.

Ann Intern Med. 1998;128:81-88.

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Most cross-sectional studies have shown an association between obesity and hypertension, and the prevalence of hypertension seems to increase with the degree of obesity (1, 2). In prospective studies, obesity has been strongly related to future risk for hypertension (3–5).

Several clinical trials have found that short-term weight loss reduces blood pressure in hypertensive patients or persons with high normal blood pressure (6–8). However, the long-term efficacy of this approach for controlling blood pressure is not well established. Because treating hypertension over a long period is costly (9), the best approach for the control of hypertension in the general population is primary prevention. The degree to which long-term weight loss effectively prevents or delays the onset of hypertension in a normotensive population has important public health implications.

We prospectively investigated body mass index (BMI) at 18 years of age and at midlife, as well as long-term and medium-term weight changes, in relation to subsequent risk for hypertension in a large cohort of U.S. female nurses without diagnosed hypertension at baseline. In a previous analysis of this cohort (10), higher BMI at midlife strongly increased the risk for developing hypertension during the subsequent 4 years of follow-up. However, this analysis did not examine BMI in early adulthood and weight changes in relation to the occurrence of hypertension. In the present analysis, we extended the follow-up to 16 years and included 13 120 additional incident cases of hypertension. The substantially greater power of this study allowed us to investigate the association of weight change with risk for hypertension and to examine whether weight loss could more effectively prevent hypertension in subgroups of the population (especially those defined by baseline BMI and age).

Methods

The Nurses' Health Study is a long-term follow-up study of female registered nurses who were 30 to 55 years of age at study entry. In 1976, 121 700 nurses responded to a mailed questionnaire on medical history and health behaviors. Follow-up questionnaires have been sent to participants every 2 years to identify incident diagnoses of hypertension and other medical events and to update information on risk factors. Further details have been reported elsewhere (11). As of 1 June 1992, the follow-up rate was 95% of potential person-years.

For the current analysis, we excluded women who, at baseline, reported high blood pressure (or use of antihypertensive medications) or a history of myocardial infarction, angina pectoris, stroke, coronary artery surgery, diabetes mellitus, or any cancer other than nonmelanoma skin cancer (n = 19 654). If any of these conditions developed during follow-up, the women were excluded from subsequent follow-up intervals. We also excluded women for whom information on height (n = 127) or weight at age 18 years (n = 19 447) was missing. The analytic cohort consisted of 82 473 women.

Measurement of Exposures

The baseline questionnaire solicited information on age, current weight, height, parity, oral contraceptive use, smoking status, family history of myocardial infarction, menopausal status, postmenopausal use of hormones, and other variables. Updated information on most of these variables was collected on biennial follow-up questionnaires. In 1980, we asked participants about weight at 18 years of age and current alcohol consumption. Starting in 1986, we assessed the level of physical activity in detail.

Body mass index was used as a measure of obesity. Current BMI was updated every 2 years by using the most recent body weight. Women were categorized into 10 groups by using whole-number cut-points of current BMI and by deciles of BMI at age 18 years to provide a reasonable number of participants in each category. The lowest category was used as the referent.

We calculated long-term weight changes (from 18 years of age to the beginning of each 2-year follow-up interval) and medium-term weight changes (from 1976 to the beginning of each 2-year follow-up interval). Women were divided into nine groups: weight loss of 10 kg or more, loss of 5.0 to 9.9 kg, loss of 2.1 to 4.9 kg, loss or gain of 2.0 kg or less, gain of 2.1 to 4.9 kg, gain of 5.0 to 9.9 kg, gain of 10.0 to 19.9 kg, gain of 20.0 to 24.9 kg, and gain of 25 kg or more. The stable weight group (loss or gain $\leq$2.0 kg) was the referent. For medium-term weight change, we examined the effects of weight loss sustained for a longer period by grouping women according to weight changes from 1976 to the beginning of the current interval and from 1976 to the beginning of the previous interval. Thus, in this analysis, women were categorized into a specific weight-change group only if their weight changes from 1976 to the current interval and to the previous interval fell into the same category. Otherwise, they were classified into an unstable weight group.

In a subsample of 184 participants living in the Boston area, self-reported weights were highly correlated with measured weights (r = 0.96; mean difference, 1.5 kg) (12). In another sample of 118 younger nurses aged 25 to 42 years, recalled weights at 18 years of age were highly correlated with weights at 17 to 21 years of age that were recorded on nursing-school physical examination forms (r = 0.87; mean difference, 1.4 kg) (13).

Ascertainment of Hypertension

Incident cases of hypertension were identified by self-reports of physician-diagnosed high blood pressure. On biennial follow-up questionnaires, we asked whether high blood pressure (except that occurring during pregnancy) had been diagnosed by a physician and, if so, the date of diagnosis. By 1992, 16 395 incident cases of hypertension had been diagnosed.

The validity of self-reported diagnosis of hypertension was assessed in a random sample of 100 nurses who had reported a diagnosis of high blood pressure on the 1982 questionnaire (14). Of the 85 women who responded to a supplementary questionnaire, all but 1 confirmed their previous reports of hypertension; 62 of the 85 women gave written permission for review of their medical records. We obtained records for 51 women; all of them had blood pressure measurements higher than 140/90 mm Hg, and 39 (77%) had blood pressure measurements greater than 160/95 mm Hg. To investigate the likelihood of false-negative responses, blood pressure was measured in another sample of 194 nurses living in the Boston area. Among the 161 women without a previous self-report of hypertension, 7% had a blood pressure higher than 140/90 mm Hg but none had a blood pressure greater than 160/95 mm Hg. In addition, self-reported physician diagnosis of hypertension is a strong predictor of myocardial infarction and stroke in this cohort (15); this finding provided further biological evidence that the self-reported diagnosis of hypertension is a valid measure in our study.

Statistical Analysis

Follow-up started in 1976 when the baseline questionnaire was returned; follow-up time accrued until the date of diagnosis of hypertension, use of

antihypertensive medications, myocardial infarction, angina pectoris, coronary artery surgery, stroke, diabetes mellitus, any cancer other than nonmelanoma skin cancer, death, or 1 June 1992, whichever came first. Women were not included in the analysis during an interval if information on their current weight was missing or if they had been pregnant for at least 6 months during the previous 2-year interval. These women, however, could reenter the analyses in the subsequent follow-up intervals.

Relative risk was used as the measure of association and was computed as the incidence in a specific category of BMI or weight change divided by the rate in the reference category. We used proportional hazards analyses to compute age-adjusted and multivariate-adjusted relative risks with 95% CIs (16, 17). Weight change and BMI were treated as continuous variables in the models to test linear trends and to compute relative risks for each one-unit increase in BMI and weight change. We calculated the population attributable risk percentages that were attributable to long-term and medium-term weight gain compared with weight change of 2 kg or less (18). Stratified analyses were performed to examine whether age and baseline BMI modified the relation between weight change and risk for hypertension.

Role of Study Sponsors

Amgen, Inc., approved the proposal for data analysis but was not involved in analyzing, interpreting, or reporting the data.

Results

By 1992, 16 395 incident cases of hypertension had been diagnosed during 923 544 person-years of follow-up. In an age-adjusted analysis, higher current BMI was strongly associated with an increasing risk for hypertension (**Table 1**). This association was not altered after adjustment for height, family history of myocardial infarction, parity, oral contraceptive use, menopausal status, postmenopausal use of hormones, and cigarette smoking. Compared with women who had a BMI less than 20 kg/m^2, women with a BMI of 31 kg/m^2 or more had a multivariate relative risk of 6.31 (95% CI, 5.80 to 6.87). This increase in risk for hypertension was monotonic with BMI; even for women with a BMI of 20.0 to 20.9 kg/m^2, the risk was significantly elevated (relative risk, 1.15 [CI, 1.04 to 1.27]). In the multivariate model in which BMI was treated as a continuous variable, an increase in BMI of 1 kg/m^2 was associated with a 12% increase in risk for hypertension.

Table 1. Relative Risk for Subsequent Hypertension According to Body Mass Index*

BMI	Cases, *n*	Person-Years of Follow-up	Relative Risk (95% CI)†	Multivariate Relative Risk (95% CI)‡
Current BMI				
<20.0 kg/m^2	742	98 691	1.00 (reference)	1.00 (reference)
20.0–20.9 kg/m^2	962	109 863	1.15 (1.04–1.26)	1.15 (1.04–1.27)
21.0–21.9 kg/m^2	1356	128 229	1.35 (1.23–1.48)	1.36 (1.24–1.49)
22.0–22.9 kg/m^2	1401	111 158	1.56 (1.43–1.71)	1.57 (1.44–1.72)
23.0–23.9 kg/m^2	1557	105 038	1.80 (1.64–1.96)	1.82 (1.66–1.98)
24.0–24.9 kg/m^2	1621	91 387	2.12 (1.94–2.32)	2.15 (1.97–2.35)
25.0–25.9 kg/m^2	1477	69 815	2.52 (2.30–2.75)	2.55 (2.33–2.79)
26.0–27.9 kg/m^2	2251	82 271	3.26 (3.00–3.55)	3.33 (3.06–3.62)
28.0–30.9 kg/m^2	2482	73 505	4.10 (3.77–4.46)	4.20 (3.86–4.57)
≥31.0 kg/m^2	2546	53 587	6.12 (5.63–6.65)	6.31 (5.80–6.87)
Continuous§	16 395	923 544		1.116 (1.113–1.120)
P for trend				<0.001
BMI at age 18 years				
≤18.2 kg/m^2	1572	89 749	1.00 (reference)	1.00 (reference)
18.3–19.1 kg/m^2	1483	98 300	1.01 (0.94–1.08)	1.02 (0.94–1.09)
19.2–19.7 kg/m^2	1400	90 671	1.10 (1.02–1.18)	1.11 (1.03–1.20)
19.8–20.4 kg/m^2	2036	126 996	1.18 (1.10–1.26)	1.19 (1.11–1.27)
20.5–20.9 kg/m^2	1207	78 920	1.14 (1.06–1.23)	1.15 (1.06–1.24)
21.0–21.5 kg/m^2	1688	103 436	1.23 (1.15–1.32)	1.24 (1.15–1.33)
21.6–22.2 kg/m^2	1571	87 483	1.38 (1.28–1.48)	1.38 (1.28–1.48)
22.3–23.3 kg/m^2	1883	95 946	1.54 (1.44–1.65)	1.54 (1.43–1.65)
23.4–25.0 kg/m^2	1669	77 753	1.69 (1.57–1.81)	1.68 (1.57–1.81)
>25.0 kg/m^2	1886	74 289	2.29 (2.13–2.46)	2.28 (2.12–2.45)
Continuous§	16 395	923 544		1.083 (1.077–1.089)
P for trend				<0.001

* BMI = body mass index.
† For current BMI, relative risks were adjusted for age (5-year categories). For BMI at age 18 years, relative risks were adjusted for age (5-year categories) and weight change since age 18 years (9 categories).
‡ Adjusted for age (5-year categories), height (continuous), family history of myocardial infarction (yes or no), parity (nulliparous, 1 to 2 births, 3 to 4 births, ≥5 births), oral contraceptive use (never, current, or past), menopausal status (premenopausal or postmenopausal), postmenopausal use of hormones (never, current, or past), and smoking status (never; past; current: 1 to 14 cigarettes/d, 15 to 34 cigarettes/d, ≥35 cigarettes/d, or unknown quantity). For BMI at age 18 years, relative risks were also adjusted for weight change since age 18 years (9 categories) in addition to the above variables.
§ For 1-kg/m^2 increment in BMI, derived from a continuous multivariate model.

Higher BMI at 18 years of age was associated with an increased risk for hypertension later in life after we controlled for age, subsequent weight change, and other covariates (P for trend < 0.001). Women whose BMI at 18 years of age was greater than 25 kg/m^2 had a relative risk of 2.28 (CI, 2.12 to 2.45) compared with women whose BMI at 18 years of age was 18.2 kg/m^2 or less. The increase in risk with BMI at 18 years of age was also monotonic. For every 1-kg/m^2 increase in BMI at 18 years of age, risk for hypertension increased 8%.

Relative risks for subsequent hypertension according to long-term (12 to 50 years) weight change after age 18 years are shown in **Table 2**. When we used the group with stable weight (weight change ≤ 2 kg) as the referent, weight loss was associated with a significantly lower risk for hypertension. After we controlled for age, BMI at age 18 years, and other covariates, the risks were reduced by 15% for weight loss of 5.0 to 9.9 kg and by 26% for a weight loss of 10 kg or more. In contrast, weight gain substantially increased risk for hypertension; a five-fold increase in risk was noted among women who gained more than 25 kg after age 18 years. Even modest weight gains were associated with increased risks; women gaining 2.1 to 4.9 kg had a 29% increase in risk, and women gaining 5.0 to 9.9 kg had a 74% increase. This association seemed to be approximately linear (P for trend < 0.001). A 1-kg increase in weight was associated with a 5% increase in risk for hypertension.

In a model that contained both current BMI and weight change after age 18 years, weight change was still significantly associated with risk for hypertension after current BMI was held constant (relative risk, 1.93 [CI, 1.75 to 2.12] for weight gain ≥25 kg). This finding suggests that both attained BMI and history of weight change are independent predictors of risk for hypertension. Among women with the same current BMI, those who had a larger previous weight gain after 18 years of age were at higher risk for hypertension than those who gained less weight.

Table 3 presents the association between medium-term (2 to 14 years) weight changes after 1976 (weight changes during midlife) and risk for hypertension. Consistent with the effects of long-term weight changes, medium-term weight loss was associated with a significantly lower risk for hypertension; even modest weight gain markedly increased the risk. Because of high recidivism in weight loss, we sought to determine whether sustained weight loss would have a stronger protective effect by regrouping women according to their weight changes in the current and previous intervals. As expected, women who maintained their weight loss for at least 2 years had a substantially lower risk for hypertension (risk reductions, 24% for weight loss of 5.0 to 9.9 kg and 45% for loss ≥10 kg).

To determine whether baseline BMI modified the relation between long-term weight change and risk for hypertension, we stratified the data by the tertiles of BMI at age 18 years (**Figure 1**). For women who were in the first and second tertiles of BMI at age 18 years (<22 kg/m^2), subsequent weight loss after age 18 years did not appreciably reduce risk for hypertension. However, subsequent weight gain was associated with a marked increase in risk compared with women who had stable weight. In contrast, for women who were in the highest tertile of BMI at age 18 years (≥22 kg/m^2), subsequent weight loss substantially decreased risk for hypertension; the relative risks were 0.72 (CI, 0.62 to 0.84) for weight loss of 5.0 to 9.9 kg and 0.57 (CI, 0.48 to 0.67) for loss of 10 kg or more. Weight gain in this group was also associated with an increase in risk.

To examine whether age modified the relation between long-term weight change and risk for hypertension, we stratified women by age (**Figure 2**). Among younger women (<45 years), a strong asso-

Table 2. Relative Risk for Subsequent Hypertension According to Weight Change since Age 18 Years

Weight Change since Age 18 Years	Cases, *n*	Person-Years of Follow-up	Relative Risk (95% CI)*	Multivariate Relative Risk (95% CI)†
Loss ≥10 kg	212	18 746	0.75 (0.64–0.87)	0.74 (0.64–0.87)
Loss 5.0–9.9 kg	368	35 230	0.85 (0.76–0.96)	0.85 (0.75–0.96)
Loss 2.1–4.9 kg	605	63 692	0.91 (0.82–1.00)	0.91 (0.82–1.00)
Loss or gain ≤2.0 kg	1174	128 495	1.00 (reference)	1.00 (reference)
Gain 2.1–4.9 kg	1869	165 565	1.28 (1.19–1.38)	1.29 (1.20–1.39)
Gain 5.0–9.9 kg	3246	212 016	1.72 (1.61–1.84)	1.74 (1.62–1.86)
Gain 10.0–19.9 kg	5122	209 456	2.65 (2.48–2.82)	2.70 (2.53–2.89)
Gain 20.0–24.9 kg	1751	47 146	3.92 (3.63–4.23)	4.06 (3.76–4.38)
Gain ≥25.0 kg	2048	43 199	4.97 (4.61–5.35)	5.21 (4.84–5.62)
Continuous‡	16 395	923 544		1.047 (1.046–1.049)
P for trend				<0.001

* Adjusted for age (5-year categories) and body mass index at age 18 years (in deciles).

† Adjusted for age (5-year categories), body mass index at age 18 years (in deciles), height (continuous), family history of myocardial infarction (yes or no), parity (nulliparous, 1 to 2 births, 3 to 4 births, ≥5 births), oral contraceptive use (never, current, or past), menopausal status (premenopausal or postmenopausal), postmenopausal use of hormones (never, current, or past), and smoking status (never; past; current: 1 to 14 cigarettes/d, 15 to 34 cigarettes/d, ≥35 cigarettes/d, or unknown quantity).

‡ For 1-kg weight increment, derived from a continuous multivariate model.

Table 3. Relative Risk for Hypertension According to Weight Change from 1976

Weight Change	Cases, *n*	Person-Years of Follow-up	Relative Risk (95% CI)*	Multivariate Relative Risk (95% CI)†
Weight change from 1976 to most recent measurement				
Loss ≥10 kg	134	7443	0.65 (0.54–0.78)	0.64 (0.53–0.76)
Loss 5.0–9.9 kg	358	21 240	0.81 (0.73–0.91)	0.81 (0.72–0.90)
Loss 2.1–4.9 kg	1101	69 269	0.95 (0.86–1.02)	0.95 (0.88–1.01)
Loss or gain ≤2.0 kg	3677	278 435	1.00 (reference)	1.00 (reference)
Gain 2.1–4.9 kg	4102	233 339	1.28 (1.22–1.34)	1.27 (1.22–1.33)
Gain 5.0–9.9 kg	3057	136 450	1.56 (1.48–1.64)	1.55 (1.48–1.64)
Gain 10.0–19.9 kg	1947	59 240	2.10 (1.98–2.23)	2.10 (1.97–2.23)
Gain 20.0–24.9 kg	266	6533	2.33 (2.04–2.66)	2.33 (2.04–2.67)
Gain ≥25.0 kg	197	4041	2.84 (2.43–3.32)	2.85 (2.44–3.33)
Continuous‡	14 839	815 988		1.042 (1.039–1.045)
P for trend				<0.001
Weight changes sustained for ≥2 years				
Loss ≥10 kg	47	3029	0.56 (0.41–0.75)	0.55 (0.40–0.74)
Loss 5.0–9.9 kg	72	4842	0.77 (0.60–0.98)	0.76 (0.60–0.97)
Loss 2.1–4.9 kg	266	18 407	0.92 (0.80–1.05)	0.91 (0.80–1.04)
Loss or gain ≤2.0 kg	1487	122 898	1.00 (reference)	1.00 (reference)
Gain 2.1–4.9 kg	1538	86 445	1.38 (1.28–1.48)	1.38 (1.28–1.48)
Gain 5.0–9.9 kg	1046	46 827	1.61 (1.48–1.75)	1.61 (1.48–1.75)
Gain 10.0–19.9 kg	710	20 855	2.19 (1.99–2.41)	2.18 (1.98–2.40)
Gain 20.0–24.9 kg	39	1179	1.82 (1.31–2.54)	1.82 (1.31–2.54)
Gain ≥25.0 kg	62	1323	2.79 (2.13–3.65)	2.79 (2.13–3.65)
Unstable weight	7005	351 479	1.32 (1.24–1.40)	1.31 (1.24–1.39)
P for trend				<0.001

* Adjusted for age (5-year categories) and body mass index in 1976 (in deciles).
† Adjusted for age (5-year categories), body mass index in 1976 (in deciles), height (continuous), family history of myocardial infarction (yes or no), parity (nulliparous, 1 to 2 births, 3 to 4 births, ≥5 births), oral contraceptive use (never, current, or past), menopausal status (premenopausal or postmenopausal), postmenopausal use of hormones (never, current, or past), and smoking status (never; past; current: 1 to 14 cigarettes/d, 15 to 34 cigarettes/d, ≥35 cigarettes/d, or unknown quantity).
‡ For 1-kg weight increment, derived from a continuous multivariate model.

ciation was found between weight change and risk for hypertension after adjustment for age, BMI at age 18 years, and other covariates (*P* for trend < 0.001). The relative risks were 0.56 (CI, 0.41 to 0.77) for weight loss of 10 kg or more and 6.90 (CI, 5.96 to 7.99) for weight gain of at least 25 kg. Among older women (≥55 years), the association was attenuated; the relative risks were 0.86 (CI, 0.66 to 1.12) for weight loss of 10 kg or more and 3.72 (CI, 3.23 to 4.29) for gain of at least 25 kg. For middle-aged women (45 to 54 years), the magnitude of the association was intermediate.

We also examined whether baseline BMI in 1976 and age modified the relation between medium-term weight change and risk for hypertension. Generally, the results were consistent with those for long-term weight change. Among women who had a BMI less than 21 kg/m^2 in 1976, subsequent weight loss did not reduce risk for hypertension, whereas weight gain dramatically increased risk. Among women with a BMI of at least 25 kg/m^2 in 1976, subsequent weight loss was associated with a substantial risk reduction (relative risk, 0.73 [CI, 0.63 to 0.84] for weight loss of 5.0 to 9.9 kg; relative risk, 0.52 [CI, 0.43 to 0.63] for loss ≥10 kg). The risk reduction was even greater for weight loss sustained for at least 2 years (relative risk, 0.66 [CI, 0.47 to 0.92] for weight loss of 5.0 to 9.9 kg; relative risk, 0.47 [CI, 0.34 to 0.65] for loss ≥10 kg). The association between medium-term weight change and risk for hypertension was much stronger in younger women than in older women.

To adjust for a possible confounding effect of alcohol consumption, we conducted an additional analysis that excluded the 1976 to 1980 follow-up because alcohol intake was assessed in 1980. Adjustment for alcohol intake did not appreciably change

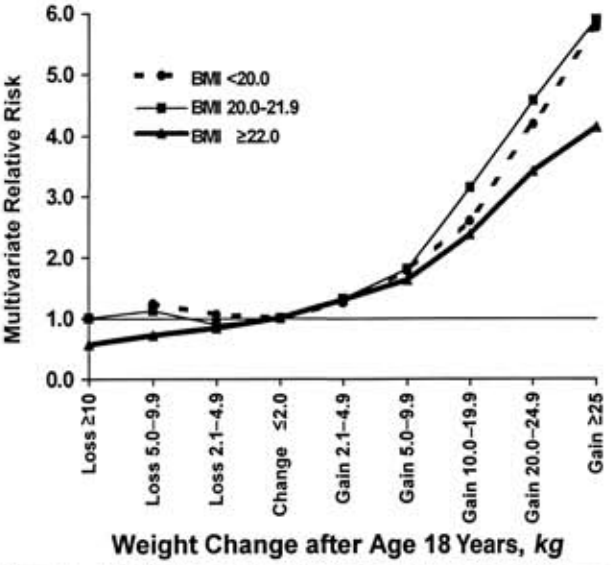

Figure 1. Multivariate relative risk for hypertension according to weight change after age 18 years within strata of body mass index (*BMI*) at age 18 years. Adjusted for age, BMI (measured in kg/m^2) at age 18 years, height, family history of myocardial infarction, parity, oral contraceptive use, menopausal status, postmenopausal use of hormones, and smoking status.

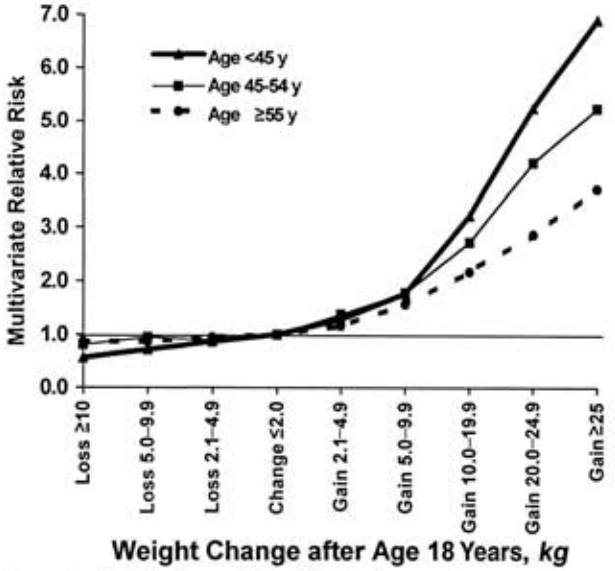

Figure 2. Multivariate relative risk for hypertension according to weight change after age 18 years within strata of age. Adjusted for age, body mass index at age 18 years, height, family history of myocardial infarction, parity, oral contraceptive use, menopausal status, postmenopausal use of hormones, and smoking status.

the associations seen in the complete follow-up. In addition, adjustment for physical activity, assessed in 1986, did not materially change the associations of BMI and weight changes with subsequent risk for hypertension. To exclude the possibility of detection bias, we limited the analysis to women who had had their blood pressure checked in the previous 2 years; this analysis did not materially change the associations of BMI and weight changes with risk for hypertension.

The population attributable risk for hypertension in women with long-term weight gain after age 18 years was 48% (CI, 45% to 50%) compared with women who had stable weight. For medium-term weight gain during midlife, the population attributable risk was 21% (CI, 19% to 22%).

Discussion

Higher BMI at midlife was strongly related to an increased risk for subsequent hypertension. Although the association of BMI at 18 years of age with subsequent hypertension seemed weaker than the association between BMI at midlife and hypertension, it was still appreciable after we controlled for weight change later in life. Long-term and medium-term weight loss was associated with a substantially reduced risk for subsequent hypertension, and weight gain was related to a markedly increased risk. Sustained weight loss had a stronger apparent protective effect. The benefit from weight loss was largely limited to women who had a higher baseline BMI, and it seemed to be greater in younger women than in older women.

In previous cross-sectional studies, body weight or BMI has been positively associated with prevalence of hypertension in a continuous, monotonic manner (1, 2). This association has been found in populations from industrialized and nonindustrialized areas (19, 20). Data from prospective studies, such as the Framingham Study and the Normative Aging Study, have confirmed this association (4, 21, 22). Our study is consistent with previous studies indicating a strong, monotonic relation between BMI at midlife and subsequent risk for hypertension. In addition, higher BMI in early adult life was also a significant risk factor for hypertension in later adulthood after adjustment for subsequent weight changes.

Many clinical trials have shown that short-term weight loss often results in a significant reduction in blood pressure and potentiates the effects of antihypertensive drugs among hypertensive patients or persons with high normal blood pressure (23–25). MacMahon and colleagues (26) summarized five randomized trials of weight reduction in hypertensive patients and reported that a 9.2-kg weight loss decreased systolic blood pressure by 6.3 mm Hg and diastolic blood pressure by 3.1 mm Hg, on average. Although short-term weight loss seems to be a promising method for reducing blood pressure among hypertensive patients, the efficacy of this approach in the primary prevention of hypertension is not well established. Because as many as 50 million Americans, or one in four adults, are classified as hypertensive and 2 million new cases of hypertension are diagnosed each year (27, 28), an effective means of preventing hypertension has great clinical and public health importance.

In studies that examined weight change and subsequent blood pressure in normotensive persons, weight change was found to be the most important predictor of subsequent blood pressure after adjustment for initial blood pressure (5, 29, 30). In the Framingham Study (22), risk for hypertension was related to weight change after 25 years of age. Our data provide powerful evidence that long-term and medium-term weight gain dramatically increase the incidence of hypertension and that weight loss substantially reduces the incidence. This relation seems to be approximately linear across the range of weight changes.

In our stratified analyses, the apparent protective effect of weight loss was much stronger in women with a higher baseline BMI. For women with a lower baseline BMI, subsequent weight loss did not reduce risk for hypertension, possibly because the weight lost in these women may have largely consisted of lean mass rather than fat mass. However,

subsequent weight gain (which would consist primarily of fat mass) substantially elevated risk for hypertension.

In previous studies, the relation of weight to blood pressure varied with age. Although the relation exists among all age groups, it seems to be stronger for younger adults and to gradually weaken with age (31, 32). Overweight was associated with a greater relative risk for hypertension in adults 20 to 45 years of age than in those 45 to 65 years of age (33). We found that the apparent protective effect of weight loss and the adverse effect of weight gain were stronger in younger women than older women. This effect probably occurred because most of the variation in weight among younger adults of the same sex and height is due to differences in adipose mass. Many, but not all, elderly persons lose substantial amounts of lean body mass, often because of greatly reduced physical activity. As a result, variation in lean body mass can contribute to a greater degree to differences in weight and changes in weight, thereby reducing the validity of weight and weight change as measures of adiposity (34). Indeed, in one elderly group, BMI was similarly associated with lean mass and fat mass (35).

The mechanisms leading to hypertension in obese persons are not completely known. It is hypothesized that increased sympathetic nervous system activity, insulin resistance and hyperinsulinemia, sodium retention, and enhanced vascular reactivity are involved in the development of hypertension (36). Some investigators (37, 38) have reported a decrease in plasma renin activity and plasma aldosterone levels after weight loss; this suggests that the renin–angiotensin–aldosterone axis may play a role in causing hypertension in obese persons.

In summary, a substantial body of evidence indicates that excess body fat and weight gain as an adult appreciably increase risk for hypertension. Thus, maintaining a lean body weight throughout adulthood seems to be beneficial in the primary prevention of hypertension. For women who are already overweight, weight loss is an effective strategy for reducing risk for hypertension. These prospective data in women offer strong support for the 1995 U.S. weight guidelines to avoid adult weight gain with increasing age (39).

Acknowledgments: The authors thank the participants in the Nurses' Health Study for their continuing dedication and commitment. They also thank Leiming Li, Mark Shneyder, and Karen Corsano for unfailing assistance.

Grant Support: By research grants CA 40356 and DK 46200 from the National Institutes of Health and by grants from Amgen, Inc.

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It was an element in Doctor Sloper's reputation that his learning and his skill were very evenly balanced; he was what you might call a scholarly doctor, and yet there was nothing abstract in his remedies—he always ordered you to take something. Though he was felt to be extremely thorough, he was not uncomfortably theoretic; and if he sometimes explained matters more minutely than might seem of use to the patient, he never went so far (like some practitioners one had heard of) as to trust to the explanation alone, but always left behind him an inscrutable prescription. There were some doctors that left the prescription without offering any explanation at all; and he did not belong to that class either, which was after all the most vulgar.

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