Weight Gain and the Risk of Developing Insulin Resistance Syndrome

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OBJECTIVE — Obesity and weight gain have been associated independently with hypertension, hyperinsulinemia, and dyslipidemia; however, prior research has not looked at the relation between weight gain from early adulthood to middle age and the development of this cluster of risk factors, known as insulin resistance syndrome.

RESEARCH DESIGN AND METHODS — The association between weight gain over 30 years (defined as the difference between measured weight in middle age and participant recall of their weight at age 20) and the odds of developing insulin resistance syndrome at middle age was examined in a population-based sample of 2,272 eastern Finnish men.

RESULTS — Each 5% increase in weight over the reported weight at age 20 was associated with nearly a 20% greater risk of insulin resistance syndrome by middle age, after adjustment for age and height. Moreover, there was a strong graded association between categories of weight gain and risk of insulin resistance syndrome. Men with weight increases of 10–19%, 20–29%, or ≥30% since age 20 were 3.0, 4.7, or 10.6 times more likely to have insulin resistance syndrome, respectively, by middle age, compared with men within 10% of their weight at age 20. Adjustments for age, height, physical activity, smoking, education, and parental history of diabetes did not alter these findings.

CONCLUSIONS — The odds of having developed the hemodynamic and metabolic abnormalities that characterize insulin resistance syndrome by middle adulthood were increasingly higher the greater the weight gain over the preceding 30 years. This study adds to the literature identifying deleterious effects of weight gain from young to middle adulthood.

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Epidemiological, experimental, and clinical evidence shows that obesity and weight gain are associated with increased risk for cardiovascular diseases (CVDs) and events and type 2 diabetes, and with risk factors for these disorders, including hypertension, dyslipidemia, glucose intolerance, and insulin resistance (1–9). Weight loss may reduce these risk factors and could delay or prevent the onset of CVD, type 2 diabetes, and other diseases associated with increased weight (3). Weight fluctuates to some degree throughout one's life and is known to increase with age. Mechanisms of weight gain and the amount and duration of increased weight in relation to known risk factors for CVD and type 2 diabetes are less well understood.

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Abbreviations: CVD, cardiovascular disease; dBP, diastolic blood pressure; IHD, ischemic heart disease; KIHD, Kuopio Ischemic Heart Disease Risk Factor Study; sBP, systolic blood pressure; WHR, waist-to-hip ratio.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Few individuals at risk of CVD or type 2 diabetes have only one risk factor (10). Usually, several hemodynamic and metabolic abnormalities cluster together in an individual. Various combinations of these factors have been referred to as Reaven's syndrome, syndrome X, the deadly quartet, metabolic cardiovascular syndrome, and others (11). Because resistance to insulin-stimulated glucose uptake appears to be a primary mechanism underlying these abnormalities, the currently recommended term is insulin resistance syndrome (11,12). Some definitions of insulin resistance syndrome imply that obesity is an essential component; however, Reaven (13) argues that because all of the elements of insulin resistance syndrome can be seen in nonobese individuals and can develop independently of obesity, obesity should not be included.

There is a direct correspondence between insulin action and relative weight (14), and, as noted, weight gain is associated with incident hypertension and glucose intolerance (1,8,9). However, few studies have specifically investigated the association between increases in weight over time and development of insulin resistance syndrome. Accordingly, we examined the relationship between weight gain from early to middle adulthood and occurrence of insulin resistance syndrome, defined as the co-occurrence of hyperinsulinemia, dyslipidemia, and hypertension, in a population sample of middle-aged eastern Finnish men.

RESEARCH DESIGN AND METHODS

Subjects

Subjects were from the Kuopio Ischemic Heart Disease Risk Factor Study (KIHD), a study designed to investigate unestablished risk factors for ischemic heart disease, carotid atherosclerosis, and related outcomes in a population-based sample of eastern Finnish men (15). Of the 3,433 eligible men aged 42, 48, 54, or 60 years residing in or around the town of Kuopio, 198 were excluded because of death, serious disease, or migration from the area. A total of 2,682 (82.9%) agreed to participate in the study.

Baseline examinations were conducted between March 1984 and December 1989. No significant differences have been found between participants and nonparticipants (16). For this study, men treated for diabetes with insulin (n = 6) and those with missing data on weight at age 20, on weight at the baseline examination (n = 207), or on any covariates (n = 197) were excluded, leaving 2,272 subjects in the analyses.

Assessment of weight and weight gain

Weight. Current weight was measured at the baseline exam using a balance scale. Weight at age 20 was assessed from a self-report questionnaire administered at baseline.

Percent weight gain. Percent weight gain was calculated as weight change (difference in measured baseline weight and recalled weight at age 20) divided by the age 20 weight, multiplied by 100.

BMI. BMI was calculated as weight (kilograms) divided by height (meters) squared.

Waist-to-hip ratio (WHR). WHR at baseline was calculated as the ratio of waist circumference (average of one measure taken after inspiration and one taken after expiration at the midpoint between the lowest rib and the iliac crest) to hip circumference (measured at the level of the trochanter major).

Assessment and definition of insulin resistance syndrome

Venous samples were obtained after fasting and abstinence from smoking for 12 h, abstinence from alcohol for 3 days, and abstinence from analgesics for 7 days. After a 30-min supine rest, blood was drawn without tourniquet, using Terumo Venoject VT-100 PZ vacuum tubes (Terumo, Tokyo). Samples were cooled immediately on ice (4°C). After centrifugation, serum was frozen (−80°C) and stored until assay.

Blood glucose. Blood glucose level was determined from fresh blood samples with the glucose dehydrogenase method after precipitation of the proteins with trichloroacetic acid (Granutest 100; Merck, Darmstadt, Germany).

Serum insulin. Serum insulin level was determined from frozen serum samples with a Novo Biolabin radioimmunoassay kit (Novo Nordisk, Bagsvaerd, Denmark).

Lipids. HDL cholesterol was separated from fresh serum samples using precipitation and ultracentrifugation (17). Cholesterol contents of lipoprotein fractions and serum triglycerides were measured enzymatically (Boehringer Mannheim, Mannheim, Germany).

Systolic blood pressure (sBP) and diastolic blood pressure (dBP). Blood pressure was measured with a random-zero sphygmomanometer (Hawksley, London, U.K.) by a trained observer. Consistent with current guidelines (18), sBP and dBP were each calculated as the average of two measurements, taken at min 5 and 10 of a 10-min seated rest.

Medications. Information on medication for hypertension, diabetes, and other disorders was obtained from a self-administered questionnaire and confirmed during the medical interview. Medications were grouped and coded by a nurse using the Nordic Pharmacopoeia coding system.

Insulin resistance syndrome. Insulin resistance syndrome cases were identified if they met the following criteria at the baseline examination: *1*) hypertension, sBP ≥160 mmHg or dBP ≥95 mmHg (19) or use of antihypertensive medication; 2) hyperinsulinemia, fasting serum insulin ≥11.7 mU/l (upper tertile of the baseline distribution of serum insulin); and 3) dyslipidemia, serum HDL cholesterol <1.0 mmol/l, or serum triglycerides ≥2.3 mmol/l (20).

Five additional subjects were classified as cases because they were hypertensive and dyslipidemic and showed evidence of hyperglycemia at baseline, with fasting blood glucose ≥6.7 mmol/l (21) or reported history of diabetes controlled by diet or oral medication.

Assessment of baseline covariates

Age. Age at baseline was modeled by dummy-coded variables for ages 48, 54, and 60 years, with age 42 as the referent.

Height. Height was measured at the baseline exam and modeled continuously (centimeters).

Smoking. Cigarette smoking was assessed by self-report. Nonsmokers (people who never smoked) were the reference category, with a dummy-coded variable for former smokers and a continuous variable for current smokers (pack-years).

Physical activity. Physical activity was assessed at baseline by using a 12-month leisure-time history modified from the Minnesota Leisure Time Physical Activity Questionnaire to represent the 16 most common leisure-time physical activities of middle-aged Finnish men and by including self-reported intensity of physical activity (22). For each activity on the questionnaire, subjects reported either not engaging in the activity or the frequency per month over the preceding year, average duration per occasion, and intensity level. Metabolic units were assigned for each activity according to reported intensity. Details on methods of calculation, reliability, and validity of these measures have been described elsewhere (16). Analyses used an intensity-dependent measure of total duration of physical activity that previously predicted type 2 diabetes in this population (23).

Education. Education, assessed as self-reported years of school completed, was modeled continuously.

Parental diabetes. Parental history of diabetes was assessed from self-report and modeled by a dummy-coded variable for each parent's history.

Statistical analysis

The relationship between percentage of gained weight and odds of having insulin resistance syndrome was examined using age- and height-adjusted unconditional logistic regression models. Subsequent models included covariates for age, height, physical activity, smoking, education, and maternal and paternal history of diabetes. Two sets of analyses were performed. Initially, percentage of gained weight was entered into the models continuously. In the second set of analyses, percentage of gained weight was divided into approximate quartiles: <10% of weight at age 20 (reference category), 10–19, 20–29, and ≥30%. Men whose baseline weight was the same or less than their self-reported weight at age 20 (n = 238) were included in the first quartile. (Separate analyses with these 238 men as the reference category produced results nearly identical to those reported and did not provide useful information regarding the impact of minimal weight gain [1–15 lb] on insulin resistance syndrome.) Less than 2% of all participants (n = 44) lost ≥10% of their reported age 20 weight by the baseline exam and thus constituted too small of a group to examine separately. Tests for trend, in odds ratios and other variables, were calculated by comparing adjacent categories of percent weight gain (24). A trend test was interpreted as significant if all comparisons achieved the specified criterion, which in this study was adjusted for three comparisons and set at $P < 0.0167$ (0.05/3).

Additional analyses compared insulin resistance syndrome cases with noncases on subject characteristics, with age adjustment. Significance values were computed using paired t tests or χ^2 tests, as appropriate. Subject characteristics also were examined by the categories of percentage of

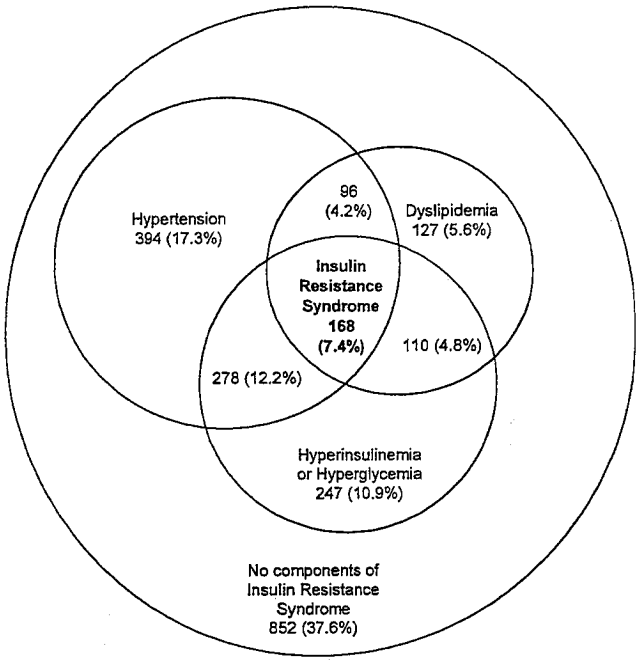

Figure 1—*Distribution of insulin resistance syndrome and its components among 2,272 men.*

gained weight. Analyses were conducted using LOGISTIC and GLM procedures in SAS (SAS Institute, Cary, NC), version 6.12.

RESULTS — Figure 1 presents the distribution of the three components of insulin resistance syndrome. There were 168 men (7.4%) who had hypertension, hyperinsulinemia, and dyslipidemia at baseline, thus meeting the criteria for insulin resistance syndrome. Approximately 55% of participants had one or two components of insulin resistance syndrome, whereas 852 men (37.6%) had none.

Compared with men without insulin resistance syndrome, those with the syndrome were significantly older and heavier, had greater WHR and BMI in middle age, and were more likely to report a positive maternal history of diabetes (Table 1). Additionally, prevalence of obesity (BMI ≥28 kg/m²) was significantly higher among men with than among those without insulin resistance syndrome. Participants with and without the insulin resistance syndrome did not differ in self-reported weight at age 20 (68.2 vs. 67.6 kg), although those with the syndrome gained significantly more weight by middle age (31.1 vs. 18.5% of age 20 weight).

Weight gain and odds of having insulin resistance syndrome

Percentage of gained weight from young to middle adulthood was significantly associated with prevalence of insulin resistance syndrome at baseline. Modeled continuously, percentage of gained weight was associated with an odds ratio of 1.04 (β coefficient, 0.0359; 95% CI 1.04–1.05) for insulin resistance syndrome, after age and height adjustment. In other words, each 5% increase over the reported age 20 weight was associated with nearly 20% higher odds of having insulin resistance syndrome in middle age. Adjustments for physical activity, smoking, education, and parental history of diabetes did not alter this finding.

With percentage of gained weight modeled categorically, a strong, positive, graded association was observed between categories of weight gain and odds of having insulin resistance syndrome (Table 2). Compared with men who gained <10% of their age 20 weight, those who gained 10–19, 20–29, or ≥30% were approximately 3, 4.7, and 10.6 times more likely, respectively, to have insulin resistance syndrome in middle age, after adjusting for age and height. Associations were relatively unchanged after adjustment for physical activity, smoking, education, and parental history of diabetes. The test for trend by comparison of adjacent categories was significant ($P < 0.0167$), indicating significantly increasing risk with increasing weight gain.

Because fasting insulin may be a less reliable marker of insulin sensitivity and thus a less accurate measure of hyperinsulinemia among people with impaired glucose tolerance (25), we also examined the association between weight gain and insulin resistance syndrome while excluding participants whose baseline fasting glucose was ≥6.7 mmol/l ($n = 20$) or who reported diabetes controlled by diet or oral medications ($n = 4$). Results were essentially identical to those reported above (data not shown).

Table 1—*Baseline subject characteristics of 2,272 men with (cases) and without (noncases) insulin resistance syndrome*

Characteristics	Cases	Noncases	*P* value
n	168	2,104	—
Weight at baseline (kg)	89.1 ± 0.91	79.7 ± 0.26	<0.0001
WHR at baseline	0.99 ± 0.005	0.94 ± 0.001	<0.0001
Age (years)	54.3 ± 0.41	52.8 ± 0.11	<0.0003
Height (cm)	173.1 ± 0.47	172.9 ± 0.13	<0.78
BMI at baseline (kg/m²)	29.7 ± 0.27	26.6 ± 0.08	<0.0001
Obesity (%)	63.7	29.3	<0.0001
Physical activity (min/week)	75.2 ± 10.70	85.3 ± 3.02	<0.36
Education (years)	9.3 ± 0.26	8.7 ± 0.07	<0.02
Smoking status (%)			
Never	20.8	27.1	<0.08
Former	45.2	39.0	<0.11
Current	33.9	33.8	<0.98
Parental history of diabetes (%)			
Mother	27.4	19.0	<0.008
Father	5.4	6.9	<0.45

Data shown are age-adjusted means ± SEM or prevalence (%). Obesity was defined as BMI ≥28 kg/m². *P* values are from *t* tests or χ^2 tests comparing cases and noncases.

Table 2—*Odds ratios and 95% CIs for insulin resistance syndrome among 2,272 men by categories of percent weight gained from age 20 to age at the baseline examination*

Percent weight gain	Odds ratio (95% CI)
Model 1	
<10	1.00 (Referent)
10–19	3.08 (1.57–6.06)
20–29	4.69 (2.42–9.09)
≥30	10.61 (5.72–19.68)
Model 2	
<10	1.00 (Referent)
10–19	2.89 (1.46–5.70)
20–29	4.51 (2.32–8.77)
≥30	10.20 (5.46–19.05)

Model 1 was adjusted for age and height; Model 2 was adjusted for age, height, physical activity, smoking, education, and maternal and paternal history of diabetes.

Weight gain and subject characteristics

Table 3 presents age-adjusted means ± SEM or prevalence (%) of subject characteristics across the categories of percentage of gained weight. The proportion of insulin resistance syndrome cases increased from 1.8 to 16.5% from the lowest to the highest weight-gain categories. Not surprisingly, significant trends across categories were noted for weight at middle age and self-reported weight at age 20: men with the most weight gain were the heaviest in middle age and had the lowest weight at age 20. This group had the correspondingly highest average BMI and WHR in middle age. Trends across weight-gain categories for other characteristics listed in Table 3 were not significant, although the pattern for smoking status is informative. Men with the largest weight gain were more likely to be former smokers (49.8%) than were those whose weight remained relatively stable (30.3%).

Weight gain and individual components of insulin resistance syndrome

To examine the effects of weight gain on individual components of insulin resistance syndrome, we calculated a series of unconditional logistic regression models with percentage of gained weight modeled either continuously or categorically and with hypertension, hyperinsulinemia, or dyslipidemia as the outcomes. Percentage of gained weight from age 20 to middle age was significantly associated with each component of insulin resistance syndrome and most strongly related to hyperinsulinemia. Modeled continuously, the odds ratio for percentage of gained weight was 1.04 (β coefficient, 0.0355; 95% CI 1.03–1.04) for hypertension, 1.02 (β coefficient, 0.0202; 95% CI 1.01–1.03) for dyslipidemia, and 1.07 (β coefficient, 0.0649; 95% CI 1.06–1.08) for hyperinsulinemia, after age and height adjustment. In other words, each 5% increase over reported age 20 weight was associated with a 19% greater chance of becoming hypertensive, an 11% greater chance of becoming dyslipidemic, and a 38% greater chance of being hyperinsulinemic by middle age.

With weight gain modeled categorically, men who had gained 10–19, 20–29 or ≥30% of their age 20 weight were at increasingly greater risk of having hypertension, dyslipidemia, and hyperinsulinemia by middle age, compared with men who had relatively stable weight (Table 4). Adjustments for risk factors did not change the associations.

Weight gain and insulin resistance syndrome by history of ischemic heart disease (IHD)

Metabolic and hemodynamic abnormalities associated with insulin resistance syndrome also underlie CVD (10,13), and it is conceivable that associations between weight gain and occurrence of insulin resistance syndrome could vary according to history of CVD. Thus, we recalculated the logistic regression models separately for participants with and without prevalent IHD at baseline. Participants were considered to have prevalent IHD if they reported a history of angina pectoris or prior myocardial infarction during the baseline medical interview; currently used anti-angina medication; or had positive findings of angina according to the Rose Questionnaire (26).

Table 3—*Subject characteristics by category of percent weight gain*

	Percent weight gain			
	<10	10–19	20–29	≥30
Cases/*n* (%)	12/673 (1.8)	31/587 (5.3)	38/486 (7.8)	87/526 (16.5)
Weight at baseline (kg)	71.0 ± 0.36	78.3 ± 0.38	83.0 ± 0.42	92.2 ± 0.40
Weight at age 20 (kg)	70.1 ± 0.28	68.1 ± 0.30	66.7 ± 0.33	64.8 ± 0.032
WHR at baseline	0.91 ± 0.002	0.94 ± 0.003	0.96 ± 0.003	0.99 ± 0.003
Age (years)	52.7 ± 0.20	52.7 ± 0.22	52.8 ± 0.24	53.6 ± 0.23
Height (cm)	172.2 ± 0.23	172.8 ± 0.25	173.3 ± 0.27	173.6 ± 0.26
BMI at baseline (kg/m²)	23.9 ± 0.10	26.2 ± 0.11	27.6 ± 0.12	30.6 ± 0.11
Physical activity (min/week)	86.3 ± 5.34	91.0 ± 5.71	81.3 ± 6.28	78.0 ± 6.05
Education (years)	8.5 ± 0.13	9.1 ± 0.14	8.8 ± 0.15	8.6 ± 0.15
Smoking status (%)				
Never	29.7	28.6	25.7	21.5
Former	30.3	39.0	41.6	49.8
Current	40.0	32.4	32.7	28.7
Parental history of diabetes (%)				
Maternal	16.8	20.6	20.8	20.9
Paternal	7.3	7.5	6.4	5.7

Data are means ± SEM or prevalence (%). Mean percentage of gained weight across categories was 1.6, 14.9, 24.5, and 42.7%, respectively. Weight at baseline, weight at age 20, WHR at baseline, and BMI at baseline had a Bonferroni-adjusted *P* for trend ≤0.017.

Table 4—*Odds ratios and 95% CIs for hypertension, dyslipidemia, and hyperinsulinemia among 2,272 men by categories of percent weight gained from age 20 to age at the baseline examination*

	Percent weight gain			
	<10	10–19	20–29	≥30
Model 1				
Hypertension	1.00 (Referent)	1.98 (1.56–2.53)	2.72 (2.12–3.50)	4.61 (3.59–5.92)
Dyslipidemia	1.00 (Referent)	1.69 (1.26–2.27)	1.92 (1.42–2.60)	2.86 (2.15–3.81)
Hyperinsulinemia	1.00 (Referent)	2.62 (1.94–3.53)	6.40 (4.77–8.60)	14.63 (10.87–19.70)
Model 2				
Hypertension	1.00 (Referent)	1.94 (1.52–2.47)	2.65 (2.06–3.42)	4.36 (3.39–5.62)
Dyslipidemia	1.00 (Referent)	1.74 (1.29–2.34)	2.01 (1.48–2.74)	3.12 (2.33–4.18)
Hyperinsulinemia	1.00 (Referent)	2.53 (1.87–3.42)	6.39 (4.74–8.61)	14.71 (10.87–19.91)

Data are odds ratios (95% CI). Cases: n = 936 for hypertension; n = 501 for dyslipidemia; n = 803 for hyperinsulinemia. Model 1 was adjusted for age and height; Model 2 was adjusted for age, height, physical activity, smoking, education, and maternal and paternal history of diabetes.

Results were essentially unchanged from the full model. There were 102 cases of insulin resistance syndrome among 1,724 men without IHD. After age and height adjustment, men with weight gain of 10–19, 20–29, or ≥30% or more had 2.9 (95% CI 1.3–6.7), 4.7 (95% CI 2.1–10.6), and 9.5 (95% CI 4.4–20.5) greater odds of insulin resistance syndrome in middle age, relative to men within 10% of their age 20 weight. Among the 548 men with a history of IHD, there were 66 cases of insulin resistance syndrome. Weight gain was associated with 3.7 (95% CI 1.1–12.0), 4.6 (95% CI 1.4–14.7), and 11.8 (95% CI 4.1–34.1) greater odds of insulin resistance syndrome, respectively, across weight gain categories. Adjustment for risk factors did not affect the associations between weight gain and insulin resistance syndrome in men with or without prevalent IHD.

CONCLUSIONS — This study shows that middle-aged men who gained >10% of their age 20 weight were significantly more likely to have developed hypertension, hyperinsulinemia, and dyslipidemia, the characteristic clustering of risk factors known as insulin resistance syndrome, over the intervening years, than were men whose weight remained stable. Risk of developing insulin resistance syndrome was increased by nearly 20% for every 5% gain in weight from age 20 to an average age of 53. This increased risk was independent of age, height, physical activity, smoking, education, and parental history of diabetes. To our knowledge, this is the first study to examine the association between weight gain from early to middle adulthood and the occurrence of insulin resistance syndrome.

Information in this study was obtained cross-sectionally; however, a temporal distinction is possible for weight gain because we have data on weight at two time points. Our findings suggest that weight gain preceded the development of insulin resistance syndrome; however, lack of information on insulin levels, blood pressure, triglycerides, and HDL levels of these men at age 20 did not allow us to examine if any characteristics of insulin resistance syndrome were present in young adulthood, before weight gain. Nonetheless, several lines of evidence support the interpretation that the insulin resistance syndrome seen in 7% of our sample occurred after weight gain. Weight gain can lead to hyperinsulinemia and is associated with glucose intolerance and insulin resistance (8,27,28). Similarly, obesity is known to be an insulin-resistant state and is strongly associated with hyperinsulinemia (29,30). Nearly 64% of our cases met the criterion for obesity at baseline (Table 1), whereas obesity was nearly nonexistent among cases (n = 1) and noncases (n = 23) at age 20. Interestingly, however, more than one third of our cases were not obese, and yet weight gain in adulthood apparently triggered metabolic alterations that contributed to insulin resistance syndrome in these men. The pattern of association between weight gain and insulin resistance syndrome among nonobese men was similar to that found in the entire sample, with increasingly greater weight gain related to increasingly higher odds of insulin resistance syndrome (data not shown). Moreover, in the full sample, post hoc adjustment for baseline WHR, a reliable indicator of abdominal obesity, did not diminish the observed dose-response pattern of associations, which remained significant, although the point estimates were decreased somewhat (odds ratios: 1.0, 2.0, 2.5, and 4.5 from lowest to highest weight-gain categories, respectively).

Insulin resistance most commonly occurs as a result of increasing weight, lack of exercise, aging, or diseases or drugs that antagonize the actions of insulin (31) and may be strongly influenced by genetic factors (32). We suspect that the weight gain experienced from young to middle adulthood by our subjects contributed to a state of insulin resistance and resulting hyperinsulinemia, hypertension, and dyslipidemia in middle age. That weight gain was more strongly associated with hyperinsulinemia than with hypertension or dyslipidemia (Table 4) is consistent with this interpretation and supports the notion that insulin resistance underlies metabolic and hemodynamic disturbances characteristic of insulin resistance syndrome (11,12,30). We also have found that hyperinsulinemia at baseline predicts incident dyslipidemia and hypertension 4 years later in the KIHD population (33).

Our data indicate that weight gain contributes to metabolic and hemodynamic abnormalities before clinical manifestation of IHD. Weight gain predicted the likelihood of insulin resistance syndrome in middle age equally well in men with and without prevalent IHD at baseline. Indeed, risk of having insulin resistance syndrome according to weight-gain categories was similar in men with and without IHD. Prevalence and incidence of CVD are higher in individuals with multiple metabolic disorders compared with those with one or fewer abnormalities (10). Thus, interventions to reduce weight and prevent further weight gain among men already exhibiting

insulin resistance syndrome and before clinical IHD could contribute to a decrease in clinically significant CVD and its associated costs and consequences.

One limitation of this study is the use of self-reported weight at age 20. Measured weight at both times would have been ideal because self-reported weight tends to be biased toward underreporting (34), particularly among overweight individuals (35). However, several studies indicate that subjects' reports of their weight during young adulthood are reasonably accurate and can be reliably used in epidemiological investigations when measured weight is not available (35–37). Lissner et al. (38) found that weight during young adulthood may have important implications for health in later life and may be captured by using weight at age 20. Also, a recent report from the Atherosclerosis Risk in Communities study (39) found that weight change, calculated as the difference between self-reported weight at age 25 and measured weight some 30 years later, was associated with carotid artery wall thickness among men and white women. In the present study, we were able to assess the association between self-report of current weight and measured weight among a subset of our participants. At baseline, current smokers ($n = 608$) completed the Prochaska smoking questionnaire, which includes a question on current weight. Self-reported weight and measured weight were highly correlated in this sample ($r = 0.95$; $P < 0.0001$). Within the categories of percent weight change, this correlation ranged from 0.83 to 0.96, indicating that self-reports of current weight were no more or less accurate based on the amount of weight gained from young to middle adulthood.

Another limitation is the lack of information on timing or pattern of weight gain among our participants. These patterns may be related to health outcomes in an important way (5,27,40,41). Prevalence of overweight increases with advancing age (42), suggesting that weight gain in adulthood occurs gradually over time. Unfortunately, we do not know if the weight gain experienced by our participants was gradual from age 20 or if most of their weight increase occurred closer to the baseline examination, although it seems unlikely that these men experienced dramatic weight gains immediately before the baseline exams. We also were not able to examine the impact of diet or physical activity from young to middle adulthood on weight gain and development of insulin resistance syndrome. We do know that most of our participants were in the Finnish Army at age 20 during the post World War II years, when food was less plentiful, and it is likely that they were more physically active as younger men than in later years as they approached middle age. Also, as these men aged, the standard diet in Finland became higher in fat and calories (43). Almost all of the men started out at approximately the same BMI (22.6 kg/m^2 for noncases and 22.7 kg/m^2 for cases at age 20). The men who gained the most weight—presumably caused by increased dietary energy intake, decreased physical activity, genetic predisposition, or some combination of the three—were at the greatest risk of developing insulin resistance syndrome.

Findings from this study of middle-aged white men may not be generalizable to nonwhite populations or to women; however, results are consistent with a recent study that found an increased risk of CVD deaths among women who gained weight from age 18 to middle age (44). Our findings support the evidence that hypertension, diabetes, and dyslipidemia are biological consequences of obesity (45–47) and confirm that insulin resistance syndrome can occur in nonobese individuals (13).

In summary, this study adds to the extant literature identifying deleterious effects of weight gain and obesity from young adulthood to middle age. Public health strategies must be targeted at reducing high-calorie diets and increasing physical activity if they are to have any chance of reversing recent trends in obesity (42) and avoiding associated adverse health consequences. Additionally, these findings point to the need to identify individuals early, before significant weight gain and before conditions develop that are difficult to manage and that may lead to overt diseases such as CVD and type 2 diabetes.

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