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# Metabolic risks identified by the combination of enlarged waist and elevated triacylglycerol concentration[1,2]

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## ABSTRACT

**Background:** Abdominal fat and circulating triacylglycerols increase with age, which indicates lipid overaccumulation. Enlarged waist (EW) with elevated triacylglycerols (ET) could identify adults at metabolic risk.

**Objective:** Using thresholds for EW and ET observed among the youngest adults, we estimated for all adults the prevalence of combined EW and ET (EWET) and described the metabolic risks associated with EWET.

**Design:** In a cross-sectional, weighted sample of 9183 adults, we used two-dimensional displays to provide thresholds for EW (men: ≥ 95 cm; women: ≥ 88 cm) and fasting ET (≥ 1.45 mmol/L) and estimated the characteristics of EWET among adults of all ages.

**Results:** The population prevalence of EWET in 18–24-y-olds was 6%; it rose with age until age 55–74 y (prevalence: 43%) and then was lower among the elderly. Persons with EWET were more likely ($P < 0.0001$) to have adverse mean (± SEE) concentrations of risk variables in adjusted analyses (fasting insulin: 43 ± 3 pmol/L; HDL cholesterol: −0.27 ± 0.02 mmol/L; apolipoprotein B: 0.20 ± 0.01 g/L; fasting glucose: 0.71 ± 0.07 mmol/L; uric acid: 50 ± 2 μmol/L) and to have diabetes (relative risk: 3.2) than were persons without EWET. Compared with a similar-size subpopulation with high body mass index, persons with EWET were older and had more dyslipidemia, hyperglycemia, and hyperuricemia. Compared with "metabolic syndrome," EWET identified more persons who were younger and had greater LDL-cholesterol and apolipoprotein B concentrations. Compared with "prediabetes," EWET identified more persons with hyperinsulinemia, dyslipidemia, and hyperuricemia.

**Conclusions:** EWET identifies a syndrome of lipid overaccumulation associated with metabolic risk and accelerated mortality after middle age. Prospective studies should evaluate this simple indicator. *Am J Clin Nutr* 2003;78:928–34.


**KEY WORDS** Adult, anthropometry, body mass index, glucose intolerance, hyperinsulinemia, hyperlipidemia, hypertension, hyperuricemia, insulin resistance, metabolic syndrome X, metabolic diseases, obesity, risk assessment

## INTRODUCTION

Many investigators assume that insulin resistance is the fundamental metabolic defect that underlies a cluster of conditions called syndrome X, the deadly quartet, metabolic syndrome, or dysmetabolic syndrome (1–6). However, insulin resistance might be an effect rather than a cause (7). An alternative syndromic concept might be defined more fundamentally by the limited capacity of the human body to buffer and dispose of lipid fuels (8, 9). During periods when lipid availability exceeds this capacity, adipocytes would expand—especially in the intraabdominal compartment—to store the excess fuel. In parallel, the blood concentrations of certain lipids would become chronically elevated. A state of lipid overaccumulation would lead to ectopic deposition of lipids in nonadipose tissues, where insulin resistance (10, 11) and other metabolic dysfunctions would arise.

For this population-based study, we postulated that a state of lipid overaccumulation could be recognized as a combination of abdominal enlargement and elevated concentration of circulating triacylglycerols (12). We established normative threshold values for an enlarged waist (EW) circumference and elevated triacylglycerols (ET) by assessing only the youngest adults, because abdominal size and triacylglycerol concentration increase with adult age and metabolic risk (13–16). Accordingly, establishing the thresholds with values from any subpopulation but the youngest adults would be inappropriate. We defined our category of lipid overaccumulation as the occurrence in one person of both EW and ET (EWET). Using the thresholds derived from the youngest adults, we examined the associations of EWET with hyperinsulinemia, insulin resistance, dyslipidemia, hyperglycemia, hyperuricemia, and hypertension among adults through age 90 y.

We report here the testing of cross-sectional relations in adulthood between our marker of lipid overaccumulation (EWET) and continuous metabolic risk variables. We also compare the estimated subpopulation identified by EWET with other estimated subpopulations identified by 3 alternative, dichotomous risk markers: *1*) high body mass index (BMI; in kg/m$^2$): a BMI above a threshold chosen to yield an estimated subpopulation similar in size to the subpopulation with EWET; *2*) metabolic syndrome: ≥ 3 of 5 risk factors defined by the Third Report of the Adult Treatment Panel (MS-ATPIII) of the National Cholesterol Education Program (5, 17); and *3*) prediabetes: impaired fasting glucose (IFG) or impaired glucose

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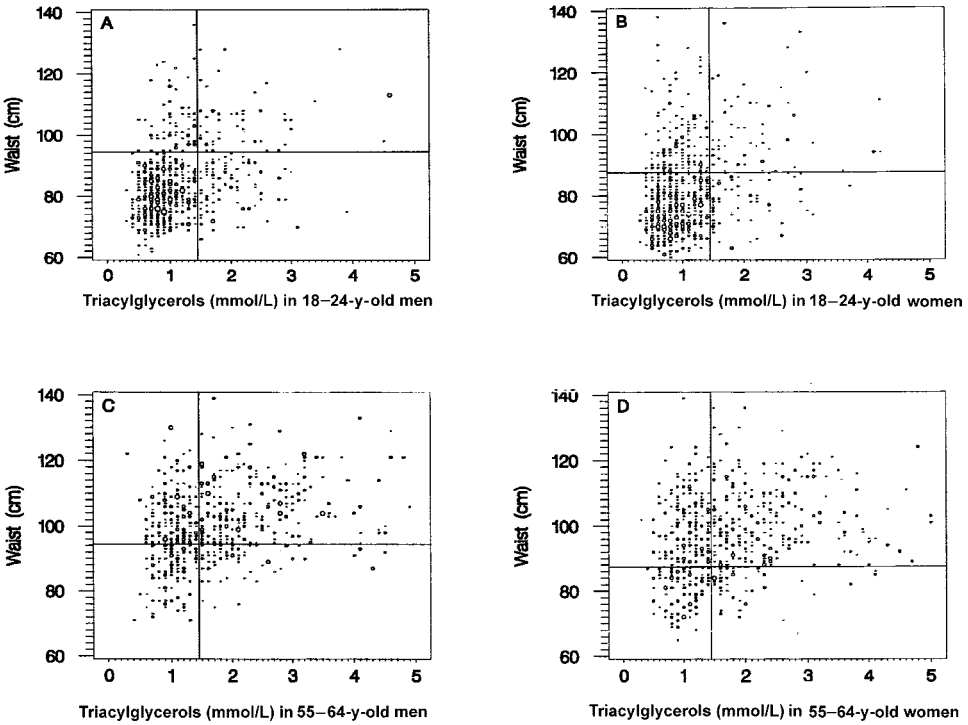


**FIGURE 1.** Estimated US population distribution according to waist circumference and concentration of fasting serum triacylglycerols, by sex and 2 age strata. Survey participants contributing to each plot: $n$ = 685 (A), 715 (B), 545 (C), and 559 (D).

tolerance (IGT), or both, shown by a 2-h oral-glucose-tolerance test (18).

## SUBJECTS AND METHODS

Our analytic population was drawn from the third National Health and Nutrition Examination Survey (NHANES III), a probability sample of the noninstitutionalized civilian US population studied in 1988–1994 (19). This complex, multistage survey oversampled non-Hispanic blacks and Mexican Americans. Our final analytic population contained 4448 male and 4735 female participants who were aged 18–90 y, were not pregnant, and had fasted for 8–19 h before their laboratory examination and for whom data on basic anthropometry and serum triacylglycerol concentration were available. Participants were asked to complete a household interview and a standardized examination, including measurement of the standing waist circumference (in the horizontal plane at a point marked just above the right ilium on the midaxillary line, at minimal respiration; 20, 21).

Serum triacylglycerol concentrations were measured enzymatically after hydrolysis to glycerol (Hitachi 704 Analyzer; Boehringer Mannheim, Indianapolis); the CV was 3–5% over the study and across the clinical range. Additional details of all laboratory procedures are available elsewhere (22). Calculations of LDL-cholesterol concentrations were limited to participants with triacylglycerol concentration $< 4.5$ mmol/L (a requirement of the Friedewald equation; 23) who fasted $\geq 9$ h. Analyses for serum apolipoprotein B were conducted only during phase 1 of NHANES III (1988–1991).

Laboratory values for insulin, glucose, and glycated hemoglobin were omitted for 63 participants who described themselves as current insulin users. For participants with valid fasting values of insulin and glucose, we estimated insulin resistance by using the homeostasis model assessment of insulin resistance (24), defined as fasting insulin (pmol/L) $\times$ fasting glucose (mmol/L)/22.5. Participants 40–74 y old, with the exception of insulin users, underwent a 2-h oral-glucose-tolerance test with 75 g glucose. On the basis of self-reported histories of diabetes and the oral-glucose-tolerance test, we classified these participants as having diabetes (nongestational, unspecified type), isolated IFG ($6.1 \leq$ fasting glucose $< 7.0$ mmol/L), isolated IGT ($7.8 \leq$ 2-h glucose $< 11.1$ mmol/L), combined IFG and IGT, or normal glucose tolerance (25).

### Statistical analysis

We used NHANES III sampling weights along with SAS/Graph (release 8.2; SAS Institute Inc, Cary, NC), and SUDAAN (release 8.0; Research Triangle Institute, Research Triangle, NC) software to estimate the represented population sizes, the prevalences of EWET, and the distributions of associated risk variables. Our analyses thereby incorporated weights that accounted for unequal selection probabilities (clustered design, planned oversampling, and differential nonresponse) (26). On the basis of the weights assigned, we estimated that our analytic sample represented a total of 100 113 964 US adults aged 18–90 y, 50.5% of whom were women.

We prepared sex-specific, age-stratified, bubble plots of population distribution by the values for waist circumference (to nearest cm) and triacylglycerol concentration (to nearest mmol/L) (**Figure 1**). The area of each circle on these plots is proportional to the estimated number of US men or women represented by those intersections. We established normative thresholds for waist circumference and triacylglycerol concen-

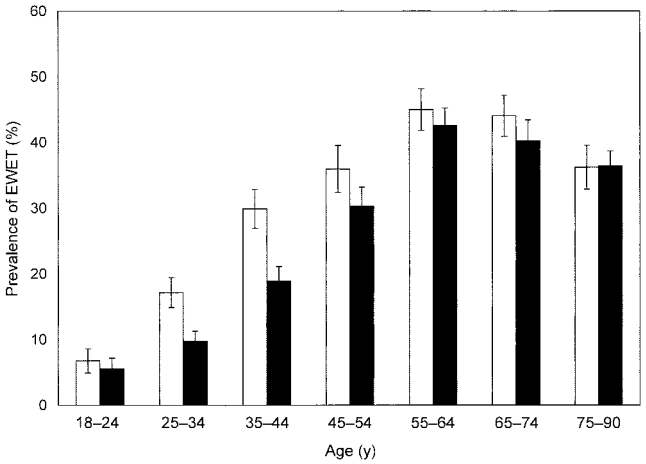


**FIGURE 2.** Mean (± SEE) prevalence of enlarged waist and elevated triacylglycerols (EWET) by age groups, estimated for the noninstitutionalized civilian US population, 1988–1994. The number of survey participants in each age group was 459–932 men (□) and 480–990 women (■).

tration by visual inspection of the plots restricted to subjects aged 18–24 y (Figure 1, A and B). For both sexes we noted predominant, rounded clusters in the lower left region that appeared to end just below waist threshold values of 95 cm (37.4 inches) for men and 88 cm (34.6 inches) for women and just below a triacylglycerol threshold of 1.45 mmol/L (128 mg/dL) for both sexes. We applied these threshold boundaries to all of our sex-specific, two-dimensional, graphic displays, thus establishing consistent quadrants for the plots of estimated persons in each age range. Subpopulations of persons whose values were above both thresholds (ie, located in the upper right quadrant) were defined as having EWET.

Mean values of risk variables in the adult population were estimated by linear regression with adjustment for sex, age, age squared, and race or ethnicity (non-Hispanic white, non-Hispanic black, Mexican American, other). No exclusions or adjustments were made for self-reported use of oral medications.

For the comparison of EWET with each alternative dichotomous marker, we estimated the 2 subpopulations that were discordant for marker status (ie, EWET-positive with negative alternative marker; EWET-negative with positive alternative marker). In the 2 discordant subpopulations, we compared prevalences (unadjusted) of adverse risk levels and then compared the mean values of risk variables with adjustments for sex, age, and race or ethnicity.

## RESULTS

### Prevalence of EWET by age and its relation to continuous risk variables

At age 18–24 y, the mean (± SEE) estimated US prevalence of EWET was 6.2 ± 1.1%. This estimate rose through consecutive decades of age to 55–64 y (43.7 ± 2.4%) and 65–74 y (42.1 ± 2.3%), but the prevalence was lower (36.4 ± 1.9%) at age 75–90 y. In the age groups from 25 to 44 y, the prevalence in men was higher than that in women (**Figure 2**). For both sexes combined, at age 18–90 y, the estimated prevalence of EWET was 24.8 ± 0.9%. We also estimated prevalences of 19.6 ± 0.5% for EW with low triacylglycerol concentration, 12.3 ± 0.6% for low waist circumference with ET, and 43.3 ± 1.1% for low waist circumference with low triacylglycerol concentration.

Compared with adults without EWET, those with EWET had significantly higher mean values for conventional risk variables and lower mean concentrations of HDL cholesterol (**Table 1**). These adverse differences were most pronounced for insulin, homeostasis model assessment of insulin resistance (**Figure 3**), and uric acid irrespective of age or sex. The risk variables related to lipids, glucose, and blood pressure also had strong associations with EWET, although they were less consistent by age and sex (data not shown).

### EWET compared with high body mass index

Within our estimated population of 100.1 million adults, a threshold BMI of ≥ 29.25 identified a subpopulation (high BMI) similar in size (24.9 million) to that identified by EWET (24.8 million). A majority within the estimated population was concordant for EWET and high BMI: 14.3 ± 0.7% met the criteria for both conditions, and 64.6 ± 0.9% were concordant

**TABLE 1**
Risk factors for adults with and without enlarged waist circumference and elevated triacylglycerols (EWET) from the third National Health and Nutrition Examination Survey, 1988–1994[1]

| Risk factor | With EWET[2] | Without EWET[2] | Difference[3] |
|---|---|---|---|
| Fasting insulin (pmol/L) | 93.2 ± 2.8 [2359] | 50.4 ± 0.9 [6321] | 42.8 ± 3.0 |
| log Fasting insulin | 4.38 ± 0.02 [2359] | 3.81 ± 0.02 [6321] | 0.58 ± 0.03 |
| HOMA-IR [(pmol · mmol) · $L^{-2}$ · $22.5^{-1}$] | 25.9 ± 0.9 [2356] | 12.1 ± 0.2 [6305] | 13.8 ± 0.9 |
| HDL cholesterol (mmol/L) | 1.10 ± 0.02 [2412] | 1.37 ± 0.01 [6731] | −0.27 ± 0.02 |
| LDL cholesterol (mmol/L) | 3.48 ± 0.04 [1774] | 3.21 ± 0.02 [4838] | 0.27 ± 0.03 |
| Total:HDL cholesterol | 5.49 ± 0.10 [2412] | 3.98 ± 0.04 [6730] | 1.51 ± 0.10 |
| Apolipoprotein B (g/L) | 1.18 ± 0.02 [1156] | 0.99 ± 0.01 [3320] | 0.20 ± 0.01 |
| Fasting glucose (mmol/L) | 5.98 ± 0.07 [2368] | 5.27 ± 0.01 [6342] | 0.71 ± 0.07 |
| Glycated hemoglobin (%) | 5.56 ± 0.04 [2383] | 5.21 ± 0.02 [6702] | 0.35 ± 0.03 |
| Uric acid (μmol/L) | 359 ± 2 [2395] | 309 ± 2 [6638] | 50 ± 2 |
| Systolic blood pressure (mm Hg) | 124.8 ± 0.5 [2431] | 120.1 ± 0.4 [6746] | 4.7 ± 0.6 |
| Diastolic blood pressure (mm Hg) | 76.7 ± 0.3 [2431] | 72.8 ± 0.2 [6744] | 3.9 ± 0.3 |

[1] Means and difference of means are estimated for the US population aged 18–90 y with adjustments for sex, age, age squared, and race or ethnicity. HOMA-IR, homeostasis model assessment of insulin resistance.
[2] $\bar{x}$ ± SEM; no. of observations in brackets.
[3] ± SEE. For all risk variables in this table, the difference between means was highly significant ($P < 0.0001$).

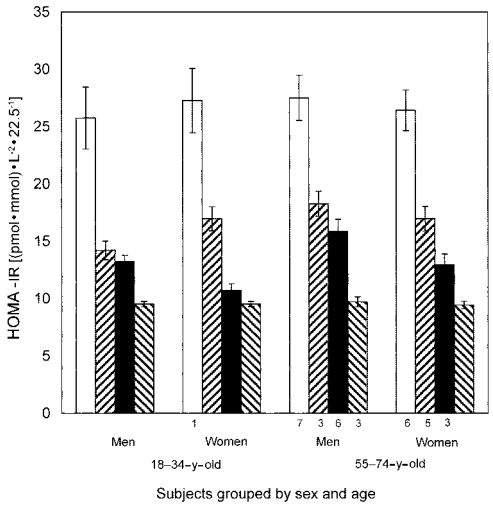


**FIGURE 3.** Mean (± SEM) estimated homeostasis model assessment of insulin resistance (HOMA-IR) according to 4 classes of waist circumference and triacylglycerol concentration (□, enlarged waist and elevated triacylglycerol; ▨, enlarged waist and low triacylglycerol; ■, low waist circumference and elevated triacylglycerol; ▧, low waist circumference and low triacylglycerol), by sex and 2 age strata. Insulin users were excluded. The numbers of survey participants contributing to each mean value was 126–812 men and 103–856 women. The numbers beneath columns indicate the estimated percentage of participants reporting the use of medication to lower blood sugar.

by meeting neither criterion. The discordant subpopulations were of equal size (**Table 2**), but the subpopulation with EWET alone was older ($\bar{x}$ age: 54.7 y compared with 42.6 y; $P < 0.0001$).

For all lipid variables, fasting glucose, glycated hemoglobin, uric acid, and systolic blood pressure, persons with EWET alone had higher unadjusted prevalences of adverse values than did persons with high BMI alone (Table 2). For all lipid variables (including LDL cholesterol; $P = 0.017$), fasting glucose ($P = 0.011$), and glycated hemoglobin ($P = 0.022$), the adjusted mean values were higher for persons with EWET alone. For fasting insulin and systolic blood pressure ($P = 0.014$), the adjusted mean values were higher for persons with high BMI alone.

### EWET compared with the metabolic syndrome

There were 8730 adult NHANES III participants with sufficient data (fasting triacylglycerol, fasting glucose, blood pressure, sex-specific waist circumference, and sex-specific HDL cholesterol) to allow the identification of either EWET or MS-ATPIII (5), and this sample represented an adult population of 95.5 million. The prevalence of MS-ATPIII was 23.1 ± 1.0%. Most of this population was concordant for EWET and MS-ATPIII, including 16.0 ± 0.8% who met the criteria for both conditions and 67.5 ± 1.1% who met neither criterion. Of those who were discordant for EWET and MS-ATPIII, the subpopulation with EWET alone was larger (Table 2) and younger ($\bar{x}$ age: 48.4 y compared with 53.1 y; $P = 0.0016$) than was the group with MS-ATPIII alone.

EWET alone identified more persons with high-risk concentrations of LDL cholesterol and apolipoprotein B than did MS-ATPIII alone (Table 2), and the adjusted mean concentrations were higher for these 2 variables (for LDL cholesterol: $P = 0.024$). However, HDL cholesterol, fasting glucose, blood pressure (3 of the 5 risk variables that define MS-ATPIII), fasting insulin, insulin resistance, and glycated hemoglobin were more likely to be adverse in the group with MS-ATPIII alone. The adjusted mean value for the ratio of total to HDL cholesterol was similar ($P = 0.10$) in these 2 subpopulations.

### EWET in relation to diabetes and prediabetes

Participants 40–74 y old who either reported having diabetes or underwent an oral-glucose-tolerance test ($n = 3800$) were estimated to total 42.4 million adults. Among those with EWET, an estimated 25.4 ± 1.7% had diabetes; among those without EWET, the estimated diabetes prevalence was 8.0 ± 0.8% (relative risk: 3.2; 95% CI: 2.5, 4.0). The relative risk for diabetes was lower for men (2.6; 95% CI: 1.9, 3.6) than for women (4.0; 95% CI: 3.0, 5.3). Among the persons with diabetes, 64.7 ± 2.7% were estimated to have EWET; of the nondiabetic adults in the same age range, an estimated 31.9 ± 1.2% had EWET.

After excluding the 6.1 million persons with diabetes, we estimated that 8.9 million had prediabetes, a dysglycemic state defined by IFG, IGT, or combined IFG and IGT (18). Of those with prediabetes, an estimated 4.0 million also had EWET (a concordant subpopulation). Of the 27.4 million with normal glucose tolerance (ie, without prediabetes), 19.8 million also did not have EWET (concordant). The discordant subpopulation with EWET alone was larger than that with prediabetes alone (Table 2), but these discordant subpopulations were of similar mean age (54.3 y compared with 55.7 y; $P = 0.19$).

The estimated subpopulation with EWET alone had higher unadjusted prevalences (Table 2) of adverse values related to hyperinsulinemia, insulin resistance ($P = 0.062$), all lipid variables, and uric acid than did the subpopulation with prediabetes alone. Persons with prediabetes alone had higher prevalences of fasting hyperglycemia (a criterion of prediabetes) and systolic hypertension ($P = 0.017$). With the exception of fasting glucose, glycated hemoglobin, and blood pressures, the adjusted mean values of risk variables were more adverse for the subpopulation with EWET alone.

### Potential efficiency of screening for EWET

On the assumption that measuring waist circumferences is simpler and less expensive than obtaining a fasting blood specimen or blood pressure reading, we used these NHANES III data to illustrate how the community-based screening of adults could benefit logistically from screening for EWET. Of the noninstitutionalized US population aged 18–90 y, we estimated that 44.4 ± 0.8% (slightly higher for the men and lower for the women) would exceed the threshold for waist circumference (**Table 3**). Thus, 56% of adults initially screened in this manner might be immediately determined not to have EWET and would thereby not have any need for a blood test. Table 3 further illustrates how the logistical simplicity of EWET is more advantageous for younger adults than for older adults. Among younger adults (aged 18–34 y), 75% would avoid a blood test, whereas, among older adults (aged 55–74 y), only 31% would do so. At age 75–90 y, the proportion avoiding a blood test would rise to 38% (37% for men and 39% for women).

**TABLE 2**
Risk factor comparisons for subpopulations of participants in the third National Health and Nutrition Examination Survey who were discordant for enlarged waist in combination with elevated triacyglycerols (EWET) and high BMI (≥ 29.25), for EWET and metabolic syndrome, and for EWET and prediabetes[1]

| | | EWET compared with high BMI | | | EWET compared with MS-ATPIII | | | EWET compared with prediabetes | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Prevalence of high risk | | | Prevalence of high risk | | | Prevalence of high risk | | |
| Risk factor | High-risk threshold | EWET alone ($n$ = 10.6 million) | High BMI alone ($n$ = 10.6 million) | Difference between means[2] | EWET alone ($n$ = 8.9 million) | MS-ATPIII alone ($n$ = 6.8 million) | Difference between means[2] | EWET alone ($n$ = 7.6 million) | Prediabetes alone ($n$ = 4.9 million) | Difference between means[2] |
| | | % | % | | % | % | | % | % | |
| Fasting insulin (pmol/L) | ≥ 71 | 36.7 ± 2.5[3] | 44.9 ± 2.9 | −8 ± 3[4] | 31.9 ± 2.2[5] | 42.4 ± 2.0 | −5 ± 2 | 44.7 ± 3.1[5] | 27.4 ± 3.2 | 16 ± 2[6] |
| HOMA-IR | ≥ 18 | 38.0 ± 2.6 | 41.4 ± 2.6 | −0.9 ± 0.9 | 30.0 ± 2.2[5] | 47.8 ± 2.3 | −3.1 ± 0.7[6] | 40.3 ± 2.9 | 30.1 ± 3.5 | 2.9 ± 0.7[6] |
| HDL cholesterol (mmol/L) | < 1.16 | 58.3 ± 2.8[5] | 39.0 ± 2.1 | −0.13 ± 0.03[6] | 41.7 ± 3.3[5] | 64.5 ± 2.0 | 0.19 ± 0.03[6] | 58.4 ± 4.2[5] | 34.8 ± 2.8 | −0.22 ± 0.03[6] |
| LDL cholesterol (mmol/L) | ≥ 3.36 | 62.1 ± 2.7[5] | 46.9 ± 2.1 | 0.18 ± 0.07 | 61.5 ± 3.0 | 51.7 ± 3.5 | 0.17 ± 0.07 | 67.1 ± 3.7[7] | 50.2 ± 3.8 | 0.37 ± 0.10[6] |
| Total:HDL cholesterol | ≥ 5 | 58.5 ± 2.5[5] | 20.4 ± 1.6 | 1.22 ± 0.16[6] | 41.3 ± 3.2 | 42.6 ± 2.6 | −0.22 ± 0.13 | 58.1 ± 4.0[5] | 25.3 ± 2.9 | 1.15 ± 0.23[6] |
| Apolipoprotein B (g/L) | ≥ 1.20 | 50.3 ± 3.9[5] | 18.9 ± 2.2 | 0.18 ± 0.02[6] | 42.4 ± 4.8 | 32.4 ± 4.2 | 0.08 ± 0.03[4] | 54.9 ± 4.2[5] | 29.2 ± 4.0 | 0.19 ± 0.03[6] |
| Fasting glucose (mmol/L) | ≥ 6.1 | 20.5 ± 1.7[5] | 10.8 ± 1.2 | 0.33 ± 0.13 | 6.0 ± 1.2[5] | 33.9 ± 2.4 | −0.51 ± 0.07[6] | 0[5] | 34.0 ± 2.8 | −0.30 ± 0.404[6] |
| Glycated hemoglobin (%) | ≥ 5.5 | 45.7 ± 2.7[5] | 35.9 ± 2.3 | 0.17 ± 0.07 | 36.9 ± 3.8[5] | 51.7 ± 2.4 | −0.25 ± 0.04[6] | 38.9 ± 3.3 | 45.0 ± 3.7 | −0.02 ± 0.04 |
| Uric acid (μmol/L) | ≥ 370 | 37.0 ± 2.9[7] | 27.7 ± 1.8 | 9 ± 5 | 37.4 ± 2.3 | 35.9 ± 2.5 | −6 ± 5 | 38.2 ± 3.3[7] | 27.0 ± 2.8 | 25 ± 7[6] |
| Systolic blood pressure (mm Hg) | ≥ 130 | 41.6 ± 2.2[5] | 29.3 ± 2.2 | −3.0 ± 1.2 | 24.4 ± 2.1[5] | 61.5 ± 3.0 | −10.4 ± 1.2[6] | 39.2 ± 2.2 | 48.3 ± 2.9 | −2.1 ± 1.5 |
| Diastolic blood pressure (mm Hg) | ≥ 85 | 18.6 ± 2.1 | 19.3 ± 1.7 | −0.3 ± 0.6 | 13.4 ± 2.1[5] | 32.8 ± 2.6 | −4.7 ± 0.7[5] | 22.1 ± 2.0 | 23.2 ± 2.7 | 0.8 ± 0.7 |

[1] HOMA-IR, homeostasis model assessment of insulin resistance; MS-ATPIII, metabolic syndrome defined by Adult Treatment Panel III.
[2] Difference, (mean for subpopulation with EWET alone) − (mean for subpopulation with alternative marker alone), adjusted for sex, age, age squared, and race or ethnicity (no. of survey participants ranged from 555 to 2241).
[3] $\bar{x}$ ± SEE.
[4] $P < 0.01$.
[5] Significantly different from alternative marker alone (ie, high BMI, MS-ATPIII, or prediabetes), $P < 0.001$.
[6] $P < 0.001$.
[7] Significantly different from alternative marker alone (ie, high BMI, MS-ATPIII, or prediabetes), $P < 0.01$.

**TABLE 3**
Estimated yields of screening the US adult population (100.1 million in 1988–1994) for enlarged waist circumference and for elevated triacylglycerols

| Sex and age range | Subpopulation estimate[1] | Enlarged waist[2] | Enlarged waist and elevated triacylglycerols[3] |
|---|---|---|---|
| All adults [$n$ (%)] | | | |
| Men, 18–90 y old | 49.6 (100) | 22.4 (45) | 13.4 (27) |
| Women, 18–90 y old | 50.5 (100) | 22.1 (44) | 11.4 (23) |
| Younger adults [$n$ (%)] | | | |
| Men, 18–34 y old | 20.3 (100) | 5.4 (27) | 2.7 (13) |
| Women, 18–34 y old | 18.5 (100) | 4.3 (23) | 1.5 (8) |
| Older adults [$n$ (%)] | | | |
| Men, 55–74 y old | 9.7 (100) | 6.9 (71) | 4.3 (45) |
| Women, 55–74 y old | 10.7 (100) | 7.2 (67) | 4.4 (42) |

[1] Estimated subpopulations are in millions of the noninstitutionalized civilian US population. This exercise assumed no previous knowledge of metabolic or hypertensive risk in the population.
[2] Enlarged waist circumference was defined as ≥ 95 cm for men and ≥ 88 cm for women.
[3] Elevated triacylglycerols was defined as a concentration of ≥ 1.45 mmol/L.

## DISCUSSION

We have proposed that EWET, a relatively simple, dichotomous risk marker, may identify adults who are at metabolic risk because of lipid overaccumulation. Our population-based, cross-sectional analysis showed a rising prevalence of EWET through middle age, which is consistent with an accumulative process. The leveling off of this syndrome after age 55 y and the declining prevalence after age 74 y (Figure 2) suggest that persons who have experienced several decades of excessive lipid burden may eventually also experience higher mortality rates.

We might ask: through what mechanisms might abdominal obesity and elevated circulating triacylglycerols become associated with more familiar risk factors such as conventional dyslipidemia, hyperinsulinemia, glucose intolerance, hyperuricemia, and hypertension? Lipid fuels are primarily the long-chain fatty acids that circulate through blood in their esterified form (relatively stable triacylglycerols inside lipoproteins) or in their nonesterified form (relatively unstable free fatty acids). The increased delivery of lipolytic products from enlarged

intraabdominal fat depots to the liver could result in a higher concentration of circulating VLDL and LDL particles (27, 28), whereas enhanced clearance of selected triacylglycerol-rich lipoprotein particles could depress the concentration of HDL cholesterol (29). At the same time, excessive fluxes of lipid fuels would lead to the ectopic accumulation of intracellular or subfascial fatty acid metabolites in nonadipose tissues (eg, liver, skeletal muscle), which would cause them to become insulin-resistant (10, 11, 30). Compensatory hyperinsulinemia would result (31) and would contribute through renal or other mechanisms to hyperuricemia (32, 33) and hypertension (32, 34). The increased delivery of lipolytic products to the liver would also promote hepatic gluconeogenesis (35), whereas the long-term accumulation of fatty acid metabolites in the pancreas could impair insulin secretion (36). This combination of processes would lead to hyperglycemia and an increased risk of type 2 diabetes (37).

The use of abdominal size and circulating triacylglycerol concentration to estimate risk is not new. Investigators in Quebec have pointed out that a "hypertriglyceridemic waist" could serve to identify men with hyperinsulinemia, elevated apolipoprotein B, and small, dense LDL particles (38). Without reference to the age dependence of abdominal size and triacylglycerol concentration, they assigned cutoffs for waist circumference ($\geq$ 90 cm) and triacylglycerol concentration ($\geq$ 2.0 mmol/L) that were rounded for simplicity. In cross-sectional studies limited to several hundred men, they found that the hypertriglyceridemic waist was positively associated with angiographically assessed coronary artery disease, dyslipidemia, hyperglycemia, and hyperinsulinemia (38–40).

Our study has built on the reports from Quebec by using population-based survey data that include both sexes. In contrast with the approach taken in Canada, we assigned threshold values for waist circumference and triacylglycerol concentration that were based on the examination of two-dimensional plots obtained only from young adults. The thresholds we obtained in this manner are consistent with other research observations. An analysis of white adults participating in NHANES III found that obesity-associated risk factors were most efficiently predicted at waist thresholds of 96 cm for men and 86 cm for women (41). Our proposed value of 95 cm for men is similar, and it also falls between the mean baseline waist circumference for incident cases and noncases among middle-aged Finnish men followed prospectively for the onset of diabetes (42) or coronary heart disease (43). A longitudinal description of non-African American adolescents from Texas found that, by age 18 y, the waist circumference of males was 6 cm larger than that of females (44); this sex difference was similar to the 7-cm difference between our proposed thresholds of 95 cm for men and 88 cm for women. Our threshold triacylglycerol concentration estimate of 1.45 mmol/L falls midway between the mean baseline concentration in adults who later acquired type 2 diabetes and that of those who did not, as reported from Texas (45) and Finland (42).

Although waist circumference is not commonly measured in clinical practice, the excellent reproducibility (46) and simplicity of this measurement should facilitate its adoption. Obtaining a standardized waist measurement is no more complicated than properly obtaining the standardized weight and height needed for calculating a BMI, and a waist circumference conveys a concept of obesity that may be easier for patients to understand. In addition, a tape measure is less expensive and more portable than are a good-quality stadiometer and scale. Cross-sectional studies within North American populations of European ancestry showed that waist circumference, even without triacylglycerol measurement, is more closely associated with multiple cardiovascular disease risk factors than is BMI (14, 41).

In our era of apparently increasing obesity and diabetes (47), it becomes more important than ever for clinicians to identify efficiently those persons who will most likely benefit from preventive or therapeutic interventions. Public health programs also need efficient markers for monitoring the prevalence of metabolic risks in communities (surveillance) and for evaluating the effectiveness of community-based attempts to prevent chronic disease. Traditional approaches to these requirements have depended on the assessment of many biochemical, physiologic, and anthropometric variables. However, the various campaigns against high cholesterol, hypertension, diabetes, and overweight may be missing an opportunity to focus on a more primary pathophysiologic pathway—possibly a key component of the "common soil" (48) from which grow major portions of type 2 diabetes and cardiovascular disease.

We have presented evidence that EWET could serve as a simple marker for a syndrome of lipid overaccumulation that would help to identify either persons in whom or communities in which "lipotoxicity" (9) might be doing the most harm. Used in community-based trials, EWET might also reveal which interventions could most effectively prevent or reverse this process of accumulation. However, our data are only cross-sectional. Missing from our evidence is any indication that EWET does, over time, predict the most important ultimate outcomes such as cardiovascular events, major disability, or premature mortality. Population-based, prospective studies already showed that triacylglycerol concentration provides significant prediction of cardiovascular risk (49, 50). However, the use of EWET instead of triacylglycerol concentration would have the advantage of substantially reducing the number of venipunctures and blood samples required from the population being assessed. Nevertheless, prospective studies will be necessary to prove the utility of EWET as a simple indicator of metabolic risks.

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