Background: Recent clinical guidelines on the health risks of obesity use body mass index (BMI; calculated as weight in kilograms divided by the square of height in meters) and waist circumference, but the waist-hip ratio may provide independent information.

Methods: To assess the joint and relative associations of BMI, waist circumference, and waist-hip ratio with multiple disease end points, we conducted a prospective cohort study of 31,702 Iowa women, aged 55 to 69 years and free of cancer, heart disease, and diabetes, assembled by random sampling and mail survey in 1986. Study end points were total and cause-specific mortality and incidence of site-specific cancers and self-reported diabetes, hypertension, and hip fracture over 11 to 12 years.

Results: The waist-hip ratio was the best anthropometric predictor of total mortality, with the multivariable-adjusted relative risk for quintile 5 vs 1 of 1.2 (95% confidence interval, 1.1-1.4), compared with 0.91 (95% confidence interval, 0.8-1.0) for BMI and 1.1 (95% confidence interval, 1.0-1.3) for waist circumference. The waist-hip ratio was also associated positively with mortality from coronary heart disease, other cardiovascular diseases, cancer, and other causes. The waist-hip ratio was associated less consistently than BMI or waist circumference with cancer incidence. All anthropometric indexes were associated with incidence of diabetes and hypertension. For example, women simultaneously in the highest quintiles of BMI and waist-hip ratio had a relative risk of diabetes of 2.9 (95% confidence interval, 1.8-4.6) vs women in the lowest combined quintiles.

Conclusion: The waist-hip ratio offers additional prognostic information beyond BMI and waist circumference.

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Excess weight, often measured as increased body mass index (BMI; calculated as weight in kilograms divided by the square of height in meters) or increased weight for height, has long been considered a risk factor for many chronic diseases. In the past 2 decades, visceral or abdominal obesity, as reflected anthropometrically by an increased waist circumference or waist-hip ratio, has also emerged as an important predictor of risk for obesity-related diseases. However, as discussed in a recent review, it is unclear which measure of abdominal obesity best characterizes risk. Recent guidelines addressing obesity recommend waist circumference over waist-hip ratio, as waist circumference is simpler to measure and interpret and correlates well with visceral fat measured by computed tomography. Yet, waist circumference also is highly correlated with BMI and thus reflects general, and abdominal, obesity.

Most reports associating abdominal obesity with disease have examined men or younger women, have focused on 1 or 2 diseases at a time, or have failed to consider the contribution of abdominal obesity independent of general obesity. Understanding the roles of different patterns of obesity in multiple diseases is important, given the steady increase in body weight during the past 2 decades in the United States. The main aim of the Iowa Women's Health Study was to assess the association of body fat distribution and disease incidence in a large cohort of older women. Previously reported findings from this cohort had limited follow-up. This report extends the follow-up and reports the joint and relative associations of BMI, waist circumference, and waist-hip ratio with disease risk in older women.
SUBJECTS AND METHODS

THE IOWA WOMEN’S HEALTH STUDY

In January 1986, a mailed questionnaire was completed by 41836 (42.7%) of 98030 randomly selected women, between the ages of 53 and 69 years, who had a valid Iowa driver’s license in 1985. Although driver’s license information indicated that respondents were 3 months older than non-respondents, had a lower BMI by 0.4, and were more likely to live in rural counties of Iowa, the associations of body weight with mortality and cancer incidence were similar in respondents and nonrespondents.1 The baseline questionnaire included standard questions on educational level, smoking status and amount, usual alcohol intake during the past year, hormone replacement therapy status, and reproductive history. Participants were asked 3 questions about whether they participated in any leisure time exercise and, if so, the frequency of moderate- and heavy-intensity activities. These latter 2 questions were combined to create a 3-level activity score (low, medium, and high). A food frequency questionnaire was used to assess dietary intake.12 Prevalent activity score (low, medium, and high). A food frequency questionnaire or implausible energy intake (≥2520 or ≥7184 kJ/d).

COHORT FOLLOW-UP

Information on the vital status of the cohort was collected by several methods. Participant identifiers (name, address, social security number, birth date, and maiden name) were linked by computer to death certificates at the State Health Registry of Iowa for 1986 through 1996. To identify deaths outside of Iowa and nonfatal, noncancer end points, mailed follow-ups were undertaken in 1987 (91%), 1989 (90%), 1992 (83%), and 1997 (79%) (response rates are given in parentheses); the vital status of nonrespondents was identified by linkage with the National Death Index. We estimate that 99% of deaths in the cohort have been identified. Underlying causes of deaths were coded according to the International Classification of Diseases, Ninth Revision (ICD-9).14 For deaths occurring in Iowa, underlying causes were assigned by the Iowa Department of Health; for deaths outside of Iowa, underlying causes were assigned by an experienced nosologist following International Classification of Diseases, Ninth Revision (ICD-9) rules.

Cancer incidence was identified by computer linkage with the State Health Registry of Iowa, a National Cancer Institute–supported Surveillance, Epidemiology, and End Results cancer registry. Other incident disease end points were obtained during follow-up surveys as the first positive self-report of a physician’s diagnosis.

DATA ANALYSIS

For this report, we examined mortality from all causes and from 4 mortality subsets: coronary heart disease (CHD), all other cardiovascular disease (CVD), cancer, and all other causes, for which the percentages of deaths were 18%, 13%, 47%, and 22%, respectively. We also examined the incidence of any cancer and common sites in women (breast, lung, colon, uterus, and ovary). Finally, we examined the incidence of self-reported high blood pressure, diabetes, and hip fracture, the latter 2 of which have been shown to be self-reported reasonably accurately in this cohort or elsewhere.6,13,16 Although self-reports of myocardial infarction and stroke were collected, we chose to present CHD- and CVD-related mortality instead, as potentially more valid end points.

Of the 41836 women, we first excluded from consideration women who were premenopausal (n=569); then, women who reported a baseline history of cancer, heart disease, or diabetes (n=9426); and then, women who had missing data on BMI and waist-hip ratio (n=139). This left 31702 for analysis. For incidence analyses of high blood pressure, prevalent cases at baseline were excluded. For uterine and ovarian cancer incidence, women who had undergone a hysterectomy and a bilateral ovariectomy, respectively, were also excluded. For multivariable analyses, we also excluded women who were deemed to have invalid dietary data (n=2167), namely, 30 or more items missing on the food frequency questionnaire or implausible energy intake (<2520 or ≥10 584 kJ/d).

Person-years of follow-up for computation of mortality rates were calculated as the time elapsed from completion of the baseline questionnaire to either the end of 1996 or death. For cancer incidence, person-years accumulated from baseline until (1) identified emigration from Iowa (approximately 0.3% annually); (2) identification of a (first) registered cancer diagnosis; (3) death; or (4) December 31, 1996, whichever occurred first. For other, self-reported incident end points, person-years were the sum of the known disease-free period plus half of the period between questionnaires, during which the diagnosis was first made; for women without incident end points, person-time continued until their last completed questionnaire.

Women were categorized according to quintiles (or tertiles when there were few end points) of the baseline anthropometric variables among the total cohort at risk. Age-adjusted relative risks (RRs), their 95% confidence intervals (CIs), and the P value for trend in RRs were calculated by Mantel-Haenszel methods.17 Multivarially adjusted RR and their 95% CIs were computed by proportional hazards regression using SAS statistical software (program PHREG; SAS Institute Inc, Cary, NC). Covariates were those variables found to be important risk factors in previous Iowa Women’s Health Study analyses.6,7,9,18,19 We computed multivariately adjusted RRs first for BMI, waist-hip ratio, and waist circumference separately. We then included BMI and waist-hip ratio simultaneously in a model to examine their independence. We did not include BMI and waist circumference in the same model because they were highly correlated. However, we did cross classify BMI and waist circumference according to recent obesity guidelines2 and computed age-adjusted odds ratios for pooled end points using unconditional logistic regression. (Person-years were omitted from the tables but are available on request from one of us [A.R.F.]).
circumference, and waist-hip ratio with multiple disease end points.

RESULTS

DESCRIPTIVE DATA

The cohort included 31,702 postmenopausal women who at baseline were free of cancer, heart disease, and diabetes. The Pearson product moment correlation of BMI with waist circumference was 0.82; BMI with waist-hip ratio, 0.40; and waist circumference with waist-hip ratio, 0.72. Body mass index and waist-hip ratio were associated with most lifestyle variables examined (Table 1). For example, among nondietary factors, BMI and waist-hip ratio were associated negatively with educational level, estrogen use, physical activity, alcohol intake, and multivitamin use. Body mass index, but not waist-hip ratio, was also associated negatively with ever smoking, whereas waist-hip ratio, but not BMI, was associated positively with age.

MORTALITY

All Cause

A total of 2476 participants died. In the age-adjusted models, BMI and waist circumference showed U-shaped associations with all-cause mortality (Table 2). After adjustment for other risk factors, women with general obesity were not at increased risk of death: the relative risks for the fifth vs first quintiles were 0.91 (95% CI, 0.8-1.0) for BMI and 1.1 (95% CI, 0.9-1.3) for waist circumference. In contrast, there was a graded risk of mortality across quintiles of waist-hip ratio, with an age-adjusted RR of 1.5 (95% CI, 1.4-1.8) and a risk factor–adjusted relative risk of 1.2 (95% CI, 1.1-1.4) for a comparison of extreme quintiles. When BMI and waist-hip ratio were in the multivariate models together, the RRs were 0.79 (95% CI, 0.7-0.9) comparing extreme quintiles of BMI and 1.4 (95% CI, 1.2-1.6) for waist-hip ratio. Figure 1 shows that there was a positive age-adjusted association of mortality with waist-hip ratio for each stratum of BMI. The highest mortality stratum was that with the lowest BMI and highest waist-hip ratio. Elimination of ever smokers from Figure 1 reduced the 3 highest RRs (in the high waist-hip ratio and low BMI quintiles), but they remained elevated (RRs, 1.2-1.7).

Coronary Heart Disease

Body mass index, waist-hip ratio, and waist circumference were associated positively with CHD-related mortality (438 deaths), with multivariately adjusted RRs for the fifth vs first quintiles of 1.7, 1.9, and 2.2, respectively (Table 2). When BMI and waist-hip ratio were in the same model, the RRs decreased to 1.3 (95% CI, 0.9-1.9) for BMI and to 1.8 (95% CI, 1.2-2.7) for waist-hip ratio but still suggested that general and abdominal obesity contribute to CHD. A stratified analysis also indicated that a higher BMI and waist-hip ratio were associated with greater CHD-related mortality among the total sample (not shown) and among the never smokers (Figure 2).

Other CVD

The waist-hip ratio was associated positively, BMI was associated negatively, and waist circumference was not associated with other CVD-related deaths (326 deaths) (Table 2). The RRs for the highest vs lowest quintiles of BMI and waist-hip ratio were 0.60 (95% CI, 0.4-0.9) and 1.7 (95% CI, 1.1-2.7), after adjustment for covariates and each other.

Cancer

The number of participants who died of cancer was 1156. Body mass index, waist-hip ratio, and waist circumfer-

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Table 1. Prevalence of Various Baseline Characteristics Within Quintiles of BMI or Waist-Hip Ratio, Iowa Women’s Health Study, 1986

<table>
<thead>
<tr>
<th>Variable†</th>
<th>Within BMI Quintile</th>
<th>Within Waist-Hip Ratio Quintile</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Age ≥60 y</td>
<td>62</td>
<td>63</td>
</tr>
<tr>
<td>Education &gt; high school</td>
<td>45</td>
<td>43</td>
</tr>
<tr>
<td>Smoked (ever)</td>
<td>44</td>
<td>36</td>
</tr>
<tr>
<td>Parous (yes)</td>
<td>88</td>
<td>91</td>
</tr>
<tr>
<td>Estrogen use (current)</td>
<td>13</td>
<td>13</td>
</tr>
<tr>
<td>Physical activity (high)</td>
<td>29</td>
<td>29</td>
</tr>
<tr>
<td>Alcohol (any)</td>
<td>52</td>
<td>51</td>
</tr>
<tr>
<td>Multivitamin use (current)</td>
<td>37</td>
<td>35</td>
</tr>
<tr>
<td>Energy intake (&lt;6300 kJ/d)</td>
<td>34</td>
<td>33</td>
</tr>
<tr>
<td>Fruit and vegetables (≥30/wk)</td>
<td>72</td>
<td>75</td>
</tr>
<tr>
<td>Red meat (&lt;7/wk)</td>
<td>67</td>
<td>65</td>
</tr>
<tr>
<td>Fish and seafood (≥1/wk)</td>
<td>69</td>
<td>71</td>
</tr>
<tr>
<td>Whole grain (≥10/wk)</td>
<td>46</td>
<td>47</td>
</tr>
</tbody>
</table>

*BMI indicates body mass index.
†n = 31,702 for nondietary variables and 29,535 for dietary variables.
ence were not significantly associated with cancer-related mortality after adjustment for other risk factors (Table 2).

Other Causes

Body mass index was associated negatively, waist-hip ratio was associated positively, and waist circumference was not associated with the residual group of deaths (556 deaths) (data not shown). The RRs for the highest vs the lowest quintiles of BMI and waist-hip ratio were 0.51 (95% CI, 0.4-0.7) and 1.5 (95% CI, 1.1-2.0), respectively, after adjustment for covariates and each other.

CANCER INCIDENCE

Any Cancer

Cancer incidence (3738 events) tended to be associated positively with all 3 anthropometric variables, with RRs between 1.1 and 1.4 for the highest vs the lowest quintiles (Table 3).

Table 2. Association of Anthropometric Variables With Mortality From All Causes, Coronary Heart Disease, Other Cardiovascular Diseases, and Cancer, IWHS, 1986 to 1996*

<table>
<thead>
<tr>
<th>Mortality End Point</th>
<th>Anthropometric Measurements</th>
<th>Variable</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>P for Trend</th>
<th>RR (95% CI) for Multivariable-Adjusted Models (Quintile 5 vs 1)</th>
<th>Separate§</th>
<th>Combined¶</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cause BMI</td>
<td>n</td>
<td>589</td>
<td>467</td>
<td>444</td>
<td>429</td>
<td>547</td>
<td>.05</td>
<td>.91 (0.8-1.0)</td>
<td>0.79 (0.7-0.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist-hip ratio</td>
<td>RR</td>
<td>1.0</td>
<td>0.76</td>
<td>0.74</td>
<td>0.71</td>
<td>0.91</td>
<td>.09</td>
<td>1.2 (1.1-1.4)</td>
<td>1.4 (1.2-1.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>95% CI</td>
<td>...</td>
<td>0.7-0.9</td>
<td>0.7-0.8</td>
<td>0.6-0.8</td>
<td>0.8-1.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist circumference</td>
<td>n</td>
<td>367</td>
<td>411</td>
<td>492</td>
<td>555</td>
<td>651</td>
<td>.001</td>
<td>1.2 (1.1-1.4)</td>
<td>1.4 (1.2-1.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist circumference</td>
<td>RR</td>
<td>1.0</td>
<td>1.1</td>
<td>1.2</td>
<td>1.3</td>
<td>1.5</td>
<td>.01</td>
<td>1.2 (1.1-1.4)</td>
<td>1.4 (1.2-1.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>95% CI</td>
<td>...</td>
<td>0.9-1.2</td>
<td>1.1-1.4</td>
<td>1.2-1.5</td>
<td>1.4-1.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other causes BMI</td>
<td>n</td>
<td>447</td>
<td>473</td>
<td>439</td>
<td>473</td>
<td>644</td>
<td>.001</td>
<td>1.1 (1.0-1.3)</td>
<td>...</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist-hip ratio</td>
<td>RR</td>
<td>1.0</td>
<td>0.99</td>
<td>0.90</td>
<td>0.93</td>
<td>1.3</td>
<td>&lt;.001</td>
<td>1.2 (1.1-1.4)</td>
<td>1.4 (1.2-1.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>95% CI</td>
<td>...</td>
<td>0.9-1.1</td>
<td>0.8-1.0</td>
<td>0.8-1.1</td>
<td>0.8-1.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist circumference</td>
<td>n</td>
<td>47</td>
<td>75</td>
<td>80</td>
<td>96</td>
<td>140</td>
<td>&lt;.001</td>
<td>1.3 (1.2-1.6)</td>
<td>1.8 (1.2-2.7)</td>
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<tr>
<td>Waist circumference</td>
<td>RR</td>
<td>1.0</td>
<td>1.5</td>
<td>1.6</td>
<td>1.7</td>
<td>2.6</td>
<td>&lt;.001</td>
<td>1.2 (1.5-2.3)</td>
<td>...</td>
<td></td>
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<tr>
<td>95% CI</td>
<td>...</td>
<td>1.0-2.1</td>
<td>1.1-2.2</td>
<td>1.2-2.5</td>
<td>1.3-3.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other cardiovascular diseases BMI</td>
<td>n</td>
<td>77</td>
<td>62</td>
<td>48</td>
<td>69</td>
<td>70</td>
<td>.70</td>
<td>0.72 (0.5-1.1)</td>
<td>0.60 (0.4-0.9)</td>
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<tr>
<td>Waist-hip ratio</td>
<td>RR</td>
<td>1.0</td>
<td>0.77</td>
<td>0.60</td>
<td>0.86</td>
<td>0.89</td>
<td>.01</td>
<td>1.3 (1.2-1.9)</td>
<td>1.7 (1.1-2.7)</td>
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<tr>
<td>95% CI</td>
<td>...</td>
<td>0.5-1.1</td>
<td>0.4-0.9</td>
<td>0.6-1.2</td>
<td>0.6-1.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist circumference</td>
<td>n</td>
<td>45</td>
<td>59</td>
<td>62</td>
<td>66</td>
<td>94</td>
<td>.003</td>
<td>1.4 (0.9-2.1)</td>
<td>1.7 (1.1-2.7)</td>
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<tr>
<td>Waist circumference</td>
<td>RR</td>
<td>1.0</td>
<td>1.4</td>
<td>1.0</td>
<td>1.2</td>
<td>1.5</td>
<td>.10</td>
<td>1.2 (0.8-1.8)</td>
<td>...</td>
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<tr>
<td>95% CI</td>
<td>...</td>
<td>0.9-2.0</td>
<td>0.7-1.5</td>
<td>0.8-1.7</td>
<td>1.2-2.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer BMI</td>
<td>n</td>
<td>269</td>
<td>234</td>
<td>210</td>
<td>199</td>
<td>244</td>
<td>.06</td>
<td>1.0 (0.8-1.2)</td>
<td>0.92 (0.7-1.1)</td>
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</tr>
<tr>
<td>Waist-hip ratio</td>
<td>RR</td>
<td>1.0</td>
<td>0.84</td>
<td>0.77</td>
<td>0.72</td>
<td>0.89</td>
<td>.003</td>
<td>1.2 (0.9-1.4)</td>
<td>1.2 (0.98-1.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>95% CI</td>
<td>...</td>
<td>0.7-1.0</td>
<td>0.6-0.9</td>
<td>0.6-0.9</td>
<td>0.7-1.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist circumference</td>
<td>n</td>
<td>187</td>
<td>209</td>
<td>247</td>
<td>242</td>
<td>271</td>
<td>.003</td>
<td>1.2 (0.9-1.4)</td>
<td>1.2 (0.98-1.5)</td>
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<tr>
<td>Waist circumference</td>
<td>RR</td>
<td>1.0</td>
<td>1.0</td>
<td>0.84</td>
<td>0.88</td>
<td>1.2</td>
<td>.31</td>
<td>1.2 (0.96-1.4)</td>
<td>...</td>
<td></td>
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</tr>
<tr>
<td>95% CI</td>
<td>...</td>
<td>0.8-1.2</td>
<td>0.7-1.0</td>
<td>0.7-1.1</td>
<td>0.97-1.4</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

* IWHS indicates Iowa Women’s Health Study; RR, relative risk; CI, confidence interval; BMI, body mass index; n, number of deaths; and ellipses, data not applicable.
† Considering one anthropometric variable at a time with adjustment for age. The average number of person-years per quintile was approximately 67 000.
‡ Cut points were 22.80, 24.87, 27.06, and 30.21 for BMI; 0.762, 0.805, 0.848, and 0.901 for waist-hip ratio; and 74.3, 80.0, 87.3, and 96.0 cm for waist circumference.
§ Considering one anthropometric variable at a time with adjustment for age, educational level (< high school, high school, or > high school), physical activity (low, medium, or high), alcohol intake (0, < 4, or > 4 g/d), smoking status (current, former, or never), pack-years of cigarette smoking (continuous), age of first live birth (nullipara, < 30 years, or ≥ 30 years), estrogen use (current, former, or never), vitamin use (yes, no, or unknown), and energy, whole grain, fruit and vegetable, fish, and red meat intake and Keys score (all in quintiles). All-cause, coronary heart disease-related, and other cardiovascular disease-related mortality also adjusted for high blood pressure (yes or no).
¶ Considering BMI and waist-hip ratio in a single model with adjustment for all of the same variables as given in the previous footnote.
Breast Cancer

Body mass index and waist circumference were moderately strongly associated with breast cancer incidence ($n=1299$), with risk factor–adjusted RRs for extreme quintiles being 1.6 and 1.7, respectively (Table 3). The RR for waist-hip ratio was smaller (RR, 1.3) and attenuated further when BMI was in the model (RR, 1.1). However, those in the lowest combined quintiles of BMI and waist-hip ratio were at the lowest risk of breast cancer (Figure 3).

Colon Cancer

The associations of anthropometric variables with colon cancer ($n=462$) (Table 3) mirrored those for breast cancer.

Lung Cancer

Body mass index was associated negatively with lung cancer incidence ($n=386$), even after multivariate adjustment (Table 3). In contrast, the waist-hip ratio and waist circumference were not associated independently with lung cancer incidence. Elimination of ever smokers left only 52 persons with incident lung cancers, among whom the age-adjusted RRs across quartiles of BMI were 1.00, 0.58, 0.62, 0.34, and 0.56 ($P = .09$ for trend). There was no age-adjusted association of waist-hip ratio and waist circumference with lung cancer among never smokers.

Uterine Cancer

Body mass index and waist circumference were strong predictors of uterine cancer incidence ($n=298$), with approximately 4-fold higher incidence for the fifth vs the first quintile but little association across the middle quintiles (Table 3). The association of waist-hip ratio with uterine cancer incidence was eliminated with adjustment for, or stratification by, BMI (Table 3 and Figure 4).

Ovarian Cancer

Body mass index was not associated, and waist circumference and waist-hip ratio were positively but not monotonically associated, with ovarian cancer incidence ($n=141$) (Table 3). The risk factor–adjusted RR comparing extreme quintiles of waist-hip ratio was 2.0 (95% CI, 1.1-3.7), and this value was not changed after adding BMI to the model.

INCIDENCE OF OTHER DISEASES

Diabetes

Body mass index, waist-hip ratio, and waist circumference were strong risk factors for incidence of self-reported diabetes ($n=1578$) (Table 4). Among the 3 anthropometric variables, waist circumference displayed the greatest RRs. As shown in Figure 5, BMI and waist-hip ratio appeared to contribute independently to diabetes incidence; the age-adjusted RR of diabetes for the highest combined quintiles vs the lowest was exceptionally high, 29 (95% CI, 18-46).

High Blood Pressure

All 3 anthropometric variables were associated positively with incidence of self-reported high blood pressure ($n=4077$). Relative risks were approximately 2.0 for...
Table 3. Association of Anthropometric Variables With Incidence of Various Cancers, IWHS, 1986 to 1996*

<table>
<thead>
<tr>
<th>Type of Cancer</th>
<th>Anthropometric Measurements</th>
<th>Variable</th>
<th>Age-Adjusted Models†</th>
<th>RR (95% CI) for Multivariable-Adjusted Models (Quintile 5 vs 1)</th>
<th>P for Trend</th>
<th>Separate§</th>
<th>Combined|</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Quintiles‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
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<tr>
<td>Any BMI</td>
<td></td>
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<td>701</td>
<td>705</td>
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</tr>
<tr>
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<td>785</td>
<td>870</td>
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<td>651</td>
<td>717</td>
<td>675</td>
<td>769</td>
<td>926</td>
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<td>275</td>
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<td>266</td>
<td>238</td>
<td>281</td>
<td>326</td>
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<td>Colon BMI</td>
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<td>73</td>
<td>91</td>
<td>104</td>
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<td>82</td>
<td>105</td>
<td>116</td>
<td>.007</td>
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<td>67</td>
<td>90</td>
<td>97</td>
<td>129</td>
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<tr>
<td>Lung BMI</td>
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<td>61</td>
<td>54</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Waist-hip ratio</td>
<td></td>
<td>68</td>
<td>73</td>
<td>82</td>
<td>75</td>
<td>87</td>
<td>.26</td>
</tr>
<tr>
<td>Waist circumference</td>
<td></td>
<td>97</td>
<td>94</td>
<td>57</td>
<td>58</td>
<td>80</td>
<td>.003</td>
</tr>
<tr>
<td>Uterus BMI</td>
<td></td>
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<td>37</td>
<td>39</td>
<td>54</td>
<td>129</td>
<td>&lt;.001</td>
</tr>
<tr>
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<td>56</td>
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<td>&lt;.001</td>
</tr>
<tr>
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<td>45</td>
<td>52</td>
<td>119</td>
<td>&lt;.001</td>
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<tr>
<td>Ovarian BMI</td>
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<td>19</td>
<td>33</td>
<td>34</td>
<td>.27</td>
</tr>
<tr>
<td>Waist-hip ratio</td>
<td></td>
<td>10</td>
<td>0.95</td>
<td>0.68</td>
<td>1.2</td>
<td>1.2</td>
<td>.13</td>
</tr>
<tr>
<td>Waist circumference</td>
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<td>10</td>
<td>1.1</td>
<td>0.65</td>
<td>1.5</td>
<td>1.3</td>
<td>.14</td>
</tr>
</tbody>
</table>

*Abbreviations are explained in the first footnote to Table 2.
†Considering one anthropometric variable at a time with adjustment for age. The average number of person-years per quintile was approximately 62 000 for all cancer, 64 000 for breast cancer, 65 000 for colon and lung cancer, 44 000 for uterine cancer, and 54 000 for ovarian cancer.
‡Cut points are given in the third footnote to Table 2.
§Considering one anthropometric variable at a time with adjustment for age, educational level (< high school, high school, or > high school), physical activity (low, medium, or high), alcohol intake (0, < 4, or ≥ 4 g/d), smoking status (current, former, or never), pack-years of cigarette smoking (continuous), age of first live birth (nullipara, < 30 years, or ≥ 30 years), estrogen use (current, former, or never), vitamin use (yes, no, or unknown), and energy, whole grain, fruit and vegetable, fish, and red meat intake and Keys score (all in quintiles).
\|Considering BMI and waist-hip ratio in a single model with adjustment for all of the same variables as given in the previous footnote.
highest vs lowest quintiles of each variable (Table 4), suggesting that both general and abdominal obesity are risk factors. The age-adjusted RR for highest vs lowest combined quintiles of BMI and waist-hip ratio (Figure 6) was 2.8 (95% CI, 2.4-3.3).

**Hip Fracture**

Body mass index was associated inversely with occurrence of self-reported hip fracture (n=484), whereas waist-hip ratio was associated slightly positively and waist circumference was not at all associated with hip fracture (Table 4). In the multivariate model including both anthropometric variables, the RRs comparing extreme quintiles were 0.49 (95% CI, 0.4-0.7) for BMI and 1.6 (95% CI, 1.1-2.2) for waist-hip ratio. Figure 7 depicts the contrasting age-adjusted joint associations of BMI and waist-hip ratio with hip fracture.

**POOLED END POINT**

Recently, an expert panel proposed joint BMI (6 classes from underweight [BMI, <18.5] to obesity class 3 [BMI, ≥40]) and waist circumference (≤88 or >88 cm) cut points to stratify patients for risk of diabetes, hypertension, and CVD. The left half of Table 5 summarizes the expert consensus panel’s categories of risk for the different body size groupings, and the right half shows estimated risk based on Iowa Women’s Health Study data. For this analysis, we excluded participants with hypertension at baseline and used 2 pooled end points, namely, (1) occurrence of incident diabetes, incident hypertension, or any CVD-related death (including CHD); or (2) occurrence of incident diabetes, hypertension, hip fracture, or cancer or all-cause death. Because waist circumference and BMI were highly correlated, there were few women in either the high BMI and low waist circumference category or the low BMI and high waist circumference category (Table 5). The age-adjusted odds ratios from our cohort for the composite end point of diabetes, hypertension, or death from CVD seemed to correspond to the consensus risk categories. However, BMI was not predictive of the broader end point (also including cancer incidence, hip fracture incidence, and all deaths) in women with waist circumferences of 88 cm or less. Adjustment of the data for other covariates, including smoking, did not materially alter these odds ratio estimates.

**COMMENT**

Our main aim was to examine the joint risk and RR of general obesity vs abdominal obesity on multiple health outcomes in a cohort of older women initially free of cancer, heart disease, and diabetes and followed up for 11 to 12 years. Our hypothesis was that the relative contributions of BMI (primarily a marker of general obesity), waist-hip ratio (primarily a marker of abdominal obesity), and waist circumference (a marker of general and abdominal obesity) would vary among diseases. Understanding the various patterns of obesity that lead to different diseases may offer clues to their etiologies and help guide clinical decision making.

**MORTALITY**

General obesity appeared to be a poor predictor of total mortality in these older women, but abdominal obesity, as measured by waist-hip ratio, showed a positive, monotonic, and independent association with total mor-
tality. As reported after 5 years of follow-up, the women with the highest risk of death in this cohort were those with a low BMI and a high waist-hip ratio (Figure 1). This was also true, although attenuated, among the women in the highest quintile of BMI carried an increased risk of CHD-related mortality or incidence. Abdominal obesity appears to be a particularly good indicator of the adverse metabolic risk factor profile (ie, hyperinsulinemia, dyslipidemia, hypertension, and impaired fibrinolytic capacity), which increases the risk of CHD. In contrast with CHD, other cardiovascular-related deaths were positively associated with waist-hip ratio and negatively associated with BMI, when adjusted for each other. Cancer-related mortality was only weakly associated with measures of obesity.

The finding that “other causes” of death showed a positive association with waist-hip ratio but a negative association with measures of general obesity is difficult to interpret. The component causes of the other deaths were a heterogeneous mix, including injury and poisoning, chronic pulmonary disease, and acute conditions that developed during follow-up. There were too few events to analyze every cause of death separately. However, risk of death from injury or poisoning, deaths that cannot easily be attributed to biological effects of obesity, appears to be elevated, albeit nonsignificantly, among women with greater body

### Table 4. Association of Anthropometric Variables With Incidence of Self-Reported Diabetes, High Blood Pressure, and Hip Fracture, IWHS, 1986 to 1996

<table>
<thead>
<tr>
<th>Mortality End Point</th>
<th>Anthropometric Measurements</th>
<th>Variable</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>P for Trend</th>
<th>RR (95% CI) for Multivariable-Adjusted Models (Quintile 5 vs 1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>BMI</td>
<td>n</td>
<td>63</td>
<td>122</td>
<td>184</td>
<td>407</td>
<td>802</td>
<td>&lt;.001</td>
<td>13.1 (9.8-17.3)</td>
</tr>
<tr>
<td></td>
<td>RR</td>
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<td>1.9</td>
<td>2.9</td>
<td>6.6</td>
<td>13.8</td>
<td></td>
<td>6.5 (4.9-8.8)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>95% CI</td>
<td>. . .</td>
<td>1.4-2.5</td>
<td>2.2-3.8</td>
<td>5.0-8.5</td>
<td>10.6-17.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>73</td>
<td>137</td>
<td>214</td>
<td>411</td>
<td>743</td>
<td></td>
<td>&lt;.001</td>
<td>11.3 (8.6-14.7)</td>
</tr>
<tr>
<td></td>
<td>RR</td>
<td>1.0</td>
<td>1.9</td>
<td>3.0</td>
<td>6.0</td>
<td>11.5</td>
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<td>5.1 (3.9-6.8)</td>
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<td>1.4-2.5</td>
<td>2.3-3.9</td>
<td>4.7-7.7</td>
<td>9.0-14.6</td>
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<td></td>
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<tr>
<td>Waist circumference</td>
<td>n</td>
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<td>94</td>
<td>190</td>
<td>402</td>
<td>837</td>
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<td>1.2-2.3</td>
<td>2.5-4.6</td>
<td>5.5-9.6</td>
<td>12.6-21.7</td>
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<td>High blood pressure</td>
<td>BMI</td>
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<td>709</td>
<td>764</td>
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<td>906</td>
<td>881</td>
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<td>RR</td>
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<td>1.4</td>
<td>1.7</td>
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<td>1.9 (1.7-2.2)</td>
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</tr>
<tr>
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<td>95% CI</td>
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<td>818</td>
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<td>875</td>
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<td>1.9 (1.8-2.2)</td>
</tr>
<tr>
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<td>1.5 (1.3-1.7)</td>
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<tr>
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<td>1.8-2.2</td>
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<td></td>
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<tr>
<td>Waist circumference</td>
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<td>737</td>
<td>824</td>
<td>909</td>
<td>896</td>
<td></td>
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<td>2.4 (2.1-2.6)</td>
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<tr>
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<td>1.1</td>
<td>1.5</td>
<td>1.8</td>
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<tr>
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<td>1.3-1.6</td>
<td>1.6-2.0</td>
<td>2.1-2.5</td>
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<tr>
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<td>91</td>
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<td>100</td>
<td>106</td>
<td></td>
<td>.14</td>
<td>1.1 (0.8-1.6)</td>
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<td>1.1</td>
<td>1.3</td>
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<td>1.6 (1.1-2.2)</td>
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<td>93</td>
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<td>.56</td>
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<td>0.6-1.1</td>
<td>0.7-1.2</td>
<td></td>
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</table>

*Abbreviations are explained in the first footnote to Table 2.
†Considering one anthropometric variable at a time with adjustment for age. The average number of person-years per quintile was approximately 60,000 for diabetes, 37,000 for high blood pressure, and 61,000 for hip fracture.
‡Cut points are given in the third footnote to Table 2.
§Considering one anthropometric variable at a time with adjustment for age, educational level (<high school, high school, or > high school), physical activity (low, medium, or high), alcohol intake (0, <4, or ≥4 g/d), smoking status (current, former, or never), pack-years cigarette smoking (continuous), age of first live birth (nullipara, <30 years, or ≥30 years), estrogen use (current, former, or never), vitamin use (yes, no, or unknown), and energy, whole grain, fruit and vegetable, fish, and red meat intake and Keys score (all in quintiles).
∥Considering BMI and waist-hip ratio in a single model with adjustment for all of the same variables as given in the previous footnote.
size. This may reflect residual effects of lower socioeconomic status on injury- and poisoning-associated mortality, although we did adjust for educational level. Future research should address whether general or abdominal obesity contributes to other preventable diseases or, conversely, whether the underlying diseases alter body composition.

INCIDENCE

The incidence of self-reported diabetes was strongly associated with all of the measures of obesity. Women in the highest quintiles of BMI and waist-hip ratio had a dramatic RR of 29 compared with women in the lowest combined quintiles. These findings are consistent with those of previous prospective studies, and emphasize the role of general and abdominal obesity in causing insulin resistance and, ultimately, diabetes. However, even women in the lowest quintile of BMI had a markedly elevated diabetes risk if they also had a high waist-hip ratio (Figure 5), suggesting the potentially pivotal role of visceral adipose tissue in insulin resistance.

Weight loss improves insulin sensitivity, and efforts are under way to determine whether weight control and other lifestyle modifications can prevent the onset of diabetes.

The incidence of reported hypertension was slightly more strongly associated with general obesity than abdominal obesity, although those at highest risk (RR, approximately 3.0) of hypertension were in the highest quintiles of BMI and waist-hip ratio. Previous studies have also suggested a somewhat stronger association of high blood pressure with generalized obesity than with abdominal obesity, with insulin resistance as the potential mechanism most commonly evoked.

Women with a higher BMI reported a decreased occurrence of hip fracture than did women with a lower BMI, similar to other prospective studies and in line with increased estrogen levels in obese women. In contrast, hip fracture incidence was not related to waist circumference, and hip fracture incidence increased with higher waist-hip ratio adjusted for BMI. Possible explanations are that women with a high waist-hip ratio are...
Abdominal fat distribution does not appear to further
increase risk of diabetes, hypertension, and CVD
beyond general obesity, with breast, colon, and uterine
cancer.45,46 but few have examined abdominal obesity.
Nevertheless, our data do corroborate that use of BMI
and waist circumference—have too few women to be useful.
BMI and low waist circumference or low BMI and high
waist circumference—have too few women to be useful.
BMI and low waist circumference or low BMI and high
waist circumference—have too few women to be useful.
BMI and low waist circumference or low BMI and high
waist circumference—have too few women to be useful.
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waist circumference—have too few women to be useful.
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waist circumference—have too few women to be useful.
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waist circumference—have too few women to be useful.
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waist circumference—have too few women to be useful.
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waist circumference—have too few women to be useful.
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waist circumference—have too few women to be useful.
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waist circumference—have too few women to be useful.
BMI and low waist circumference or low BMI and high
waist circumference—have too few women to be useful.
BMI and low waist circumference or low BMI and high
waist circumference—have too few women to be useful.
BMI and low waist circumference or low BMI and high
waist circumference—have too few women to be useful.
BMI and low waist circumference or low BMI and high
waist circumference—have too few women to be useful.
BMI and low waist circumference or low BMI and high
waist circumference—have too few women to be useful.
BMI and low waist circumference or low BMI and high
waist circumference—have too few women to be useful.
BMI and low waist circumference or low BMI and high
waist circumference—have too few women to be useful.
BMI and low waist circumference or low BMI and high
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waist circumference—have too few women to be useful.
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waist circumference—have too few women to be useful.
BMI and low waist circumference or low BMI and high
waist circumference—have too few women to be useful.
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waist circumference—have too few women to be useful.
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LIMITATIONS

The potential drawbacks of this study warrant consideration. The covariates and some nonfatal end points were self-reported, but we chose nonfatal end points that are self-reported fairly accurately. We did not have data on blood pressure, lipid levels, or other potentially valuable physiologic measures. Misclassification of these self-reported variables may have led to bias, although it is difficult to imagine that bias would account for different patterns of associations for different anthropometric indexes. Anthropometric indexes were self-measured, but we have documented their validity. It is possible that relations between body size and disease differ according to the duration of obesity or the age of the study population. Furthermore, even though we excluded women with known heart disease, cancer, and diabetes at baseline, other or subclinical diseases could have caused some of these older women to have lost weight before baseline. However, it was previously shown that excluding women with weight loss since the age of 50 years did not alter mortality results appreciably. Finally, these results apply to older white women and may not generalize to other ethnic groups, to younger women, or to men.

CONCLUSIONS

Clinical guidelines using BMI and waist circumference indeed identify older women at risk of diabetes, hypertension, and CVD. The high correlation between BMI and waist circumference, however, leads to categories that actually contain few women. Waist-hip circumference further identifies women at increased risk of death and several other important illnesses; it could be considered for additional risk stratification.

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REFERENCES


Correction

Missing Disclaimer. In the article by Durning and Cation titled “The Educational Value of Autopsy in a Residency Training Program” published in the April 10 issue of the ARCHIVES (2000;160:997-999), a disclaimer was omitted from the acknowledgments in the right-hand column on page 999. Preceding the Reprints address, the disclaimer paragraph should have read as follows: “The views expressed herein are those of the authors and do not reflect the official policy or position of the US Air Force, the US Department of Defense, or the US government.” The journal regrets the error.