More on Body Fat Cutoff Points

To the Editor: We read with interest the recent article by Oreopoulos et al[1] that reported the association between body composition and chronic heart failure. In the article, the authors state that "…WHO [World Health Organization] has also proposed a definition of obesity as greater than 25% body fat in men and greater than 35% body fat in women," with the 1995 WHO Technical Report[2] serving as the reference for this statement. As a matter of fact, the mentioned WHO Technical Report makes no recommendation regarding the criteria of percentage of body fat (PBF) for the diagnosis of obesity.

However, the WHO Technical Report refers to a Swedish study in which the *average* PBF (by underwater weighing) was 25% in men and 30% in women aged 45 to 49 years:

> Using underwater weighing of 200 healthy Swedish men and women aged 45-78 years, Bjontorp & Evans[3] reported changes in the percentage of weight that is represented by body fat. At 45-49 years, men averaged 25% fat; this seemed to stabilize at 38% at age 60-65 years. Women had more body fat than men at 45-49 years (30%) and stabilized at an average of 43% at 55-59 years. Between 60 and 78, neither men nor women showed much change in percentage body fat.[2, p378]

Thus, the WHO report did not set any threshold of PBF for defining obesity.

Despite that fact, several authors have continued to misquote the PBF threshold. The misquotation appears to have begun in an article published in 1998,[4] which stated that "Obesity is characterised by an increased amount of body fat, defined in young adults as body fat >25% in males and >35% in females, corresponding to a body mass index (BMI) of 30 kg/m^2 in young Caucasians" and attributed these thresholds to the WHO Technical Report.[2] Moreover, subsequent studies[5-10] continued referring to that article[4] and/or the 1995 WHO Report[2] as the primary source for the PBF thresholds.

In 2004, a WHO Expert Committee stated without reference that "…overweight (≥25 kg/m^2) corresponded to 31-39% (mean 35%) body fat in females and 18-27% (mean 22%) body fat in males. If these criteria for the percentage body fat for overweight and obesity are applied to the Asian populations, the corresponding BMIs can be calculated with country-specific equations."[11]

These are quoted as "facts" without a sound scientific basis because no original scientific validation has been published.

In summary, an initial misrepresentation of a WHO Technical Report has led to a trail of subsequent misquotations. To date, there is no validated threshold of body fatness for defining obesity.

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In reply: We greatly appreciate the interest of Ho-Pham et al in our article[1] and in percentage of body fat (PBF) cutoff points in general. To provide as detailed a response as possible, Oreopoulos has allied herself with Lavie and Romero-Corral, who cowrote the accompanying editorial,[2] and Snitker, the author of a recent letter on a related topic[3] and an unpublished correspondence with *Mayo Clinic Proceedings* criticizing the use of the World Health Organization (WHO) 1995 Technical Report[4] to support specific cutoff points for PBF.

We enjoyed reading the historical account of the misattribution of the WHO 1995 Technical Report[4] as recommending specific PBF cutoff points, which 3 of us (A.O., C.J.L., A.R.-C.) have inadvertently used as well.[1,5-8] We note that a guideline statement of the American Association of Clinical Endocrinology/American College of Endocrinology[9] and an article by a recognized expert[10] both define PBF cutoff points of 25% in men and 35% in women for obesity. One of these would probably be a better reference to use, although we admit that neither publication provides any rationale. Incidentally, these cutoff points are close to the means for PBF in the 13,601 adult participants in the Third National Health and Nutrition Examination Survey (NHANES III), which are 24.8% for men and 36.7% for women.[7]

The major contribution of the 1995 WHO Technical Report[4] was to define the normal range of body mass index

(BMI; calculated as weight in kilograms divided by height in meters squared) in adults as between 18.5 and 24.9 (with additional thresholds at 30 and 40), later elevated to official standards of both the WHO[11] and the National Institutes of Health.[12] The consensus on these numbers provided a foundation for Gallagher et al[13] to propose PBF cutoffs as the empirical age-, sex-, and race-specific PBF correlates of the now canonical BMI thresholds. According to Gallagher et al, a BMI between 25 and 29.9 corresponds to a PBF of 20% to 25% in men and of 32% to 38% in women, generally allowing for a higher PBF with advancing age and in Asians compared with others[13]; the studies of Romero-Corral et al[7] and of Jackson et al[14] provide PBF correlates of a BMI of 25 in the same range as Gallagher et al. We used the thresholds of Gallagher et al in our study of patients with chronic heart failure[1] as an example of the *obesity paradox*, ie, the observation that in some chronic conditions, a high BMI is associated with improved survival. We found that when body composition was quantified as its individual components, a high lean body mass and a low fat mass percentage were independently associated with advantageous prognostic factors; body fat thresholds are important because BMI misclassified body fatness status (in either direction) in a large proportion of our patients,[1] as also shown by Romero-Corral et al in the general population[7] and in a cohort with coronary heart disease.[8]

A debatable aspect of the approach by Gallagher et al is the fact that it allows for a higher degree of obesity in Asians and the elderly. Such group differences are to be expected when a uniform BMI threshold is applied to groups that differ in their relation between PBF and BMI. The finding that health risks are evident at a lower BMI in Asians than in other populations[14] begs the question of whether higher PBF cutoffs are indeed appropriate in this group. Only prospective studies of individuals in whom PBF has been measured can ascertain whether Asians and the elderly are particularly tolerant of a high PBF. Nevertheless, the Gallagher et al adjustments for demographics and age are small and do not detract from the soundness of the basic principle.

Using universal PBF cutoffs points of 25% in men and 35% in women, we have found that the obesity paradox in patients with coronary heart disease extends not only to BMI but also to PBF,[5] thereby advancing the understanding of this phenomenon. In another study,[16] we have defined *normal weight obesity* among 6171 individuals whose BMI was in the normal range (18.5-24.9) as those whose PBF was in the highest tertile, ie, greater than 23.1% in men and greater than 33.3% in women. Normal weight obesity was associated with a high prevalence of metabolic syndrome, similar to that observed in overweight individuals. More importantly, normal-weight obese women had more than a 2-fold increased risk of cardiovascular mortality.

In conclusion, our research has shown that PBF cutoffs in the 20% to 25% range in men and 30% to 38% in women are useful to identify individuals at risk of metabolic disease who are possibly "misclassified" by BMI and to provide insights into the obesity paradox as it applies to various conditions. It has not been within the scope of our research to determine whether a hypothetical "elbow" exists on the risk curve, to define actionable trigger points for clinical recommendations, or to examine how any of these might vary by age or ethnicity. We reiterate our call[6] for research and guidelines to establish evidence-based cutoff points for PBF, as was done years ago for BMI.

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Frequency of Herpes Zoster Recurrence

To the Editor: We read with great interest the study by Yawn et al,[1] published in the February 2011 issue of *Mayo Clinic Proceedings,* which found that the frequency of herpes zoster (HZ) recurrence in a community population was higher than previously reported. The reported results are somewhat unexpected. It is generally accepted that the lifetime incidence of a second episode of HZ in immunocompetent individuals is between 1% and 5% and that the recurrence is typically many years after the first episode. A number of issues need to be clarified about the study by Yawn et al before the relevance of these findings can be determined.

First, the diagnosis of HZ in the study by Yawn et al[1] was established clinically. The clinical diagnosis of HZ can be difficult and is subject to error. In a zoster prevention study,[2] HZ was ruled out by laboratory testing (polymerase chain reaction or viral culture) in 24% of patients with a clinical diagnosis of HZ, suggesting that clinical diagnosis can on occasion be incorrect. No previous unreported case of HZ was revealed in closeout interviews with patients in that study.[2] Similarly, a prospective study of HZ diagnoses by general practitioners in the United Kingdom found 17% of diagnoses to be incorrect.[3] More specifically, of the 230 patients diagnosed clinically as having HZ, only 204 cases were confirmed by immunofluorescence and/or polymerase chain reaction. Of the 26 patients who had no evidence of HZ on laboratory tests, 10 patients had herpes simplex, and the rest had other dermatological diseases.[3] In the study by Yawn et al,[1] only 25% of the recurrent episodes were confirmed by laboratory analysis, but it is unclear whether the first episode was also confirmed by laboratory results.

We recently conducted a study of 173 patients (median age, 75 years) with postherpetic neuralgia. In these patients, the median duration of postherpetic neuralgia was 23 months (range, 2-207 months).[4] None of the patients presented with HZ during the follow-up visit or had a history of HZ. We realize that the number of people involved is low compared with the cohort in the study by Yawn et al, but they presented with both the main risk factors that, according to that study, predict the likelihood of recurrences.

Another point in need of clarification is the choice by Yawn et al to include in the analysis the 139 individuals (8.3% of the total population sample) who were immunocompromised at the time of the index HZ episode.[1] It is known that the risk of HZ and its recurrence is increased in persons with a compromised immune system. Indeed, HZ rates of 29.4 to 51.5 per 1000 person-years have been reported among adults infected with the human immunodeficiency virus,[5] and high rates have also been reported in persons with systemic lupus erythematosus, rheumatoid arthritis, granulomatosis with polyangiitis (Wegener), and inflammatory bowel disease.[5] For most of these conditions, data are insufficient to determine how much of the risk is attributable to the underlying disease vs its treatment. Hence, the inclusion of immunocompromised people may represent a bias.

Finally, the authors discuss the possibility of an innate (possibly genetic) predisposition for HZ, which has received attention in studies of HZ in families. We have recently examined the possibility that a family history of HZ represents a risk factor for zoster development, but our findings could not confirm the hypothesis.[4]

Given the ready availability and the safety profile of the HZ vaccine, we agree that it is important to identify additional categories of people who could benefit from it. However, in our opinion, well-designed prospective studies are needed to ascertain the real likelihood of recurrences in the general population.

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In reply: The very thoughtful letter by Drs Volpi, Gatti, and Pica indeed highlights some important issues in studying HZ occurrence and recurrence. We agree that not all clinical diagnoses of HZ are truly HZ. That is one reason why we thoroughly reviewed the medical records of all potential cases to further evaluate the clinical diagnosis of HZ. In addition to having been diagnosed as having HZ by a physician, our study patients had to have documented pain or other dysesthesias plus a vesicular or a crusted-over rash in a dermatomal pattern. We also reviewed visits in the 3 months after the initial visit to confirm that no later testing was performed that may have changed the initial diagnosis of HZ (eg, to a diagnosis of herpes simplex).[1] As a result of this follow-up process, more than 86 cases from the 1996-2001 incident cohort and 10 additional possible "recurrences" from the final recurrence data were removed. Despite this careful abstracting and follow-up, we agree that some of the recurrences may be conditions other than HZ and that a large prospective study with laboratory confirmation would be preferable; however, implementing such a study on a community basis would pose practical difficulties.

Using the same data as Volpi et al, we conclude that the use of a clinical HZ diagnosis is justified. The data they reference state that 17% to 25% of clinical HZ diagnoses may be incorrect (this is assuming limited effort to rule out herpes simplex and other differential diagnoses); stated conversely, this suggests that 75% to 83% of clinical HZ diagnoses are correct.[2,3] In our cohort, it is true that 75% of the cases did not have laboratory testing, but at least 75% of them are then likely to be correctly diagnosed, which means that, overall, at least 81% of the recurrences in our study are likely to have indeed been HZ. If we used this 81% to adjust our recommendations for patients who are not immunocompromised, the recurrence rate would still be considerably higher than the 1% to 5% lifetime recurrence rate suggested by Volpi et al.

We also agree that most people report they have never had shingles previously. In our original study of HZ "incident cases,"[1] a careful review of the patients' medical records for up to 40 years before the date of the "incident case" demonstrated that about 6% of the 1669 patients had a previous medical record notation of HZ with typical rash and pain that was not mentioned in the clinical notes of the current HZ case. Long-term patient recall has been documented repeatedly to be faulty.[4]

To provide community-based recurrence rates, we chose to include all patients in the community but stratified calculations of recurrence rates by immune status (immunocompromised or immunocompetent). As expected, the rate of recurrence was higher in those who had an indication of immune compromise compared with those who did not. The question raised by Volpi et al as to what constitutes an immunocompromised group is important, requires further study, and is beyond the scope of our study and article.

Our study provides an important estimate for a community (not a clinical trial) population with an average of 8 years of follow-up, longer than in any of the administrative database studies or the Shingles Prevention Study.[2,5] Until the results of a prospective, population-based study have been published, we think that our study provides useful information to help physicians discuss HZ recurrence with their patients.

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