

# The Fitness, Obesity, and Health Equation

## Is Physical Activity the Common Denominator?

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**T**HE MODERN LIVING ENVIRONMENT IN DEVELOPED COUNTRIES is characterized by low daily energy expenditure and an abundant and inexpensive food supply, making positive energy balance common. The result is a rightward skewing of the body mass index (BMI) distribution and an increasing prevalence of obesity.

Indisputable evidence links obesity to health problems, including risk of cardiovascular disease, type 2 diabetes, some cancers, and all-cause mortality.<sup>1</sup> These associations are dose-related, temporally consistent, and biologically plausible, which support a causal hypothesis. Physical inactivity also has a dose-related, temporally consistent, and biologically plausible relationship to the same health outcomes as those as for obesity,<sup>2</sup> and both obesity and inactivity have similar patterns of association with clinical risk indicators such as blood pressure, fasting plasma glucose, and inflammatory markers.<sup>3-5</sup> Furthermore, declines in average daily energy expenditure are a likely underlying cause of the obesity epidemic.<sup>6</sup>

However, the majority of studies examining obesity and health have not adequately accounted for physical activity. When physical activity has been considered, investigators have often relied on simple self-report questionnaires in which inaccuracy can increase proportionally with the respondent's weight. Failure to adequately quantify physical activity when examining the risks of obesity is similar to exploring risk factors for cancer and misclassifying tobacco use. Physical activity and weight are closely linked and each must be measured accurately and considered carefully when examining the other.

Previous investigations, including studies from our group, have examined the individual and joint associations of cardiorespiratory fitness (CRF) and body habitus to health outcomes. Use of maximal exercise tests to quantify CRF provides an objective evaluation of an individual's recent activity patterns and accounts for 70% to 80% of the variance in detailed activity records.<sup>7</sup> Cardiorespiratory fitness is stronger than self-reported physical activity as a predictor of many health outcomes, most likely because fitness measure-

ments are less prone to misclassification and because factors other than activity may influence both fitness and health through related biological factors.<sup>8</sup> For example, the age and examination year-adjusted relative risks for all-cause mortality in 1263 men with type 2 diabetes are 1.8 for inactivity but 2.9 for low fitness.<sup>9</sup>

Obese individuals with at least moderate CRF have lower rates of cardiovascular disease (CVD) or all-cause mortality than their normal-weight but unfit peers. In fact, death rates in the former group are about one half those of the latter.<sup>10</sup> These results are similar whether BMI, percent body fat, body fat mass, or waist circumference is used as the body habitus measure<sup>11</sup> and are consistent for women and men<sup>11,12</sup> and for men with type 2 diabetes.<sup>13</sup> These results also pertain to nonsmokers and after exclusion of individuals with chronic disease or deaths within the first 5 years of follow-up.<sup>11</sup> Moreover, 150 minutes a week of moderate intensity physical activity is sufficient to avoid the low-fitness category. These results are consistent with those reported in 24 studies identified in a systematic review on physical activity, CRF, obesity, and health.<sup>14</sup>

Two reports in this issue of *JAMA* examine activity and BMI as predictors of health outcomes, with somewhat divergent results.<sup>15,16</sup> Wessel and colleagues<sup>16</sup> report that women with low self-reported functional ability had higher risks of CVD outcomes than women with higher levels of fitness. In contrast, BMI and fat distribution were not associated with CVD risk. These findings are consistent with studies showing that adequate levels of activity or fitness confer health benefits for women and men in normal-weight, overweight, and obese categories.<sup>11,13,17,18</sup> In contrast, Weinstein and colleagues<sup>15</sup> report that BMI is stronger than physical activity in predicting incident type 2 diabetes and that physical activity has little effect on the relation of BMI to diabetes. They report significant inverse gradients of risk across categories of physical activity for 3 different methods of assessing activity although the associations became nonsignificant after adjustment for BMI in 2 of the 3 analyses.

Key questions raised by the 2 articles in this issue of *JAMA* are why is the association between physical activity and incident diabetes substantially reduced when adjusted for BMI as reported by Weinstein et al<sup>15</sup> and why is there little evi-

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dence of a protective effect for activity in overweight or obese women? And, conversely, why do Wessel et al<sup>16</sup> observe a substantially lower risk for adverse CVD events in obese and nonobese physically active women yet no association between body habitus and CVD outcomes?

Differences between these 2 studies, as well as the difference between the findings of Weinstein et al<sup>15</sup> and other published work on this topic, may be due to differences among study populations, methods, and outcomes. Wessel et al<sup>16</sup> followed-up women with clinical indications for coronary angiography, whereas Weinstein et al<sup>15</sup> followed-up apparently healthy women in the health care profession. Although related, study outcomes also differed—adverse CVD events<sup>16</sup> and type 2 diabetes.<sup>15</sup> Valid assessment of habitual physical activity is difficult. Wessel et al<sup>16</sup> used 2 measurements—an estimate of CRF by the Duke Activity Status Index,<sup>19</sup> which was previously validated against maximal oxygen uptake, and a self-reported physical activity questionnaire. Their results for Duke Activity Status Index are similar to other findings for objectively measured cardiorespiratory fitness and mortality,<sup>11-13,18</sup> as were their results when using the self-reported questionnaire. The 2 studies used different measures of self-reported physical activity; therefore, it is possible that the one used by Wessel et al is more accurate than the one used by Weinstein et al, highlighting another difference in the 2 studies. The questionnaire used by Weinstein et al<sup>15</sup> has acceptable reliability and shows modest correlations with other self-reported physical activity measures but apparently has not been validated with a gold standard, such as maximal oxygen uptake or doubly labeled water, as was the case for Duke Activity Status Index.<sup>19</sup> There are other differences in methods. Wessel et al<sup>16</sup> and other recent studies<sup>11-13,18</sup> obtained baseline data at a clinical examination, whereas Weinstein et al<sup>15</sup> did not have such information. This may have led to greater misclassification for some variables such as the likelihood of detecting subclinical disease, which could result in health status influencing the combined associations among activity, BMI, and incident disease.

The findings of Wessel et al<sup>16</sup> and Weinstein et al<sup>15</sup> provide a timely opportunity to examine an ongoing debate and offer a resolution. The results presented by Weinstein et al<sup>15</sup> suggest that increased BMI is substantially more important for incident diabetes, and Wessel et al<sup>16</sup> suggest that inactivity or low fitness is a greater threat to health in terms of CVD outcomes. In recent years, the “fitness vs fatness” issue has led to controversy and heated debate. Although the debate may never be fully resolved, the relative contribution of fitness and obesity to overall health and risk actually may be a trivial matter because a common treatment is already available for both low fitness and excess body weight. Increasing regular physical activity results in predictable increases in fitness, and it is widely accepted that regular physical activity is a core component of successful weight loss programs and, more importantly, of long-term weight loss

maintenance. In essence, physical activity is the common denominator for the clinical treatment of low fitness and excess weight, making the “fitness vs fatness” debate largely academic. Thus, physicians, researchers, and policymakers should spend less energy debating the relative health importance of fitness and obesity and more time focusing on how to get sedentary individuals to become active. With 40 to 50 million adults in the United States currently not obtaining the recommended amount of daily physical activity,<sup>2</sup> motivating the individuals to incorporate physical activity into their daily lives, whether to lose weight or reduce risk of chronic disease, will have substantial health and financial benefits at an individual and societal level.

In summary, the majority of studies show that regular physical activity has health benefits at any weight, and for those who want or need to lose weight, physical activity is a critical component of long-term weight management. Consequently, physical activity promotion should be a foundation of clinical therapy and public health policy, whether to promote health or weight control. The medical community needs to lead in communicating the importance of physical activity for health and weight maintenance. Just as weight is addressed in some manner at nearly every physician visit, so should attention be given to recommending the accumulation of 30 minutes a day of moderate intensity physical activity at least 5 days of the week. This can be obtained through brisk walking, bicycling, swimming, or activities of daily life such as housework or gardening.

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# Pharmacotherapy of Chronic Fatigue Syndrome

## Another Gallant Attempt

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**A**S THE ABILITY TO TREAT THE PHYSICAL MANIFESTATIONS of many illnesses improves, physicians grapple more seriously with their emotional, social, and symptomatic dimensions. For example, palliative care is now a critical healing art, while oncology begins to contend with the long-term sequelae of the curative regimens for which it has labored so long to craft. Today, quality-of-life instruments and symptom rating scales are essential metrics of health status and outcomes.

Among the illness symptoms that are now addressed in the context of clinical practice and research, fatigue seems the most refractory to measurement and management. Although fatigue is a recognized complication of certain conditions and treatments—advanced cancers and multiple sclerosis, and a consequence of radiation and recombinant interferon therapy—the tools and techniques used to assess and ameliorate fatigue and the comprehension of its pathogenesis are decidedly inferior to those for other prevalent symptoms like pain and nausea.

Absent optimal metrics and explanations for fatigue, this symptom also elicits the least attention and sympathy. This reality most affects those for whom no underlying illness or treatment can be identified as the proximate cause of their persisting fatigue. Efforts over the past quarter century have attempted to characterize such patients, leading to a series of working definitions of which the most widely used, however still imperfect, parses cases into those with idiopathic chronic fatigue and those with more global and debilitat-

ing features that have been termed *chronic fatigue syndrome* (CFS).<sup>1-4</sup>

As defined, CFS is largely an acquired sporadic condition that affects, arguably, as many as 420 individuals per 100 000 population—adults more often than children and women more often than men.<sup>5,6</sup> Speculations as to its pathogenesis abound: that it arises from a chronic infection, a brain or mood disorder, a sleep disturbance, an immune dysfunction, an autonomic or neuroendocrine imbalance, etc.<sup>3,4,7</sup> The data strongly reject the infectious hypotheses and discern a subtle, but still nebulous, problem in regulation of hypothalamic-pituitary-adrenal and related hormonal axes.<sup>8,9</sup>

With the description of CFS have come countless proposals to treat it with drugs, biological agents, dietary interventions, and behavioral and exercise strategies. The self-help sections of bookstores and numerous Web sites beckon to desperate patients with promises of simple solutions for renewed health and energy. Among the strategies that were studied rigorously, only 2 emerged with some consistency as meaningfully beneficial for many patients: cognitive-behavioral therapy and graded exercise.<sup>4,8,10-15</sup> These are demanding therapies and not universally embraced because of a misperception that their nature places blame for the fatigue on the patient for failing to manifest sufficiently healthy behaviors and habits. Thus, drugs remain the favored solution, should any prove effective.

Unfortunately, pharmacological approaches have failed to resolve CFS. This is not to say that drugs have no place

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See also p 1195.