And What About Exercise? Fitness and Risk of Death in “Low-Risk” Adults

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Leafing through this morning’s Sunday paper, I could not help but feel a sense of unease about our current state of preventive medicine. A lead article in the opinion section argued that most of the elements of the “annual physical exam” are “in many ways pointless or (worse) dangerous.” Routine electrocardiograms are of “no use.” Another essay attacked the government’s guidelines for dietary salt reduction, noting that the “eat-less-salt argument has been surprisingly controversial. . . . Not because the food industry opposes it, but because the evidence to support it has always been so weak.” Yet another writer praised the mayor of New York City for his efforts to institute a ban on sugary beverages, a proposed ban that has run into much opposition.

So controversy continues about salt, sugar, and the annual physical. And what about exercise? Just a few days before, a front-page news story had described a study finding that some people could be “harmed” by exercise. Among 1687 patients who were enrolled in 6 separate studies of rigorous exercise, approximately 10% saw worsening of measures traditionally thought to improve with exercise; these measures included blood pressure, high-density lipoprotein cholesterol, triglycerides, and fasting insulin levels. The news story included questions about current guidelines that call for at least 150 minutes of moderate-level exercise per week. The guidelines are based on “a weak form of evidence . . . that compared the health of people who exercised with that of people who did not.”

Within the context of these ongoing controversies that focus on our approach to fundamental lifestyle issues, Barlow and colleagues report in the current issue of the Journal of the American Heart Association on the association of cardiorespiratory fitness and long-term risk of death among adults classified as low risk by the Framingham Risk Score. The authors performed symptom-limited exercise tests in >11,000 healthy adults without diabetes mellitus who were followed up for 27 years, during which time >1000 died. There was a strong gradient of risk, as decreasing levels of fitness predicted increased risk of all-cause and cardiovascular death, irrespective of sex, smoking status, or baseline Framingham Risk Score. The authors argue that their findings have “important implications for clinical practice” in that low-risk adults should be considered appropriate candidates for higher doses of aerobic exercise.

Barlow and colleagues’ well-done investigation is wholly consistent with a remarkably robust body of literature on the epidemiological association between levels of cardiorespiratory fitness and risk of death. Across a wide spectrum of baseline risk, from severe heart failure to “low-risk” asymptomatic adults, lower levels of fitness predict higher rates of death. How should we respond to these findings? We can frame our responses to the literature on fitness and to Barlow and colleagues’ report within clinical, public health, and research contexts.

Clinical implications: Barlow et al focused on patients deemed to be at low risk on the basis of the Framingham Risk Score, a global risk assessment that incorporates age, sex, smoking status, blood pressure, and cholesterol levels. Although risk scores have been promoted widely, remarkably little evidence exists to show that their routine use leads to improved clinical outcomes. Furthermore, risk scores have been criticized for yielding inconsistent values; recent work has highlighted remarkably high levels of predictive uncertainty, as levels of risk can depend not only on clinical characteristics but also on which risk instrument and risk variables are measured. The study by Barlow et al effectively represents a refinement of the Framingham Risk Score, a refinement based on the addition of cardiorespiratory fitness. It is difficult for us to determine how important this refinement is because the authors do not present data on improved discrimination or reclassification. And even so, the study, as well

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What About Exercise?

The American Heart Association

Barlow and colleagues argue that their data support widespread prescription of higher doses of exercise even among low-risk adults. To date, though, there are no large-scale randomized trials supporting exercise recommendations. One small trial of sedentary obese women found that as little as 72 minutes of exercise per week could lead to potentially meaningful improvements in physical fitness. A large-scale observational study of >400,000 adults suggested that even as little as 15 minutes of exercise per day predicted a 14% reduction in risk of death. Some of us worry that that might misinterpret public health recommendations to mean that anything less than 150 minutes of exercise per week is of no value and therefore not worth pursuing at all. To add to the confusion, we now are aware of data suggesting that some adults might be harmed by exercise. It is critically important to avoid oversimplifications that overlook nuanced quantitative and qualitative issues: Just as not all fats are the same and not all carbohydrates are the same, not all exercise, whether of short or long duration, is equivalent either.

Public health implications: Current US guidelines recommend that most adults seek to engage in at least moderate-level exercise for ≥150 minutes a week (eg, 30 minutes a day for 5 days a week). Barlow and colleagues argue that their data support widespread prescription of higher doses of exercise even among low-risk adults. To date, though, there are no large-scale randomized trials supporting exercise recommendations. One small trial of sedentary obese women found that as little as 72 minutes of exercise per week could lead to potentially meaningful improvements in physical fitness. A large-scale observational study of >400,000 adults suggested that even as little as 15 minutes of exercise per day predicted a 14% reduction in risk of death. Some of us worry that that might misinterpret public health recommendations to mean that anything less than 150 minutes of exercise per week is of no value and therefore not worth pursuing at all. To add to the confusion, we now are aware of data suggesting that some adults might be harmed by exercise. It is critically important to avoid oversimplifications that overlook nuanced quantitative and qualitative issues: Just as not all fats are the same and not all carbohydrates are the same, not all exercise, whether of short or long duration, is equivalent either.

Research implications: On the basis of what we know to date, exercise can be an extraordinarily powerful preventive intervention, an intervention that might prevent premature death, myocardial infarction, stroke, cancer, depression, dementia, and disability. Nevertheless, in contrast to the situation with blood pressure and cholesterol treatment, there is remarkably little randomized trial evidence supporting routine exercise prescription. Perhaps this is because it is much more difficult to prescribe an exercise regimen to which people will adhere than it is to prescribe pills. So far, trials have focused either on surrogate measures or on special populations, like those with heart failure or glucose intolerance. The ongoing LIFE trial (Lifestyle Interventions and Independence for Elders; ClinicalTrials.gov Identifier: NCT01072500) is assessing the value of routine exercise in sedentary healthy elderly adults, and although it is powered primarily to evaluate effects on mobility, it might yield some important insights on the effects of exercise prescription on cardiovascular health. There also could be a role for public health research into the effects of public policies on levels of physical activity. Community planners can consider a variety of interventions, including installation of pavements and increased numbers of neighborhood recreational facilities. It is arguably even more difficult to randomize community interventions than it is to randomize clinical lifestyle interventions, though some investigators have demonstrated an ability to randomize neighborhoods or schools to various types of public health efforts. Another potentially valid research methodology involves exploitation of “natural experiments,” such as differential implementation of smoking bans across political borders.

Over the past 50 years, we have seen remarkable declines in death rates due to myocardial infarction and stroke. A good part of the improvements can be traced to management of classic risk factors. The recently announced “Million Hearts Initiative” will seek to exploit 4 evidence-based interventions: aspirin in appropriate settings, blood pressure reduction, cholesterol reduction, and smoking cessation. Even if the initiative is successful in preventing millions of heart attacks and strokes, cardiovascular disease will remain a leading cause of death and disability. It is wholly appropriate that we are exploring other modes of prevention, including exercise, but at the same time we should have the humility and discipline to figure out how to develop robust levels of evidence that will enable us not only to confidently improve public health, but also to better enjoy our encounters with the Sunday newspaper.

Disclosures

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