Physical Activity
Can There Be Too Much of a Good Thing?

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It is widely acknowledged that physical activity in some way, shape, or form is beneficial to a person’s health, a concept that has been around for >2 millennia, having been first espoused by Hippocrates: “Eating alone will not keep a man well; he must also take exercise.”1 Therefore, it should come as no surprise that in this issue of Circulation, Armstrong and colleagues present findings from The Million Women’s Study that highlight the beneficial effects on the risk of coronary heart disease, cerebrovascular disease, and venous thromboembolism that regular moderate physical activity confers on active healthy, middle-aged women in the United Kingdom.2 Findings from the current study have brought some clarity with respect to the questions of how much, how often, and how hard, middle-aged women need to do physical activity to accrue the greatest vascular benefits.

The key findings from this article relate to the frequency, intensity, and total amount of physical activity that were associated with optimal vascular benefits among middle-aged women. Interestingly, the relationship between the frequency of activity (either strenuous or any) and vascular risk was not linear but rather U-shaped; in women who engaged in strenuous activity (defined as “enough to cause sweating or a fast heart rate”), the optimal frequency of activity in terms of vascular risk reduction was 2 to 3 times per week which was associated with significant relative risk reductions of 17% to 19% in comparison with the rarely/never group. Any further increase in the frequency of strenuous exercise beyond that point was associated with an increased vascular risk. For any activity, which mainly included walking, gardening, and housework, the optimal frequency was 4 to 6 times per week (in comparison with rarely/never), which was associated with a slightly greater 17% to 25% reduction in the risk of vascular outcomes in this population. And, as with the frequency of activity, there was also no evidence of a linear association between the total amount of physical activity and reductions in vascular risk; the greatest difference in vascular risk occurred between the least active women (<40 excess metabolic equivalent [MET] hours per week) versus all other groups.

Ascertaining a valid and reliable measure of physical activity and its relationship with health outcomes requires that numerous hurdles be overcome. Physical activity must be measured (preferably at >1 time point) in a large enough sample of people for a long enough period of time to accrue a sufficient number of events for estimates of the association between physical activity and vascular disease to be derived. Reliably estimating the volume of physical activity is notoriously challenging. This has in part been due to the inherent difficulties in accurately measuring not only the frequency of physical activity, but also its type, intensity, and duration, and variations in activity level over time, as well. Comparability between studies has also been impeded by a general lack of consistency as to which activities constitute physical activity. For example, The Million Women Study is one of the few large-cohort studies to measure housework and to include it as a form of moderate physical activity.

In many ways, the current study has been able to overcome these methodological challenges by sheer virtue of its size and length of follow-up. Between 1996 and 2001, >1.1 million healthy British women with a mean age of 56 years were recruited into the study.3 At baseline, the women were asked how often they did any exercise and how often they did strenuous exercise. At a resurvey 3 years later, 44% of participants reported how many hours they spent each week on a range of physical activities including housework, gardening, walking, or exercise that caused sweating or a fast heart rate. When relying on self-report data of this type, it is crucial to understand how valid the methods for assessing the exposure are. In a previous publication from the same group, the authors examined the level of agreement between activity measured at the 2 time points.3 For strenuous activity, absolute agreement for questionnaires 2 years apart was 52% (κweighted=0.51), and, for any physical activity, the absolute agreement for questionnaires 2 years apart was 47% (κweighted=0.58), suggesting that there was moderate agreement between the studies or, in other words, the level of physical activity that women reported doing was in reasonable agreement with what was actually done.

Over the course of 9 years of follow-up and after excluding women who may have been asymptomatic for serious disease at the commencement of the study, there were >49 000 cases of incident coronary heart disease, >17 000 strokes, and 14 500 venous thromboembolism events. In comparison with being inactive, doing any form of exercise at least once a week was associated with the greatest reductions in the risk of incurring any of these vascular events. Increments in the amount of physical activity beyond once a week were associated with smaller benefits up to a certain point beyond which there were no gains in terms of reduced risk of vascular outcomes. The point of inflection depended on the type of vascular event, and...
the intensity of activity, as well. But, in general, undertaking
moderate exercise on 4 to 6 days of the week was associated
with the greatest reductions in relative risk estimates in com-
parison with women who were inactive. For strenuous exer-
cise, in comparison with never, restricting the activity to 2 to 3
days of the week was optimal. It is noteworthy that increases
in the frequency of strenuous exercise to >3 times per week
were associated with significantly increased vascular risk (in
comparison with strenuous exercise 2–3 times per week).

The possibility of confounding is always a concern with
observational data. In the current study, the women who
reported doing strenuous exercise daily comprised only 3.2%
of the population in comparison with 47% of women in the
reference group who reported no strenuous exercise. And,
rather counterintuitively, the prevalence of current smokers
was similar in both groups at 25%, considerably higher than
the prevalence estimates for women who did strenuous exer-
cise between 1 and 6 times per week. Even though the results
were adjusted for smoking (and other risk factors), the authors
acknowledge that residual confounding may have persisted
and, thus, may have explained some of the association between
physical activity and vascular risk in the most active women.

Although the current findings are consistent with the litera-
ture, they are not directly comparable with those from other
cohorts because the metric used to quantify the absolute vol-
ume of activity in The Million Women Study was the excess
MET as opposed to the more commonly used MET. A MET
is the ratio of the metabolic rate of an activity to the rate of
energy expended while sitting quietly: 1 MET is the rate of
energy expenditure while at rest, so a 3 MET activity (such as
housework) expends 3 times the energy used by the body at
rest. Therefore, a 3 MET activity undertaken for 60 minutes
is equivalent to 180 MET-minutes (or 3 MET-hours) of physi-
cal activity. Moderate-intensity exercise, such as walking,
gardening, and housework, typically equates to 3 to 6 METs,
whereas vigorous activity (such as cycling) is estimated to be
≥6 METs. In contrast, an excess MET is defined as the
excess energy expenditure associated with any given activity
above that of the basal metabolic rate obtained by subtract-
ing 1 MET from each multiplier before calculations (ie, the
excess MET associated with walking for 60 minutes is 120
MET-minutes [or 2 excess MET-hours as opposed to 3 MET-
hours]). Calculating excess MET-hours takes into account
the differences in the proportion of energy expenditure attrib-
able to resting metabolic rate during low versus high activities
and thus is a better indicator for assessing the actual amount
of energy expended as a result of physical activity. For example,
in low-intensity activities such as housework (which accounts
for more than half of all activity in the current study),5 the
proportion of energy expenditure attributable to resting metabolic
rate is higher than of high-intensity activities.6

The use of excess MET-hours versus MET-hours to esti-
mate physical activity levels between studies is likely to
explain some of the observed variation in reported activity lev-
els between comparable populations. For example, in the
current study, the amount of physical activity in women reporting
any exercise varied from 58 excess MET-hours in the rarely/
ever active group to 79 excess MET-hours per week in the
daily category. In comparison, among women (average age,
50 years) in the European Prospective Investigation into
Cancer and Nutrition (EPIC) mean MET-hours per week were
50 in the inactive group and 145 MET-hours in the most active
group. Finally, data from the Nurses’ Health Study (mean
age, 64 years) show considerably lower levels of total physi-
cal activity with an average of 1.3 MET-hours per week in
the least active group to 37.6 MET-hours in the most active
group; these low activity levels in the latter study are likely
to reflect in part the noninclusion of household activity.8 But,
irrespective of how physical activity was calculated, women in
The Million Women Study were all at the more active end of
the spectrum, and, thus, the generalizability of the findings to
women who are largely inactive remains unclear.

Current recommendations suggest that, for cardiovascular
health, adults should be doing at least 30 minutes of moder-
ate-intensity aerobic activity at least 5 days per week in bouts
of ≥10 minutes, or 25 minutes of vigorous aerobic activity
at least 3 days per week, or a combination thereof.9 In total,
this amount of activity would equate to ≈8 to 12 MET-hours
per week. In the current study, even women who reported
doing no physical activity at study baseline still accrued >15
excess MET-hours per week (after excluding housework) pre-
dominantly through walking and gardening.3 In comparison,
in England, nationally representative data indicate that only
28% of women aged 55 to 64 years10 (and a similar percent-
age in the United States11) meet the recommended guidelines
for physical activity. Part of the disparity in prevalence esti-
mates between the current study and national figures is likely
to be a consequence of the healthy-volunteer effect. However,
because women in the study had similar levels of other vascu-
lar risk factors (such as smoking and body mass index) com-
parable to that of the general population, it is unlikely that
they differed that dramatically from the rest of the population
in terms of physical activity levels. Rather, the aforementioned
differences in how physical activity is defined and measured
between studies are likely to explain some of the variation.

In conclusion, in healthy, active, middle-aged women, mod-
erate and frequent physical activity was optimal for vascular
risk reduction. These findings may offer some hope – and
perhaps even a dash of inspiration – to the estimated 30% of
adults worldwide who struggle to achieve the recommended
levels of physical activity.14 To paraphrase Hippocrates, walk-
ing may well be woman’s best medicine.

Disclosures
None.

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