



Editorial

Screening with the exercise test: time for a guideline change?

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This editorial refers to 'Reasons for terminating an exercise test provide independent prognostic information: 2014 apparently healthy men followed for 26 years' by J. Bodegard *et al.*, doi:10.1093/eurheartj/ehi278

Exercise testing as a screening modality must be considered in a new light given the paper by Bodegard *et al.*¹ and three other recent screening studies. First, this paper demonstrates the importance of using cardiac endpoints for evaluating cardiac tests. When adjusting for age, men who stopped exercising exclusively because of impaired breathing had a two-fold increased risk of dying from coronary heart disease (CHD) and a 3.5-fold increased risk of dying from pulmonary causes when compared with men who stopped due to volitional fatigue. Although all-cause mortality must be the primary endpoint of intervention studies, this is not the case for cardiac tests, where the goal is to determine which patients should be considered for a cardiac intervention to improve outcome. The authors demonstrated that certain responses predict pulmonary endpoints more so than cardiac. Secondly, this data set of 2014 asymptomatic Norwegians and two studies of asymptomatic Americans have clearly demonstrated the substantial risk ratios generated by the standard exercise test when combined with other risk factors.

From the Cooper Clinic comes the largest screening study of the exercise test to predict CHD in a self-selected population of asymptomatic men.² It was a prospective study performed between 1970 and 1989, with an average follow-up of 8 years. There were 25 927 healthy men, 20–82 years of age at baseline (mean 43

years) who were free of CHD and who were evaluated in the Cooper preventive medicine clinic. During follow-up there were 612 deaths from all causes and 158 cardiac deaths. The sensitivity of an abnormal exercise test to predict cardiac death was 60%. The age-adjusted relative risk of an abnormal exercise test for CHD death was 21 times in those with no risk factors, 27 times in those with one risk factor, 54 times in those with two risk factors, and 80 times in those with three or more factors.

The usefulness of a screening exercise test along with risk factors has been recently demonstrated in the Framingham population.³ Included were 3043 members of the Framingham Heart Study offspring cohort without CHD (1431 men and 1612 women; age, mean 45) who were followed for 18 years. The risk of developing CHD was evaluated considering three exercise test variables: (i) ST-segment depression, (ii) failure to achieve target heart rate, and (iii) exercise capacity. In multivariable analyses that adjusted for age and Framingham CHD risk score, among men, ST-segment depression or failure to achieve target heart rate doubled CHD risk, whereas a greater exercise capacity predicted lower CHD per risk. In this random sample of asymptomatic men, ST-segment depression, failure to reach target heart rate, and exercise capacity provided additional prognostic information in age- and Framingham risk score-adjusted models, particularly among those in the highest risk group.

In a previous analysis of their screening study, our Norwegian colleagues⁴ concluded that integration of multiple exercise test parameters and conventional risk factors improved CHD risk assessment substantially—especially in smokers with high cholesterol.

These three studies (*Table 1*) lead to the logical conclusion that exercise testing should be part of the preventive health recommendations for screening healthy, asymptomatic individuals along with risk factor assessment.

The opinions expressed in this article are not necessarily those of the Editors of the *European Heart Journal* or of the European Society of Cardiology.

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Table 1 Three contemporary studies reporting exercise testing to screen apparently healthy individuals that considered multiple exercise test response and risk factors together with extended follow-up for hard endpoints

Study	Sample size	Years follow-up
Cooper clinic	25 927 men	8
Norway	2014 men	26
Framingham	3043 men/women	18

No other cardiac screening technology has studies matching these in numbers tested and years of follow-up.

The following rationales justify this conclusion:

- (1) Three contemporary studies have demonstrated impressive incremental risk ratios for the synergistic combination of the standard exercise test and risk factors.
- (2) Other more costly modalities without the availability or documented favourable test characteristics of the exercise test are currently being promoted for screening.
- (3) Physical inactivity has reached epidemic proportions and what better way to make our patients conscious of their deconditioning, than having them do an exercise test that can also 'clear them' for exercise?
- (4) An MET increase in exercise capacity corresponds to a 10 to 20 % improvement in survival in all populations studied⁵ as well as a 5% decline in health care costs.⁶

The additional risk classification power documented by the data from Norway (2000 men, 26-year follow-up), the Cooper clinic (26 000 men, 8-year follow-up), and Framingham (3000 men, 18-year follow-up) provide convincing evidence that the exercise test should be added to the screening process. In addition, exercise capacity itself has substantial prognostic predictive power. Given the emerging epidemic of physical inactivity, inclusion of the exercise test in the screening process sends a strong message to our patients, that we consider their exercise status as important.

Although the risk of an abnormal exercise test is apparent from these studies, the iatrogenic problems resulting from screening must be considered (i.e. employment, insurance, etc.). The recent US Preventive Services Task Force statement contends that 'false positive tests are common among asymptomatic adults, especially women, and may lead to unnecessary diagnostic testing, over treatment and labelling'. This statement summarizes the current US Preventive Services Task Force (USPSTF) recommendations on screening for CHD and the supporting scientific evidence and updates the

1996 recommendations on this topic. The complete information on which this statement is based, including evidence tables and references, is available in the background article and the systematic evidence review, available through the USPSTF website (<http://www.preventiveservices.ahrq.gov>) and through the National Guideline Clearinghouse (<http://www.guideline.gov>).⁷ In the majority of asymptomatic people, screening with any test or test add-on, is more likely to yield false positives than true positives. This is the mathematical reality associated with all of the available tests.

However, if screening could be performed in a logical way with test results used to decide on therapies, rather than leading to invasive interventions, insurance or occupational conundrums, then the recent results summarized earlier should be applied to preventive medicine policy. Owing to the inherent difficulties, few preventive medicine recommendations are based on randomized trials demonstrating improved outcomes but rely on reasonable assumptions from available evidence. There is now sufficient evidence for recommending a routine exercise test every 5 years for asymptomatic men >40 and women >50 years of age, especially if one of the potential benefits is the adoption of an active lifestyle.⁸

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