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Who exceeds ATP-III risk thresholds? Systematic examination of the effect of varying age and risk factor levels in the ATP-III risk assessment tool☆

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ABSTRACT

Objective. We sought to determine the levels of risk factors required to exceed threshold values of intermediate (≥10%) or high (>20%) predicted 10-year risk for coronary heart disease using the Adult Treatment Panel III (ATP-III) Risk Assessment Tool.

Methods. Continuous risk factor values were entered into the risk assessment tool to examine levels of predicted 10-year risk. Both individual risk factors and the joint effects of varying multiple risk factors were systematically examined.

Results. Women only exceed 10% risk at ages ≥70 with single risk factors of HDL-cholesterol levels <30 mg/dL or systolic blood pressure >170 mm Hg. Women ≤65 only exceed 10% risk if they are smokers with low HDL-cholesterol levels. In contrast, single risk factors can cause men over 45 to exceed 10% or 20% predicted 10-year risk. Combinations of only modestly elevated risk factors cause many men to exceed 10% risk at ages ≥45, and to exceed 20% risk at ages ≥55.

Conclusions. Because such high-risk factor levels are required for men <45years and women <65 years to exceed ATP-III risk thresholds, additional means for risk communication may be needed for individuals with elevated risk factors in these age ranges.

Introduction

The major assumption underlying current prevention guidelines is that the intensity of preventive treatment should match the level of absolute risk (Expert Panel, 2002). Accordingly, the National Cholesterol Education Program's Third Adult Treatment Panel (ATP-III) developed a multivariable risk assessment tool (National Cholesterol Education Program, 2002) to estimate absolute 10-year risk for fatal and non-fatal myocardial infarction using seven traditional risk factors: sex, age, total cholesterol, HDL-cholesterol, systolic blood pressure, smoking status, and current treatment for hypertension. The tool is accessible to any health care provider or patient through the National Heart, Lung, and Blood Institute website (National Cholesterol Education Program, 2002).

This risk estimate can be used by clinicians to communicate risk and determine the need for medical therapy. In the ATP-III algorithm, individuals with diabetes or estimated 10-year risk >20% are considered to be at high risk, and they are recommended for immediate drug therapy to lower risk (Expert Panel, 2002). Those with a predicted 10-year risk of 10% to 20% are considered to be at intermediate risk. Within this stratum, clinicians and patients have the option to begin drug therapy, or they may pursue additional noninvasive testing to further stratify risk and assist in decision-making regarding drug therapy. Finally, those with estimated 10-year risk <10% are considered by the algorithm to be "low" risk. Newer guidelines (Grundy et al., 2004) recommend the incorporation of risk factor counting to guide risk classification and LDL-cholesterol (LDL-c) treatment goals in these individuals. Patients with <10% 10-year risk and 0–1 traditional risk factors are considered "lower risk" and have a LDL-c goal of <160 mg/dL, and those with 2 or more risk factors are considered "moderate" risk with a LDL-c goal of <130 mg/dL.

Prior studies have examined the *prevalence* of different risk strata (i.e., proportion of the population with 10-year predicted risk <5%, 5% to <10%, 10% to 20%, ≥20%) (Ford et al., 2004; Keevil et al., 2007; Persell et al., 2006), while others have examined the *predictive performance* of the ATP-III risk assessment tool in different populations (D'Agostino et al., 2001; Daviglus et al., 2004) and in younger individuals (Berry et al., 2007). It appears relatively easy for clinicians to identify very low risk and very high-risk individuals based simply on the absence of risk factors or the presence of multiple elevated risk factors (Grover et al., 1995). However, because covariates are weighted in risk prediction equations, risk estimates may not be intuitive (Ridker and Cook, 2005) for the majority of patients. Thus, a more thorough understanding of the *intrinsic properties* of the ATP-III

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risk assessment tool itself would be useful to clinicians. The objective of the present study was to perform a systematic evaluation of the ATP-III online risk assessment tool to determine: what levels of risk factor burden are required to exceed treatment thresholds of ≥10% or >20%, and which age, sex and risk factor combinations are classified by the tool as "low" risk even in the face of high-risk factor burden.

Methods

The online risk assessment tool from ATP-III incorporates age, sex, total and HDL-cholesterol levels, smoking status, systolic blood pressure, and treatment for hypertension into a multivariable regression equation to estimate the 10-year risk for hard CHD (coronary death or non-fatal myocardial infarction). We entered data into the ATP-III online risk assessment tool for men and women using 5 year intervals from ages 30 (the minimum age allowed) to 75 years. Our approach did not use specific individuals or a specific population; instead, it allowed us to examine the effects of varying individual risk factors and aggregate risk factor burden on predicted 10-year risks for coronary events using the ATP-III online risk assessment tool. This tool is based on equations derived from the Framingham cohorts (Expert Panel, 2002).

Risk calculation procedure for single risk factors

To compare the effect of individual risk factor levels on 10-year predicted risk, we varied single risk factor levels, holding the other risk factor levels constant at approximate age-adjusted national means (systolic blood pressure: 130mm Hg; total cholesterol: 200 mg/dL; HDL-cholesterol: 45 mg/dl for men and 55 mg/dl for women) (Gregg et al., 2005). Using the entire range of values permitted by the risk assessment tool, we varied total cholesterol from 130 to 320 mg/dL in increments of 10 mg/dL, HDL-cholesterol from 20 to 100 mg/dL in increments of 5 mg/dL, and systolic blood pressure from 90 to 200 mm Hg in increments of 10 mm Hg. We also compared the predicted risks for smoking vs. non-smoking status and for treatment with antihypertensive therapy vs. no treatment, holding other risk factor levels constant as described above. For example, to determine the effect of untreated systolic blood pressure on 10-year risk in a 45-year old woman, we set total cholesterol equal to 200 mg/dL, HDL-cholesterol to 55 mg/dL, and smoking status and antihypertensive therapy to "no" while we varied systolic blood pressure from 90 mm Hg to 200 mm Hg.

Risk calculation procedure for multiple risk factors

To examine the effect of risk factor combinations on 10-year risk estimates, we varied the levels of all risk factors in every possible combination for all ages. After consideration of average and at-risk values of risk factors, we present representative risk factor levels as follows. For total cholesterol, we included values of 160 mg/dL, 200 mg/dL, and 240 mg/dL. For systolic blood pressure, we included 110 mm/Hg, 130 mm Hg, and 150 mm Hg. For HDL-cholesterol in men, we included 25 mg/dL, 35 mg/dL, and 45 mg/dL. For HDL-cholesterol

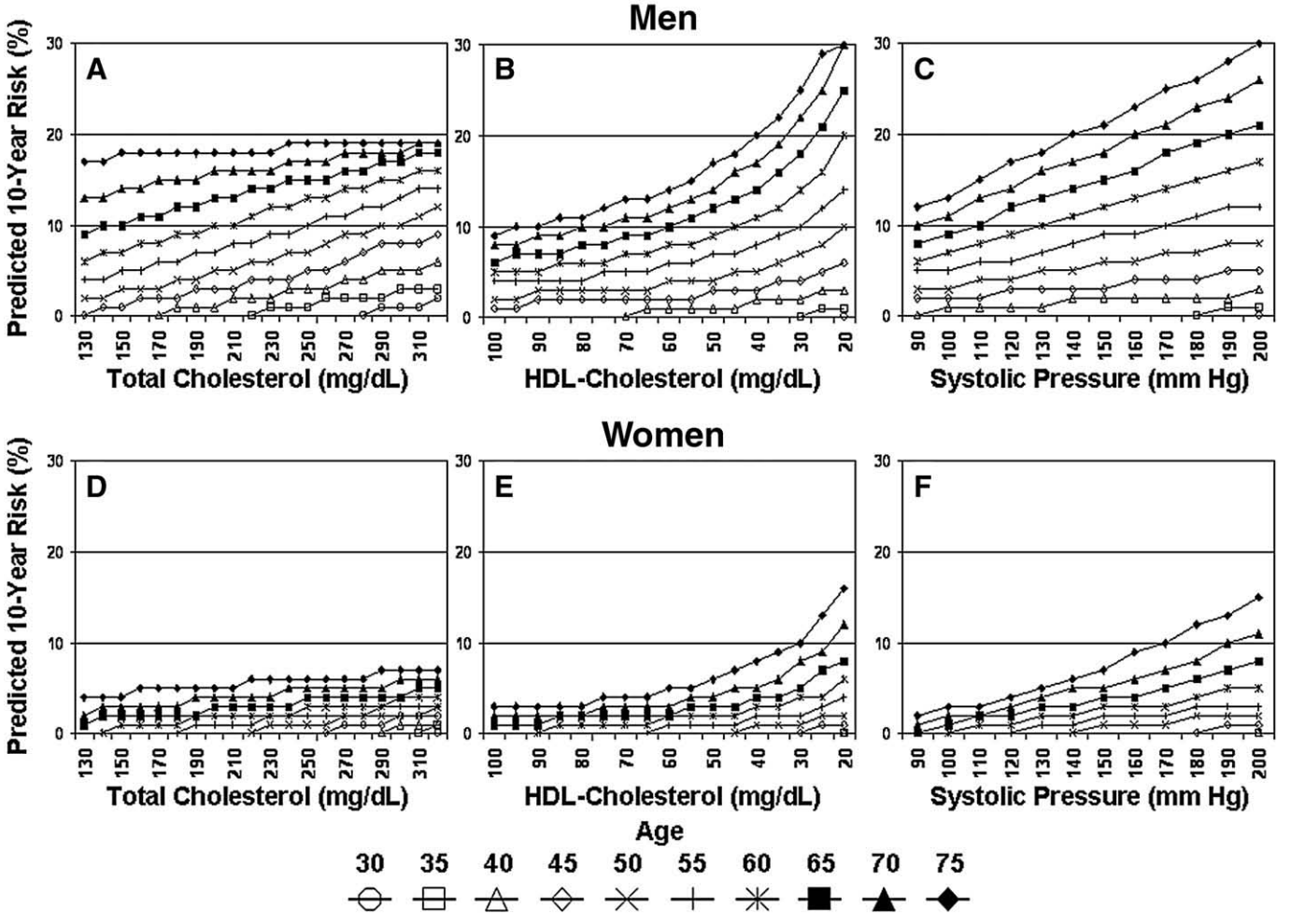

Fig. 1. Ten-year predicted risks, using the ATP-III Risk Assessment Tool, across levels of single risk factors in men (Panels A–C) and women (Panels E–F) at selected ages, with other risk factors held constant at approximate age-adjusted average values.