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Cost-effectiveness of the non-laboratory based Framingham algorithm in primary prevention of cardiovascular disease: A simulated analysis of a cohort of African American adults☆

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ABSTRACT

The non-lab Framingham algorithm, which substitute body mass index for lipids in the laboratory based (lab-based) Framingham algorithm, has been validated among African Americans (AAs). However, its cost-effectiveness and economic tradeoffs have not been evaluated. This study examines the incremental cost-effectiveness ratio (ICER) of two cardiovascular disease (CVD) prevention programs guided by the non-lab versus lab-based Framingham algorithm. We simulated the World Health Organization CVD prevention guidelines on a cohort of 2690 AA participants in the Atherosclerosis Risk in Communities (ARIC) cohort. Costs were estimated using Medicare fee schedules (diagnostic tests, drugs & visits), Bureau of Labor Statistics (RN wages), and estimates for managing incident CVD events. Outcomes were assumed to be true positive cases detected at a data driven treatment threshold. Both algorithms had the best balance of sensitivity/specificity at the moderate risk threshold (> 10% risk). Over 12 years, 82% and 77% of 401 incident CVD events were accurately predicted via the non-lab and lab-based Framingham algorithms, respectively. There were 20 fewer false negative cases in the non-lab approach translating into over $900,000 in savings over 12 years. The ICER was −$57,153 for every extra CVD event prevented when using the non-lab algorithm. The approach guided by the non-lab Framingham strategy dominated the lab-based approach with respect to both costs and predictive ability. Consequently, the non-lab Framingham algorithm could potentially provide a highly effective screening tool at lower cost to address the high burden of CVD especially among AA and in resource-constrained settings where lab tests are unavailable.

1. Introduction

Current American Heart Association statistics depict a disproportionately high burden of cardiovascular disease (CVD) in African Americans (AAs) with an estimated 50% of adults having some form of CVD compared to 39% of the general United States (US) adult population (Benjamin et al., 2017). To address these disparities, evidence-based prevention guidelines recommend absolute CVD risk assessment as a crucial step in primary prevention. Specifically, these guidelines recommend tailoring the choice and intensity of preventive interventions based on an individual's absolute CVD risk score calculated using risk assessment algorithms (Jr et al., 2013; World Health Organization, 2007). The absolute CVD risk score represents the likelihood that a certain constellation of risk factors will lead to CVD related disability or death over a given time period (Hayman et al., 2011).

To date, > 360 algorithms have been developed to estimate absolute CVD risk (Damen et al., 2016). However many require laboratory (lab) measures such as lipids and are focused on hard coronary events, instead of general CVD events that also includes stroke and peripheral vascular disease - conditions that are more prevalent in AAs (Gaziano et al., 2008; Beswick et al., 2008). Although lipid tests are generally available in most US clinical settings, they are resource intensive and may be difficult to do in underserved communities which are frequently lost to follow-up. Moreover, developing countries in Africa and

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elsewhere have limited access to lab testing making it impractical to rely entirely on lab-based algorithms. In recent years, progress has been made in developing resource efficient non-lab based algorithms that focus on general CVD events (Kariuki et al., 2013)—a move that if demonstrated to be cost-effective could increase their clinical utility for early detection and timely management of CVD risk in underserved communities and resource constrained settings.

Previously, we have identified the non-lab Framingham algorithm, developed by D'Agostino and colleagues (D'Agostino et al., 2008), as superior in performance and methodological soundness compared to other non-lab based algorithms (Kariuki et al., 2013). The algorithm has also been externally validated in the Atherosclerosis Risk in Communities (ARIC) dataset where its overall performance was comparable to the lab-based Framingham algorithm, with no racial differences between the AA and white cohorts (Kariuki et al., 2017). Both the non-lab and lab-based Framingham algorithms are similar, except for the substitution of body mass index (BMI) for lipids in the former (D'Agostino et al., 2008).

Although external validation was crucial in benchmarking transportability of the non-lab Framingham algorithm to AAs (Kariuki et al., 2017), its feasibility and appeal to policy makers and clinicians in resource constrained settings is dependent on the associated economic and performance trade-offs. This study evaluates these tradeoffs by evaluating the incremental cost-effectiveness ratio (ICER) of a simulated CVD prevention program guided by the non-lab Framingham algorithm versus another guided by the lab-based Framingham algorithm in a cohort of AA adults enrolled in the ARIC study. In particular, do the extra costs of lab tests over BMI measures justify their routine use on a sound societal cost basis especially at initial primary care or community based screening?

2. Methods

2.1. Data source

We conducted a secondary analysis using the ARIC dataset. The recruitment process, study protocols, and criteria used to adjudicate CVD events in this study have been reported elsewhere (Investigators A, 1989). In brief, the ARIC study is an ongoing biracial prospective epidemiologic study to examine the causes of atherosclerosis and its clinical sequelae and the variation in cardiovascular risk, cost of care, and disease by race, gender, location, and date (Investigators A, 1989). In this analysis, our sample includes 2690 randomly selected AA participants aged 45 to 64 years, who at baseline examination (i.e., 1987–1989) were free of CVD and had no missing data on the variables of interest (i.e., covariates included in both algorithms) during 12-year of follow-up. The lab-based Framingham algorithm covariates include; age, systolic blood pressure (SBP), antihypertensive medication use, smoking status, diabetes status, high-density lipoprotein (HDL) and total cholesterol (TC). The non-lab Framingham algorithm substitutes BMI for lipids (HDL and TC) in the lab-based Framingham algorithm (D'Agostino et al., 2008). Both algorithms predict general CVD events (coronary heart disease, stroke and peripheral vascular disease) and are freely available as online or downloadable interactive risk calculator (Framingham Heart Study, 2008).

All the participants were under continuous sentinel surveillance by the ARIC investigators for the development of CVD events and death (Investigators A, 1989). Investigators did not intervene in subjects' diagnosis and treatment. We truncated this analysis at the twelfth year of follow-up to match the period used to derive the Framingham algorithms (D'Agostino et al., 2008).

2.2. The WHO prevention guidelines

To estimate the ICER of the non-lab Framingham algorithm, we compared its performance to the lab-based Framingham algorithm in a simulated CVD prevention program guided by the World Health Organization's (WHO) CVD prevention guidelines (Table 1) (World Health Organization, 2007). We did not use the American Heart Association comprehensive CVD prevention guidelines because they are dated (published in 2002) and limited by their narrow focus on hard coronary events (Pearson et al., 2002). The WHO prevention guidelines have a broader focus on general CVD, including coronary heart disease, stroke and peripheral vascular disease, making them more relevant to AAs.

Using subjects' baseline characteristics, absolute CVD risk scores were calculated for each of the 2690 eligible AA participants using both algorithms. At-risk scores below a data driven risk threshold were considered normal and hence indicated for usual care (lifestyle management) (Stone et al., 2013) while higher risk categories received the appropriate therapies as outlined in Table 1 (World Health Organization, 2007). With rising risk comes more intense preventive measures. Specifically, monitoring very high risk patients is recommended every 3–6 months instead of 6–12 months, blood pressure should be treated when > 130/80 instead of 140/90, lipid therapy initiated, and low dose aspirin is recommended daily. These increases have cost implications as detailed below.

We made treatment eligibility dichotomous whereby only individuals who had an absolute CVD risk score equal or greater than the data driven treatment threshold were indicated for treatment (Rosner and Bernard, 2011). If the treatment threshold was met, the participant entered into one of three treatment arms depending on their absolute CVD risk score. At the end of each year, the cohort was then assigned to 1 of 4 health states: CVD free, non-CVD death, non-fatal CVD events and fatal CVD events. These states determined follow-on prevention or treatment of events.

Since the risk threshold at which preventive treatments are initiated is usually selected to optimize utilization of resources (World Health Organization, 2007), we selected the risk category (identified in section on Results: Outcomes) at which both algorithms demonstrated the best balance of sensitivity and specificity in the ARIC dataset using the roctab command in Stata© as recommended by Reichenheim (Reichenheim, 2002).

2.3. Cost effectiveness formula

Since the ICER is dependent on the costs and outcomes associated with each of the two simulated CVD prevention programs guided by the non-lab and lab-based Framingham algorithms, we computed the ratio using the formula described by Drummond (Drummond and Drummond, 2005).

$$\text{ICER [non-lab vs. lab]} = \frac{\Sigma t = {}_1^{12}\ [\Delta S_t + \Delta V_t + \Delta D_t + \Delta FN_t]/(1+d)^t}{\Sigma t = {}_1^{12}\ [\Delta CVD_t\ ]/(1+d)^t} \quad (1)$$

- o ΔS_t, ΔV_t, ΔD_t, ΔFN_t = difference in cost between non-lab and lab-based approach in screening (S), preventive visits (V), preventive drugs (D), and management of CVD in false negatives (FN) in year t. These labels are bolded in Tables 2 & 5 tabulating the unit and cumulative costs, respectively.
- o ΔCVD_t = the difference between the non-lab and lab-based approach in the number of CVD events predicted in year t
- o d = the discount rate (assumed constant 0.03) (Weinstein et al., 1996).

Costs are calculated as the product of unit expenses for screening, preventive visits, drugs and treatment of false negative cases (Table 2) times the number of individuals identified as meeting the treatment threshold by each algorithm and the associated false negative cases (shown later in Table 3). The outcomes are determined by the true positive cases detected as meeting the data driven treatment thresholds by each algorithm (Table 3).