

CORRESPONDENCE

Letters to the Editor

Fantastic Voyage Through Cardiology: From 1969 to 2008

Hecht and Colmer (1) deserve praise for their fantastic account of 2 generations of cardiology encompassed in 1 still-living patient. As I reviewed their wonderful presentation of historical text, images, and videos, I could not help but reminisce about the joy of discovering, as a medical student, the numerous interventions possible in cardiology practice. During my cardiology fellowship training, publication of Waller's (2) account of "crackers, breakers, stretchers, drillers, scrapers, shavers, burners, welders and melters" in the future treatment of coronary artery disease only added to the excitement about the specialty.

In my old age, however, I have become equally impressed with the power of public health measures and the impact of prevention (3,4). Aspirin, beta-blockers, statins, and the control of blood pressure and cholesterol play a crucial role in reducing cardiovascular morbidity and mortality (4). Similarly, policy-based initiatives (4,5) and other public health measures that reduce population exposure to risk factors or support health-improving behaviors, such as smoking cessation, increased physical activity, and a diet rich in fruits and vegetables, play important roles, although they are by no means as glamorous as the interventions described by Hecht and Colmer (1) or chronicled by Waller (2).

Several studies from the U.S., New Zealand, Scotland, England, Wales, Ireland, and Finland suggest that 45% to 75% of the decline in coronary mortality can be attributed to risk factor changes, and the remaining 25% to 55% to treatments (6). In fact, improved risk factor levels explained 53% to 72% (and treatments only 23%) of the decline in coronary mortality in Finland (7). It would be highly instructive to learn from Hecht and Colmer how the spectrum of risk factors and major preventive practices changed during this fantastic voyage. In the words of the legendary broadcaster, Paul Harvey, providing this account may tell "the rest of the story" (8).

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Please note: The findings and conclusions in this letter are those of the author and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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Reply

We are delighted to respond to Dr. Mensah's query regarding the changes in risk factors and major preventive practices during the 2 generations of the "fantastic voyage" (1). Sadly, there is a large gap between progress in prevention and the spectacular progress in diagnostic testing and intervention. This prevention gap may be attributed to several factors:

1. In primary prevention, there is a disconnect between risk assessment by risk factor analysis (Framingham Risk Score, Procam, European Society of Cardiology) and the actual risk determined by events, which is much more accurately predicted by coronary calcium scanning (2,3).
2. Despite the superiority of coronary calcium scanning to identify candidates for aggressive prevention, its widespread use for screening has been road-blocked by demands for randomized controlled trials showing its effect on outcomes. This criterion has never been fulfilled by the Framingham Risk Score, Procam, European Society of Cardiology, or, for that matter, by nuclear stress testing, rest and stress echocardiography, cardiac catheterization, and most interventions. Nonetheless, they are accepted as gospel.
3. This "deadly double standard" (4) and the continued reliance on risk-factor-based prognostication will continue to deprive high-risk patients of the possibility of early identification, with an unconscionable and unnecessary increased morbidity and mortality.
4. Indeed, there has been an explosion of risk factor identification (including high-sensitivity C-reactive protein), none of which

have added to the area under the receiver-operator characteristic curve for the standard risk factors' ability to prognosticate. We think that there has not been and will not be a major breakthrough in prevention, akin to what has dramatically occurred in diagnostic testing and intervention, until risk factors are used not for risk assessment, but to identify treatable causal factors after risk has more accurately been established by the level of subclinical atherosclerosis (5).

5. To those who raise cost effectiveness concerns related to widespread screening for subclinical atherosclerosis, reduction in the cost of calcium scanning to the level of mammography will make it the most cost-effective modality.
6. Finally, in both secondary and primary prevention, there has been a misplaced focus on simple changes in the treated risk factors, for example, low-density lipoprotein, rather than on measures of subclinical atherosclerosis and disease activity and endothelial function to evaluate the response of the disease, rather than the risk factors, to treatment.

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No Benefit From Cardiac Resynchronization Therapy in Asymptomatic Patients

We congratulate Linde et al. (1) on the meticulously carried out REVERSE (REsynchronization reVERses Remodeling in Systolic left vEntricular dysfunction) trial that addressed the question of the clinical benefit of cardiac resynchronization therapy (CRT) in patients with New York Heart Association (NYHA) functional class II and I heart failure (1). Unfortunately, the composite primary end point as defined per the study protocol was negative. Still, the authors conclude that CRT, in combination with optimal medical treatment (\pm defibrillator), reduces the risk for heart failure hospitalizations and improves ventricular structure and function in NYHA functional class II and I. In our opinion, the

later statement is not supported by the presented data, which shows no benefit for NYHA functional class I patients (odds ratio: 0.87; 95% confidence interval: 0.37 to 2.03) in their subgroup analysis (Fig. 4 of Linde et al. [1]).

This disagreement raises the more philosophical question: whether these subgroup analyses make sense if the primary end point is negative—maybe due to a lack of statistical power? It seems that the well-known players such as wide QRS and low left ventricular ejection fraction are positive predictors for CRT success but not NYHA functional class I. Another intriguing finding of this subgroup analysis is that patients on diuretics did improve, whereas those not on diuretics did not. However, the use of diuretics reduced mortality and prevented hospital admissions in this patient population, which raises the question of whether the use of diuretics by themselves may have accounted for the documented beneficial effect (clinical composite end point, hospitalizations) in the CRT ON group and whether this confounding variable was corrected for in the main analysis (2).

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Reply

We thank Dr. Osswald and colleagues for their interest in our paper (1). The REVERSE (REsynchronization reVERses Remodeling in Systolic left vEntricular dysfunction) study was designed as one population of New York Heart Association (NYHA) functional class I to II heart failure (HF) patients. We agree that the primary end point did not reach statistical significance (2), with 16% of patients worsened in the cardiac resynchronization therapy (CRT) ON group and 21% in the CRT OFF group ($p = 0.10$). The clinical composite response was designed for severe HF patients and, to our knowledge, has not previously been used in mildly symptomatic or asymptomatic HF patients (3).

The fact that the primary end point did not reach statistical significance despite substantial improvement in left ventricular (LV) dimensions accompanied by a significantly reduced time to first HF related hospitalization might be due to the difference in utility of this end point or that the observation period was not long enough to demonstrate effects in NYHA functional class I to II patients. Dr. Osswald and colleagues are concerned about the