Commentaries and Author’s Response

Aronow’s “Should the NCEP III Guidelines Be Changed in Elderly and Younger Persons at High Risk for Cardiovascular Events?”

What Do We Do for the Very Old?

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DR. ARONOW makes a strong case for lowering the target low-density lipoprotein level for patients treated with statins (1). I will limit my comments to one aspect of his discussion—when and how to treat very old people.

The current National Cholesterol Education Program (NCEP) guidelines call for lowering the cholesterol of those patients who have a 10-year risk for coronary disease of >20% (2). Might that not include all very old people? The figure below presents 10-year risks of mortality from heart disease as a function of age and gender. At age 75, men have a 16% and women a 12% chance of dying from heart disease in the next 10 years. And that is just mortality; it doesn’t include chance of developing nonfatal heart disease, which is at least as high as the mortality rate.

This raises a question: Is it possible to prospectively define a subset of 75 year olds that do not have a >20% 10-year risk of heart disease? I doubt it. If not, then does that mean that all 75 year olds should be on statins? Even if it is possible to define such a group of 75 year olds, does anyone think they can identify a group of 80 year olds with a <20% 10-year cardiovascular disease risk?

This is the problem encountered when one takes guidelines originally constructed with one population in mind (the middle aged) and applies it to another population (the very old).

It is certainly possible that someday we will recommend that all 75 year olds be on statins, but we do not know that at this time. What we do know from the MRC/BHF (Medical Research Council/British Heart Foundation) trials is that 70–80 year olds with preexisting coronary disease and/or other vascular disease and/or diabetes and elevated cholesterol experience a 5.1% absolute reduction in new vascular events over 5 years when treated with statins (3).

The PROSPER (Prospective Study of Pravastatin in the Elderly at Risk) study of 70–82 year olds with a somewhat lower prevalence of risk factors reported an absolute reduction in new heart attacks or stroke of 2.1% over 3 years of follow-up (4).

These are impressive results and justify more aggressive treatment of older people with elevated cholesterol plus vascular disease or diabetes. What we do not know is what to do with those persons older than age 80. A reasonable approach would be to treat octogenarians if they resemble the subjects of the MRC/BHF trial; i.e., preexisting vascular disease and/or diabetes plus elevated cholesterol. Dr. Aronow has published a series of observational studies of institutionalized men and women with a mean age of 81, showing that those treated with statins had lower heart attacks, strokes, and heart failure than those not treated (5–9). Selection bias would be powerful in such a very old, institutionalized population. I doubt that we can learn about safety and efficacy of statins in various categories of very old people without randomized controlled trials.

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REFERENCES
Preventive Gerontology: Edging Ever Closer to the “Barrier to Immortality”

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Ever since James Fries (1) framed the central argument for “Preventive Gerontology” (a neologism coined shortly after the publication of his article) (2) and its goal of squaring the human survival curve in his classic 1980 New England Journal of Medicine article entitled, “Aging, Natural Death, and the Compression of Morbidity,” I have followed with great fascination the impressive accumulation of evidence for the efficacy of aggressive preventive measures to enhance both vitality and longevity across the entire human life span. Increasingly, this evidence reflects findings in studies that have included persons of truly old age, even some who are approaching or have even surpassed the maximal average age at death under Utopian conditions projected by Fries at 85 ± 4 years, the “barrier to immortality” for our species. Indeed, in the Special Article in this issue, Aronow (3) recommends revisions of NCEP-III guidelines to extend hyperlipidemic preventive treatment to octogenarians and nonagenarians based upon his study of residents of a long-term care facility and review of the recent literature in this field.

In his original hypothesis [considerably expanded in the Successful Aging movement (4)], Fries placed primary emphasis upon maintenance at all ages of a healthful lifestyle (in a healthy environment). This was to be accomplished principally through enhanced education, continuing social engagement, robust physical activity, avoidance of substance abuse and environmental hazards, and optimal nutrition (both qualitatively and quantitatively).

However, fueled by the breathtaking advances of biomedicine in recent decades, the platform of Preventive Gerontology for midlife and beyond has shifted ever more toward identification of predisposing disease risk factors, aggressive disease detection at clinical and subclinical stages, and interventions to control those risk factors and disease progression by maintaining key indices of health within acceptable boundaries, especially by pharmacological means. Given the primacy of cardiovascular disease (CVD) as the leading cause of death among adults, and its exponential escalation with advancing age, this effort has focused upon a tetrad of potentially modifiable risk factors that arguably account for up to 80% of CVD deaths: cigarette smoking, hypertension, dyslipidemia, and diabetes.

The latter three cluster in the worldwide contemporary epidemic of the metabolic syndrome driven by increasing overweight and obesity, a shift that threatens to nullify the remarkable gains in health and longevity of the late 20th century (widely attributed to the major decline in cigarette smoking during that era).

Five trends of the past 40 years have proven especially powerful in generating the current momentum in Preventive Gerontology in its close conjunction with Preventive Cardiology.

First, the dramatic, ongoing revolution in pharmacology has offered increasingly powerful and acceptably safe agents to intervene upon biomarkers of CVD risk. These drugs have exquisitely targeted key points in physiological regulation such as the low-density lipoprotein (LDL) receptor and the central role of hepatic hydroxymethyl glutaryl coenzyme A (HMG CoA) reductase in the control of LDL cholesterol levels. This trend can be expected to continue and indeed to accelerate as the goals of intervention become individualized to the genome of a given patient in the not-too-distant future.

Second, the ascendency of chronic disease epidemiology, randomized, controlled clinical trials (RCTs), and evidence-based medicine has provided clinicians and public health leaders with powerful tools to define an ambitious agenda of Preventive Gerontology/Cardiology for the second half of the human life span.

Third, the cumulative results of epidemiological studies and RCTs in support of early, aggressive, and demonstrably effective interventions have been critically examined by expert panels such as the NCEP (1, II, III, . . .) and JNC (1–7, . . .), commissions reconvened every few years to review latest advances and accumulated evidence in this field and issue updated recommendations. Such periodic reviews have inexorably “raised the bar” of intervention strategies by: 1) creating progressively more ambitious target levels to achieve acceptable control of the risk indices (e.g., lower LDL or non-high-density lipoprotein [HDL] cholesterol, lower blood pressure, lower fasting glucose and HgbA1c levels); such target levels have become especially low in