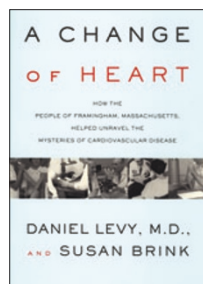


The dawn of risk factors



A Change of Heart

Daniel Levy & Susan Brink

Knopf, 2005

272 pp., hardcover, \$26.95

ISBN 0375412751

Reviewed by Eric J Topol

In 1945, Franklin D. Roosevelt suffered from severe hypertension with blood pressure measurements as high as 300/190 mmHg, had symptoms of angina and congestive heart failure, and was a cigarette smoker, before he succumbed to a cerebral hemorrhage. Amazingly little was known about an individual's susceptibility to coronary heart disease or cerebrovascular disease, although these were the leading causes of death. As now, when a high-profile individual can have an extraordinary impact on medicine, Roosevelt's death served as a wake-up call to Americans. The National Heart Institute, later known as the National Heart, Lung, and Blood Institute, was established in 1948, at a time when there were only 374 cardiologists in the country. That same year, the first phase of the Framingham Study of 5,209 individuals aged 30–59 years began.

In *A Change of Heart*, Levy and Brink review the history and impact of the Framingham Study and how “one New England town changed the practice of medicine and lifestyles of tens of millions.” As one of the original Framingham volunteer study subjects aptly put it, “It's not just for the people who live in this town. Many lives have been saved because of the Heart Study.” Indeed, the meticulous study of the original cohort and a subsequent generation (a study of 5,124 of their offspring began in 1971) has yielded an extraordinary collection of insights about heart and vascular disease.

Most importantly, the study defined risk factors for coronary disease: hypertension, obesity, hypercholesterolemia, diabetes, smoking and lack of physical activity. But pioneering the ‘risk factor’ concept had profound implications for more than just coronary disease—it became the construct of our approach for thinking about the concept of susceptibility for all chronic diseases.

Beyond creating a systematic definition of risk factors, the Framingham investigators taught us that angina occurs in women at an unexpectedly high frequency, that silent heart attacks are common, that the lifetime risk of developing hypertension is 90%, and that atrial fibrillation is a major cause of stroke. This is only a short list of some of the major contributions that the book describes. Collectively, the knowledge gleaned from the Framingham Study had such a profound effect that since 1963, when the death rate from coronary heart disease peaked, there has been a 60% reduction in death from heart disease—highly influenced by this prototypic epidemiologic study. In parallel, the percentage of smokers in

the population has decreased, from 44% to 22%. The field of preventive cardiology, focused on risk-factor modification, was born.

Although the book does a fine job in taking us through the incredible impact of Framingham discoveries, it gets off course with chapters on Ed Freis and the randomized trials he conducted on individuals with hypertension, the discovery and testing of statins, the controversy about homocysteine as a putative risk factor, and population studies of Ansel Keys regarding cholesterol and diet. These chapters detract from the main objective of enlightening the reader about the Framingham Study. For example, little is written about the stress and strain that existed between the National Heart, Lung and Blood Institute and the directors of the Framingham Study. Perhaps in striving for political correctness, the authors steered clear of examining this difficult relationship.

Regarding controversy, however, Levy and Brink take us through the two major points of peril resulting in near shutdown of the Framingham Study. The first occurred in 1969, when the original 20-year commitment made by the National Institutes of Health was fulfilled and there was serious concern over whether the NIH's investment was worth perpetuating. The second, in 2000, was related to the venture capital-backed firm Framingham Genomic Medicine, which intended to commercially benefit from the data. Especially telling was the strong protest from elderly original volunteers in the study, with comments such as “We would rather see Framingham Heart Study information and data destroyed than have it turned over to a ‘for-profit’ entity” and “The Study was initiated to help all mankind, not for financial profit to any company or individual.” Fortunately, wisdom prevailed and the commercial entity folded. Subsequently, in 2002, a study began that included collection of DNA of the individuals of the third Framingham generation.

Another shortcoming of the book is that it does not sufficiently address the limitations of the Framingham Study. Although the intrinsic problem that the population studied was almost entirely of European-American ancestry is mentioned, the fact that there were only two people of African descent in the primary cohort, and that the resulting knowledge of the natural history of cardiovascular disease may not be transferable to other racial and ethnic populations, is not adequately emphasized. Furthermore, the prominence of diabetes and the metabolic syndrome as a risk factor is not proportionately developed. That socioeconomic data have never been collected is noteworthy and would have been appropriate to include in the book in order to balance all of the impressive triumphs of the Framingham Study.

Notwithstanding these concerns, the book is outstanding and provides unique insight into this quintessential epidemiologic study, perhaps the most important population science ever conducted. It demonstrates how ignorant we were in the 1940s and 1950s in not realizing the dangers of hypertension and that it needed to be aggressively treated, that smoking was a profound risk, that our diet rich in fat was contributing to atherosclerotic plaques, and that high blood cholesterol was common and a chief offender. Moreover, breaking new ground to enroll one-half of the town's population between ages 30 and 60 to volunteer to participate in in-depth studies every two years without offering any medical treatment or advice, and the lack of bioinformatic support to track the original 80 variables of data, is altogether astounding. *A Change of Heart* does indeed achieve its objective of illuminating the transformation of American cardiovascular medicine.

Office of the Provost, Cleveland Clinic Foundation, Cleveland, Ohio 44195, USA.
E-mail: topole@ccf.org