The several faces of clinical trials: from new therapies to failed preventive strategies

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Over the past few years, editorials in various pre-eminent journals have celebrated cardiovascular drug and device therapies and interventions that have proven efficacious in double-blind, randomized, controlled trials. In wealthy countries, over the last three decades such research has led to the average lifespan being prolonged by about 6 years. Advances in cardiovascular medicine should be acknowledged, but significant areas of concern remain, such as the following: conflicts of interest and bias (e.g. financial or academic bias, or selective reporting by editors of positive trials); growing private funding for pharmaceutical and interventional research resulting in increasing financial opportunities for physicians and investigators (e.g. fees for advice that dwarf consulting payments); and unclear consent information. Furthermore, and perhaps most importantly, even with the enormous advances in treatments, prevention of cardiovascular disease is dramatically failing, and trials to address prevention are proving difficult.

In 2005, a WHO document entitled *Preventing Chronic Diseases, a Vital Investment* outlined the worldwide burden of disease, including the economic implications. The prevalence of cardiovascular disease and other chronic diseases—cancer, diabetes and chronic respiratory diseases—is clearly increasing, not only in high-income countries but also very rapidly in low-income and middle-income countries. In 2005, 35 million people were estimated to have died from these diseases; approximately 20% of these deaths were in high-income countries and 80% occurred in low-income and middle-income countries.

Although an urgent need for innovative approaches for prevention of cardiovascular disease is evident, clinical trials aiming at new strategic approaches are almost nonexistent and the work that is available is fraught with difficulties. Such an example is the Women's Health Initiative study on low-fat diet, which

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has just been published. In this 8-year study of 50,000 postmenopausal women across the USA, individuals were asked to reduce total fat intake to 20% of total calorie intake and to consume about five daily servings of fruits, vegetables and grains, or to continue with their usual eating pattern. No significant statistical reduction in the incidence of heart disease, stroke or cancer (breast or colon) was reported. Several issues arise from these findings. First, primary development and prevention of disease could take decades rather than only 8 years as was tested in this study. Second, many intervention participants were unable to maintain a strict low-fat diet, which reflects the fact that such profound population-wide changes to high-risk behaviors can be difficult to implement. Third, success in prevention strategies needs to be based on sound scientific methods and to be responsibly reported in all sources, including journals and newspapers. For example, articles in high-profile newspapers hailing these types of study results as revolutionary or definitive does nothing to address the emerging world epidemics of obesity and diabetes, which are partly caused by high-fat and high-calorie diets, as described in the WHO document.

In summary, over the past three decades, findings of controlled clinical trials applied to patients with cardiovascular disease have significantly contributed to a better quality and prolongation of life. Concerns about how these studies are conducted, such as interactions between industry, physicians and investigators, patients, and editors, should be continuously addressed. The increasing prevalence of cardiovascular disease across the world, however, also needs to be addressed. This can be done only by realistic approaches to modify high-risk behaviors. Clinical preventive trials, tailored to the various target populations (e.g. by age, community traits, culture, etc.) and based on sound scientific methods, should be only one of these approaches.

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Competing interests

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