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# Medical Research

## A Better's Guide

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Any complex machine (e.g., washing machine, television, or car) comes with an owner's manual that explains how to use it. Another associated document, seldom seen by consumers, is a detailed description of all the parts and how they are connected. We shall call this the blueprint.

Likewise, there are two types of health research. Some researchers are, in effect, searching for the "owner's manual" for the human body—the living conditions that produce the best health. This research includes epidemiology, which suggests cause-and-effect relationships; animal experiments, such as those that test ideas arising from epidemiology; and human intervention studies, such as controlled trials, which provide the most reliable evidence. We call this lifestyle research. Like an owner's manual, it tends to focus on the prevention of problems. In contrast, other researchers, the large majority, try to fill in the human "blueprint." Blueprint research, often referred to as reductionism or mechanistic research, includes studies of gene expression, neurotransmitters, cell adhesion molecules, and biochemical pathways. The results of this research, like actual blueprints, often guide treatment.

Which type of research is more useful (per dollar spent)? Lifestyle research, it seems fair to say, has produced the lion's share of useful results.<sup>1-3</sup> Consider coronary heart disease (CHD). In the Nurses' Health Study,<sup>4</sup> the results suggest that about 80% of the coronary events could be prevented by lifestyle changes. For instance, replacement of 5% of energy from saturated fat with unsaturated fat would reduce risk by about 40%.<sup>5</sup> Vigorous or moderate exercise was associated with 30% lower risk.<sup>4</sup> In the Lyon Diet Heart Study,<sup>6</sup> a randomized clinical trial, a Mediterranean diet high in n-3 fatty acids caused a 70% reduction in coronary events. Blueprint research has produced nothing this impressive. In this arena, its most useful result has probably been the development of statin drugs, which lower cholesterol. In randomized trials, these drugs reduced CHD by about one third.<sup>7-11</sup> However, credit for this must be allocated to both types

of research. It was lifestyle research that suggested that lowering cholesterol would reduce CHD. Moreover, the expense of statin drugs limits their use to persons at high risk,<sup>12</sup> whereas the changes suggested by lifestyle research, which cost little, are available to all.

Consider cancer. Lifestyle research has identified several powerful causative and preventive factors. Smokers and nonsmokers differ in their rate of lung cancer by a factor of 10 or more. Van't Veer et al.<sup>13</sup> estimated that if everyone in the Netherlands increased their intake of fruits and vegetables by 100 grams/day, cancer rates would fall by about 20%. Whole-grain consumption is associated with a decrease in risk of one third.<sup>14,15</sup> A randomized study reported a halving in cancer mortality in subjects taking a selenium supplement,<sup>16</sup> supporting what epidemiology and animal studies had previously suggested.<sup>17,18</sup> Again, these improvements are available to all, at little cost. Nothing so useful against cancer has come from blueprint research.

Consider diabetes. In a study of Americans at high risk for type 2 diabetes, participants who took metformin (the product of blueprint research) reduced their risk of type 2 diabetes by about 30%. But participants assigned to intensive lifestyle intervention (based on lifestyle research, of course) reduced their risk by about 60%.<sup>19</sup>

Yet blueprint research has received the lion's share of research funding. A rough indication of this is the number of articles published in each area. We selected 100 papers at random from the latest 1 million articles in MEDLINE, most of which were published in 2000–2001. We classified all full papers in any area of health research ( $n = 28$ ) as either lifestyle or blueprint. Blueprint papers outnumbered lifestyle papers by a ratio of 5 to 1. Along similar lines, a survey of the *Journal of the American Medical Association* and the *New England Journal of Medicine* found that articles about treatment far outnumbered articles about prevention.<sup>20</sup>

Blueprint research has also received the lion's share of intangible resources. The Nobel Prize for medicine should be given, according to Nobel's will, to those who "have conferred the greatest benefit on mankind," yet in the last 50 years has never honored lifestyle research. A particularly conspicuous omission is the discovery that smoking causes cancer, one of the most beneficial

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health-related discoveries of the last century. The resource imbalance has no end in sight, as exemplified by genomic medicine.

The novelist Vladimir Nabokov wrote that a certain review of his work seemed to be so exactly wrong that it would make perfect sense when seen in a mirror. Likewise, the current situation—the relative allocation of resources to the two types of research—seems exactly the opposite of what it should be, at least if health improvement is the goal.

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