

# *Will salt reduction benefit consumers?*

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## Introduction

Aside from water, salt is the most ubiquitous food ingredient consumed by humankind. Salt is a nutrient that is essential to life and good health. Having originally evolved from a marine environment, the human body's salt:water ratio is critical to metabolism. Human plasma contains 0.9% salt (sodium chloride) to maintain the electrolyte balance. In the normal course of metabolism, we routinely eliminate sodium along with most other waste materials, and the minimum balance must be replenished if we are to survive. Most of our salt intake comes from foods, and some comes from water. Of course, any activity resulting in excessive loss of sodium, such as exercise, has to be counterbalanced by increased salt consumption to make up this additional loss.

In a strikingly clear and comprehensive manner, a recent paper titled "Central Regulation of Sodium Appetite," by Joel Geerling and Arthur Loewy (2008) of the Department of Anatomy and Neurobiology, Washington University School of Medicine in St. Louis, MO, elaborates the multiple mechanisms responsible for our appetite for salt. The physiological apparatus we have evolved over the eons to maintain a fully operational cardiovascular system is largely dependent on maintaining both a balance and sufficient quantities of the 2 nutrients most essential to life, water and salt. This fundamental system is can be found in fish, reptiles, and all mammals.

This multifactorial system is so robust and includes so many fail-safe and redundant mechanisms that it continues to function after large sections of its system are shut down. Using a complex cascade of physiological functions, from powerful hormonal systems such as the renin-angiotensin-aldosterone system (RAAS) to pressure-sensitive baroreceptors in the brain, this water thirst and salt

appetite mechanism moderates our behavior so that we are driven to quickly replenish the volume and osmotic balance of our blood so that it is pressurized sufficiently for our heart to pump it throughout the circulatory system.

If we do not replenish the sodium, our metabolic system shifts to a sodium-sparing mode with multiple significant consequences for us. Reductions in sodium intake are initially accompanied by significant increases in the RAAS system. Although this reaction is designed to sustain osmotic balance and pressure, an elevated RAAS has negative effects on the structural condition of our circulatory system and smooth muscle cells and stimulates inflammatory agents within the body. For people with hypertension, increased RAAS activity predicts an increased potential for heart attacks and for the increased insulin resistance that often accompanies low-sodium diets. Thus, reductions of sodium in the diet have to be considered very cautiously.

## The Debate

The major effect of increased sodium chloride intake is on blood pressure, which has been shown to be a risk factor for cardiovascular diseases. A large number of studies have demonstrated that blood pressure rises progressively with increased sodium chloride intake. However, there is a well-recognized heterogeneity in the blood pressure response to changes in sodium chloride intakes (Institute of Medicine, 2004). Approximately one-third of normotensive individuals experience a drop in blood pressure when salt consumption is restricted, whereas in one-quarter of the population, blood pressure actually increases under the same circumstance (Miller et al., 1987).

The response to salt intake is also highly dependent on other factors in the diet. If individuals have inadequate intakes of other dietary electrolytes such as potassium, calcium, and magnesium, they are much more likely to be salt sensitive. Further evidence comes from the well-known Dietary Approaches to Stop Hypertension (DASH) trials. When a control diet was compared with the DASH diet while sodium intake and body weight were maintained at constant levels, systolic blood pressure was reduced as much as 11.4 mmHg for hypertensives (Appel et al., 1997).

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Thus far, the preponderance of medical research carried out on the salt and health issue has been observational in nature and almost exclusively based on epidemiological analysis. Unfortunately, most of these studies have relied solely on blood pressure as a proxy or surrogate for cardiovascular outcomes. The question is really whether a reduction in the consumption of salt will reduce the risk of heart attack and stroke—definitive health outcomes.

When outcomes are studied, the results are somewhat different (Kagan et al., 1985; Alderman et al., 1995; Cutler, 1997; Tunstall-Pedoe, 1997; Alderman et al., 1998; Valkonen, 1998; Cohen, 1999; He et al., 1999; Tuomilehto et al., 2001; Hooper et al., 2002; Grobbee et al., 2003; Nagata et al., 2004; Cohen et al., 2006; Cook et al., 2007; Geleijnse, et al., 2007).

Figure 1 illustrates the results of the impact of low salt intakes on health outcomes. As mentioned, a significant breakthrough was made in the DASH study (Figure 2). Here it was determined that a balanced diet, replete with the recommended levels of fruits and vegetables and low-fat dairy products, had a significant impact on reducing blood pressure. A study was carried out to show the impact of both the DASH diet and salt reduction a few years later (Sacks et al., 2001).

When the DASH sodium trial is examined, it is immediately apparent that moving to a DASH-type balanced diet (bottom line) has a significantly greater impact on blood pressure than lowering salt consumption. Dropping from the current level of sodium consumption to the recommended dietary level reduced the systolic pressure by an average of 2.1 mmHg. However, simply changing from a regular diet to the DASH diet (vertical lines), without any changes to sodium consumption, reduced the systolic blood pressure by 5.9 mmHg, almost 3 times the drop resulting from the sodium reduction. This clearly explains why Mediterranean people enjoy an excellent cardiovascular status despite their higher salt consumption. The im-

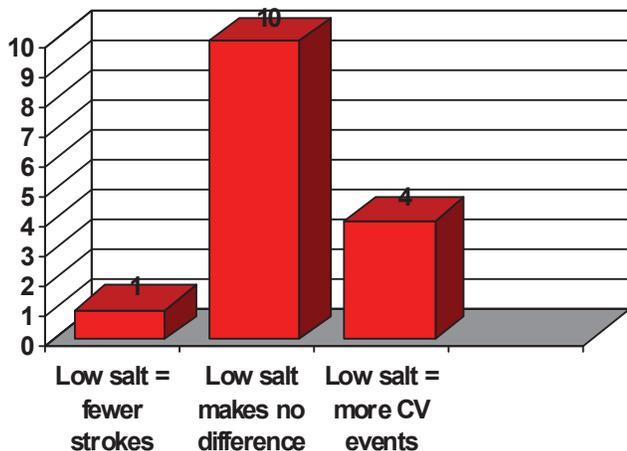
port of sodium on the blood pressure of hypertensives is modest (and of no significance to normotensive people, the majority of the population; Freeman and Petitti, 2002). However, salt reduction advocates inevitably give salt reduction more significance than the DASH diet itself.

Until recently, the question remained whether reducing salt intakes in the population would save the thousands of lives predicted by salt-reduction advocates. In the publication "Salt—The Forgotten Killer," published by the Center for Science in the Public Interest, Jacobson (2005) states that reducing salt consumption by half would save 150,000 lives per year in the United States, in spite of the considerable body of documented knowledge indicating that these claims may lack scientific merit (Dole, 1951; Miller et al., 1987; Laragh and Sealey, 1992; Alderman et al., 1995; Feldman et al., 1996; Midgley et al., 1996; Taubes, 1998; Freedman and Petitti, 2001; Robertson, 2003; Alderman, 2006). Even experts on the Institute of Medicine panel on dietary reference intakes for electrolytes and water acknowledge that there is a gap in knowledge on the health consequences of dietary salt restriction (Egan, 2003; Institute of Medicine, 2004). Nevertheless, ongoing salt-reduction advocacy efforts and general media attention to this issue may induce the food industry and consumers to cut back significantly on salt utilization or consumption. The potential negative health impact of a population-wide reduction in sodium intake, as described in the scientific literature, is the primary subject of this supplemental statement.

As indicated previously, the RAAS system plays a critical role in regulating blood volume and systemic vascular resistance, which together influence cardiac output and arterial pressure. As the name implies, there are 3 important components to this system: 1) renin, 2) angiotensin, and 3) aldosterone. Renin, an enzyme that is primarily released by the kidneys, stimulates the formation of angiotensin in blood and tissues, which in turn stimulates the release of aldosterone from the adrenal cortex. More recently, there has been a paradigm shift in our understanding of the actions of aldosterone. Indeed, seldom has there been such a renewed interest in the study of a compound that was isolated more than a half century ago as we see ongoing now with aldosterone.

Traditionally, our view has been that the primary action of aldosterone was its action on renal epithelial cells in the distal tubule and collecting duct to promote sodium reabsorption and potassium excretion. The more malignant role of aldosterone in the pathophysiological consequences of the activated renin-angiotensin-aldosterone system on vascular condition and chronic heart failure was unseen. There is now evidence for vascular synthesis of aldosterone aside from its secretion by the adrenal cortex. More recently, this hormone was found to be involved in vascular matrix impairment and endothelial dysfunction (Duprez et al., 2000; Figure 3).

The latest observations indicate that the most significant impact of aldosterone on cardiovascular and renal disease



**Figure 1. Fifteen health outcome studies of salt intake and cardiovascular (CV) outcomes.**

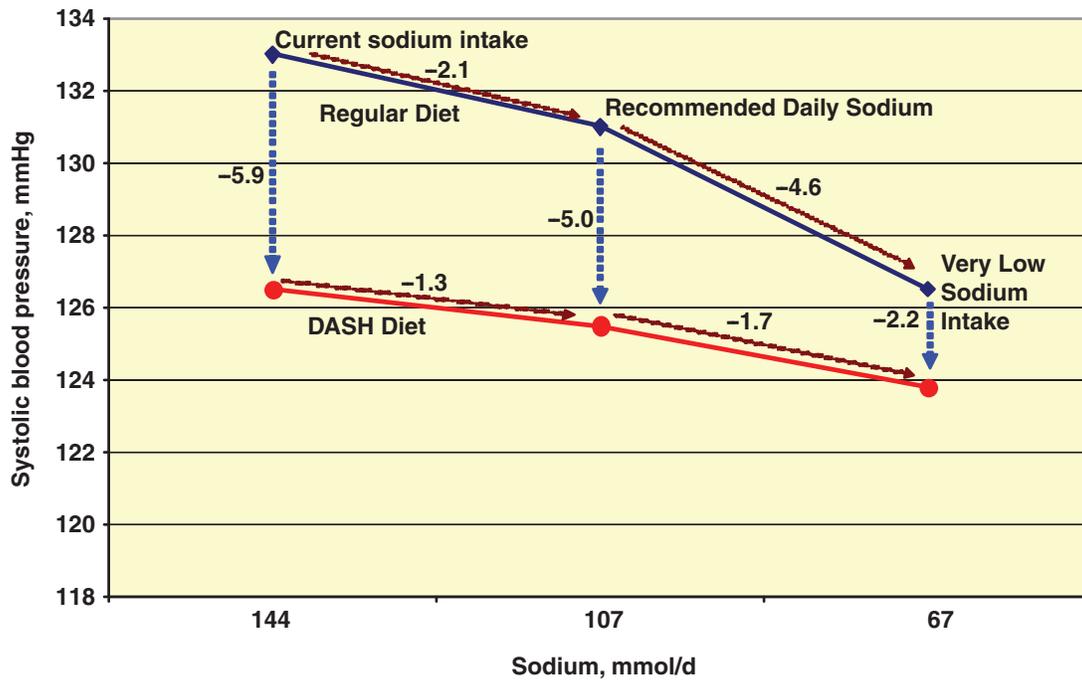


Figure 2. Dietary Approaches to Stop Hypertension (DASH) sodium trial.

results from specific actions at critical sites, including the heart, kidneys, and vasculature. Indeed, aldosterone is considered a crucial hormone for the body's cardiovascular system (Epstein, 2002). Clinical studies indicate that aldosterone, completely independent of angiotensin II and elevated blood pressure, plays a role in cardiovascular disease. In addition to its role in fluid and electrolyte balance and circulatory homeostasis, aldosterone is a critical mediator of vascular injury through its effects on endothelial function as well as through increasing vascular smooth muscle cell hypertrophy, generation of reactive oxygen species, and inhibition of norepinephrine uptake.

The addition of aldosterone antagonists to the regimens of patients with left ventricular systolic dysfunction and ongoing symptoms of heart failure, despite optimal ongoing treatment with angiotensin converting enzyme (ACE) inhibition and  $\beta$ -blockers, can substantially reduce overall mortality and the rate of sudden death in this vulnerable population. This result indicates that the aldosterone level may be a more important predictor of cardiovascular disease risk than is blood pressure.

Aldosterone interacts with mineralocorticoid receptors to facilitate thrombosis, reduce vascular compliance, and impair the baroreceptor function. It also interacts with mineralocorticoid receptors to cause myocardial and vascular fibrosis and left ventricular hypertrophy (Struthers and MacDonald, 2004; Duprez, 2005).

This more recent information explains many of the unexpected results that have been observed in the past. For instance, in an analysis of 219 patients with essential hypertension in the early 1970s, heart attacks and strokes

were observed when the plasma enzyme renin was elevated. It was concluded that renin may be a risk factor for heart attacks (Brunner et al., 1972). In 1991, Alderman et al. reported on the relationship between reduced salt-related high renin levels and increased myocardial infarction rates (Alderman et al., 1991). This relationship was once again confirmed in 1997 (Alderman et al., 1997).

A short time later, in 58 trials of hypertensive persons, reducing sodium intake to 118 mmol/24 h (urinary sodium excretion) lowered systolic blood pressure by 3.9 mmHg and diastolic blood pressure by 1.9 mmHg. In 56 trials of normotensive persons, reducing sodium intake to 160 mmol/24 h lowered systolic blood pressure by 1.2 mmHg and diastolic blood pressure by 0.26 mmHg. On the surface, this appeared to be a positive outcome; however, another consequence of this drop in sodium consumption was a significant 360% increase in the levels of plasma renin and a 320% increase in the level of aldosterone. These increases were proportional to the degree of sodium reduction and were accompanied by a significant decrease in body weight and increases in levels of norepinephrine, cholesterol, and low-density lipoprotein cholesterol (Graudal et al., 1998).

In his introduction of Michael H. Alderman as editor-in-chief of the *American Journal of Hypertension*, renowned hypertension researcher and founder of the American Society of Hypertension, John Laragh, stated that Alderman rightly "questioned the popular wisdom of unselectively advising salt avoidance for all hypertensives, and for all normotensive people—a popular public health strategy which will surely chronically raise all of their plasma renin values and may have other unintended adverse con-

# Renin-angiotensin-aldosterone system

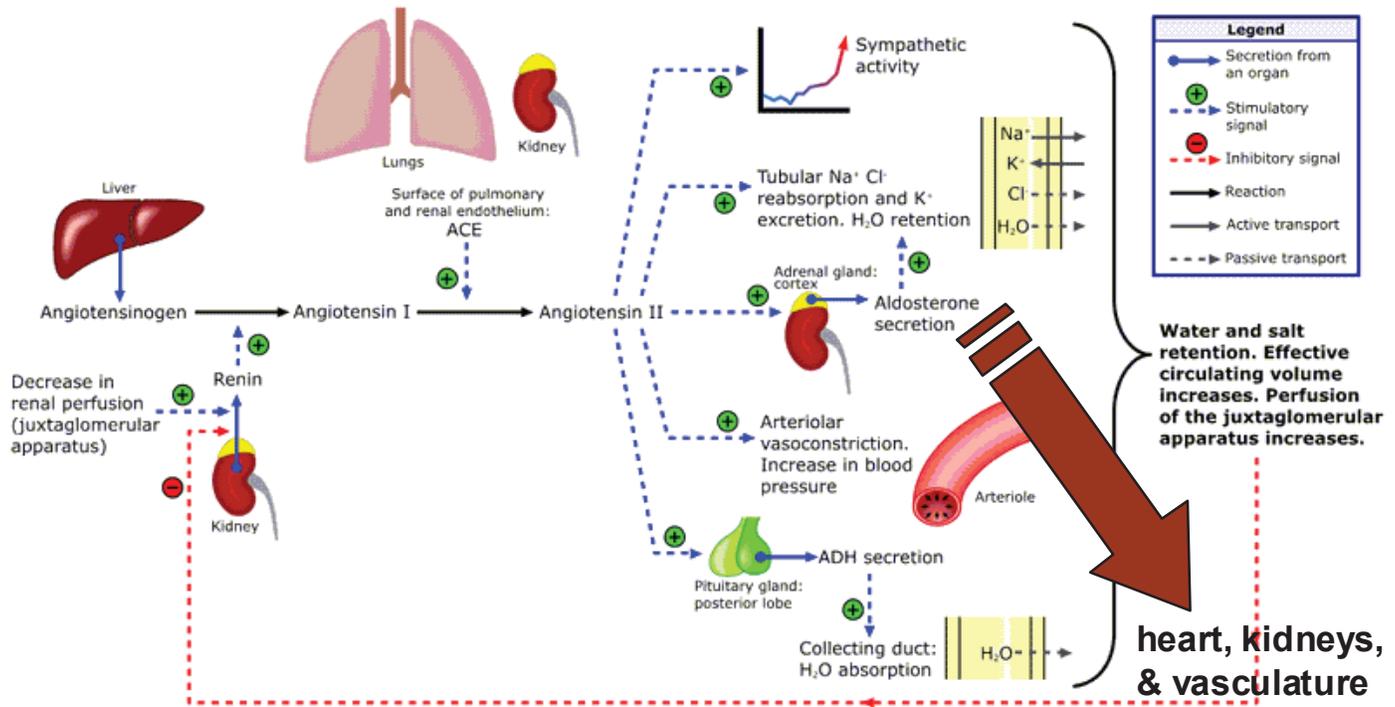


Figure 3. Renin-angiotensin-aldosterone system.

sequences” (Laragh, 2006). Why is it that this is not more widely known?

One of the serious unintended adverse consequences of salt avoidance is the negative impact of increased aldosterone levels on vascular compliance (stiffness). Vascular compliance has assumed increasing importance as a key marker of early disease of the vascular wall, a predictor of future vascular disease, and a way to monitor the effects of vasoactive agents on arterial wall stiffness (Winer et al., 2001). A significant number of recent publications have attributed increased arterial stiffness to reduced salt intakes (Resnick et al., 2000; Resnick et al., 2004).

Very recently, Shapiro et al., (2008) investigated the association between excess aldosterone, reflected by an increased aldosterone:renin ratio and pulse wave velocity (PWV) in young healthy adults to determine vascular compliance. In a single-center study, 60 subjects were evaluated for lipid profile, glucose, hs-CRP, rennin, and aldosterone. The PWV was performed as a simple, non-invasive recording and computer analysis of the 2 artery sites’ pressure waveform (Shapiro et al., 2008). The aldosterone:renin ratio was significantly and positively associated with PWV and had the potential to exhibit the direct effects of aldosterone on the vascular wall. Most significantly, the participants received instructions to consume levels of sodium proportional to energy intake, corresponding to 2,300 mg/d of sodium per 2,100 kcal, and to avoid foods notably high in sodium caused by processing or foods with salt topically added—in other words, to

comply with the upper limit daily value recommendations of the Institute of Medicine (Institute of Medicine of the National Academies, 2005). This study demonstrated that this level of intake resulted in increased aldosterone and increased arterial stiffness. Even this upper daily value limit of sodium consumption recommended by the Institute of Medicine appeared insufficient to prevent elevation of aldosterone and its consequent potential for harm.

Several reasonable conclusions can be derived from the data reported above. In the first instance, there is clear evidence that a reduction in salt intake will elicit an increased plasma aldosterone-renin output, thereby placing normotensive people at a greater risk for vascular damage and myocardial infarction. It appears likely that the derived Institute of Medicine upper limit for sodium may not be sufficient to protect a large part of the population from arterial stiffening.

This may also explain in part the publication of a recent research article by Karppanen and Mervaala (2006). They boldly stated:

In this paper, we provide evidence that strongly suggests that the progressive decrease in salt intake, which has continued in Finland for 25 to 30 years, has played an important role both in the impressive fall in the average blood pressure of the population and in the pronounced 75% to 80% decrease in both stroke and coronary heart disease mortality in the population younger than 65 years.

The authors refer to an aggressive national antisalt campaign involving influential newspapers, labeling programs, and a consensus agreement of government and scientific organizations with the food industry. The result of this effort was a drop in per capita salt consumption from 14 to 8 g/d, close to a 50% reduction. Finland is the only country that has managed to do this.

To strengthen the case for salt reduction, the authors went on to state that

Evidence is presented to indicate that the comprehensive salt reduction has also played an important part in the remarkable 5- to 6-year increase in the life expectancy of the Finnish population during the past 25 to 30 years.

The figures in that paper clearly show a dramatic drop in per capita salt intake in Finland. As the authors stated, "Finland, so far, appears to be one of the few countries where it has been possible to produce a marked population-wide reduction in salt intake."

They go on to state that salt consumption in the United States was not reduced during that same time period. Unfortunately, they did not actually record the US cardiovascular data for comparison in a relatively straightforward matter.

The Global Cardiovascular Infobase (<http://www.cvdinfobase.ca/>) makes possible a clear comparison of patterns of ischemic heart disease (IHD) in all countries over the last 35 years. The comparison of Finland to the United States is illustrated in Figure 4.

The rate of IHD has decreased in both countries. In fact, the degree of heart disease reduction is far superior in the United States, having started at a significantly higher rate in the late 1960s and dropping to a lower rate by the year 2000. Yet unlike Finland, where the per capita salt intake has steadily declined from 14 to 8 g/d, US per capita food salt consumption has fluctuated in the range of 7 to 11 g/d.

Karppanen and Mervaala (2006) were clearly wrong in attributing reduced cardiovascular disease to a reduction in salt consumption. If anything, the evidence would suggest just the opposite. Studies from 5 more European countries and Canada confirm the relationship. All these countries have significantly reduced their IHD mortality over the past 30 yr, yet none but Finland has claimed any reduction in dietary salt. In fact, in the early 1970s, the risk rate closest to Finland's was that of Canada. By the year 2000, with no salt reduction in Canada, Canadians had reduced their IHD mortality by twice as much as Finns. Finland had the *least* impressive improvement of the entire group and, as the authors boldly remind us, Finland was the only country to achieve a significant and sustained reduction in per capita salt consumption (Figure 5).

The authors' second health outcome metric was longevity. They claimed that the 5- to 6-yr increase in life expectancy experienced in Finland was also the result of the reductions in salt intake. Again, using the same country set, the United States led the group in increased life expectancy, improving fully 45% more than in Finland.

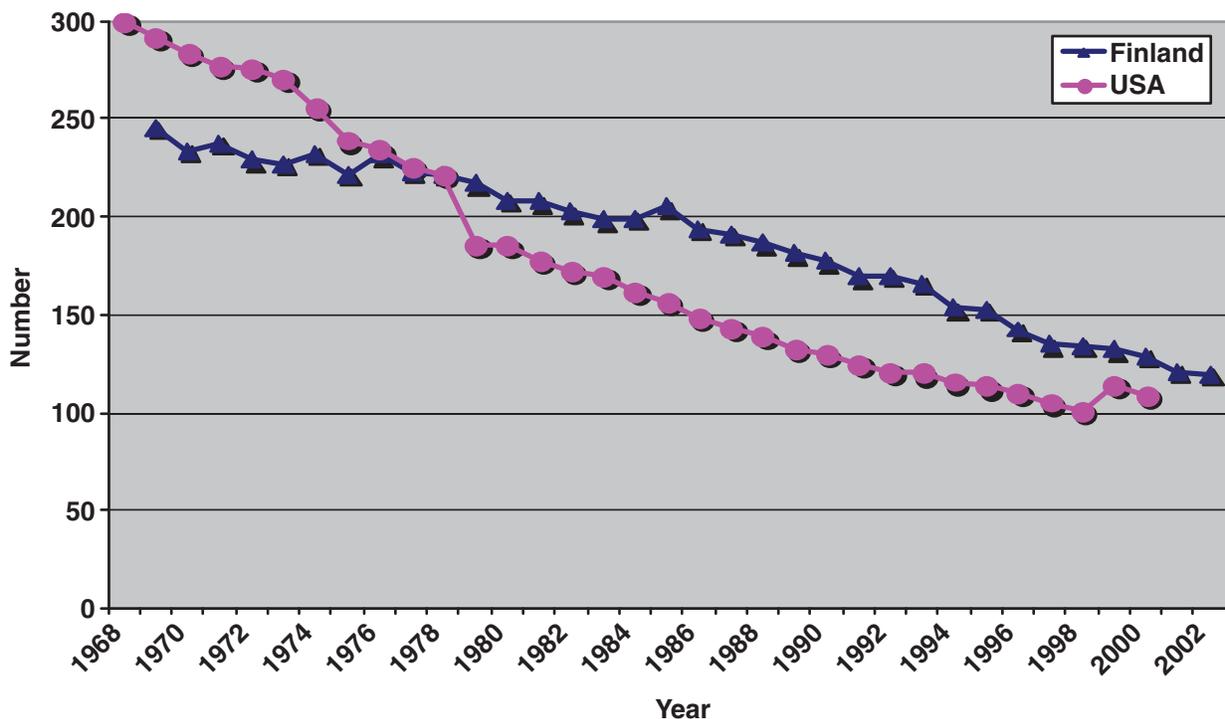


Figure 4. Age-standardized death rate from ischemic heart disease (per 100,000) in Finland and the United States between 1968 and 2002.

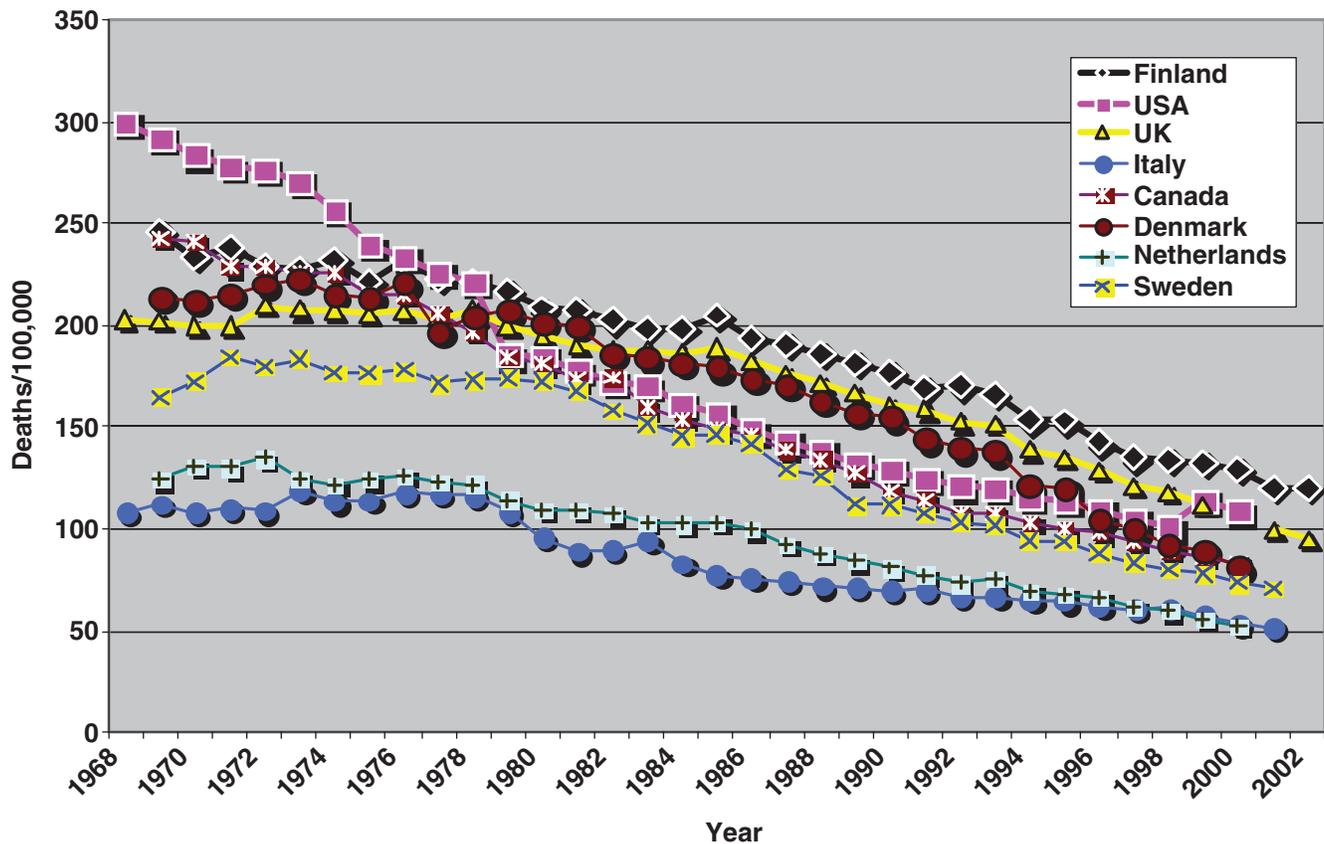


Figure 5. Ischemic heart disease in 8 countries between 1968 and 2002.

In fact, Finland's improved life expectancy appears modest when compared with those of most of its neighbors. As the authors point out, Finland was the only country to achieve salt reduction, but, as far as increases in life expectancy are concerned, the country earned a subpar health benefit for all this effort: countries with consistent salt consumption levels set the pace for extending their citizens' lives, as shown in Table 1 derived from the International Data Base of the US Census Bureau (<http://www.census.gov/cgi-bin/ipc/aggggen>). It is difficult to see how the authors attributed both the reduction in heart disease and the increase in life expectancy uniquely to a pattern of salt reduction without any attempt to compare this with real data readily available to anyone.

The evidence of health impacts of reduced salt consumption invites reconsideration of public health policy on universal sodium reduction. The study from Finland has crystallized the impacts for all to see. Finland achieved significant salt reductions, yet its progress in improving health outcomes was retarded compared with those of its neighboring countries and countries that shared similar social, economic, food, and medical systems but did not reduce salt intakes. Despite a nearly 50% reduction in the consumption of salt in Finland, no health benefits were attributable to this intervention—the most definitive lesson thus far that salt reduction will accomplish nothing.

In conclusion, the food industry is currently in the midst of a long-standing controversy centered on the use of one of its most ubiquitous ingredients—salt, a nutrient that is essential to life. The latest evidence indicates that salt reduction will not deliver the health benefits stated by the advocates of salt reduction. On the contrary, it may have the opposite effects and reduce or reverse the pattern of cardiovascular advances we have seen over the last 3 decades.

Unintended adverse consequences are what we all strive to avoid. Just as John Adams stated "we are a government of laws and not men," so too is the functioning of our physiology—processes governed by scientific laws and not the subjective opinions of humans. We stand to be in great peril if we ignore the science.

Table 1. Thirty-year increase in life expectancy in 8 countries

Country	Life expectancy increase, yr
United States	8.0
Canada	6.8
Italy	6.7
Sweden	6.0
Denmark	5.5
United Kingdom	5.5
Finland	5.5
The Netherlands	4.5

Despite vigorous salt-reduction advocacy and populist media attention to this issue, the science will eventually come to the forefront. It can only be hoped that no one suffers unintended consequences because of a rush to judgment. Fortunately, the FDA is taking a more cautious approach than the regulatory agencies in other countries and evaluating all the scientific data before rushing ahead with any policies. The FDA did this once before, when they delayed the acceptance of thalidomide while the rest of the world eagerly accepted it without a full review of the science. Prudence dictates that we tread very carefully in any consideration of a change in the regulatory status of salt to ensure that we do not do the population more harm than good.

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