Shaking up the Conventional Wisdom on Salt

What Science Really Says about Sodium and Hypertension

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Executive Summary

The notion that if you eat too much salt you will have high blood pressure has been perceived as medical gospel that most people—including this author—believed for the past three decades. But in recent years, research has emerged that challenges this once accepted truth. Headlines asking, "Is salt really bad for your blood pressure?" and declaring, "It's time to end the war on salt," have fostered growing suspicion among the public that the facts about salt and its effects on health might not be as clear cut as once believed.

Around the world, chronically elevated blood pressure affects approximately 40 percent of the adult population. In the United States, nearly one in three adults qualifies as hypertensive, which puts individuals at greater risk for many serious health events, including heart attack, heart failure, and stroke.

Considering the cost of the disease, both in terms of human suffering and the burden it places on our health care system, government agencies have made reducing the prevalence of hypertension a top priority. A public health strategy that successfully reduces hypertension rates has the potential to improve millions of lives and save millions of dollars. A misguided approach, on the other hand, would at best fail to reduce hypertension; at worst it would encourage behavioral changes that increase harm, obscure more effective means of risk reduction, and erode public trust in agencies.

For these reasons, population-wide recommendations should be rare and adhere to rigorous standards. At a minimum, such recommendations should:

- Be limited in scope and based on robust, high-quality evidence;
- Weigh and thoroughly consider unintended consequences; and
- Be more effective and less harmful than the likely alternatives.

Based on a review of the scientific literature, the results of nearly four decades of government efforts focused on sodium restriction, and the existence of other—possible more effective—means of hypertension reduction as presented in this paper, the current government recommendations on sodium fail to meet this standard.

Key findings of this study include the following:

- Humans require a certain amount of dietary sodium in order for our bodies to regulate fluid homeostasis. Too little sodium will result in the body ceasing to function, while too much can cause strain and death. However, the scientific community has yet to agree on an optimal range of sodium intake.
- At least in part, the factors that determine what amount of salt a person craves ("salt appetite") may be determined biologically and influence a person's eating behavior in unconscious ways, making it resistant to public policy efforts to lower sodium intake (which may prompt undesirable physiological responses and changes in behavior).
- Currently, government health agencies such as the U.S. Department of Health and Human Services, U.S. Department of Agriculture, and Centers for Disease Control and Prevention recommend adults consume less than 2,300 milligrams of sodium per day. This limit originated not from a process of scientific

consultation, but from government fiat, prompted by politicians, bureaucrats, and industry.

- Most human populations consume a relatively similar level of sodium that is much higher than the U.S. government recommendation, while only a handful of populations—some isolated tribal and Sub-Saharan peoples—consume less than 2,300 milligrams a day.
- Americans have not significantly increased sodium intake since such investigations began in the 1950s. This is despite increases in processed food consumption, more sodium in processed food, and significant increases in both calorie consumption and average weight.
- Lowering sodium can lower blood pressure for some people, but the response may only be seen at a certain extreme consumption level and is heterogeneous. When sodium is decreased, some individuals will experience decreases in blood pressure, some will experience no change, and some will see their blood pressure increase.
- Scientific evidence is inconsistent regarding the health benefits of moderate sodium restriction for individuals who are not hypertensive.
- People do not die as a result of high blood pressure, but rather from health effects linked to, but not necessarily caused by elevated blood pressure. As a corollary, blood pressure reduction does not always result in improved health outcomes.
- Diets consisting of sodium levels lower than the recommended level are associated with negative health outcomes, though the cause of this association is unclear.
- There is almost universal agreement within the scientific literature that other dietary factors, such as weight loss and increasing potassium intake, are as effective as sodium reduction in reducing blood pressure. Such alternative strategies also appear to be beneficial for a larger portion of the population, have a greater probability of adherence, and have less chance of unintended consequences.

Worldwide, government attempts to lower population sodium intake below the recommended limit have failed despite four decades of effort. Considering this failure and what we currently know—and do not know—about the biological effect of sodium restriction on the population at large, government health agencies engaged in efforts to lower hypertension rates should abandon their myopic and ultimately futile war on salt.

The development of high blood pressure is personal, multifactorial, not influenced by a single genetic or lifestyle factor; sodium reduction may be advisable for some, but ineffective or counterproductive for others. The most effective approach for risk reduction can only be made on an individual basis by patients and their health care providers. However, if the government is going to attempt to lower population hypertension rates, it should refocus its efforts toward helping people lose weight and increase potassium in their diet with higher consumption of fruit and vegetables. Compared with a salt-centric approach, this strategy would have a firmer grounding in science, be less likely to cause unintended harm, and may even have health benefits in addition to lowering blood pressure.

Introduction

"Some seek not gold, but there lives not a man who does not need salt." ~Cassiodorus

Health advocates are right to worry about hypertension. It is a serious condition that affects a very large percentage of people. Globally, around 40 percent of the population has elevated blood pressure, which increases the risk for strokes and heart attacks.[1] The numbers are even higher among those over 50 years old. In some countries, half or more of the older population is hypertensive.[2] Public health programs to reduce hypertension have the potential to save and improve countless lives around the globe and relieve financial pressure on national health care systems. To achieve this goal, policy makers need to identify and implement strategies that actually produce net positive outcomes and avoid those that prove to be ineffective or harmful.

That is no simple task. The heterogeneous nature of human populations, with innumerable differences in genetics and lifestyle factors, makes providing universally beneficial recommendations difficult and complicated. Thus, recommendations made to the general public should be limited in scope and firmly grounded in the most sound and robust scientific evidence.[3] On the other hand, health initiatives based on logical leaps and unsubstantiated theories erode the public's trust of health organizations and their future recommendations, and harm the public's health.

For example, the idea that dietary cholesterol raised blood serum cholesterol—and because of that raised heart disease risk—was commonly accepted medical wisdom as recently as last year. Today, it is increasingly considered erroneous for most of the population, so much so that restrictions on dietary cholesterol were left out of the most recent government dietary recommendations.[4] This occurred because of mounting evidence indicating that, for most people, cholesterol in the diet has no effect on serum cholesterol levels, and may even impart certain nutritional and heart-protective benefits.[5] The link between fat intake and certain disease risks, once medical dogma, has recently been flipped on its head. Though eating a "low fat diet" had been considered a safe recommendation to lower cardiovascular and obesity risks, much of the modern research shows variation in the risks and benefits associated with various types of fat. For example, recent studies examining milk fat have found an inverse relationship, or none at all, between full-fat dairy and diabetes, obesity,[6] and cardiovascular risk.[7]

Beginning in the 1950s, health associations began recommending for people to reduce the amount of animal fat in their diets.[8] That message was codified in the U.S. Food and Drug

The heterogeneous nature of human populations makes providing universally beneficial recommendations difficult and complicated.

Evidence warranting a public health recommendation should be robust, consistent, and, preferably, based on large randomized controlled trials.

Administration's (FDA) 1980 Dietary Guidelines, which advised Americans to:

- Reduce their intake of cholesterol and saturated fat;
- Eat foods like "eggs and organ meats" in moderation;
- Limit fatty foods like butter, cream, margarine, shortening, and coconut oil; and
- "[T]rim excess fat off meats."[9D]

This spurred the anti-saturated fat movement, leading to the promotion of alternatives like margarine and shortening.[10] While low in saturated fat, these products contain artificial trans-fatty acids, and their excessive consumption is now linked to increased cardiovascular risk.[11] Some observers outside of the research community have argued that the obesity epidemic in the U.S., which seemed to accelerate during the 1980s, was caused by the Dietary Guidelines pushing Americans to consume less fat and more carbohydrates.[12] However, evidence supporting this claim is weak, since obesity takes many years of excess energy intake to develop and because Americans did not reduce their intake of fat. In fact, we increased our intake of all the macronutrients: fat, protein, and carbohydrates, from the 1970s to the 2000s.[13] Fat intake only decreased as a percentage of total calories—meaning that carbohydrate intake rose more than fat and protein intake did.[14] And while use of animal fats, like butter and lard, declined after the 1980s and added fats, like shortening and seed oils, increased, these trends were already under way before the release of the Guidelines.[15] Whether or not the Dietary Guidelines recommendations on fat and cholesterol actually caused consumers to shift their diets in ways that made us more or less healthy is unclear, but the recent reversals on the recommendations have, at the very least, increased skepticism toward recommendations by public health agencies.[16]

Evidence warranting a public health recommendation should be robust, consistent, and, preferably, based on large randomized controlled trials (RCT)[17] that investigate real-world health outcomes of a given intervention for generally healthy individuals, not just markers that are presumed to correlate with health outcomes. Weaker evidence, such as from cohort studies that follow people with various habits over time and tracking health outcomes, can warrant action if there is a consistently strong association, as there was with tobacco smoking and cancer. Currently, not a single RCT has looked at the actual health outcomes (heart attack, strokes, or cardiovascular disease) of reducing sodium to below the government's recommended maximum sodium intake of 2,300 mg a day. While there are hundreds of studies demonstrating a link between blood pressure and dietary sodium, people do not die because of high blood

pressure, but rather from complications related to the condition, such as strokes and heart attacks. As will be discussed in this paper, results from cohort studies attempting to show an association between sodium intake level and health outcomes have been inconsistent.

The current sodium reduction paradigm, which asks the average American to cut his or her sodium intake by a third, hinges on the assumption that, because increased sodium in the diet can lead to higher blood pressure and because higher blood pressure is associated with negative health outcomes, lowering sodium in the average American's diet will reduce the incidences of strokes, heart attacks, and cardiovascular disease.[18] Is that approach supported by the evidence? This paper seeks to address that question.

If incorrect, the current sodium reduction approach will, at best, fail to reduce hypertension. At worst, it may displace genuinely effective approaches while pushing people toward potentially less healthy diets and possibly increasing health risks for some. To assess the validity of these assumptions and the sodium-reduction paradigm, this paper investigates:

- The role salt plays in human biology;
- The development of the theory of salt-driven hypertension;
- The latest research on the health effects of sodium reduction; and
- Possible alternative public policy approaches to hypertension reduction.

It concludes that while salt reduction, like dietary cholesterol restriction, may be appropriate for some, the scientific evidence does not support the universal sodium reduction recommendations.

Salt, throughout the ages and across cultures, has long been revered as a gift from the gods.

Sodium in Human Biology

Salt, throughout the ages and across cultures, has long been revered as a gift from the gods. That is not surprising, considering that salt is necessary for human survival. Our need for salt—or more precisely, sodium chloride—likely stems from the fact that life originated in Earth's primordial oceans. In order for sea-dwelling cells to make the transition onto dry land, they needed to be surrounded by a fluid similar to the salt water conditions in which they evolved.[19]

As most of us were taught as school-children, the human body is made up of 60 percent water. But not just any water; almost 25 percent of our body weight is *salt water*. This is important because salt contains two electrolytes, sodium (a positive ion) and chloride (a negative ion), which allow electrical charges to pass throughout the body and send the necessary signals to keep everything running.

While most of us are aware of the dangers posed by high blood pressure, for most of our species' existence, low pressure was the greater threat.

Just as importantly, the complex interplay between electrolytes maintains the appropriate balance of fluid. Within the body, there are several distinct fluid compartments that have their own particular electrolyte makeup. Positively charged sodium and negatively charged chloride are the primary electrolytes in the fluid outside of cells, including blood plasma, spinal fluid, and lymph fluid. In the fluid inside the cells, known as intracellular fluid, the most prominent electrolyte is potassium, which is also positively charged. Water, like sodium chloride, is a *polar* molecule that has both a positively and negatively charged end. This complimentary polarity means that water and salt are attracted to each other while sodium and potassium—both positively charged electrolytes—repel one another. It is this interplay between electrolytes and water that allows the body to maintain the correct balance of fluid both inside and outside cells and to raise or lower blood pressure inside the body.[20]

The body's response to low blood pressure. The term "blood pressure" describes the force of blood on vessel walls. Blood vessels include arteries, veins, and capillaries. Pressure is a function of two factors: the amount or volume of blood and the size of the vessels through which blood flows. For example, decrease the volume of blood through blood loss, and pressure will drop. Increase the size of the vessels and pressure will drop. Alternatively, if you increase the volume of blood or decrease the size of the vessels (for example, if cholesterol builds up in arteries), pressure will rise.

While most of us are aware of the dangers posed by high blood pressure, for most of our species' existence, low pressure was the greater threat. Without enough pressure pushing blood through the kidneys, which take waste out of the blood and put it into the urine, our bodies would be unable to supply the organs with enough clean blood to stay alive. So, when the body senses a dip in pressure, it triggers a chain reaction of effects known collectively as the renin-angiotensin-aldosterone system (RAAS) to bring pressure back up to an adequate level. In a nutshell, the function of RAAS is to prompt the body to retain sodium and water and restrict blood vessels. Water is attracted to sodium, so in order to hold onto the water, the body also needs to retain sodium instead of excreting it, along with water, into the urine. Retaining water in cells plumps up blood volume. At the same time, RAAS forces blood vessels to constrict, reducing the space through which the blood can flow. Like turning up the water to a hose, or putting a finger over the opening, these changes in volume and space increase the pressure of blood flow.

In addition to increasing blood pressure, Angiotensin II, one of the main

hormones involved in RAAS, also appears to trigger the sensation of thirst, prompting us to drink more water for the body to retain.[21] RAAS hormones may also stimulate our appetite for salt, or, at least may make us perceive saltier foods as tastier. These behavioral prompts alter our drinking and eating in order to give the body more water to retain and more sodium with which to retain it (see Sidebar 1: RAAS).[22] Together, this causes blood pressure to rise and allows the kidneys to filter an adequate supply of blood.

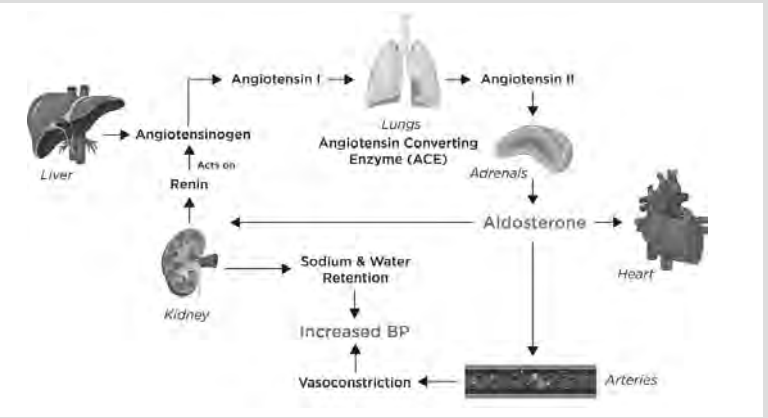
The Renin-Angiotensin-Aldosterone System (RAAS)

The renin-angiotensin-aldosterone system (RAAS or RAS) is a chain-reaction response, triggered when a person's blood pressure dips too low. Its purpose is to bring pressure back up to an adequate level. For example, if you become severely dehydrated or experience a sudden loss of blood, your blood pressure will decrease. When this happens, cells in the kidneys (which filter your blood) will sense the drop in pressure and stimulate the release of an enzyme called **renin**. Renin then flows through the bloodstream until it encounters an inactive hormone already present in the blood called angiotensinogen. When they meet, renin converts inactive angiotensinogen into the active hormone angiotensin I which then travels around the bloodstream until it encounters angiotensinconverting enzyme (ACE).

As the name implies, ACE then converts angiotensin-I into something else: **angiotensin II**. Angiotensin II or ANGII is a powerful hormone that does a number of things to increase blood pressure. First, ANGII signals the adrenal glands (organs just above the kidneys) to release **aldosterone**. Aldosterone is a hormone that triggers the kidneys to excrete potassium into the urine and to reabsorb sodium and water back into the blood. By doing this, it increase the volume of the blood and thus, blood pressure. Angiotensin II also signals the release of vasopressin (aka antidiuretic hormone or ADH). As the dual names imply, vasopressin/ADH causes both vasoconstriction (the squeezing of blood vessels) and the retention of water. Together, these effects result in the volume of blood increasing and the space through which it flows decreasing, resulting in a blood pressure rise.

Angiotensin II also triggers the sensation of thirst[1] and may stimulate our appetite for salt or, at least, may make higher levels of salt seem tastier to us.[2] This provides the body with the ingredients it needs—sodium and water—for RAAS to do its job: increase blood volume and pressure. Without enough sodium, either through dietary deficiency or a disorder that prevents sodium retention, blood pressure drops, organs fail, and the individual dies.

The purpose of RAAS is not merely to raise pressure indefinitely, but to achieve *homeostasis* or a stable balance of fluid in the body. Thus, as blood pressure increases and puts pressure on vessel walls, this stretching stimulates heart vessels to produce a substance meant to inhibit RAAS: **Atrial Natriuretic Peptide (ANP)**. This peptide stops the kidneys from releasing renin. Without renin, the body cannot produce angiotensin I and thus cannot produce angiotensin II, and without angiotensin II vasodilation stops and sodium and water can again be freely excreting; bringing blood volume and pressure back down. Therefore, in a properly functioning body, sodium intake, water consumption, and blood pressure should obtain a natural balance.



1 J.T. Fitzsimons, "Angiotensin, thirst, and sodium appetite. Physiological Reviews, Vol. 78 (1998), pp. 583–686.

2 Institute of Medicine. Appendix B: Workshop Papers. In: *Nutrient composition of rations for short-term, high-intensity combat operations* (Washington, D.C.: National Academies Press, 2005), https://www.nap.edu/read/11325/chapter/7.

* Image source: Renal Fellow Network, National Kidney Foundation, "Basic Review: The Renin-Angiotensin-Aldosterone Axis," August 27, 2009

Our predilection for salt is on par with our other most basic instincts like thirst, hunger, sexual desire, and the maternal impulse.

It is sodium's role in fluid and pressure regulation that makes the theory of dietary salt-induced hypertension so compelling. Based on the fact that the physiological mechanism for raising blood pressure is fundamentally linked to the absorption and excretion of sodium, and that many people with hypertension often seem to have higher levels of salt in their systems, the connection seems obvious. However, the body also has means to address high blood pressure and elevated blood sodium.

How the body responds to high blood pressure. As with low blood pressure, high blood pressure triggers a cascade of effects to bring pressure back to a normal level. Whether due to constriction of blood vessels or an increase in blood volume (due to retention of water and sodium), increased blood pressure causes the vessels in the heart to stretch. This stretching stimulates them to release Atrial Natriuretic Peptide (ANP), a hormone that inhibits the production of renin. Because renin is vital to the system that raises blood pressure (RAAS), it shuts down this system and prompts the body to stop constricting vessels and excrete sodium and water.

Excretion of water and sodium causes blood volume to decrease, which, along with widening blood vessels (vasodilation), results in blood pressure to dropping. Also, at least in animals, it appears to inhibit thirst and salt cravings triggered by RAAS.[23] All of these effects result in a reduction of blood pressure. Thus, in a properly functioning body with access to adequate sodium and water, blood pressure should neither be chronically too high nor too low due to dietary sodium. Yet, almost one in three Americans has chronically elevated blood pressure.[24] Clearly, something is amiss.

Evolutionary Derived Salt Need

Humanity's forbears likely evolved in hot and dry environments. Researchers believe they were also likely primarily vegetarian, which means their diets would have been salt deficient.[25] That scarcity, combined with sodium's importance in human fluid regulation and thus survival, set the stage for evolution to favor the development of a powerful urge to consume and conserve sodium.[26] As leading salt researcher Derek Denton of the University of Melbourne once put it, our predilection for salt is on par with our other most basic instincts like thirst, hunger, sexual desire, and the maternal impulse.[27] Thus, of our early human ancestors, those who were highly motivated to consume salt tended to survive, reproduce, and pass down their salt-tooth, while those without such drives died out. So, it makes sense that modern humans have a

strong predilection toward salty foods as a survival mechanism. But, the question remains: What is the optimal level of sodium intake?

The range of human sodium consumption. The Dietary Guidelines for Americans, the twice-a-decade recommendations released jointly by the U.S. Departments of Agriculture (USDA) and Health and Human Services (HHS), recommend that adults consume no more than 2,300 milligrams of sodium per day.[28] The American Heart Association recommends even less, with a maximum limit of 1,500 mg a day.[29] Both of these recommendations are much higher than the physiological minimum requirement for sodium—the absolute smallest amount of sodium humans need to continue functioning properly—which the American Heart Association estimates to be around 500 mg of sodium a day.[30]

These recommendations are considerably lower than the 3,400 mg a day the average American consumes.[31] But it is not just the U.S. Practically every human group observed by researchers appears to consume, on average, significantly higher levels of sodium than what is estimated to be physiologically necessary or even considered healthy by most health organizations.

The "normal" range for sodium intake, across cultures with diverse dietary practices, appears to be between 2,600 and 4,800 mg a day, according to a 2013 study by David McCarron of the University of California, Davis and his colleagues.[32] They analyzed 190 studies that collected 24-hour urine samples of participants, representing nearly 70,000 individuals in 45 countries. By having study participants collect all, or most, of their daily urine output, researchers are able to test the amount of sodium in it and get a highly reliable estimate of how much sodium the test subjects consumed. While sodium intake estimate from 24-hour urine samples may be limited by the fact that a person's sodium intake and even their excretion varies from day to day, it is still considered one of the most reliable methods.

Other methods of estimating sodium intake, such as keeping a diet diary, where participants record food and portions consumed, and dietary recall, where participants are asked to remember the food they ate over the last day, month, or even over years, are less reliable due to faulty memory or the participants wanting to appear to have a healthier diet than they do. The current gold-standard of sodium intake estimation is to collect multiple 24-hour urine samples to account for variation in daily diet and excretion (see Sidebar 2: estimating dietary sodium). But using single 24-hour samples, and even after accounting for age, culture, and ethnicity, McCarron

et al. found that most people consumed sodium within this relatively narrow range. Even more extraordinary, they observed that this range remained unchanged over the five decades of data they analyzed. A finding that echoed the results of other emerging research.[33]

Two years prior to McCarron's study, Harvard epidemiologists Adam M. Bernstein and Walter C. Willett published the first assessment of U.S. sodium excretion conducted over nearly 50 years. Similarly to McCarron, they found that intake appeared unchanged over that time, despite people's increased consumption of processed and highly salted foods. For their study, Bernstein and Willett's team analyzed all English language studies that reported 24-hour urine data between 1957 and 2003, accounting for just over 26,000 U.S. residents. Because hypertension rates in the U.S. had increased over the previous 20 years, the pair expected a corresponding increase in sodium intake

Estimating Dietary Sodium Intake

Measuring an individual or a population's average sodium intake is the foundation on which researchers base their observations. For example, looking at a person's health over time compared to his or her sodium intake can lead to valuable insights. On the other hand, inaccurate estimation of sodium intake can lead to erroneous conclusions. Below are the most common methods researchers employ to estimate sodium intake, including their advantages and limitations.

Dietary recall surveys include the 24-hour dietary recall, food frequency questionnaires, or an ongoing diary. They are the most convenient for participants in many ways, allowing data collection to be done remotely and are affordable, so researchers can get information from many thousands of participants. Yet, the accuracy of a self-report depends on the memory and honesty of participants who might underestimate the quantity of sodium they add in cooking or to finished dishes.

Spot urine testing requires volunteers to provide a one-time sample of urine during the day. While considered fairly accurate at estimating the average sodium intake for a population, it is not considered highly reliable to estimate an individual's intake because of daily variations in sodium consumption and variation in sodium excretion throughout the day.

24-hour urine collection asks participants to collect all, or most, of their daily urine output over a 24-hour period. It is considered a reliable means of estimating sodium intake. However, because of an increased time investment for participants, it can lead to selection bias. For example, those who are more health conscious might be more inclined to persist in the testing. Temperature and seasonal variability, in addition to incomplete samples, can lead to inaccurate data. This, as critics of recent studies argued, could result in masking of an upward trend in sodium consumption.[1]

Multiple 24-hour urine samples are the gold standard of sodium intake estimation. This requires participants to collect all of their urine on multiple random days, possibly over the course of years. While it is considered highly reliable, it is also the most time-consuming and energy-intensive for both participants and researchers, making it an impractical method of sodium estimation for most studies.[2]

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1 Paul K. Whelton, Lawrence J. Appel, Ralph L. Sacco, et al, "Sodium, blood pressure, and cardiovascular disease: further evidence supporting the American heart association sodium reduction recommendations," *Circulation*, Vol. 126 (2012), pp. 2880–2889, http://dx.doi.org/10.1161/CIR.0b013e318279acbf.

2 Rachael M. McLean "Measuring population sodium intake: a review of methods," *Nutrients*, Vol. 6 (2014), pp.4651-4662, doi: 10.3390/nu6114651

during that period. Indeed, as Bernstein and Willett note in their paper, existing evidence, such as the results of the National Health and Nutrition Examination Survey (NHANES), estimated that sodium intake had risen over 20-35 years based mostly on self-reported diet. Yet, when they conducted their analysis of sodium in urine, the pair found that mean sodium consumption was around 3,712 mg per day, and that, apart from adults over 50 years old, there was not a statistically significant rise in sodium over 46 years of data.[34]

In 2014, researchers at the U.S. Centers for Disease Control and Prevention (CDC) released their own study that examined "spot urine" samples collected as part of the NHANES survey. While they found a slight increasing trend over time, once they adjusted the results for body mass index (BMI), they found "no temporal trends in sodium excretion."[35] Adjusting for BMI is important because, as the authors note, sodium intake is strongly correlated with BMI—the larger a person is and the more calories a person takes in, the more sodium he or she will necessarily consume. Thus, adjusting for BMI allows the researchers to assess if sodium consumption has increased for people at various BMI levels. When they did this adjustment, they found no trend toward increased calorie intake. Notably, Bernstein and Willett did not adjust their results for body weight and still found no significant increasing trend in sodium intake.[36]

All studies have limitations. Methods of estimating sodium intake, as discussed, have degrees of reliability. Moreover, errors or inconsistencies in collection techniques may mask trends in sodium intake over time.[37] Still, even if these large population studies have some limitations, they provide compelling evidence that the tendency to consume higher sodium levels than the U.S. government recommendations is practically universal among human populations. The question too few are asking is: Why, if this level of sodium is excessive and leads to dangerous blood pressure imbalance, are we as a species driven to over-consume salt?

The tendency to consume higher sodium levels than the U.S. government recommendations is practically universal among human populations.

Influence on Human Sodium Consumption

Several theories try to explain what drives our high level of sodium intake, such as the ideas that:

- It is physiologically set, a concept known as sodium appetite;
- It is a maladaptation;
- We are addicted to salt; and
- High sodium intake may serve some, as yet undiscovered, benefit.

Physiological sodium appetite. The theory of an innate sodium appetite holds that humans are born with a set

Construction workers who experience frequent sodium depletion may discover they feel better after eating higher levels of salt and thus learn to consume more as part of their overall diet.

level of sodium that, if not met, triggers a desire to seek out and consume salt until the sought sodium level is restored. As numerous researchers have argued, the existence of a physiological sodium appetite would be a significant barrier for public policy aimed at reducing our salt intake.[38] However, to date researchers have been unable to prove that humans, unlike other animals, are born with a sodium appetite.

The first evidence of the existence of a sodium appetite came from psychobiologist Curt Richter, who in the 1930s conducted an experiment in which he removed the adrenal glands of rats. The adrenal glands produce aldosterone, one of the hormones necessary for RAAS. Aldosterone promotes sodium retention and prevents uncontrolled sodium excretion in order to maintain fluid homeostasis. Richter observed that the rats on a sodium restricted diet would die within a week without those glands. However, given free access to sodium and water, the rats would increase consumption enough to keep blood pressure stable and survive.[39] Rats, of course, are not humans. However, Richter observed a similar phenomenon in a three-and-half-year-old human boy whose parents reported had a voracious appetite prior to his first birthday. Placed on a sodium-restricted diet in the hospital, the boy, like the rats, died within a week. It was only during his autopsy that the doctors discovered a previously undiagnosed adrenal disorder and realized that the boy's elevated sodium intake had probably maintained a stable blood pressure and kept him alive.[40] Yet, others in similar cases of sodium loss do not always exhibit this elevated salt craving, even as they die from low blood sodium (hyponatremia).[41]

While researchers have observed that athletes, even when consuming water and sodium-electrolyte solutions, will fail to replenish what is lost during exercise,[42] it seems that individuals who are regularly sodium-depleted, like athletes and construction workers, find salt tastier[43] and generally consume more salt on average.[44] However, this may not be a function of salt hunger, but learned behavior. In other words, construction workers who experience frequent sodium depletion may discover they feel better after eating higher levels of salt and thus learn to consume more as part of their overall diet. Similarly, the boy observed by Richter may have discovered that eating salt made him feel better and developed an increased desire for the flavor. However, this is all speculation at this point.

Maladaptation. Another theory for why humans consume the amount of sodium we do is maladaptation, a trait that was useful in the past and passed down from our ancestors, but may be useless or even harmful in a modern environment. For example, over-

consuming and storing calories would have been beneficial for our ancestors who frequently experienced bouts of food scarcity and insecurity. In our current environment of calorie abundance, however, storing fat and overconsuming calories can quickly become unhealthy.

Robust evidence exists that humans' adult sodium intake is directly influenced by sodium deprivation in early life. For example, studies comparing adults' salt preference with the experience of their mothers during pregnancy found that participants whose mothers reported significant bouts of vomiting during pregnancy, and thus, dehydration, had notably higher levels of salt consumption as adults compared to children of mothers who did not report extraordinary morning sickness.[45] Similarly, major episodes of vomiting or diarrhea during infancy correlated with a persistently elevated enthusiasm for salt later in life.[46] A study of identical twins found that environmental factors, as opposed to genetic factors, played a larger role in their ability to sense saltiness, which might impact the amount of salt they eat.[47]

These early experiences with deprivation, which trigger the release of the hormones involved in the renin-angiotensin-aldosterone system, could, as researcher Stylianos Nicolaïdis theorized, "leave behind a sort of memory … that, over time, increases the readiness and strength of the ingestive response."[48] This seems like a compelling theory. The body, having experienced deprivation once, may prepare for subsequent salt famine, seeking out more salt than it needs at the moment. Supporting this theory is the recent discovery that the human body can store a limited amount of inactive sodium under the skin, but it is not clear that this storage system is as robust as the calorie-fat system, the mechanism that prompts us to overeat so that our body may store a virtually unlimited amount of energy as fat for use in periods of famine.[49]

Addiction

Like maladaptation, drug addiction can undermine our drive for self-preservation with a life-threatening appetite. Some researchers theorize that salt acts in a similar, albeit milder manner as drugs, specifically, opioids.

The theory argued by Corcores and Gold is that "salted food acts in the brain like an opiate agonist," meaning that it binds with opioid receptors in the brain, producing a similarly pleasurable effect we interpret as tasty. In support of this, researchers have observed that opioid addicts going through withdrawal will often over-consume calories and salty foods in an attempt, so the theory goes, to "self-medicate."[50] The analogy of salt as an opioid replacement is not

It may not be that salt is a drug, but that drugs are like salt.

perfect, however. Studies indicate that the elevated appetite observed in opiate addicts in withdrawal might be due to the nutritional deficiency experienced by opiate users and that as the deficiency fades, so does the increased appetite. For example, in one study of opioid-addicted rats, researchers found that in early withdrawal their valuation of sugar was inflated compared to other rats, but after two weeks, they valued sugar no higher than did other rats. An increased attraction to salt during opioid withdrawal may or may not have a similar shelf life.[51]

Addictive substances are understood to "hijack" important neural mechanisms involved in motivating reward-based behavior. They "penetrate the brain by devious artifactual routes," as Micah Leshem of the University of Haifa, phrased it. However, as Leshem noted, sodium does not operate this way. Far from "hijacking" a receptor meant for some other purpose, humans have a unique sodium receptor, designed specifically for that substance.[52]

That said, our brain's opioid system appears to be involved in salt appetite, triggering a sensation of pleasure or gratification when we consume needed sodium.[53] As noted, the basic understanding of drugs is that they work by hijacking important existing neural pathways. However, researchers have recently proposed the theory that opioid drugs piggyback on the evolution-created drive to consume sodium. So, it may not be that salt is a drug, but that drugs are like salt.[54]

Conditioning

Fundamental to the discussion of public policy addressing salt intake is the assumption that the level of salt we prefer in foods is *conditioned*. That is, because we are fed a high salt diet since childhood, we learn to like and prefer a given level of salt intake. There is only limited evidence that this is how salt preference is determined.

While other animals experience an immediate and lasting increase in salt preference in response to sodium depletion, there is little evidence that isolated incidents of deprivation—except during fetal stages or early infancy—will provoke a long-term change in the amount of salt a person desires.[55]

While studies show that the palatability of salt increases in the wake of depletion in adults, palatability returns to pre-depletion levels once sodium balance is restored. In small experiments with adults engaging in exercise, and thus sodium loss through sweat, researchers have observed that they express a preference for higher levels of salt in their food.[56] But this increased preference was transient. Even chronic bouts of sodium depletion in adult humans do not appear to affect salt preference in the long term.[57]

Furthermore, short term *increases* in salt, where people are given much more sodium than they would normally eat, do not appear to create lasting alterations in sodium intake. In 1986, Mary Bertino of the Monell Chemical Senses Center in Philadelphia and her colleagues conducted an experiment in which they gave subjects sodium tablets, added salt, or a placebo. While the pleasantness of salt went up quickly in the salt-added group, they found that "sodium excretion returned to baseline even though taste preference for salt remained high," suggesting that "the influence of diet on taste is greater than of taste on diet."[58]

On the other hand, several trials have demonstrated that long-term sodium restriction leads to a downward shift in taste preference—that is, subjects on reduced sodium diets for several months will experience an elevated perception of salt and find lower levels of salt more acceptable in particular foods compared to participants not on restricted sodium diets.[59] At least one recent study found that decreasing salt preference can be accomplished without reducing sodium in the overall diet. Such studies, testing preference for particular foods, may simply represent the ability of habituation to change a person's preference for a particular food through repeat exposure. For example, participants may acclimate to a low-salt soup so that it eventually becomes acceptable.[60]

Even assuming such a food-by-food sodium reduction could work, it is unclear *how much* this approach might be able to lower Americans' average sodium consumption overall. For example, gradual stepwise sodium reduction in foods on shelves in Finland (beginning in 1979) and the United Kingdom (in 2003) appeared to have some success in lowering overall intake, but the average level of sodium in these countries prior to reduction were 1,000 mg or more than the average American's salt intake, with which they are just now in line. It is uncertain what type of biological and behavioral response might be provoked by getting consumers to reduce sodium below that level and whether or not that is possible for most people.[61]

Benefits to higher sodium levels. Another explanation for why humans consume such a high level of sodium compared with government recommendations is that high dietary sodium serves some, as yet discovered, protective function.

Researchers, like Pavel Goldstein and Micah Leshem, a statistician and psychologist, respectively, at the University of Haifa, examined two possible benefits of a higher salt diet: growth and the moderation of depression. In their cross-sectional analysis of NHANES data and controlling for total calorie consumption, they found what appeared to be an

increase in sodium consumption during periods of growth, such as adolescence and pregnancy. They also found that dietary sodium was inversely related to depression in women, as women with less sodium in their diet were more likely to experience depression.[62] The researchers hypothesized that RAAS activation, which is associated with depression, might be inhibited by higher levels of dietary sodium.[63] In other words, dietary salt might act like a natural antidepressant.

It is also possible that higher sodium intake correlates with higher overall nutrient intake and better health. As will be discussed later, high sodium intake is correlated with higher systolic blood pressure, and there is a conflict in the literature about whether or not the typical sodium intake actually correlates with worse health.

Whether sodium levels are determined physiologically or conditioned, most researchers have found that getting subjects to adhere to low salt diets is frustratingly difficult. For example, in a 1997 trial examining the effect of weight loss and sodium reduction on blood pressure, participants were asked to reduce daily sodium intake to 1,840 mg or less. Yet, even with intense counseling, they managed only to reduce sodium to between just 2,390 mg and 2,852 mg per day.[64] In the early days of hypertension research, the 1950s, when dietary protein was thought to be the dietary culprit of hypertension, Corcoran and colleagues at the Cleveland Clinic Foundation placed 14 patients on salt or protein restricted diets. Of the 14, only four were able to achieve lower blood pressure through sodium restriction, and once they left the clinical setting, only two of the four could maintain the antihypertensive effect, leading the authors to conclude that "low sodium dietotherapy is therefore often impractical under the conditions of out-patient or office practice and demands at the very least a certain basic comprehension and compulsiveness on the part of the patient."[65]

More recently, clinical trials conducted in the 1990s—Trial of Nonpharmacologic Interventions in Elderly-TONE[66] and Trials of Hypertension Prevention II-TOHP[67]—were able to lower sodium intake by about 1,000 mg a day through intensive dietary counseling. However, both set a target sodium intake at less than 1,800 mg a day, and both failed to get the average sodium intake below 2,400 mg a day. For example, in TOHP-II participants assigned to the low sodium group lowered sodium intake from about 4,200 mg to about 2,600 mg by the sixth month of the study. But by the 36th month, average sodium intake had crept back up to 3,200 mg.[68]

Studies like this demonstrate that is possible to lower sodium intake, but for most people, that reduction stays

within the "normal" range observed by McCarron and his colleagues and Bernstein and Willett. It is possible that there is an upper and lower limit to dietary sodium, which, once crossed, triggers unconscious behavioral and physiological responses to bring consumption back into this normal range. For example, in a trial testing the effect of various sodium levels on blood pressure in hypertensive patients treated with a particular drug, researchers asked participants to maintain a very low sodium diet for several weeks of about 1,700 mg a day. Then they randomly assigned half to receive a placebo or a salt tablet that contained about 2,300 mg of sodium for four weeks, after which the groups were switched for an additional four weeks. In addition to finding no change in blood pressure due to high or low salt diets for their patients, the researchers also observed a curious trend of participants unconsciously altering their sodium intake to stay within a relatively narrow range. Participants on the placebo increased dietary sodium from about 1,700 to 2,800 mg a day. Those on the salt tablet continued to consume just 1,700 mg of sodium in their diet, while also getting 2,300 mg of sodium via salt tablet. Both groups ended up taking in between 2,800 and 3,970 mg of sodium a day from all sources, which, as the researchers noted is the observed "normal" range of human sodium intake.[69]

Thus, it might be possible to shift sodium preference within this range with conditioning, but getting people to reduce sodium *below* that range may be difficult and resource intensive. Furthermore, without a good understanding of *why* humans are driven to consume sodium in this particular range, efforts to significantly reduce sodium are as Leshem put it "not evidence-based."[70]

Development of the Salt-Heart Hypothesis

The theory that dietary salt impacts the cardiovascular system goes back to at least 300 C.E., but it was not until the 20th century that research began investigating this connection.[71] Though two French physicians had some success in lowering the blood pressure of their hypertensive patients with salt reduction[72] the results were almost immediately repudiated, and for the next four decades, "protein intoxication" remained the predominant theory for the cause of hypertension.[73]

Then in the 1940s, the idea of salt's role in blood pressure reemerged thanks to the work of Walter Kempner, a research physician at Duke University. Kempner experimented with a diet, later termed the Kempner diet, consisting of plain rice, fruit, fruit juice, sugar, or syrup and vitamin supplements. In addition to being remarkably low in fat, protein, and sodium (less than

The theory that dietary salt impacts the cardiovascular system goes back to at least 300 C.E., but it was not until the 20th century that research began investigating this connection.

194 mg a day), it was also relatively low-calorie, at 2,000 calories, and relatively high in potassium. The results of his diet on hypertension were remarkable. After a little over a month, the majority of Kempner's 500 hypertensive patients experienced improvements in their conditions, including lower blood pressure, reduction in heart size, and reduction of damage to the retina (retinopathy). Though Kempner was interested in the effect protein-restriction, other researchers seized on the idea that it was the diet's low sodium content that improved the patients' health.[74]

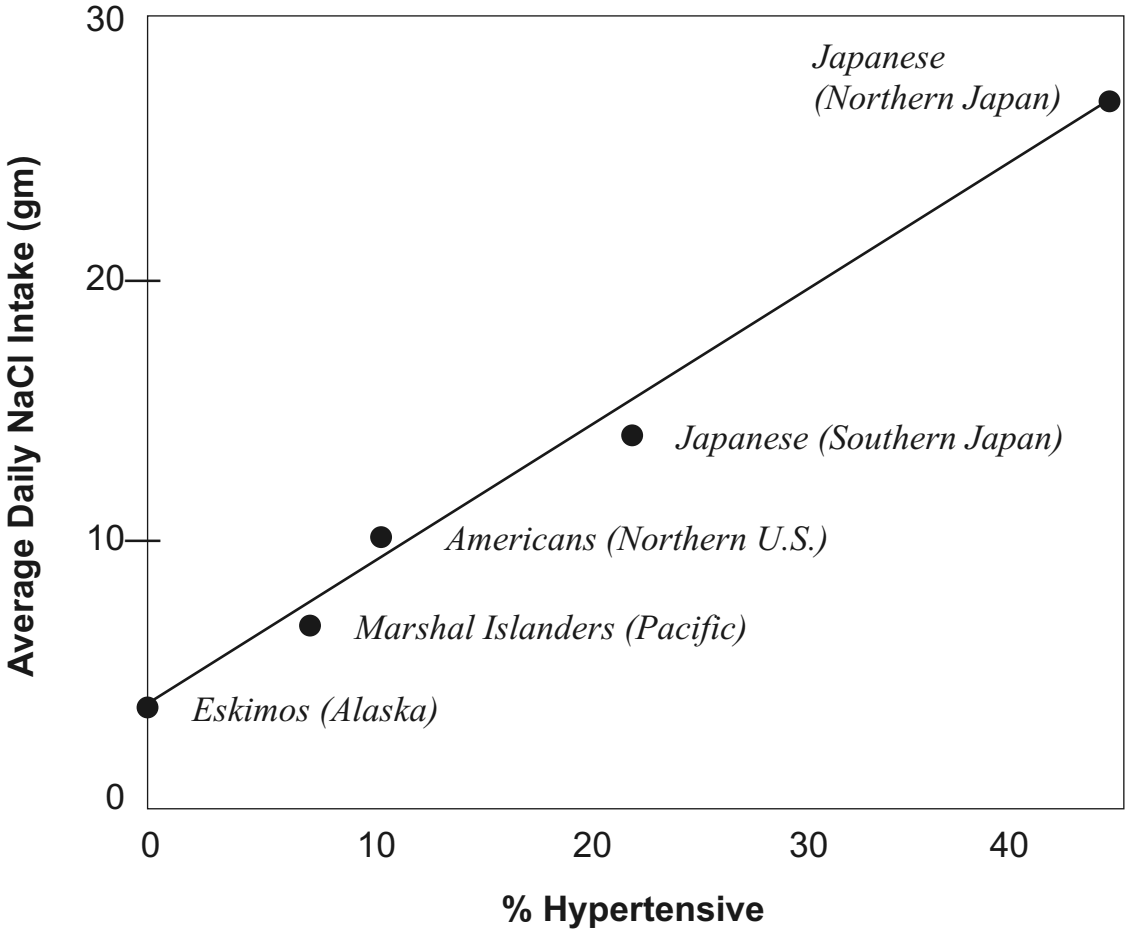
Arthur Grollman and his colleagues at the University of Texas conducted the first small controlled trials of the salt-hypertension hypothesis using both animals and humans. They confirmed that, for some patients, sodium restriction could lower blood pressure and that it was the sodium, in particular, that produced the results.[75]

Despite limitations of applying their results to the general population (since they studied only hypertensive patients), the experiments conducted by Grollman, Kempner, and others supported the link between salt and hypertension. However, it was a seminal 1960 population study by Lewis K. Dahl, an iconic hypertension researcher, who got the research community hooked on the idea that dietary sodium was the cause of chronically elevated blood pressure. Dahl and his team examined five separate populations with various levels of salt intake. They convincingly showed a nearly one-to-one correlation between salt intake and blood pressure, in a study that still influences research and public policy to this day. After analyzing 24-hour urine collections and comparing them with national purchasing behavior, self-reported diet, and an assessment of the sodium content in the food of the five different populations, Dahl concluded the results of their study suggest that "with higher average salt consumption there is higher prevalence of hypertension."[76]

Since the publication of Dahl's population study, various researchers have raised concerns about limitations of the work, such as the fact that Dahl never published information on how the data were collected and how his team controlled for biases and confounding factors like total calorie consumption and weight.[77] Dahl acknowledged that other factors may be at play in blood pressure, but he merely stated that they "have been omitted from this discussion." Pioneering medical researcher John Swales of the University of Leicester noted that "Dahl described a relationship between average daily intake of salt and the prevalence of hypertension … although the evidence used for assessing both variables was tenuous."[78] Perhaps most importantly, Dahl failed to

Table 1. Average Daily Salt Intake (based on 24hr urine excretion) Several Societies

Group	Year	Sex	Salt Intake	
			Average (g/d)	Range (g/d)
Alaskan Eskimo	1958, 1960	both	4	1-10
Marshall Islander (Pacific Ocean)	1958	both	7	1.5-13
United States (Brookhaven)	1954-1956	male	10	4-24
Japan				
Hiroshima (South, Japan)	1958	male	14	4-29
Akita (North, Japan)	1954	both	26	5-55



Source: Lewis K. Dahl, "Possible role of salt intake in the development of hypertension," 1960.

account for the relative age of the populations in his studies, an important factor since blood pressure is known to rise with age. For example, one member of his population, the Inuit (or Eskimo, as they were known at the time), had a particularly low life expectancy when Dahl and his team were gathering data. Data for Alaskan Eskimo are limited, though studies of northern Quebec Inuit put life expectancy between 1941 and 1951 at 35 years old.[79] Studies of the Inuit of the Northwest Territories of Canada found the average life expectancy to be 37 years between 1951 and 1960.[80]

However, subsequent studies failed to find a link between sodium and blood pressure *within populations*. While groups of people with higher levels of salt in their diet appeared to have higher blood pressure, when researchers examined sodium habits and blood pressure of people within these populations, they failed to find a connection between sodium and blood pressure.[81] Still, Dahl's population studies and his experiments with rats were incendiary within the public health community, in part because Dahl himself stepped out of the lab and into the policy debate, an approach that heralded the current era of advocate-scientists. Despite the limitations of his work and possibility of confounding factors, Dahl's belief in his conclusions was untempered. "The evidence that salt induces permanent and fatal hypertension is direct, quantitative and unequivocal in the rat," Dahl wrote in 1972. "Because the extensive evidence is circumstantial in man, it is therefore dismissed almost casually by some. If equal evidence had related salt to a similarly fatal but far less common disease, cancer, it would have evoked intense campaigns against it long ago." It was Dahl's work that was instrumental in developing the first Dietary Guidelines issued by the U.S. government.[82]

Development of the first dietary guidelines. The earliest dietary recommendations provided by the government, promulgated by the U.S. Department of Agriculture in 1917, aimed at stemming undernutrition in children.[83] Then in the 1970s, with the growing understanding of the role that overeating played in disease, Congress turned its attention toward setting recommended upper limits on foods. Ultimately, this would result in the inaugural Dietary Recommendations for Americans (and later the food pyramid), which, for the first time, proposed a recommended maximum daily limit on sodium intake.[84]

The U.S. Senate Select Committee on Nutrition and Human Needs first convened in 1968 with the charge to examine hunger and malnutrition, but in 1973 turned instead to address obesity, heart disease, and other illnesses influenced by diet. The

committee was helmed by Senator George McGovern (D-S.D.), who had recently come under the influence of diet-guru Nathan Pritikin, a non-physician who founded the Pritikin Longevity Center and created the temporarily popular Pritikin diet.[85] After receiving a disturbingly high cholesterol reading, McGovern began following Pritikin's dietary recommendations for lower consumption of fat, sugar, meat, salt, and processed foods. Roughly following this regime, McGovern impressively reduced his cholesterol—from 350 to 170. This led to a lifelong relationship between Pritikin and the Senator and, apparently, influenced McGovern's perspective on the issue of nutrition.[86]

While Dahl testified at the hearings, his greatest impact was felt in the number of other witnesses citing his work. For example, in 1972 the National Institute of Health began its blood pressure education programs, citing evidence from rat and population studies as the basis for the salt reduction recommendation, but ignoring the fact that many researchers raised concerns with ascribing certitude to what was preliminary and sometimes problematic research, a concern raised by several witnesses at the McGovern hearings.

American Medical Association Executive Vice President James Sammons noted that while observational studies like Dahl's suggested a "relation between salt ingestion and hypertension," they failed to substantiate the hypothesis that salt was a major contributing factor to overall hypertension rates. Furthermore, he noted that "for 80 percent of the population in this country, present salt intake has not been demonstrated to be harmful," and as such, "we believe that the recommendation of the report to set salt consumption as a national dietary goal is inappropriate."[87]

Similarly, a working party of the Royal College of Physicians of London and the British Cardiac Society noted that despite epidemiological and animal studies linking dietary salt with blood pressure, "at present we have no evidence that a reduction in the salt consumption of the whole population in the United Kingdom would widely lower blood pressure levels."[88]

While many in the scientific community were pleased with McGovern's efforts to act on what they saw as good evidence for nutrition-related diseases, some were nervous about grand proclamations on population health based on research that was still in the early stages. Doctors like Robert Olson of St. Louis University pleaded with Congress to wait for more research. "Rather than spend federal money to promulgate what may well be erroneous information, we should

carry out more research to be sure of what we are doing," Olson wrote in his report to the Committee.[89]

According to Marc Hegsted, head of the USDA's Center for Human Nutrition, when the Dietary Goals were written, most of the nutrition community opposed the goals. "I think they felt that a Senate committee had no business getting involved in recommendations that ought to be made by the scientific community."[90] When the first draft of the guidelines were made public, "all hell broke loose … practically nobody was in favor of the McGovern recommendations."[91]

Upon the release of the first McGovern report, the committee was confronted by "an unexpectedly boisterous mob of critics."[92] In addition to representatives of the food industry (who did not want the government telling people to buy less of their products), critics included representatives from the National Heart, Lung, and Blood Institute, and the American Medical Association—which wrote that the Goals had the "potential for harmful effects."[93] University of Wisconsin biochemist Alfred Harper savaged the report as one that would "appeal to those who accepted pseudoscientific reasoning,"[94] while National Academy of Sciences President and metabolism expert Philip Handler called the report "nonsense."[95]

In the first report, the recommendation provided by the committee was for Americans to reduce salt intake by 50-85 percent, down to 3 grams a day (or about 1160 mg of sodium).[96] However, the limit was later raised to five grams of salt (1940 mg of sodium) and then eight grams (3104 mg of sodium) after the report authors explained that the original limit was for *added* salt—it did not include salt already present in foods.[97]

Despite the scientific controversy, the conclusions hashed out in the Senate Select Committee, including sodium's link to hypertension, were largely accepted by the public. This was due, in part no doubt, to high-publicity efforts on the part of the government in the ensuing years to lower sodium in the food supply. The FDA, in addition to launching its sodium labeling effort in 1981, announced plans that same year to work with industry to achieve "voluntary" reductions in sodium in processed foods.[98] There was also talk of the FDA revoking the generally recognized as safe (GRAS) status of salt.[99] Food additives deemed as GRAS may be sold or used in the U.S. without any special approval or permission by the FDA under the assumption that the longstanding history of their use is sufficient evidence of their safety. Additives not considered to be GRAS, on the other hand, must be approved by the

FDA for use in given amounts in particular foods. Supporting the case against salt was a slew of new and convincing studies linking sodium to blood pressure that were published beginning in the mid-1980s.

Intersalt 1988: the most important salt study since Dahl. In 1988 the Intersalt Cooperative Research Group, a consortium of researchers at 52 research centers in 32 countries, published the results of their investigation into sodium and blood pressure. Intersalt researchers examined data from 32 countries, comprising over 10,000 participants, including blood pressure, urinary sodium, and potassium. Confounding factors, like alcohol intake, body weight, and others were also collected via questionnaire. At the time, it was the largest observational study to examine a connection between electrolytes and blood pressure.[100] The study found a positive, but weak, correlation between increasing sodium intake and blood pressure, specifically finding that mean systolic blood pressure dropped two to nine mm HG for every 100 mmol sodium decrease— that is, for every drop in sodium intake of 2,300 mg, the researchers found a drop in systolic blood pressure reading of two to nine points.[101] Essentially, this confirmed what Dahl had observed in his human and rat studies. Yet, the results received little attention, at first.

In a *New York Times* op-ed published a few months after the release of *Intersalt*, William Bennett, editor of the *Harvard Medical School Health Letter*, lamented that *Intersalt*, which "yielded the best data on salt and hypertension that we can hope for in this century," received such a lackluster reception. "It may simply have been that the practical message was undramatic: for all practical purposes, salt is a minor factor in the development of hypertension, once consumption exceeds a very low level," said Bennet.[102] It was, perhaps, this flat response that led the authors of Intersalt to revisit the data a few years later. In their 1996 paper, *Intersalt Revisited*, they applied new methodology to analyze the original data and found a much stronger association between dietary sodium and blood pressure—a threefold increase in the blood pressure benefits of reducing sodium intake.[103]

In addition to eliminating their original correction for body mass, the authors added a controversial correction for regression dilution bias (accounting for presumed errors in measurement that "dilute" the presumed relationship between two factors).[104] As the authors noted in their original study, there may have been some errors in the collection of their data, which would have "diluted" the assumed positive relationship between salt and blood pressure. Using the method of

Supporting the case against salt was a slew of new and convincing studies linking sodium to blood pressure that were published beginning in the mid-1980s.

For the vast majority of people, sodium restriction had no effect.

regression dilution bias is meant to correct for such errors. However, applying a regression dilution bias required them to make the assumption that any errors in their data diluted a stronger-than-shown relationship between sodium intake and blood pressure. If the assumption is incorrect, this new analysis method simply enhances a spurious correlation. These factors led some researchers, such as George Davey Smith, professor of epidemiology at the University of Bristol, to write that the study was "misleading," and others, like Nicholas E. Day, Director of the MRC Biostatistics Unit at the Institute of Public Health at Cambridge University, to chide that "statistical complexity should not be used to conceal inadequacies of the data."[105]

However, the most damning response to *Intersalt Revisited*, was an independent reanalysis of the data published four years later by David Freedman, a statistician at the University of California, Berkeley, and Diana Petitti, an epidemiologist and director of research at Kaiser Permanente.[106] They noticed that of the 52 centers, there were four "outliers," or four centers where sodium intake was extraordinarily low. In these centers—two examining Brazilian tribes, one in Papua New Guinea, and one in Kenya—there was the expected upward trend in blood pressure with increased sodium. However, once these outliers were removed from the data, the remaining 48 centers showed a surprising, albeit statistically insignificant inverse correlation between sodium and blood pressure. Once corrected for the four outliers, the results found no link between sodium and hypertension. In addition to fact that "the primary hypothesis of *Intersalt* was flatly contradicted," Freedman later charged that the *Intersalt* authors' continued attempts to reengineer the data in an attempt to find a correlation between salt and hypertension amounted to "data mining"—trying to find answers within data, the questions for which were not the goal of the study.[107]

Still, these concerns did not stop *Intersalt* from becoming hugely influential within the research community—with more than 600 citations since the publication of the first *Intersalt*.

Complicating things further was the fact that concurrent with the publication of *Intersalt Revisited*, in 1996 the *Journal of the American Medical Association* published a meta-analysis of controlled clinical trials, which investigated whether lowering sodium in the diet would result in decreases in blood pressure. They found that while individuals with existing hypertension experienced a small drop in systolic blood pressure, for the vast majority of people, sodium restriction had no effect. They concluded that while

sodium reduction "in older hypertensive individuals might be considered" the evidence "does not support current recommendations for universal dietary sodium restriction."[108]

Perhaps even more influential than Intersalt, in 2001 the Dietary Approaches to Stop Hypertension (DASH) trial published its results, which demonstrated that lowering sodium in the diet, consuming the "DASH diet" (high in fruits, vegetables, and low-fat dairy foods; includes whole grains, poultry, fish, and nuts; and is lower in red meat and added sugar than the typical American diet), or a combination of the two produced significant reduction in blood pressure. The DASH diet plus a very low level of sodium (1,500 mg/day) resulted in blood pressure that was seven to 11.5 point lower than those not on any diet.[109] The numbers were relatively small (just over 400 participants) and the duration of each diet was fairly short (30 days), but the results were impressive enough to convince many health bodies to endorse low sodium diets for the entire population.[110]

This back and forth within the scientific literature is, understandably, confusing to the general public. By the late 1990s there were more data available on sodium and blood pressure than ever before, but a connection between the two was murkier than ever. This murkiness was made worse by the continued calcification of the research community into camps supporting the theory that salt does cause hypertension or does not. While doctors like Paul Elliot, an epidemiologist at the Imperial College School of Medicine at St. Mary's in London and co-author of *Intersalt Revisited*, asserted that "there is a strong consensus," and "there is too much salt in the diet and it ought to be removed," others argued the evidence was not sufficient to advocate for universal sodium reduction. As Michael Alderman, president of the American Society of Hypertension and chairman of the department of epidemiology and social medicine at the Albert Einstein College of Medicine, argued, while there is some evidence involving salt consumption in blood pressure, there are not enough data showing that low salt diets are healthier. "Does a change in blood pressure by these techniques translate into a health benefit?" Alderman asked in 1996—a question he himself would seek to answer for the next two decades.[111]

Is a lower salt diet associated with better health?

Without knowing why humans consume such an apparently high level of sodium, it is difficult to fully understand the potential benefits or harms of any given consumption level. Despite this, activists within government and the research community have moved ahead with implementing national

Without knowing why humans consume such an apparently high level of sodium, it is difficult to fully understand the potential benefits or harms of any given consumption level.

and international programs to curb sodium intake, reasoning that, even if reducing salt is not dramatically beneficial for the majority of people, it will not harm health. However, emerging research, especially over the last decade, has cast serious doubt on that assumption. As with all aspects of the debate over salt, it seems, the answers are not clear cut.

While many studies have attempted to determine the connection between dietary sodium and blood pressure, very few have looked at actual health outcomes in relation to dietary sodium. By 2012, there were 23 observational studies examining health outcomes with lowering sodium:

- Six found a direct and significant association between higher sodium and poor health outcomes;
- Seven found an inverse association (showing higher sodium associated with better health outcomes),
- Two studies found a J- or U-shaped curve (with poor outcomes associated with very low or very high sodium intake); and
- Eight studies found no or mixed results.[112]

Additionally, since 2012 several researchers have published a handful of meta-analyses, attempting to integrate the results of these various studies. These too, have produced conflicting results.[113]

In fact, research teams looking at the same data have reached opposite conclusions. In 2008, a team led by Hillel Cohen of the Albert Einstein College of Medicine examined data from the third National Health and Nutrition Examination Survey, which, based on a single 24-hour dietary recall, contained estimated sodium, potassium, and calorie intake for nearly 9,000 people recruited between 1988 and 1994.[114] After adjusting the data for known cardiovascular risk factors, such as smoking, weight, serum cholesterol, and possible "confounding" factors, like potassium intake, the researchers found that people in the lowest-sodium intake group—those under 2,060 a day—were more likely to die from cardiovascular disease, compared with the highest sodium group, which consumed between 4,000 and nearly 10,000 mg of sodium a day. However, in 2011 a team led by Quanhe Yang of the CDC's Office of Public Health Genomics looked at the same data set and came to the opposite conclusion, finding that increased sodium intake is associated with higher all-cause mortality and that a higher sodium-to-potassium ratio was associated with higher all-cause and cardiovascular mortality.[115] Cohen et al claimed that the use of the sodium-potassium by

Yang et al "gives the impression of adjusting sodium for potassium, but in fact allows potassium to drive the association rather than adjust it."[116] Potassium has been repeatedly observed to lower mortality risk, particular for high sodium consumers. This, as Cohen et al alleged, allowed Yang et al "to make a statement about sodium only based on the ratio, which they might not be able to make based on a sodium model adjusted for potassium." On the other side, Yang et al claimed that the Cohen study was weaker because it included fewer participants for a shorter period of time (approximately 10 years versus Yang's 15), relied on a single dietary recall survey, and though it adjusted for potassium, it did not examine mortality association with potassium.[117]

Seeking to combine the results of the various studies, Pasquale Strazzullo and his colleagues at the University of Naples Medical School and University of Warwick analyzed the results of 13 population studies that looked at dietary salt and health outcomes like stroke and cardiovascular disease. They found a 23 percent increased risk of stroke for every increase in sodium intake of 2,000 mg and concluded that "this meta-analysis shows unequivocally that higher salt intake is associated with a greater incidence of strokes and total cardiovascular events."[118] However, critics of the study noted certain flaws and questioned their conclusions.

One criticism was that the selection of studies included leaned heavily toward those that demonstrated a connection between dietary sodium and poor health outcomes—seven out of 13 studies concluded high sodium led to worse outcomes, while they included just two studies that showed lower sodium intake caused worse health outcomes. For one of these, Strazzullo et al incorrectly interpreted the data so that a significant association between higher sodium and better outcomes was deemed insignificant.[119]

Another criticism of Strazzullo, which could be levied at many meta-analyses, is that his results are not generalizable to the healthy U.S. population because many of the populations examined in the Cohen study were *subpopulations*. For example, four of the 13 studies included only Japanese, Japanese-immigrant, or Taiwanese participants, which is important because certain cultural lifestyle factors, such as a much higher than average sodium intake or genetic variables, could make some populations more prone to certain diseases or conditions than others. Furthermore, many of the studies included in the Strazzullo survey either looked at or only found a correlation between high sodium intake and poor health outcomes in individuals who were overweight,[120] obese,[121] or smoked.[122]

Since Strazzullo et al, a number of other researchers have attempted to

The effects of sodium reduction in the general population remain unclear.

combine results of multiple data sets in order to assess the health effects of sodium reduction. Yet, the effects of sodium reduction in the general population remain unclear.

In 2011 Martin O'Donnell of the Population Health Research Institute at McMaster University and colleagues analyzed data for 28,880 individuals participating in heart disease drug trials and found that those at both the highest and lowest ends of sodium intake were most at risk of dying. In other words, they found a J-shaped curve where people at the lowest risk appeared to consume between 3,000 mg and 7,000 mg of sodium a day.[123] O'Donnell and his team found a similar result again in 2014, when as part of the Prospective Urban Rural Epidemiology (PURE) study, they examined the urine samples of more than 100,000 people from 17 countries and found that sodium intake above 7,000 mg of sodium a day was associated with a 15 percent increased risk of death, but also that intake below 3,000 mg a day was associated with a 27 percent increased risk of death.[124]

These results were echoed in December 2015, when Pablo M. Lamelas of the Population Health Research Institute in Ontario and his team published their analysis of Latin American individuals, which, after examining single urine samples from approximately 17,000 people from Argentina, Brazil, Chile, and Colombia, and tracking their health outcomes for nearly five years, found a found a similar J-shaped association between sodium, cardiovascular events, and mortality.[125]

These studies were met with vociferous criticisms, some justified. The most relevant of those criticisms pertained to the method of estimating sodium intake, with both the O'Donnell and Lemelas studies using single "spot urine" samples to estimate sodium (see sidebar: Estimating Dietary Sodium). While considered reliable for estimating average sodium consumption for the average person, the estimates can be off by several thousand milligrams for consumers at the very highest and lowest ranges.[126] Furthermore, the accuracy of spot-urine tests is affected by the time of day the urine is collected, since urine excretion rates vary throughout any 24-hour period.[127] Of course, these two studies are not the only ones to use spot urine samples. Many of the studies surveyed in previous meta-analyses use even less reliable methods like dietary recall surveys to estimate sodium intake—as did nine of the studies included in Strazzullo et al.[128]

However, some studies that have examined the sodium-mortality connection in generally healthy populations using the more accurate 24-hour urine collection method still indicate a connection between low

sodium levels and higher death rates. In 2011, Katarzyna Stolarz-Skrzypek of the University of Leuven and her colleagues conducted the first longitudinal population study, which followed the same 3,600 Europeans for an average of eight years. After excluding patients who had a history of cardiovascular disease, they collected a single 24-hour urine sample and compared it to outcomes including blood pressure, hypertension, stroke, heart attacks, and heart failure during the follow-up period. They found that, while higher sodium was independently associated with higher systolic blood pressure, "this association did not translate into a higher risk of hypertension or [cardiovascular disease complications]."[129] Instead, they found that lower sodium intake correlated with higher rates of cardiovascular death. Critics claimed the study was " disappointingly weak," pointing to, among other things, the use of a single 24-hour urine sample.[130]

In 2014, Niels Graudal of Copenhagen University Hospital and his colleagues published their own meta-analysis, which looked at 27 studies, including most of those in the Strazzullo meta-analysis. The analysis included 25 cohort studies and two randomized controlled trials—clinical trials that randomly assign participants to either a "control" group or an "intervention," such as sodium reduction. Similar to the PURE study, Graudal et al found a J-shaped curve, with the lowest risk for individuals consuming between 2,645mg and 4,945 mg of sodium a day, with higher rates of death in the upper and lower range. Critics of the study, such as Feng J. He and Graham A. MacGregor of the Queen Mary University of London,[131] contended that the studies included were flawed and that one had been withdrawn from the Cochrane Library.[132] However, as Graudal and team responded, the retracted paper was not part of the meta-analysis, but was a source for a data set from a different and higher quality study. Yet, that data, and many of the data sets, are limited—in the same was Strazzullo et al was—by the fact that many of the populations are non-generalizable. As Graudal et al noted, their critics often rely on the same studies to make their case that sodium should be reduced for the general population.[133]

It is always possible that higher mortality, even in these apparently healthy groups, is related to some other dietary or lifestyle factor not measured by such investigations. As a result, low sodium intake could be an effect rather than a cause leading to increased mortality. As with questions about *why* humans are driven to consume a normal sodium intake between 2,000 and 5,000 mg, research should seek to answer why lower sodium intakes are associated with higher mortality rates.

Low sodium intake could be an effect rather than a cause leading to increased mortality.

Broad public health recommendations ought to be based on the consistent results of randomized controlled trials.

In opposition to these recent findings of a J- or U-shaped curve, Nancy Cook and her colleagues at the Harvard Medical School published their own meta-analysis in 2014 and found not a curve, but a linear relationship between higher sodium and cardiovascular death. The authors concluded there was a 17 percent increased risk for every 1,000 mg increase in sodium consumption.[134] Their data were drawn from Phases I and II of the Trials of Hypertension Prevention (TOHP), clinical trials studies designed to test the effect of several non-pharmacological approaches to reducing blood pressure in people with blood pressure toward the high end of the normal range. In October 2016, Cook et al released a follow-up that reiterated what they found in 2014—no J-shaped curve in relation to sodium and mortality.[135] However, despite the existence of a trend, there was no statistically significant difference in mortality between the low sodium group and the control group.[136]

Who might benefit from sodium restriction? Randomized controlled trials (RCTs) are those in which participants are randomly assigned to either a control group—those receiving no treatment or intervention—and those in the intervention group or groups—those receiving a medication or treatment. For example, pharmaceutical trials will randomly assign patients to receive medications or a placebo; the researchers do not know to which group patients are assigned. Often, such studies will run interventions for a period of time, then the participants will be switched to the other group. This allows researchers to reduce possible bias and to isolate the effects of a given treatment apart from other factors, such as lifestyle and genetics, which might influence the outcomes of a given treatment.

Broad public health recommendations ought to be based on the consistent results of randomized controlled trials. Unfortunately, there have been only a handful of RCTs investigating the relationship between sodium and health outcomes. None of these have examined outcomes, like mortality or cardiovascular disease rates, for sodium intake at or below 2,300 mg a day.[137] However, evidence from observational studies can sometimes merit public recommendations, if the results unambiguously point to public health harm. An example of this is the connection between smoking cigarettes and cancer. While RCTs were not and, for ethical reasons, could not be performed, researchers conducting observational studies observed an unambiguous positive relationship between smoking and the development of cancer. By contrast, the results of observational studies on dietary sodium and health outcomes have been ambiguous.

The strongest evidence for a causal relationship between dietary sodium and blood pressure has been observed in one particular group: those who are already hypertensive (though there is evidence linking sodium intake and blood pressure in non-hypertensives). It is in this same group that the evidence, though weaker, indicates a possible relationship between sodium restriction and health outcomes, but again, the evidence is ambiguous.

For example, in a recent meta-analysis of evidence regarding dietary sodium's impact on health outcomes, the authors identified only five quality RCTs that looked at heart disease, stroke, or mortality.[138] Of these five:

- None observed sodium intake levels at or below 2,300 mg.
- One examined gross morbidity and found no difference between the treatment and control groups as indicated by hospitalization or death.[139]
- Two examined the risk of developing hypertension, and found that weight loss and reduced sodium intake reduced hypertension risk.[140]

Only one investigated the relationship between sodium intake and cardiovascular disease events, like stroke, heart attack, arrhythmia, and heart failure.[141] This study's participants were all pre-hypertensive elderly patients (60 to 80 years old) using anti-hypertensive medication, and more than half were obese. Researchers randomly assigned participants to regimens of a) weight loss, b) lowered sodium intake, c) a combination of lowered sodium and weight loss, or d) "usual care" (the control group). They observed that while blood pressure was significantly reduced in both the weight loss group and the sodium reduction groups—who lowered their intake to between 2,400 and 2,800 mg a day—blood pressure maintenance was best among those in the combined weight loss and sodium reduction group.[142] However, there was no significant difference in the rates of cardiovascular events between any of the intervention groups and the control group.

As noted, there is controversy surrounding the observational studies looking at sodium restriction's effect on health outcomes in both normotensive and hypertensive subjects. For example, in 1995 the American Society of Hypertension's Michael Alderman and colleagues followed a group of 2,937 individuals being treated for mild to moderate hypertension for approximately four years. They reported that mortality in the whole group, particularly in men, was inversely related to sodium intake—the lower the sodium intake the higher the associated risk of death (assessed via 24-hour urine collection).[143]

However, this study, is limited and has been criticized because participants were recruited from a hypertension lowering drug trial and instructed to restrict sodium intake in the five days leading up to the first urinary assessment.[144] Thus, it might not reflect the participants "true" normal sodium intake, and those who might have been at the greatest risk might have restricted sodium most intensely.

In a 2016 study, researchers using a single morning urine sample estimated the sodium intake for more than 60,000 normotensive and more than 60,000 hypertensive individuals in an attempt to identify risks related to various levels of sodium intake in the two populations.[145] They found that high levels of sodium intake—more than 7,000 mg a day—was associated with higher rates of cardiovascular events and death in hypertensives. They did not find this in the non-hypertensive population. On the other hand, low sodium intake (below 3,000) was also associated with increased death rates in hypertensives as well as within the normotensive population. For most hypertensive populations, whether or not sodium reduction is employed as a blood pressure reduction strategy, it likely should be done in combination with other effective therapies, including increasing dietary potassium.[146]

While the study has many of the limitations of other observational studies, the findings add to what another recent clinical trial of a blood pressure medication found: For those with the highest blood pressure (over 143 systolic), lowering pressure using medication reduced bad health outcomes, but for those in the middle and low ranges, it was unhelpful.[147] Together, they provide compelling, if limited, support to the hypothesis that only those with high blood pressure and high levels of sodium intake may see cardio-protective benefits from reducing sodium in their diet. However, hypertensives who already consume moderate or low levels of sodium may not see the same cardio-protective benefits from further reducing sodium and may even experience worse outcomes.[148]

Finally, evidence provides support for physicians to test sodium reduction in combination with weight loss for their pre-hypertensive and hypertensive patients who are overweight or obese. Based on experimental studies of non-pharmacological approaches to lowering blood pressure (such as TONE and TOHP), sodium reduction in combination with weight loss appears to be more effective for overweight hypertensives than either approach alone (though both can lower blood pressure).[149] This makes sense, since weight loss has blood pressure-lowering effects independent of dietary sodium levels. It is also possible that lowering overall caloric intake necessarily reduces dietary

sodium, so that each approach magnifies the other's effects.

Additionally, sodium reduction creating a "bland" diet may aid in weight loss, and thus blood pressure reduction. As Robert Alexander McCance, one of the first researchers to conduct sodium reduction experiments on humans, discovered in 1936, sodium restriction affects appetite. McCance and several of his medical students put themselves on a salt-free diet for about 10 days and induced sodium depletion through sweating. While their blood pressure and pulses remained stable, all the subjects experienced weight loss and a loss of appetite.[150] McCance noted that even normally unsalted foods like fruit seemed bland and that even his cigarettes were tasteless. Thus, it may be the case that moderate sodium reduction may benefit overweight hypertensives, not by reducing sodium-related blood pressure, but perhaps by inducing weight loss, which itself would lower blood pressure.

Effect of sodium restriction on healthy individuals

Graudal argued in 2016 that while randomized control trials have found a positive dose-response relationship to dietary sodium in non-hypertensive individuals who consume sodium at levels above the observed normal human range (approximately 5,700 mg a day), these studies found no such linear relationship in non-hypertensives individuals consuming sodium within the observed average human range.[151] And while some studies have found better outcomes associated with lower sodium in certain groups, like overweight[152] and obese individuals,[153] other studies have observed *worse* health outcomes at lower levels of sodium (versus average) intake in other groups. For example, two recent studies linked low sodium with higher mortality rates in those with type I[154] and type II diabetes.[155]

In 2011 Merlin Thomas of the Baker IDI Heart and Diabetes Institute in Australia and his team at the Biochemistry of Diabetic Complications Lab tracked data for type I diabetic patients for 10 years.[156] They found a non-linear (J-shaped) relationship between mortality and sodium Independent of age, sex, kidney disease, and other factors. They observed that diabetic patients were more likely to die if they had very low or very high sodium intake.

Similarly, Elif Ekinci and her team at the Endocrine Centre at the University of Melbourne tested 24-hour urine samples of more than 600 type II diabetics and measured their health for nearly 10 years.[157] They also found that sodium was linked to higher mortality rates in an *inverse* linear fashion. That is, Ekinci et al observed that the lower the sodium excretion in their type II diabetics, the higher their risk for dying.

It may be the case that moderate sodium reduction may benefit overweight hypertensives, not by reducing sodium-related blood pressure, but perhaps by inducing weight loss, which itself would lower blood pressure.

Sodium reduction, for certain hypertensives, may do more harm than good.

As noted, some research even indicates that sodium reduction, for certain hypertensives, may do more harm than good. At least one study found that men being treated for hypertension were more at risk of having a heart attack if their sodium intake was lower, though this study was limited by the fact that participants were instructed to "avoid high sodium foods" prior to being tested. It is possible those at the highest risk were most motivated to restrict sodium prior to the test.[158] Still, the growing body of evidence of possible harmful effects of sodium restriction among diabetics—a group into which nearly 30 million Americans fall[159] calls for "caution before applying salt restriction universally," as Thomas and his team wrote in the conclusion of their study.[160]

Researchers have also observed some worrying effects of sodium restriction on generally healthy populations, such as potentially harmful changes to blood lipid profile. For example, in 2011 Graudal and his team reviewed the effects of low sodium diets on blood pressure, cholesterol, and triglycerides among other health markers.[161] They found that low sodium diets (below 2,700 mg) correlated with a lower systolic blood pressure (by 1 or 2 points), but was also linked to a 2.5 percent increase in cholesterol and a 7 percent increase in triglycerides. Other studies have also found that sodium reduction in healthy individuals can result in higher levels of insulin[162] and may increase insulin resistance, which has been implicated in the development of diabetes and cardiovascular disease.[163]

Heterogeneous blood pressure response to sodium

While many factors, such as diet and lifestyle, may affect why individuals with lower sodium intake have worse health outcomes, one aspect is gaining increased attention from the scientific community: the fact that people do not always have the same blood pressure response to sodium.

For decades, researchers have observed that certain individuals will have a much more significant change in blood pressure when the level of dietary sodium is altered. Those whose blood pressure is prone to increase as sodium in the diet increases are referred to as "salt sensitive." Those whose blood pressure increases when sodium in the diet is *decreased* are deemed "inverse salt sensitive." Most people, however, are "salt-resistant," and will see no, or minimal changes in blood pressure with even very large increases or decreases in sodium intake. The breakdown of these various salt-response types within populations is unknown, but one expert on salt sensitivity, Robin A. Felder of the University of Virginia, estimates that about three quarters of people are salt resistant and thus will have little or no blood pressure change in response to dietary sodium changes,

while 17 to 25 percent are salt sensitive and about 11 percent are inverse salt sensitive.[164]

Cause of salt sensitivity. The reasons why certain individuals might be salt sensitive and the mechanism for how it increases blood pressure are not well understood. Salt sensitivity may be caused by multiple intertwining factors, such as kidney damage, hormonal imbalance, blood vessel problems (endothelial dysfunction), and central nervous system malfunction.[165] Underlying these theories is the general consensus that salt sensitivity is in a person's genes, though the trait might only be expressed under certain conditions. As Lewis K. Dahl began his seminal study of salt and hypertension in the 1960s, he suspected a genetic role in the development of the disease. To test the theory, he separated experimental rats into groups based on their blood pressure responses to dietary sodium and bred like-responders together—insensitive rats with insensitive rats and salt-sensitive rats with other salt-sensitive rats. By doing this, Dahl was able to predictably breed generations of rats that were highly sensitive to changes to sodium in the diet or completely resistant to dietary sodium—now known as Dahl salt-sensitive rats and Dahl salt-resistant rats, breeds that are still used today in clinical testing.[166]

So while the genetic variants involved in salt sensitivity and how they operate are not yet well understood, there are some theories for particular genes. For example, the expression of some genes has been associated with a reduced ability for the kidneys to excrete sodium. These genetic variations could provide an explanation why certain populations, like those of African descent, are more sensitive to blood pressure changes related to salt intake and are more likely to develop hypertension.[167] For example, genes known to cause impaired sodium excretion have been found to be more common in black South Africans than in their white compatriots.[168]

Another compelling emerging theory about the genesis of salt-sensitivity involves the gut microbiome—the community of bacteria that live in the digestive tract.[169] These microbes are responsible for numerous beneficial processes within guts, including breaking down undigested food into useful energy sources, synthesizing vitamins, and maintaining immunity in the gut to prevent inflammation. However, researchers are increasingly investigating the possibility that imbalance within this community of microbes may lead to disorders, including diabetes, allergies, obesity, and hypertension.[170]

For example, suspecting that certain bacteria might be able to inhibit the renin-angiotensin-aldosterone system, researchers tested the effect of milk fermented with *Lactobacilli helveticus*

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Salt sensitivity should be an important part of the discussion about dietary sodium and health.

(*L. helveticus*) or a placebo on hypertensive patients. After 21 weeks of use, researchers observed a mean drop of 6.7 points in systolic pressure and 3.6 points in diastolic pressure among those drinking the lactobacilli-laced milk.[171] Similar studies with this strain of lactobacillus have found similar results, such as one published just this year that gave hypertensive patients a small (30 gram) daily ration of Grana Padano, an aged Italian cheese fermented with *L. helveticus*.[172] As with the milk, the cheese-eating hypertensive patients lowered their blood pressure by five to sixs points compared with the placebo.[173]

Whatever its cause, salt sensitivity should be an important part of the discussion about dietary sodium and health. For individuals and populations, sensitivity, resistance, or inverse sensitivity will impact how helpful or potentially harmful sodium restriction may be as a matter of public policy. Most likely, salt sensitivity is caused by a combination of genetic predisposition and environmental exposure. This complex and, likely unique, interplay between risk factors underscores why sweeping recommendations may not be appropriate for large swaths of the population.

What does all this research mean?

Though some researchers continue to insist there is broad agreement about the health impacts of sodium reduction for the general population, there is high-quality evidence challenging this position. While hypertensives—especially those who are salt sensitive and especially those who consume much more than the average level of sodium—may benefit from reducing salt in their diet, plenty of research suggests that for the majority of the population, lowering sodium will not have positive impacts on blood pressure or cardiovascular outcomes. In some, such as type I[174] and type II diabetics (10 percent of the American population), sodium restriction may result in worse health outcomes.[175]

This uncertainty calls for caution in making population-wide recommendations and calls for randomized controlled trials examining the actual health effects of reducing sodium intake from the average to the low level recommended by government and health agencies for healthy individuals.

While there is much research suggesting that dietary salt levels influence human health, *how* it influences health, *how much* is optimal, and *for whom* salt reduction may benefit or harm is far from clear. Thus, the current U.S. effort attempting to push everyone to lower sodium to a level almost unheard of in human populations is, at best, useless. At worst, it may be influencing Americans to alter their diets in a less healthy way.

Alternative Approaches to Combating Hypertension

While the body of research on sodium may be inconclusive, many of the studies looking at sodium's effect on blood pressure—even though they disagree on the sodium's effect—have consistently observed that a different dietary ingredient may play just as important a role in health outcomes as sodium, if not more: potassium. In addition to addressing other factors associated with the development of hypertension, like as obesity, chronic dehydration, and gut microbiome imbalance, correcting potassium deficiency presents a promising new avenue for treating and preventing hypertension.[176]

While the purpose of Strazzullo's study was to examine studies looking at the relationship between sodium and cardiovascular risk, five of the 13 studies it analyzed also considered the role of potassium and found an *inverse* relationship between mortality and poor health outcomes and potassium in the diet.[177] Of the additional 12 studies considered by Graudal in 2014, three examined the relationship between potassium and blood pressure and found that either higher potassium intake or a lower potassium-to-sodium ratio (meaning the amount of potassium was closer to being on par with sodium intake) was associated with lower risk of cardiovascular disease, stroke, and death.[178]

The 2013 Prospective Urban Rural Epidemiology study by O'Donnell and colleagues found that potassium intake seemed to be *inversely* associated with overall mortality—the higher the potassium intake, the less likely participants were to die from cardiovascular or other causes.[179] Similarly, Cook et al, in their most recent analysis, found a linear relationship between increasing sodium and poor health outcomes, but they also found that the sodium-potassium ratio was an even stronger predictor of health outcomes.[180]

Researchers have long suspected that other nutrients, including potassium, calcium, and magnesium, may play a role in blood pressure and health outcomes. Despite increasing evidence of their role, little attention has been given to them in public policy seeking to lower population blood pressure, though it might be easier to *increase* one or all of these nutrients than it would be to significantly lower sodium.

For example, one 2003 study found that increasing potassium intake by about 1,700 mg intake was virtually as effective in reducing blood pressure as cutting salt intake by 1,700 mg a day.[181] Increasing potassium and intake of other minerals is demonstrably effective at lowering blood pressure in the elderly,[182] among black patients,[183] and individuals who are not hypertensive.[184] This is a significant finding because,

It is not high blood pressure, generally, that kills people, but associated events, such as heart attack and stroke.

according to the CDC, 98 percent of the U.S. population is potassium deficient, leading one to wonder if nutrient deficiency, as opposed to sodium excess, might be a cause of elevated blood pressure.[185] Evidence indicates that this deficiency, at least in certain populations, may play a role in hypertension as well as in the development of other disease like diabetes and metabolic syndrome.[186] Furthermore, recent research into the dietary guidelines finds that meeting the minimum requirement for potassium while adhering to the recommended maximum for sodium is virtually impossible, since many potassium-rich foods also contain significant levels of sodium.[187]

Body mass is another major predictor of hypertension.[188] This is especially important for those of African heritage who are both at higher risk for hypertension and for being overweight or obese than non-Hispanic whites.[189] In fact, studies that have examined the effect of both sodium and weight reduction on blood pressure found that weight loss had a more significant effect on blood pressure over time than did sodium reduction—though a combination was more effective than either approach alone.[190]

Chronic dehydration is another theory that seeks to explain why hypertension and other diseases are so prevalent in Western societies beyond sodium intake. For example, hypertension researcher Simon N. Thornton, of the University of Lorraine in France, suggests that even the most heroic efforts to curtail sodium intake would do nothing to stop the activation of the renin-angiotensin-aldosterone-system—and thus, the activation of hormones implicated in vasoconstriction, hypertension, and poor health outcomes—unless low blood volume was remedied. This is a thought-provoking theory because RAAS, and potentially elevated blood pressure, may be triggered by chronically low blood volume resulting from dehydration. And recent research indicates that the hormones released by RAAS are associated with such complications, independent of their effect on blood pressure.[191] Evidence supporting the idea that increased fluid intake results in long-term reductions in water is scarce. But, as noted, it is not high blood pressure, generally, that kills people, but associated events, such as heart attack and stroke.

There is some evidence that increased water intake is associated with better cardiovascular outcomes, regardless of its effect on blood pressure. For example, higher levels of water seems to be inversely correlated with fatal coronary heart disease (that is, people with higher water intake are less likely to have coronary heart disease)[192] and mortality rates following a stroke.[193] According to the Centers for Disease

Control and Prevention, as much as 75 percent of Americans do not drink enough water and may be chronically dehydrated.[194] Considering the interplay between water, blood volume, RAAS, and sodium, it is plausible that chronic dehydration plays a role in hypertension-related outcomes. Along with increased consumption of potassium-rich vegetables and fruits, increased water intake may provide a novel strategy to reduce hypertension-related risks in the general population.[195]

In the wake of increasingly conflicting research and 40 years of public policies apparently failing to alter American's sodium intake levels, such approaches merit consideration as a means of lowering hypertension risk and health improvement at the population-level.

Conclusion

Considering the difficulty and limited success of sodium reduction efforts, the uncertain health outcomes that could result from large sodium reductions, and the robust clinical evidence pointing toward the effectiveness of alternative approaches, potassium consumption, weight loss, and water intake should be given much more attention in government recommendation for population-wide hypertension advice than is the current practice.

When it comes to sodium and health, we know disappointingly little. However, there is ample evidence to indicate that individuals' response to sodium is contextual. Some people respond well to sodium restriction, while others might have negative outcomes, and the majority of people have no response at all. This emerging evidence, though neither perfect nor definitive, should give health agencies pause before making blanket recommendations on salt or hypertension-risk reduction.

The best way to prevent or treat hypertension is to create individual plans that accounts for a person's unique genetic makeup and lifestyle and to monitor the effects of such changes. For some people, such as older hypertensives consuming very high levels of salt, this plan might include sodium restriction. However, based on current evidence, sodium restriction is not effective for blood pressure reduction in the majority of people and does not impart health improvements. Yet, the continued focus on this approach has obscured other strategies, particularly increasing potassium, which has been repeatedly shown to be effective at lowering blood pressure. With our currently limited understanding of what drives our salt intake, the benefits high sodium diets may have, and what effects low salt diets might have on individual and population health, our current policy of pushing sodium reduction to the entire population is ineffective.

The best way to prevent or treat hypertension is to create individual plans that accounts for a person's unique genetic makeup and lifestyle and to monitor the effects of such changes.

Based on the evidence that does exist, government agencies and health organizations—if they are going to do anything—should refocus attention away from a salt-only approach and instead emphasize dietary strategies that promise to result in net benefits for a larger portion of the population and are unlikely to cause negative unintended consequences. Advising people to consume much more of their daily calories from fruits and vegetables, which would increase potassium and other nutrient intake, based on current research, would likely result in lower blood pressure for a larger portion of individuals without having negative unintended consequences. An approach focused on increased water and potassium via fruits and vegetables may be easier for consumers to follow than significant sodium reduction and promises to have health benefits in addition to blood pressure reduction.[196]

NOTES

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