**CAHS website posting**

*“The Alignment of National/International Sodium Guidelines with Current Evidence” – A CAHS Forum*

On May 14-16, 2014, the CAHS co-convened (with the World Heart Federation [WHF] ) a Consensus Conference on Nutrition, held at the Population Health Research Institute of McMaster University and Hamilton Health Sciences. In a series of expert presentations followed by extensive discussion and debate, the invited participants examined current research and knowledge about the effects on cardiovascular events of a wide range of dietary nutrients. The WHF and the CAHS had put in place explicit guidelines in regard to conflict of interest, financial sponsorship, and program committee responsibilities (publically available on the conference website [**http://www.nutritioncvd2014.com/body.cfm?id=1**](http://www.nutritioncvd2014.com/body.cfm?id=1) ).

CAHS took responsibility for a Symposium on Dietary Sodium: “*The Alignment of National/International Guidelines with Current Evidence*,” while the WHF managed other nutrients. In the sodium portion of the meeting, the agenda included speakers from the Global Burden of Diseases Group, the Canadian Sodium Working Group, the WHO Sodium Guidelines Group, and the American Heart Association Guidelines Committee. Their presentations provided essential context for presentations of new data (including the June 2013 report of the IOM Sodium Intake in Populations Expert Panel) challenging some of the evidence for recommendations for stringent restriction of dietary sodium.

**Summary of Points with Reasonable Levels of Agreement among Speakers**

**Stuart MacLeod**, MD, PhD, FRCPC of University of British Columbia, a fellow of CAHS who is a clinical pharmacologist, chaired a workshop of the speakers on dietary sodium on the third day of the meeting and was charged with developing a summary of the dietary sodium proceedings. **John Cairns**, MD, FRCPC, the President of CAHS who is a cardiologist, was a member of the conference organizing committee and worked with Dr MacLeod on the preparation of the summary.

MacLeod and Cairns are recognized for their research in fields outside of nutrition and the relationship of dietary sodium to blood pressure and cardiovascular events. Neither of them identifies a conflict of interest arising from public views about dietary sodium, participation in the guidelines of national agencies for dietary sodium, conduct of dietary sodium research or research support or compensation from the food industry. In the following they attempt to summarize the salient points around which they perceived reasonable levels of agreement among the participants in the meeting, although no formal consensus of views was undertaken.

1. Elevated blood pressure increases the risk of cardiovascular events (MI, stroke, CV death).
2. Most published reports indicate a positive association between dietary sodium intake and blood pressure
3. Observational studies generally have shown that excessive dietary sodium intake is associated with increased rates of cardiovascular events
4. Comprehensive assessment of national and subnational dietary surveys and 24-hour urine collections, find that sodium intake is high in every region of the world, and is especially high from Eastern Europe through to Southeast Asia.  In the majority of countries intake exceeds 3 g/d, and in about half of countries it exceeds 4 g/d. Average intake by adults in Canada is estimated at 3.4g of sodium daily; 85% of men and 60-80% of women consume more than 2300 mg/day.
5. In the 25% of the population with a blood pressure above 131/78 mmHg sodium reduction reduces blood pressure up to a mean of 5.5/3.0 mmHg depending on baseline blood pressure. In the 75% of the population with a blood pressure below 131/78 mmHg there is a minimal effect of sodium reduction on blood pressure.
6. Reduction of blood pressure by lowering dietary sodium is a surrogate for reduced cardiovascular events. There is epidemiological evidence for reduced CV events by lowering excessive dietary sodium, but no consistent evidence for the benefit of lowering dietary sodium below 3400 mg/day. There are many deficiencies identified in the observational trials, including unreliable measurement of 24 hr. urinary sodium, confounding by other nutrients and antihypertensive medications, and use of blood pressure as a surrogate for CV events.
7. There is no consistent RCT evidence for reduction of CV events by reducing dietary sodium. The complexities and costs of large and definitive RCTs have deterred efforts to mount such trials.
8. Most government agencies recommend dietary sodium intake be reduced to 2000-2300 mg/day, with recommendations as low as 1500 mg/day for those at higher than average risk of CV events.
9. There is some evidence indicating a “J-“ or “U- shaped” relationship between dietary sodium and CV events, with excess CV events occurring at levels not only above, but also below an optimal range. The precise limits of this range cannot be identified on the basis of available data. There are unresolved concerns about potential “reverse causality” in relation to low sodium takes.
10. The IOM report concluded a) there is a positive relationship between higher levels of sodium intake and risk of CVD, consistent with existing evidence on blood pressure as a surrogate marker of CVD risk, b) evidence from studies on direct health outcomes is insufficient and inconsistent regarding an association between sodium intake below 2300 mg/day and either risk or benefit of CV outcomes and c) direct evidence on health outcomes does not support recommendations to lower sodium intake within subgroups (diabetes, chronic renal disease, pre-existing CVD) to 1500 mg/day or less.
11. It seems likely that people consuming more than 3.4 g of sodium per day could safely reduce their intake.
12. The most important source of excess sodium intake on a population basis is through processed food. There is general agreement as to the likely public health benefits of reducing sodium in the food supply and the unlikelihood of harm even to those whose dietary sodium intake is already lower than average.
13. Legitimate scientific debate about the evidence supporting national dietary guidelines is essential to the advancement of knowledge, but may place the public health efforts of government agencies at risk by engendering uncertainty and confusion in the public and among physicians. Leading scientists should be encouraged to reach agreement on major elements of the evidence and support efforts to lower excessive sodium intake.

All sodium speakers were asked to identify the key points in regard to their topic. These were submitted by all but 2 of the speakers, whose key points were inferred from their publically available summary slides [**http://www.nutritioncvd2014.com/body.cfm?id=1**](http://www.nutritioncvd2014.com/body.cfm?id=1) ).

**The following is a listing of the sodium symposium speakers, the titles of their talks, and the key messages they have identified to the meeting working group (or summarized in their slide presentations)**

1. **Dariush Mozaffarian**

**Harvard School of Public Health.**

**“The American Dietary Sodium Guidelines from the Global Perspective”**

• Based on a new meta-analysis of RCTs, sodium intake is linearly associated with higher BP, with stronger effects at older ages, in Blacks, and among those with high BP.

• Based on our comprehensive assessment of national and subnational dietary surveys and 24-hour urine collections, sodium intake is high in every region of the world, and is especially high from Eastern Europe through to Southeast Asia.  The majority of countries in the world exceed 3 g/d, and about half exceed 4 g/d.

• While optimal levels of sodium intake are difficult to determine precisely, based on observed associations between sodium intake and CVD and gastric cancer, and on established effects of sodium on BP, optimal intake of sodium is approximately 2 g/d.

• Based on current sodium intakes, the influence of sodium on BP, the relationship of BP to CVD, and current rates of CVD, all assessed in subgroups by country, time, age, and sex, 1.65 million CVD deaths/year are attributable to sodium intake > 2 g/d.

• Four in 5 of these deaths occur in low and middle income countries, and 2 in 5 occur prematurely (< age 70).

Mozaffarian D, Fahimi S, Singh GM, et al. Global sodium consumption and death from cardiovascular causes. N Engl J Med 2014;371:624-34.

**(2) Mary L’Abbé**

**University of Toronto.**

**“Guidelines for Canada and the WHO”**

 The following key messages were inferred from Dr L’Abbe’s summary slide:

* Lowering sodium intake reduces blood pressure in adults and children and has no adverse effect on blood lipids, catecholamine levels, or renal function.
* Evidence from prospective cohort studies showed a positive association between sodium intake and stroke, fatal stroke and fatal coronary artery disease events – (although all the evidence was graded as LOW or VERY LOW)
* WHO Recommendations resulting from evidence review:

 Less than 2000 mg sodium/day to reduce blood pressure in adults

 A maximum of 2000 mg sodium/day to control blood pressure in children

 Applies to all individuals except for clinical populations excluded from the analysis

 Is based on high quality data from trials on blood pressure. Evidence on direct health outcomes was of lower quality.

WHO. Guideline: Sodium intake for adults and children. Geneva, World Health Organization (WHO), 2012. [www.who.int/publications/en](http://www.who.int/publications/en)

**(3) Jamy Ard**

**Wake Forest School of Medicine.**

**The IOM Report: Sodium Intake in Populations: Assessment of Evidence**

• The IOM Consequences of Reducing Sodium Intake in Populations Report was a direction function of the task assigned by the Centers for Disease Control (CDC) which identified the following key objectives: (1) summarize the quality of literature reviewed; (2) comment on the benefits and adverse consequences of reduced population sodium intake, particularly to levels of 1,500 to less than 2,300 mg/day; (3) speak specifically to key demographic and disease affected sub-groups; (4) discuss implications for population-based strategies to reduce sodium; and (5) identify gaps in data and methodology and propose ways to address them.

• In response to its charge, the committee focused its examination of evidence on the associations between dietary sodium intake and direct health outcomes, with the preponderance of evidence available being outcomes related to cardiovascular disease events and mortality.

• The key questions that guided the literature search were “What is the effect of reducing dietary sodium intake in (1) all individuals compared to habitual intake on health outcomes; and (2) individuals with hypertension, pre-hypertension, those aged 51 years and older, African Americans, and individuals with diabetes, chronic kidney disease, or congestive heart failure compared to habitual intake on health outcomes?”

• The committee was unable to define quantitatively high or low sodium intakes because of wide ranging differences in methodologies and a lack of consistent definitions across studies. Therefore, sodium intake was qualitatively defined within the context of each study.

• The committee concluded that the available evidence was consistent with efforts to reduce excessive sodium intake, but it was not consistent with previous efforts to lower sodium to 1,500 mg per day (i.e., a specific target). Furthermore, there was no specific evidence found to support treating specific sub-groups differently from the general population.

• The effects of reducing sodium intake on blood pressure are clear. However, the ideal sodium intake for optimal health and minimal adverse health effects is not clear from literature reviewed.

Institute of Medicine. Sodium intake in populations: assessment of evidence. 2013. Washington, DC: National Academies Press, May 2013 (http://www.iom.edu/Reports/2013/Sodium-Intake-in-Populations-Assessment-of-Evidence.aspx).

**(4) Theodore Kotchen**

**Medical College of Wisconsin.**

**“Mechanisms of NaCl-induced Increases in Blood Pressure and CVD”**

• Salt sensitivity of blood pressure is primarily related to a “natriuretic handicap”, due to:
a) intrinsic renal pathology
b) extrinsic influences such as aldosterone, sympathetic nervous system activity

• High NaCl intakes are associated with an increased prevalence of CV disease, due primarily to blood pressure

• NaCl reduction results in lower blood pressure and a decreased incidence of CV disease

Kotchen TA, Cowley AW, Frohlich ED. Salt in health and disease – A delicate balance. N Engl J Med 2013;368(13):1229-37.

**(5) David McCarron**

**University of California-Davis:**

 **“Normal Range of Human Sodium Intake”**

**and**

**(6) Michael Alderman,**

**Albert Einstein College of Medicine:**

**“Dietary Sodium and Cardiovascular and All-Cause Mortality”**

2013 IOM Report – Sodium Intake in Populations

 - BP is surrogate for CVD, but not Na+ effect on morbidity/mortality (M/M)

 - BP is one of several physiologic consequences of Na+ intake

 - BP and M/M are discordant in many outcome studies

• “Excess” Na+ is to be avoided, but level was undefined

• Subpopulations should be treated in the same manner as general populations

• Evidence of harm in subgroups from sodium intakes <1500mg/d

• Insufficient/inconsistent data as to benefit/harm from Na+ <2300 mg/d

Published Data Subsequent to IOM Report

• Outcomes data has defined –“Excessive,” deficient and optimal range

 - Meta-analysis of 25 studies of M/M …..Graudal et al

 - Three new reports …consistent with Graudal et al

 - Presentation of PURE Study…O’Donnell et al (publication pending)

 - Optimal range 2600-5000 mg/d…mean 3700-3800 md/d

 - Deficient <2600 md/d……Excessive > 5000 mg/d

• Populations surveys, RCT’s and physiology have identified a healthy urinary sodium range

 - Normal range–overlaps that defined by morbidity/mortality outcomes data

 - US / worldwide Na+ intake is well within this normal range

 - Sodium content of food supply does not dictate intake

 - UK initiative has significantly reduced foodNa+,but not intake

Physiology of Na+ Impact on CV Regulation and Na+ Appetite

• Modulation through RAS and Aldosterone

• Other cations and anions (K+, Ca2+, Mg2+, Cl-)modulate Na+ BP effect

• Neural circuits responsive to Angiotensin II and Aldosterone regulate Na+ appetite

• Renin levels predict mean of optimal intake – 3600 mg/d

• Renin and aldosterone levels increase exponentially at intakes <2600 mg/d

Policy Implications

• Modify worldwide Na+ guidelines to reflect current science

 - Following Dietary Reference Intake Guide-IOM (2006) for defining a dietary reference intake (DRI)

• Establish 2600 to 5000 mg/d as healthy range

 - Avoid intakes below 2600 and above 5000md/d

 - Guideline is for all populations

• New guidelines should only be modified by consistent/sufficient data that:

 - Abrogate the Findings and Conclusions of the 2013 IOM Report

 - Counter the supporting data published subsequently

Alderman MH. Reducing dietary sodium. The case for caution. JAMA 2010; 303: 448-9.

**(7) Niels Graudal**

**Copenhagen University Hospital.**

**“Association of Sodium Intake with Health Outcomes and Surrogate valuables; Focus on reducing sodium intake below 2300mg”**

• In the 75% of the population with a blood pressure below 131/78 mmHg there is a minimal effect of sodium reduction on blood pressure.

• In the 25% of the population with a blood pressure above 131/78 mmHg sodium reduction reduces blood pressure up to a mean of 5.5/3.0 mmHg depending on baseline blood pressure.

• Sodium reduction increases renin, aldosterone, noradrenalin, cholesterol and triglyceride independently of baseline blood pressure.

• In the general population a low sodium intake below 2600 mg is associated with increased cardiovascular disease and all-cause mortality.

• In the general population a high sodium intake above 4900 mg is associated with increased cardiovascular disease and all-cause mortality.

• In the general population the lowest frequency of cardiovascular disease and all-cause mortality is found in persons with a sodium intake in the range of 2600-4900 mg.

Graudal NA, Hubeck-Graudal T, Jürgens G. Effects of low sodium diet vs. high-sodium diet on blood pressure, renin, aldosterone, catecholamines, cholesterol, and triglyceride (Cochrane Review). Am J Hypertens 2012;25:1-15.

**(8) Martin O’Donnell**

**National University of Ireland.**

 **“Recent observations - PURE and other data”**

* Low sodium, compared to moderate intake, is associated with activation of the RAAS when sodium intake falls below 3g/day. Prospective cohort studies, reporting a J-shaped association between sodium intake and CVD/mortality, report an increased risk of CV events below 3g/day (versus moderate intake).
* Sodium is a physiological requirement, a nutrient that is essential to normal human physiology. Accordingly, intake recommendations should target a ‘range’ of optimal intake, rather than a threshold (e.g. <1.5g/day)
* No large randomized controlled trials have been completed, and none are underway, to determine whether lowering sodium intake below moderate/average intake range reduces mortality or cardiovascular events.
* In people with high sodium intake, lowering sodium intake will lower blood pressure without activating RAAS. There is a generally consistent association between high sodium intake (compared to low or moderate intake) and an increased risk of death and CV events. Therefore, there is good evidence to support benefit and none to suspect harm, for reducing high sodium intake.
* In people consuming a moderate sodium intake (2.3-4.6g/day), lowering sodium intake will lower blood pressure (modestly) and activate RAAS. No prospective cohort study has reported a lower risk of mortality or cardiovascular events in groups consuming low sodium intake (<2g/day), compared to moderate intake, in the overall cohort. Therefore, there is conflicting evidence as to whether there is a benefit of lowering sodium intake in this group to low intake levels, which is particularly an issue for those with normal blood pressure, as there is likely to be no benefit from lowering their blood pressure. Lowering sodium intake within the moderate range would appear reasonable in those with hypertension.
* There is no population that has achieved a mean sodium intake recommended by current guidelines, other than niche hunter-gatherer populations. Therefore, there is a major question about whether achieving a target of low sodium intake (<2g/day) is feasible.
* Evidence from observational research studies are an important part of developing guidelines for an essential nutrient such as sodium.

O’Donnell MJ, Mente A, Rangarajan S, et al. Urinary sodium and potassium excretion, mortality, and cardiovascular events. N Engl J Med 2014;371:612-23.

**Dr O’Donnell created the following chart in an attempt to depict areas of Consensus and Uncertainty**

|  |  |
| --- | --- |
|  | **Systolic Blood Pressure** |
| <130mmHg | 130-140mmHg | >140/90mmHg |
| **Sodium Intake** | >4.6g/day(>2 teaspoons salt) |  |  |  |
| 2.3-4.6g/day(1-2 teaspoons salt) |  |  |  |
| < 2.3g/day(< 1 teaspoon salt) |  |  |  |

|  |  |
| --- | --- |
|  | Consistent evidence and consensus on clear need for sodium reduction |
|  | Inconsistent evidence, but most agree that modest sodium reduction may be reasonable within this range in those with hypertension |
|  | Very inconsistent and conflicting evidence. No consensus on whether sodium should be reduced to this range in any population  |

**(9) Lawrence Appel**

**Johns Hopkins Medical Institutions.**

**“The case for population-wide sodium reduction”**

The following key messages were inferred from Dr Appel’s summary slide:

* Elevated blood pressure is the leading cause of preventable death worldwide
* Reduced sodium intake lowers BP in a dose response fashion, with greater BP reductions when Na < 2,300 mg/d
* Major methodological issues limit the usefulness of recent studies as a basis for guiding policy, much less reversing recommendations
* The estimated benefits of sodium reduction are substantial and warrant major public health efforts to reduce salt intake
* Prevailing recommendations align with best evidence and do not warrant any change in policy

Appel LJ, Frohlich ED, Hall JE et al. The importance of population-wide sodium reduction as a means to prevent cardiovascular disease and stroke: A call for action from the American Heart Association. Circulation 2011; 123:1138-43.