AHRQ Evidence Review: Effects of Sodium and Potassium Intake on Chronic Disease Outcomes and Related Risk Factors

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Disclaimers and Disclosure

- This presentation is based on my experiences in conducting systematic reviews to support development of DRIs under contract to the Agency for Healthcare Research and Quality (AHRQ).
  - DRAFT Evidence Report (Effects of Dietary Sodium and Potassium Intake on Chronic Disease Outcomes and Related Risk Factors) is being revised to address peer and public review comments
- I'm a coauthor of the evidence report. None of the authors can answer inquiries regarding the report directly.
- The views expressed in this presentation are my own, and should not be construed as an official endorsement by the AHRQ or the U.S. Department of Health and Human Services.
- I have no COIs to disclose.

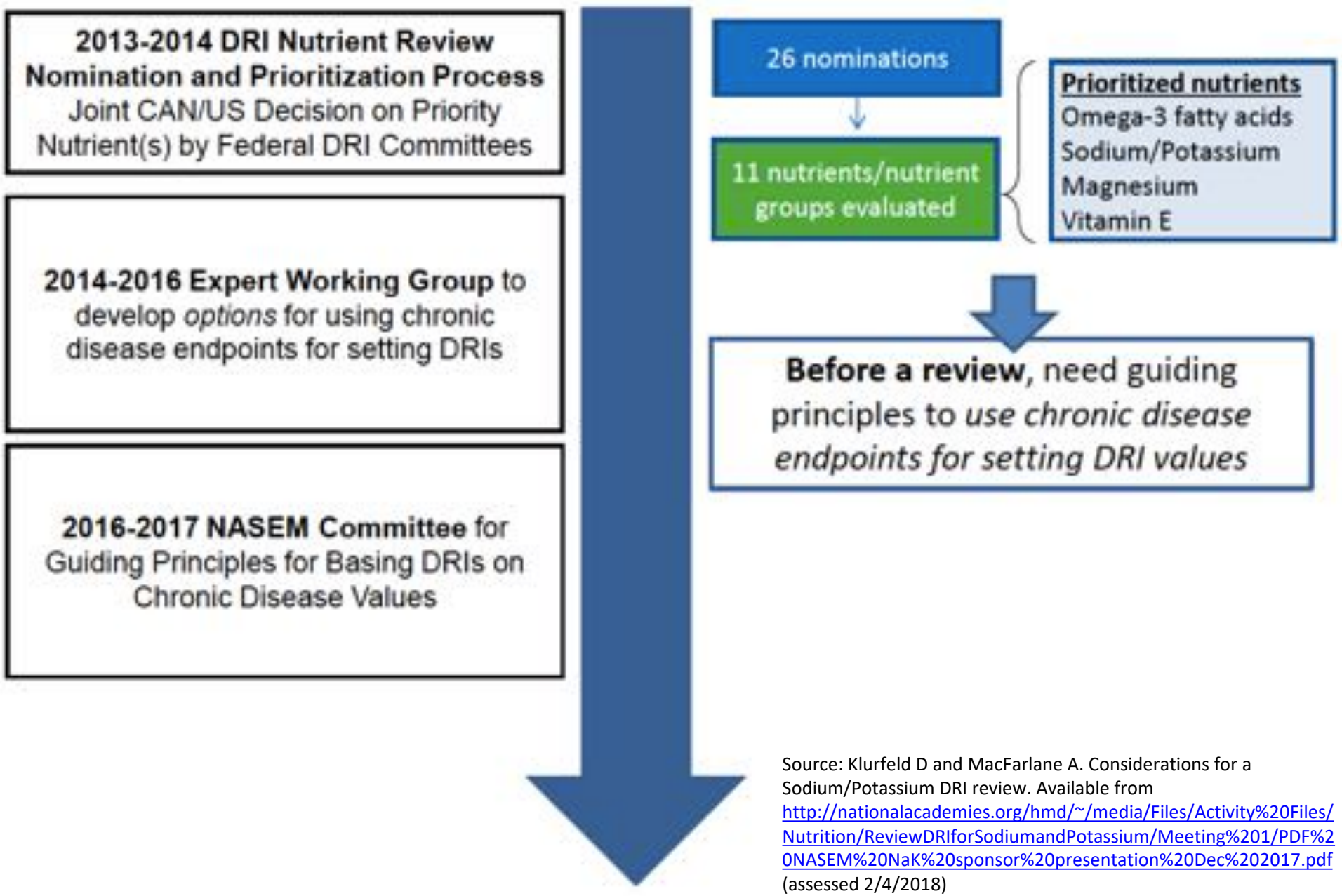
Background (I)

- Dietary Reference Intakes (DRIs) are nutrient reference values that support many program, policy and regulatory initiatives.
- These values, which vary by age and gender, include:
  - Recommended Dietary Allowance (**RDA**):
    - average daily level of intake sufficient to meet the nutrient requirements of nearly all (97%-98%) healthy people.
  - Adequate Intake (**AI**):
    - established when evidence is insufficient to develop an RDA and is set at a level assumed to ensure nutritional adequacy.
  - Tolerable Upper Intake Level (**UL**):
    - maximum daily intake unlikely to cause adverse health effects.

Background (II)

- DRIs are set based on an expert consensus process.
  - ad hoc committees convened by the Food and Nutrition Board of the Health and Medicine Division (formerly Institute of Medicine) of the National Academies of Sciences, Engineering, and Medicine (NASEM)
  - "Traditional DRIs" are (often, not always) set based on nutrient adequacy endpoints using a risk assessment framework: need dose-response trials to set EARs
- The commission of a systematic (evidence) review for nutrients under review is now an integral part of the DRI process.
  - Vitamin D & Calcium (2010): first DRIs incorporated a SR in the process
  - Sodium & Potassium (2017 to present)

Using Chronic Disease Endpoints for Setting DRIs



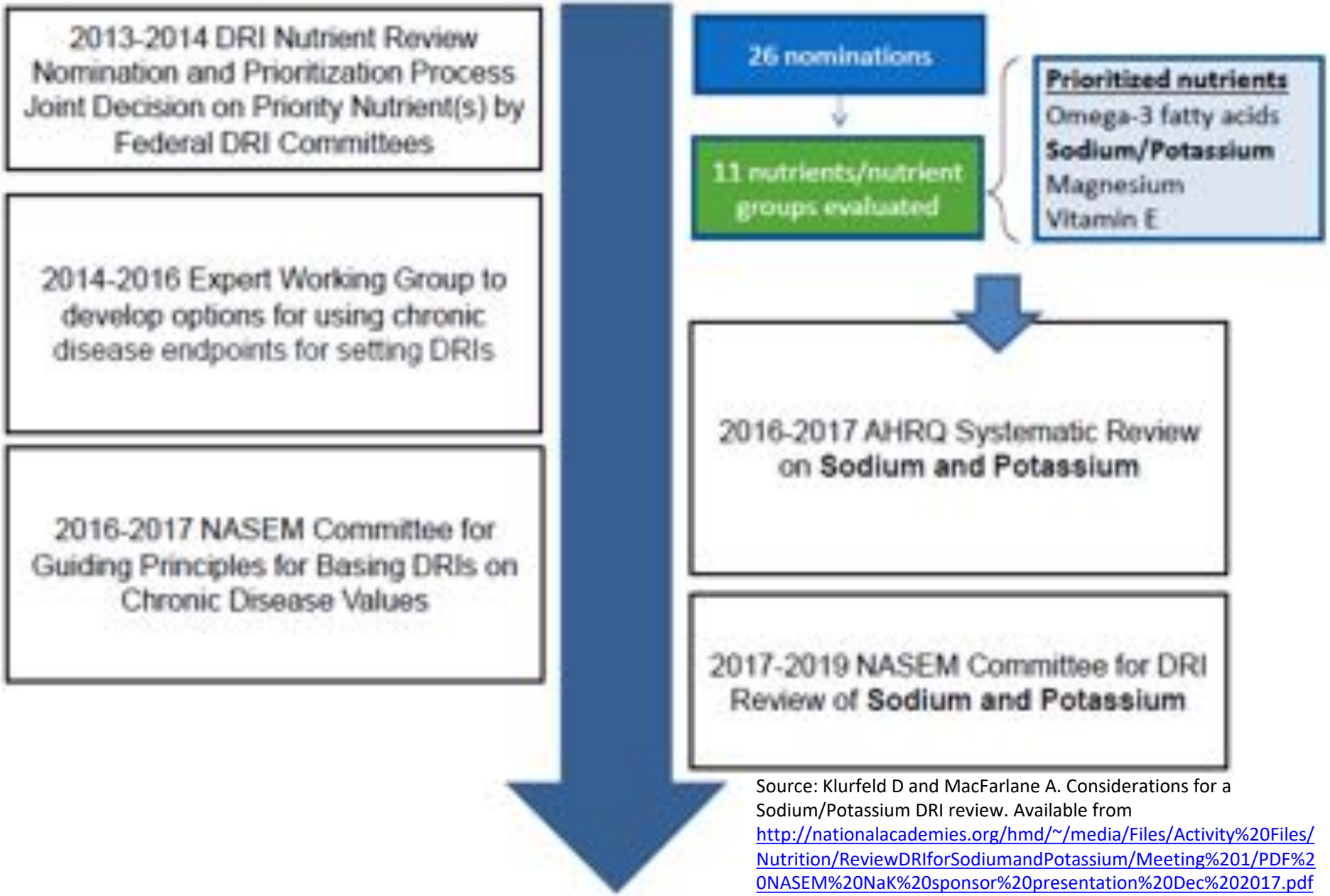
Source: Klurfeld D and MacFarlane A. Considerations for a Sodium/Potassium DRI review. Available from http://nationalacademies.org/hmd/~/media/Files/Activity%20Files/Nutrition/ReviewDRIforSodiumandPotassium/Meeting%201/PDF%20NASEM%20NaK%20sponsor%20presentation%20Dec%202017.pdf (assessed 2/4/2018)

Methods for Setting "Chronic Disease DRIs"

- NASEM Guiding Principles for using chronic disease endpoints (August 2017): potential use of observational evidence

Source: http://www.nationalacademies.org/hmd/Activities/Nutrition/ChronicDiseaseEndpointsinFutureDRIs.aspx

Independent Systematic Review to Support the Development of Sodium and Potassium DRIs



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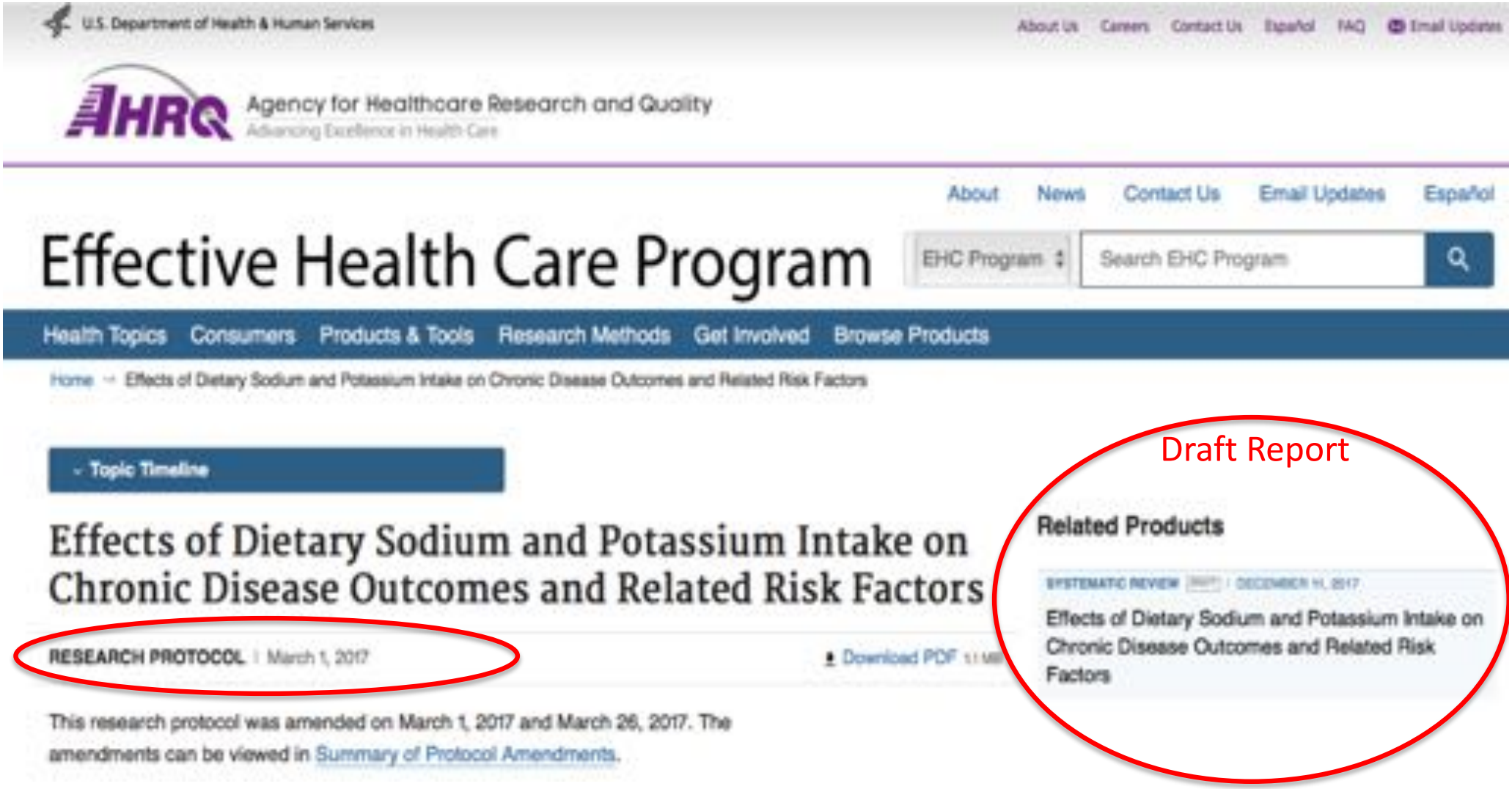
Draft Report is Currently Being Revised



Source: https://effectivehealthcare.ahrq.gov/topics/sodium-potassium/research-protocol

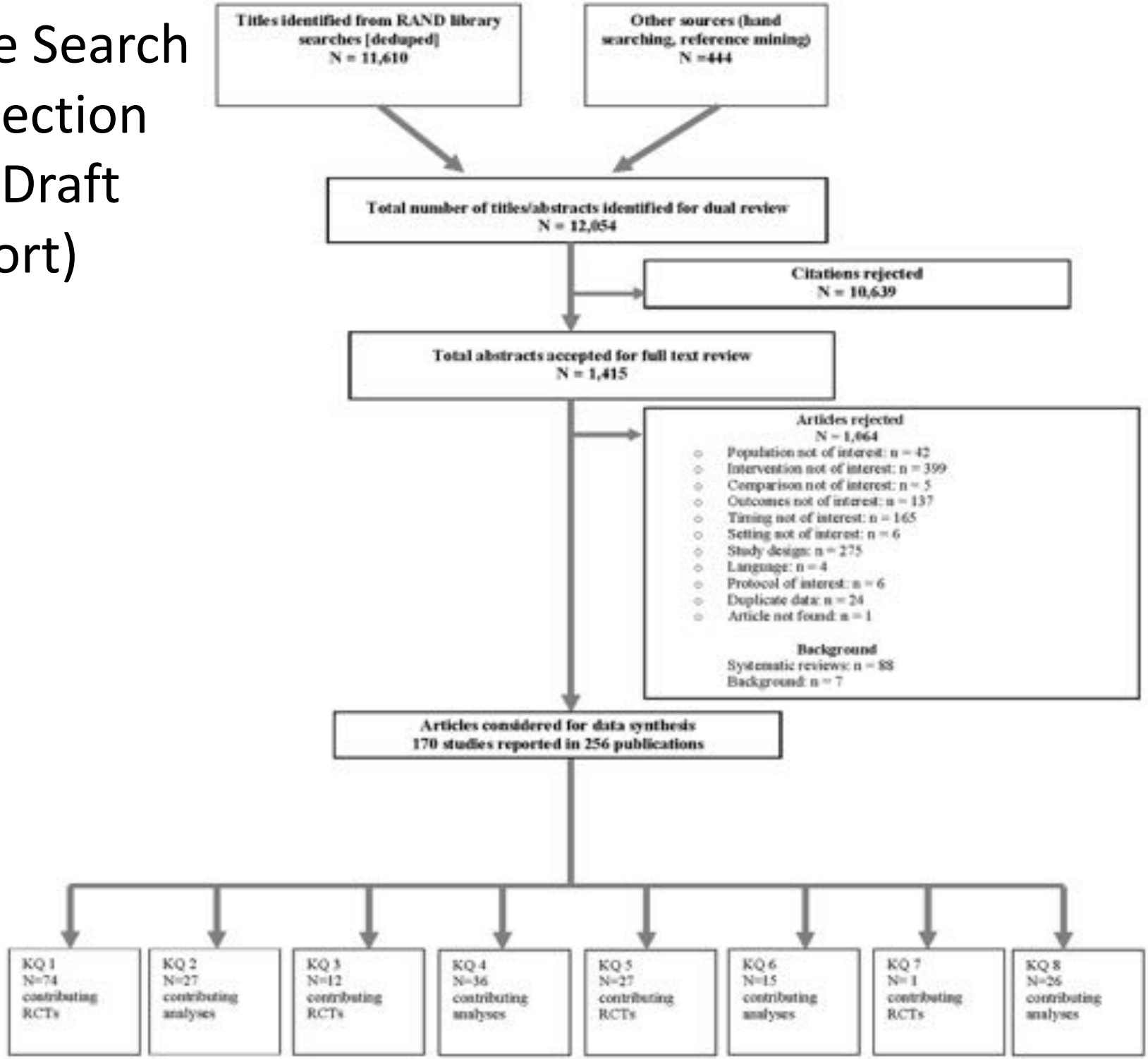
Reviewed in relation to sodium:	AHRQ SR	2005 Na/K DRI	2015 DGAC
Blood Pressure	√	√	√[a]
Incident hypertension	√		
Achievement of prespecified blood pressure goals	√		
All-cause mortality	√	√	
CVD morbidity and mortality	√		√[b]
CHD morbidity and mortality	√	√	
Stroke	√	√	
Myocardial infarction	√		
Renal morbidity and mortality (chronic kidney disease; creatinine clearance; serum creatinine; glomerular filtration rate; end stage renal disease; albuminuria or proteinuria; acute kidney injury)	√	√	
Kidney stones	√	√	
Adverse events (requiring coronary revascularization procedures; atherosclerotic revascularization procedures; left ventricular hypertrophy; hospitalization for heart failure; hospitalization for any cause of coronary heart disease or cardiovascular disease)	√		
Sodium balance		√	
Chloride balance		√	
Serum concentration		√	
Plasma renin activity		√	
Blood lipids concentration		√	
Insulin resistance		√	
Calcium excretion		√	
Bone mineral density		√	
Left ventricular mass		√	
Pulmonary function		√	
Gastric cancer		√	

Reviewed in relation to potassium:	AHRQ SR	2005 Na/K DRI	2015 DGAC
Blood Pressure	√	√	√[a]
Incident hypertension	√		
Achievement of prespecified blood pressure goals	√		
All-cause mortality	√	√	
CVD morbidity and mortality	√	√	√[b]
CHD morbidity and mortality	√		
Stroke	√	√	
Myocardial infarction	√		
Renal morbidity and mortality (chronic kidney disease; creatinine clearance; serum creatinine; glomerular filtration rate; end stage renal disease; albuminuria or proteinuria; acute kidney injury)	√	√	
Kidney stones	√	√	
Adverse events (requiring coronary revascularization procedures; atherosclerotic revascularization procedures; left ventricular hypertrophy; hospitalization for heart failure; hospitalization for any cause of coronary heart disease or cardiovascular disease)	√		
Potassium balance		√	
Serum potassium concentration		√	
Prevention of bone demineralization		√	
Bone loss		√	
Prevention of impaired pulmonary function		√	
Salt-sensitive blood pressure		√	
Hypolakemia		√	

Sub-questions

- a. Do other minerals (e.g., potassium, calcium, magnesium) modify the effect of sodium?
- b. Among subpopulations defined by sex, race/ethnicity, age (children, adolescents, young adults, older adults, elderly), and for women (pregnancy and lactation).
- c. Among subpopulations defined by hypertension, diabetes, and obesity health status.

Literature Search and Selection Flow (Draft Report)



Risk of Bias for Sodium Exposure Assessment Methods in Prospective Cohort Studies

- Low RoB:
  - Multiple days (more than four on average, preferably non-consecutive) 24-hour urines with reported quality control measures (i.e., instructions given, measure of completeness of collection, e.g., creatinine, urine volume, questionnaire)
- Moderate RoB:
  - One to four 24-hour urine specimens with reported quality control measures or correction for regression dilution bias with repeated 24-hour urine collection on a sample of participants.
  - Multiple days of food diaries
  - Multiple non-consecutive days (more than 4) 24-hour diet recalls or food records or correction for regression dilution bias with repeated (non-consecutive) 24-hour diet recalls for a sample of participants
- High RoB:
  - One or multiple 24-hour urine without any reported quality control measures
  - Timed-urine collection of less than 24 hours
  - Single-day food diaries/records or 24-hour diet recalls
  - Spot urine with or without use of a prediction equation for estimating 24-hour excretion

Food Frequency Questionnaire (FFQ) measure was excluded

Risk of Bias for Potassium Exposure Assessment Methods in Prospective Cohort Studies

- Low RoB:
  - Multiple non-consecutive days (more than 4) 24-hour diet recalls or food records
  - Multiple (more than four, preferably non-consecutive) 24-hour urines with reported quality control measures (i.e., instructions given, measure of completeness of collection, e.g., creatinine, urine volume, questionnaire)
- Moderate RoB:
  - One to four 24-hour urine specimens or correction for regression dilution bias with repeated 24-hour urine collection on a sample of participants
  - Two to four non-consecutive 24-hour recalls/food records or correction for regression dilution bias with repeated (non-consecutive) 24-hour diet recalls for a sample of participants.
  - FFQ validated for potassium intake within a subset of the study population against duplicate diets or multiple 24-hour urine collections
- High RoB:
  - One or multiple 24-hour urine specimen without quality control measures
  - Use of more than one 24-hour urine specimen without any reported quality control measures
  - Timed-urine collection of less than 24 hours
  - FFQ other than that specified above under Moderate RoB
  - Single-day food records
  - Single day of 24-hour recall
  - Spot urine specimen(s) with or without use of an equation for estimating 24-hour excretion

Definitions of the Levels of Strength of Evidence

Grade	Definition
High	We are very confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has few or no deficiencies. We believe that the findings are stable, i.e., another study would not change the conclusions
Moderate	We are moderately confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has some deficiencies. We believe that the findings are likely to be stable, but some doubt remains
Low	We have limited confidence that the estimate of effect lies close to the true effect for this outcome. The body of evidence has major or numerous deficiencies (or both). We believe that additional evidence is needed before concluding either that the findings are stable or that the estimate of effect is close to the true effect
Insufficient	We have no evidence, we are unable to estimate an effect, or we have no confidence in the estimate of effect for this outcome. No evidence is available or the body of evidence has unacceptable deficiencies, precluding reaching a conclusion

Major Challenges

- Direct evidence on dose/intake-response relationship from trials is scarce (and often no evidence on chronic disease endpoints)
- Observational evidence is limited by the biases or errors in exposure assessment
- Methodology for synthesizing different types of evidence is in its infancy

Most Important Take Away Messages

- AHRQ evidence review is a public good
  - All data will be made publicly available
  - Can be used (as is or reanalyzed) to support other guideline development
- AHRQ evidence review does NOT make clinical/public health recommendations
- Final report is currently scheduled to be posted on March 6 (one day before the NASEM DRI review of sodium and potassium public workshop)

Thank you for your attentions!

- I cannot answer any question with regards to the results or conclusions of the evidence report.
- I am happy to answer any question related to evidence review methods and process.