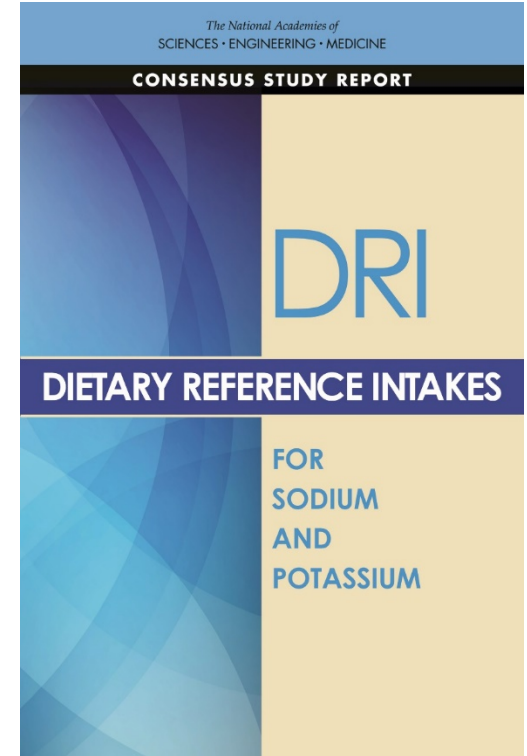


Dietary Reference Intakes for Sodium and Potassium



Presentation Outline

- **Presentation**
 - Overview of the Task
 - Potassium and Sodium DRIs for Adequacy
 - Potassium and Sodium DRIs for Toxicity
 - Potassium and Sodium DRIs Based on Chronic Disease
 - Risk Characterization and Special Considerations
 - Future Directions
- **Questions and Answers**

Overview of the Task

Statement of Task

Assess current relevant data and update, as appropriate, the DRIs for sodium and potassium

- Consider:
 - Deficiency
 - Inadequacy
 - Toxicities
 - Chronic disease endpoints
- Incorporate:
 - DRI Organizing Framework
 - *Guiding Principles Report*
 - *AHRQ Systematic Review*

DRI Organizing Framework

Step 1: Review and select the indicator(s) that will inform the DRIs

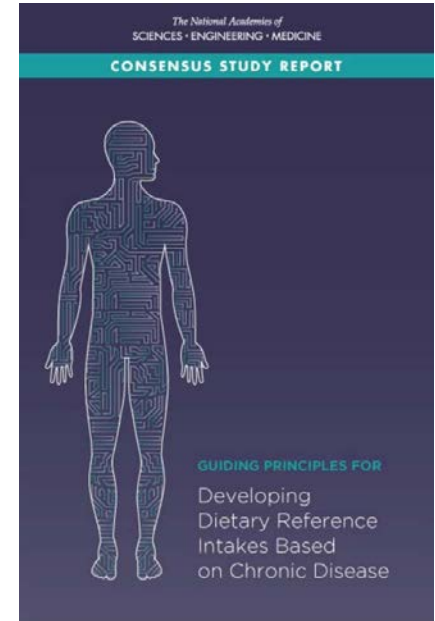
Step 2: Assess intake-response relationships and establish DRI values

Step 3: Compare current population intake levels to DRI values

Step 4: Discuss public health implications and special considerations

Guiding Principles Report

- Provides guidance for establishing DRIs based on chronic disease
- In general, DRIs based on chronic disease are:
 - Established when there is **at least moderate strength of evidence** for both causal and intake-response relationships
 - Ideally based on the chronic disease of interest, although **qualified surrogate markers** can be used as supporting evidence



Expansion of the DRI Model

- **DRI for Adequacy**
 - Refers to EARs, RDAs, and AIs
- **DRI for Toxicity**
 - Refers to the UL
 - Retain, but based on **toxicity endpoints**
- **DRI Based on Chronic Disease**
 - Refers to the **Chronic Disease Risk Reduction Intake (CDRR)**

Potassium and Sodium DRIs for Adequacy

Potassium DRI for Adequacy

- Findings
 - There is **no sensitive biomarker** of potassium requirements
 - Available **balance studies** do not rigorously measure intake and all forms of losses, limiting their ability to estimate potassium requirements
- Conclusions
 - None of the reviewed indicators offer sufficient evidence to establish potassium EARs and RDAs
 - Median intakes in **apparently healthy groups of people** are appropriate for establishing the potassium AIs

Potassium Adequate Intakes

- **Infants, 0-6 Months**
 - Based on estimates from breast milk
- **Infants, 7-12 Months**
 - Based on estimates from breast milk and complementary foods
- **Children, 1-18 Years**
 - Estimates from NHANES 2009-2014 and CCHS Nutrition 2015
 - Stratified by sex and age groups
- **Adults, ≥ 19 Years**
 - Apparently healthy group of people
 - Normotensive
 - Without history of CVD
 - Estimates from NHANES 2009-2014 and CCHS Nutrition 2015
 - Stratified by sex and life stage

Potassium Adequate Intakes (mg/d)

Age	Infants	Children	Males	Females	Pregnancy	Lactation
0-6 m	400					
7-12 m	860					
1-3 y		2,000				
4-8 y		2,300				
9-13 y			2,500	2,300		
14-18 y			3,000	2,300	2,600	2,500
19-30 y			3,400	2,600	2,900	2,800
31-50 y			3,400	2,600	2,900	2,800
51-70 y			3,400	2,600		
> 70 y			3,400	2,600		

Potassium Adequate Intakes (mg/d)

Age	Infants	Children	Males	Females	Pregnancy	Lactation
0-6 m	400					
7-12 m	860					
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19-30 y			3,400	2,600	2,900	2,800
31-50 y			3,400	2,600	2,900	2,800
51-70 y			3,400	2,600		
> 70 y			3,400	2,600		

■ **Increased** compared to *2005 DRI Report*
■ **Decreased** compared to *2005 DRI Report*

Compared to Previous Values

- Updated potassium AIs are **reduced** for individuals 1 year of age and older
 - No longer based on evidence from potassium supplementation trials
 - Additional benefits on chronic disease risk reduction considered for establishing a potassium CDRR

Sodium DRI for Adequacy

- Findings
 - Blood sodium concentrations and hyponatremia are not indicators of usual sodium intake or status
 - Balance studies do not offer sufficient data for determining sodium requirements
 - Insufficient and inconsistent evidence of harmful effects of low sodium intake on:
 - Type 2 diabetes, glucose tolerance, and insulin sensitivity
 - Blood pressure
 - Plasma lipid concentrations
 - Cardiovascular disease and all-cause mortality

Sodium DRI for Adequacy

- Limitations of observational studies reporting U- or J-shaped relationships
 - Population included in sample, such as pre-existing conditions
 - Possible confounding, especially by reverse causation
 - Use of **spot urine** to estimate 24-hour urinary excretion
 - Bias in the estimates—overestimate at lower levels and underestimate at higher levels of intake
 - Different sodium intake assessment methods within the same study population have been shown to lead to different estimates and intake-response relationships

Sodium DRI for Adequacy

- **Conclusions**

- None of the reviewed indicators of sodium requirements offer sufficient evidence to establish EAR and RDA values
- Median population intakes are not suitable for establishing the sodium AI because they exceed the sodium CDRR
- The **lowest levels of sodium intake evaluated in randomized trials** and evidence from the **best-designed balance study** conducted among adults were congruent and are appropriate values on which to establish the sodium AIs

Sodium Adequate Intakes

- **Infants, 0-6 Months**
 - Based on estimates of breast milk
- **Infants, 7-12 Months**
 - Based on estimates of breast milk and complementary foods
- **Children, 1-18 Years**
 - Extrapolated from adult AI using sedentary Estimated Energy Requirements
- **Adults, ≥ 19 Years**
 - Lowest sodium intake from DASH-Sodium Trial and 8 other randomized controlled trial
 - Best-designed balance study in adults with neutral balance with heat stress at 1,525 mg/d sodium intake
 - Insufficient evidence of adverse health effects at low levels of intake

Sodium Adequate Intakes (mg/d)

Age	Infants	Children	Males	Females	Pregnancy	Lactation
0-6 m	110					
7-12 m	370					
1-3 y		800				
4-8 y		1,000				
9-13 y			1,200	1,200		
14-18 y			1,500	1,500	1,500	1,500
19-30 y			1,500	1,500	1,500	1,500
31-50 y			1,500	1,500	1,500	1,500
51-70 y			1,500	1,500		
> 70 y			1,500	1,500		

Sodium Adequate Intakes (mg/d)

Age	Infants	Children	Males	Females	Pregnancy	Lactation
0-6 m	110					
7-12 m	370					
1-3 y		800				
4-8 y		1,000				
9-13 y			1,200	1,200		
14-18 y			1,500	1,500	1,500	1,500
19-30 y			1,500	1,500	1,500	1,500
31-50 y			1,500	1,500	1,500	1,500
51-70 y			1,500	1,500		
> 70 y			1,500	1,500		

■ Increased compared to 2005 DRI Report
■ Decreased compared to 2005 DRI Report

Compared to Previous Values

- Updated sodium AIs are **similar** to the previous values
 - Reaffirmed values for infants 7-12 months, children 14-18, and adults 19-50 years of age
 - Reduced values for children 1-13 years of age due to a different approach in extrapolation
 - Did not establish different values adults >50 years of age
 - Limited data on adults > 70 years of age

Potassium and Sodium DRIs for Toxicity

Potassium UL

- Findings

- Very high, acute doses of supplemental potassium can lead to adverse effects and death
- Supplementation slightly increases blood potassium concentrations, but no evidence of hyperkalemia among adults with normal kidney function
- No consistent pattern of reported adverse events in potassium supplementation trials

Potassium UL

- **Conclusion**
 - There is insufficient evidence of potassium toxicity risk within the apparently healthy population to establish a potassium UL.
- The conclusion is the **same** as was reached in the 2005 DRI Report

Sodium UL

- Findings

- Very high, acute doses of sodium can lead to adverse events and death
- Two crossover trials provided evidence that intake of more concentrated doses of sodium may lead to more adverse effects, but no specific toxicological indicator could be identified
- Headaches have been reported to be less prevalent during some low-sodium trials, but effect is not well characterized

Compared to Previous Values

- **Conclusion**
 - There is insufficient evidence of sodium toxicity risk within the apparently healthy population to establish a sodium UL.
- This is **different** from the conclusion reached in the 2005 DRI Report
 - Under the expanded DRI model:
 - UL is now based on *toxicological* risk
 - Blood pressure and chronic disease indicators were not reviewed in context of establishing ULs

Potassium and Sodium DRIs Based on Chronic Disease

DRI Based on Chronic Disease

- The Committee's Approach
 - Use strength of evidence rating across a **body of evidence**
 - Considered both **causality** and **intake-response**
 - Guided by the GRADE system, which considers:
 - Study Design
 - Risk of bias
 - Inconsistency
 - Indirectness
 - Imprecision
 - Publication bias

AHRQ Systematic Review

- Primary source of evidence for key indicators
- Strength of evidence for blood pressure in the *AHRQ Systematic Review*
 - Downgraded due to **heterogeneity** (inconsistency) for both potassium and sodium
- Committee conducted additional meta-analyses
 - To explore sources of heterogeneity
 - To examine the intake-response relationship

Potassium DRI Based on Chronic Disease

- Strength of Evidence for Relationships with Potassium Intake
 - Insufficient or low
 - All-cause mortality
 - Cardiovascular disease
 - Coronary heart disease
 - Myocardial infarction
 - Stroke
 - Kidney stones
 - Chronic kidney disease
 - Osteoporosis
 - Type 2 diabetes
 - Moderate
 - Potassium supplementation significantly reduces systolic and diastolic **blood pressure**
 - Lack of dose-response with potassium intake
 - Effect appeared restricted to those with hypertension at baseline
 - Heterogeneity of effect across studies that could not be adequately explained

Potassium Chronic Disease Risk Reduction Intake

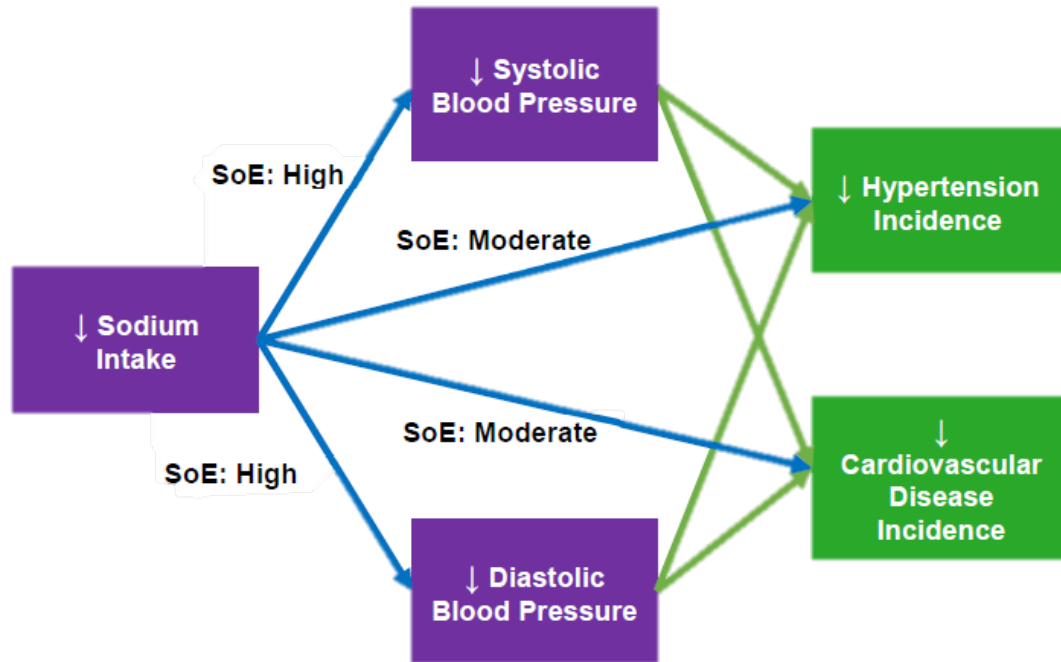
- **Conclusion**

- Although there is moderate strength of evidence for a causal relationship between potassium supplementation and reductions in blood pressure, a potassium CDRR could not be established because:
 - Heterogeneity across studies,
 - Lack of evidence for an intake-response relationship, and
 - Lack of supporting evidence for benefit of potassium on cardiovascular disease

Sodium DRI Based on Chronic Disease

- Strength of Evidence for Causal Relationship with Reductions in Sodium Intake
 - Insufficient
 - Cardiovascular mortality
 - Myocardial infarction
 - Left ventricular mass
 - Stroke
 - Osteoporosis
 - Kidney disease
 - Moderate
 - All-cause mortality
 - Cardiovascular disease incidence
 - Hypertension incidence
 - High
 - Systolic blood pressure
 - Diastolic blood pressure

Relationship Between Indicators



- Continuous measures (changes in numerical values)
- Dichotomous Outcomes (changes in risk or incidence)

- ➡ Evidence from sodium randomized controlled trials
- ➡ Evidence for blood pressure as a surrogate marker from other studies

Sodium DRI Based on Chronic Disease

Intake Range (mg/d)	Strength of Evidence for Intake-Response Relationship Between Reduction in Sodium Intake and Chronic Disease Risk
> 4,100	Moderate up to 5,000 mg/d
2,300-4,100	High
< 2,300	Low down to 1,000 mg/d

Sodium Chronic Disease Risk Reduction Intake

- **Conclusions**

- There is moderate to high strength of evidence for both a causal relationship and an intake-response relationship between sodium and several interrelated chronic disease indicators: **cardiovascular disease**, **hypertension**, **systolic blood pressure**, and **diastolic blood pressure**
- Evidence from these indicators can be synthesized to inform the development of a **sodium CDRR**

Sodium Chronic Disease Risk Reduction Intake

- **Adults, 19-70 Years**
 - Lowest level of intake for which there was sufficient strength of evidence to characterize a chronic disease risk reduction
- **Adults, >70 Years**
 - Extrapolated from adults, 19-70 years
- **Children, 1-18 Years**
 - Extrapolated from adult CDRR using sedentary Estimated Energy Requirements

For sodium, the CDRR is the intake above which intake reduction is expected to reduce chronic disease risk within an apparently healthy population

Sodium Chronic Disease Risk Reduction Intakes

Population Group

Recommendation

Children, 1-3 years

Reduce intakes if above 1,200 mg/d

Children, 4-8 years

Reduce intakes if above 1,500 mg/d

Children, 9-13 years

Reduce intakes if above 1,800 mg/d

Children, 14-18 years

Reduce intakes if above 2,300 mg/d

Adults, ≥ 19 years

Reduce intakes if above 2,300 mg/d

Sodium 2005 UL and 2019 CDRR (mg/d)												
Age	Infants		Children		Males		Females		Pregnancy		Lactation	
	2005 UL	2019 CDRR	2005 UL	2019 CDRR	2005 UL	2019 CDRR	2005 UL	2019 CDRR	2005 UL	2019 CDRR	2005 UL	2019 CDRR
0-6 m	ND	ND										
7-12 m	ND	ND										
1-3 y			1,500	1,200								
4-8 y			1,900	1,500								
9-13 y					2,200	1,800	2,200	1,800				
14-18 y					2,300	2,300	2,300	2,300	2,300	2,300	2,300	2,300
19-30 y					2,300	2,300	2,300	2,300	2,300	2,300	2,300	2,300
31-50 y					2,300	2,300	2,300	2,300	2,300	2,300	2,300	2,300
51-70 y					2,300	2,300	2,300	2,300				
> 70 y					2,300	2,300	2,300	2,300				

Sodium 2005 UL and 2019 CDRR (mg/d)												
Age	Infants		Children		Males		Females		Pregnancy		Lactation	
	2005 UL	2019 CDRR	2005 UL	2019 CDRR	2005 UL	2019 CDRR	2005 UL	2019 CDRR	2005 UL	2019 CDRR	2005 UL	2019 CDRR
0-6 m	ND	ND										
7-12 m	ND	ND										
1-3 y			1,500	1,200								
4-8 y			1,900	1,500								
9-13 y					2,200	1,800	2,200	1,800				
14-18 y					2,300	2,300	2,300	2,300	2,300	2,300	2,300	2,300
19-30 y					2,300	2,300	2,300	2,300	2,300	2,300	2,300	2,300
31-50 y					2,300	2,300	2,300	2,300	2,300	2,300	2,300	2,300
51-70 y					2,300	2,300	2,300	2,300				
> 70 y					2,300	2,300	2,300	2,300				

Risk Characterization and Special Consideration

Risk Characterization

- **The Committee's Approach**

- Compare updated DRI values to intakes in U.S. and Canadian populations
 - NHANES 2009-2014
 - CCHS Nutrition 2015
 - FITS 2016
- Comparison to the potassium and sodium AIs
 - Groups with intakes \geq AI assumed to have low prevalence of inadequate intake
 - Extent of inadequacy for groups with intakes $<$ AI cannot be made
- Comparison to the sodium CDRRs
 - Proportion with intakes in which sodium reduction is expected to reduce chronic disease risk in the population

Potassium Risk Characterization

- By DRI Age, Sex, and Life-Stage Groups in U.S. and Canada

Groups	Percent with Intakes > AI
Children	23-53%
Adults	17-40%
Pregnant	32-48%
Lactating	41-51%

- By Race/Ethnicity in the U.S.
 - Potassium intakes lowest among non-Hispanic blacks across DRI groups

Potassium Special Considerations

- **Excessive sweat losses**
 - Exposure to high temperatures and high levels of physical activity can increase potassium losses through sweat
- **Individuals taking medications that affect potassium retention and excretion**
 - ACE-I, ARBs, certain diuretics can affect potassium homeostasis
 - ACE-I and ARBs are among first line pharmaceutical agents for hypertension treatment
 - Drugs are commonly used in patients with heart failure

Potassium Special Considerations

- **Individuals with adrenal insufficiency**
 - Rare condition characterized by hypokalemia
- **Individuals with chronic kidney disease**
 - At risk of hyperkalemia, hypokalemia
- **Individuals with type 2 diabetes**
 - May be at increased risk of hyperkalemia
 - Higher potassium intake may slow decline of kidney function

Sodium Risk Characterization

- By DRI Age, Sex, and Life-Stage Groups in U.S. and Canada

Groups	Percent with Intakes > AI	Percent with Intakes > CDRR
Children	95-99%	62-99%
Adults	85-99%	34-98%
Pregnant	98-99%	70-94%
Lactating	98-99%	76-99%

- By Race/Ethnicity in the U.S.
 - Non-Hispanic white adults tended to have higher sodium intakes

Sodium Special Considerations

- **Normotensive and Hypertensive Individuals**
 - Larger effects in blood pressure reduction seen in hypertensive
 - **Benefits of sodium reduction are applicable to both**
- **Excessive sweat losses**
 - Exposure to high temperatures and high levels of physical activity can increase sodium losses through sweat
- **Orthostatic hypotension**
 - Characterized by symptomatic low blood pressure
 - Sodium intake may need to be guided by a healthcare provider

Sponsors

- Centers for Disease Control and Prevention
- Food and Drug Administration
- Health Canada
- National Institutes of Health
- Public Health Agency of Canada
- U.S. Department of Agriculture

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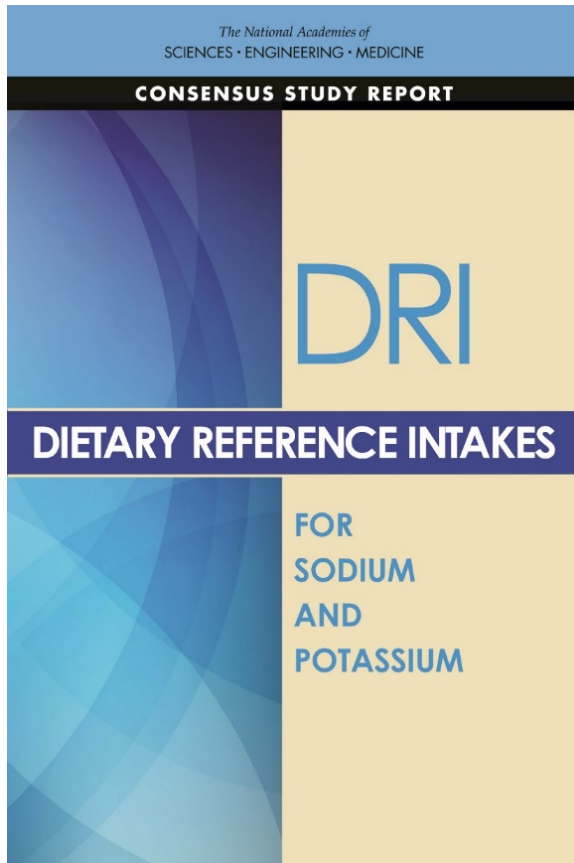
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