Evidence for Dietary Risk Factors and Albuminuria

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Objectives

- Describe recent research on the relationship between high levels of urine albumin and risk of mortality
- Summarize the relationship between weight loss and level of proteinuria
- Incorporate information on the level of sodium restriction recommended for patients with Chronic Kidney Disease (CKD) in clinical practice

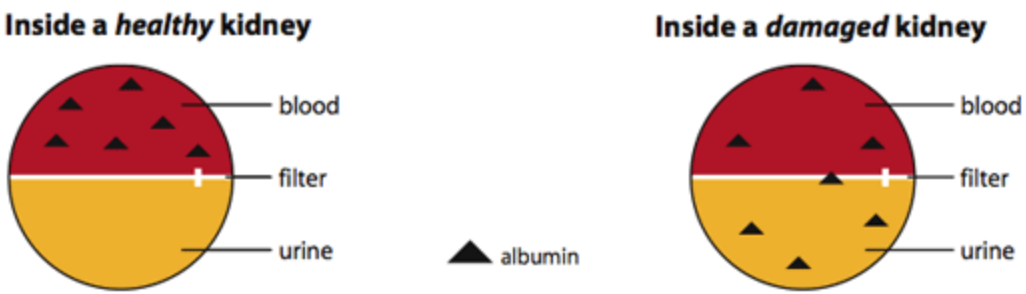
Topics

- Brief review of urine albumin and albuminuria
- Brief review of risk factors for albuminuria
- Potential dietary factors for albuminuria
  - Sodium
  - Protein

Review of Urine Albumin

- Urine albumin measures albumin in the urine
- May be earliest sign of CKD and marks severity of kidney damage
- Reducing urine albumin may be associated with slower progression of CKD
- Albuminuria is a risk factor for cardiovascular disease (CVD)
  - Increased inflammation
  - Oxidative stress
  - Marker of endothelial dysfunction

A Healthy Kidney Does Not Let Albumin Pass into The Urine



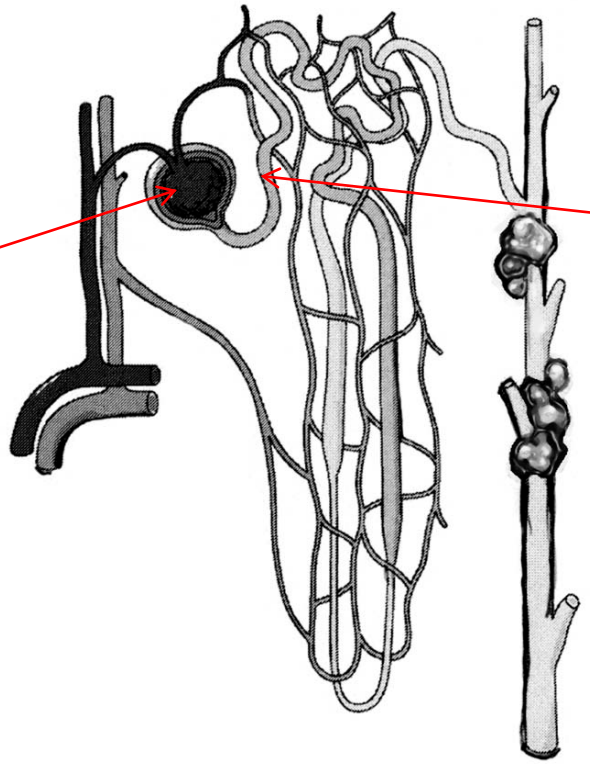
http://nkdep.nih.gov/resources/explaining_kidney_test_results.htm

Proteins are Filtered Based on Size, and are Reabsorbed within the Tubules

- Low-molecular-weight proteins cross the glomerular barrier (filter)
- High-molecular-weight proteins normally do not cross the barrier into the tubule
- Albumin is a medium-molecular-weight protein, and most of the albumin in the tubules is reabsorbed

Most Protein that Crosses the Glomerular Barrier Is Reabsorbed within the Tubule

Glomerulus
- Filtration



Tubule
- Reabsorption
- Secretion

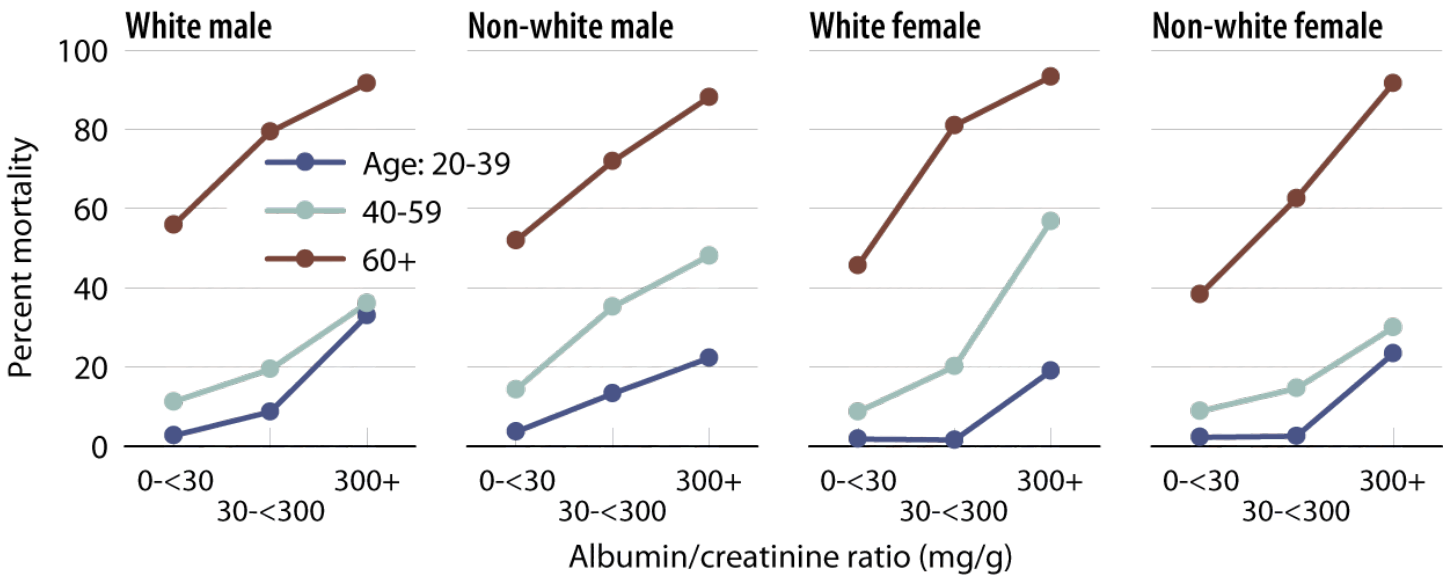
Catalog.niddk.nih.gov/ImageLibrary/

Damaged Kidneys Allow Albumin to Cross the Filtration Barrier into the Urine

- Increased glomerular permeability may allow albumin (and other proteins) to cross the glomeruli into the urine.
- High levels of protein within the tubules may exacerbate kidney damage.
- High levels may exceed tubules' ability to reabsorb.

High Levels of Albuminuria are Associated with Mortality

NHANES 1988 – 1994 participants



USRDS Annual Report 2010

Strong Heart Study (SHS): Albuminuria was Significant, Independent Risk Factor for Heart Disease

- SHS cardiovascular risk calculator includes questions on microalbuminuria and macroalbuminuria (Do you have….?)
- Other factors include age, gender, systolic blood pressure, low density lipoprotein (LDL), diagnosis of diabetes and smoking, high density lipoprotein (HDL), or triglycerides (TG).

In Diabetes Mellitus (DM), Urine Albumin > 30 mg/g is Associated with Greater Risk of Kidney Disease

- Normal urine albumin levels vary based on age and gender.
- Some studies use < 25 mg/g for women, < 17 mg/g for men.

Assessing Urine Albumin is a Standard of Care for People with Type 2 Diabetes

Assessing Urine Albumin in Type 2 DM

1. **Screen:** Check UACR at diagnosis and yearly
2. **Diagnosis:** Positive diagnosis albuminuria if UACR is greater than 30mg/g on 2 separate occasions
3. **Monitor:** Recheck UACR every year

   More frequent monitoring may be needed in patients with changing clinical status or after therapeutic interventions.

   (Do not monitor urine albumin in dialysis patients)

http://www.ihs.gov/MedicalPrograms/Diabetes/HomeDocs/Resources/DiabetesTopics/Treatment/DM_urine_albumin_screening.pdf

Urine-Albumin-to-Creatinine Ratio (UACR) Quantifies All Levels of Urine Albumin

- UACR is a continuous variable
- The term microalbuminuria describes urine albumin levels *not* detected by dipstick test
  - 30 mg/g – 300 mg/g
- The term macroalbuminuria describes urine albumin > 300 mg/g

RISKS FACTORS FOR ALBUMINURIA

Risk Factors

- Known Risk Factors
  - Hypertension
  - Diabetes
  - Obesity
  - Smoking
- Possible Risk Factors
  - High sodium intake
  - Excessive protein intake

Blood Pressure Medications May Lower Urine Albumin but Increase Risk for Hyperkalemia

Medications:

- Angiotensin converting enzyme inhibitors (ACEi)
- Angiotensin receptor blockers (ARBs)
- Restrict dietary potassium when serum level is high
- Salt substitutes may be rich in potassium

Good Diabetes Control May Help Prevent Albuminuria

- Diabetes Complication and Control Trial
  - Type 1 diabetes
- United Kingdom Prospective Diabetes Study
  - Type 2 diabetes

American Diabetes Association

Advanced Glycation End Products (AGEs) Form Spontaneously

- AGEs form by nonenzymatic, sequential glycation and oxidation reaction of sugars with free amino groups on proteins, lipids, and nucleic acids.
- The initial reaction is reversible depending on concentration.
- AGEs accumulate in plasma and tissues.
  - Increased levels found in DM and CKD
  - May accumulate with aging

Bohlender et al., 2005

AGEs Alter Protein Structure And Function

- Almost any protein can be glycosylated
  - Example: Hemoglobin
    - A1c
- Slow turnover proteins particularly prone to modification
  - Glomerular basement membrane thickening

Goldin et al., 2006; Peppa et al., 2003

AGEs Binding to Receptors May Promote Inflammatory Response

- Receptors for AGEs upregulate as AGEs accumulate.
- Activation (binding) may induce release of proinflammatory and profibrogenic cytokines.

Schmidt et al., 2001

Obesity May be Associated with Albuminuria

- Obesity is associated with CKD
  - Meta-analysis (Wang et al, 2008)
- High Body Mass Index (BMI) and abdominal obesity are associated albuminuria in Type 2 Diabetes
  - Look AHEAD [Action for Health in Diabetes] (Kramer et al, 2009)

Obesity and Diabetes may have Similar Effects on Kidney Function

- Hyperfiltration
- Hypertrophy
- Albuminuria

Intentional Weight Loss Associated with Decreased Proteinuria

- Weight loss is associated with decreased proteinuria
  - Dietary restrictions
  - Exercise
  - Antiobesity medications
  - Bariatric surgery
- No data to evaluate effect on CKD progression

Afshinnia et al., 2010

Smoking is Associated with Abuminuria

- Dose-dependent increase in urine albumin in the general population
- Independent predictor of elevated urine albumin in primary hypertension
- Independent risk factor for onset and progression of albuminuria in DM 1 and DM 2
- May increase risk for progression of renal failure in patients with primary renal disease

Orth, *2002*

Possible Risk Factors: Diet

- **Sodium**
- Protein

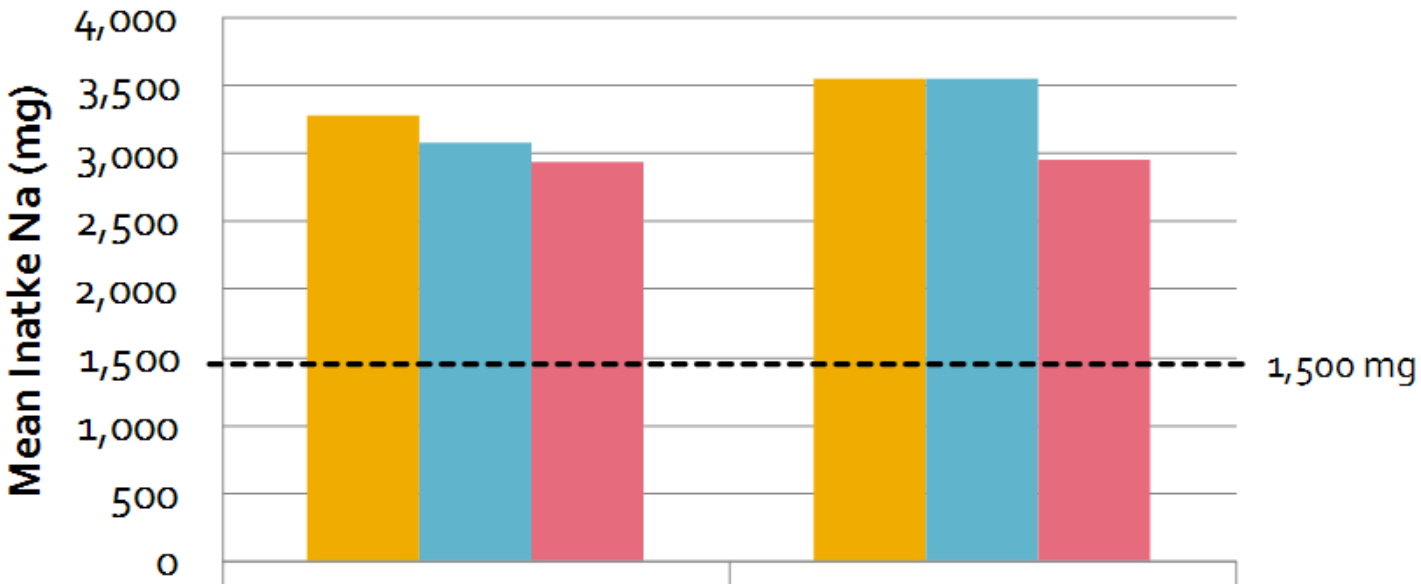
Dietary Guidelines 2010: Reduce Sodium Intake

- The 2010 recommendations include:
  - 2,300 milligrams sodium
  - 1,500 milligrams sodium
    - Hypertension
    - Diabetes
    - CKD
    - African Americans
    - People 51 years and older

Reducing Sodium Intake May Reduce Urine Albumin Levels

- Population studies
  - Higher sodium intake associated with increased urine albumin excretion in the Netherlands
    - More pronounced with obesity (Verhave, 2004)
- Literature review
  - Suggests increasing salt consumption associated with worsening urine albumin (Jones-Burton, 2006)
- Data from randomized control trials (RCTs) are lacking

Navajo Adults: Sodium Intake Higher Than Recommended

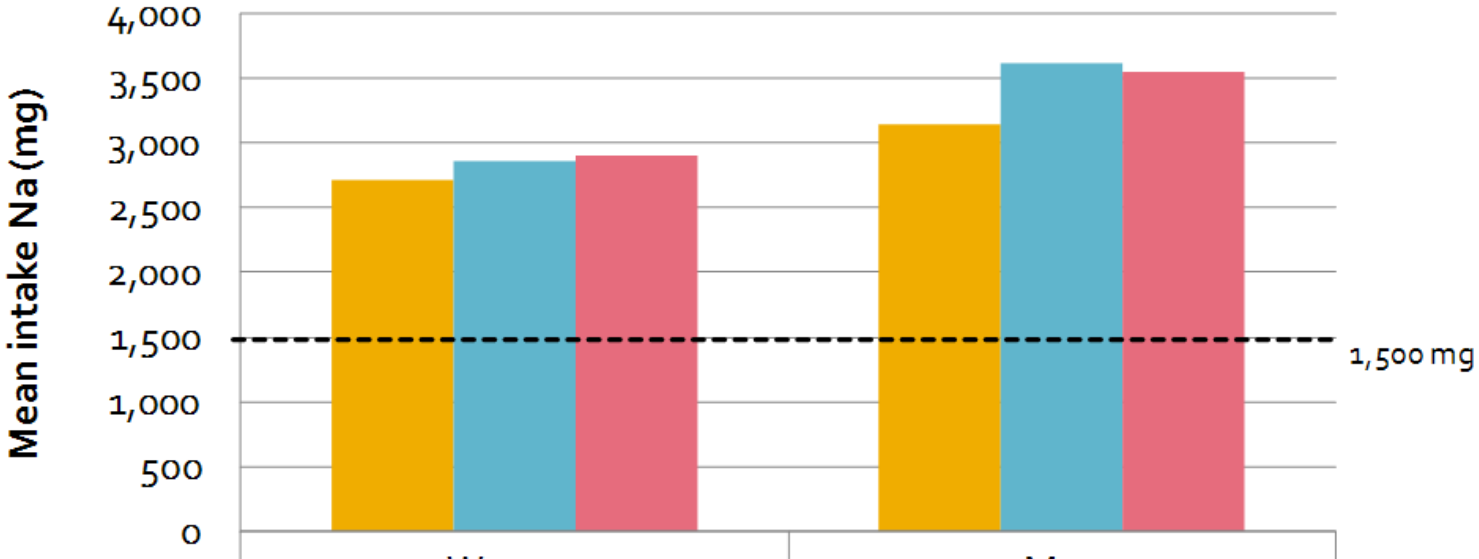


	Women		Men	
20-39	3,268	(SEM 113)	3,544	(SEM 135)
40-59	3,072	(SEM 211)	3,542	(SEM 234)
60 plus	2,938	(SEM 155)	2,945	(SEM 285)

Adapted from Ballew et al, 1997

SEM = standard error of mean

SHS: Sodium Intake Higher Than Recommended

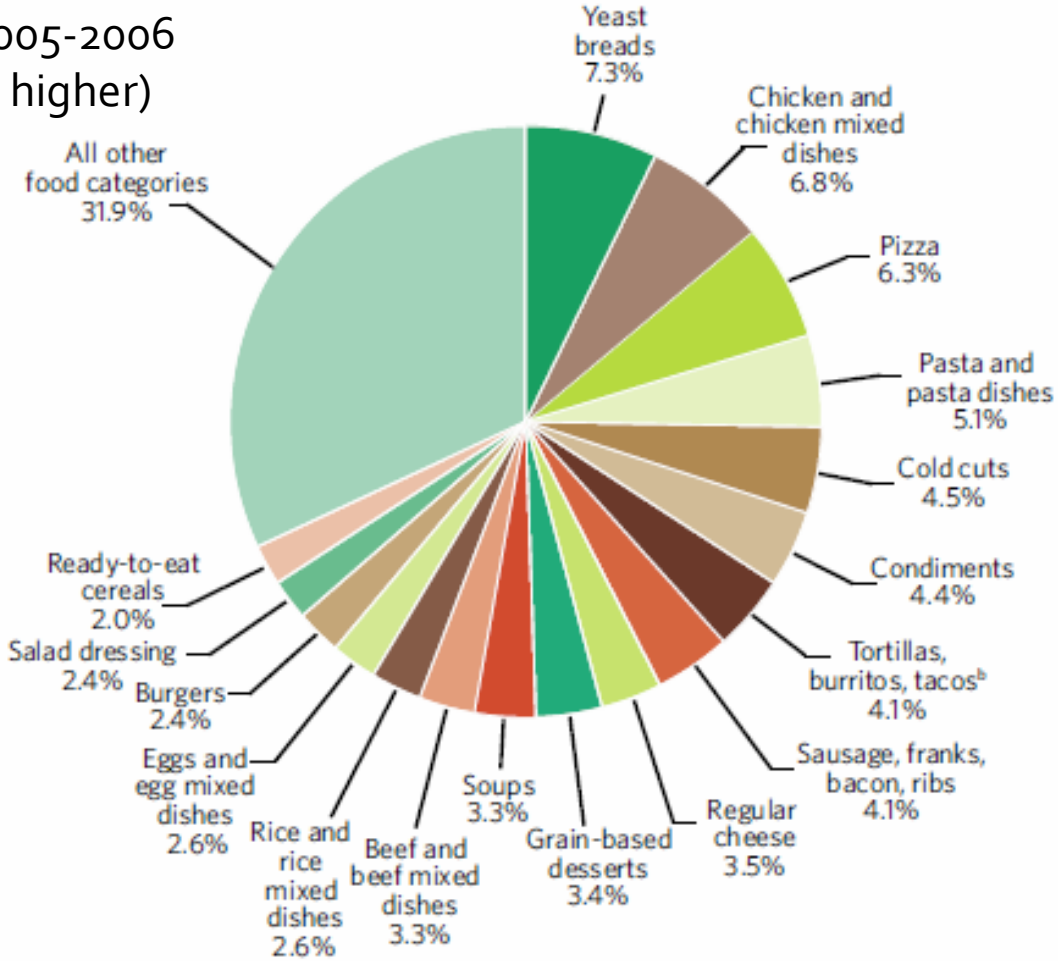


	Women	Men
Arizona	2,717 ± 1,306	3,143 ± 1,611
Dakotas	2,858 ± 1,449	3,608 ± 2,188
Oklahoma	2,897 ± 1,274	3,544 ± 1,705

Adapted from Stang et al, 2005

Sources of Sodium in U.S. Diet

NHANES 2005-2006
(ages 2 and higher)

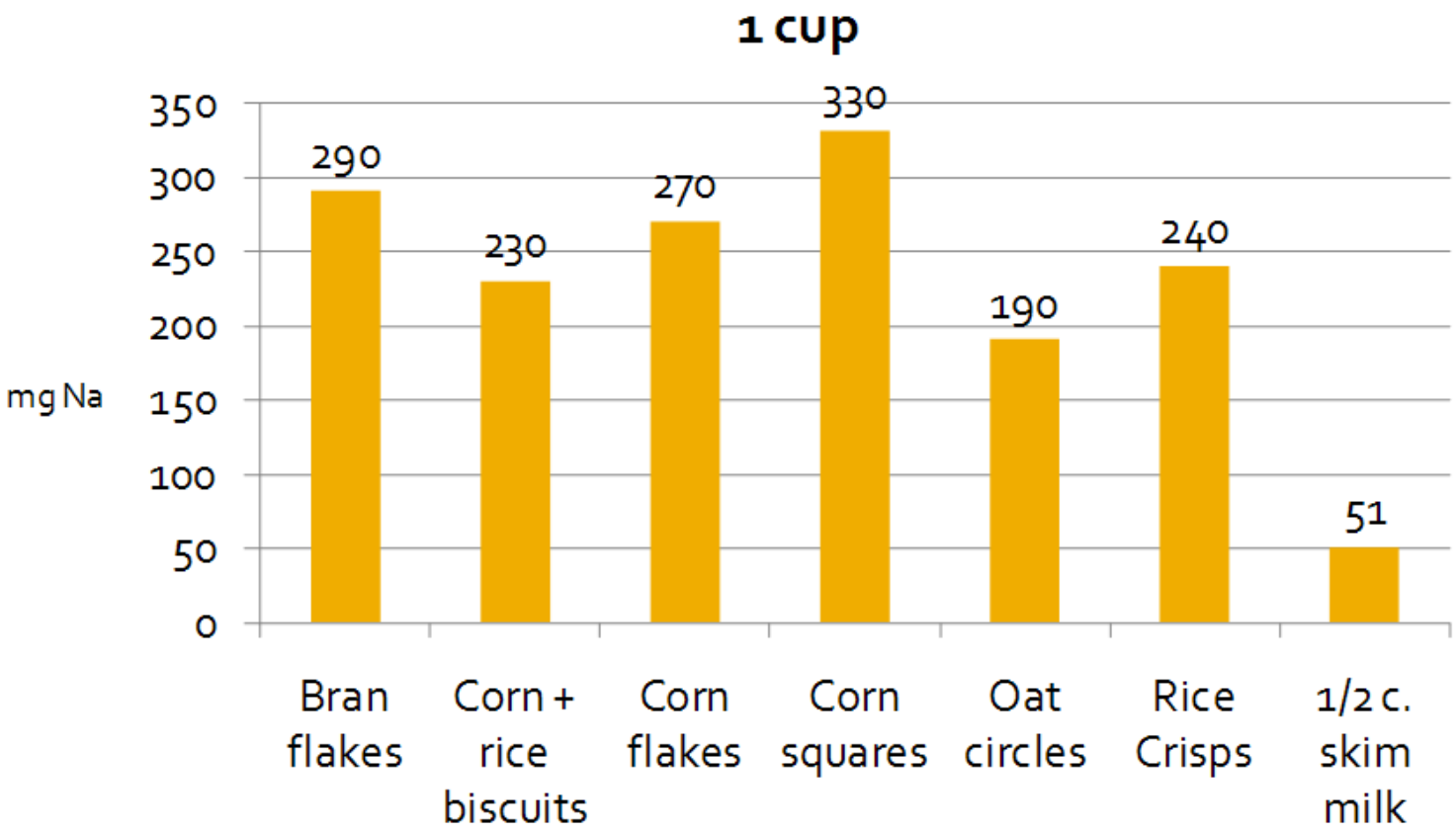


http://www.health.gov/dietaryguidelines/dga2010/DietaryGuidelines2010.pdf

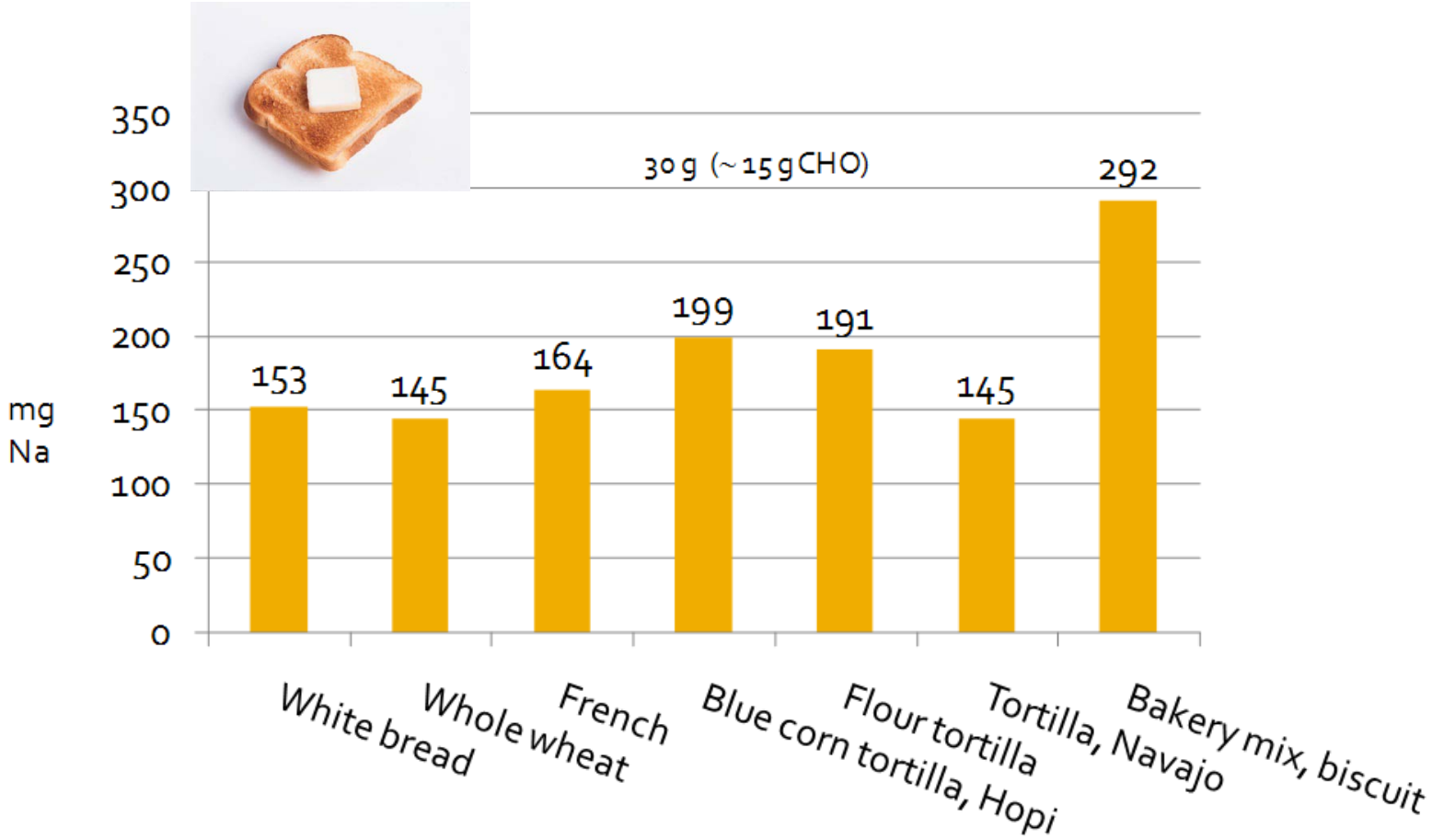
All Nutrient Analysis Data is from usda.gov

- Food Distribution Program on Indian Reservations Commodity Facts Sheets
  - http://www.fns.usda.gov/fdd/programs/fdpir/cfs_fdpir.htm
- Nutrient Data Laboratory
  - http://www.nal.usda.gov/fnic/foodcomp/search/

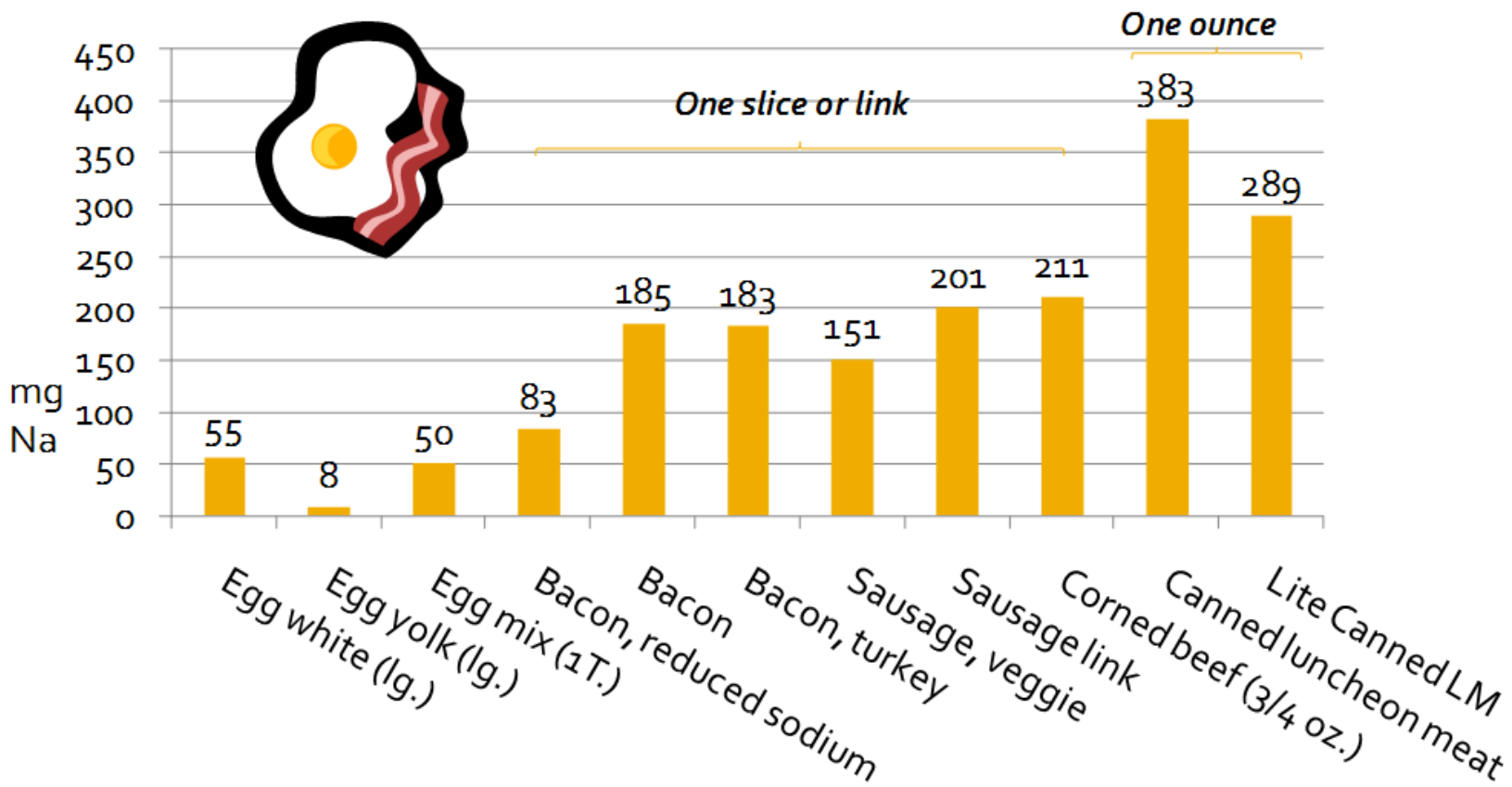
Commodity Cold Cereals Vary in Sodium Content



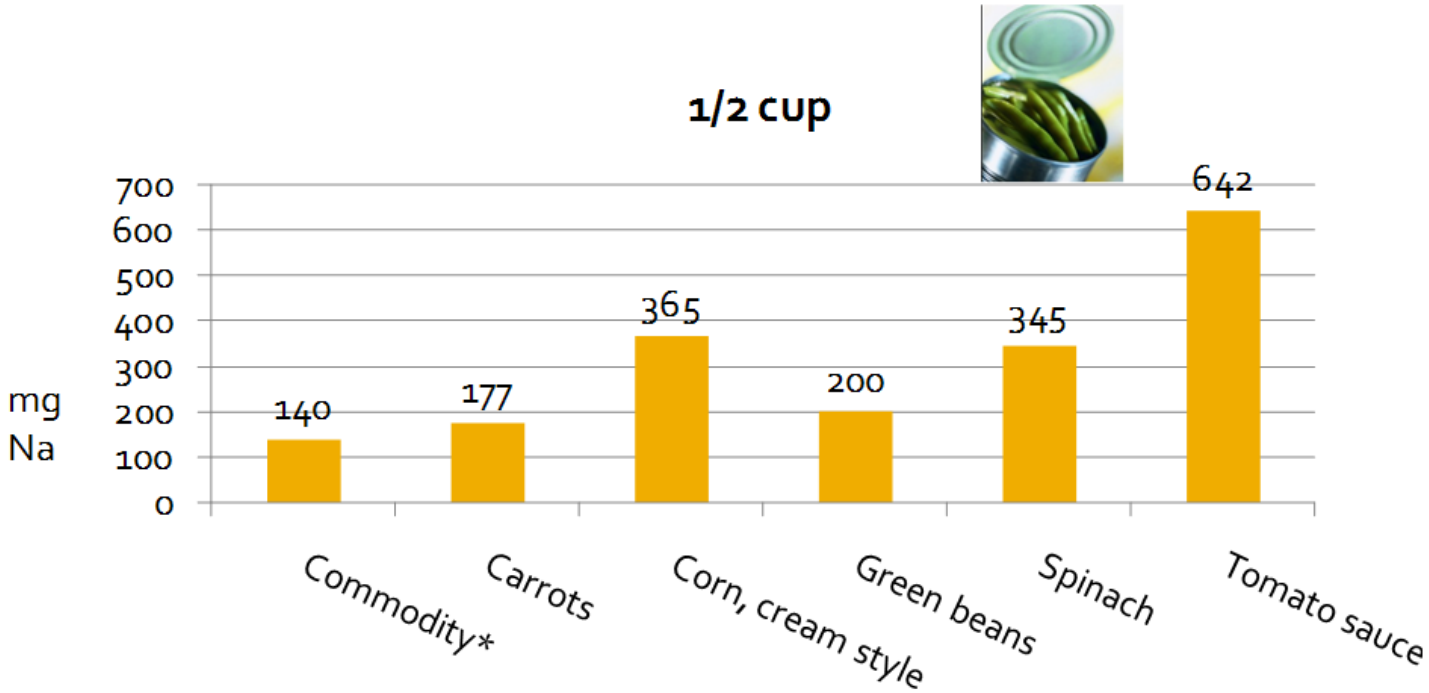
Bread Adds Up when Limiting Sodium



Breakfast Meat Adds a Lot of Sodium

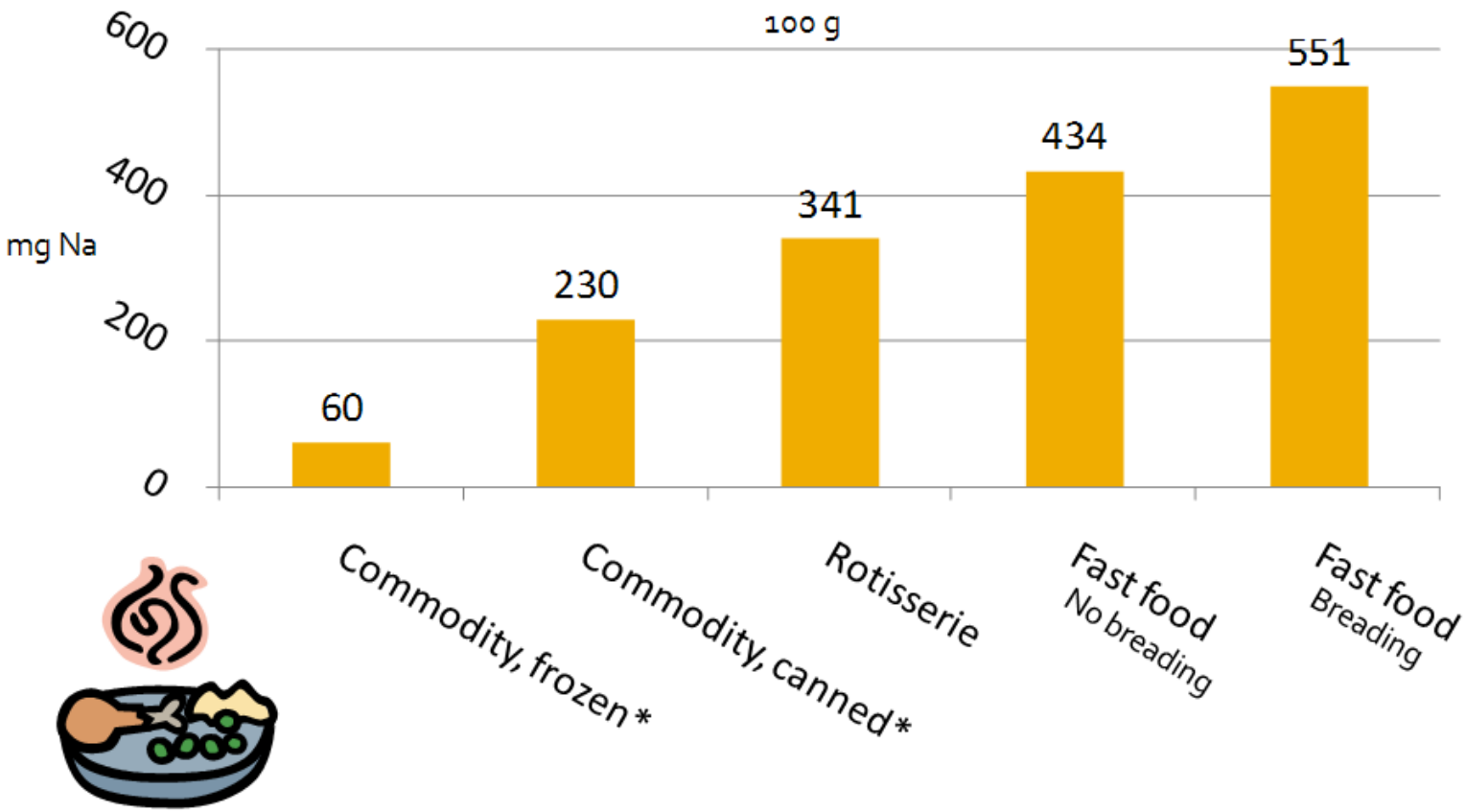


Commodity Canned Vegetables May be Lower in Sodium Than Most Store Brands



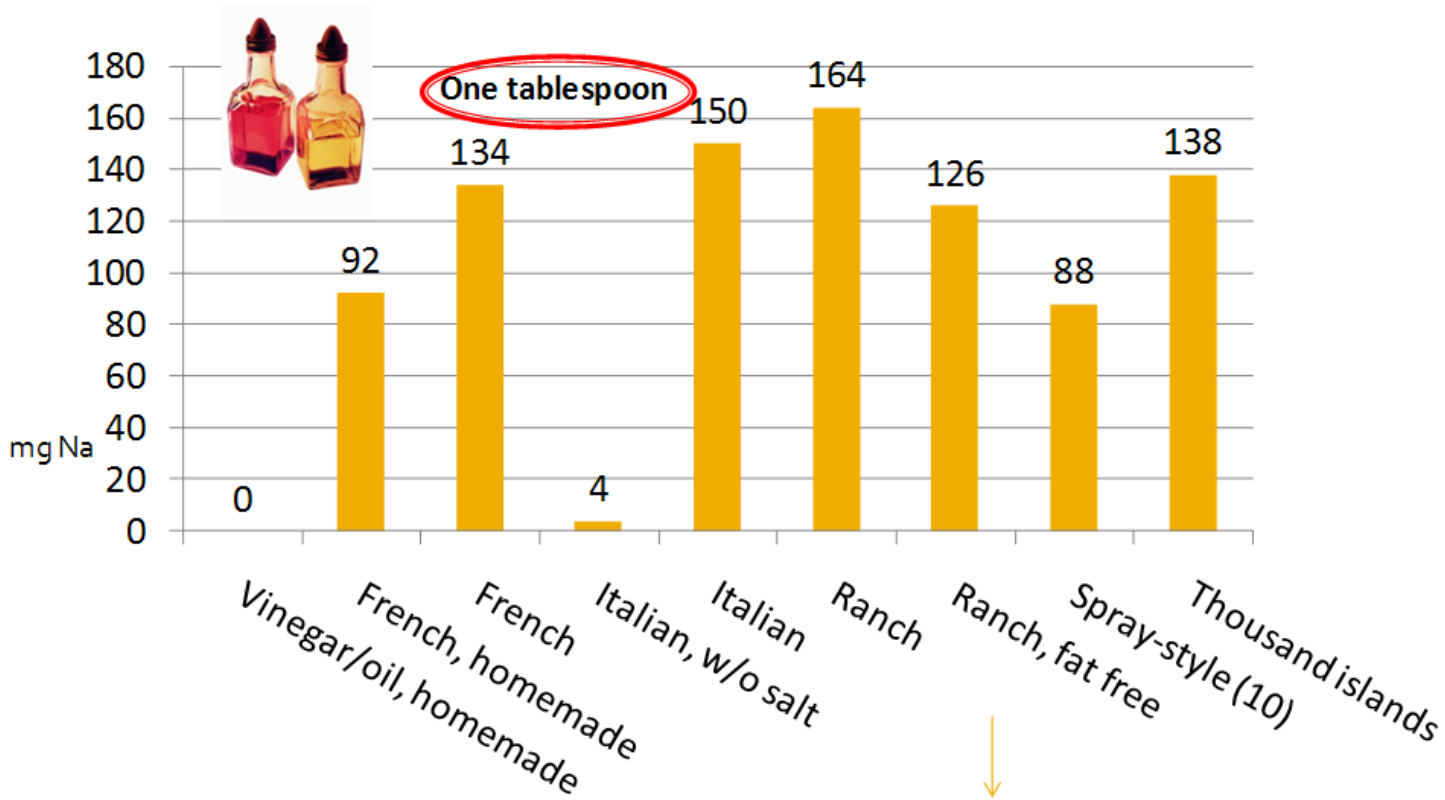
***Commodity carrots, corn, cream-style corn, green beans, green peas, spinach, tomatoes (diced), tomato sauce; mixed vegetables have 120 mg per 1/2 cup.**

Sodium Content Varies by Source and Preparation of Chicken



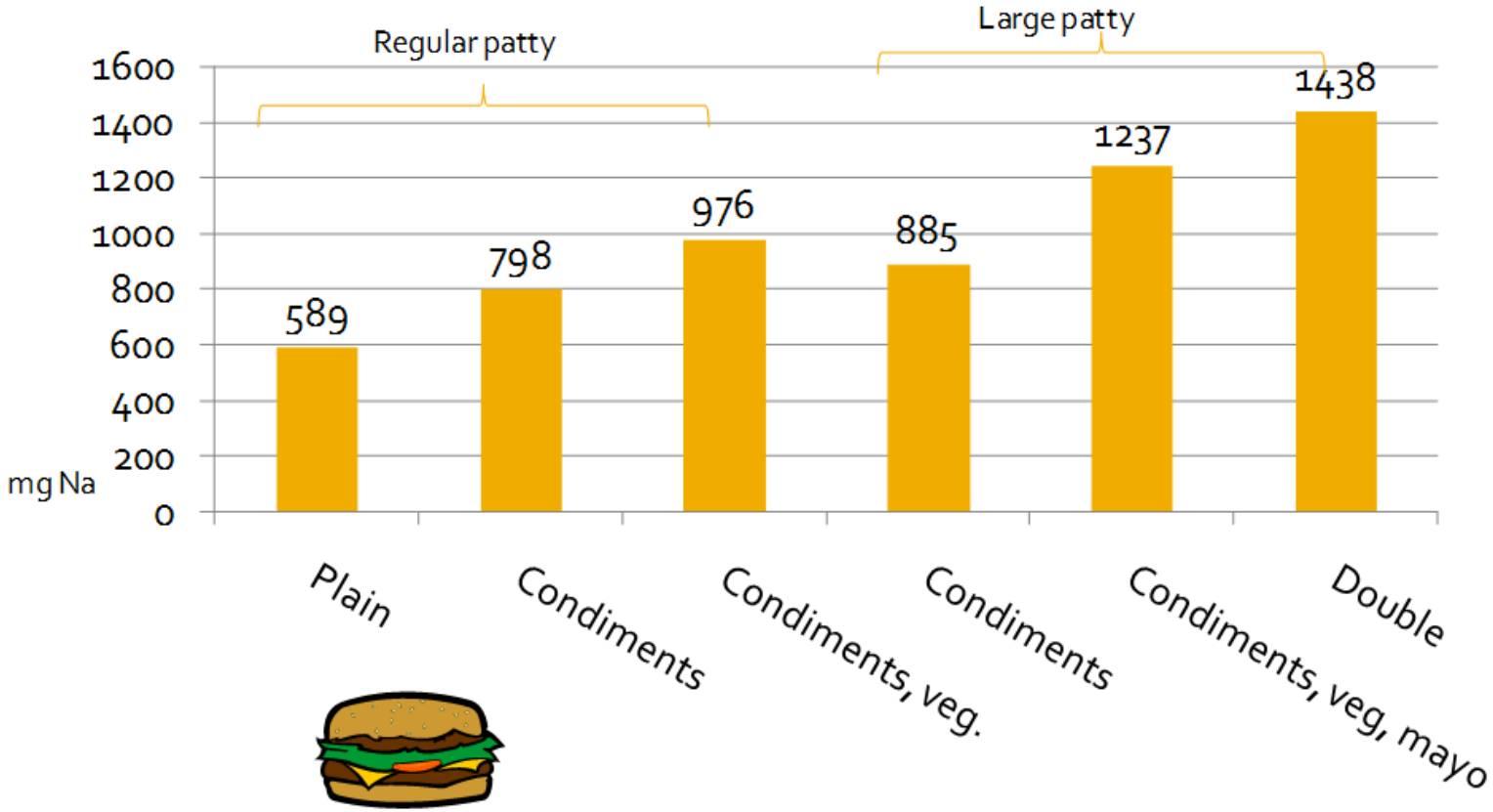
* 85 gram serving (3 oz.)

Vinegar and Oil on Salad Helps with 1,500 mg Sodium Budget

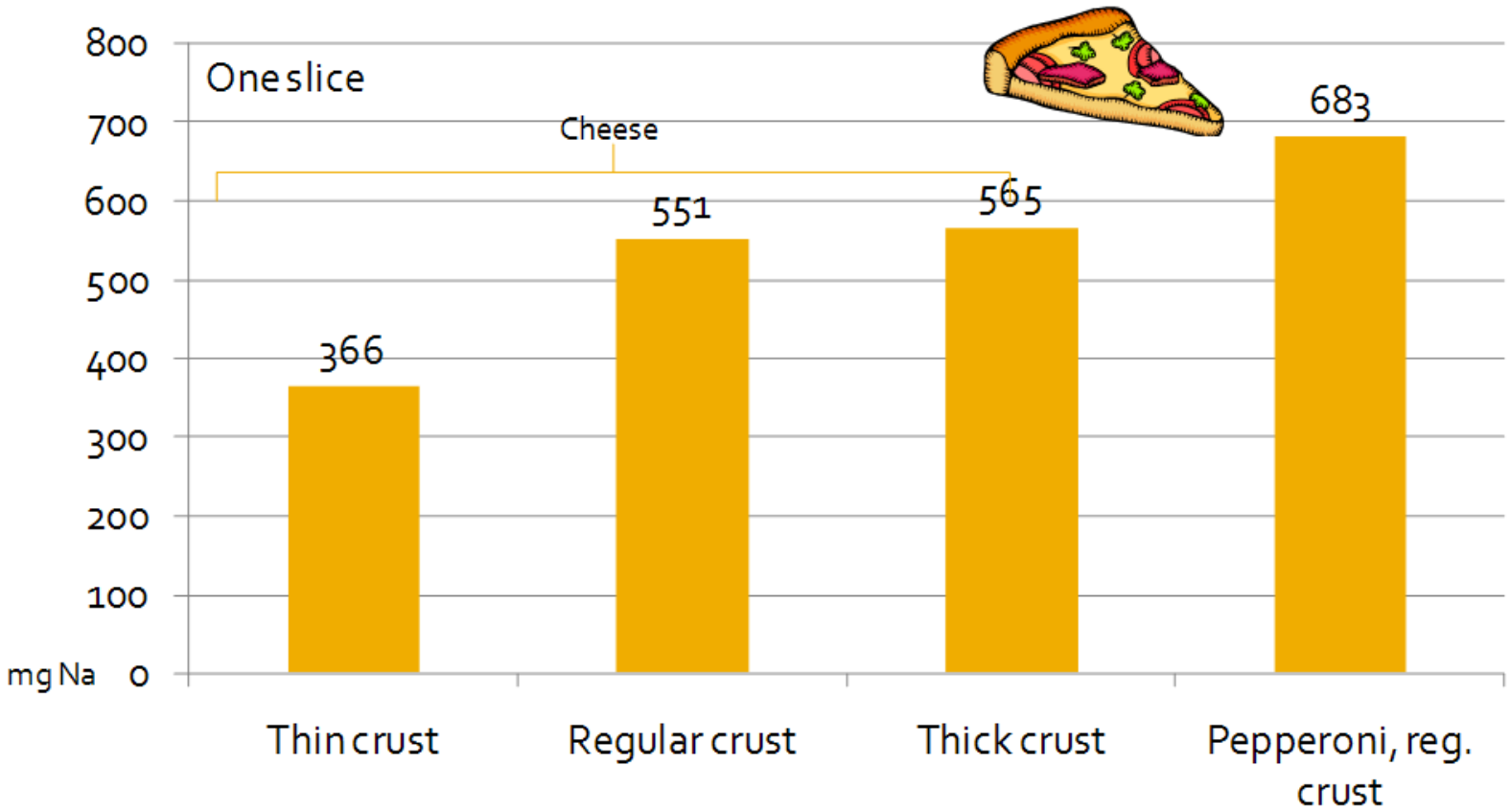


A serving of fat-free or light salad dressing may be 2 tbsp.

A Large Double Cheeseburger has Almost 1,500 mg Sodium

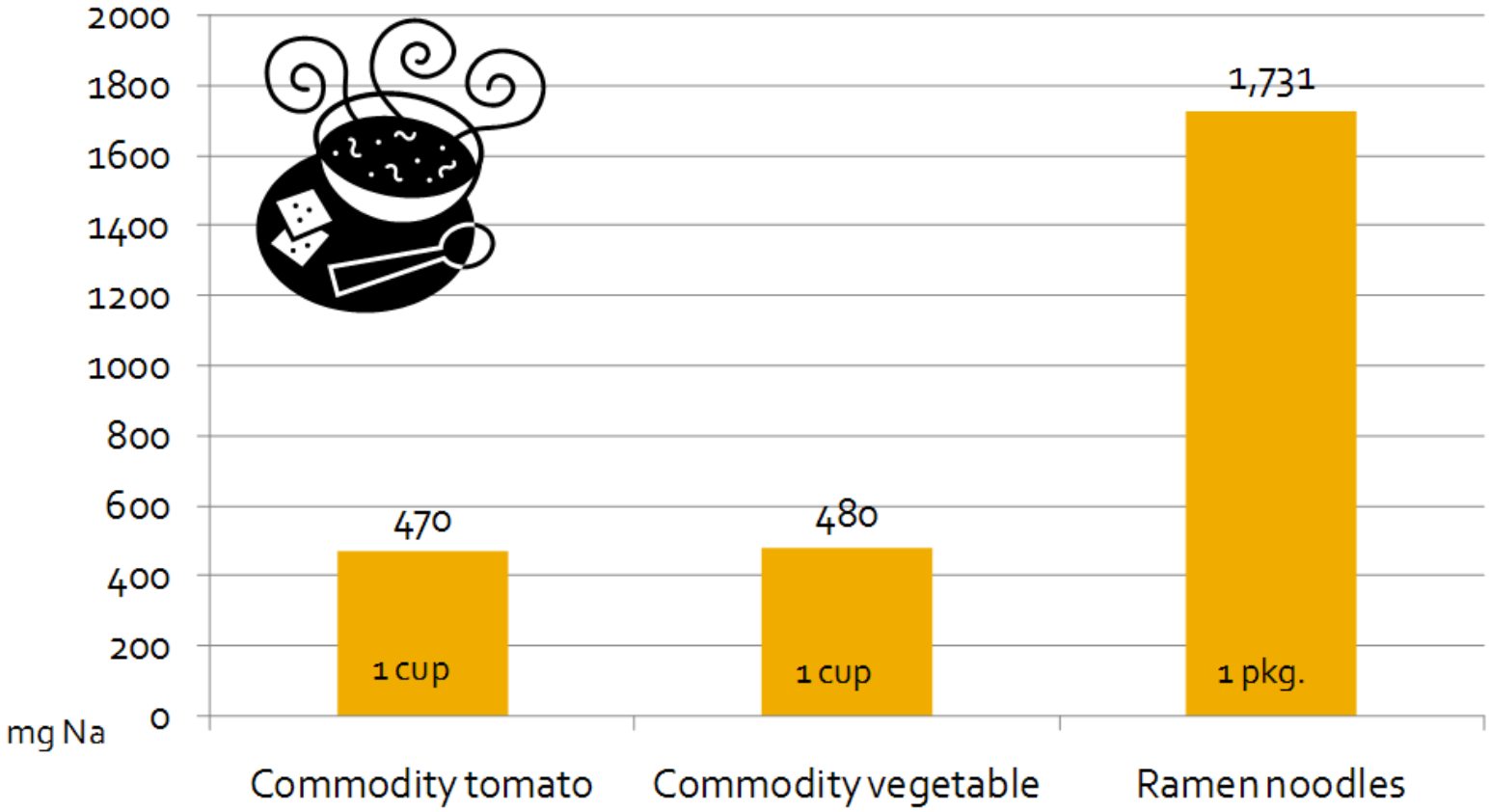


If You're Having Pizza, Thin-Crust is a Lower Sodium Choice

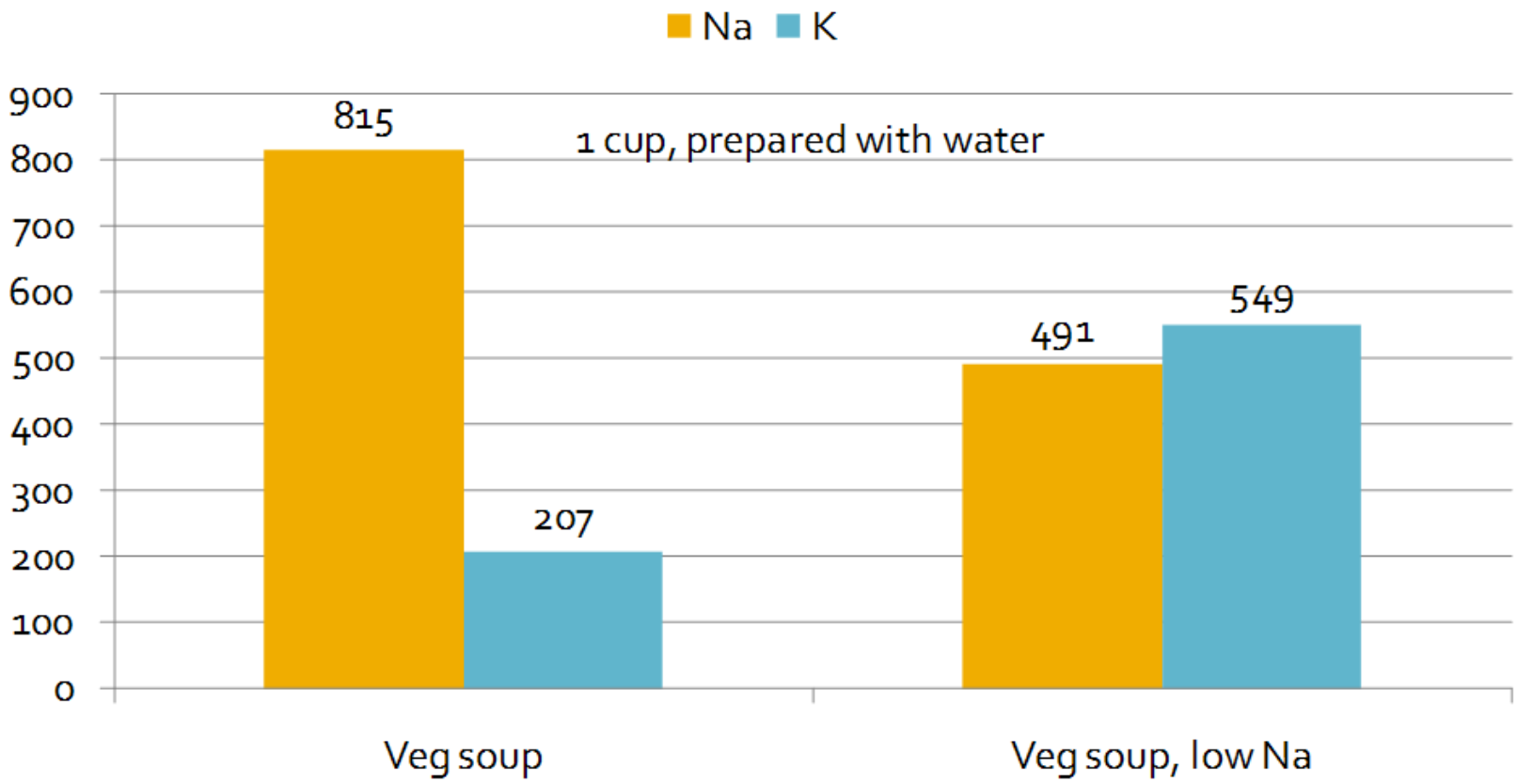


But who only eats one slice?

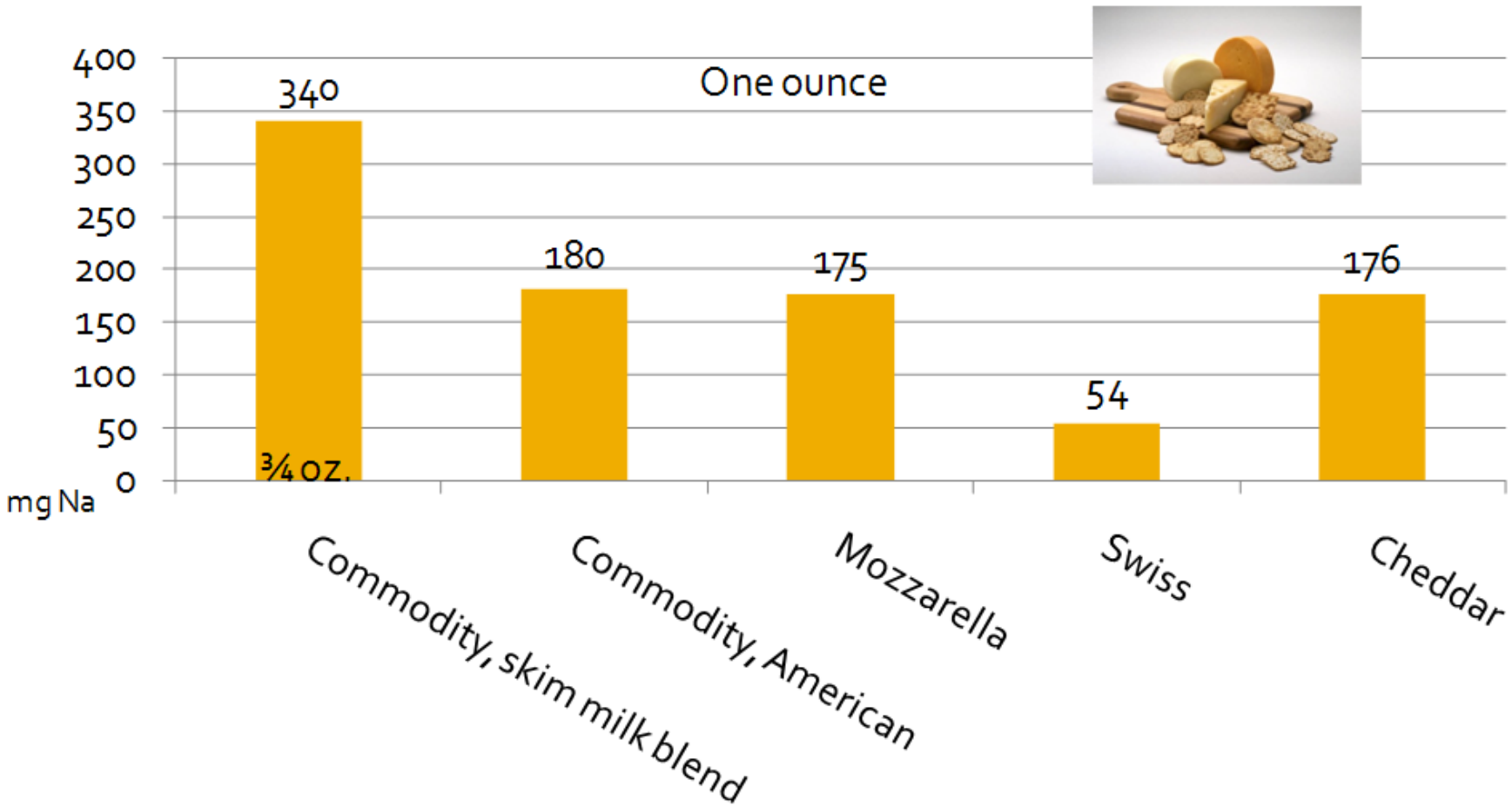
Soup Can be a Source of Sodium



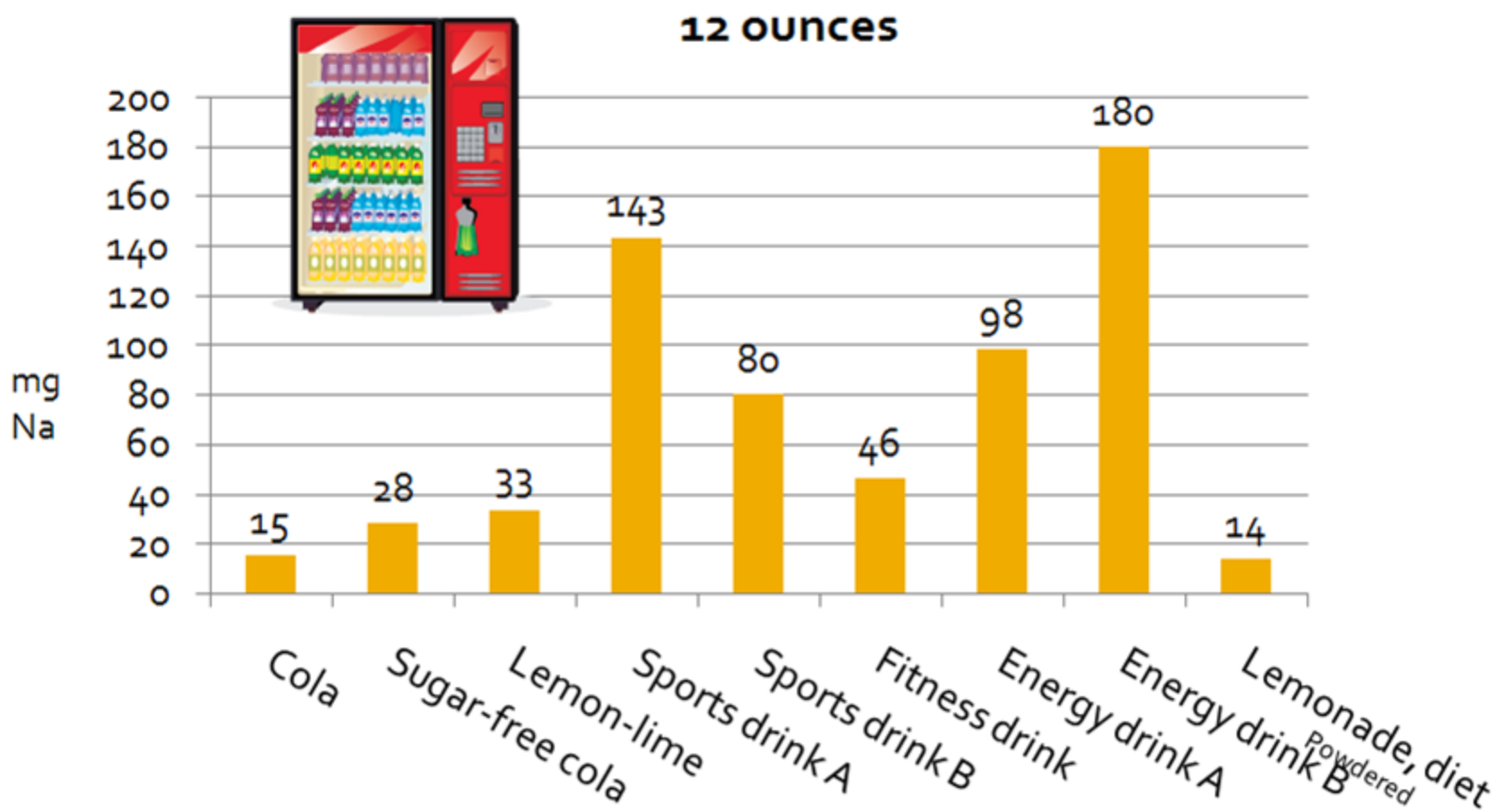
Lower-Sodium Canned Soups May Have Potassium Chloride Instead



Cheese Matters when Counting Sodium (Crackers Count Too)



Read Beverage Labels for Sodium



Look for Sodium on Food Labels

The amount listed is for one 1-cup serving. If you eat two servings, the amount doubles.

Nutrition Facts

Serving Size: 1 cup (228g)

Servings Per Container: 2

Amount Per Serving	
Calories: 260 **Calories from Fat:** 120	
	% Daily Value*
Total Fat 13g	20 %
Saturated Fat 5g	25 %
Trans Fat 2g	
Cholesterol 30mg	10 %
Sodium 660mg	28 %
Total Carbohydrate 31g	10%
Dietary Fiber 0g	0 %
Sugars 5g	
Protein 5g	

Vitamin A	4%	Vitamin C	2%
Calcium	15%	Iron	4%

* Percent Daily Values are based on a 2,000 calorie diet.

This package has two 1-cup servings.

One serving has 660 milligrams of sodium.

One serving has 28% Daily Value of sodium.

- 5% or less is low.
- 20% or more is high.

For this food label, 28% Daily Value is **high** for sodium.

% Daily Value for sodium is based on 2,400 mg

NKDEP How to Read a Food Label

Summary: Sodium and Albuminuria

- Sodium intake is associated with albuminuria in certain populations
- *New* 1,500 mg sodium per day for CKD, DM
  - Fast foods are high in sodium
  - Read Nutrition Facts labels for sodium

Possible Risk Factors: Diet

- Sodium
- **Protein**

Relationship Between Urine Albumin and Dietary Protein is Not Clear

- Type of protein may make a difference
  - Animal protein may be associated with higher urine albumin

Animal Protein Intake May be Associated with Higher Urine Albumin

- Two or more servings of red meat per week may increase risk of microalbuminuria.

  Nurses Health Study (Lin J et al., 2010)

- Nondairy animal foods are associated with albuminuria.

  Multiethnic Study of Atherosclerosis (Nettleton et al., 2008)

- High protein intake is associated with urine albumin for both hypertension and diabetes (but not if renal function is normal).

  NHANES III (Wrone et al., 2003)

Lowering Dietary Protein May Help Reduce Urine Albumin or Proteinuria

- Low-protein diet may slow increase in urine albumin level for insulin-dependent diabetes.

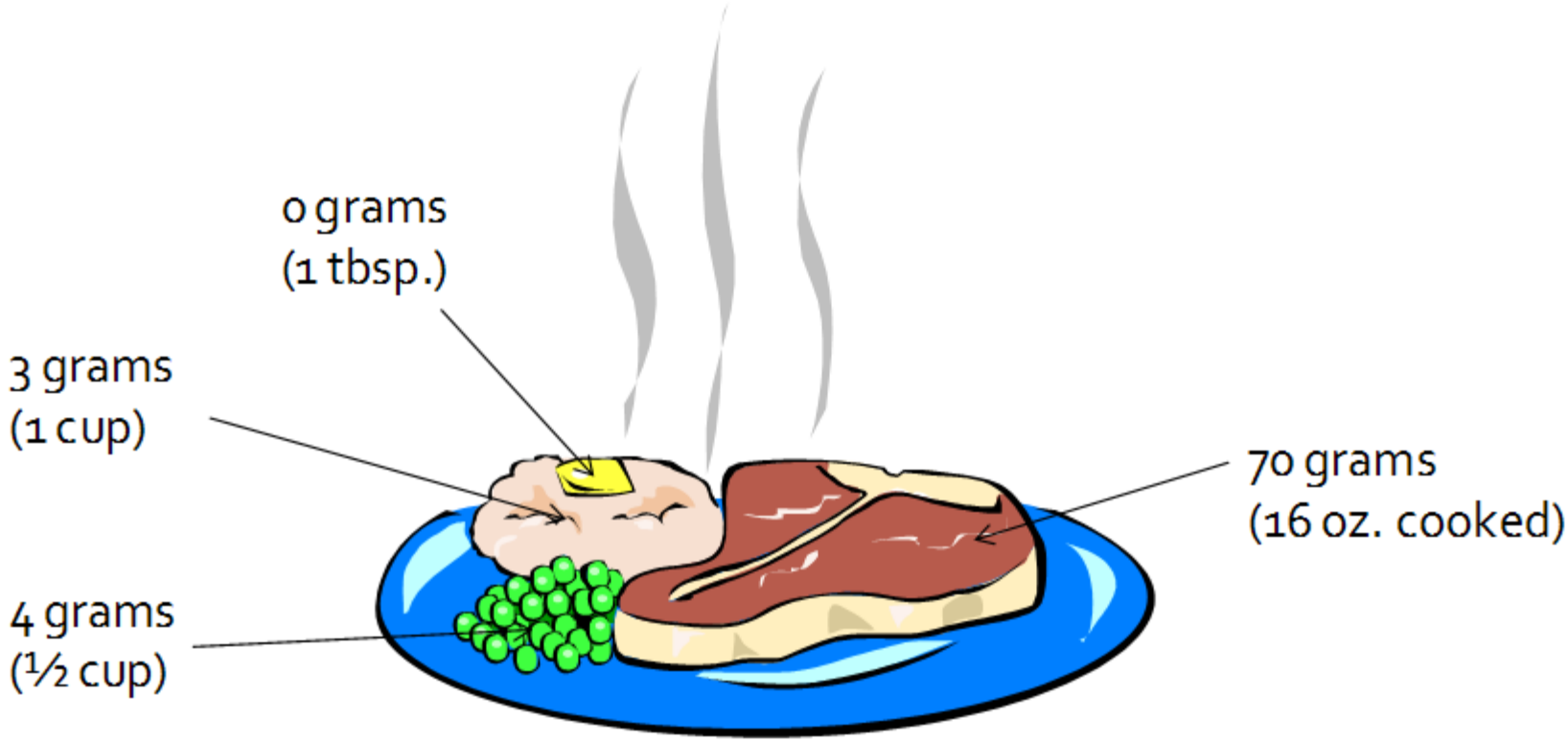
  (Pedrini et al, 1996)
- Use of supplemented very-low-protein diet is associated with decrease in proteinuria.

  (Chauveau et al, 2007)

Type of Animal Protein Still Controversial in Diabetes

- Red meat > chicken > fish
  - UAER lower with chicken (compared to beef) in T2 DM with macroalbuminuria [Brazil] (de Mello et al, 2006)
  - UAER lower with chicken (compared to beef) in T2 DM with microalbuminuria [Brazil] (Gross et al, 2002)
  - Risk of microalbuminuria lower with fish protein in T1 diabetes [Sweden] (Mollstein et al, 2001)

Many of Us Eat More Protein than Recommended

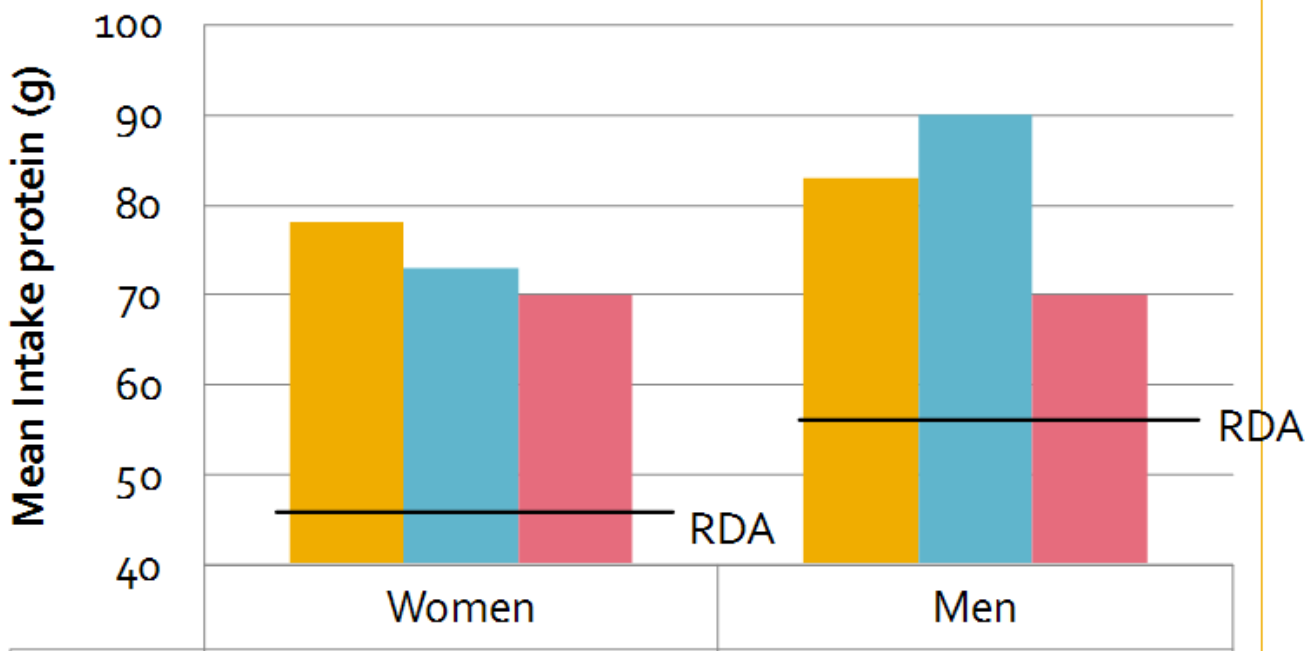


One tbsp. commodity buttery spread has 85 mg sodium

How Much Protein Do We Need?

- The Recommended Daily Allowance (RDA) for protein is based on weight.
- **RDA: 0.8 grams of protein/ kilogram body weight**
- Reference man weighs 70 kg
  - He needs about 56 grams of protein per day
- Reference woman weighs 57 kg
  - She needs about 46 grams of protein per day

Navajo Adults: Protein Intake Higher Than Recommended

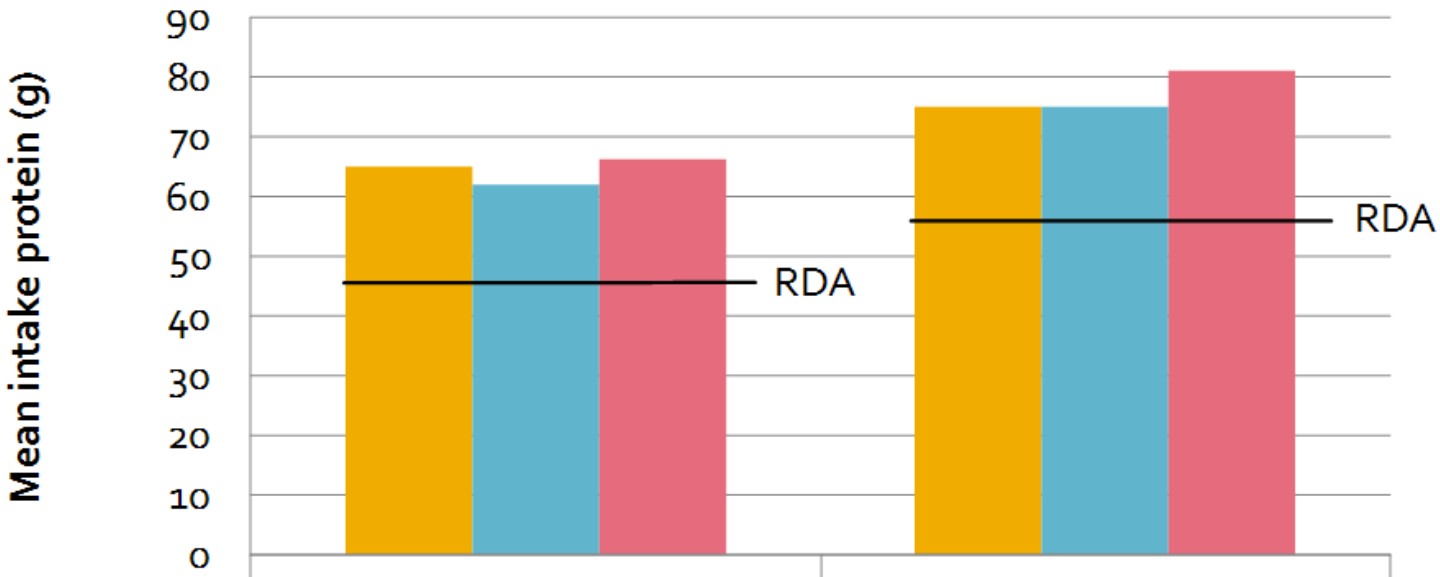


	Women		Men	
20-39	78	(SEM 3)	83	(SEM 3)
40-59	73	(SEM 4)	90	(SEM 4)
60 plus	70	(SEM 3)	70	(SEM 7)

SEM = standard error of mean

Adapted from Ballew et al, 1997

SHS: Protein Intake Higher Than Recommended



	Women	Men
Arizona	65 ± 31	75 ± 38
Dakotas	62 ± 30	75 ± 42
Oklahoma	66 ± 29	81 ± 40

Adapted from Stang et al, 2005

Where is the Protein?

Fruit (1/2 c.)
0-1 gram

Vegetables (1/2 c.)
2-3 grams

Milk (1 c.)
8 grams

Meat (3 oz.)
21 grams

Egg (1)
6 grams

Beans (1/2 c.)
4 grams

Grains (1/2 c.)
3- 4 grams

What Counts as a Serving of Meat?

- 3 ounces (21 grams)
  ≈ size of a deck of cards

This is more than one serving of meat

Protein: Summary

- Protein intake may be associated with albuminuria (animal > plant protein)
- Many of us eat more protein than recommended

Summary: Work Towards Smaller Portions of Foods Rich in Protein

Possible Interventions for Reducing Urine Albumin

- Blood pressure control
  - ACEi and ARBs
    - Gentle reminder: Please don't reach for the salt substitute
- Weight reduction
- Tobacco cessation
- Aim for less than 1,500 mg sodium per day
- Reduce protein intake, if excessive

Thank you!

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