

Feasibility of using spot urines for WHI CVD association studies

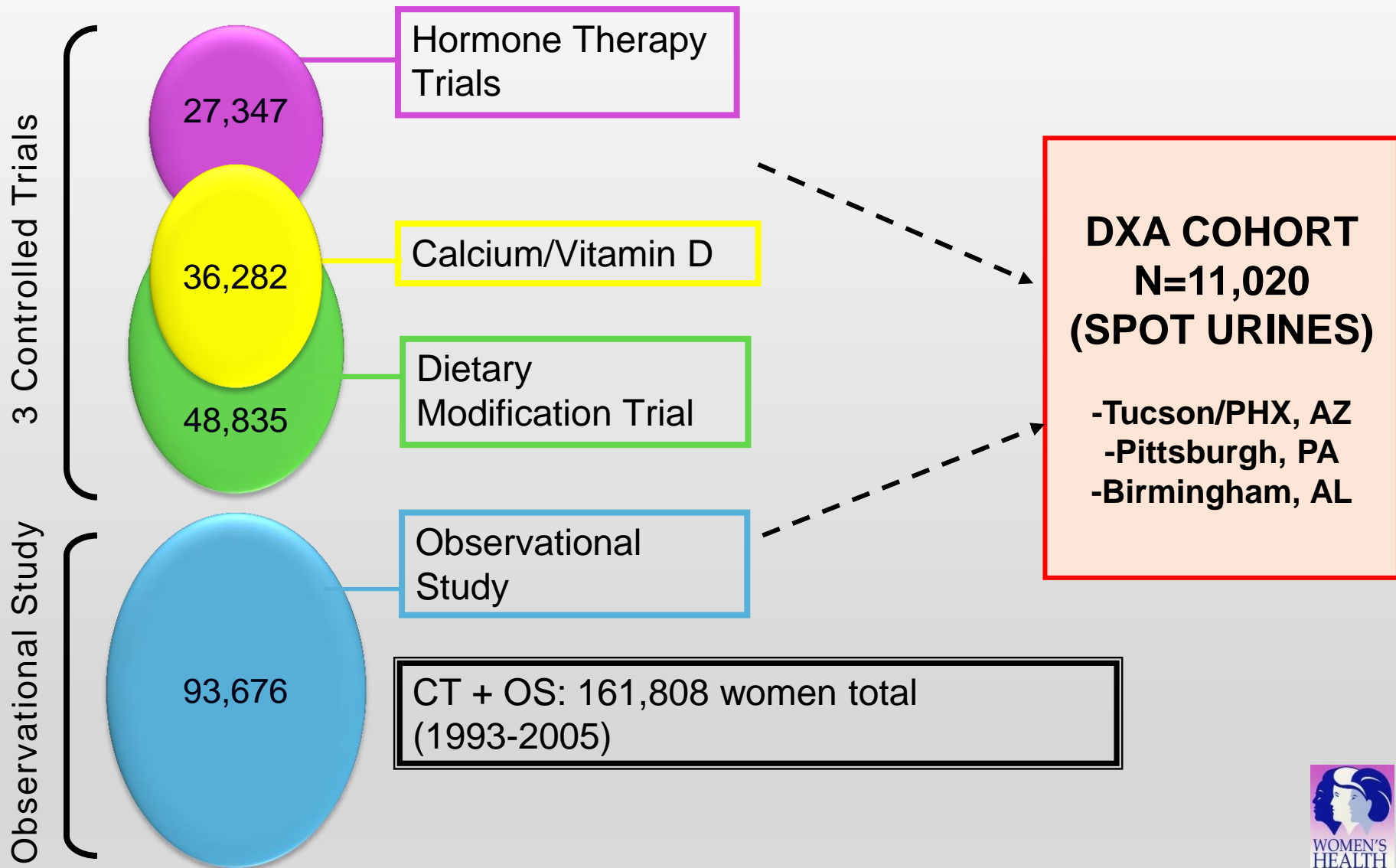
AS 525 Feasibility Study 2105

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WHI Components



Introduction

■ Sodium, potassium and cardiovascular disease?

↑ sodium intake ↑ risk CVD Moderate evidence	↑ sodium intake ↑ risk hypertension Higher evidence	Potassium and blood pressure Insufficient evidence
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■ Dietary self-reports of sodium (Na) and potassium (K) are biased. Biomarkers may be used to derive calibrated intake estimates.



Huang Y, Van Horn L, Tinker LF, Neuhaus ML, Carbone L, Mossavar-Rahmani Y, Thomas F, Prentice RL, Measurement error corrected sodium and potassium intake estimation using 24-hour urinary excretion. *Hypertension*. Feb 2014;63(2):238-244.

■ Biomarker-calibrated estimates may be used in diet/disease association analyses.



Carbone L, Johnson KC, Huang Y, Pettinger M, Thomas F, Cauley J, Crandall C, Tinker L, Susan LeBoff M, Wactawski-Wende J, Bethel M, Li W, Prentice R. Sodium Intake and Osteoporosis. Findings from the Women's Health Initiative. *J Clin Endocrinol Metab*. Feb 10 2016:jc20154017.

Introduction

- 24-hour urine collections have been the gold standard for estimating sodium and potassium intakes
 - 90% excreted sodium ~ dietary intake
 - 80% excreted potassium ~ dietary intake
- 24-hour urine collections are burdensome to collect.
- Spot urines are more practical than 24-hour urine collections epidemiologically, but measurement properties are uncertain.



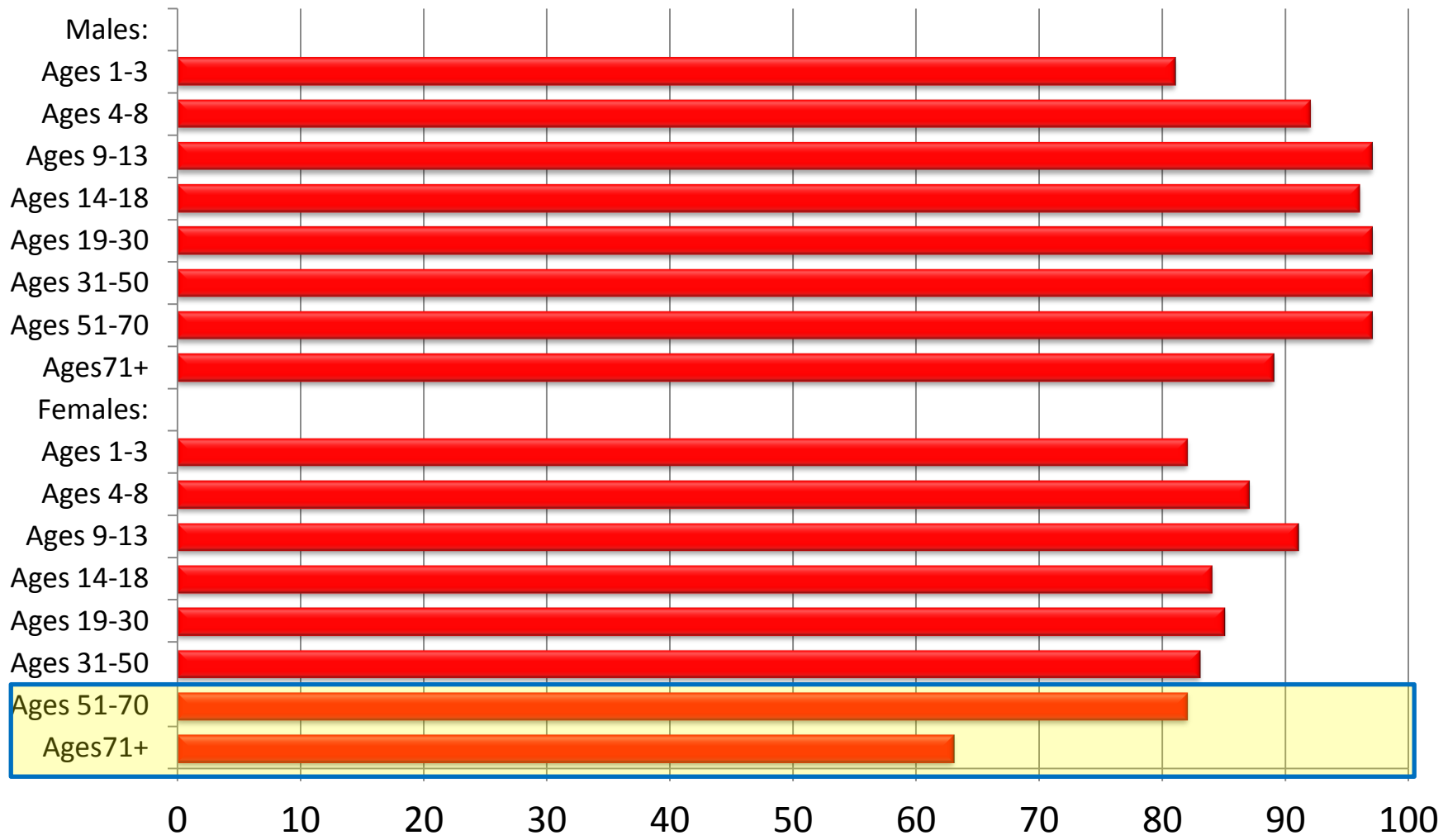
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US Dietary Guidelines for Americans

- **Daily Nutritional Goals Based on Dietary Reference Intakes and Dietary Guidelines Recommendations**
 - **2300 mg sodium/day**: Women and men 51 years of age and older
- **Hypertension?**
 - DGAC concurs with 2013 AHA/ACC Lifestyle Guideline
 - **“No more than 2,400 mg of sodium/day.”**
 - **“Further reduction of sodium intake to 1,500 mg/d can result in even greater reduction in blood pressure.”**



Sodium: Percent of age/sex group with usual intakes above the UL



The Salty Six

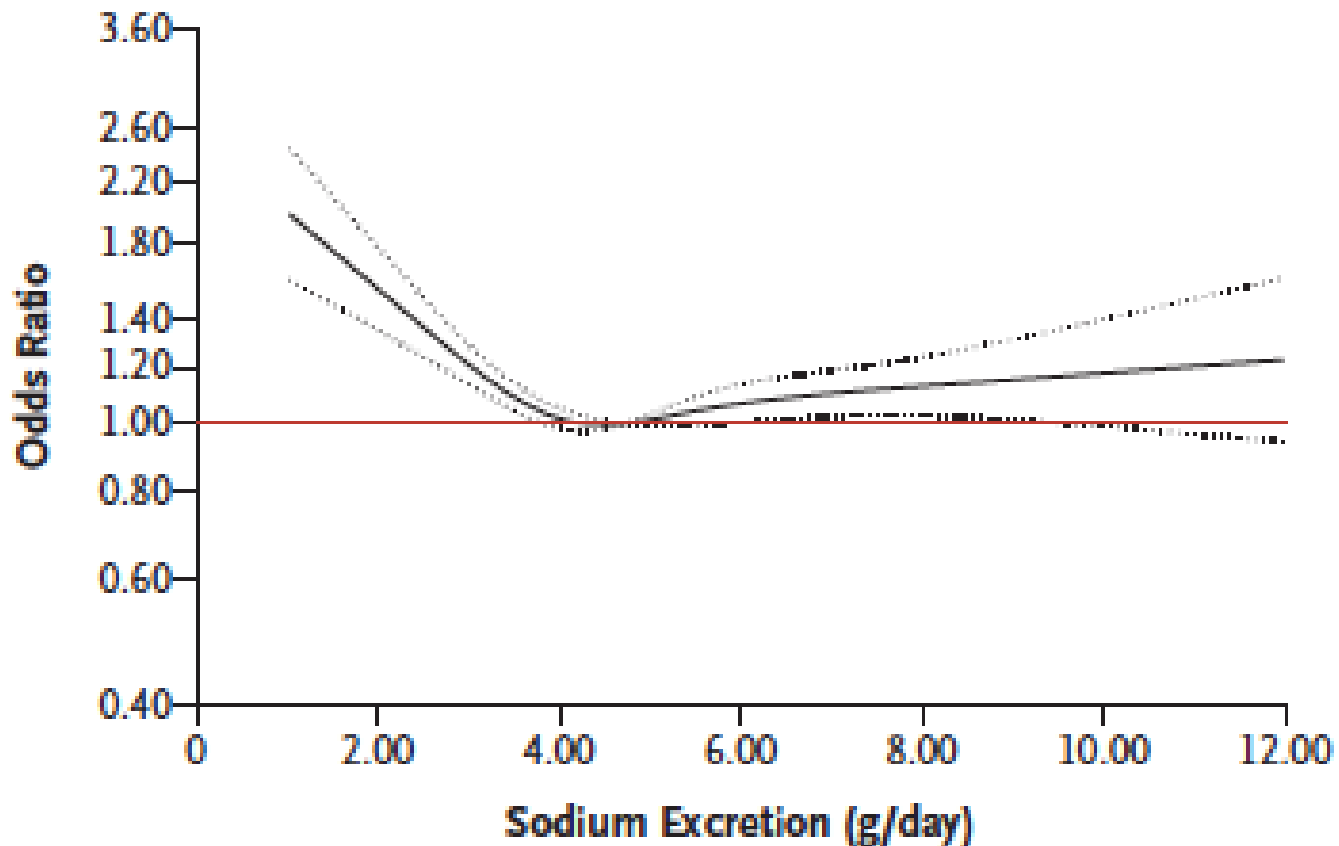
- Breads and rolls
- Cold cuts and cured meats
- Pizza
- Soup
- Sandwiches
- Poultry

Sodium Snipits

- 1 slice bread ~147 mg sodium
- 1 oz potato chips ~140 mg sodium
- >75% sodium from processed, prepackaged and restaurant foods
- Only ~10% of sodium from salt during cooking or at the table

“The optimal range of sodium intake for cardiovascular health is controversial.”

A Estimated Sodium Excretion and Risk of Death or Cardiovascular Events



No. of Events	101	1,023	1,437	597	126	25
No. at Risk	1817	30,124	46,663	18,395	3885	756



Purpose of AS 525

To elucidate the measurement properties of spot urine-derived sodium and potassium excretion compared with 24-hour urine excretion.

Moving toward: Feasibility of using WHI spot urines to augment research on risk of sodium intake on CVD in postmenopausal women.

Study Design & Lab Methods

Nutrition and Physical Activity Assessment Study (NPAAS): Feeding Study

n = 153 WHI Extension 2010-2015 from Seattle WHI area (2011-2013)

14-day feeding study, provided participants replications of their usual diet

Day 13: Morning first void spot urine at home followed by 24-hour collection

Day 14: Brought urine collections to clinic

NPAAS Feasibility Study of Spot and 24-hour urine measurement properties

n = 150 NPAAS feeding study with a spot & 24-hour urine

Aliquots from the spot and 24-hour urines frozen at -70° C

Sodium and potassium analyzed by ion selective electrode

Creatinine, an adjustment factor linking the spot and 24-hour sodium and potassium concentrations, assayed by spectrophotometric detection of a colored creatinine-picrate complex

Statistical Methods – Estimating 24HR Na and K from Spot Urines

- **Statistical analyses generated calibration equations for estimating 24-hour sodium and potassium excretion from spot urines and study subject characteristics.**
- **Calibration equations for creatinine-adjusted sodium, potassium and sodium/potassium ratio**
 - **developed separately by regressing 24-hour excretion levels on spot urine measurements**
 - **subject characteristics on the basis of Aikake information criterion (AIC).**
 - **age, body mass index (BMI), physical activity, education, season, and race**

Results

Table 1a: Participant Characteristics (n = 150)

	Mean (or n)	SD (or %)
Age, years (during study)	75.4	3.5
Race/Ethnicity		
White	143	95%
Other	7	5%
Education		
< College	26	17%
≥ College	123	82%
Smoking Status		
Current	3	2%
Former or Never	147	98%

Results

Table 1b: Medications and Diet (n = 150)

	Mean (or n)	SD (or %)
Taking anti-hypertension associated medication*	66	44%
Taking diuretics **	24	16%
Energy intake, kcal***	1921	291
Sodium intake, mg***	2511	676
Potassium intake, mg***	3111	631

* ACE inhibitors, angiotensin II receptor blockers, beta blockers, calcium channel blockers, diuretics (non-specified indication)

** Diuretics (loop, n=5; thiazide and thiazide-like, n=14; combinations, n=5)

*** Not biomarker-calibrated

Results

Table 2. Urinary excretions in spot urine and 24-hour urine (geometric means)

	Sodium (MEq/L)		Potassium (mEq/L)		Creatinine (mg/L)	
	<u>Spot</u>	<u>24-hour</u>	<u>Spot</u>	<u>24-hour</u>	<u>Spot</u>	<u>24-hour</u>
Excretion	59.5	45.2	27.5	31.3	545	441
Excretion ratio Na or K/creatinine*	0.110	0.104	0.051	0.070		
* Na or K (mEq/L)/creatinine (mg/L)						

Results

Table 3. Calibration equation coefficients and R² (% Variation) regressing log-transformed 24 hour urine on spot urine (creatinine adjusted)

Beta coefficients (SE) and R ² % Variation						
	Sodium		Potassium		Sodium/Potassium	
	Beta	R ²	Beta	R ²	Beta	R ²
Intercept	-1.64 (0.12)		-1.74 (0.19)		0.36 (0.16)	
Spot urine	0.29 (0.06)	16.9%	0.37 (0.05)	26.7%	0.33 (0.06)	18.0%
Race (White)	--		0.17 (0.09)	1.7%	-0.26 (0.15)	1.7%
Current smoking	-0.27 (0.19)	1.3%	--		--	
Education		5.1%		2.7%		
HS	-0.13 (0.11)		-0.01 (0.08)		--	
>HS	0.23 (0.09)		0.14 (0.06)		--	
Overall R ²		23.3%		31.1%		19.7%
Overall r (√R ²)		0.48		0.56		0.44

Conclusions

- Suggestive that spot urine may serve as a reasonable replacement for 24-hour urine for assessing sodium and potassium intake in the WHI.
- WHI has the potential to cost-effectively use existing spot urine biospecimens to research the association of sodium and potassium intakes as risk factors for CVD.



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WOMEN'S HEALTH INITIATIVE

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