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& CLINICAL RESEARCH

Developing Nutritional Pattern Interventions

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Outline

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- Types of dietary intervention studies
- Dietary patterns
  - Process of designing interventions of dietary patterns
  - Common issues
  - Common mistakes
- The future (actually the present)

Types of Dietary Intervention Studies

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- Feeding studies
  - Complete feeding
  - Partial feeding
- Behavioral interventions
- Pill supplements (vitamins, minerals) studies
- Mixed interventions

4 NHLBI-Supported Feeding Studies Focused on Diet and Blood Pressure (BP)

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DASH (Dietary Approaches to Stop Hypertension)

- Focus: overall dietary pattern on BP

DASH-Sodium

- Focus: salt, alone or combined with DASH diet, on BP

OmniHeart (Optimal Macronutrient Intake to Prevent Heart Disease)

- Focus: replacement of some carbohydrate with protein or unsaturated fat

OmniCarb

- Focus: amount and type of carbohydrate

Complete Feeding Study: DASH

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- Why this design: test dietary pattern by controlling multiple, relevant nutrients without the confounding effect on incomplete adherernce
- Study population: 'uber' volunteers, with high BP - the primary outcome
- Duration of feeding: 11 weeks
- Feasibility: really expensive, logistical challenges, specialized centers

Objective and Design of DASH: A Randomized Controlled Feeding Study

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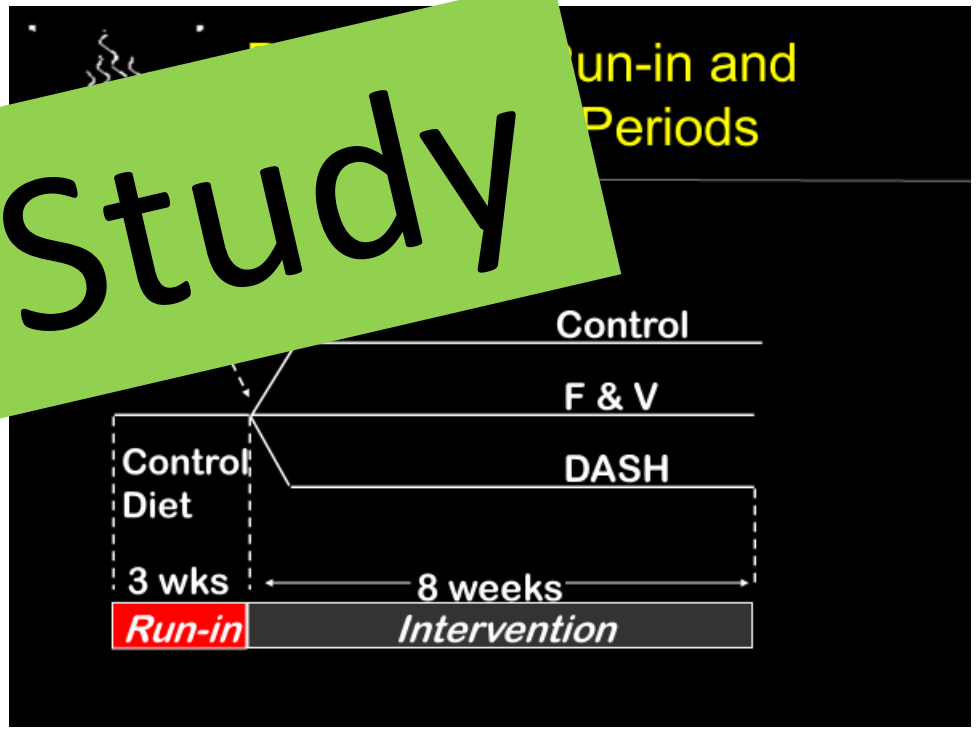
Efficacy Study



Main Results: DASH diet lowers BP, with striking results in persons with hypertension

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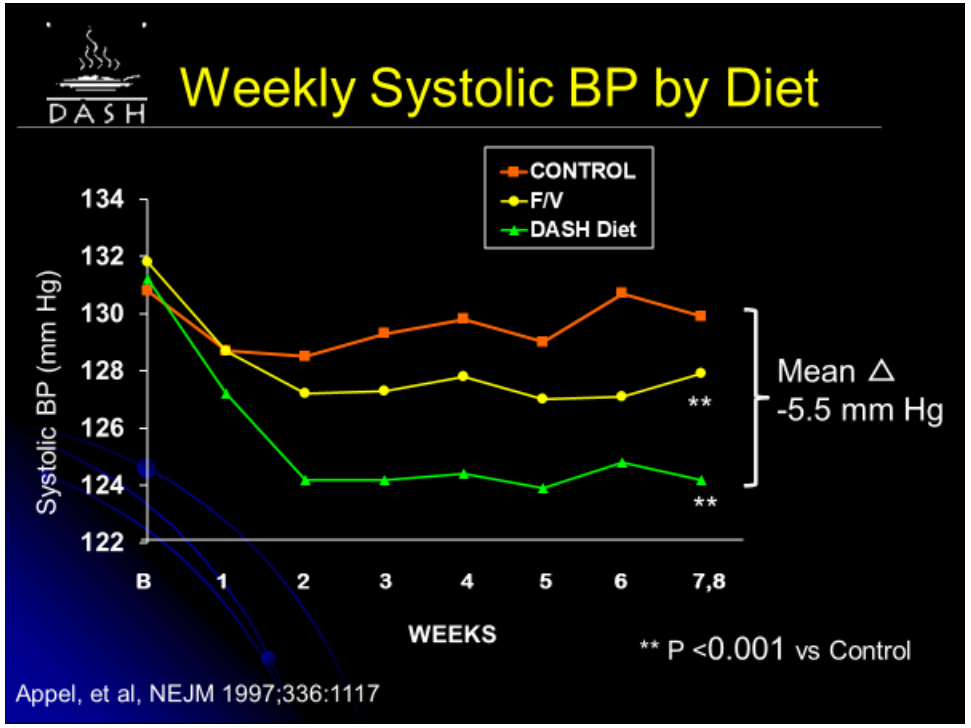

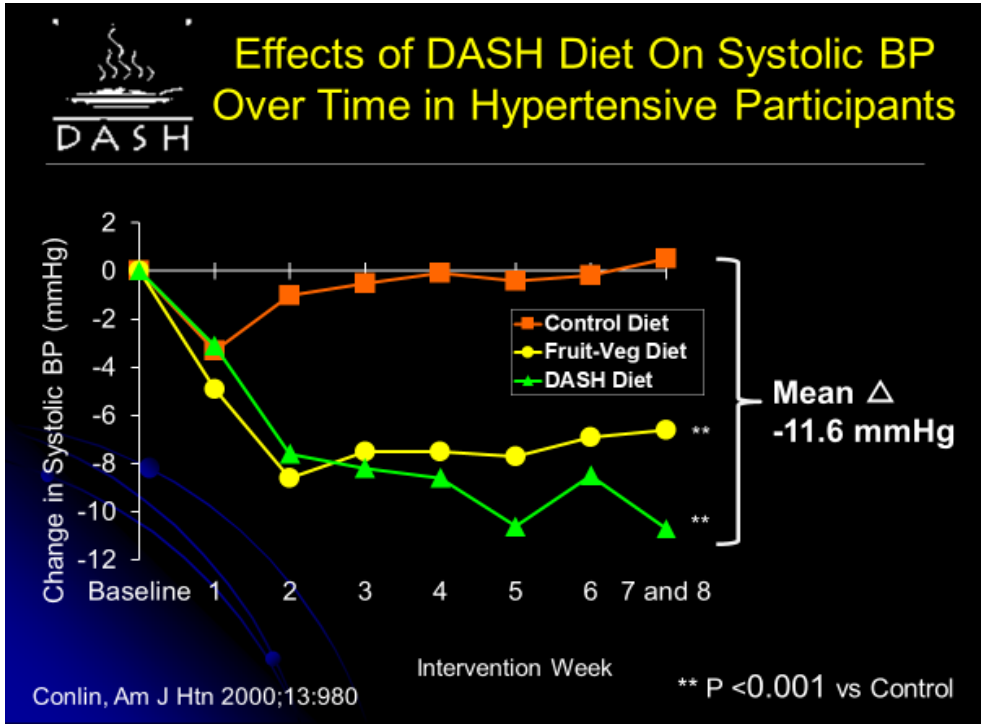

Design Process of DASH: Start with Nutrient Targets

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Steps in Our Process

1) Set nutrient targets of diets
   - Variable
   - Fixed
2) Conduct the trial
3) Describe diets in terms of food groups and # of servings
4) Develop description of the diets to communicate results

Feeding Protocol

- All foods and beverages provided for 11 weeks
- Seven day meal cycle
- All food had to be consumed
- No additional food allowed
- Discretionary beverage allowance
- One on-site meal: Monday - Friday
- All other meals consumed off-site
- Weight maintenance: kcal adjusted periodically to maintain stable weight

Measurement Protocols

- End-of-Study in DASH
  - Blood pressure: 5 days of BP measurements, resulting in very precise estimates of change from baseline
  - Fasting blood: lipids, nutritional biomarkers, biorepository of serum, plasma, [whole blood]
  - 24 Hour Urine: sodium, potassium, urea nitrogen, calcium, phosphorus
- Possibilities
  - Stool for microbiome
  - Remote monitoring, e.g. continuous glucose monitoring
  - Functional assessments, e.g. pulmonary function tests, timed walk

Impact of DASH Trial on Prevention Policy

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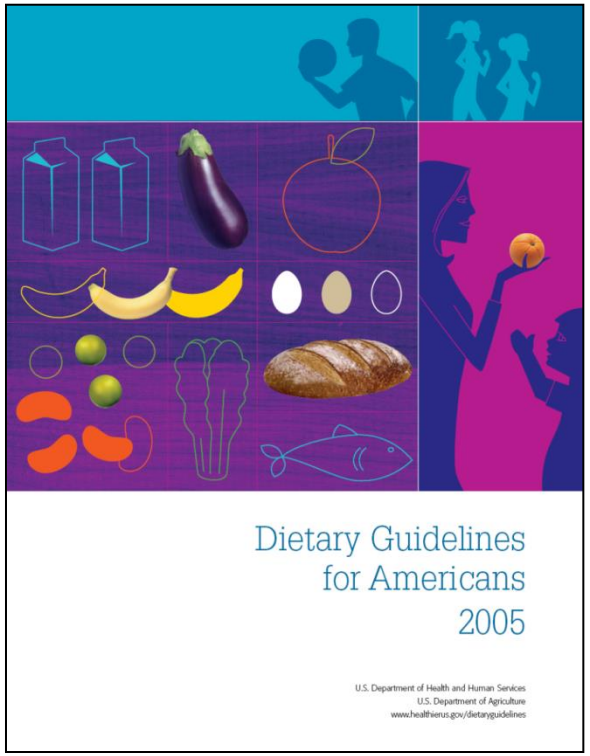
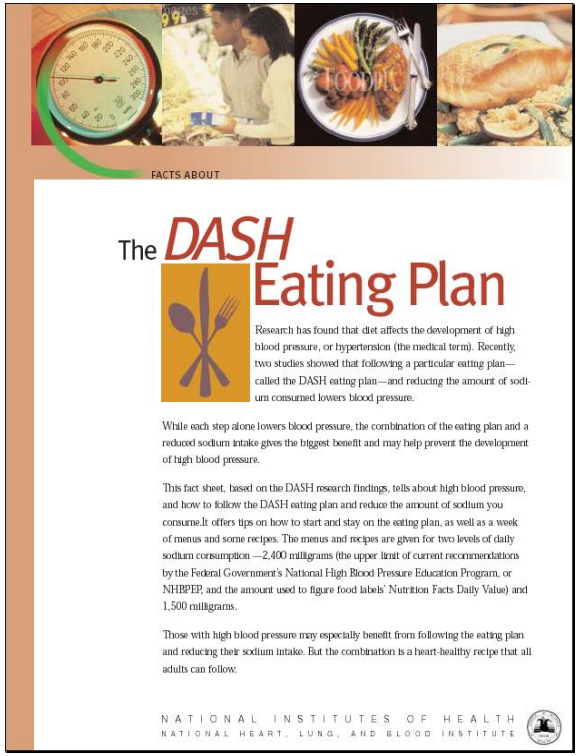
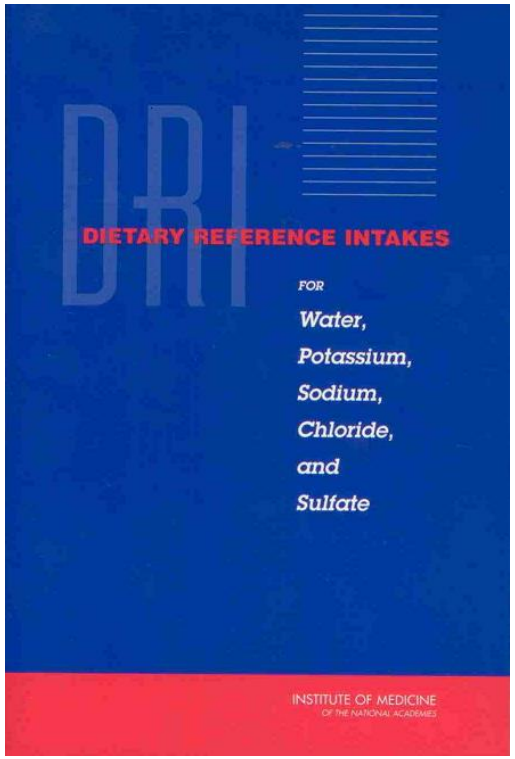
2005 Dietary Guidelines for Americans



JNC VII – Hypertension Prevention and Treatment Guidelines



IOM Report on Dietary Reference Intakes for Electrolytes



Observations

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- Feeding studies are really expensive
- Easier and less expensive to test:
  - supplementation than restriction
  - single nutrients than whole patterns
- Older persons adhere better than younger persons
- NIH, especially NHLBI, not interested in clinical trials, as evidenced by:
  - the barriers for investigator-initiated trials
  - inability of NIH staff to launch major initiatives

Costs of Feeding Studies

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	Sample Size	Duration of Feeding	Total Costs	Per Participant Costs
DASH	459	11wk	$7.8 m	$17k
DASH-Sodium	412	14 wk	$11.8 m	$29k
Omni Heart	160	19 wk	$6.2 m	$39k
Omni Carb	160	21 wk	$10.3 m	$64k

Selected Design Issues: Diet (1)

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- By what process does one construct a dietary pattern?
  - what are the key characteristics of the dietary pattern? nutrients or foods?
  - what is the dose?
- What is the control condition?
- Approach to highly correlated nutrients/concepts
  - e.g. fiber and glycemic index
- How much effort to describe baseline diet and physical activity

Selected Design Issues: Diet (2)

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- Approach to kcal intake and weight
  - Options
    - » Stable weight (isocaloric)
    - » Weight loss (hypocaloric)
- What is the approach to nutrients other than kcal?
  - keep absolute amount of other nutrients constant?
  - keep nutrient density constant?

Macronutrient Goals, % kcal

	CARB*	PROT	UNSAT
Carbohydrate	58	48	48
Protein	15	*25*	15
Fat	27	27	37
Monounsaturated	13	13	21
Polyunsaturated	8	8	10
Saturated	6	6	6

*Similar to DASH diet, except that the carbohydrate content of DASH was 55% kcal and its protein content 18% kcal.

Absolute Intake (mmol/d) of Na and K in DASH and DASH-Na Trials by Kcal Level

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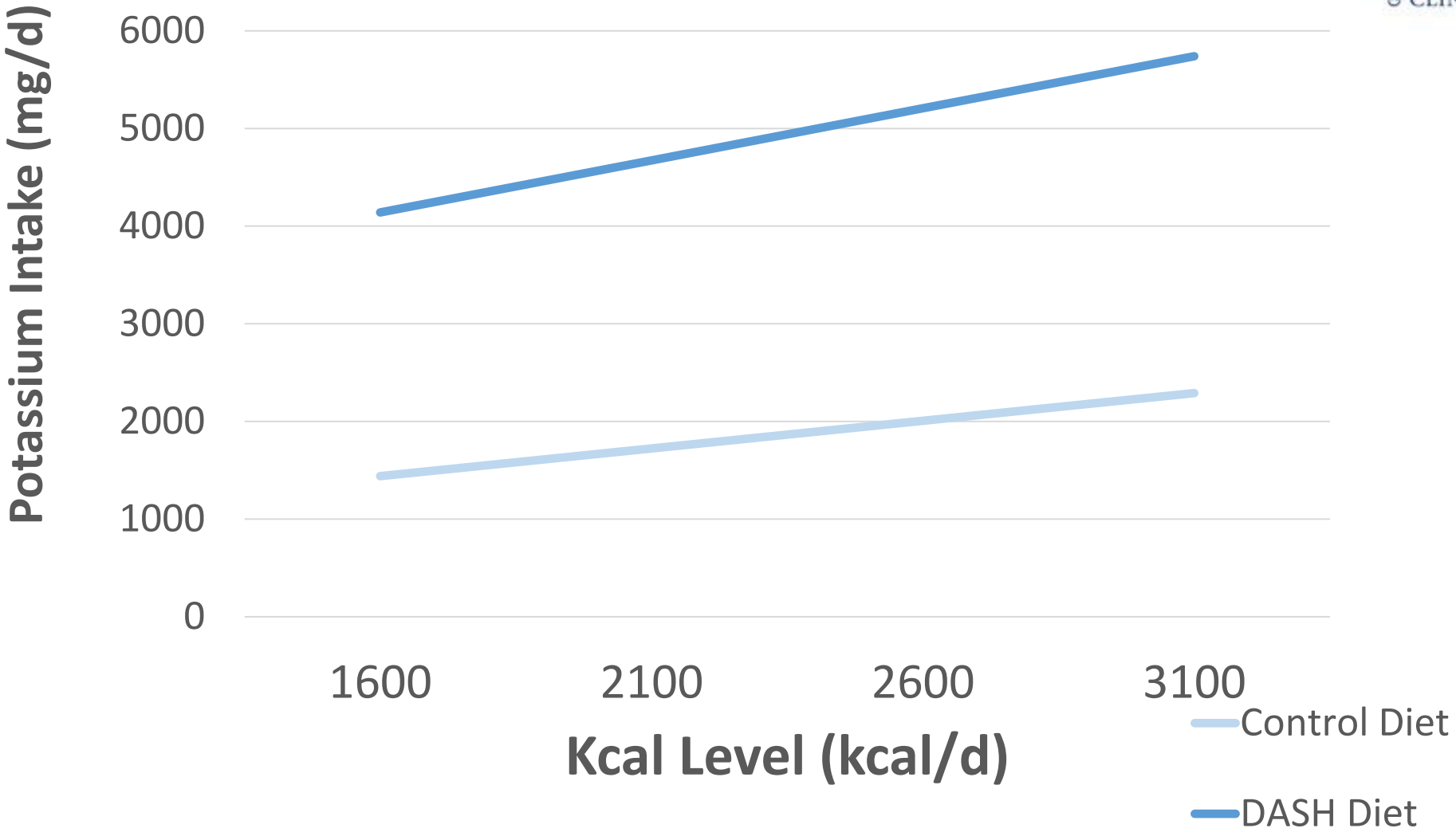
	Potassium (mmol/d)		Sodium Intake (mmol/d)		
Kcal level	DASH Diet		Lowest Level	Intermediate Level	Higher Level
1600	101		40	80	120
2100	118		50	100	150
2600	133		60	120	180
3100	150		70	140	210

Amount of Potassium in DASH and Control Diets by Kcal Level



Common Mistakes

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- Recruitment
  - Inadequate resources
- Wrong population to assess effects, especially true for secondary outcomes
- Suboptimal measurement of outcomes
- Insufficient duration to affect outcome
- Overoptimistic effect sizes

Alternative Approaches to Research Facility-Based, In-Person Feeding Studies

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- Shipping food from central production facility
  - Beltsville Agricultural Research Center
- Distributing food through existing meal delivery, mass production systems
  - Meals on Wheels
  - Company feeding operations