Dietary Patterns and Biomarkers of Inflammation and Endothelial Activation

in the Multi-Ethnic Study of Atherosclerosis (MESA)

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Inflammation, Diet & Cardiovascular Disease (CVD)

- Studies have shown that inflammation is involved the development of atherosclerosis and overt CVD
- Diet has been shown to be significantly related to CVD
- Diet → *inflammation* → CVD ?

Nutrients, Foods, Dietary Patterns & Inflammation

- Nutrients
  - Fatty acids: PUFA ↓, *trans* fat ↑
  - Antioxidant vitamins & related nutrients (lycopene, lutein) ↓
  - Fiber ↓
- Foods & Beverages
  - Nuts ↓
  - Fruits & vegetables ↓
  - Tea ↓
  - Alcohol ↓
- Dietary patterns

  Empirically-derived patterns
  - "Western"↑
  - "Prudent" ↓

Hypotheses

- Empirically-derived dietary patterns in the Multi-Ethnic Study of Atherosclerosis (MESA) will be similar to those previously reported with unique aspects due to ethnic and corresponding dietary diversity of the population.
  - "Western"-type pattern: ↑ biomarkers of inflammation and endothelial activation
  - "Prudent"-type pattern: ↓ biomarkers of inflammation and endothelial activation

Study Design

- Cross-sectional, baseline analysis of 5,089 male and female MESA participants
  - 2,407 men and 2,682 women
  - 43% White, 24% Black, 20% Hispanic, 13% Chinese
- Exclusionary criteria
  - Extreme energy intake/ implausible dietary data (*N* = 630)
  - Diabetes (*N* = 919)
  - Use of oral steroids and asthma medications (*N* = 134)

Methods: Diet Assessment

- Modified Block style 120-item food frequency questionnaire (FFQ)
- Responses categorized into 47 food groups
  - Foods & beverages quantified in servings/d
  - Mixed dishes allocated to multiple food groups
  - Foods with high consumption (e.g., coffee/tea creamers, pizza) or unique attributes (e.g., avocado/guacamole) were defined as a single food groups.
  - Cold cereals categorized as whole or refined grain based on brand name reported

Methods: Biomarkers of Inflammation & Endothelial Activation

- C-reactive protein (CRP)
  - ***N* = 5,053**
- Interleukin-6 (IL-6)
  - ***N* = 4,953**
- Homocysteine
  - ***N* = 5,073**
- Soluble Intracellular Adhesion Molecule-1 (sICAM-1)
  - ***N* = 2,068**
- Soluble E-selectin
  - ***N* = 777**

Statistical Analysis

- Principal Components (PCA) used to derive dietary patterns (SAS PROC FACTOR)
  - Dietary pattern score =
    sum of servings/day of each food group x food group loading value
- General linear model regression (PROC GLM) used to calculate log-transformed biomarker means according to quintiles of each dietary pattern
- *P*-trend calculated with dietary pattern score treated as a continuous variable

Statistical Analysis

- Multivariable model:
  - Age (y)
  - Gender
  - Race/ethnicity (White, Back, Hispanic, Chinese)
  - Examination site (Chicago, St. Paul, New York, Los Angeles county, Baltimore county, Forsyth county)
  - Education (<HS, = HS, >HS)
  - Energy intake (kcal/d)
  - Physical activity (active leisure & inactive leisure MET-min/wk)
  - Smoking (status & pack y)
  - Supplement use (at least weekly vs. not)

Food loading values for each dietary pattern

Fats & Processed Meats	*Vegetables & Fish*	*Beans, Tomatoes & Refined Grains*	*Whole Grains & Fruit*
Fats & oils (0.65)	Dark yellow vegetables (0.77)	Legumes (0.76)	Whole grains (0.59)
High-fat & processed meats (0.64)	Cruciferous vegetables (0.75)	Tomatoes (0.73)	Fruit (0.55)
Fried potatoes (0.60)	Other vegetables (0.62)	Refined grains (0.60)	Seeds, nuts & peanut butter (0.46)
Salty snacks (0.50)	Fish (0.60)	High fat cheeses, cream sauce (0.57)	Green leafy vegetables (0.39)
Desserts (0.48)	Other soups (0.58)	Avocadoes & guacamole (0.52)	Low-fat milk (0.33)
High fat cheeses, cream sauce (0.42)	High-fat Chinese dishes (0.41)	Red meat (0.46)	Cottage/ricotta cheese (0.31)
Vegetables, fruit, soy foods (> -0.14)	Coffee (-0.22)	Tea (-0.12)	Refined grains (-0.20)

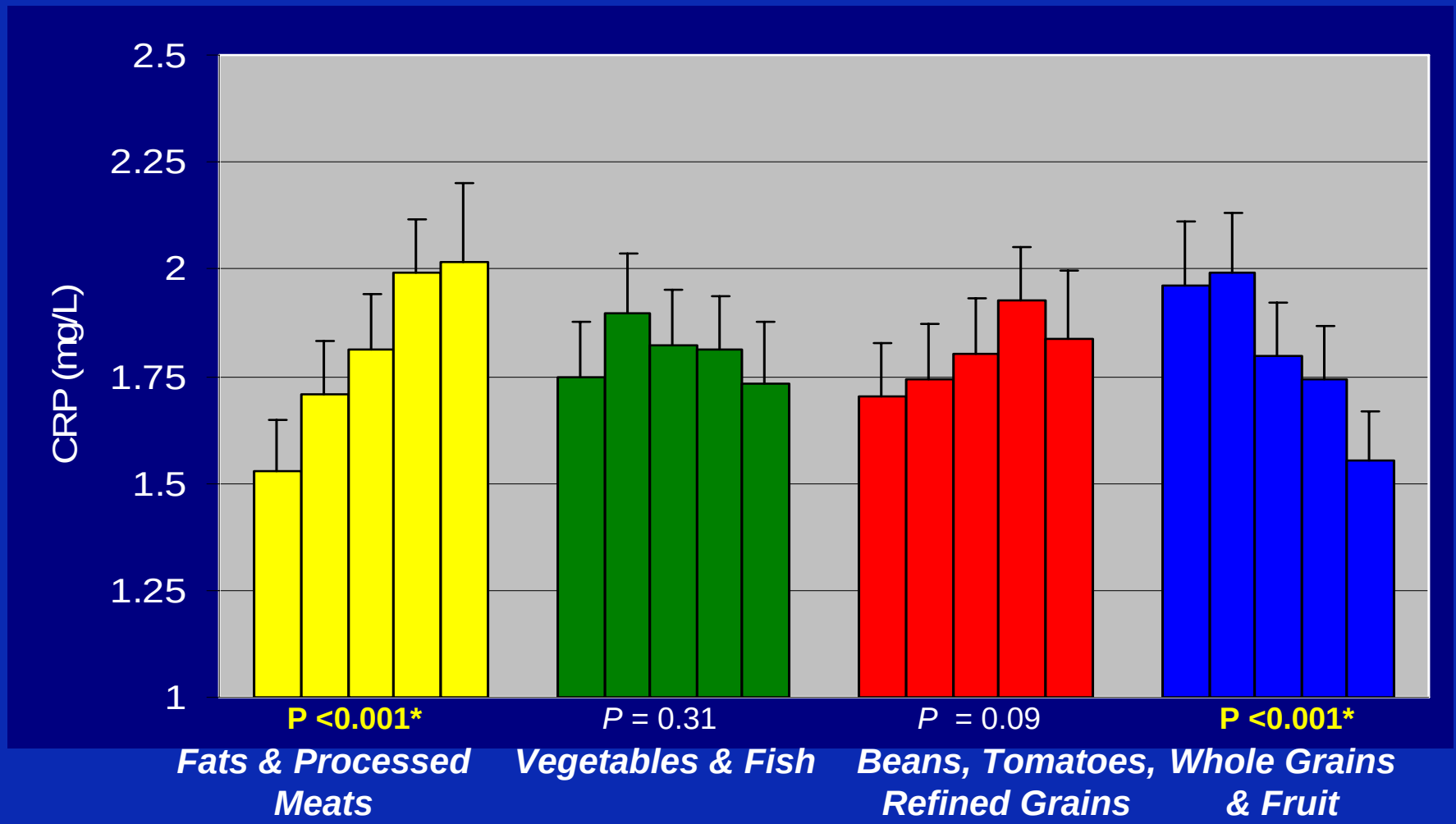
Race/ethnicity: Dietary Pattern Quintile 5

	Fats & Processed Meats	*Vegetables & Fish*	*Beans, Tomatoes & Refined Grains*	*Whole Grains & Fruit*
	Q5	**Q5**	**Q5**	**Q5**
White	**51.1** ↑	**22.0** ↓	**30.1** ↓	**64.5** ↑
Black	**35.5** ↑	**23.1** ↑	**12.1** ↓	**21.4** NS
Hispanic	**12.1** ↓	**11.4** ↓	**55.6** ↑	**10.9** ↓
Chinese	**1.4** ↓	**43.4** ↑	**2.3** ↓	**3.1** ↓

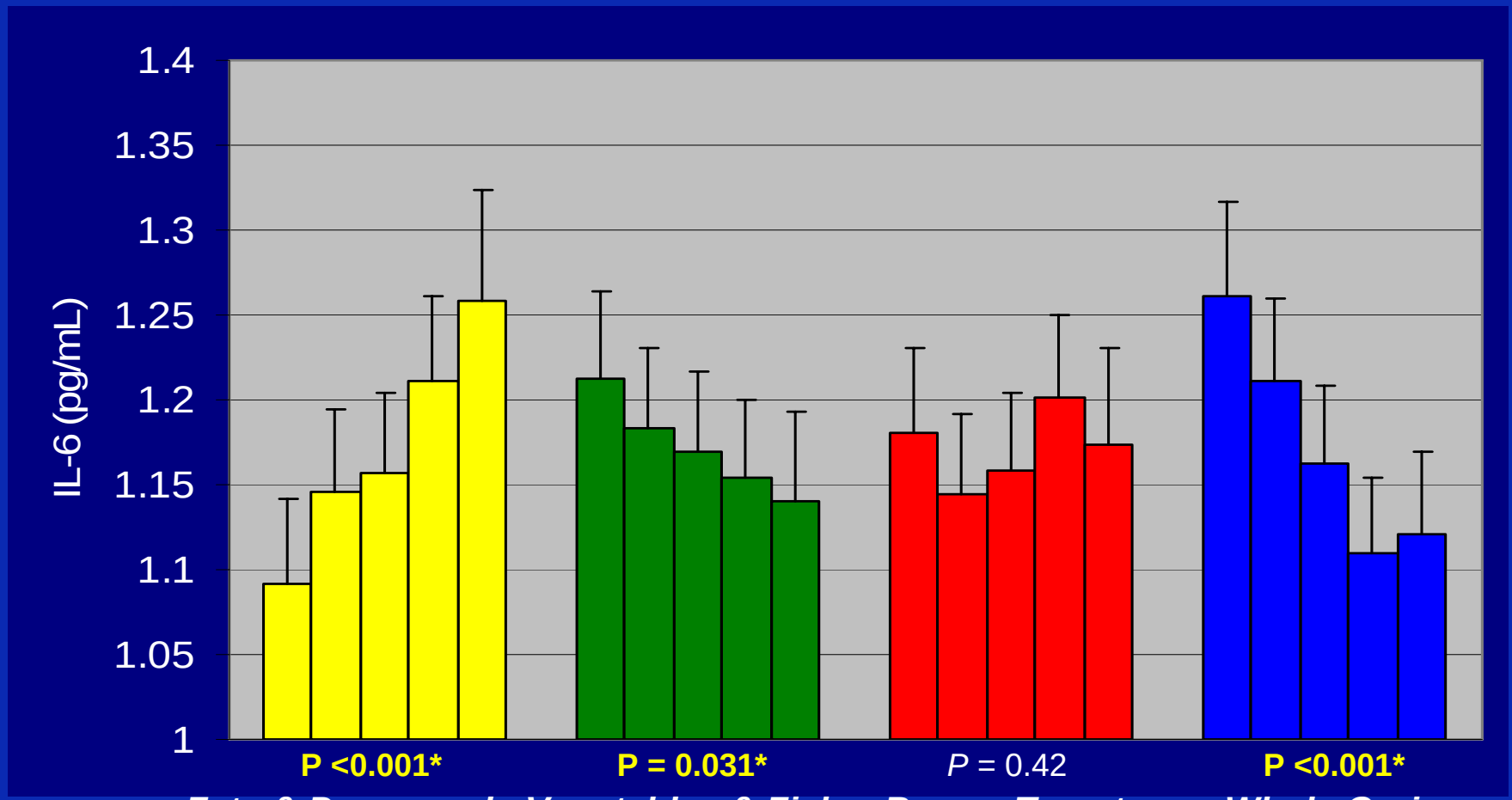
Unadjusted values; Arrows indicate direction of trends across dietary pattern scores ($P<0.05$), unless indicated non-significant (NS).

Dietary Patterns and Biomarkers of Inflammation & Endothelial Activation

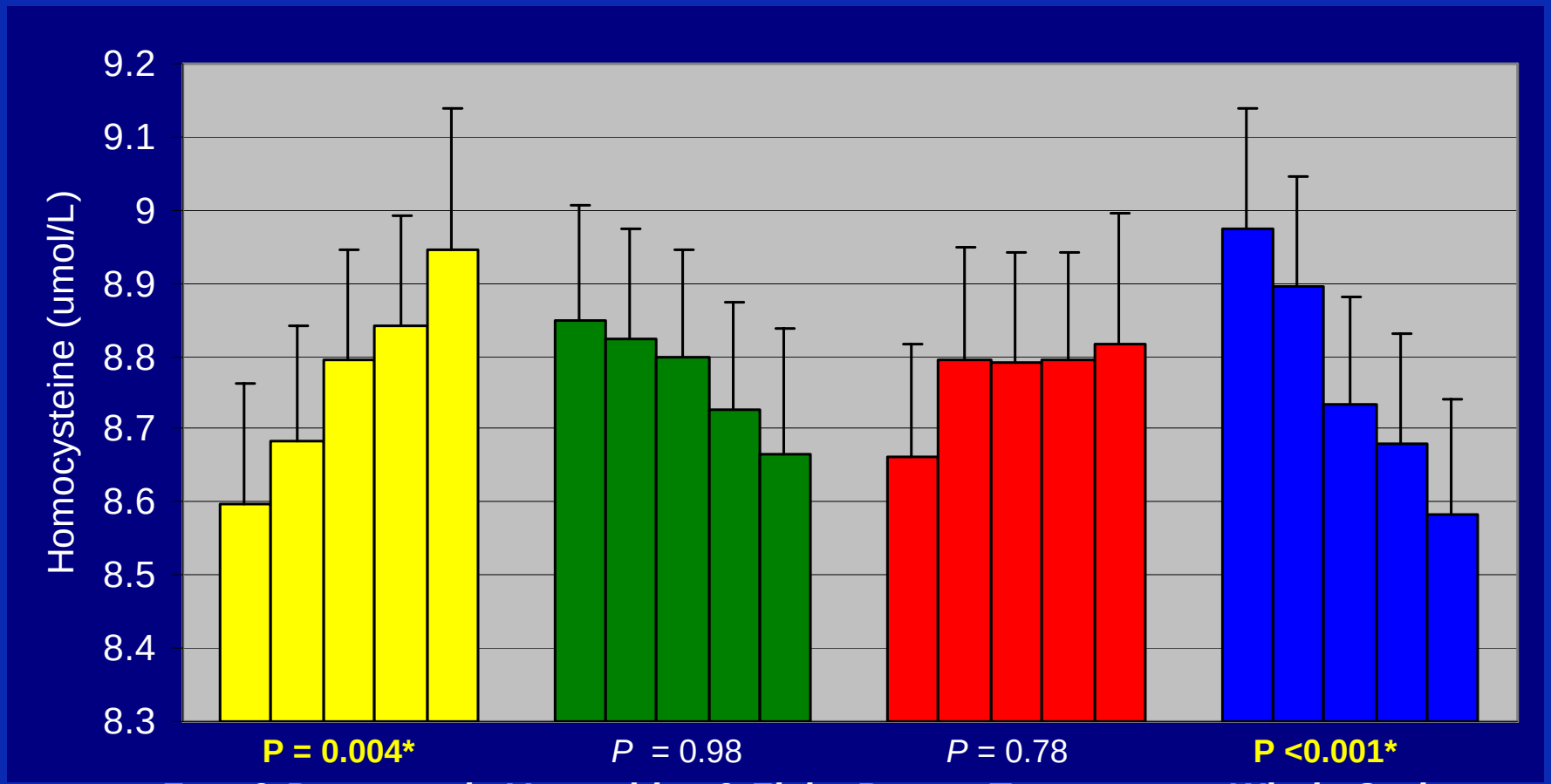
CRP concentrations across dietary pattern score quintiles



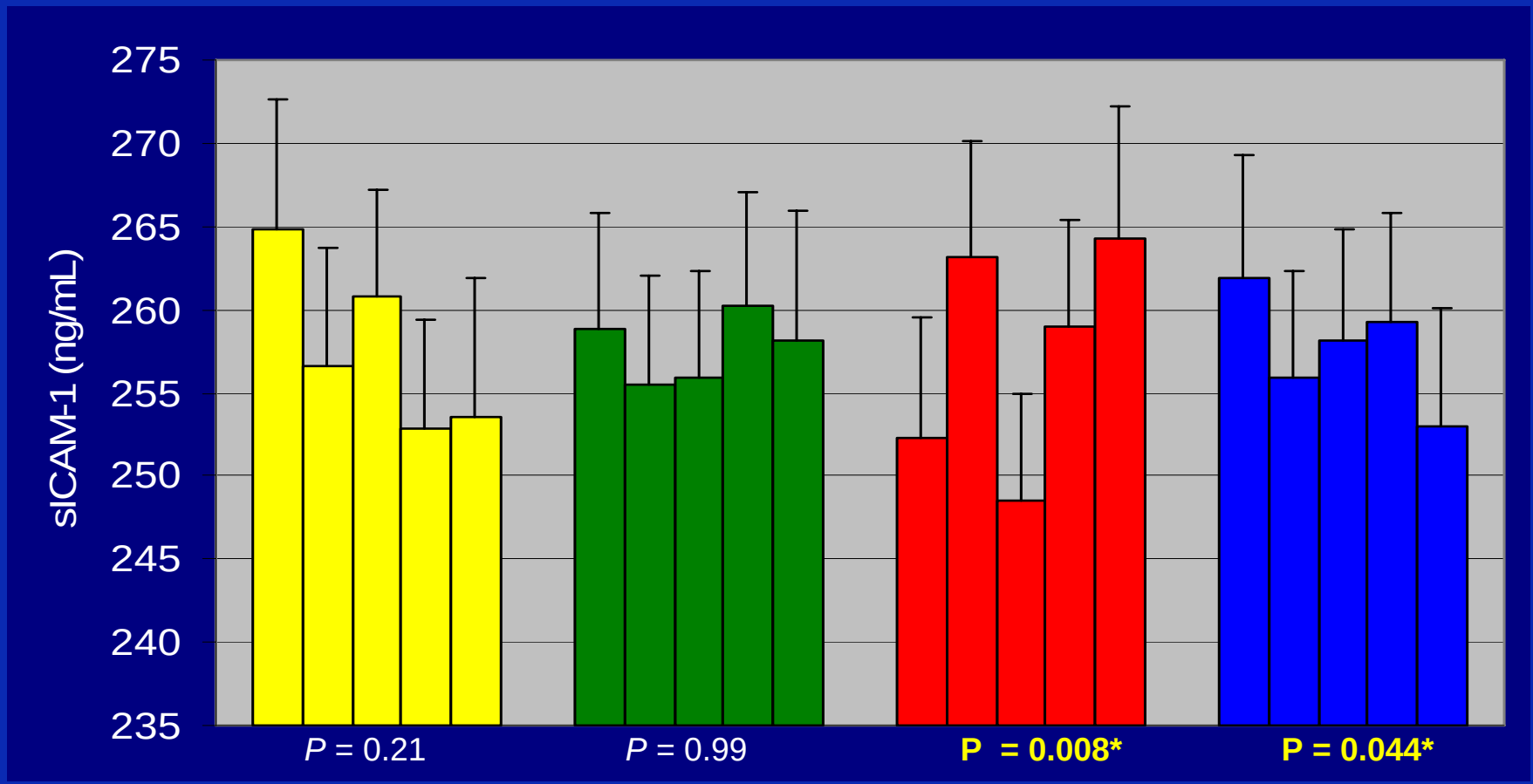
IL-6 concentrations across dietary pattern score quintiles



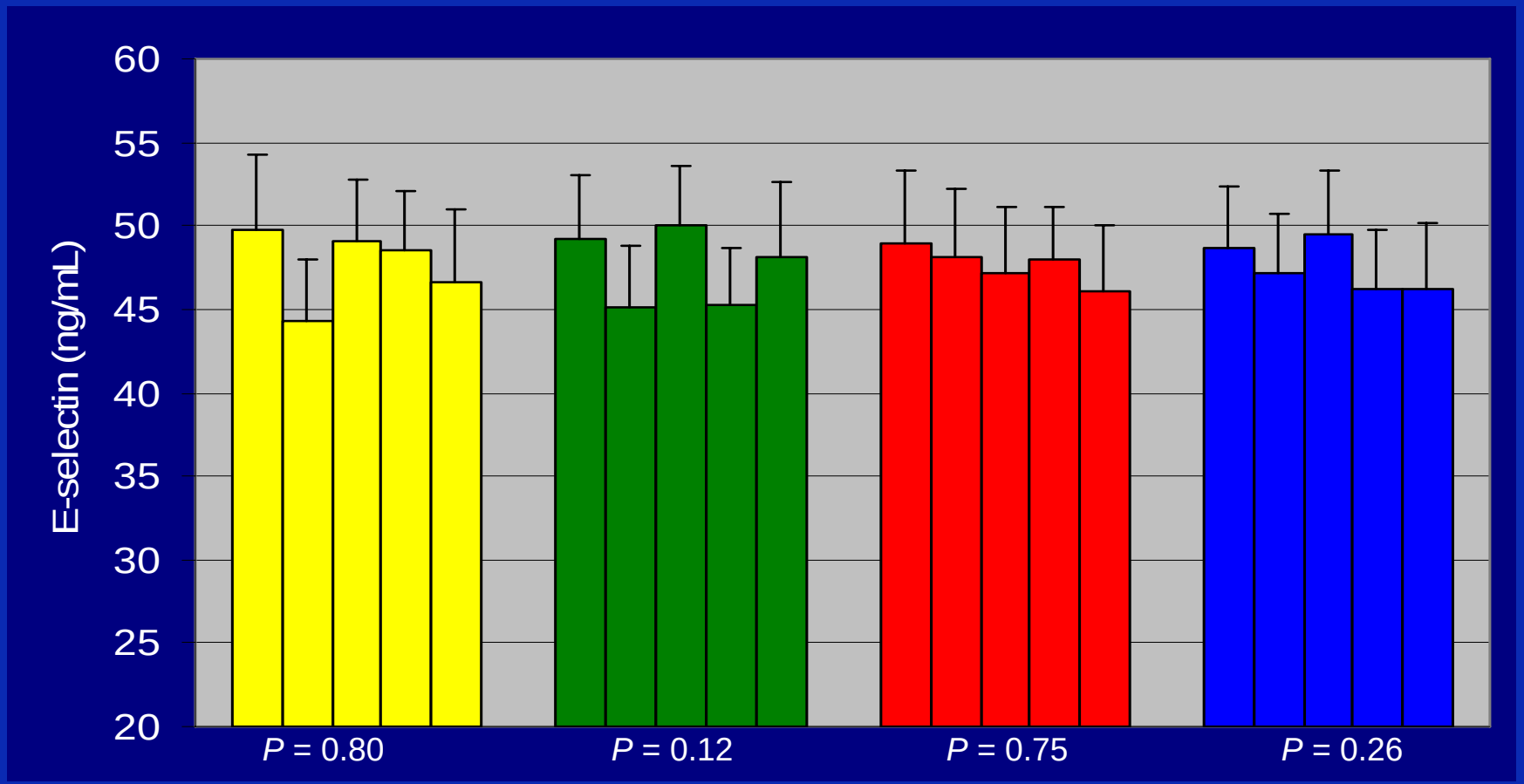
Homocysteine concentrations across dietary pattern score quintiles



sICAM-1 concentrations across dietary pattern score quintiles



E-selectin concentrations across dietary pattern score quintiles



Limitations

- Cross-sectional analysis so cause-effect relations cannot be concluded
- Subjective nature of factor analysis
- Other foods or dietary patterns may be more importantly related to inflammation
- Reduced power for sICAM-1 and E-selectin

Conclusions

- *Fats & Processed Meats*
  - ↑ CRP, IL-6, homocysteine
- *Whole Grains & Fruit*
  - ↓ CRP, IL-6, homocysteine, sICAM-1
- *Vegetables & Fish*
  - ↓ IL-6
- *Beans, Tomatoes & Refined Grains*
  - ↑ sICAM-1

★ Adjustment for waist circumference and CVD risk factors had minimal impact

★ Associations were not modified by gender or race/ethnicity

Thank You

Questions?

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Additional Analyses

- Mechanism model 1:
  - Multivariable model **+ waist circumference**
    - Attenuated previously significant associations with IL-6
    - Attenuated association between sICAM-1 and *Whole Grains & Fruit* dietary pattern
- Mechanism model 2:
  - Multivariable model + waist circumference **+ fasting insulin, glucose, LDL, HDL, and systolic blood pressure (SBP)**
    - Return of significance for IL-6 and *Fats & Processed Meats* association (*P* = 0.026)

Nutrient composition of dietary patterns

		Fats & Processed Meats	*Vegetables & Fish*	*Beans, Tomatoes & Refined Grains*	*Whole Grains & Fruit*
Energy	**Q1**	**1258**	**1514**	**1426**	**1644**
(kcal/d)	**Q5**	**2601**	**2008**	**2317**	**2099**
Fat	**Q1**	**30.8**	**34.1**[NS]	**34.8**	**37.1**
(%energy)	**Q5**	**37.8**	**34.4**[NS]	**35.3**	**31.5**
Sat fat	**Q1**	**8.2**	**11.6**	**10.3**	**11.1**
(%energy)	**Q5**	**12.8**	**9.5**	**11.4**	**10.0**
MUFA	**Q1**	**11.7**	**12.4**	**12.9**	**13.6**
(%energy)	**Q5**	**13.7**	**12.7**	**12.9**	**11.5**
PUFA	**Q1**	**8.2**	**7.3**	**8.2**	**9.1**
(%energy)	**Q5**	**7.8**	**8.8**	**8.0**	**7.1**
Protein	**Q1**	**16.5**	**14.0**	**16.1**	**160.**
(%energy)	**Q5**	**15.0**	**18.1**	**15.7**	**16.3**
CHO	**Q1**	**54.8**	**50.4**	**50.0**	**47.2**
(%energy)	**Q5**	**46.3**	**49.3**	**49.5**	**52.9**
Fiber	**Q1**	**23.7**	**14.5**	**16.7**	**14.4**
(g/d)	**Q5**	**10.9**	**21.8**	**20.9**	**23.1**

Participant Characteristics according to *Fats & Processed Meats* pattern*

	Q1	Q3	Q5
Female (%)	63.1	54.1	41.2
Age (y)	63.6	61.6	59.5
High school (%)	72.6	85.0	90.7
Inactive leisure (MET-hr/wk)	24.4	28.3	31.5
Smoker (%)	5.9	15.2	25.8
Supplement users (%)	66.6	60.8	48.6
Waist circumference	92.3	97.1	101.8

**P* trend across pattern scores significant for all (*P* <0.05)

Participant Characteristics according to *Vegetables & Fish* pattern*

	Q1	Q3	Q5
Female (%)	47.8	53.3	55.9
Age (y)	61.8	61.7	61.0
High school (%)	84.0	86.1	83.4
Active leisure (MET-hr/wk)	38.4	41.8	42.8
Smoker (%)	22.0	13.1	10.5
Supplement users (%)	53.1	60.5	62.4
Waist circumference	98.1	97.3	93.1

**P* trend across pattern scores significant for all with the exception of %with HS degree

Participant Characteristics according to *Beans, Tomatoes & Refined Grains**

	Q1	Q3	Q5
Female (%)	57.1	54.9	48.9
Age (y)	63.9	61.7	59.1
High school (%)	88.1	87.9	69.8
Active leisure (MET-hr/wk)	43.7	40.6	38.1
Smoker (%)	15.6	13.7	18.4
Supplement users (%)	61.2	60.6	51.0
Waist circumference	95.2	95.9	99.5

**P* trend across pattern scores significant for all (*P* <0.05)

Participant Characteristics according to *Whole Grains & Fruit* pattern*

	Q1	Q3	Q5
Female (%)	40.0	55.1	57.8
Age (y)	59.0	61.5	63.8
High school (%)	72.0	84.6	91.4
Active leisure (MET-hr/wk)	32.7	39.6	50.3
Smoker (%)	19.2	13.5	11.1
Supplement users (%)	44.8	57.8	70.1
Waist circumference	95.4^{NS}	97.1^{NS}	96.5^{NS}

**P* trend across pattern scores significant for all with the exception of waist circumference

Traditional CVD risk factors*

	Fats & Processed Meats			*Whole Grains & Fruit*		
	Q1	Q2	Q3	Q1	Q2	Q3
LDL (mg/dL)	116.5	118.3	120.8* ↑	119.0	118.0	115.6* ↓
HDL (mg/dL)	51.5	51.7	51.2	51.7	51.5	52.2
Insulin (pmol/L)	40.0	44.2	48.5* ↑	46.2	43.3	40.4
Glucose (ng/dL)	95.2	96.1	96.0	96.6	95.5	95.2* ↓
SBP (mm/Hg)	125.2	124.3	125.7	125.7	125.2	124.0
Waist (mg/dL)	94.6	97.0	99.6	97.5	96.8	95.0* ↓

**P* trend = <0.05, Mean values adjusted for MODEL 2: center, race/ethnicity, age, gender, education, physical activity, smoking, supplement use, and total energy intake.

Traditional CVD risk factors*

	Vegetables & Fish			*Beans, Tomatoes, RG*		
	Q1	Q2	Q3	Q1	Q2	Q3
LDL (mg/dL)	117.4	117.1	119.0	118.0	118.4	115.9* ↓
HDL (mg/dL)	52.5	51.7	50.7	52.2	52.2	50.9* ↓
Insulin (pmol/L)	43.7	43.6	41.8	43.7	43.4	43.6* ↓
Glucose (ng/dL)	95.2	96.4	95.6	95.4	95.9	95.7
SBP (mm/Hg)	125.0	126.1	124.6	123.5	125.7	126.8
Waist (mg/dL)	96.9	96.6	95.7* ↓	96.2	96.6	97.0

**P* trend = <0.05, Mean values adjusted for MODEL 2: center, race/ethnicity, age, gender, education, physical activity, smoking, supplement use, and total energy intake.