Whole Grains & Hypertension

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Emily D'Antonio

Flint et al., 2009

Why Whole Grains?

- **Potassium**
  - Improve **endothelial cell function** ~ relaxing artery walls
- **Phytochemicals**
  - **Protective compounds** produced by plants
  - Complement fruits & vegetables
- **Low glycemic-index foods**
  - Lower/slower glucose present in blood after eating → **reduce insulin resistance**
- **Fiber**
  - Increases **satiety** → lower total energy intake → healthier weight

Flint et al., 2009, Webb, 2013

Knowledge gap

- Limited prospective data in **men**
- Previous studies had not **quantitatively** estimated whole-grain intake in **grams**
    - ***Objective:*** Quantitatively estimate the association of whole-grain intake (grams/day) with risk of incident hypertension in men.
- Longitudinal prospective cohort design

Flint et al., 2009

Population

- **The Health Professionals Follow-Up Study**
  - **31,684** male **health professionals** (dentists, optometrists, osteopaths, pharmacists, podiatrists, veterinarians)
  - 45-75 y/o at enrollment in 1986
  - Studied for 18 years
- **Exclusion criteria:**
  - Prevalent cancer, stroke, CVD, hypertension, missing diet information

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Exposure Measurement

- **Baseline questionnaire** ~ completed every **2 years**
  - Personal & family Medical history
  - Lifestyle
  - Demographics
- **Food Frequency Questionnaire** ~ completed every **4 years**
  - Specific questions regarding grain foods
  - Nutrient composition database created & updated to reflect trends in food consumption + availability

Flint et al., 2009

Outcome Measurement

- Whole-grain intakes categorized into **quintiles** using cumulative average update method
  - Translated into grams/day according to **dry-weight** of ingredients
- **Incident** hypertension **self-reported**
  - Calendar year/month recorded

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Confounding

- **Reported at baseline questionnaire:**
  - Family history of CVD, hypertension
  - Cigarette smoking status (current, former, never)
  - Total energy, fruit, vegetables, alcohol, potassium, magnesium, total fiber, folate, & cereal fiber
  - Height & weight → BMI calculated & categorized
  - Physical activity level - number of hours/week → categorized
- Controlled for in analyses

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Statistical Analysis

- **Hazard Regression**
  - Present a model of the association between **time-varying whole-grain intake** & incident hypertension
  - Relative Risk Ratios (95% Confidence Intervals) reported
- All analyses adjusted for age & total energy
- Multivariate analysis further adjusted for covariates

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Results

- 9,227 cases of incident hypertension (29% of cohort)

TABLE 1
Baseline characteristics and mean energy-adjusted intakes by quintile of whole-grain intake in 31,684 men: Health Professionals Follow-Up Study, 1986[1]

	Quintile of whole-grain intake				
	1	2	3	4	5
Median intake (g/d)[2]	3.3	9.8	17.1	26.9	46.0
	(0–6.5)	(6.6–13.2)	(13.3–21.4)	(21.5–34.2)	(34.3–326.4)
Age (y)	52.5 ± 9.3[3]	51.9 ± 9.2	52.4 ± 9.2	53.0 ± 9.4	53.7 ± 9.7
Current smoking (%)	16.0	11.3	7.6	5.3	3.7
BMI (kg/m^2)	25.5 ± 3.0	25.5 ± 3.1	25.4 ± 3.1	25.1 ± 2.9	24.6 ± 2.8
Family history of hypertension (%)	24.2	25.7	25.3	24.8	27.0
Family history of myocardial infarction (%)	11.6	11.8	11.6	11.1	11.4
Nutrient intake					
Total energy (kcal/d)	1996 ± 648	2050 ± 646	2075 ± 643	2031 ± 595	1876 ± 554
Whole grains (g/d)	3.2 ± 2.0	9.8 ± 1.9	17.1 ± 2.4	27.2 ± 3.7	52.4 ± 21.5
Naturally occurring bran (g/d)	0.37 ± 0.33	1.13 ± 0.56	2.06 ± 1.00	3.41 ± 1.62	6.64 ± 4.26
Naturally occurring germ (g/d)	0.15 ± 0.13	0.39 ± 0.21	0.62 ± 0.30	0.92 ± 0.44	1.80 ± 1.40
Added bran (g/d)	0.13 ± 0.48	0.62 ± 1.61	1.81 ± 3.43	3.11 ± 4.99	5.12 ± 11.32
Added germ (g/d)	0.07 ± 0.28	0.15 ± 0.56	0.25 ± 0.80	0.44 ± 1.51	0.97 ± 3.13
Cereal fiber (g/d)	3.0 ± 1.2	3.9 ± 1.3	5.3 ± 1.7	7.0 ± 2.3	10.5 ± 5.9
Total fiber (g/d)	16.3 ± 4.9	18.2 ± 4.9	20.1 ± 5.2	22.5 ± 5.6	27.2 ± 8.2
Folate (μg/d)	395 ± 230	430 ± 247	472 ± 259	516 ± 273	575 ± 316
Total carbohydrate (g/d)	218 ± 43	224 ± 38	231 ± 36	241 ± 36	262 ± 41
Total sugar (g/d)	105 ± 39	105 ± 34	107 ± 32	109 ± 31	109 ± 32
Saturated fat (g/d)	27.4 ± 6.4	26.4 ± 5.6	25.2 ± 5.4	23.8 ± 5.2	20.9 ± 5.7
Polyunsaturated fat (g/d)	13.1 ± 3.7	13.4 ± 3.4	13.4 ± 3.4	13.2 ± 3.3	13.0 ± 3.5
trans Fat (g/d)	3.19 ± 1.22	3.06 ± 1.08	2.94 ± 1.06	2.75 ± 1.03	2.33 ± 1.06
Glycemic load per day	115 ± 49	122 ± 48	127 ± 48	130 ± 46	132 ± 48
Sodium (mg/d)	3322 ± 1217	3353 ± 1154	3290 ± 1064	3283 ± 1049	3177 ± 1077
Potassium (mg/d)	3106 ± 626	3222 ± 601	3341 ± 600	3464 ± 599	3631 ± 659
Magnesium (mg/d)	295 ± 59	313 ± 53.9	335 ± 55.3	357 ± 56.7	406 ± 79.8
Vitamin E (mg/d)	36.9 ± 78.1	40.9 ± 82.1	47.0 ± 87.5	52.1 ± 90.3	67.3 ± 107.6
Food intake					
Fruit (servings/d)	2.0 ± 1.6	2.2 ± 1.6	2.4 ± 1.6	2.6 ± 1.6	2.8 ± 1.8
Vegetables (servings/d)	2.8 ± 1.6	3.2 ± 1.6	3.3 ± 1.7	3.4 ± 1.8	3.5 ± 2.0

[1] For all continuous variables, P for trend < 0.0001.
[2] Ranges in parentheses.
[3] Mean ± SD (all such values).

Relative Risks & Trend

- Dose-Response Relationship

TABLE 2
Relative risks (RRs) and 95% CIs of incident hypertension in 31,684 men by quintile of whole-grain intake: Health Professionals Follow-Up Study, 1986–2004[1]

	Quintile of whole-grain intake					
	1	2	3	4	5	*P* for trend
Median intake (g/d)[2]	3.3 (0–6.5)	9.8 (6.6–13.2)	17.1 (13.3–21.4)	26.9 (21.5–34.2)	46.0 (34.3–326.4)	—
No. of cases	1826	1917	1922	1914	1648	—
Person-years	61,137	68,966	72,196	73,184	69,877	—
Age- and energy-adjusted RR[3]	1.00	0.90 (0.84, 0.96)	0.83 (0.78, 0.89)	0.81 (0.76, 0.87)	0.72 (0.67, 0.77)	<0.0001
Multivariate-adjusted RR[3,4]	1.00	0.94 (0.88, 1.01)	0.89 (0.83, 0.95)	0.89 (0.84, 0.96)	0.81 (0.75, 0.87)	<0.0001

[1] RRs derived from proportional hazards models.
[2] Ranges in parentheses.
[3] 95% CIs in parentheses.
[4] Adjusted for age, energy, family history of coronary heart disease, family history of hypertension, smoking, alcohol, marital status, profession, height, fruit and vegetable intakes, sodium intake, physical activity, multivitamin use, and cholesterol screening.

Isolated Total Bran Intake

TABLE 3
Relative risks (RRs) and 95% CIs of incident hypertension in 31,684 men by quintile of total bran intake: Health Professionals Follow-Up Study, 1986–2004[1]

	Quintile of bran intake					
	1	2	3	4	5	*P* for trend
Median intake (g/d)[2]	0.3 (0–0.7)	1.3 (0.8–1.9)	2.8 (2.0–3.8)	5.5 (3.9–7.8)	12.0 (7.9–236.8)	—
No. of cases	1839	1988	1869	1845	1686	—
Person-years	62,258	71,499	72,080	71,933	67,590	—
Age- and energy-adjusted RR[3]	1.00	0.91 (0.85, 0.97)	0.81 (0.76, 0.87)	0.78 (0.73, 0.84)	0.76 (0.71, 0.81)	<0.0001
Multivariate-adjusted RR[3,4]	1.00	0.95 (0.88, 1.02)	0.88 (0.81, 0.94)	0.87 (0.80, 0.94)	0.85 (0.78, 0.92)	0.002

[1] RRs derived from proportional hazards models.
[2] Ranges in parentheses.
[3] 95% CIs in parentheses.
[4] Adjusted for age, energy, family history of coronary heart disease, family history of hypertension, smoking, alcohol, marital status, profession, height, fruit and vegetable intakes, sodium intake, physical activity, multivitamin use, and cholesterol screening.

Study Conclusion

Whole-grain intake was inversely associated with incidence of hypertension; independent of several healthy lifestyle markers.

Flint et al., 2009

Strengths

- **Quantitative**, more precise estimate of whole-grain intake (grams/day)
- Large sample size
- Longitudinal, prospective design -limits reverse causation
- Implemented previously validated FFQ **multiple times**
  - Reduces measurement error & possible misclassification to gather a more accurate average intake
- Findings consistent with current literature

Flint et al., 2009

Limitations

- **Measurement error** ~ self-reported FFQ & hypertension status
- Population of health professionals
  - **Assumed knowledge** of proper nutrition & healthy behavior may weaken association
  - Already consuming high amounts of whole-grains, fruits, vegetables, etc.
  - Not at high risk for disease → less incidence observed
- Association only observed in men
- Residual confounding

Flint et al., 2009

Future Research & Implications

- Dietary recommendation to **increase whole-grain intake** to reduce risk of hypertension & chronic disease occurrence
- Apply to more populations / characteristics to **generalize** results
  - Randomized, double-blind, controlled trials
- Observe **at risk** populations
- Further investigate the health benefits of **bran intake**

Flint et al., 2009

Thank You!