



## **Health Research – A Review of Recent Findings**

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**Senior Director of Nutrition and Health Research**  
**USHBC/NABC**

**IBO SUMMIT 2023** *Lublin, 3-6 July 2023*

# USHBC Health and Nutrition Research Pillars

**Know we're always learning more.**

Blueberries may promote good health in additional ways. **Areas of research:**



**Cardiovascular  
Health**



**Brain Health**



**Healthy Living**



**Insulin Response**



**Gut Health**



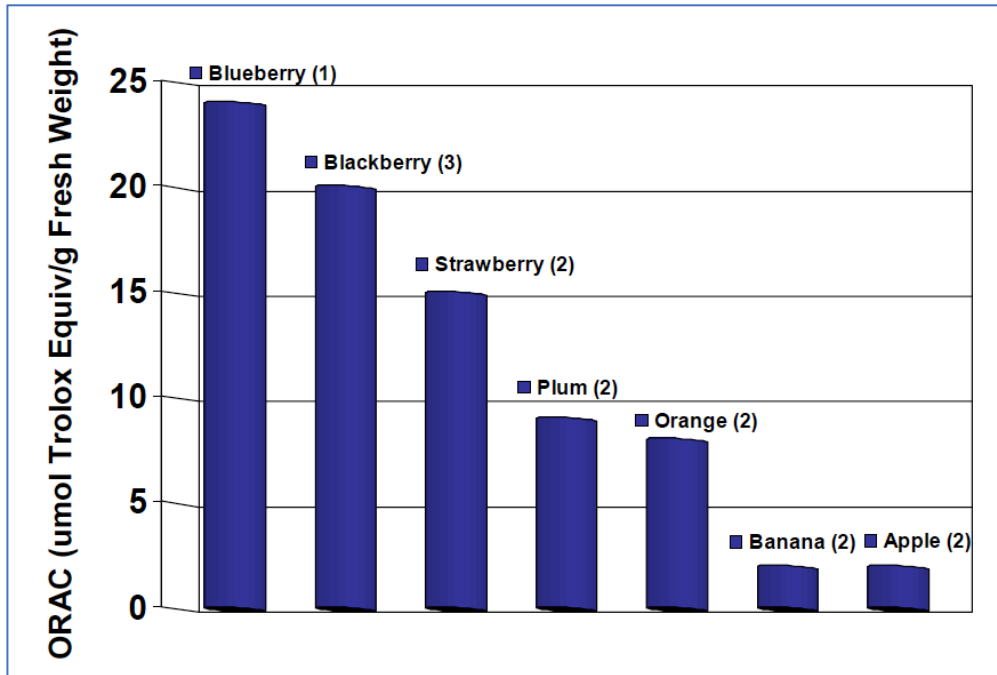
# Blueberries and Brain Health

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# Blueberries' Antioxidant Profile Sparks Research Interest



Brain Health



J Agric Food Chem. 46, 1998

## Can Foods Forestall Aging?

Some with high **antioxidant** activity appear to aid memory

**S**tudies at the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University in Boston suggest that consuming fruits and vegetables with a high-ORAC value may help slow the aging process in both body and brain. ORAC—short for Oxygen Radical Absorbance Capacity—measures the ability of foods, blood plasma, and just about any substance to subdue oxygen free radicals in the test tube.

Early evidence indicates that this antioxidant activity translates to animals, protecting cells and their components from oxidative damage. Getting plenty of the foods with a high-ORAC activity, such as spinach, strawberries, and blueberries, has so far—

• raised the antioxidant power of hu-

KEITH WELLER (KR051-1)



Cao developed the ORAC test while he was a visiting scientist at the National Institute on Aging in Baltimore, Maryland. After joining Prior's group 5 years ago, the researchers assayed commonly eaten fruits, vegetables, and fruit juices with ORAC. [See "Plant Pigments Paint a Rainbow of Antioxidants," *Agricultural Research*, November 1996, pp. 4-8.]

"The ORAC value covers all the antioxidants in foods," says Cao. "You cannot easily measure each antioxidant separately," he adds. "But you can use the ORAC assay to identify which phytonutrients are the important antioxidants."

The researchers have been testing whether antioxidants other than vitamins are absorbed into the blood and protect the cells. And the results look promising.

Ag Research Feb 1999

*"In general, blueberries are one of the richest sources of antioxidant phytonutrients of the fresh fruits and vegetables we have studied"*

*Prior et al. J Agric Food Chem, 1998*

Eur J Nutr  
DOI 10.1007/s00394-017-1400-8

ORIGINAL CONTRIBUTION

## Dietary blueberry improves cognition among older adults in a randomized, double-blind, placebo-controlled trial

Marshall G. Miller<sup>1</sup> · Derek A. Hamilton<sup>2</sup> · James A. Joseph<sup>1</sup> · Barbara Shukitt-Hale<sup>1</sup>

Eur J Nutr, 2018



Brain Health



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Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Journal of Functional Foods

journal homepage: [www.elsevier.com/locate/jff](http://www.elsevier.com/locate/jff)

Cognitive performance in relation to urinary anthocyanins and their flavonoid-based products following blueberry supplementation in older adults at risk for dementia

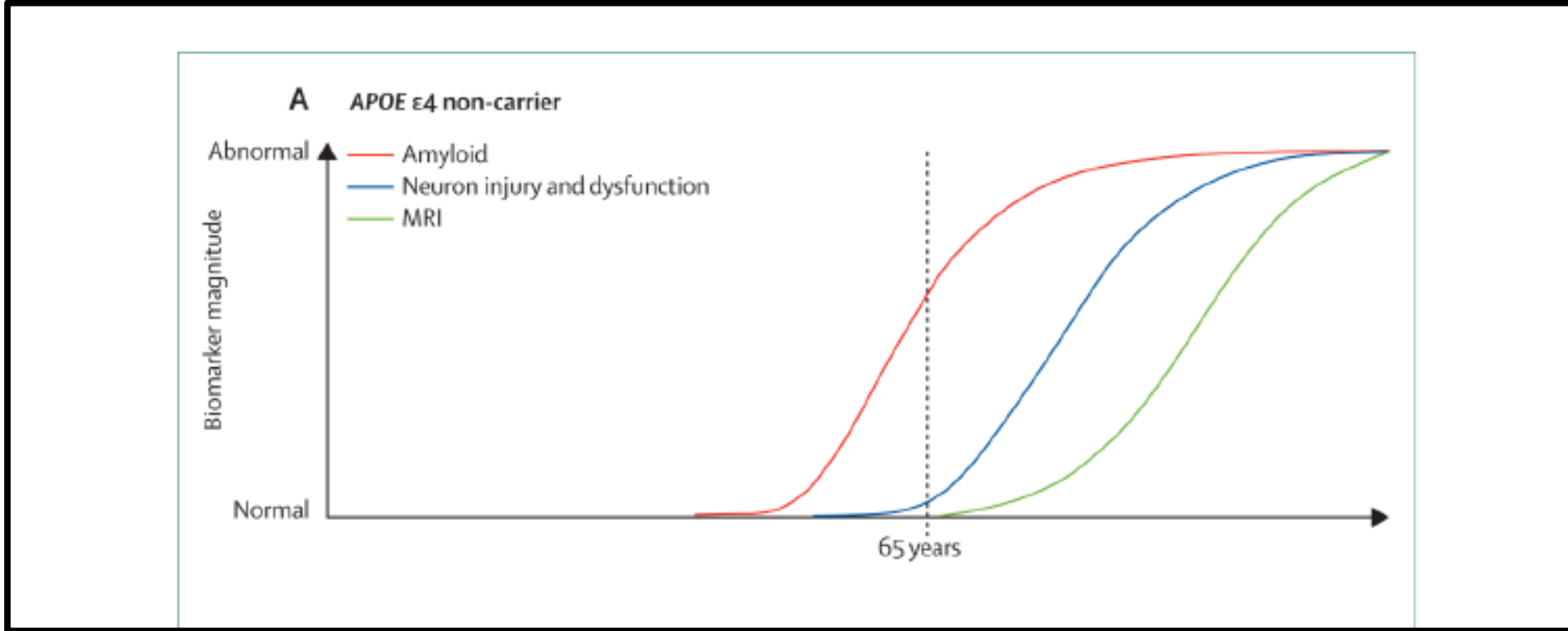
Robert Krikorian<sup>a,\*</sup>, Wilhelmina Kalt<sup>b,1</sup>, Jane E. McDonald<sup>b,1</sup>, Marcelle D. Shidler<sup>a</sup>,  
Suzanne S. Summer<sup>c</sup>, Amanda L. Stein<sup>a</sup>

<sup>a</sup> Department of Psychiatry & Behavioral Neuroscience, University of Cincinnati Academic Health Center, Cincinnati, OH, USA

<sup>b</sup> Agriculture and Agri-Food Canada, Kentville Research and Development Centre, Kentville, Nova Scotia, Canada

<sup>c</sup> Clinical Translational Research Center, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

J Functional Foods, 2020



Jack, CR Lancet Neurol, 2010



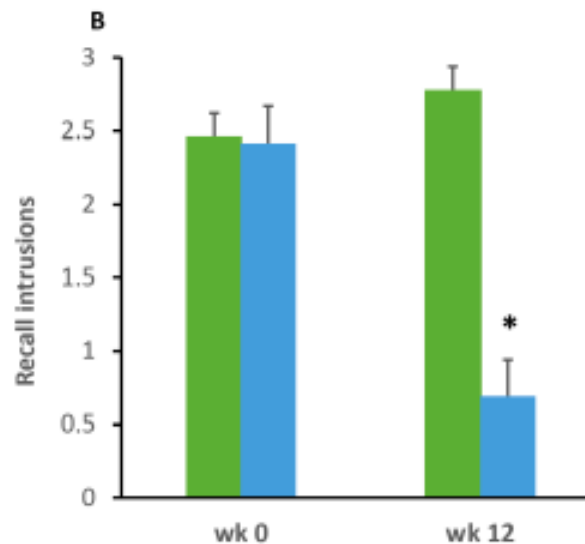
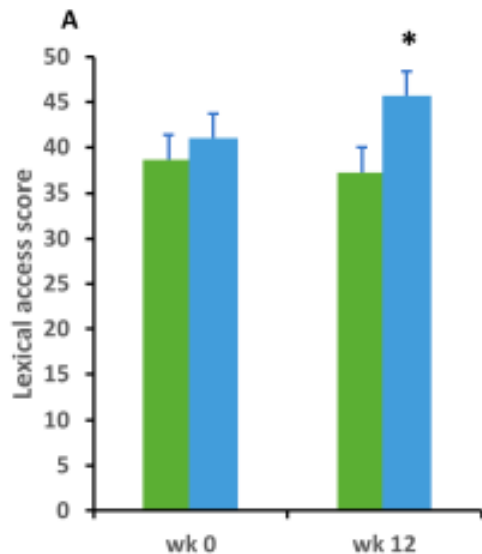
Brain Health

# Blueberry Consumption in Middle-Aged Men and Women

- Twenty-seven men and women, 50 - 65 years, who had gained weight in midlife and had subjective cognitive decline
- 12-week intervention with blueberry powder (1/2 cup equivalent) or placebo powder

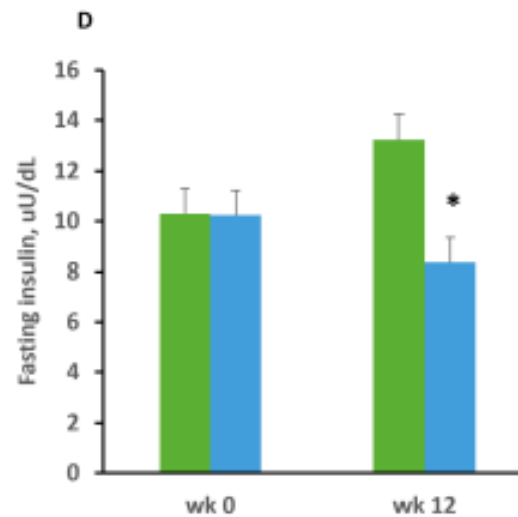
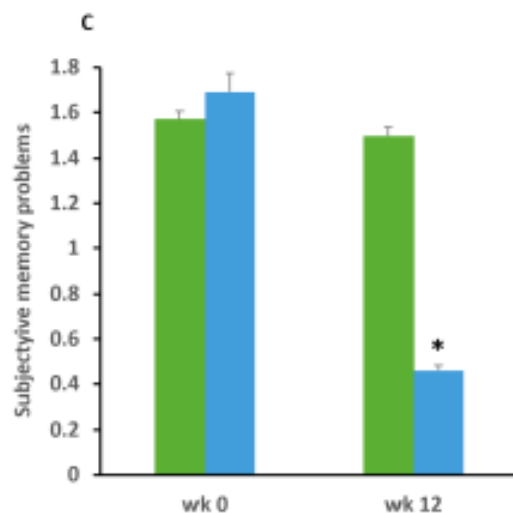


Controlled Oral Word Association Test



Fewer intrusion errors

Perceived day-to-day memory difficulties



Reduced mean fasting insulin levels





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Poland

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Lublin, 3-6 July 2023



Brain Health


*“While further studies are warranted, our results provide novel and exciting data regarding the potential of blueberry supplementation as a preventive intervention”*

*Krikorian, et al. Nutrients, 2022*



Article

## Blueberry Supplementation in Midlife for Dementia Risk Reduction

Robert Krikorian <sup>1,\*</sup>, Matthew R. Skelton <sup>2</sup>, Suzanne S. Summer <sup>3</sup>, Marcelle D. Shidler <sup>1</sup> and Patrick G. Sullivan <sup>4</sup> 

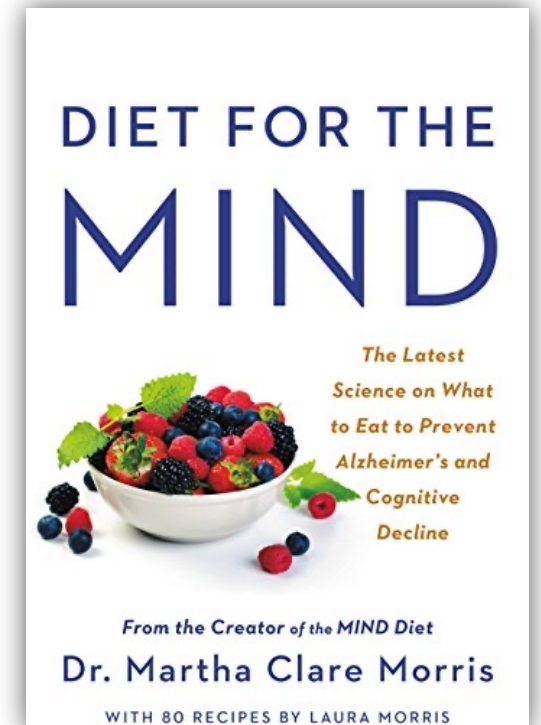
Nutrients, 2022

# The **M**editerranean-DASH **I**ntervention for **N**eurodegenerative **D**elay (**MIND**) Study

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3-year, NIH-funded, multicenter, randomized controlled trial to test the effects of the MIND diet on cognitive function in 604 individuals at risk for Alzheimer's Disease





Brain Health

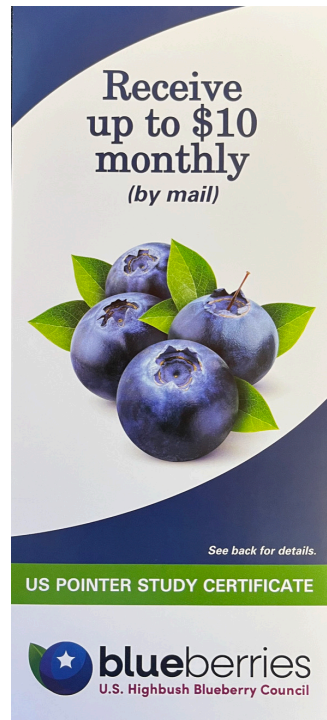
DASH	Mediterranean	MIND
Total Grains 42+/wk	Nonrefined Grains 56/wk	Whole Grains >28/wk
Vegetables 28+/wk	Vegetables 42/wk Potatoes 3-5/wk	Green Leafy 6+/wk Other Vegetables 14+/wk
Fruits 28+/wk	Fruits 21/wk	Berries (2-5 servings/d)
Dairy ≥14/wk	Dairy 14/wk	Regular Cheese ≤1 oz/week Butter <1 pat/d
Nuts, seeds & legumes ≥4/wk	Legumes 3-4/wk	Beans 3+/wk Nuts 2-5 servings/week
Lean meat, poultry fish ≤6/wk	Red meat ≤ 1/wk Fish >6/wk Poultry ≤3/wk	Lean Red Meats <4/wk Fish 1+/wk Poultry 2+/wk
Total Fat ≤ 27% of kcal Saturated Fat ≤ 6% of kcal		
Sweets ≤ 5/wk		Commercial Pastries, sweets <5/wk
Sodium ≤ 2400mg/d	Olive oil 3-4 T/d	Olive Oil >1 T/d
	Alcohol < 300mL/d but >0	Alcohol/wine 1/d

# The U.S. Pointer Study

## A Lifestyle Intervention Trial to Support Brain Health and Prevent Cognitive Decline



- 2-year, \$20 million, Alzheimer's Association-funded Study
- 2000 participants
- 5 sites



### Intervention Methods will Include:



Physical Exercise



Cognitive & Social Stimulation

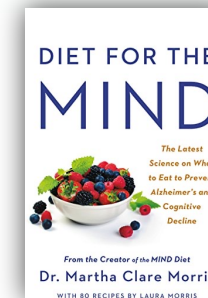


Nutritional Counseling & Modification



Improved Self-Management of Health Status

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# **Blueberries and Cardiovascular Health**

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The Journal of Nutrition  
Nutrient Physiology, Metabolism, and Nutrient-Nutrient Interactions

## Blueberries Decrease Cardiovascular Risk Factors in Obese Men and Women with Metabolic Syndrome<sup>1-3</sup>

Arpita Basu,<sup>4\*</sup> Mei Du,<sup>6</sup> Misti J. Leyva,<sup>5</sup> Karah Sanchez,<sup>4</sup> Nancy M. Betts,<sup>4</sup> Mingyuan Wu,<sup>6</sup> Christopher E. Aston,<sup>5</sup> and Timothy J. Lyons<sup>5,6</sup>

J Nutr, 2010



Cardiovascular  
Health

## Daily Blueberry Consumption Improves Blood Pressure and Arterial Stiffness in Postmenopausal Women with Pre- and Stage 1-Hypertension: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial



Sarah A. Johnson, PhD, RD, CSO; Arturo Figueroa, MD, PhD, FACSM; Negin Navaei; Alexei Wong, PhD; Roy Kalfon, MS; Lauren T. Ormsbee, MS; Rafaela G. Feresin, MS; Marcus L. Elam, MS; Shirin Hooshmand, PhD; Mark E. Payton, PhD; Bahram H. Arjmandi, PhD, RD



J Acad Nutr Diet, 2015

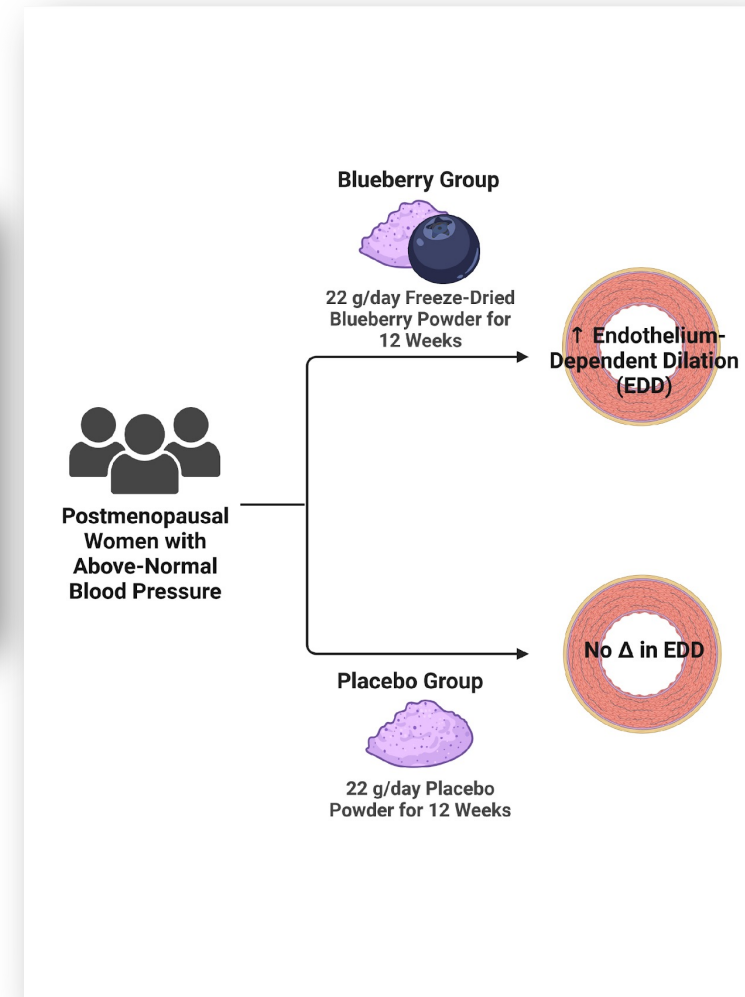


## Daily Blueberry Consumption for 12 Weeks Improves Endothelial Function in Postmenopausal Women with Above-Normal Blood Pressure through Reductions in Oxidative Stress: a Randomized Controlled Trial

Emily K. Woolf<sup>a</sup>, Janée D. Terwoord<sup>b</sup>, Nicole S. Litwin<sup>a</sup>, Allegra R. Vazquez<sup>a</sup>, Sylvia Y. Lee<sup>a</sup>, Nancy Ghanem<sup>a</sup>, Kiri A. Michell<sup>a</sup>, Brayden T. Smith<sup>a</sup>, Lauren E. Grabos<sup>a</sup>, Nathaniel B. Ketelhut<sup>b</sup>, Nate P. Bachman<sup>b</sup>, Meghan E. Smith<sup>b</sup>, Melanie Le Sayec<sup>d</sup>, Sangeeta Rao<sup>c</sup>, Christopher L. Gentile<sup>a</sup>, Tiffany L. Weir<sup>a</sup>, Ana Rodriguez-Mateos<sup>d</sup>, Douglas R. Seals<sup>e</sup>, Frank A. Dinunno<sup>b</sup>, Sarah A. Johnson<sup>a\*</sup>

Food Function, 2023

Comparing endothelial response to ascorbic acid (vitamin C) after blueberry or placebo consumption, suggests that improvement in endothelial function with blueberries is mediated in part to reduced oxidative stress







# Circle Study

Am J Clin Nutr 2019; 109:1535-1545

Blueberries improve biomarkers of cardiometabolic function in participants with metabolic syndrome—results from a 6-month, double-blind, randomized controlled trial

*Peter J Curtis,<sup>1</sup> Vera van der Velpen,<sup>1</sup> Lindsey Berends,<sup>1</sup> Amy Jennings,<sup>1</sup> Martin Feelisch,<sup>2</sup> A Margot Umpleby,<sup>3</sup> Mark Evans,<sup>4</sup> Bernadette O Fernandez,<sup>2</sup> Mia S Meiss,<sup>2</sup> Magdalena Minnion,<sup>2</sup> John Potter,<sup>1</sup> Anne-Marie Minihane,<sup>1</sup> Colin D Kay,<sup>1</sup> Eric B Rimm,<sup>5</sup> and Aedín Cassidy<sup>1</sup>*

*“The simple and attainable message to consume 1 cup of blueberries daily should be given to those aiming to improve their cardiovascular health.”*

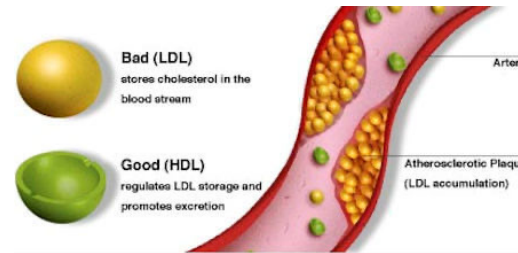
*Curtis, et al. Am J Clin Nutr, 2019*



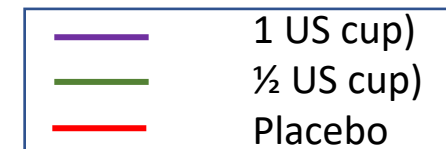
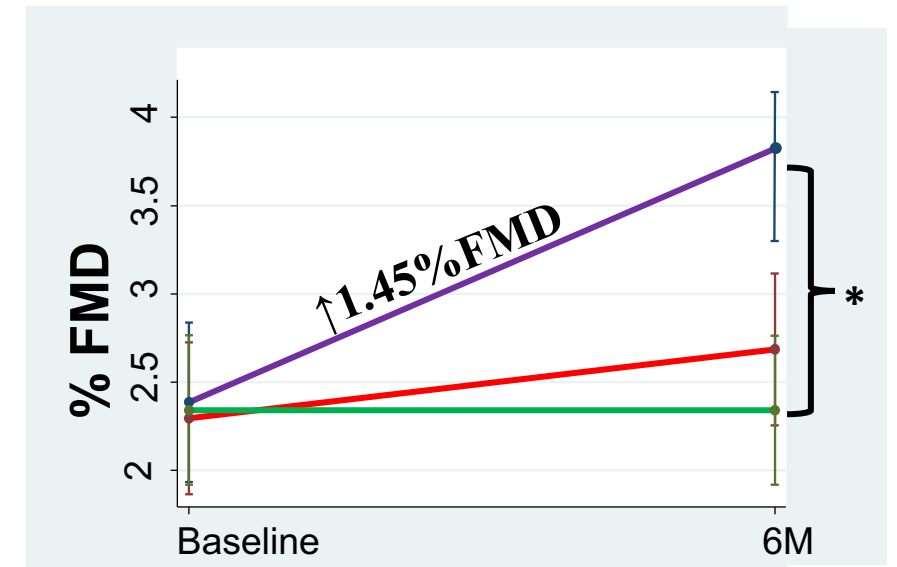
# Clinically significant improvements in robust vascular measures

## 1 cup per day

- Sustained improvement in blood flow
- Arteries more flexible (Arterial stiffness)
- HDL-Cholesterol increased



115 Overweight men & women - metabolic syndrome  
6-month intervention



# Do blueberries reduce the deleterious acute postprandial effects of energy dense meals?



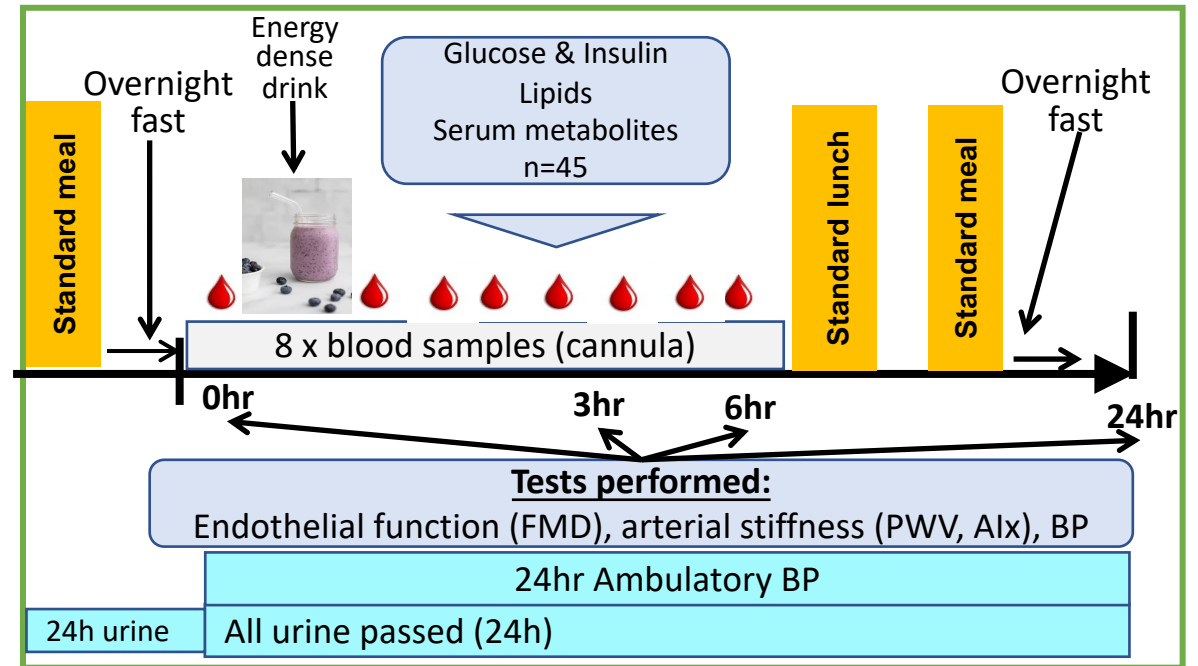
500 grams

969 kcal  
64.5 g fat  
84.5 g carb  
17.85 g protein



Burger, fries and soda

979 kcal  
40 g fat  
123 g carb  
32 g protein





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Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: <http://www.elsevier.com/locate/clnu>



Randomized Control Trials

Blueberry anthocyanin intake attenuates the postprandial cardiometabolic effect of an energy-dense food challenge: Results from a double blind, randomized controlled trial in metabolic syndrome participants



Peter J. Curtis <sup>a</sup>, Lindsey Berends <sup>a,1</sup>, Vera van der Velpen <sup>a,1</sup>, Amy Jennings <sup>b</sup>, Laura Haag <sup>a</sup>, Preeti Chandra <sup>c</sup>, Colin D. Kay <sup>c</sup>, Eric B. Rimm <sup>d</sup>, Aedín Cassidy <sup>b,\*</sup>

## Postprandial response to meal with blueberries

- ✓ Improved glucose control
- ✓ Reduced insulin
- ✓ Decreased cholesterol
- ✓ Increased HDL cholesterol



Clinical Nutrition, 2022



# Blueberries and Gut Health

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# Blueberry Consumption and Gut Microbiota in Young and Older Women






*nutrients*



Article

## Whole Blueberry and Isolated Polyphenol-Rich Fractions Modulate Specific Gut Microbes in an In Vitro Colon Model and in a Pilot Study in Human Consumers

Alexandra Ntemiri <sup>1,2</sup>, Tarini S. Ghosh <sup>1,2</sup>, Molly E. Gheller <sup>4</sup>, Tam T. T. Tran <sup>1,2</sup>,  
Jamie E. Blum <sup>4</sup>, Paola Pellanda <sup>1,2</sup>, Klara Vlckova <sup>1,2</sup>, Marta C. Neto <sup>1,2</sup>, Amy Howell <sup>3</sup>,  
Anna Thalacker-Mercer <sup>4,5</sup> and Paul W. O'Toole <sup>1,2,\*</sup>


Ntemiri A, Nutrients, 2020

- 17 women (11 young 21-39 yrs) and 6 old (65-77 yrs)
- Consumed 38 g FDBP (~1.75 cups) over 6 weeks
- Dietary enrichment with blueberries resulted in a moderate increase in diversity of the microbiota of the older women but not in younger women

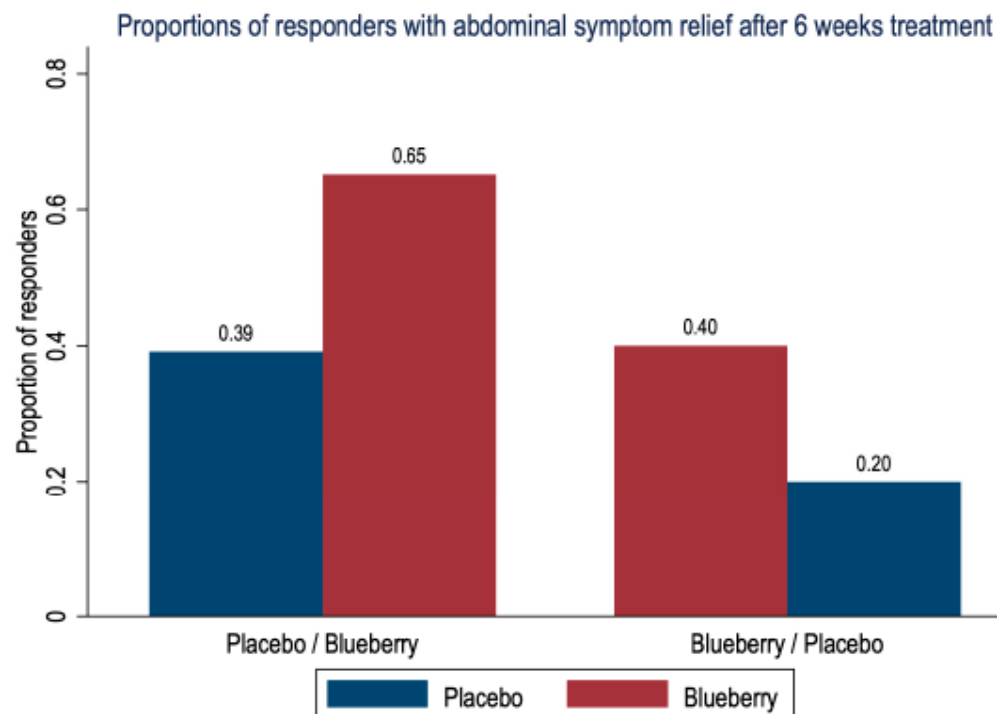
# Blueberries and Functional Gastrointestinal Disorders

Article

## Blueberries Improve Abdominal Symptoms, Well-Being and Functioning in Patients with Functional Gastrointestinal Disorders

Clive H. Wilder-Smith <sup>1,\*</sup> , Andrea Materna <sup>1</sup> and Søren S. Olesen <sup>2</sup>

- 43 participants 18-60 yrs with FGID
- 30 g FDBP (~1.25 c fresh blueberries) for 6 weeks
- Improvement in general markers of well-being, quality of life and life functioning based on Outcome Questionnaires with blueberries vs placebo



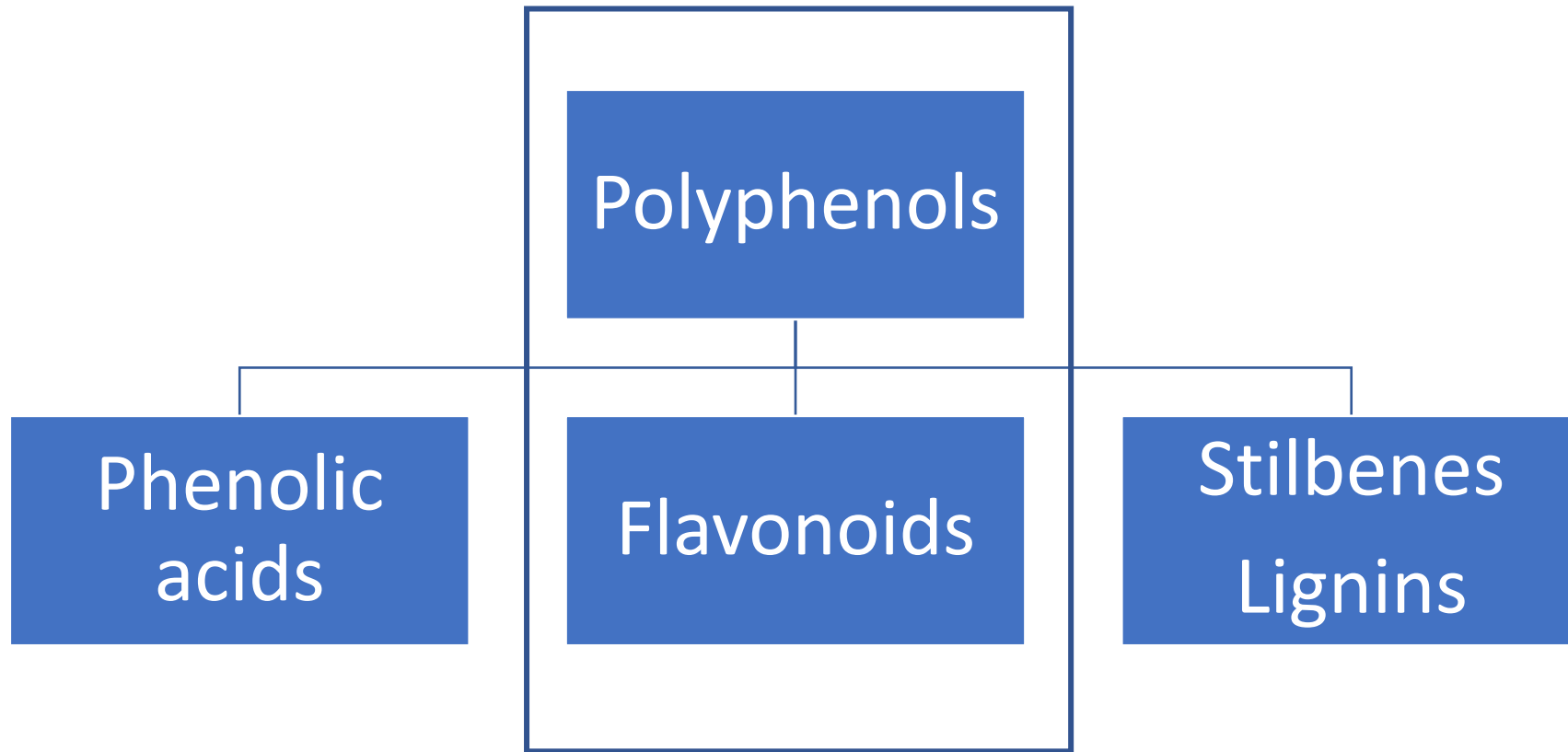
A close-up photograph of several blueberries, some in sharp focus and others blurred in the background. The berries are a deep blue color with a slightly textured surface. A white rectangular box is overlaid on the lower half of the image, containing the title and event information.

# Blueberries and Healthy Living

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# Terminology



# Bioactive Compounds in Blueberries

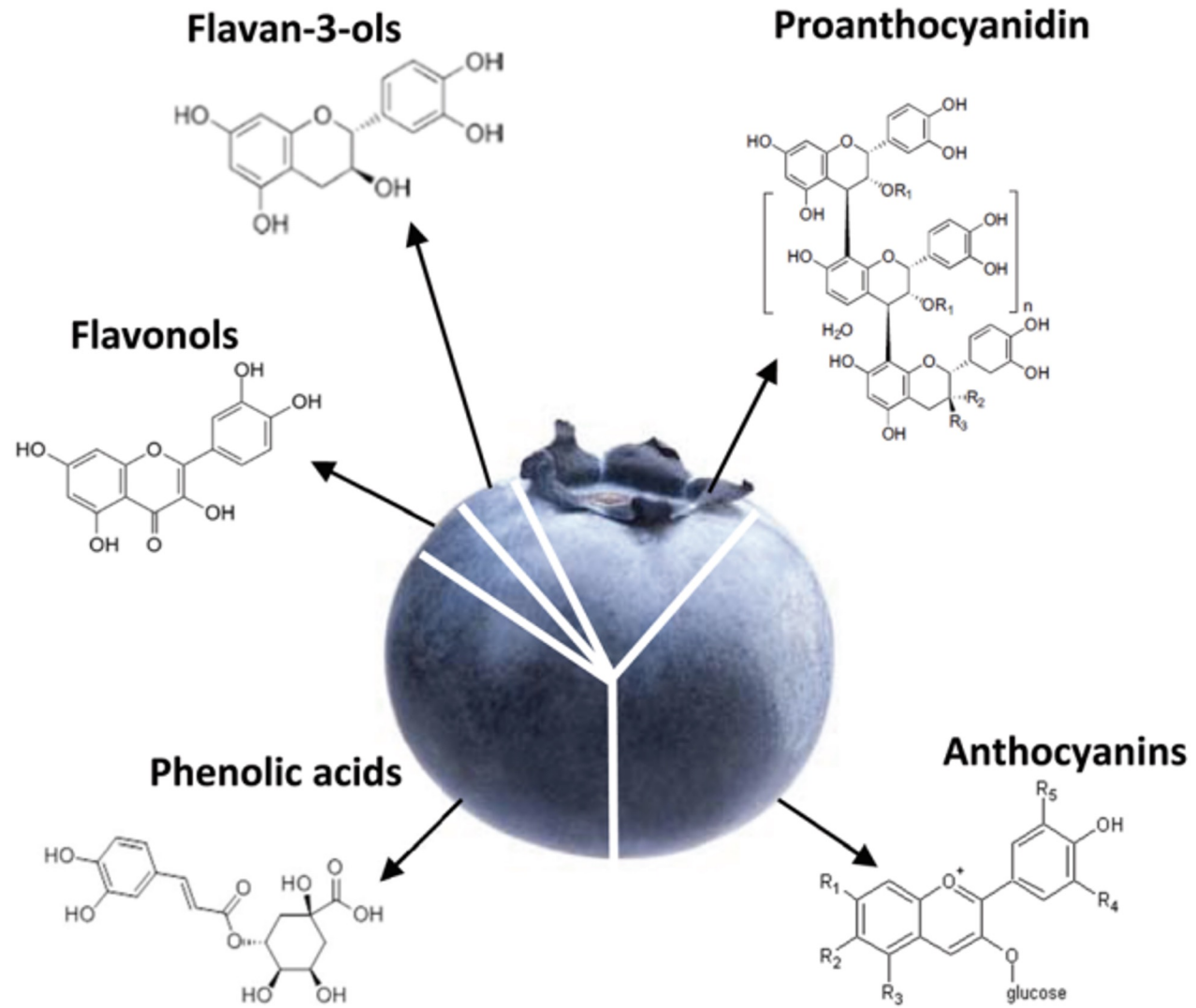
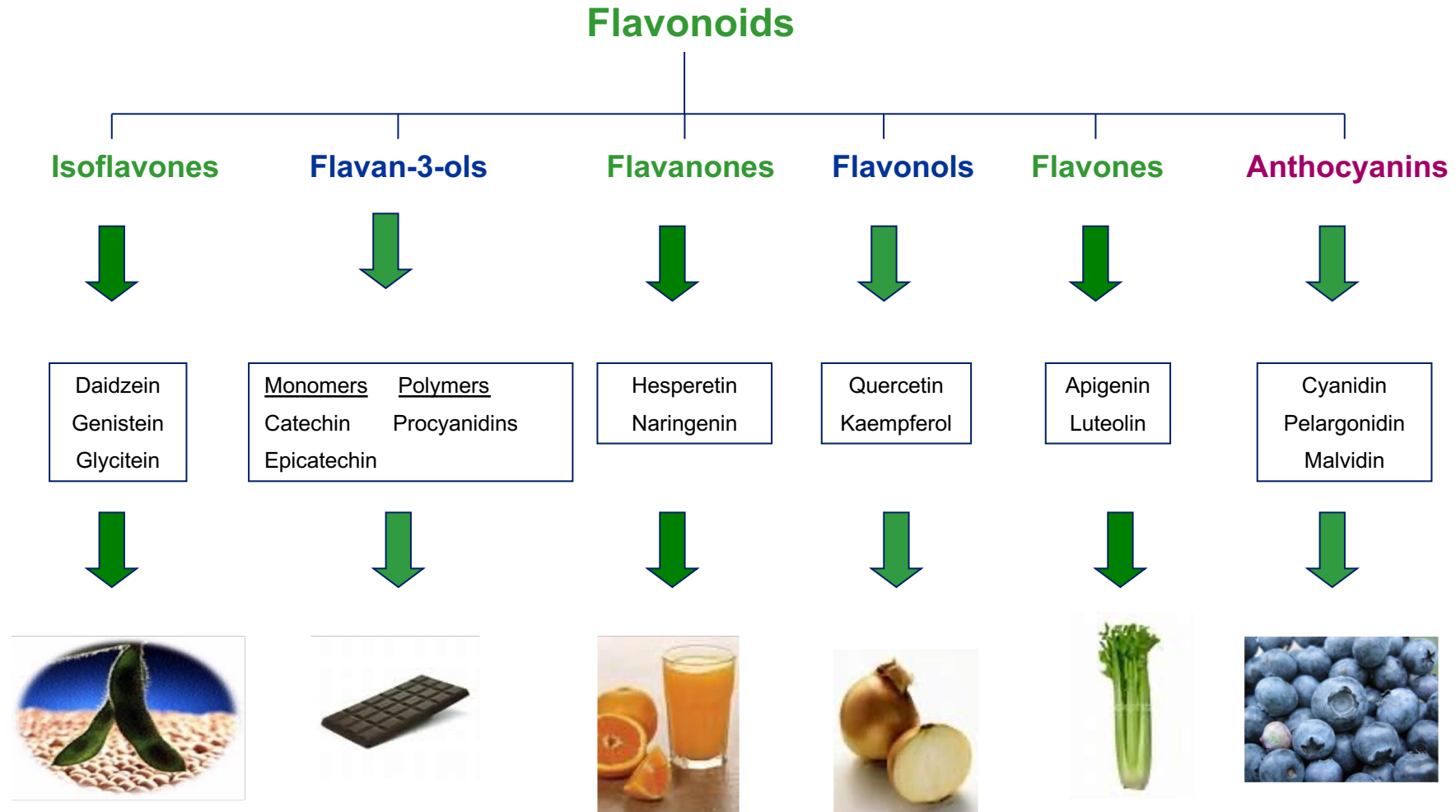


Fig. 1 Main (poly)phenol groups found in blueberries.

# Flavonoids

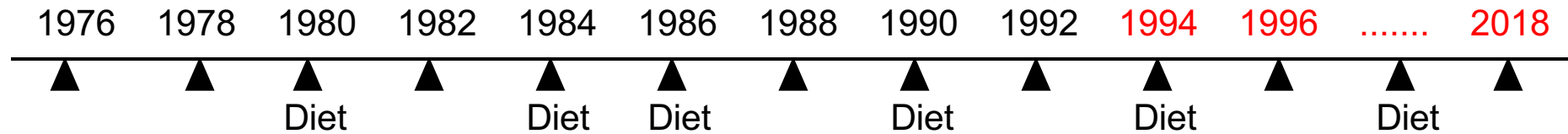
## sub-classes and sources



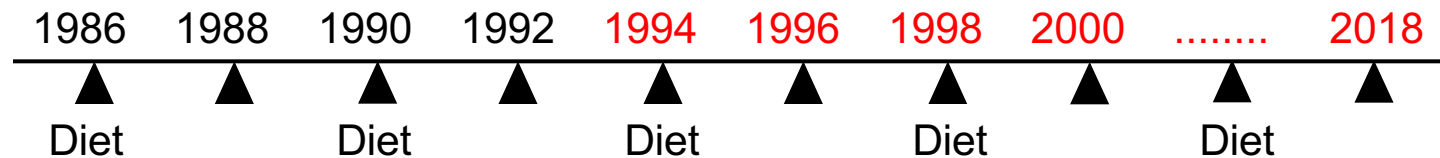
# Diet/Lifestyle Changes and Long-Term Health Outcomes

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Nurses' Health Study - 121,701 women (55,768)



Health Professionals Follow-up Study - 51,529 men (29,800)



**Every Two Years: Weight, smoking, physical activity, CVD risk factors, diseases.**  
**Every Four Years: Detailed dietary habits.**




RESEARCH ARTICLE

Open Access

# Change in habitual intakes of flavonoid-rich foods and mortality in US males and females

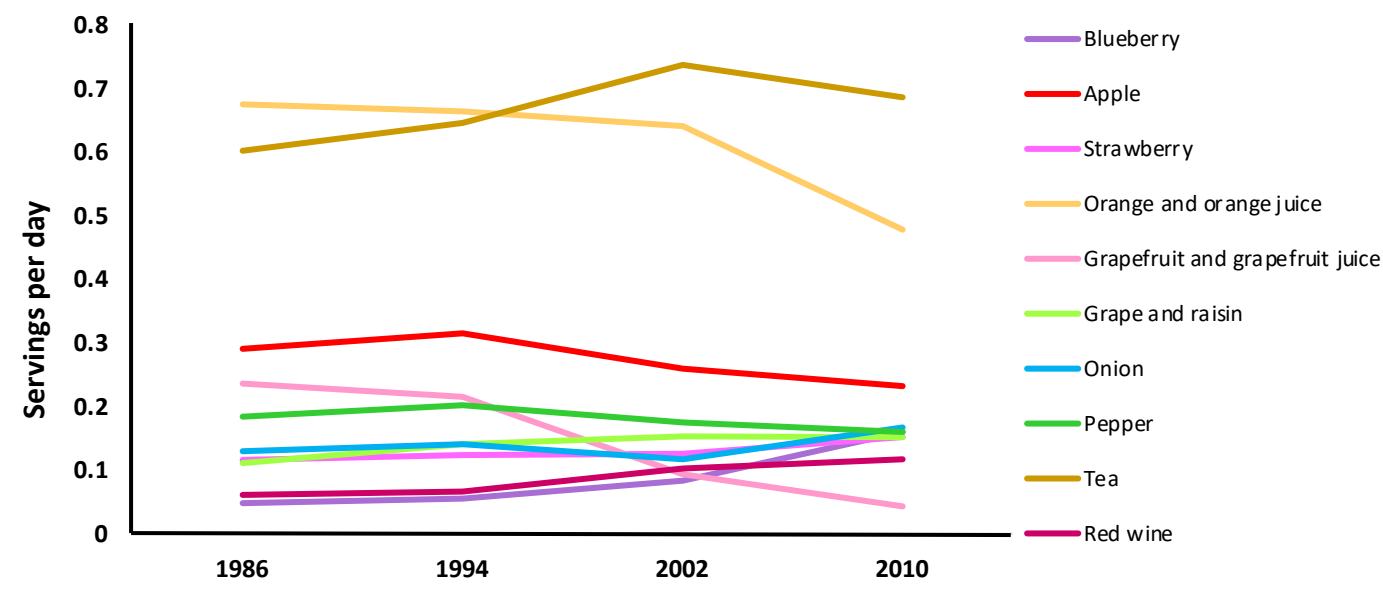


Nicola P. Bondonno<sup>1,2,3</sup>, Yan Lydia Liu<sup>4</sup>, Yan Zheng<sup>5</sup>, Kerry Ivey<sup>4</sup>, Walter C. Willett<sup>4,6,7</sup>, Meir J. Stampfer<sup>4,6,7</sup>, Eric B. Rimm<sup>4,6,7</sup> and Aedin Cassidy<sup>1\*</sup> 

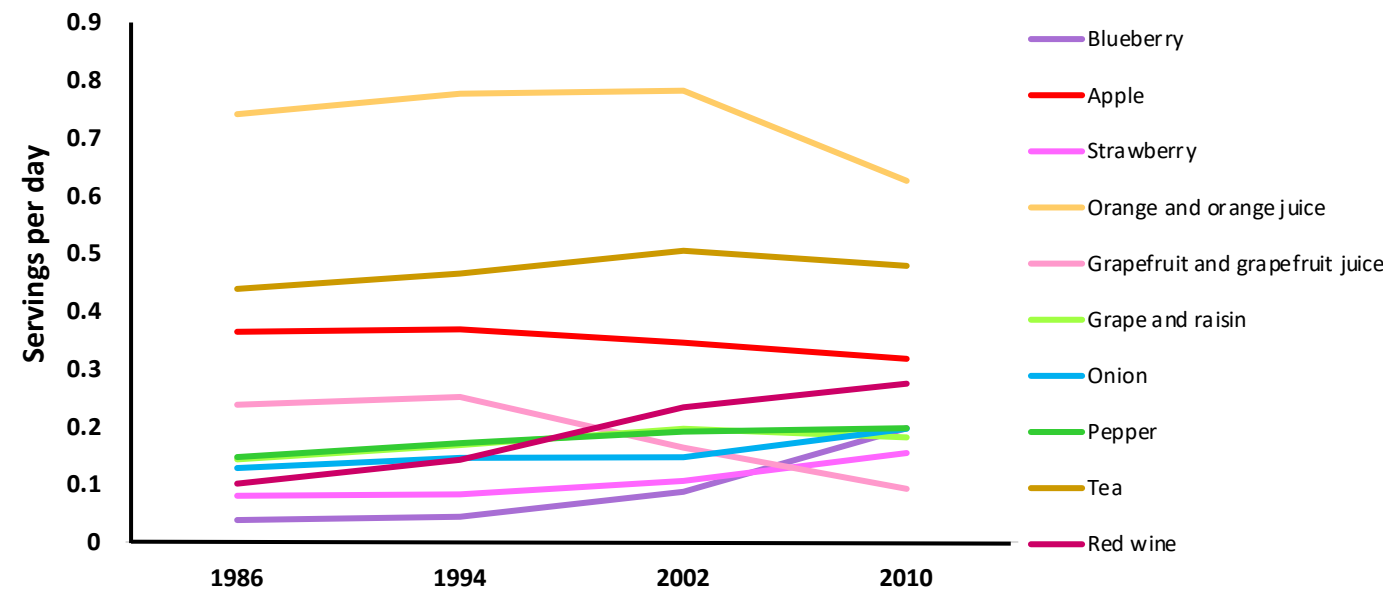
BMC Medicine, 2023

- Study Population = 55,786 females and 29,800 men
- Examined association between change in intakes of flavonoid-rich foods and risk of all-cause and cause-specific mortality
- Flavonoid-rich foods: blueberries apple, orange, orange juice, grapefruit, grapefruit juice, strawberry, tea, red wine, onion, peppers, grapes, raisins
- “Flavodiet” score created from foods that contribute >1% to total flavonoid intake (tea, apples, onions, grapefruits, blueberries, strawberries and red wine)
- Causes of death categorized as CVD-related, cancer-related, respiratory-related, neurological disease-related

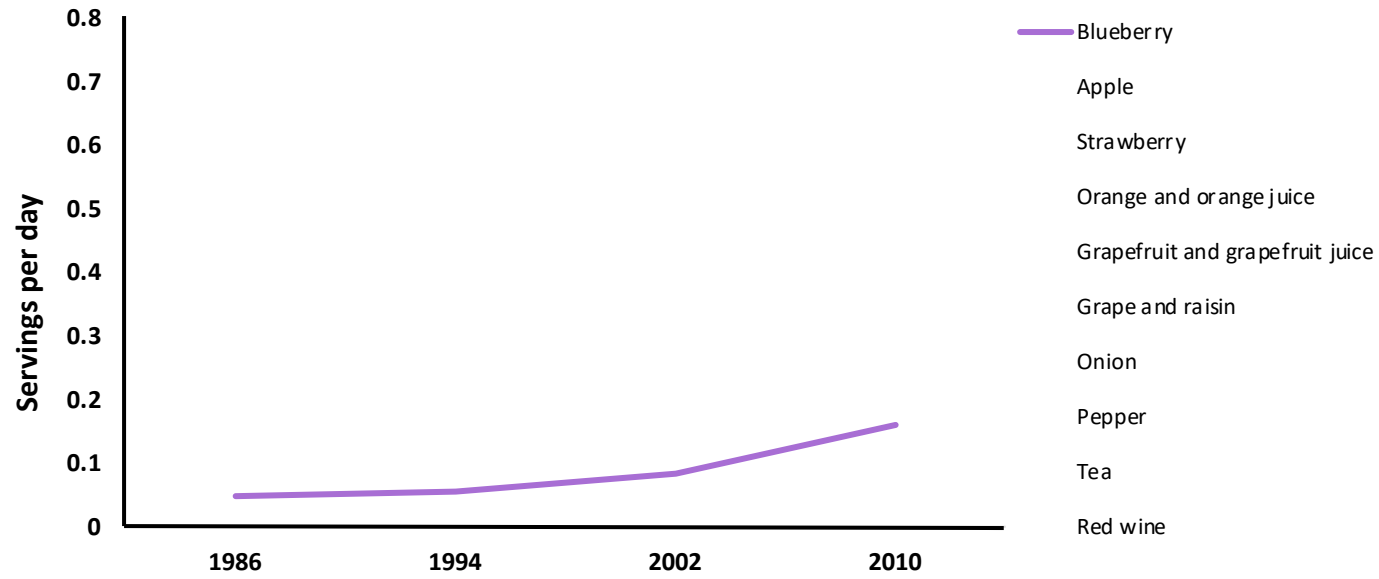
### Nurses' Health Study I



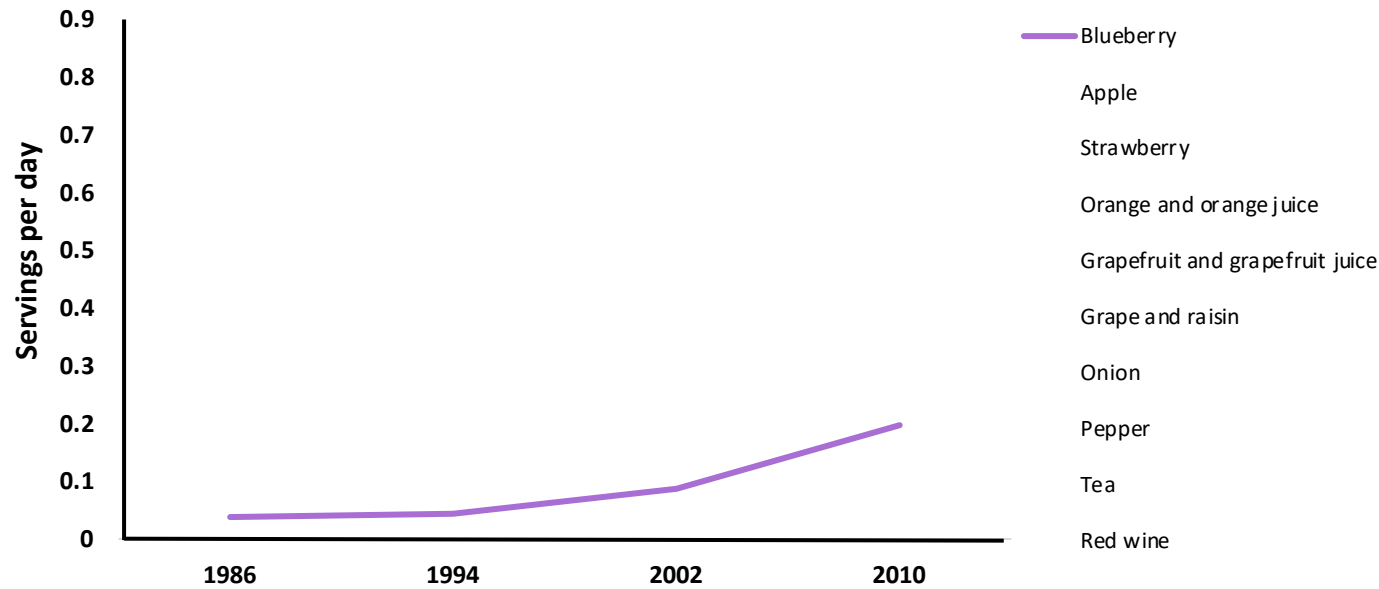
### Health Professionals Follow-up Study



### Nurses' Health Study I



### Health Professionals Follow-up Study





Healthy Living

Food	Increased Frequency	Decreased risk total mortality
Blueberries	3.5 servings/week	5%
Red wine	3.5 servings/week	4%
Peppers	3.5 servings/week	9%
Tea	7 servings/week	3%
Flavodiet Score	3 servings/day	8%
		13% neurological mortality

*Encouraging an increased intake of specific flavonoid-rich foods and beverages, namely tea, blueberries, red wine and peppers, even in middle age, may lower early mortality risk:*

Bondonno et al. BMC Medicine, 2023



# USHBC Health and Nutrition Research Pillars

**Know we're always learning more.**

Blueberries may promote good health in additional ways. **Areas of research:**



**Cardiovascular  
Health**



**Brain Health**



**Healthy Living**



**Insulin Response**



**Gut Health**

**Thank you.**



[www.blueberry.org](http://www.blueberry.org)

[www.healthprofessionals.blueberry.org/research/](http://www.healthprofessionals.blueberry.org/research/)