

## FOOD ROOTED IN BETTER CARDIOMETABOLIC HEALTH

The First Dietary Bioactive  
Guideline & Its Impact On  
Produce Consumption







# **KATIE CALLIGARO**

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**MODERATOR**



# ABOUT PBH

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PBH is 100% dedicated to helping people live happier, healthier lives by eating and enjoying more fruits and vegetables each and every day.

PBH and Have A Plant® programming are now part of the International Fresh Produce Association's (IFPA) [Foundation For Fresh Produce](#).

Our mission remains the same, yet TOGETHER, we now serve the largest community of fruit and vegetable advocates for a greater impact on consumption.



**PBH**®

**PRODUCE FOR  
BETTER HEALTH**



# THE AWARD-WINNING HAVE A PLANT® MOVEMENT REACHES MILLIONS

The award-winning Have A Plant® Movement is a way to inspire lasting behavior change by tapping into the emotional connection consumers have to the fruit and vegetable eating experience.

PBH is an undeniable resource for health & wellness professionals, given its trusted third-party credibility, breadth of nutrition and behavioral research, and strong consumer, influencer and industry reach.

**1 Billion**

social media impressions  
since the 2019 launch

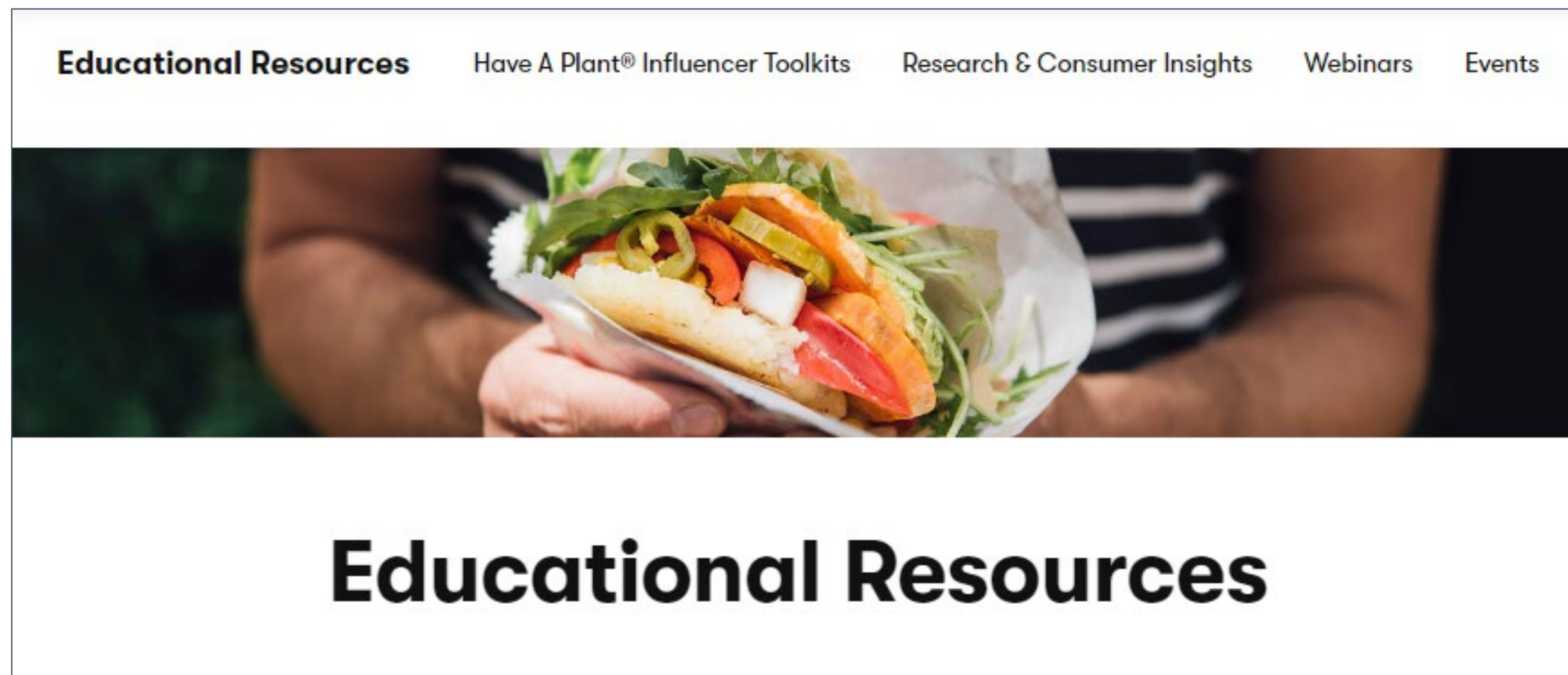
**2 Billion**

traditional media impressions  
since the 2019 launch

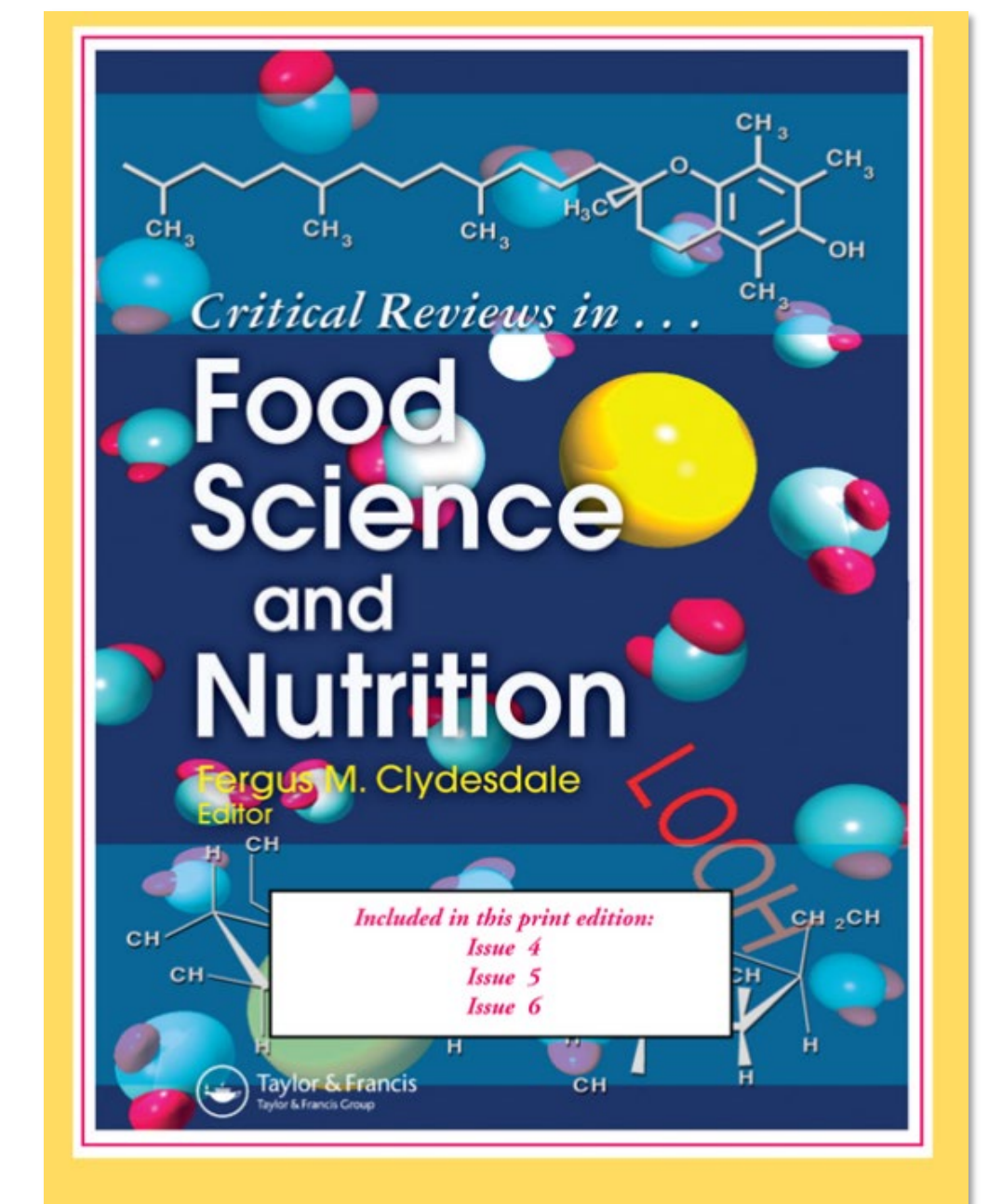
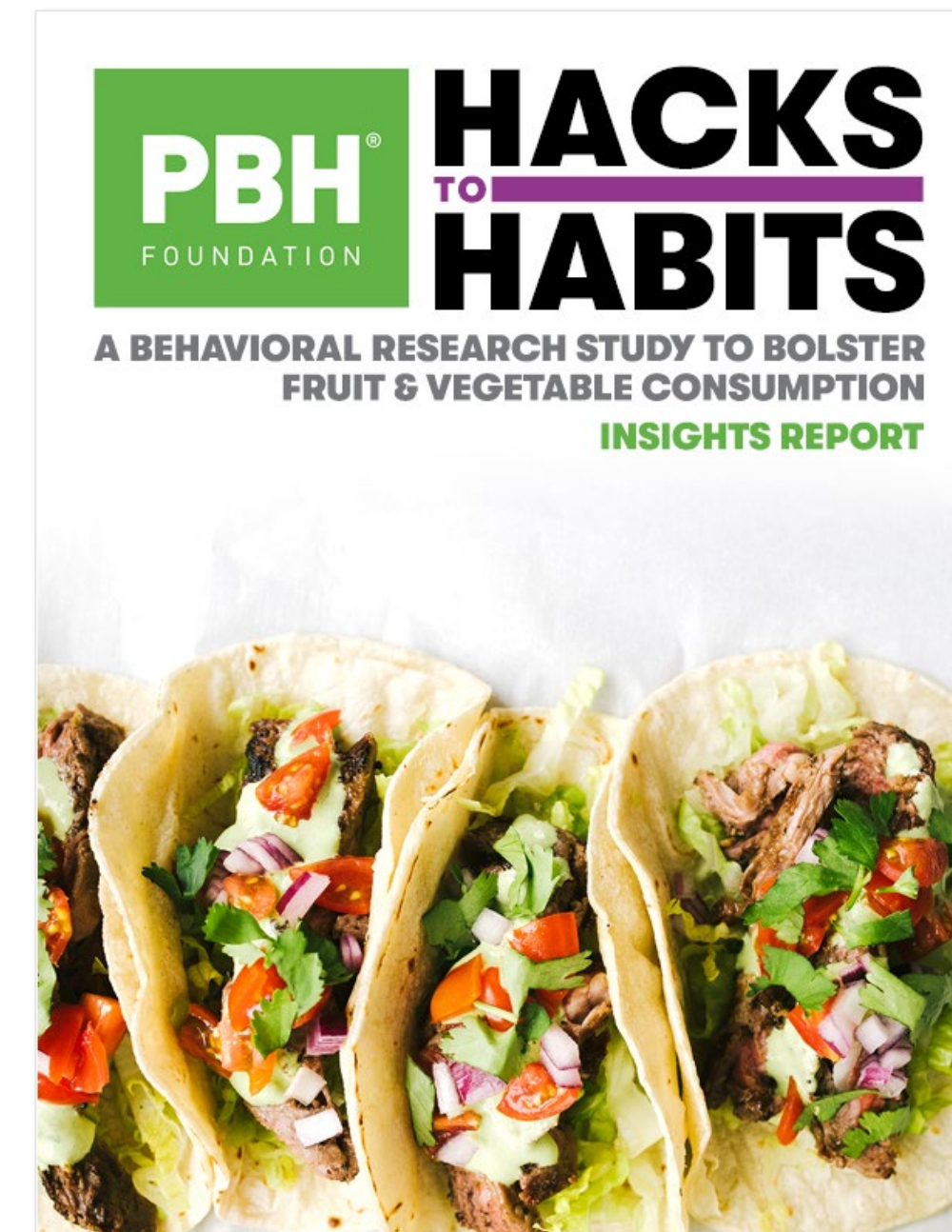




# PBH delivers innovative research as well as unique fruit and veggie insights and communication tools.



[fruitsandveggies.org/educational-resources](https://fruitsandveggies.org/educational-resources)



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## FOOD ROOTED IN BETTER CARDIOMETABOLIC HEALTH

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Its Impact On Produce Consumption



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# Overview

**1.**

Discuss the benefits of flavan-3-ols for cardiometabolic health through review of the first-ever dietary recommendation for a bioactive compound.

**2.**

Identify risks and adverse effects from supplemental intake of flavan-3-ols.

**3.**

Understand guidelines that could aid in recommendations for improving greater fruit and vegetable consumption.



# What is a dietary bioactive compound?

Constituents in foods other than those needed to meet basic human nutritional needs YET responsible for changes in health status

## Focus of intake guidelines

- Deficiencies
- Improvements in health





# Flavan-3-ols & Cardiometabolic Health

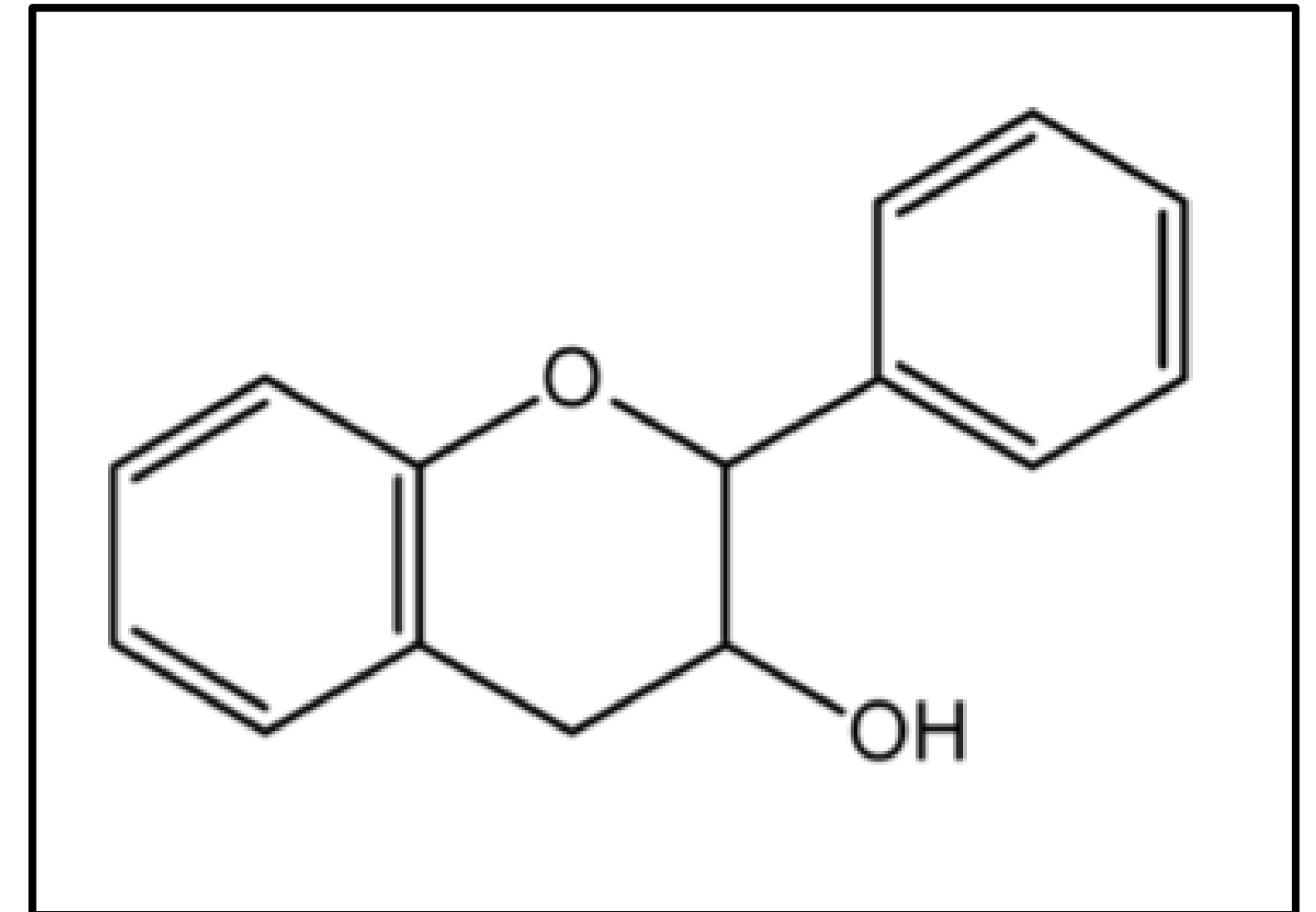
## Flavan-3-ols

Most widely consumed secondary plant metabolite in the flavonoid family

Sources include tea, apples, pears, berries, cocoa products, dark chocolate, and red wine

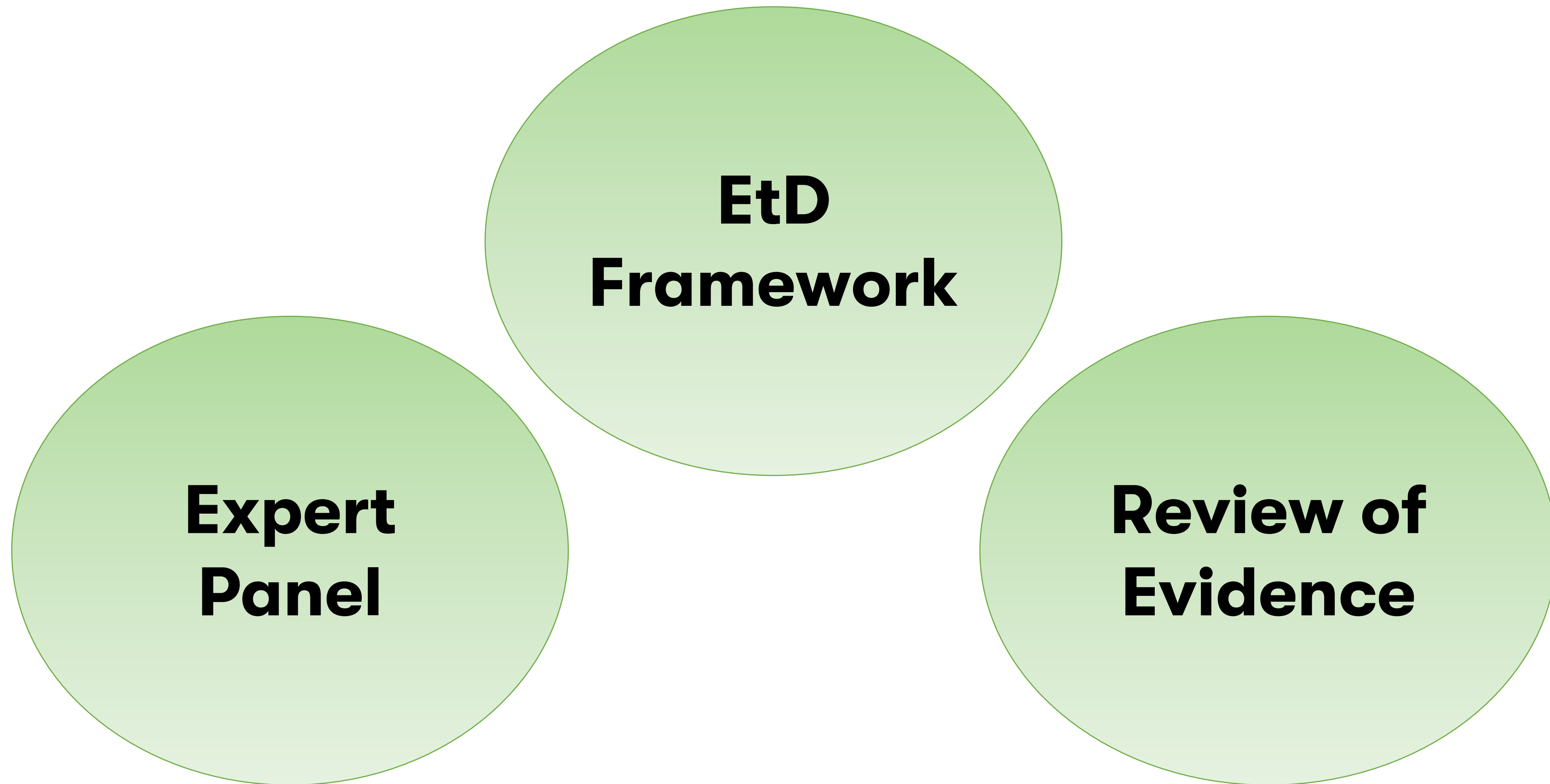
## Health-promoting properties

Functional roles include anti-oxidant, anti-inflammatory, anti-mutagenic, and anti-carcinogenic properties along with modulating effects on enzyme functionality





# Guideline Development Process





# Flavan-3-ols & Cardiometabolic Health

## Outcomes Assessed

- CVD mortality, CHD incidence, stroke and type 2 diabetes
- Blood pressure
- Endothelial function
- Glucose metabolism
- Serum lipids
- Inflammatory biomarkers

## Review Of Evidence

Data from 158 RCTs and 15 cohort studies (Raman et. Al 2019; Sesso et al. 2022)

Positions from authoritative organizations including the European Food Safety Authority and the Chinese Nutrition Society, etc.



# Flavan-3-ols & Cardiometabolic Health

Outcome Measures	Mean Difference (Summary Estimates)
Systolic Blood Pressure	-1.29 mmHg (-2.45, -0.13)
Diastolic Blood Pressure	-1.24 mmHg (-2.13, -0.34)
Acute FMD	1.15% (0.71, 1.59)
Chronic FMD	1.3% (0.59, 2.0)
Total Cholesterol	-0.06 mmol/L (-0.11, -0.001)
HDL-c	0.02 mmol/L (0.001, 0.05)
HOMA-IR	-0.29 (-0.48, 1.0)

Strength of evidence was stronger for some biomarkers.



# Flavan-3-ols & Cardiometabolic Health

## Interpreting outcomes

Each 2mm Hg increase in systolic and diastolic blood pressure increases mortality due to ischemic heart disease and stroke by 7% and 10%, respectively.

A 1% increase in FMD has been shown to reduce CVD risk by 8% and 13% in asymptomatic and diseased populations, respectively.

A 0.026 mmol/L increase in HDL-c has been reported to reduce CVD risk by 2-3%.

## Collective takeaway

Cumulative improvements in multiple cardiometabolic biomarkers may have substantial benefits to overall risk reduction at both the individual and public health level.

*Lewington et al. 2002, Gordon et al. 1989, Ras et al. 2014*



# Recommendation for Flavan-3-ols

Among the general adult population, we suggest increasing consumption of nutrient-dense foods rich in flavan-3-ols and low or absent in added sugars including but not limited to tea, apples, berries, and cocoa.

This is a food-based guideline and not a recommendation for flavan-3-ol supplements.

**Based on moderate quality research, consumption of 400 to 600mg daily of flavan-3-ols may reduce risk associated with cardiovascular disease and diabetes. Increasing consumption may help improve blood pressure, cholesterol, and blood sugar.**





# **Dose Matters:**

Balancing The Risks & Benefits of  
Flavan-3-ol Containing Supplements



# Caution – Supplementation

## Liver injury

Increases in liver enzymes such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (AP), bilirubin, and gamma-glutamyl transferase (GGT).

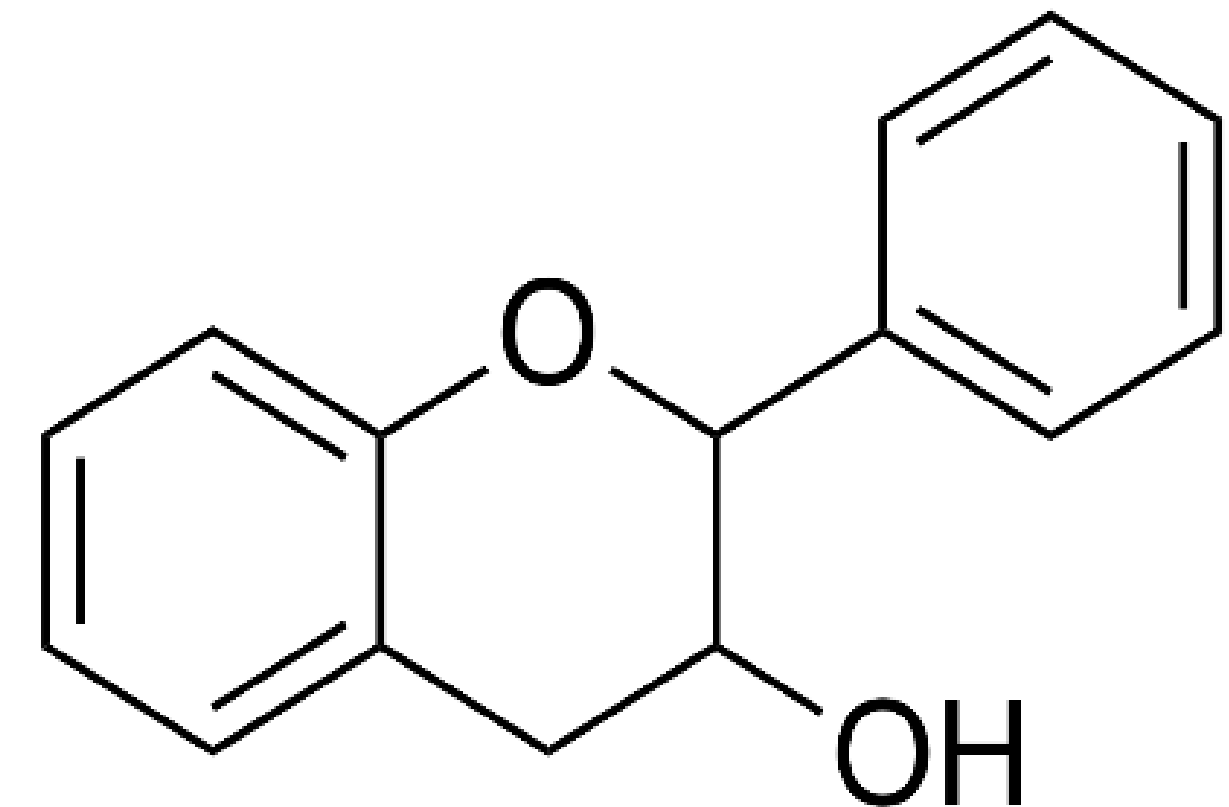
## Gastrointestinal distress

Including nausea, abdominal pain or discomfort, diarrhea or indigestion.

*Note: Clinical effects have largely been noted in studies of green tea extracts or purified epigallocatechin gallate (EGCG).*



Flavan-3-ol Structure



*Regul Toxicol Pharmacol.* 2018;95:412.



# Safety Of Green Tea & Green Tea Extracts

## Toxicity Data

A systematic review of adverse event data from 159 human intervention studies yielded findings consistent with toxicological evidence in that a limited range of concentrated catechin-rich green tea preparations resulted in adverse hepatic events in a dose-dependent manner. This occurred **when ingested in large bolus doses** but not when consumed as brewed tea or extracts in beverages or part of food matrix.

## NIH Dietary Supplement Label Database (DSLDD)

Lists a range of supplemental doses of EGCG from 140 to 1000 mg.

*Regul Toxicol Pharmacol.* 2018;95:412.

[https://ods.od.nih.gov/Research/Dietary\\_Supplement\\_Label\\_Database.aspx](https://ods.od.nih.gov/Research/Dietary_Supplement_Label_Database.aspx)



# Safety Of Green Tea & Green Tea Extracts

Outcome	Body of Evidence	Consistency	Dose Response	Biological Plausibility	Human Relevance	Confidence Rating
GI Toxicity	N=33	Yes	Yes	Strong	High	High
Hepatotoxicity	N=37	Yes	Yes	Strong	High	High
Body Weight	N=27	Yes	Yes	Medium	Limited	Moderate
Nasal-olfactory Toxicity	N=7	No	No	Medium	Limited	Very Low
Thyroid Toxicity	N=5	No	Yes	Weak	Limited	Very Low
Cardiotoxicity	N=11	No	Yes	Weak	Limited	Low

**Note:** There was also weak biological plausibility, limited human relevance, and a very low confidence rating for pancreatic, renal, reproductive, developmental, lung, spleen, lymphoid, and bone marrow toxicity.

# Safety Of Green Tea & Green Tea Extracts

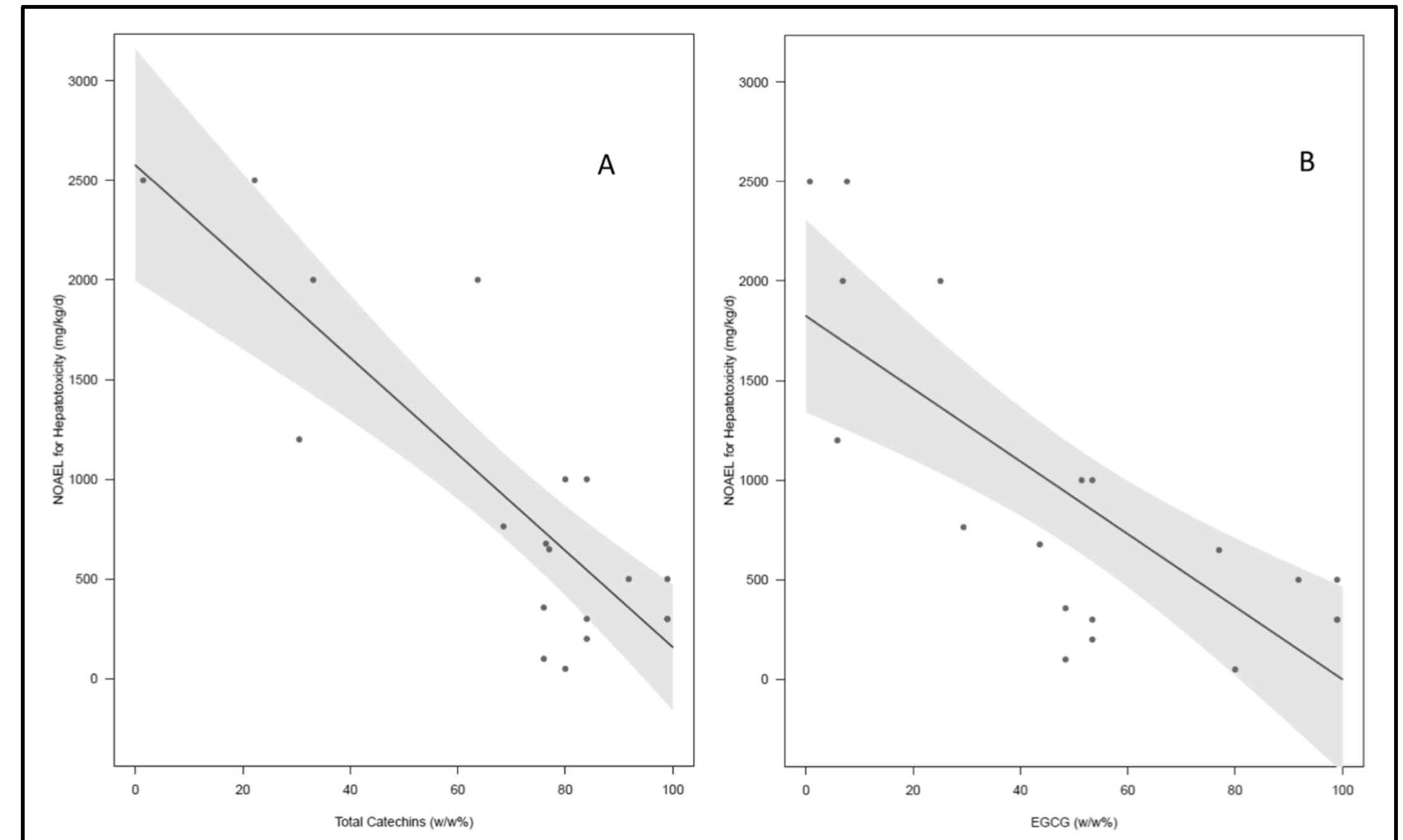
## Toxicity Data

An inverse relationship was identified between the purity of total catechins (left) and EGCG (right) with the No Observed Adverse Effect Level (NOAEL).

Toxic potential of green tea sharply rises with increasing concentrations of catechins and EGCG.

Safe intake level of **338 mg EGCG per day for supplements.**

Safe intake level of **704 mg EGCG per day for beverages.**





# Recommendations From Authoritative Bodies

## European Food Safety Authority (2018)

Catechins in green tea extracts as supplements delivering EGCG in amounts equal to or above 800 mg per day increased serum transaminases, indicative of liver injury. A safe dose was not identified.

## Health Canada (2018)

Strengthened cautionary risk statement in monograph.

## Norwegian Institute of Public Health (2019)

Concluded that intake of more than 0.4 mg of EGCG per kg of body weight per day as a bolus may cause adverse biological effects and noted an increased susceptibility to toxicity when taken under fasting conditions.

# Recommendations From Authoritative Bodies

## U.S. National Institutes of Health (2020)

States that although uncommon, liver problems have been reported in several people who took green tea products, primarily green tea extracts in pill form.

## U.S. Pharmacopeia (2020)

“Do not take on an empty stomach. Take with food. Do not use if you have a liver problem and discontinue use and consult a healthcare practitioner if you develop symptoms of liver trouble, such as abdominal pain, dark urine, or jaundice.”



# Safety of Cocoa Extracts

## Part 1

Open-label, intake-amount escalation study in which 34 healthy adults (age 35-55 years) consumed increasing amounts of cocoa flavan-3-ols (1000-2000 mg per day) over 6-weeks.

## Part 2

Randomized, double-blind, placebo-controlled trial in which participants consumed 2000 mg of cocoa flavan-3-ols or a placebo per day for 12-weeks (n=74).

No significant changes in liver panel results were noted.

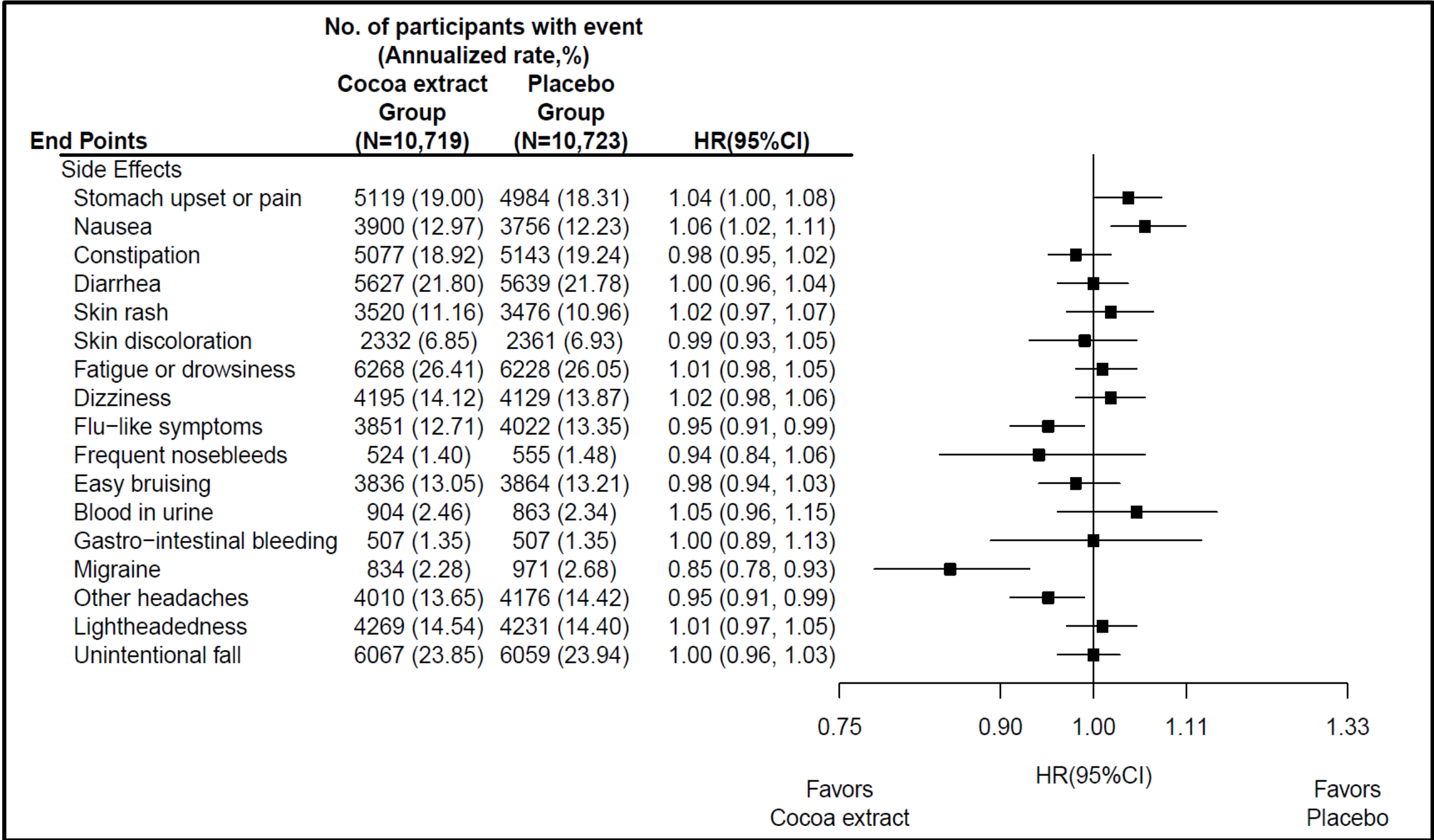
Gastrointestinal-related issues represented most of the adverse events (75%) with nausea being the most predominant. **These events were commonly reported when supplements were taken on an empty stomach.** Other less reported adverse events included vomiting and headaches.

# The COSMOS Trial

## Large 20,000 Person RCT

Those taking the active cocoa extract supplement were **6% more likely to have nausea** (HR: 1.06, 95% CI: 1.02-1.11).

In contrast, the cocoa extract supplement group had a significant 5% reduction in self-reported flu-like symptoms and other headaches (HR: 0.95, 95% CI: 0.91-0.99) and a 15% reduction in self-reported migraine (HR: 0.85, 95% CI:0.78-0.93).





# Recommendations On Cocoa Extracts From EFSA

## European Food Safety Authority (2014)

A cause-and-effect relationship has been established between consumption of **cocoa flavanols and maintenance of normal endothelium-dependent vasodilation** contributing to normal blood flow. In order to obtain the claimed effect, **200 mg of cocoa flavanols** should be consumed daily. The Panel did not evaluate safety.

# Additional Considerations

## We Considered...

The amount of galloylated flavan-3-ol derivatives in cocoa is negligible. This may be of importance because the absorption, distribution, metabolism, and excretion, and thus **biological activities of galloylated flavan-3-ols have been shown to exhibit significant differences.**

Extrapolation of information on the overall safety of flavan-3-ols was not possible. Consequently, there was insufficient evidence to identify an upper limit for flavan-3-ols in food or supplemental form.

Food slows the absorption of supplements.

**It is important for the supplement industry to stay within the guard rails of this evidence-based guideline (400-600 mg/d).**

*Adv Nutr.* 2022; online first (<http://doi.org/10.1093/advances/nmac105>).



# Guideline Recommendation

Based on moderate quality research, consumption of 400 to 600mg daily of flavan-3-ols may reduce risk associated with cardiovascular disease and diabetes. Increasing consumption may help improve blood pressure, cholesterol, and blood sugar.

This is a food-based guideline and not a recommendation for flavan-3-ol supplements as these may cause gastrointestinal irritation and/or liver injury, particularly when taken on an empty stomach.





# **Translating The Guideline Into Practice**



# Translation Of Guideline Into Practice

## How do we estimate intake of flavan-3-ols?

### Two main databases:

USDA, Database for the Flavonoid Content of Selected Foods, Release 3.3 (2018) and USDA Database for the Isoflavone Content of Selected Foods, Release 2.1 (2015)

6 flavonoid subclasses - anthocyanins, flavan-3-ols, flavanones, flavones, flavanols and isoflavones

Phenol-Explorer, Developed at INRA, Version 3.6

9 flavonoid subclasses – also chalcones, dihydrochalcones and dihydroflavonols

Bhagwat, Seema; Haytowitz, David B. (2022). USDA Database for the Flavonoid Content of Selected Foods, Release 3.3 (March 2018). Nutrient Data Laboratory, Beltsville Human Nutrition Research Center, ARS, USDA. <https://data.nal.usda.gov/dataset/usda-database-flavonoid-content-selected-foods-release-33-march-2018>.

U.S. Department of Agriculture, Agricultural Research Service. 2015. USDA Database for the Isoflavone Content of Selected Foods, Release 2.1. Nutrient Data Laboratory Home Page: <http://www.ars.usda.gov/nutrientdata/isoflav>.

Rothwell JA, Pérez-Jiménez J, Neveu V, Medina-Ramon A, M'Hiri N, Garcia Lobato P, Manach C, Knox K, Eisner R, Wishart D, Scalbert A. (2013) Phenol-Explorer 3.0: a major update of the Phenol-Explorer database to incorporate data on the effects of food processing on polyphenol content. Database, 10.1093/database/bat070.

# Adult Global Differences in Estimated Flavan-3-ol Intake

Countries	Flavan-3-ols (mg/day)	Foods
United States	170	Black tea, apple
Australia	427	Black tea
Europe, MED	282	Apple, pear, berries, red wine
Europe, Non-MED	430	Black tea
Brazil	11	Chocolate, cocoa powder, banana, apple
Mexico	121	Apple, prickly pear, strawberry, green broad bean, plum
China	173	Apple, pear, peach, green tea, black tea
South Korea	122	Apple, pear, green tea



# Flavan-3-ol Intake In The United States

Gender and age (years)	Flavan-3-ols (mg/day)	Total Flavonoids (mg/day)
Male		
20 and over	164 ± 11	213 ± 12
Females		
20 and over	175 ± 17	221 ± 18
Males and females		
20 and over	170 ± 12	218 ± 13

U.S. Department of Agriculture, Agricultural Research Service. 2022. Flavonoid Intakes from Food and Beverages: Mean Amounts Consumed per Individual, by Gender and Age, What We Eat in America, NHANES 2017-2018.

# Flavan-3-ol Intake in the US by Race/Ethnicity (≥ 20 Years)

Race/Ethnicity	Flavan-3-ols (mg/day)	Total Flavonoids (mg/day)
Non-Hispanic White	201 ± 19	248 ± 20
Non-Hispanic Black	99 ± 11	136 ± 11
Non-Hispanic Asian	219 ± 27	283 ± 28
Hispanic	73 ± 10	124 ± 12

U.S. Department of Agriculture, Agricultural Research Service. 2022. Flavonoid Intakes from Food and Beverages: Mean Amounts Consumed per Individual, by Race/Ethnicity and Age, What We Eat in America, NHANES 2017-2018.



# Flavan-3-ol Intake in the US by Family Income (≥ 20 Years)

Family Income in US Dollars	Flavan-3-ols (mg/day)	Total Flavonoids (mg/day)
\$0 - \$24,999	148 ± 19	188 ± 20
\$25,000 - \$74,999	163 ± 14	208 ± 15
\$75,000 and higher	193 ± 21	248 ± 22
All Individuals	170 ± 12	218 ± 13

U.S. Department of Agriculture, Agricultural Research Service. 2022. Flavonoid Intakes from Food and Beverages: Mean Amounts Consumed per Individual, by Family Income (in Dollars) and Age, What We Eat in America, NHANES 2017-2018.

# Dietary Sources of Flavan-3-ols

Flavan-3-ol Source	Standard Serving Size	Average Flavan-3-ols (mg)
Tea, black, brewed prepared with tap water	8 fluid ounces	269
Tea, black, brewed prepared with tap water, decaffeinated	8 fluid ounces	124
Tea, black, ready-to-drink, diet, plain and flavored	8 fluid ounces	39
Tea, black, ready-to-drink, plain and flavored	8 fluid ounces	65
Tea, green, brewed, flavored	8 fluid ounces	120
Tea, green, brewed, decaffeinated	8 fluid ounces	152
Tea, green, ready-to-drink	8 fluid ounces	28
Tea, oolong, brewed	8 fluid ounces	117
Tea, white, brewed	8 fluid ounces	163
Tea, instant, unsweetened, powder, prepared	8 fluid ounces	60

Bhagwat, Seema; Haytowitz, David B. (2022). USDA Database for the Flavonoid Content of Selected Foods, Release 3.3 (March 2018). Nutrient Data Laboratory, Beltsville Human Nutrition Research Center, ARS, USDA. <https://data.nal.usda.gov/dataset/usda-database-flavonoid-content-selected-foods-release-33-march-2018>.



# Dietary Sources of Flavan-3-ols

Flavan-3-ol Source	Standard Serving Size	Average Flavan-3-ols (mg)
<u>Fruit</u>		
Apple	1 small apple (2-3/4” dia.)	12
Banana	1 small peeled	7
Blueberries	½ cup	6
Blackberries	½ cup	31
Cranberries	½ cup	10
Grapes	½ cup	6
Peach	½ cup	8
Pear	½ cup	5
Raspberries	½ cup	6
Strawberries	½ cup	4
Cocoa, dry powder, unsweetened	1 tablespoon	13
Dark Chocolate	2 tasting squares	30
Red Wine	5 fluid ounces	23

Bhagwat, Seema; Haytowitz, David B. (2022). USDA Database for the Flavonoid Content of Selected Foods, Release 3.3 (March 2018). Nutrient Data Laboratory, Beltsville Human Nutrition Research Center, ARS, USDA. <https://data.nal.usda.gov/dataset/usda-database-flavonoid-content-selected-foods-release-33-march-2018>.

# Example Meal Plan

## Breakfast

- Oatmeal
- 1 small banana = 7 mg flavan-3-ols
- 8 oz black tea, brewed = 269 mg flavan-3-ols

## Snack

- ½ cup blackberries = 31 mg flavan-3-ols

## Lunch

- Florida sunshine salad with choice of protein
- Multigrain roll
- 1 small apple = 12 mg flavan-3-ols
- Beverage

## Snack

- 2 dark chocolate squares = 30 mg flavan-3-ols

## Dinner

- Blackened grouper and vegetables with rice
- Red wine 5 fluid oz = 23 mg flavan-3-ols

## Snack

- 8 oz decaf green tea = 152 mg flavan-3-ols

**Flavan-3-ol Intake = 524mg**



# Cost Considerations

**Apple** \$1.31 per pound (4 small apples)

**Banana** 50 cents per pound (3 bananas)

**Blackberries** \$2.00 per ½ cup

**Cocoa powder** 23 cents per 1 tablespoon


**Dark chocolate** 36 cents per tasting square

**Tea brewed at home** 3 – 5 cents per 8 fluid ounces


**Red wine** \$3.20 per 5 fluid ounces




# Practice Applications




Increasing intake of flavan-3-ol rich foods may reduce risk of cardiometabolic disease.



Caution is warranted in increasing intake through supplements.



Flavan-3-ol consumption varies among the US adult population and by recognizing barriers/facilitators intake may be increased.



Understand guidelines that could aid in recommendations for improving greater fruit and vegetable consumption.



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# Q & A

# JOIN THE MOVEMENT



Show your support by joining the Have A Plant<sup>®</sup> community at [fruitsandveggies.org/jointhenetwork](https://fruitsandveggies.org/jointhenetwork)

And don't forget to follow PBH's social channels to keep up to date on all the insights and inspiration!  
#haveaplant



September is National Fruits & Veggies Month (NFVM) and each year we celebrate Have A Plant<sup>®</sup> during this monumental moment as a way to elevate fruit and vegetable consumption to a national priority.

Start planning for NFVM 2023 now! #NFVM2023

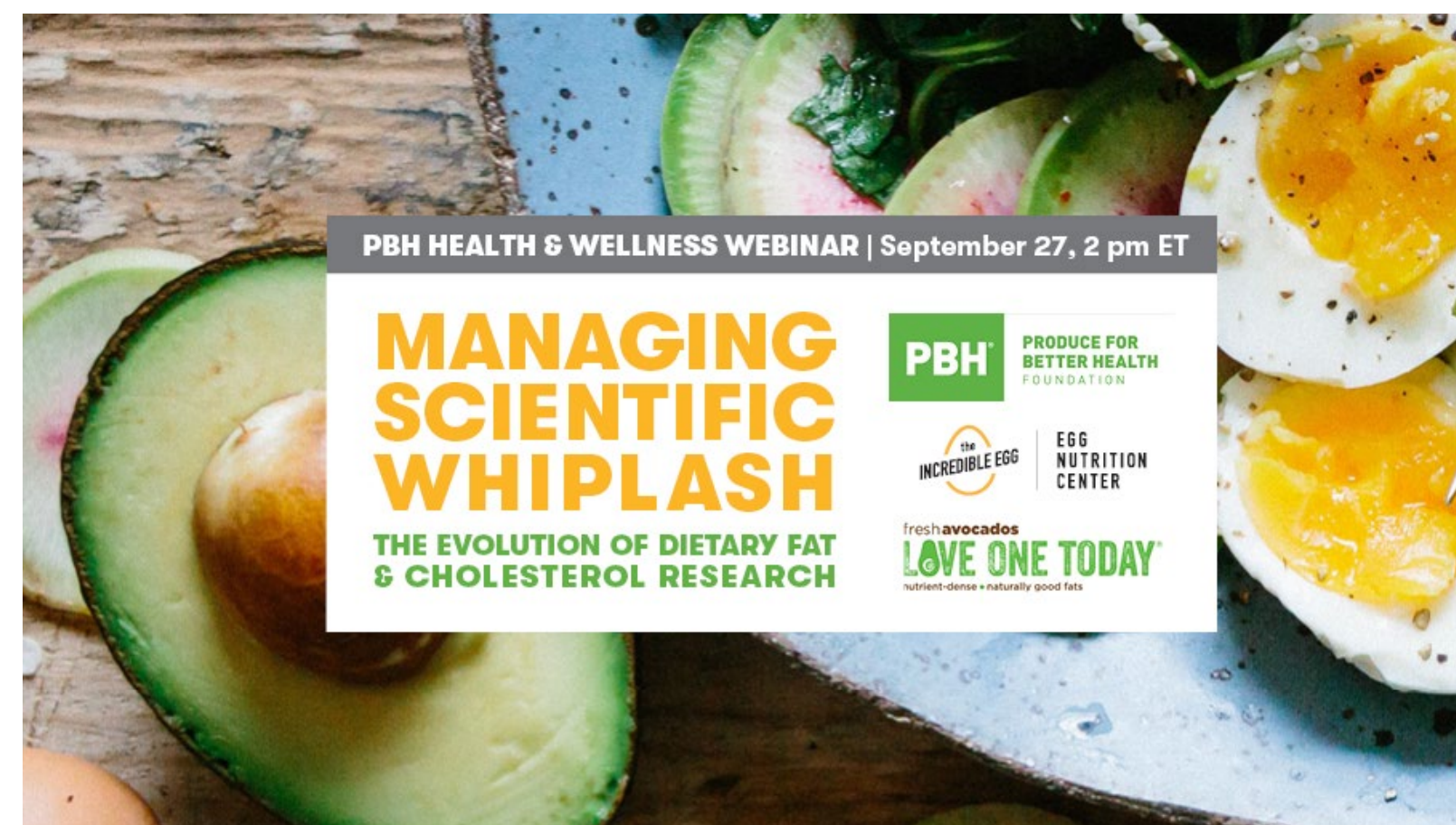


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## Visit PBH's on-demand catalog of webinars on various fruit and vegetable topics including:

- *Hacks To Habits: Unpacking The Research For Retail, Foodservice & Communication Professionals*
- *Managing Scientific Whiplash: The Evolution Of Dietary Fat & Cholesterol Research*
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**WE ARE SO HAPPY  
YOU'RE WITH US!**

