The Food Environment, Microbial Bile Acid Metabolism, and Cancer Disparities

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Disclosures

None

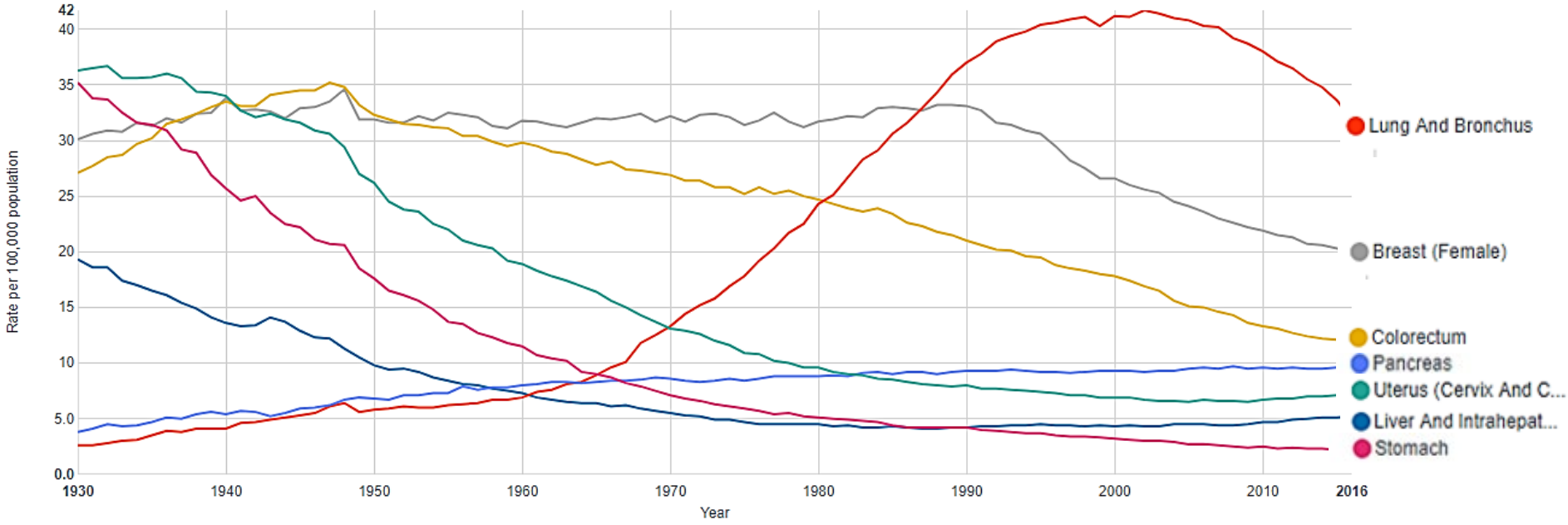
Learning Objectives

1. Evaluate the evidence and identify research gaps in the relationship of microbial ecology and function with cancer risk.
2. Consider the association of diet and microbes with health disparities.
3. Determine how research can be translated into action steps to provide individuals access to interventions.

CRC is a leading cause of cancer incidence and death

Trends in death rates, 1930-2016

Females



Per 100,000, age adjusted to the 2000 US standard population.

Data sources: National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention, 2017

Higher CRC burden in individuals that identify as Black

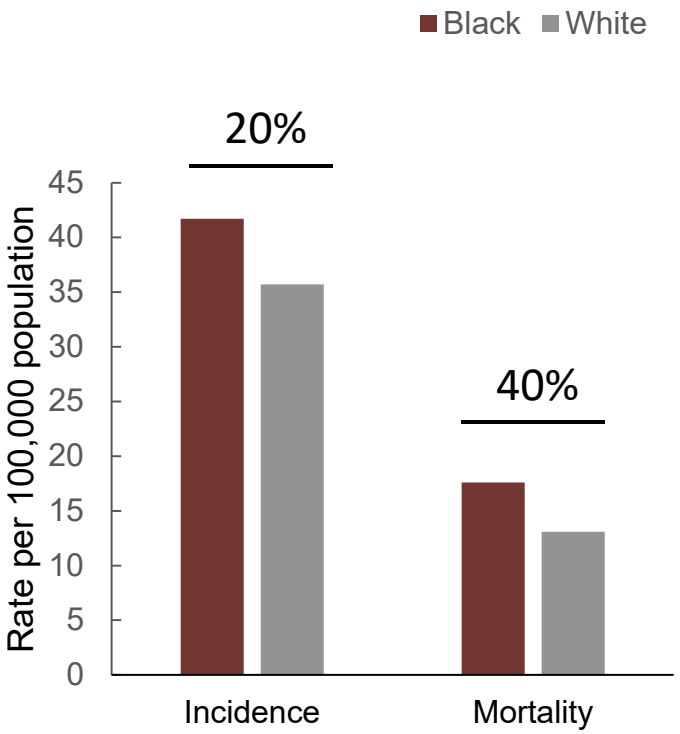
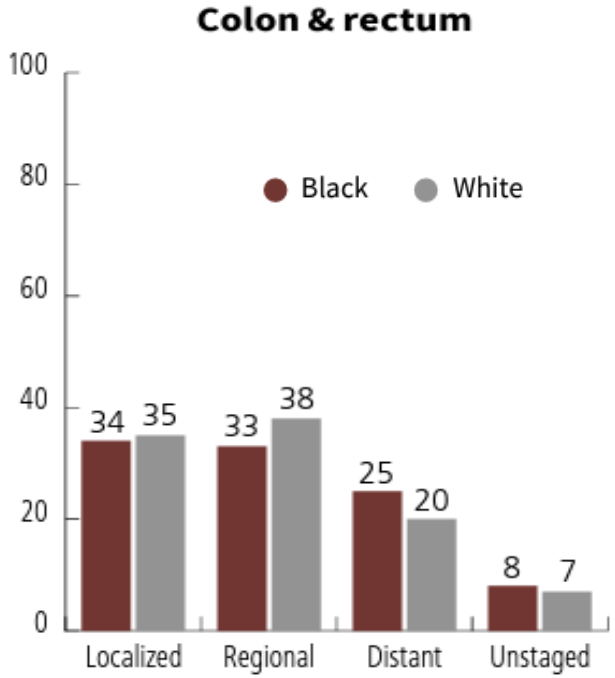
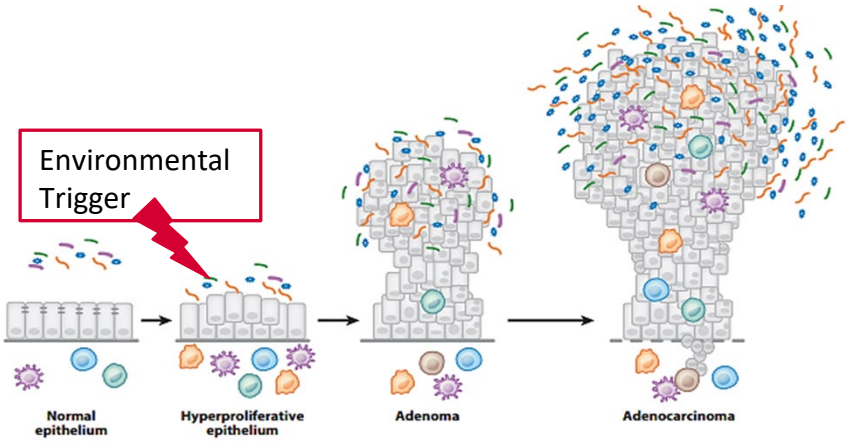


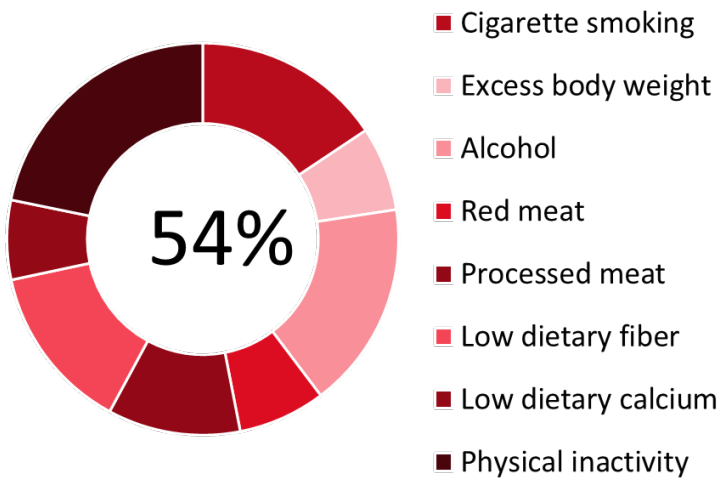
Figure 4. Stage Distribution for Selected Cancers in Black and White People, US, 2014-2018



Source: Surveillance, Epidemiology, and End Results (SEER) Program, 18 Registries, National Cancer Institute, 2021. ©2022, American Cancer Society, Inc., Surveillance and Health Equity Science

The majority of CRCs are the result of modifiable risk factors

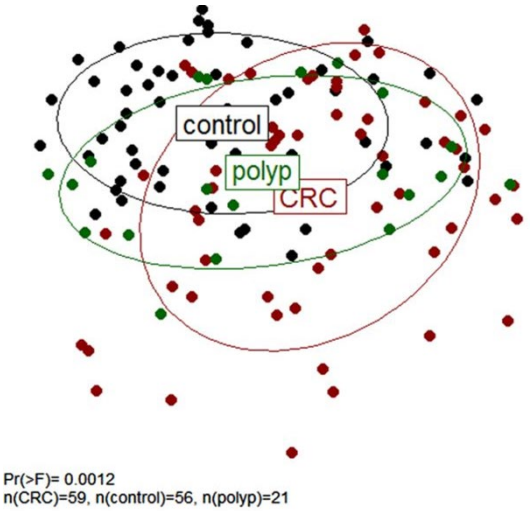


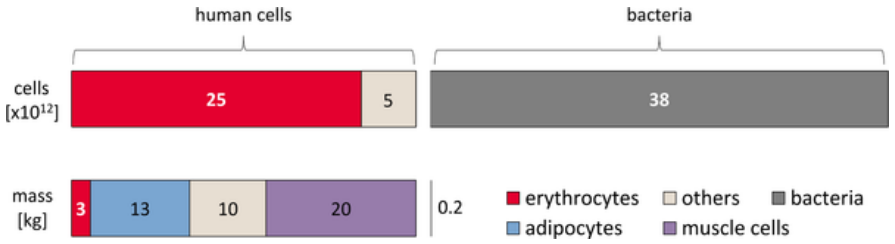


Brennan and Garrett. (2016) *Annual Review of Microbiology*

Islami F et al. (2018) *CA Cancer J Clin*

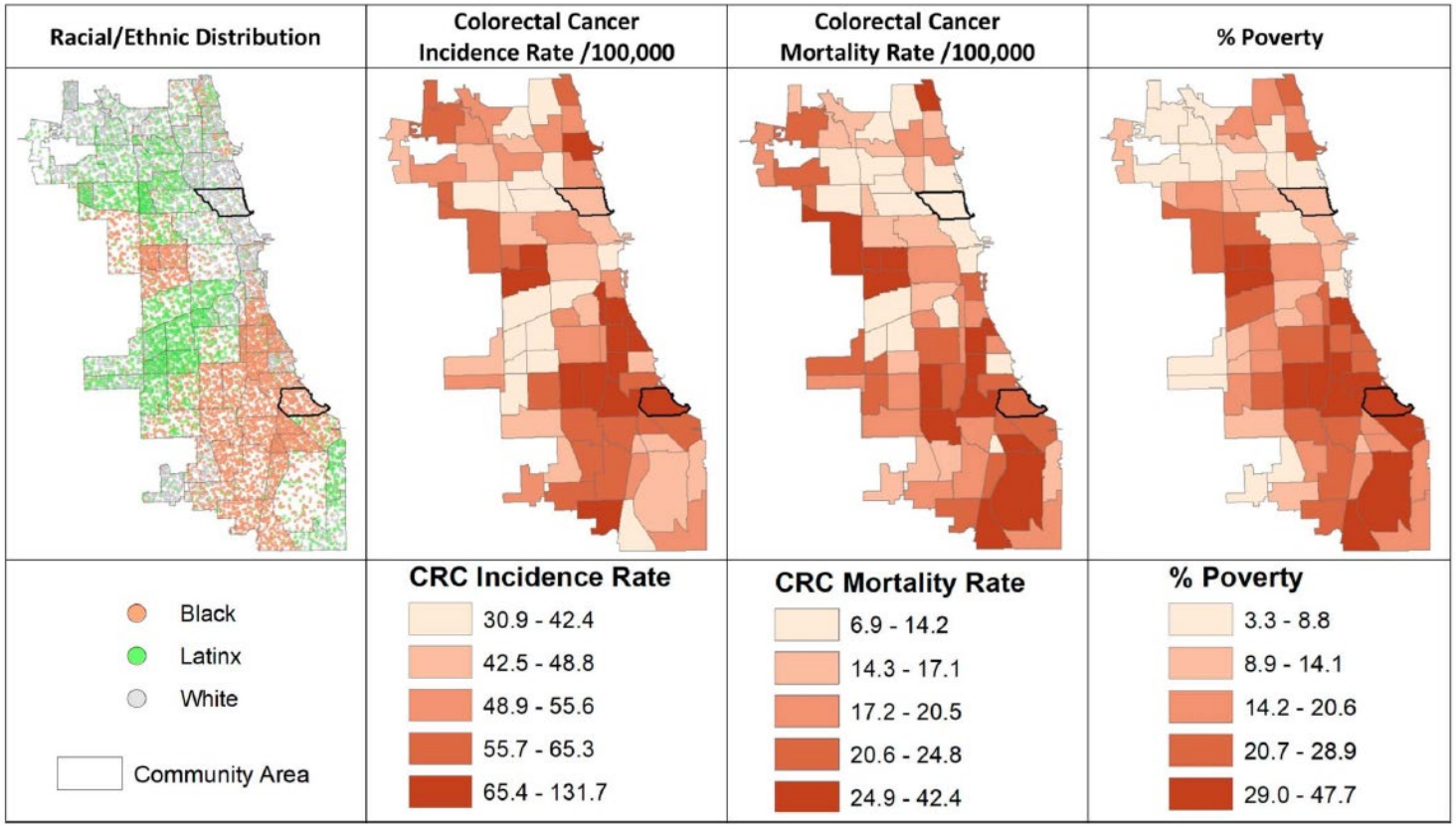
Gut microbiome is strongly influenced by diet and is a risk factor for CRC





Sender R et al. (2016) *PLoS Biol*
Burkhardt Flemer et al. (2015) *Gut*

Economic and structural inequalities are barriers to dietary quality

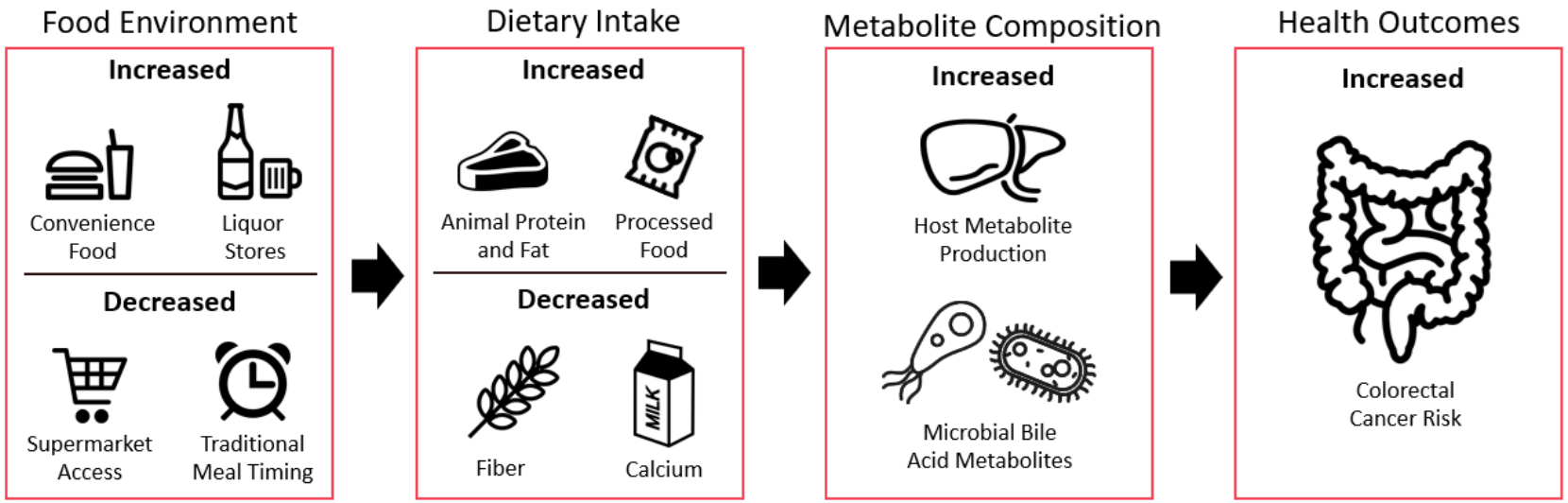


Wolf, Kim, and Tussing-Humphreys (2023) *American Journal of Gastroenterology*

Economic and structural inequalities are barriers to dietary quality

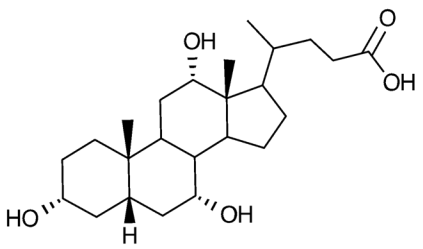
 **Travel further to the nearest supermarket**	Zenk SN et al. (2005) *Am J Public Health* Li W et al. (2017) *J Nutr Health Aging*
 **Small food outlets with fewer healthier food items**	Zenk SN et al. (2014) *Am J Public Health* Singleton CR et al. (2021) *Public Health Nutr*
 **↓ quality of whole foods and ↑ microbial load**	Jackson KA et al. (2011) *J Food Prot* Zenk SN et al. (2006) *Ethn Dis*
 **Saturation of fast-food restaurants and liquor stores**	Morland K et al. (2002) *Am J Prev Med* Block JP et al. (2004) *Am J Prev Med*
 **Predatory marketing of convenience foods and beverages**	Hilmers A et al. (2012) *Am J Public Health*

Inequitable food environment and cancer disparities

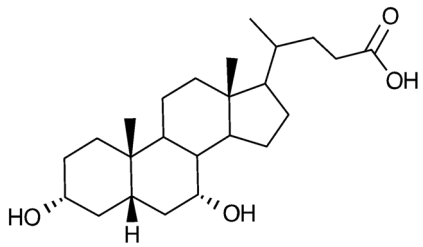


Wolf et al. (2021) *mSystems*

Bile acids at the nexus of diet, microbes, and CRC risk



Cholic acid



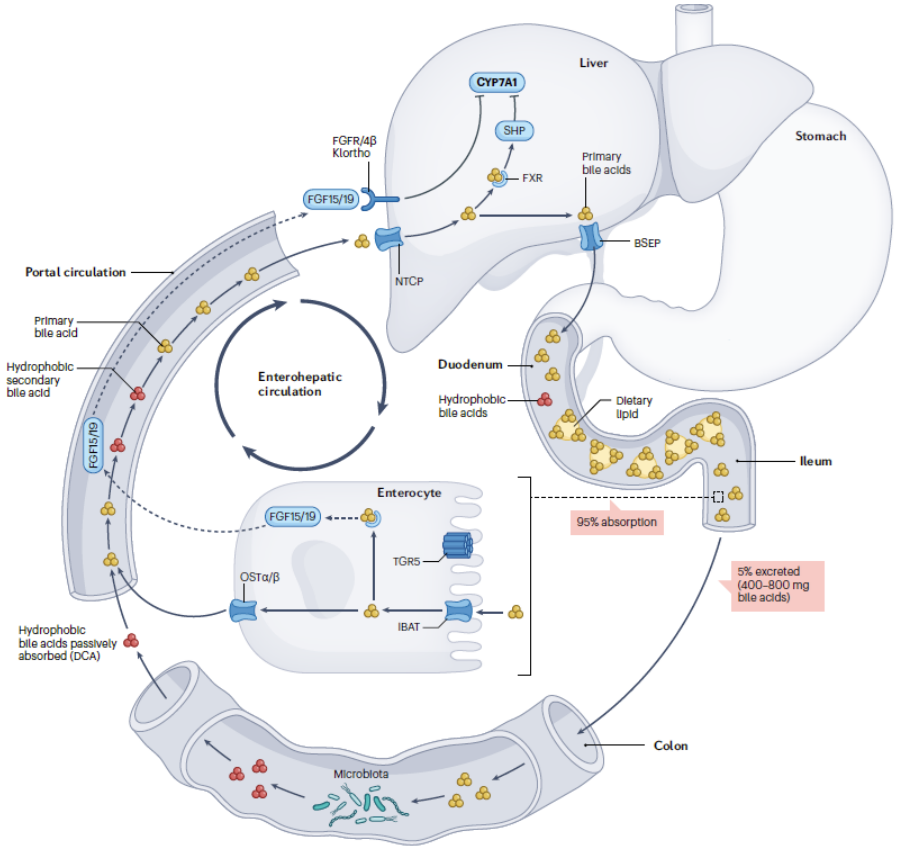
Chenodeoxycholic acid

Emulsify dietary fats

Aids absorption of lipids, cholesterol, and fat-soluble vitamins

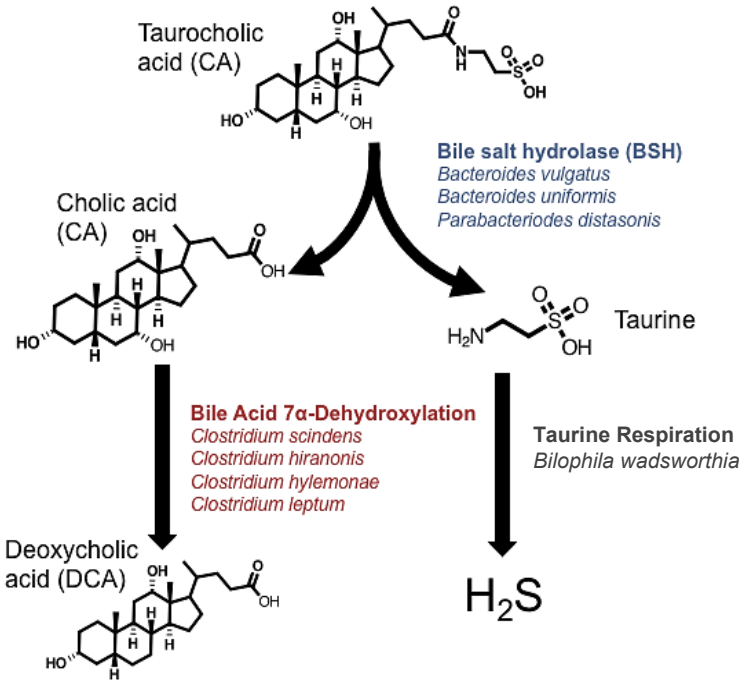
Ligands for immune and cell signaling pathways

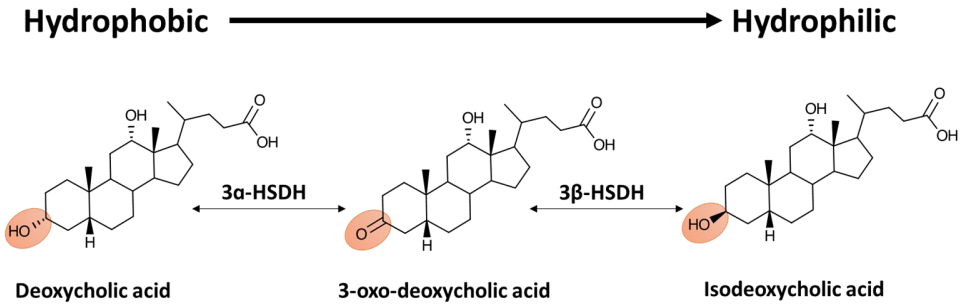
Approximately 5% of bile acids escape reabsorption



Ridlon JM and Gaskins HR (2024) *Nat Rev Gastroenterol Hepato*

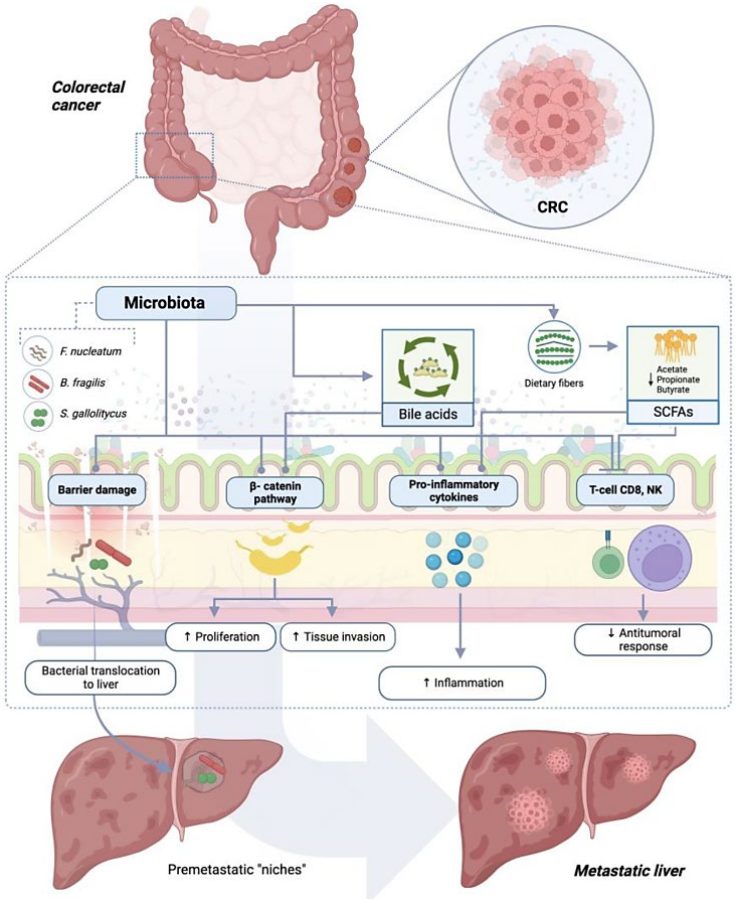
Receptor affinity and cytotoxicity of bile acids impacted by microbial metabolism





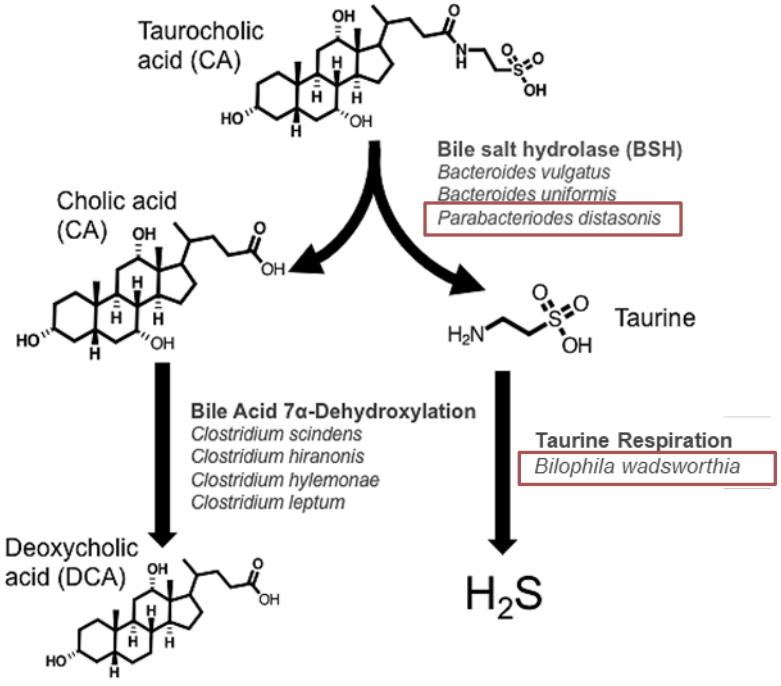
Ridlon JM et al. (2020) *Gut Microbes*

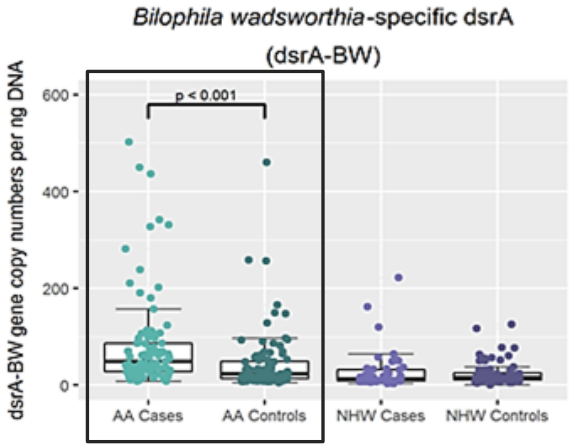
Accumulation of hydrophobic bile acids promotes CRC

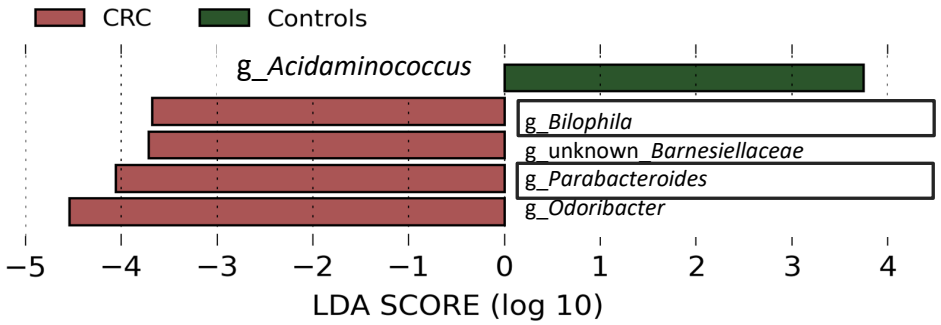


Mingnini I et al. (2024) *J Clin Med*

Bacteria that produce hydrophobic bile acids associated with CRC

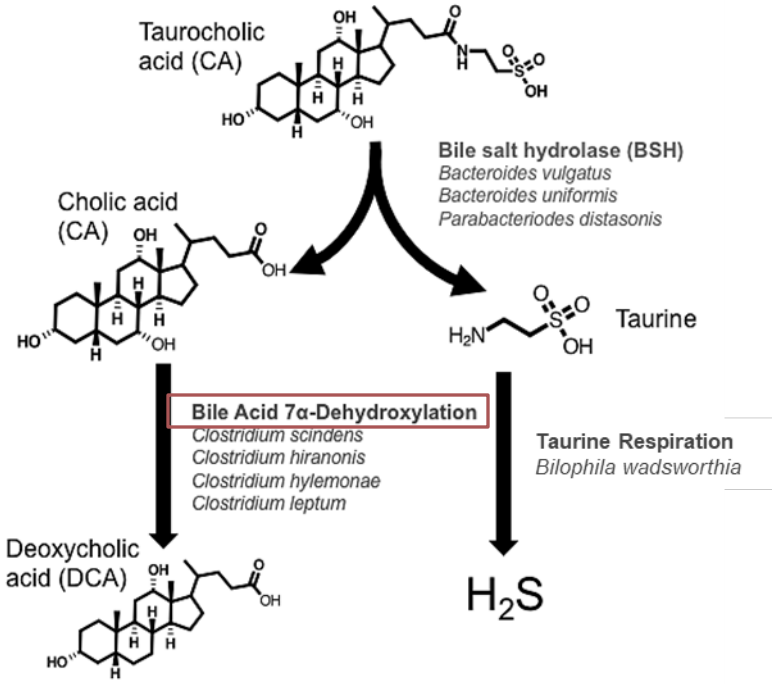


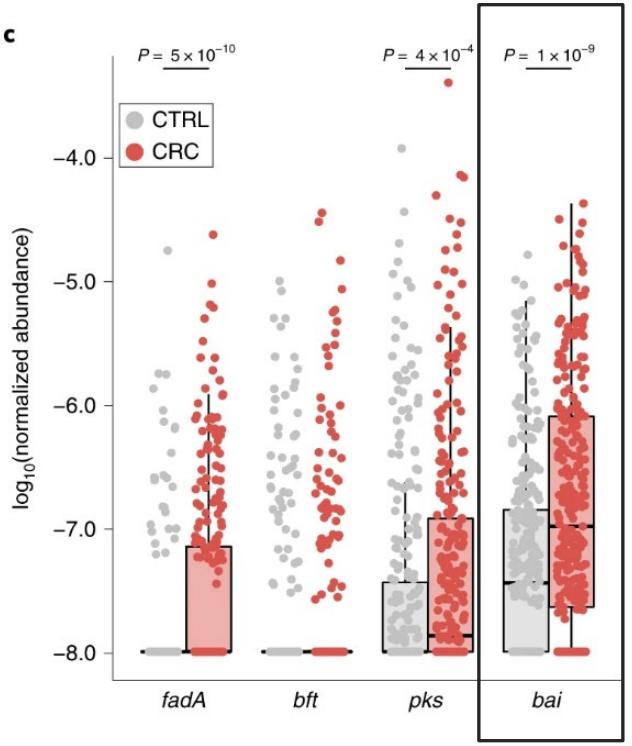




Yazici and Wolf et al. (2017) *Gut*

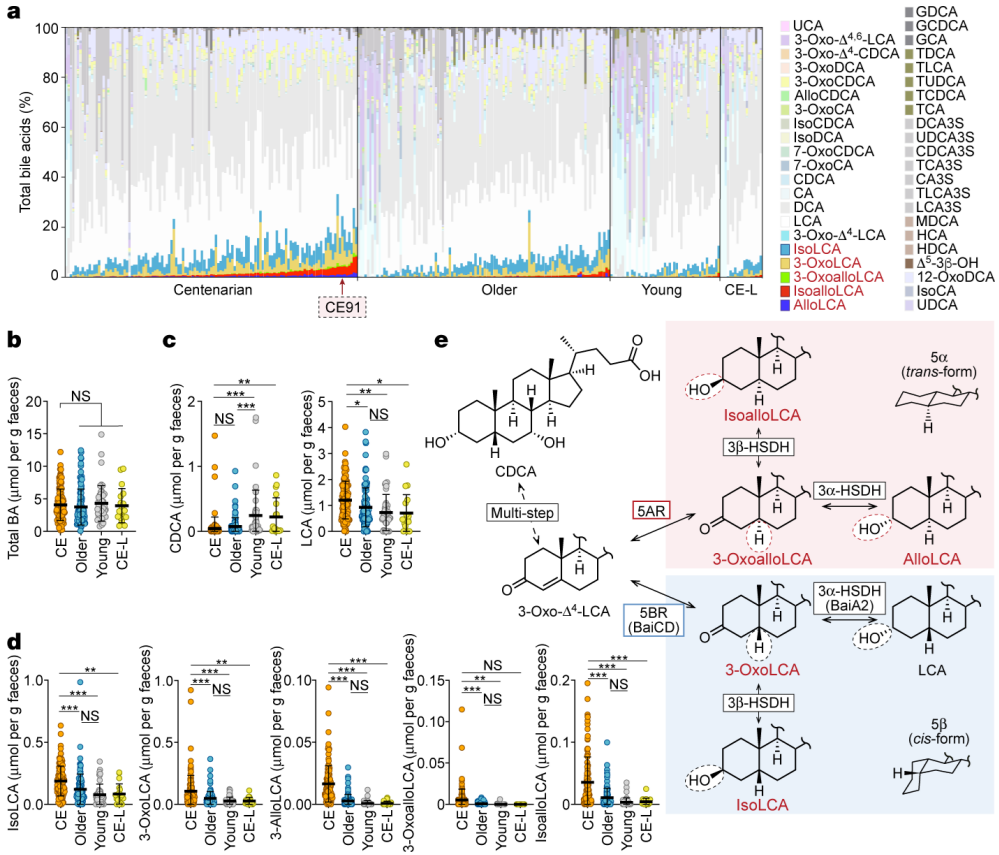
Bacteria that produce hydrophobic bile acids associated with CRC





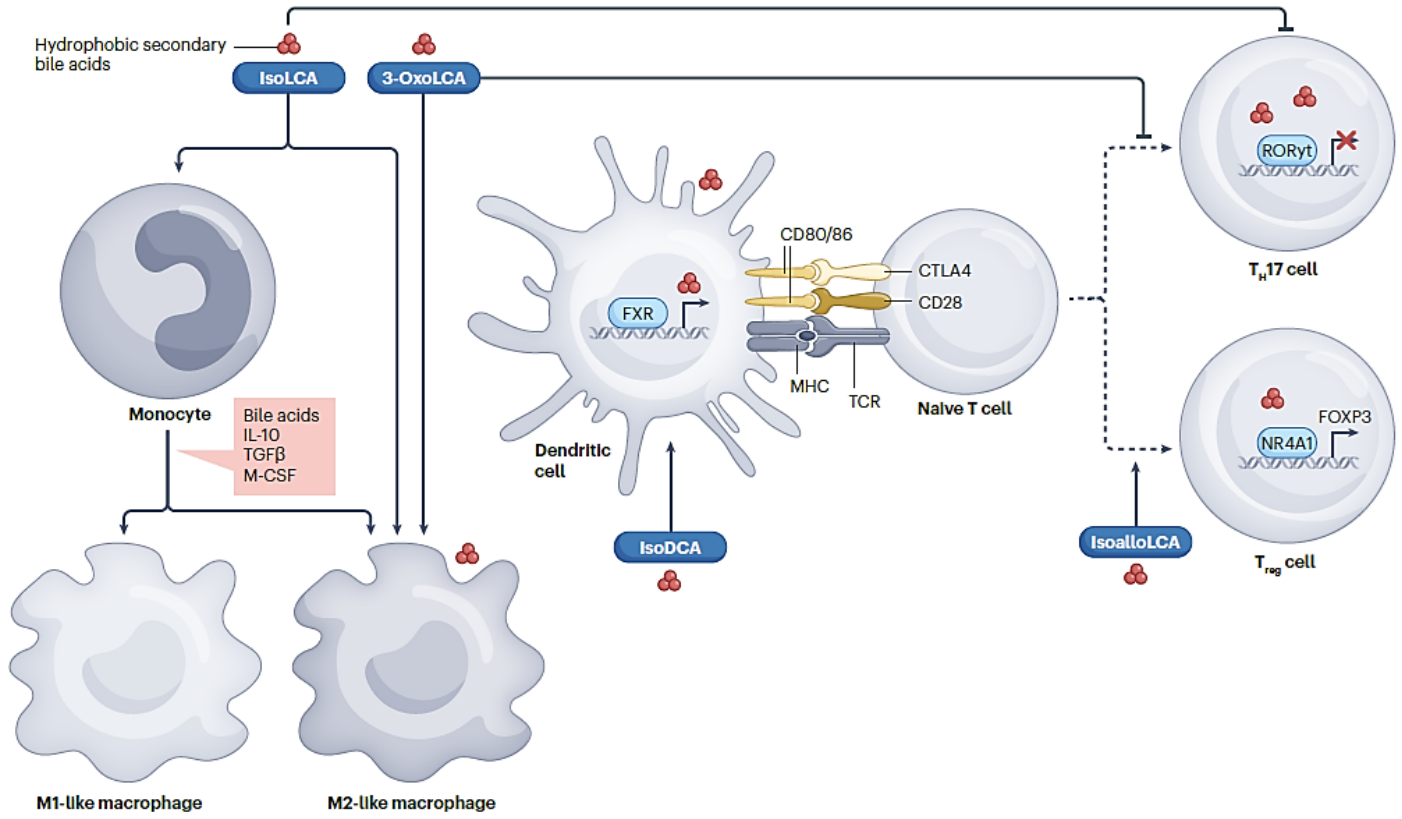
Wirbel J and Pyl PT et al. (2019) *Nature Medicine*

Hydrophilic bile acids are enriched in centenarians



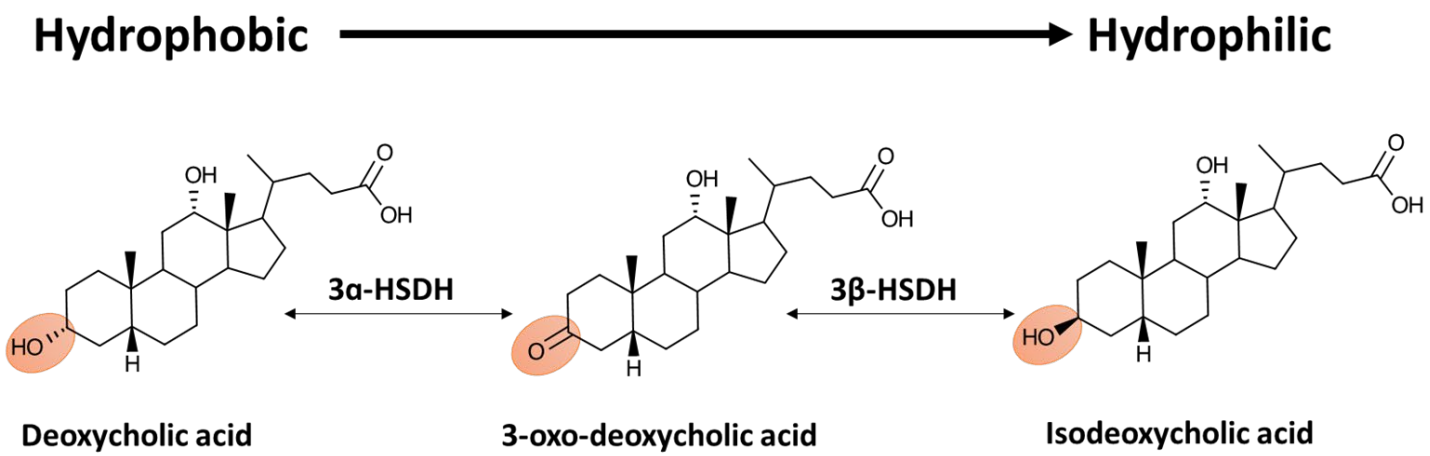
Sato Y, *et al.* (2021) *Nature*

Anti-inflammatory impact of hydrophilic bile acids may promote colonic health



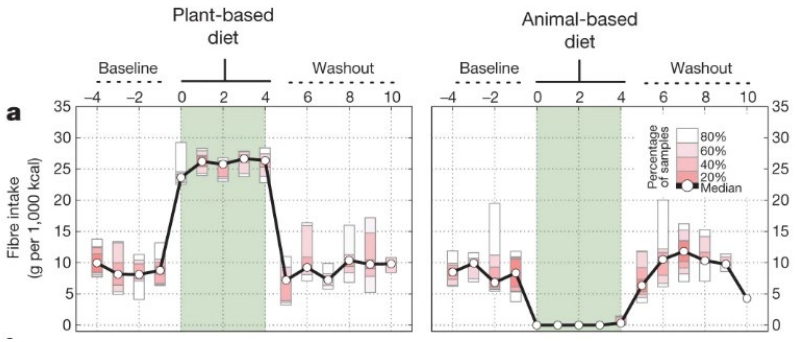
Ridlon JM and Gaskins HR (2024) *Nat Rev Gastroenterol Hepato*

What role does diet play?



Dietary Patterns?

Plant vs. Animal Based Diet

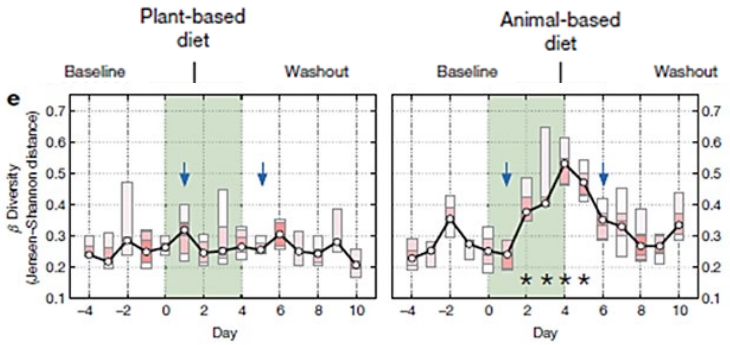


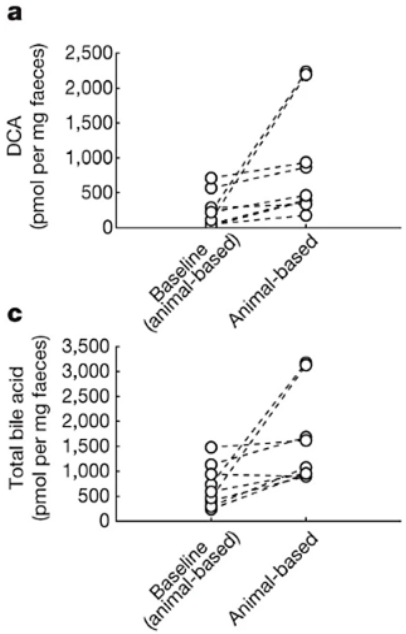
Diet	Meal	Food item
Plant-based diet	Breakfast	Granola cereal
	Lunch	Jasmine rice
		Fresh onions
		Fresh tomato
		Fresh butternut squash
		Fresh garlic
		Frozen peas
		Steamed lentils
		Chili powder
		Cumin
		Coriander seed
		Vegetable oil
		Salt
	Dinner	Jasmine rice
		Fresh cauliflower
		Fresh carrots
		Fresh onions
		Fresh green chile
		Fresh garlic
		Steamed lentils
		Frozen spinach
		Fresh tomato
		Vegetable oil
		Mustard oil
		Chili powder
		Cumin
		Coriander seed
	Snacks	Fresh banana
		Fresh mangoes
		Fresh papayas
		Banana chips

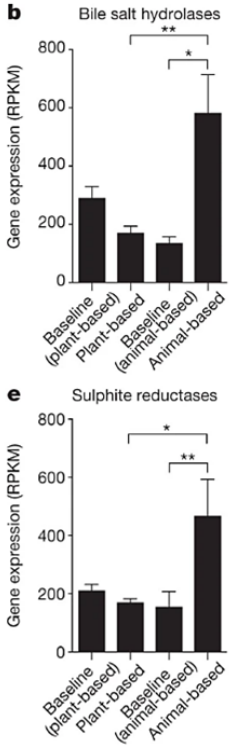
Diet	Meal	Food item
Animal-based diet	Breakfast	Cooked bacon
		Scrambled eggs
		Brewed coffee
		Half & half cream
	Lunch	Pork spare ribs
		Beef brisket
	Dinner meats	Salami
		Prosciutto
	Dinner cheeses	Blue
		Cheddar
		Caerphilly
		Camembert
	Snacks	Salami
		Mozarella string cheese
		Pork rinds

David L, *et al.* (2014) *Nature*

Hydrophobic bile acids linked with animal based diet







David L, *et al.* (2014) *Nature*

Western diet vs. Rural South African Diet

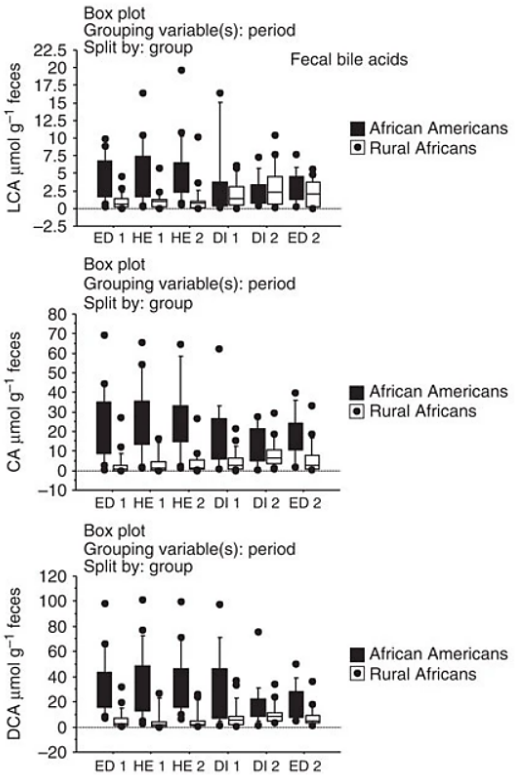
a) High Fat, Low Fibre Intervention Diet for Africans

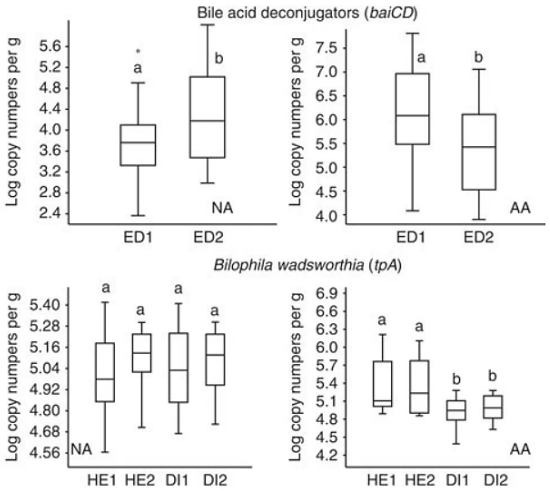
	Breakfast	Lunch	Dinner
Day 1	Beef Sausage Links Pancakes	Hamburger French Fries	Meatloaf Rice
Day 2	Beef Kielbasa Grits	Meatballs Spaghetti	Salisbury Steak Noodles
Day 3	Breakfast Steak Hash Browns	Chili w Meat Rice	Roast Beef Mashed Potatoes & Gravy
Day 4	Corned Beef Hash Potatoes	Beef Hotdog Baked Beans	T-Bone Steak Macaroni & Cheese
Day 5	Beef Bacon Rice Krispies	Beef Stew Potatoes	Fried Liver & Onions Rice
Day 6	Beef Sausage Patty Biscuits	Stuffed Bell Peppers Rice	Beef BBQ Ribs Steak Fries

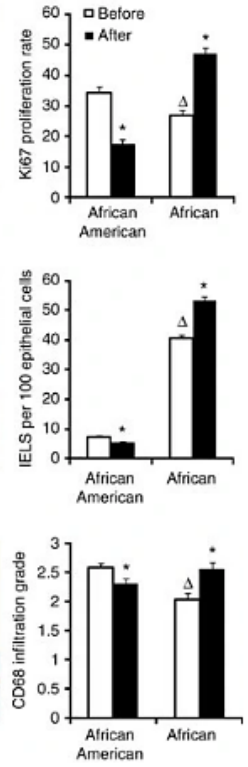
b). High Fibre, Low Fat Diet for African Americans

	Breakfast	Lunch	Dinner
Day 1	Hi-Maize Corn Fritters	Hi-Maize Corn Dogs w Veggie Dog	Okra/Tomatoes/Hi-Maize Meal
	Salmon Croquettes w Hi-Maize RS	Homemade Tater Tots	Hi-Maize RS Corn Muffins Black-eye Peas
	Spinach/Red Pepper & Onions	Mango slices	Pineapple Black Tea
Day 2	Buttermilk Corn Biscuits	Catfish Nuggets breaded with	Lentils
	Banana	Hi-Maize RS	Rice
	Hi-Maize RS Cheese Grits	Hi-Maize Hushpuppies	Hi-Maize Cornbread
	Scrambled Egg Substitute	Kale Salad w Hi-Maize Croutons	African Potato Salad Guava Juice
Day 3	ProNutro Cereal	Navy bean soup	Fish Taco (Tilapia)

Hydrophobic bile acids linked with western diet

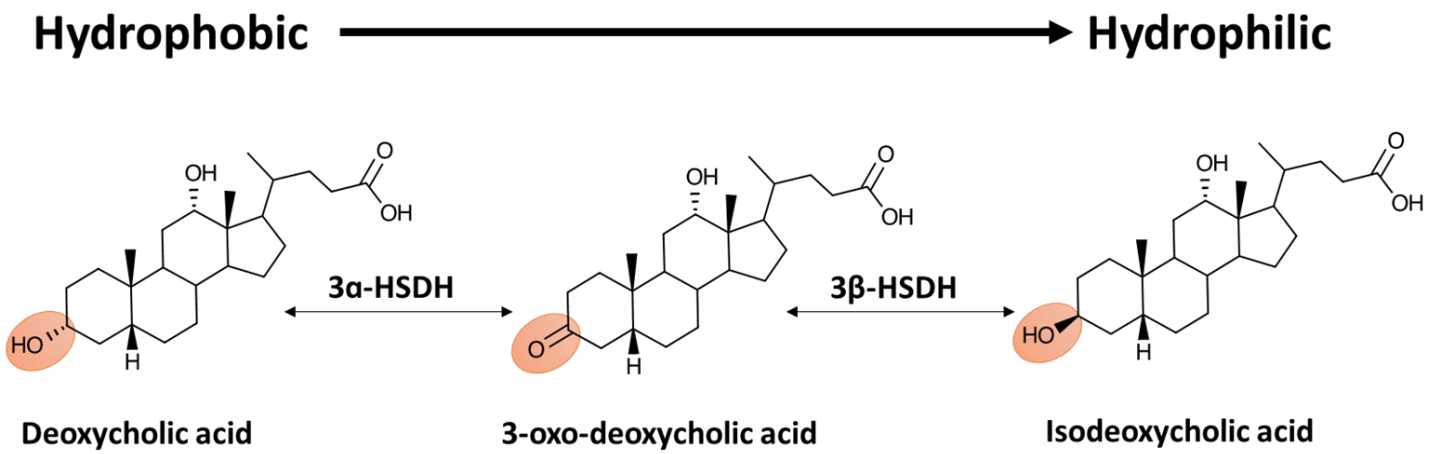






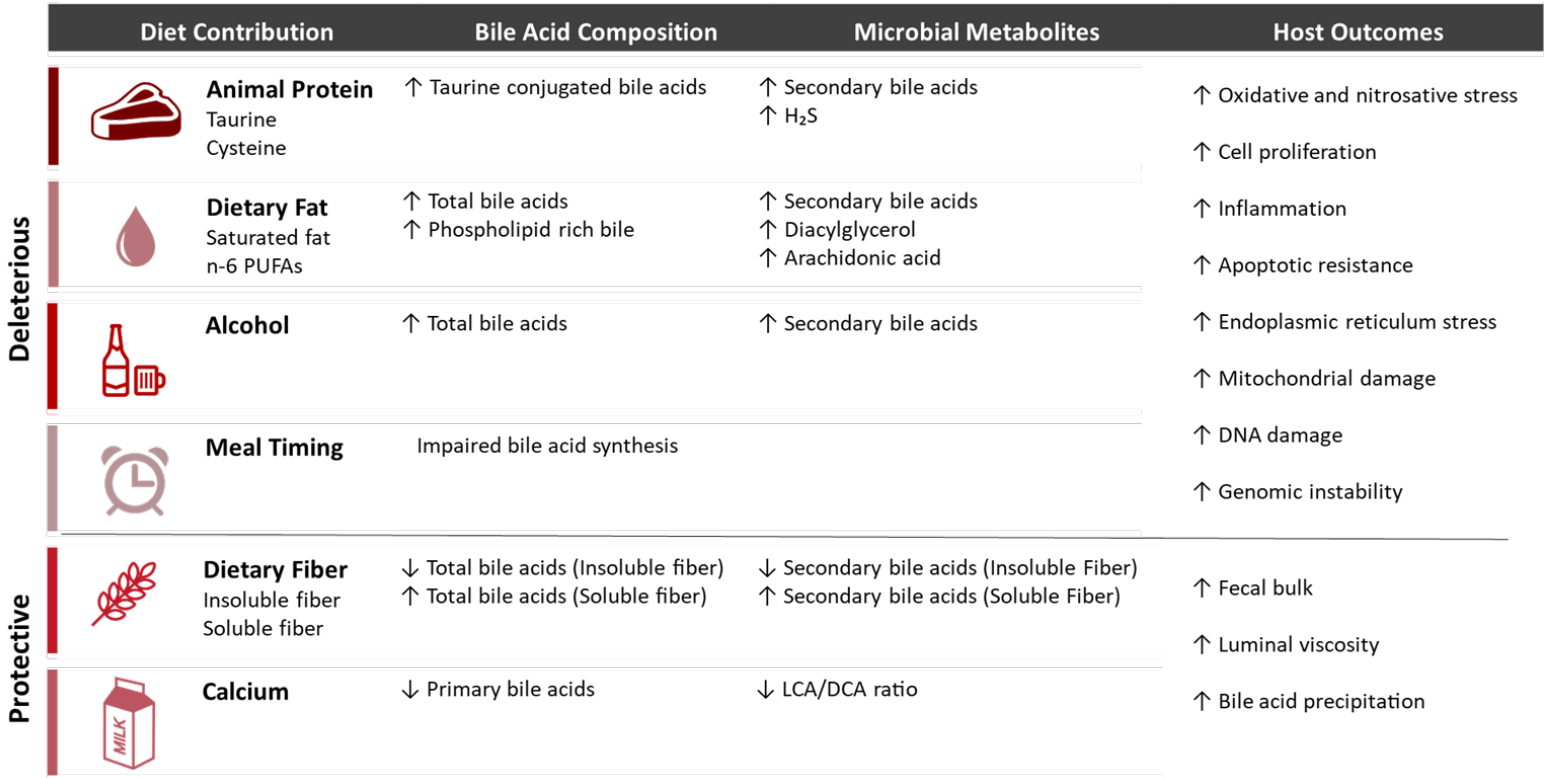
O'Keefe S, *et al.* (2015) *Nature Communications*

Impact of dietary pattern on hydrophilic bile acid production unknown



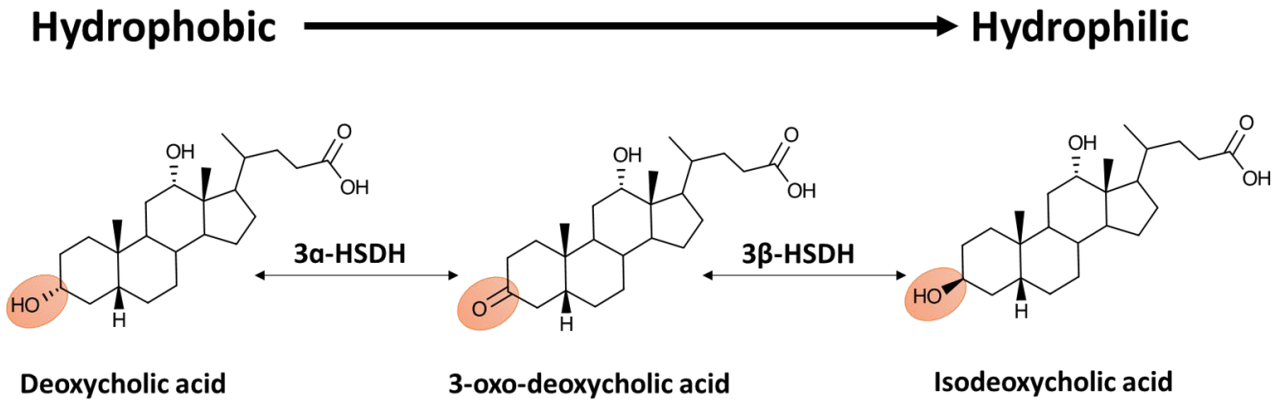
Individual nutrients?

Work done mostly in rodent studies

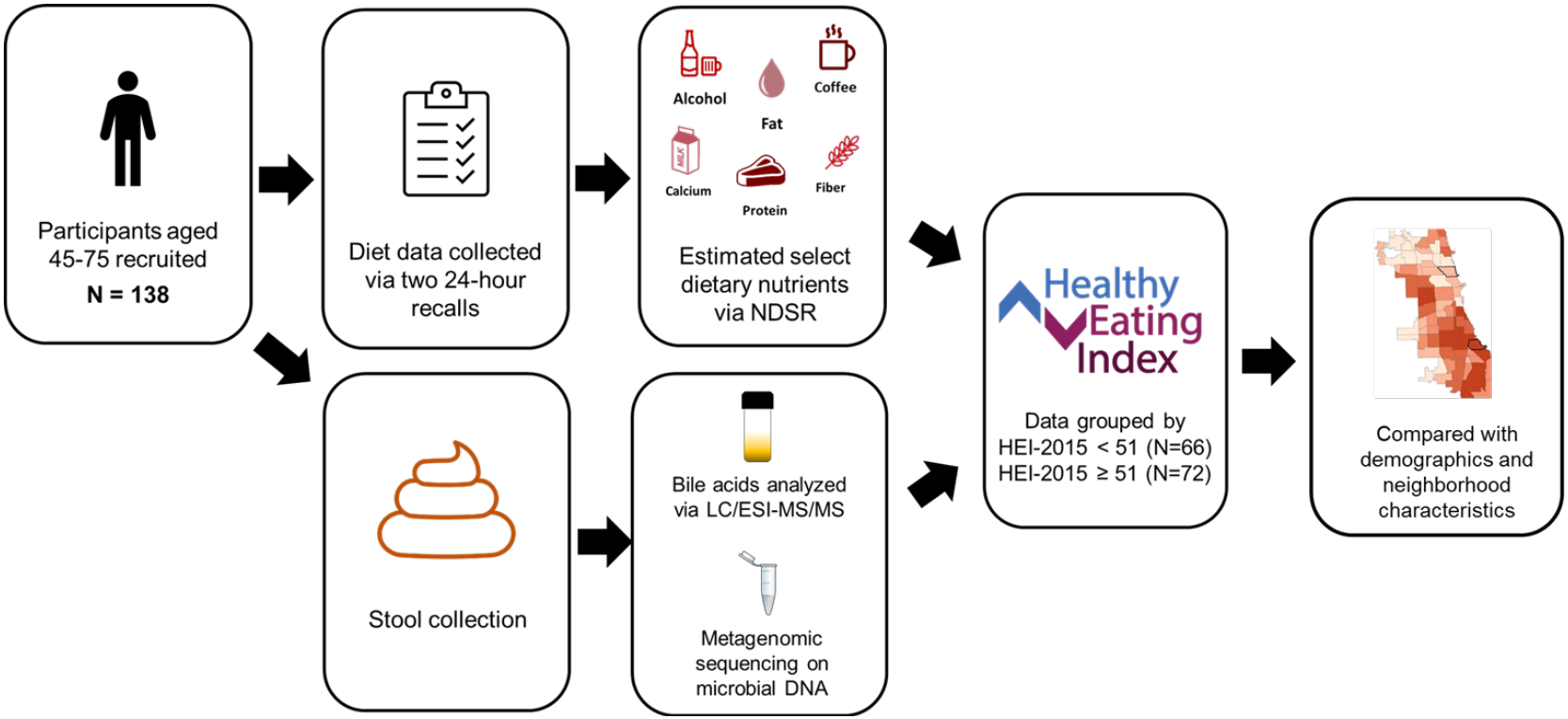


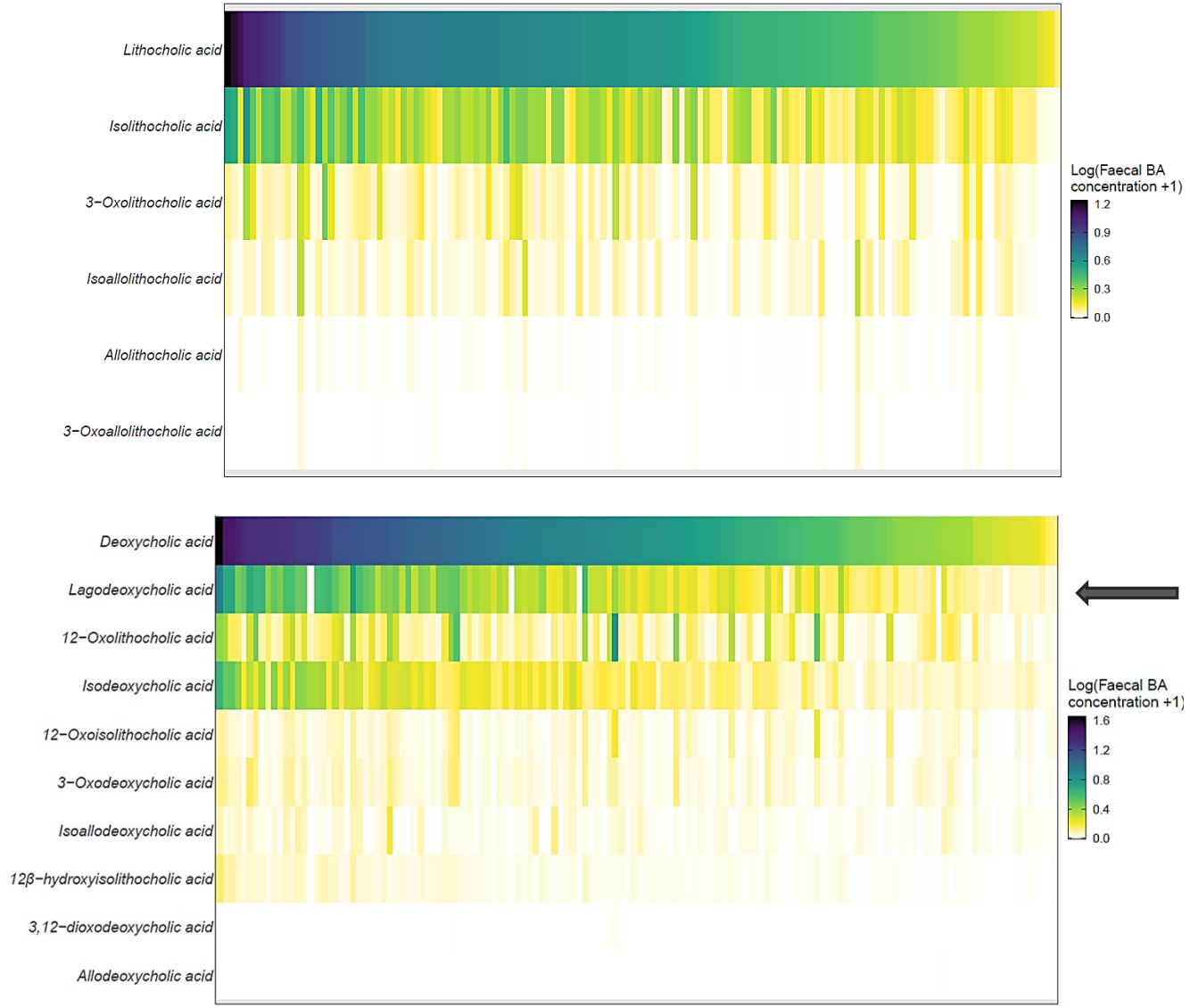
Wolf et al. (2021) *mSystems*

Effect of individual nutrients on bile acid composition is not well known



Data collection and methods



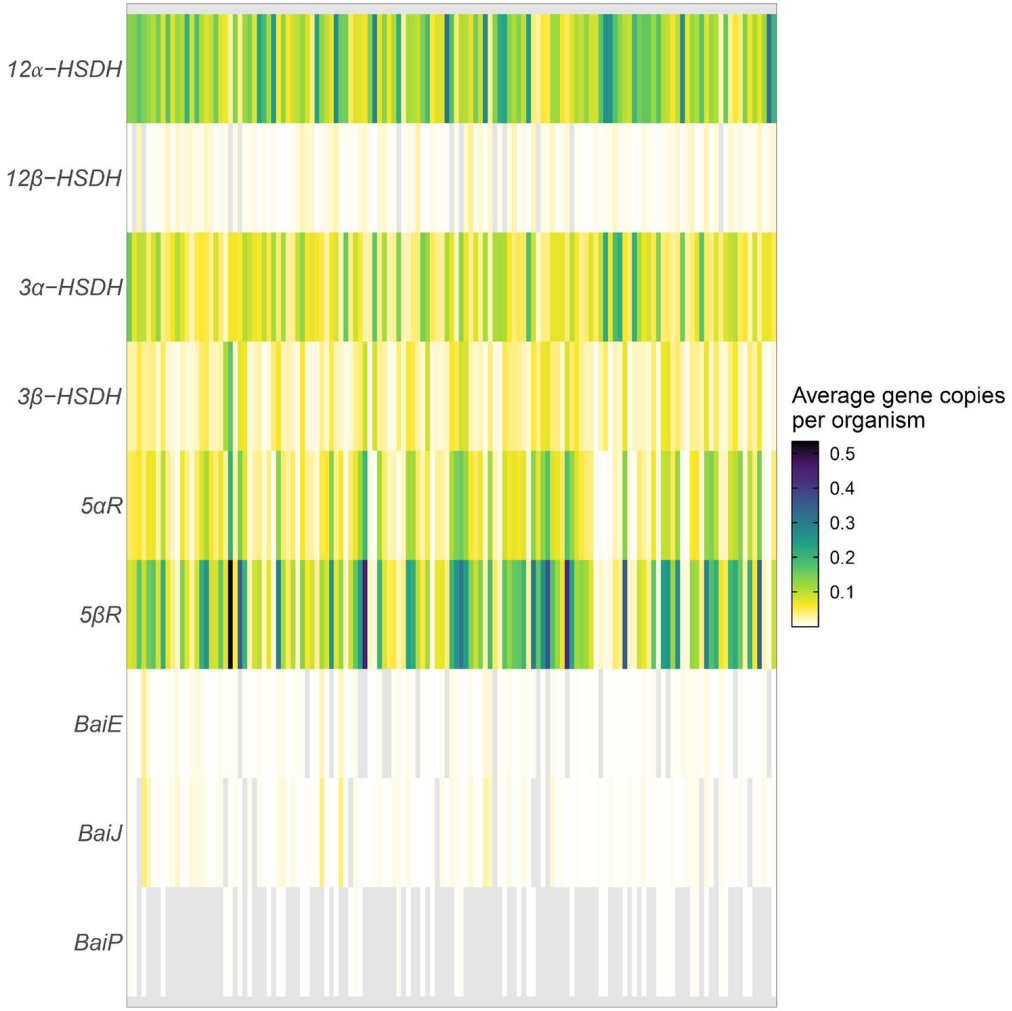


Most abundant derivative

Three most abundant forms constitute 14% of the fecal bile acid pool

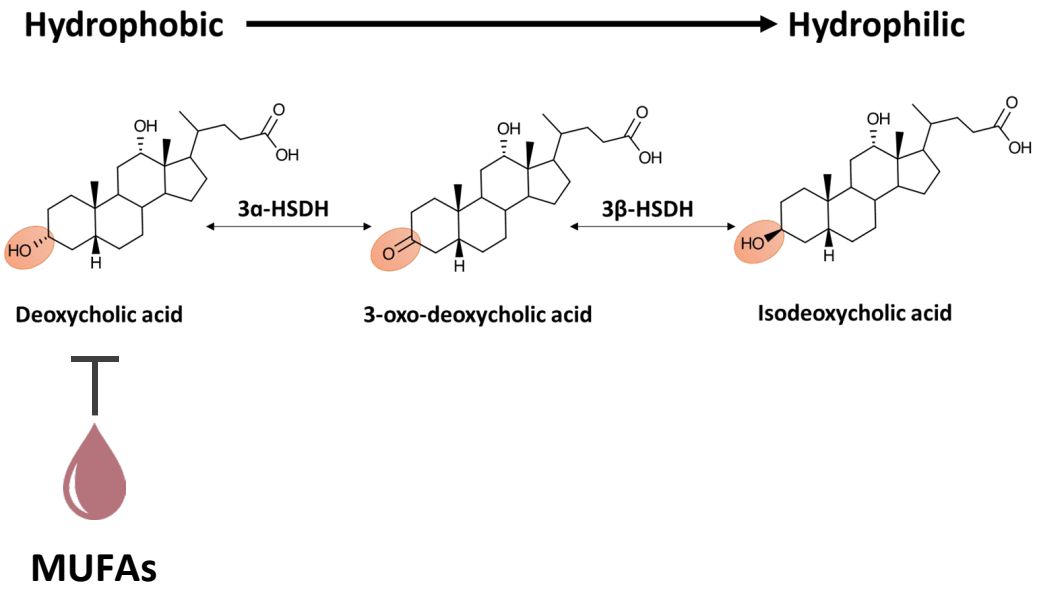
Wolf et al. (2025) *J Nutr*

Microbial genes for the formation of hydrophilic bile acids were highly abundant



Wolf et al. (2025) *J Nutr*

Effect of diet on secondary bile acid metabolites



In practice:

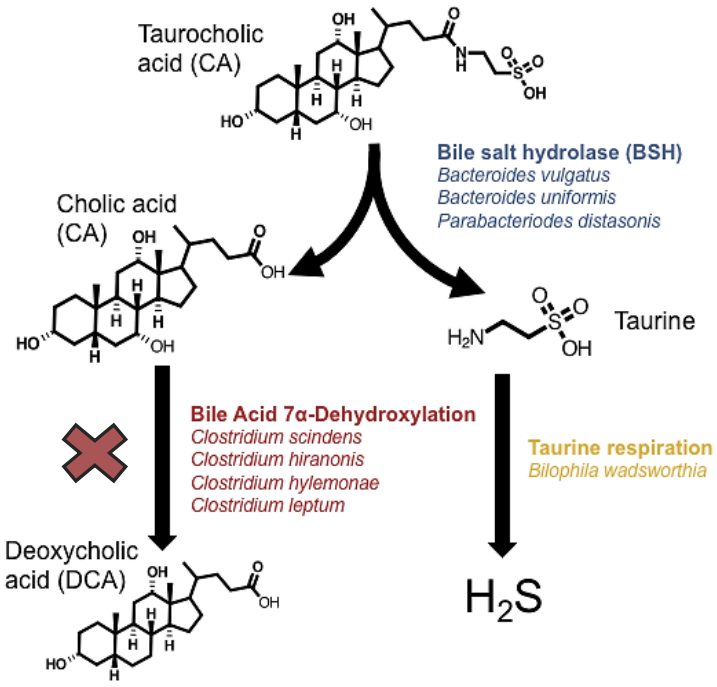
Dietary Fats in Relation to Total and Cause-Specific Mortality in a Prospective Cohort of 521 120 Individuals With 16 Years of Follow-Up

Pan Zhuang, Yu Zhang, Wei He, Xiaoqian Chen, Jingnan Chen, Lilin He, Lei Mao, Fei Wu, and Jingjing Jiao | AUTHOR INFO & AFFILIATIONS

Circulation Research • Volume 124, Number 5 • https://doi.org/10.1161/CIRCRESAHA.118.314038

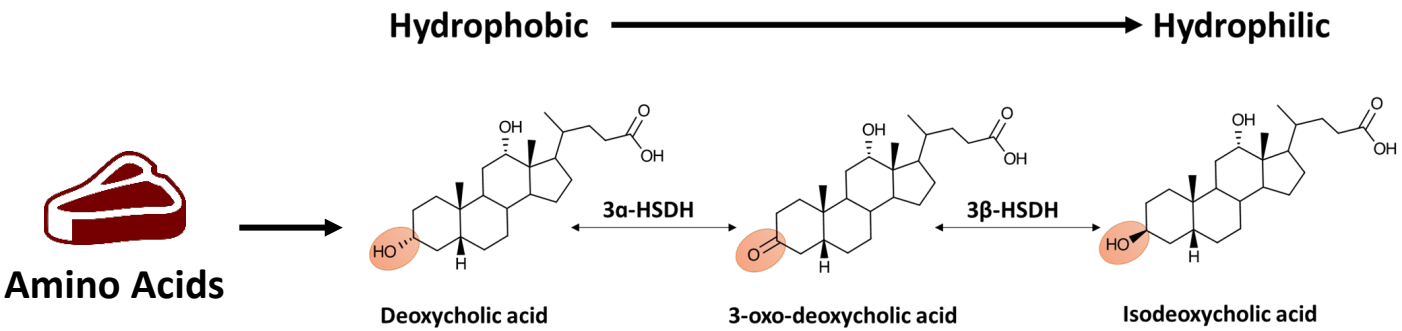
Replacing 5% of the energy from SFAs with plant MUFAs was associated with 11% lower CRC mortality

Olive oil may inhibit bacterial growth

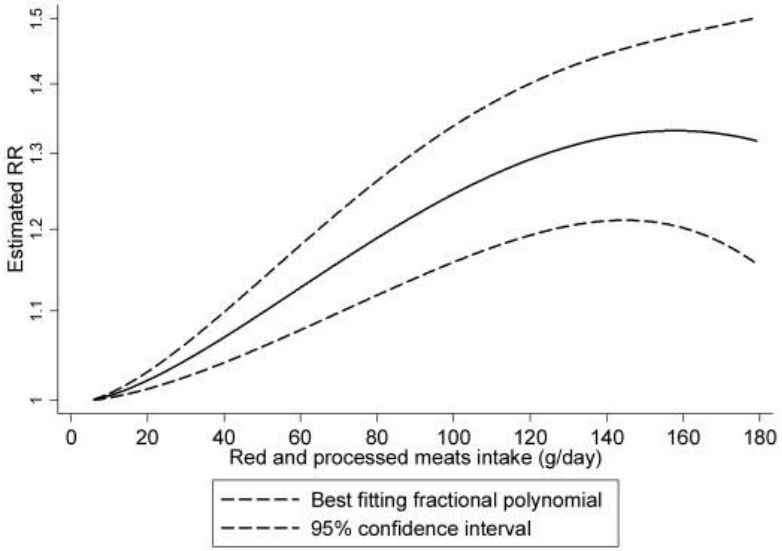


microorganism[b]	control	Picual virgin olive oil (VOOP2)	Arbequina virgin olive oil (VOOA2)	olive oil (OO2)
L. acidophilus	<0.01	>4.59	>4.59	>4.59
L. monocytogenes	0.13 (0.03)[c]	>4.82	>4.82	>4.82
S. mutans	0.24 (0.07)	>4.79	>4.79	>4.79
B. bifidum	0.71 (0.07)	>4.95	>4.95	>4.95
E. faecium	0.07 (0.02)	>4.84	>4.84	>4.84
E. faecalis	<0.01	>4.94	>4.94	>4.94
S. aureus	<0.01	>4.60	>4.60	>4.60
C. perfringens	0.36 (0.01)	>5.38	>5.38	>5.38
S. sonnei	0.07 (0.05)	2.43 (0.13)	3.47 (0.75)	1.79 (0.01)
Bacteroides sp.	<0.01	>5.11	>5.11	>5.11
Yersinia sp.	0.09 (0.01)	>4.58	>4.58	>4.58
E. coli	<0.01	1.76 (0.01)	1.22 (0.01)	0.72 (0.01)
S. enterica	0.44 (0.05)	>5.11	>5.11	2.67 (0.16)
C. albicans	<0.01	<0.01	<0.01	<0.01

Effect of diet on secondary bile acid metabolites



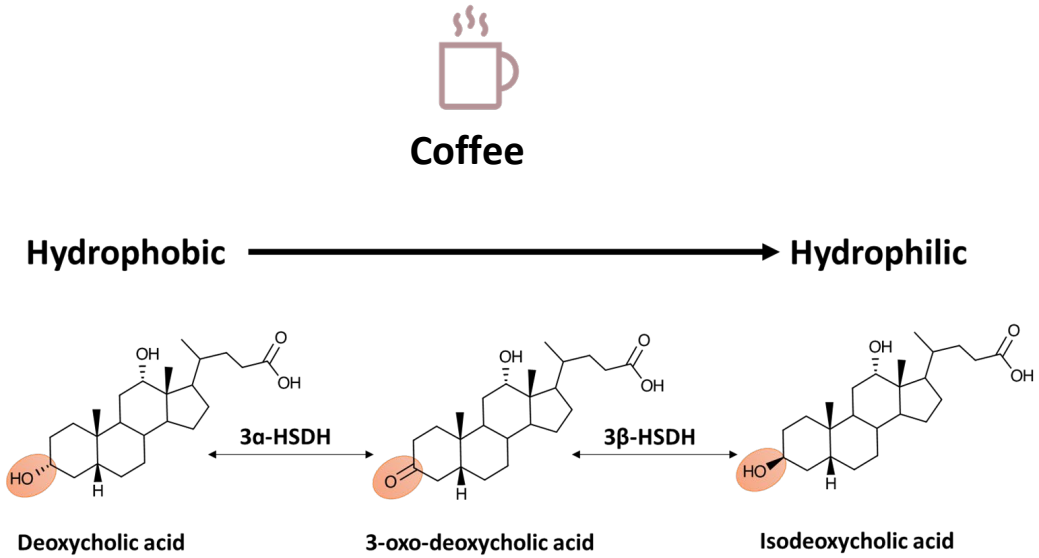
In practice:



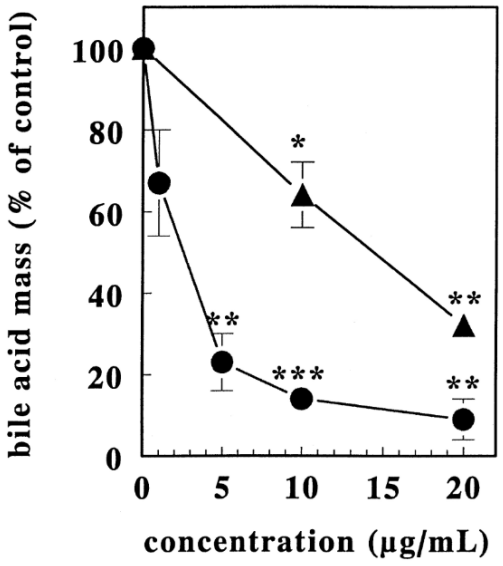
If you eat red meat, limit consumption to no more than ~3 12–18 oz portions per wk. Consume very little, if any, processed meat.

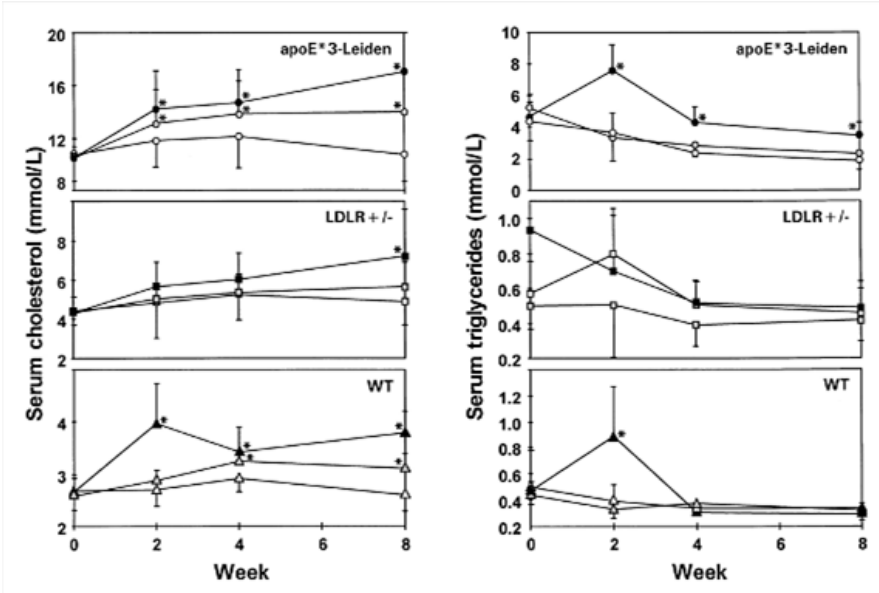
Chan et al. (2011) *Plos One*

Effect of diet on secondary bile acid metabolites



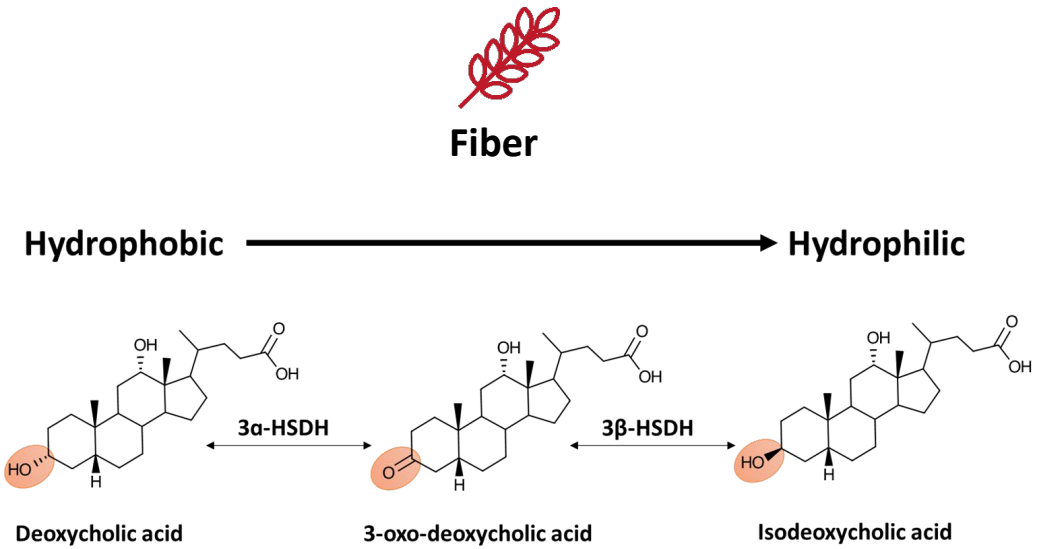
In practice:



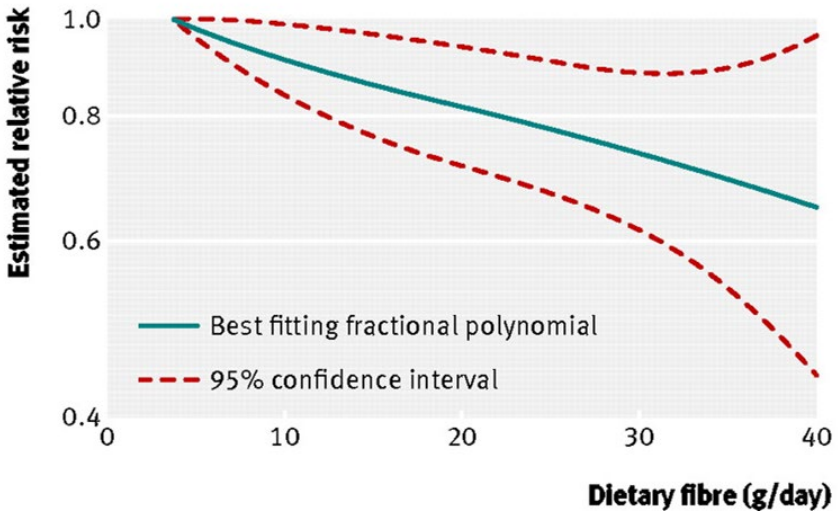


No recommendation. Associations between coffee intake and CRC are mixed. There is compelling evidence that unfiltered coffee increases serum cholesterol by inhibiting bile acid synthesis.

Effect of diet on secondary bile acid metabolites



In practice:

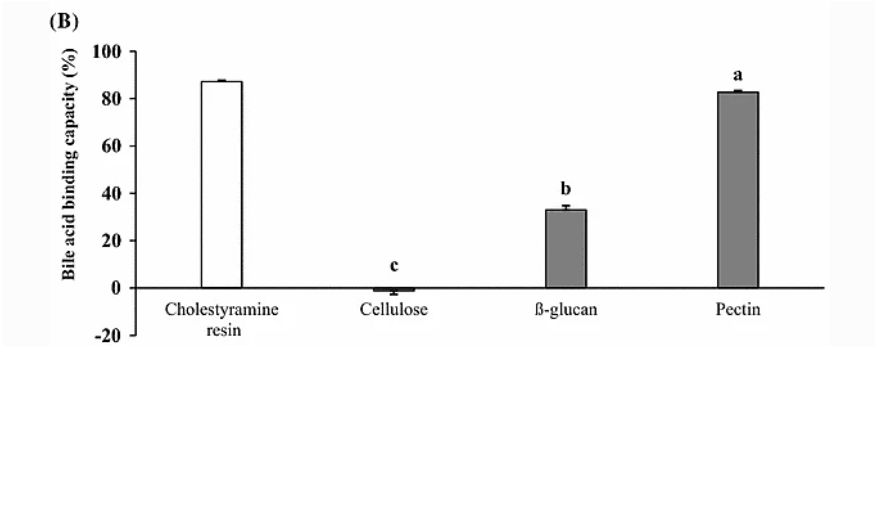


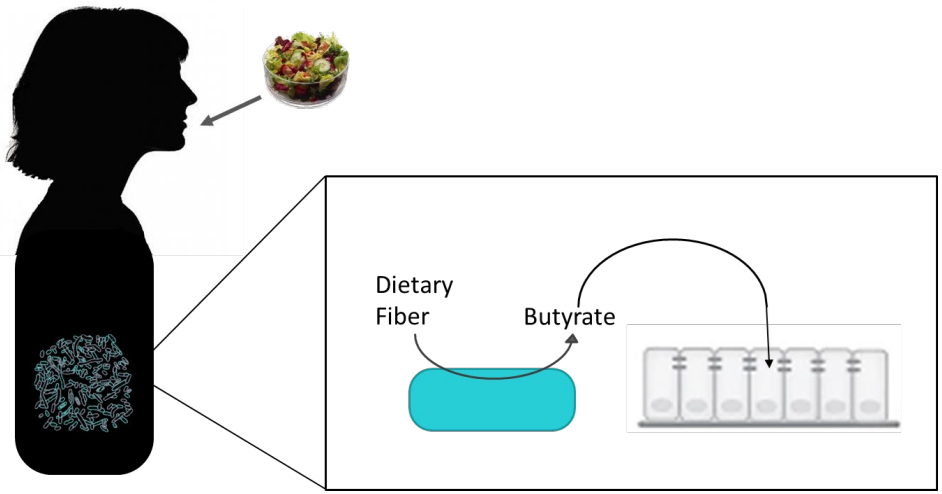
2017	DIET, NUTRITION, PHYSICAL ACTIVITY AND COLORECTAL CANCER		
		DECREASES RISK	INCREASES RISK
STRONG EVIDENCE	Convincing	Physical activity[1,2]	Processed meat[3] Alcoholic drinks[4] Body fatness[5] Adult attained height[6]
	Probable	Wholegrains Foods containing dietary fibre[7] Dairy products[8] Calcium supplements[9]	Red meat[10]

Eat a diet rich in whole grains, vegetables, fruit, and beans.

Aune et al. (2011) *BMJ*

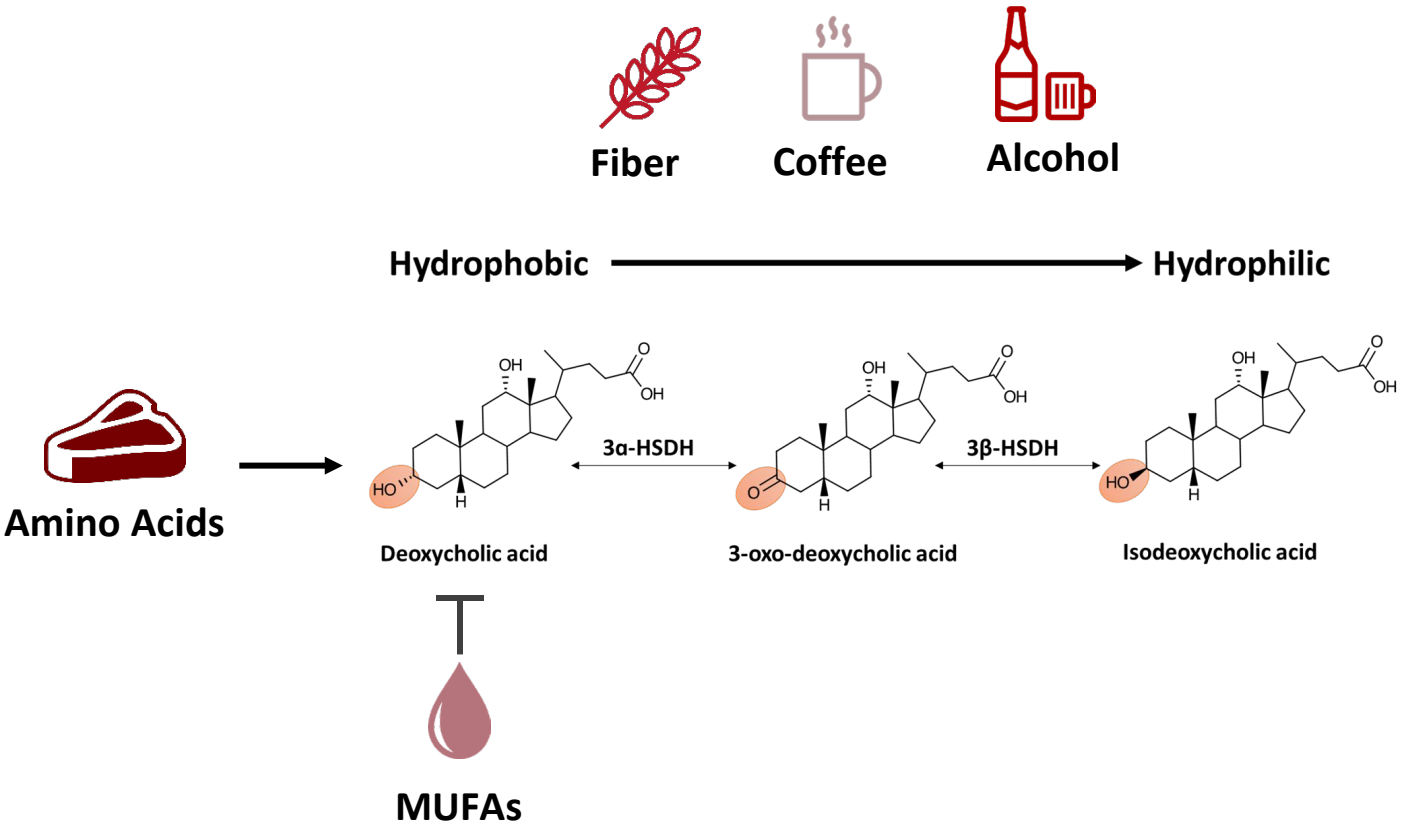
Fiber likely impacts bile acid composition through a variety of mechanisms



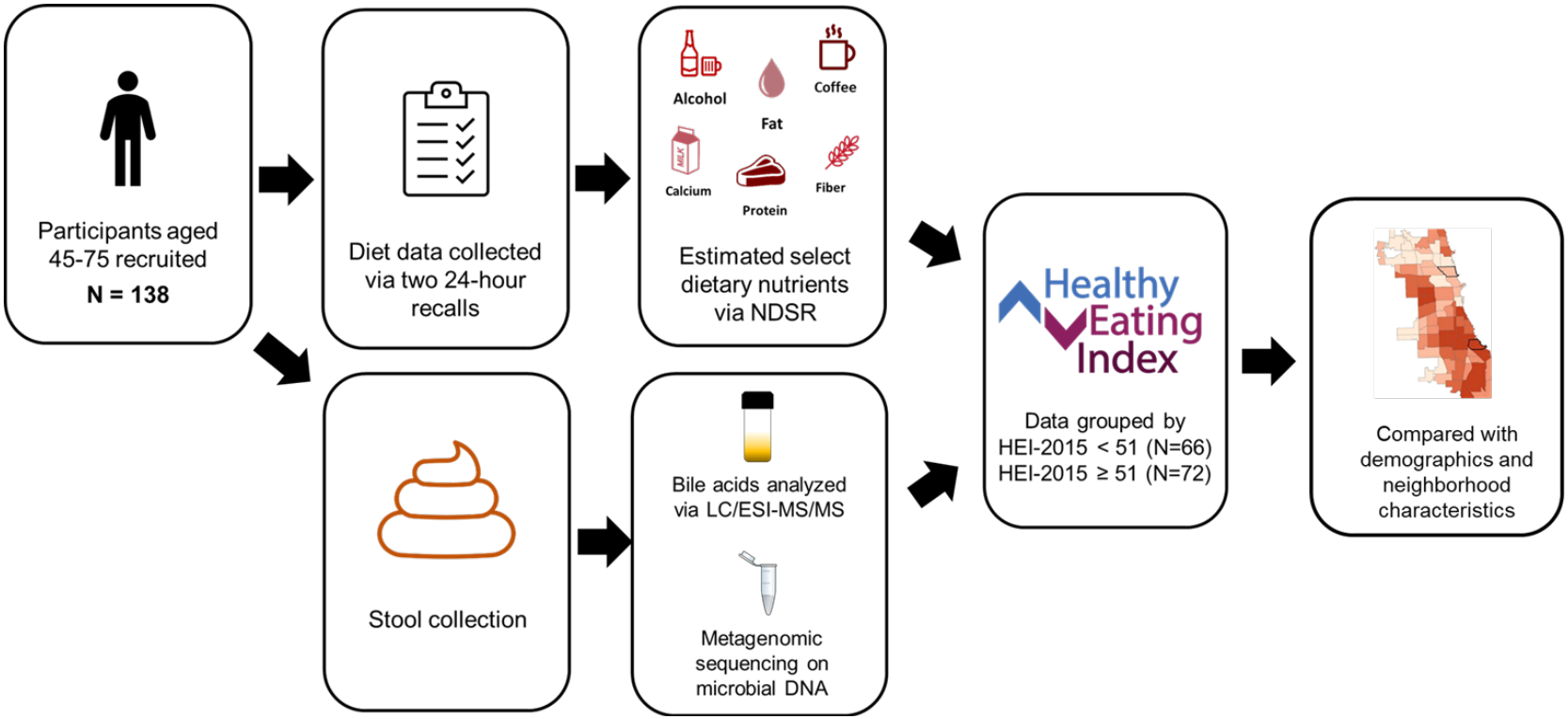


Truong NH, Lee S, & Shim SM. (2016) *Appl Biol Chem*

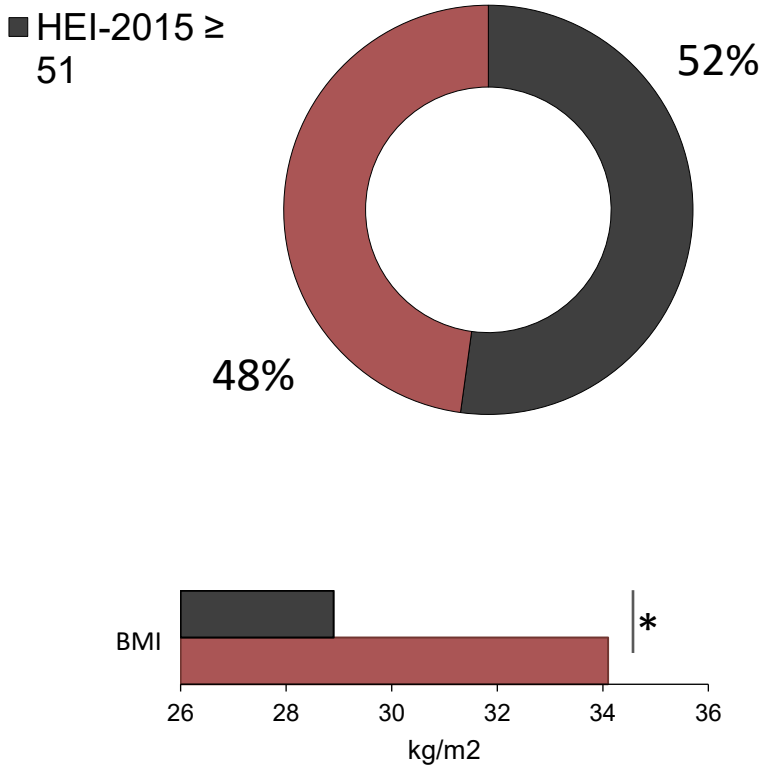
Summary: Effect of diet on secondary bile acid metabolites

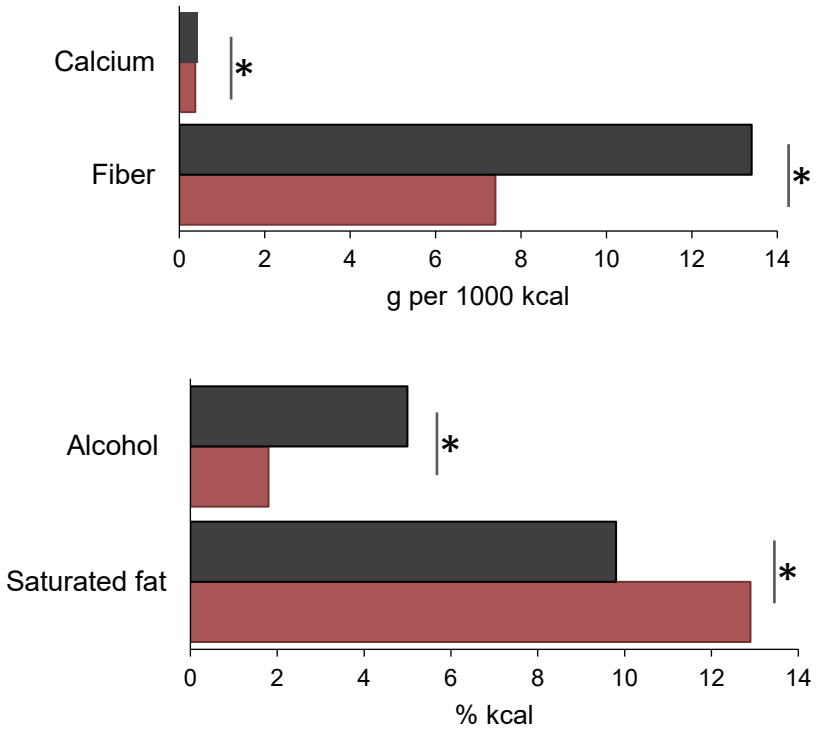


Data collection and methods

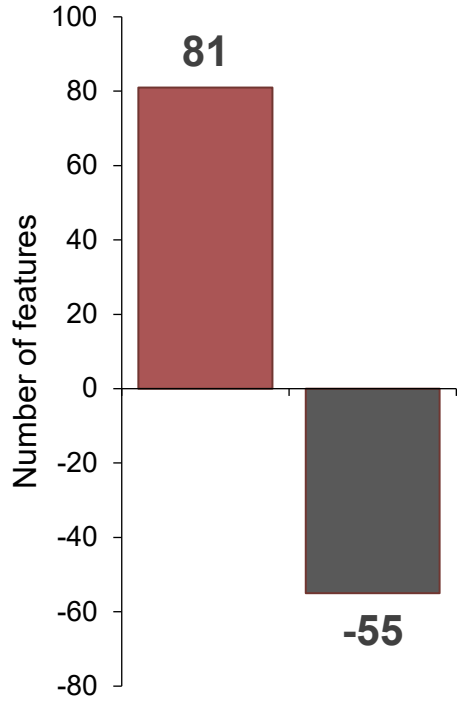


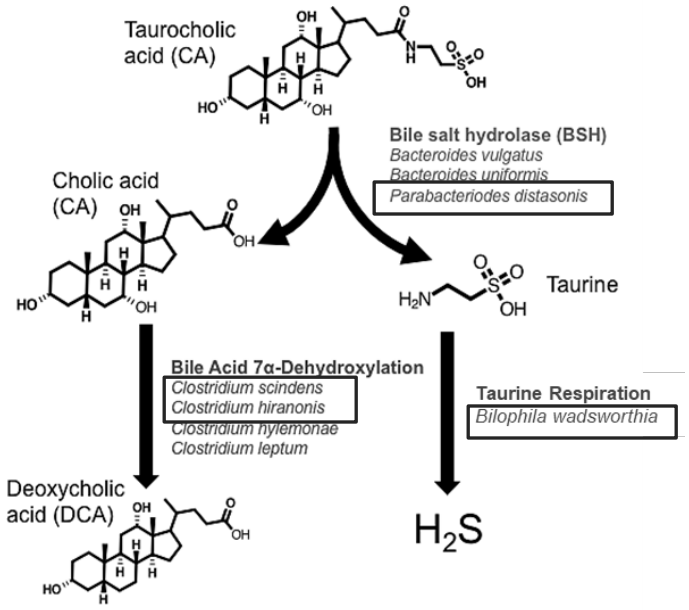
Diet characteristics and BMI



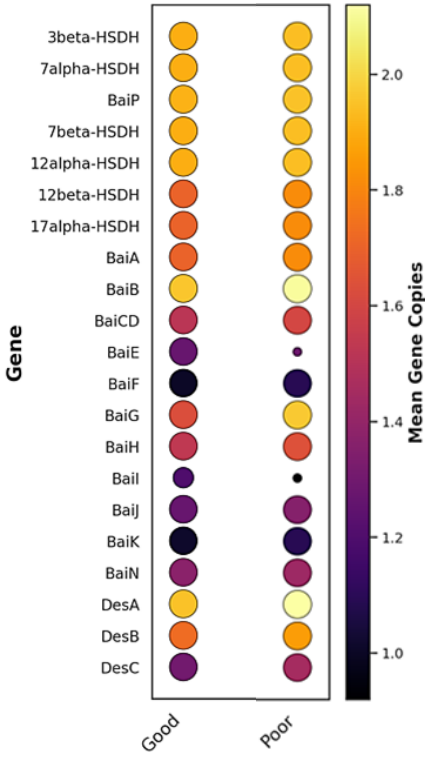


Dietary quality impacts the metagenome



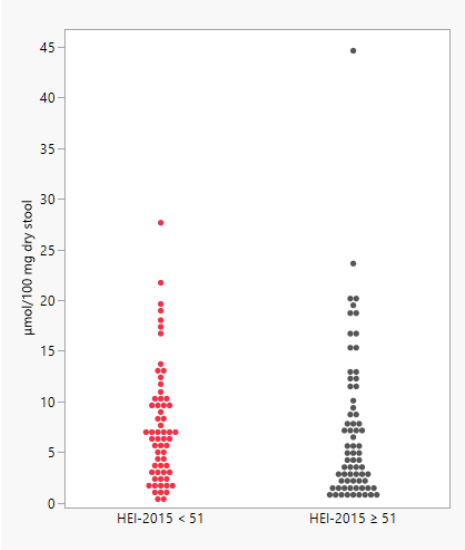


Differences in bile acid genes

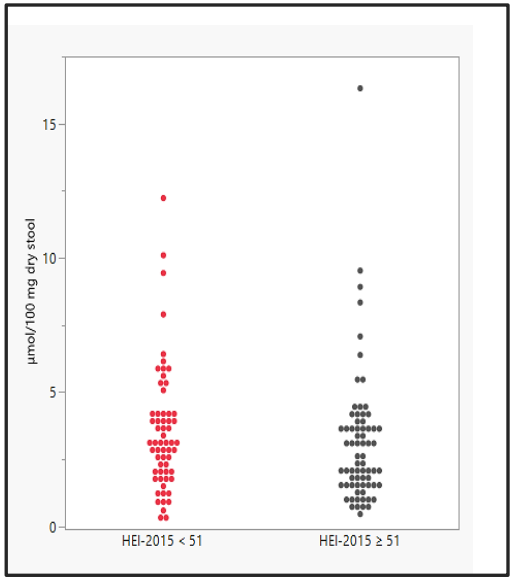


Pius Sarfo Buobu

Poor dietary quality increases hydrophobic bile acids

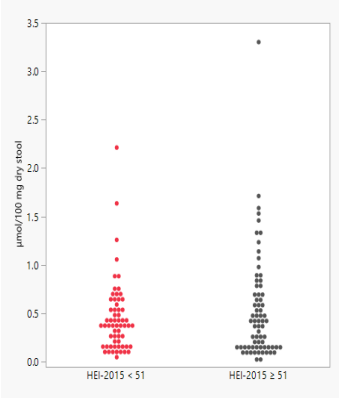


DCA

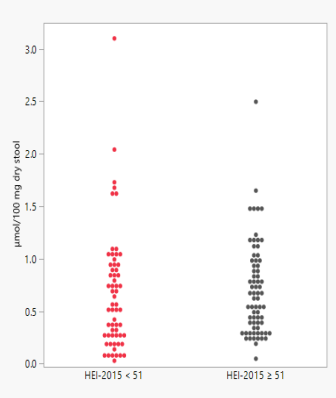


LCA

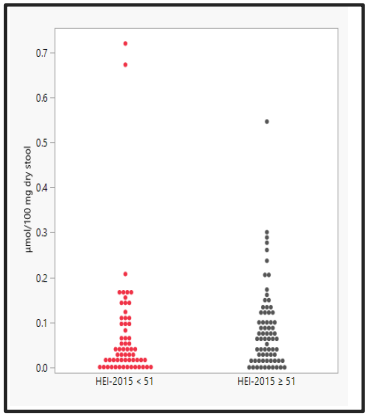
Poor dietary quality reduces hydrophilic bile acids



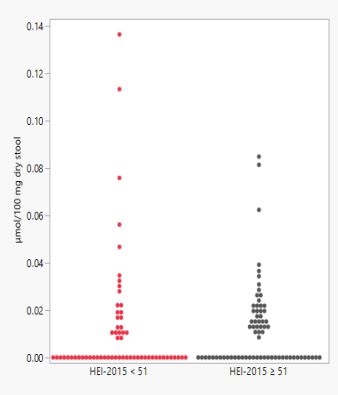
Iso-DCA



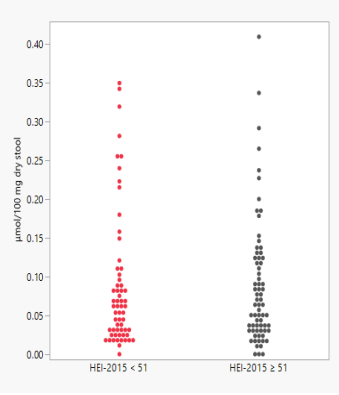
Iso-LCA



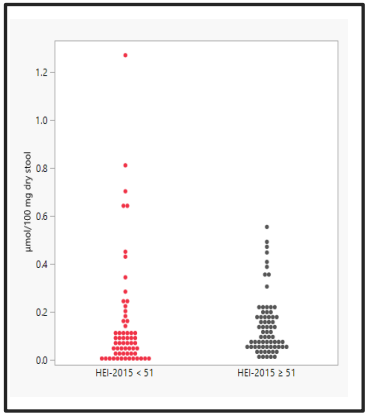
Iso-allo-DCA



Allo-LCA



3-oxo-DCA



3-oxo-LCA

Multivariable Modeling Predicting Fecal Bile Acid Metabolites

Dependent Variables	Major Secondary Bile Acids		Bile Acid Metabolites that Drive Treg Expansion		
	Deoxycholic Acid (DCA)	**Lithocholic Acid (LCA)**	**Iso-allo-LCA**	**Allo-LCA**	**Iso-allo-DCA Iso-DCA Iso-LCA 3-oxo-LCA**
Independent Variables	**Higher HEI-2015** ↓	**Higher HEI-2015** ↓	**Higher % kcal ETOH** ↑	**Higher % kcal ETOH** ↑	**Race = White** ↑
	Controlling for: • BMI • Race • % kcal ETOH	Controlling for: • BMI • Race • % kcal ETOH	Controlling for: • HEI-2015 • BMI	Controlling for: • HEI-2015 • BMI • Race	Controlling for: • HEI-2015 • BMI • % kcal ETOH

Generalized linear modeling, backward selection
% kcal ETOH included in model selection given not captured in HEI-2015

In practice:

Dependent Variables	Major Secondary Bile Acids		Bile Acid Metabolites that Drive Treg Expansion		
	Deoxycholic Acid (DCA)	Lithocholic Acid (LCA)	Iso-allo-LCA	Allo-LCA	Iso-allo-DCA Iso-DCA Iso-LCA 3-oxo-LCA
Independent Variables	Higher HEI-2015	Higher HEI-2015	Higher % kcal ETOH	Higher % kcal ETOH	Race = White
	Controlling for: • BMI • Race • % kcal ETOH	Controlling for: • BMI • Race • % kcal ETOH	Controlling for: • HEI-2015 • BMI	Controlling for: • HEI-2015 • BMI • Race	Controlling for: • HEI-2015 • BMI • % kcal ETOH

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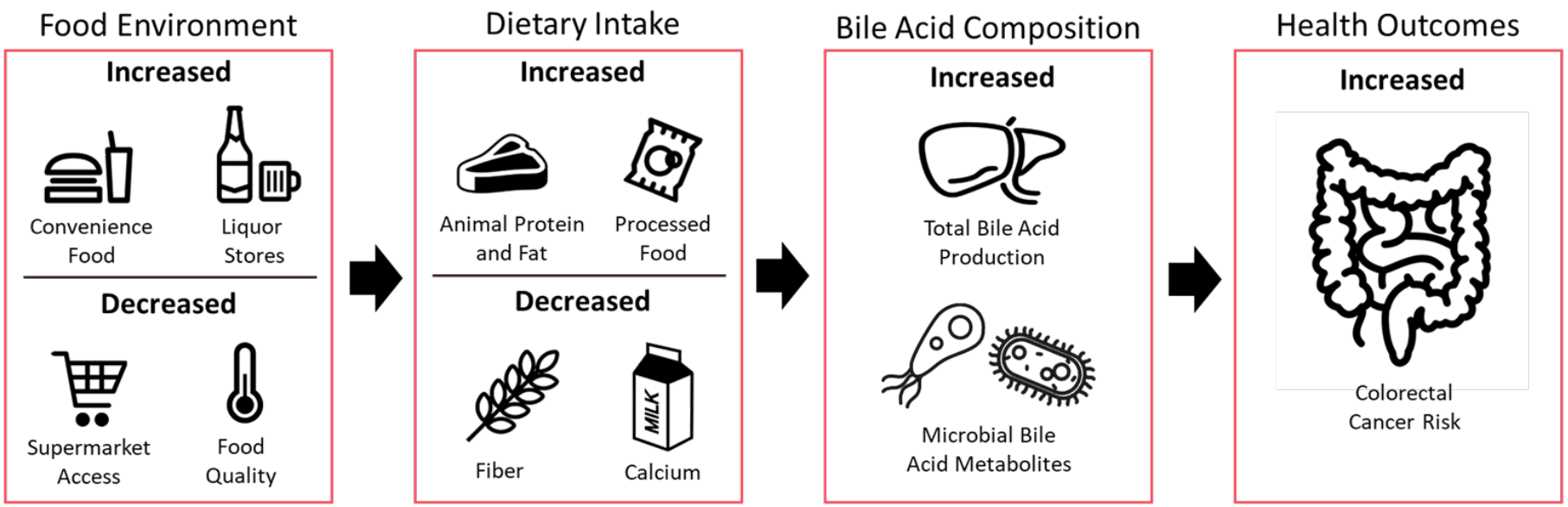
Results consistent with AICR recommendations to reduce colorectal cancer risk

Inequitable food environment and cancer disparities

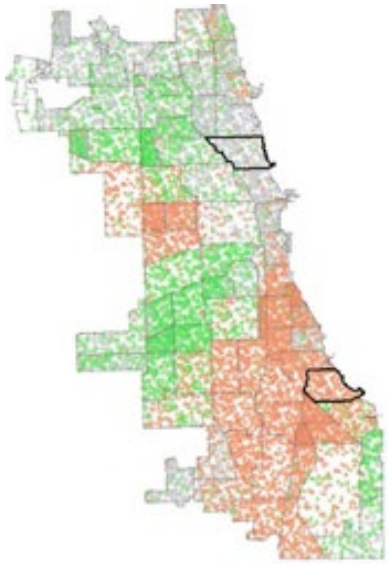


Adapted from Wolf et al. (2021) *mSystems*

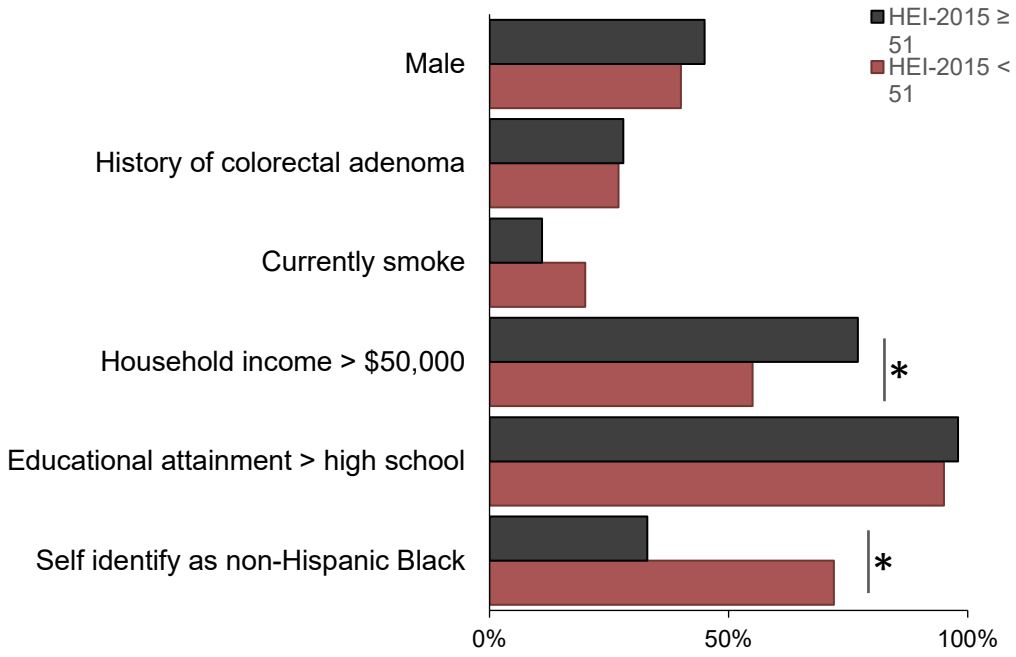
Socioenvironmental barriers to diet quality

Sage Kim

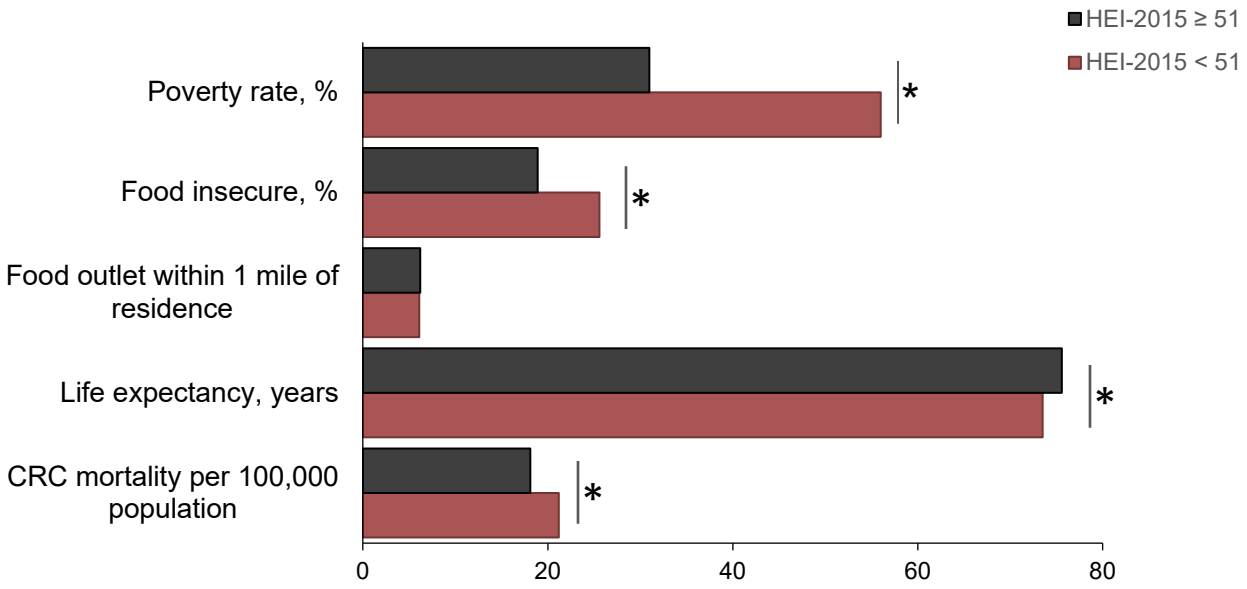
Lisa Tussing-Humphreys



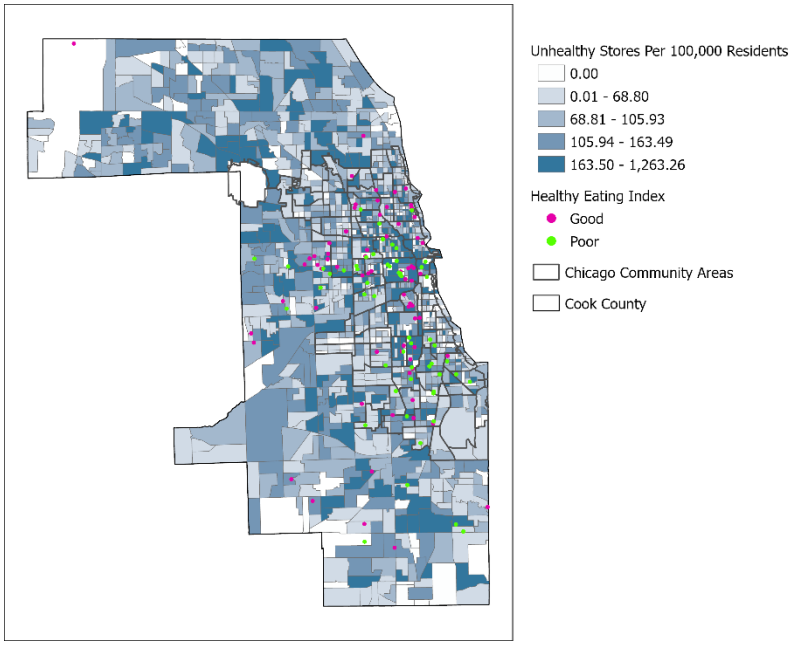
Participant characteristics

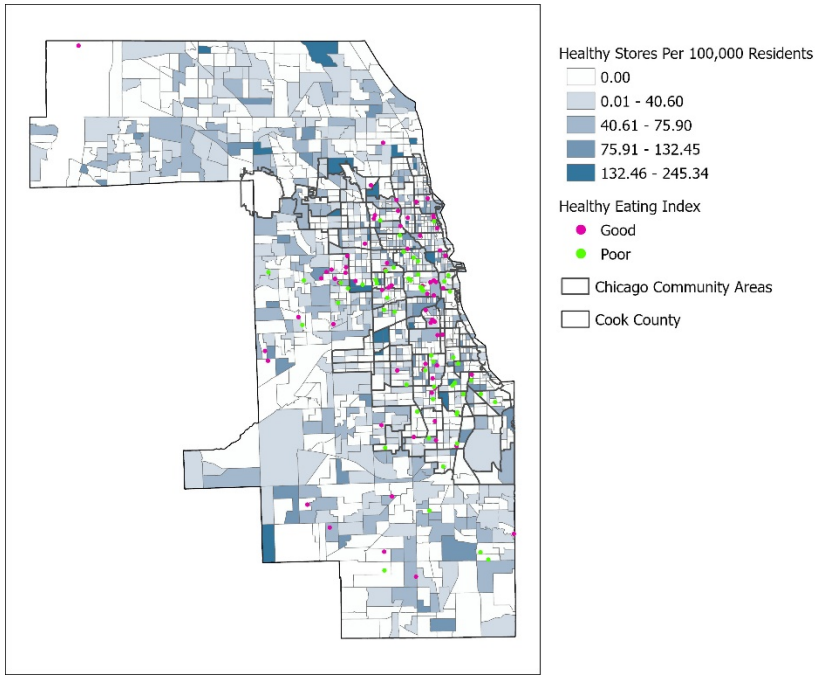


Participant neighborhood characteristics at census tract



Unhealthy and healthy food stores in Chicago food environment





Approximately 80% of 3280 “grocery stores” were miscategorized!

Major findings

- Secondary bile acid derivatives are significant contributors to the fecal bile acid pool
- Dietary quality and individual nutrients may impact bile acid accumulation and conversion by gut microbes.
- Dietary quality is likely impacted by physical and economic barriers to nutrition.

What’s next?

Characterization of microbial steroid metabolism pathways

M2 macrophage differentiation in response to BA derivative treatment

Psychosocial stress on bile acid accumulation and metabolism

Many thanks

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Any questions?

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