# Gut Microbial and Metabolomic Signatures of Ultra-Processed Food Intake

THE HARVARD CHAN MICROBIOME IN PUBLIC HEALTH CENTER

Mengxi Du, PhD, MPH, RD, Kai Wang, PhD, Runzhe Yao, BS, Yujia Lu, MS, Jiaxian Shen, PhD, Ana Nogal, PhD, Hanseul Kim, PhD, Wenjie Ma, ScD, Frank B. Hu, MD, PhD, Andrew T. Chan, MD, MPH, Curtis Huttenhower, PhD, Mingyang Song, MBBS, ScD

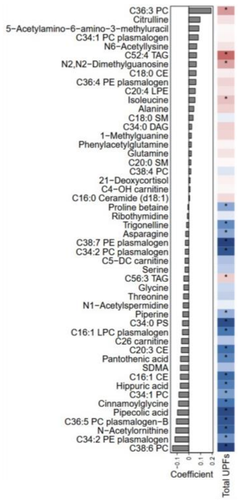
## BACKGROUND

### Ultra-processed foods (UPFs)

- **29%** ↑ risk for CRC in men
- **18%** and **20%** ↑ risk for advanced adenomas of the colon and rectum
- **45%** ↑ risk of early-onset conventional adenomas
- **65%** ↑ risk for mortality due to CVD among CRC survivors

### Colorectal Cancer (CRC)

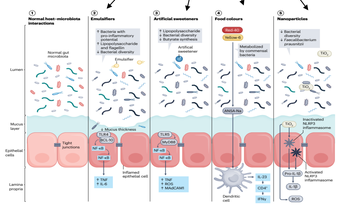
- One of the most prevalent cancers (**~159,000 new cases** and **~1.4 million** survivors in 2026)
- Leading cause of cancer deaths
- Most strongly associated with suboptimal dietary intake




**Carcinogens** (*e.g., processed meat, N-nitroso compounds*)




**Obesity**




**Food Additives Altering Gut Microbiome/Gut Permeability**

- Emulsifiers
- Artificial sweeteners
- Food colors
- Nanoparticles

## OBJECTIVE

**Identify microbial and metabolomic signatures of UPF intake**

- Do individuals with varying levels of UPF intake have different gut microbial composition?
- Which species are associated with UPF intake?
- Do UPFs exhibit distinct stool metabolomic signatures?

## ACKNOWLEDGEMENTS

**Funding Support**

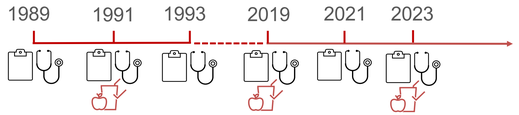
NIH NATIONAL CANCER INSTITUTE
NIH NIDDK
American Cancer Society

**All participants and staff of the Nurses' Health Study II and Micro-N Study**
**Song Lab, HutLab, Chan Lab, MGH CTEU, Hu Research Group**

## Methods

**Microbiome Among Nurses (Micro-N) Study**

Nurses' Health Study II enrolled 116,429 women in 1989




*Updated every 2 years*
- Self-reported questionnaires
- Medical records

*Updated every 4 years*
- Validated food frequency questionnaires (FFQs)

Nurses' Health Study Micro-N Microbiome Among Nurses

Micro-N initiated in 2019 and recruited nurses from NHS II

**Shotgun metagenomic sequencing**

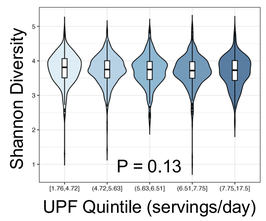
**Taxonomic profiles** **Functional profiles**

Fecal samples from 20,000 women who participated in NHS II

**High-throughput Metabolomic Profiling**
liquid chromatography-mass spectrometry (LC-MS)

Matched cases and controls
- Diverticulitis (n=121 pairs)
- Type 2 Diabetes (n=137 pairs)
- Liver Disease (n=430 pairs)
- Colorectal Adenoma (n=885 pairs)

## RESULTS



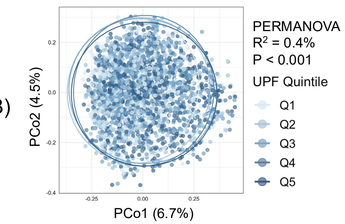
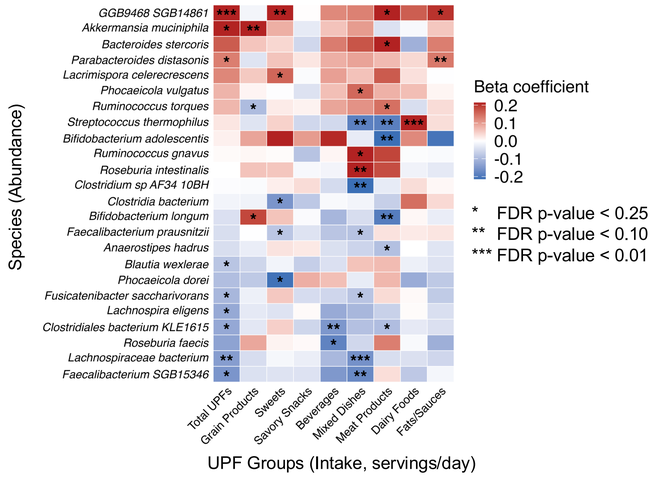




**Figure 1. UPF Intake Not Associated with Broad Microbial Community Measures**
Associations between UPF intake and gut microbial composition were evaluated in 2,288 women in the Micro-N study. (A) Shannon diversity did not differ significantly across UPF intake quintiles. (B) Principal coordinate analysis showed substantial overlap in microbial community composition across UPF intake groups, although PERMANOVA detected a small but statistically significant association.

## CONCLUSIONS

- UPF intake does not strongly alter overall microbiome structure
- UPF intake was linked to modest but targeted microbial shifts, including depletion of butyrate-producing taxa
- UPFs were associated with a broad and coordinated stool metabolomic fingerprint across multiple food items



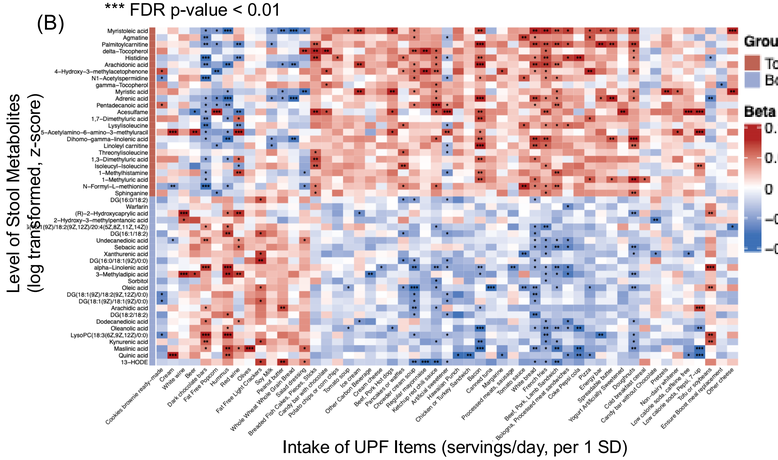




**Figure 2. Gut Microbial and Metabolomic Signatures of UPF Intake**
(A) Species-level associations were estimated using MaAsLin3 models. Different UPF categories showed distinct microbial association patterns. (B) Associations between 73 individual UPF items and 322 stool metabolites were evaluated using multivariable linear models. Stool metabolomic profiles showed coordinated association patterns that were substantially stronger and more systematic than microbiome compositional changes.