Integrative approaches to reduce cancer disparities: diet and the gut microbiome

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2023 FLASCO Puerto Rico Oncology Symposium
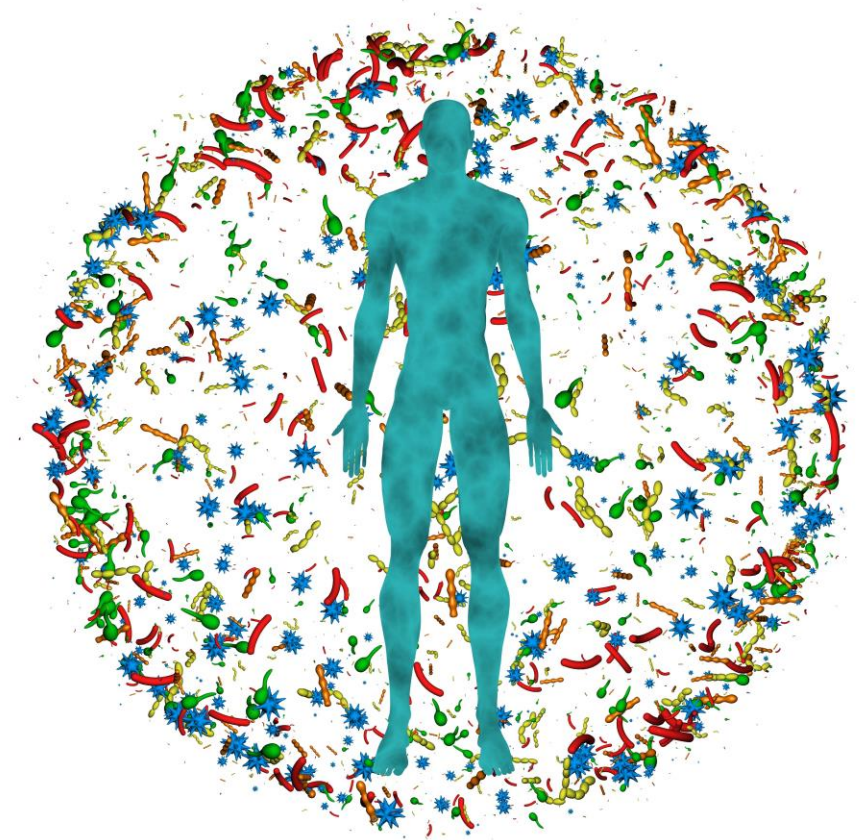
MOFFITT
CANCER CENTER
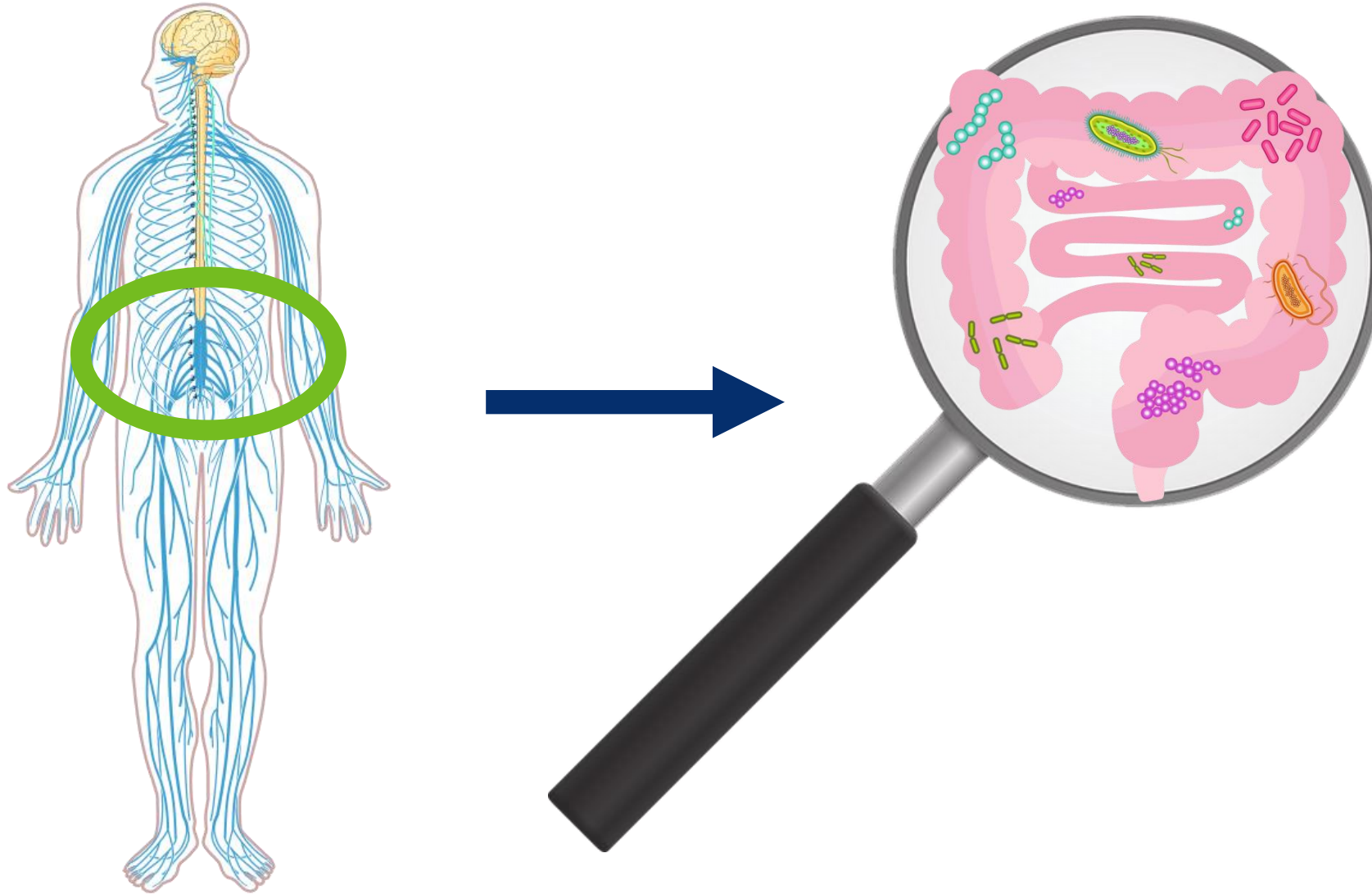
Disclosures

No financial relationships to disclose

What is the microbiome?

- Trillions of microorganisms in & on our bodies

- Some microbes are similar across humans, others are special to you

- Critical for maintaining health
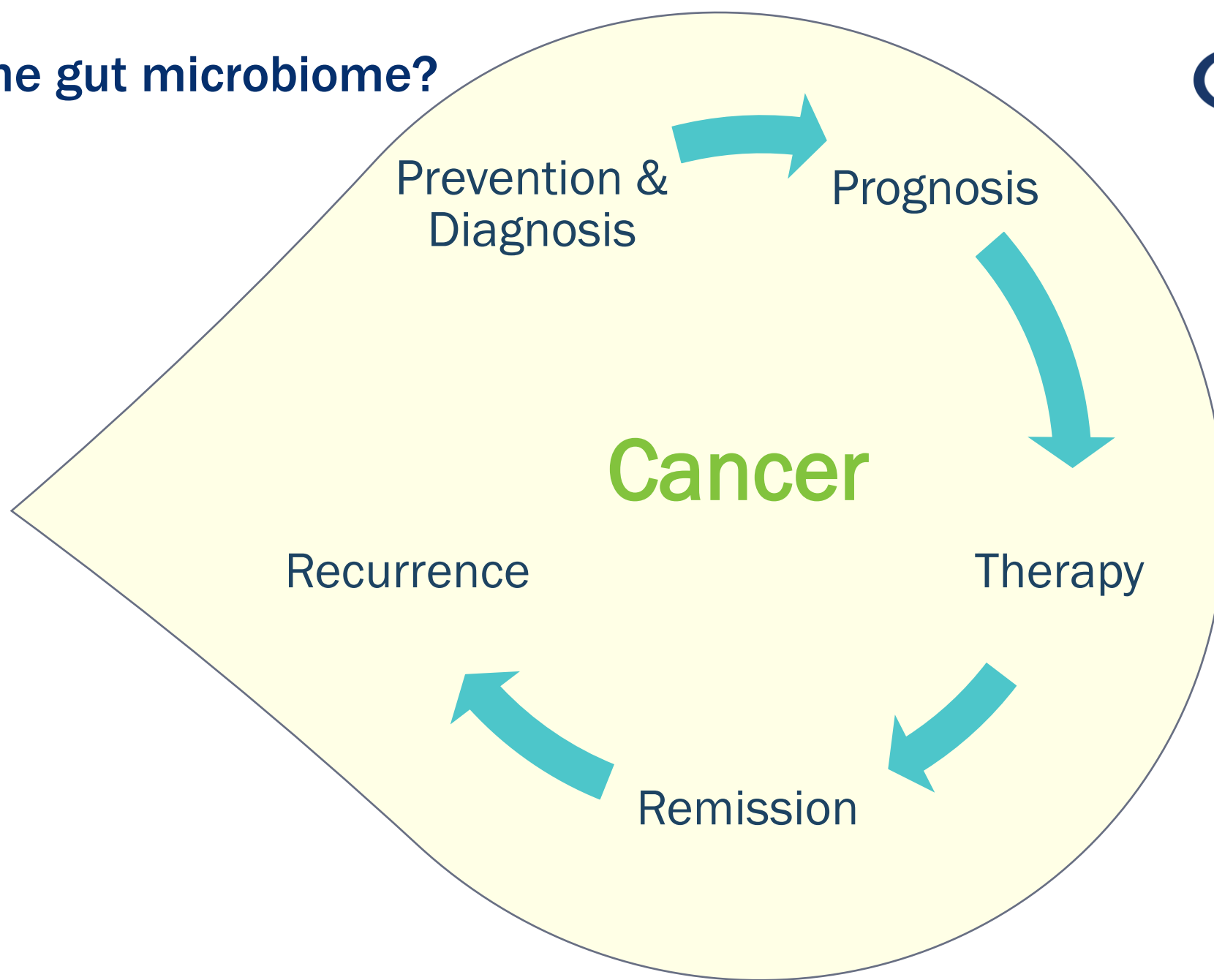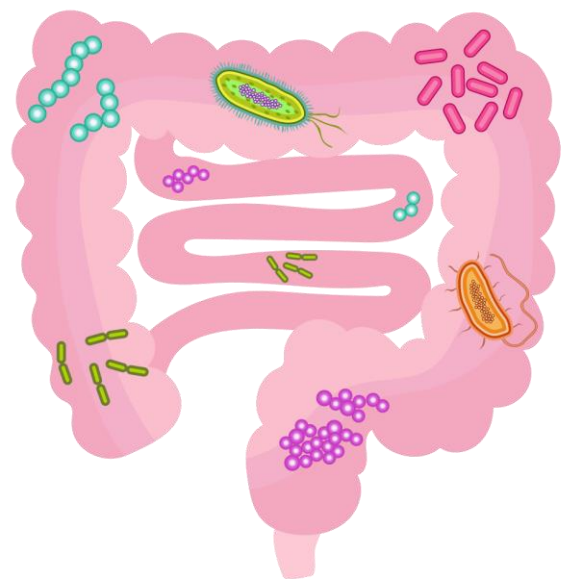
- Potentially modifiable

What is the gut microbiome?

97% of microbes live in our "gut"

Why should we study the gut microbiome?

Cancer

Prevention & Diagnosis → Prognosis → Therapy → Remission → Recurrence

The Gut Microbiome & Colorectal Cancer

- 2nd leading cause of cancer death among US men & women

- 5-year relative survival rates:
  - 90% for stages I/II
  - 71% for stage III
  - 13% for distant (stage IV)

- ~30% to 40% of CRC patients who undergo potentially curative surgery ultimately relapse

- Need to ID <u>potentially modifiable</u> biomarkers of have poor CRC outcomes

The Gut Microbiome & Colorectal Cancer Outcomes

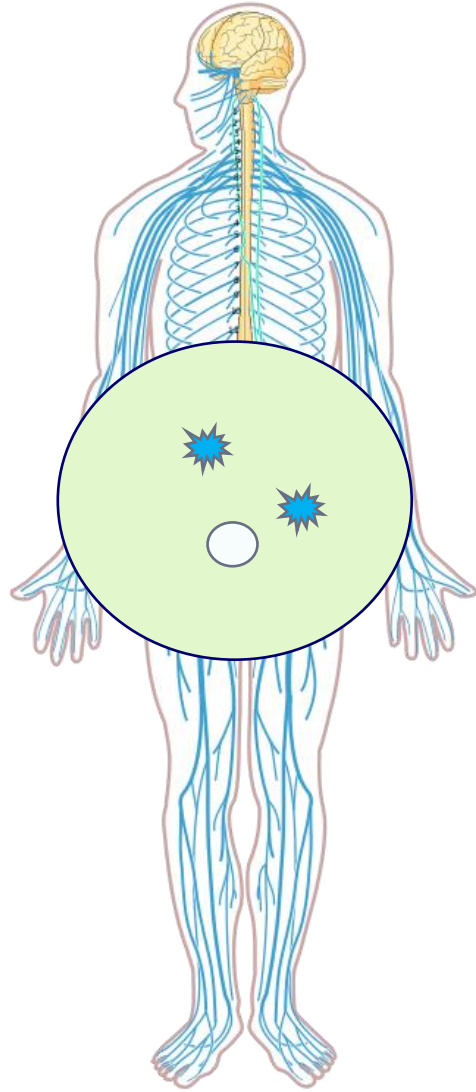Men & women diagnosed w/ colorectal cancer
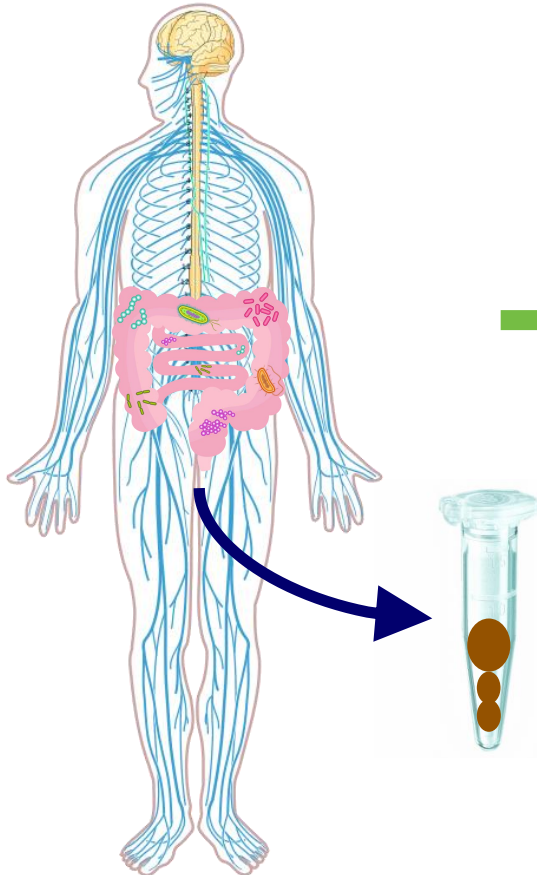
> 2 years

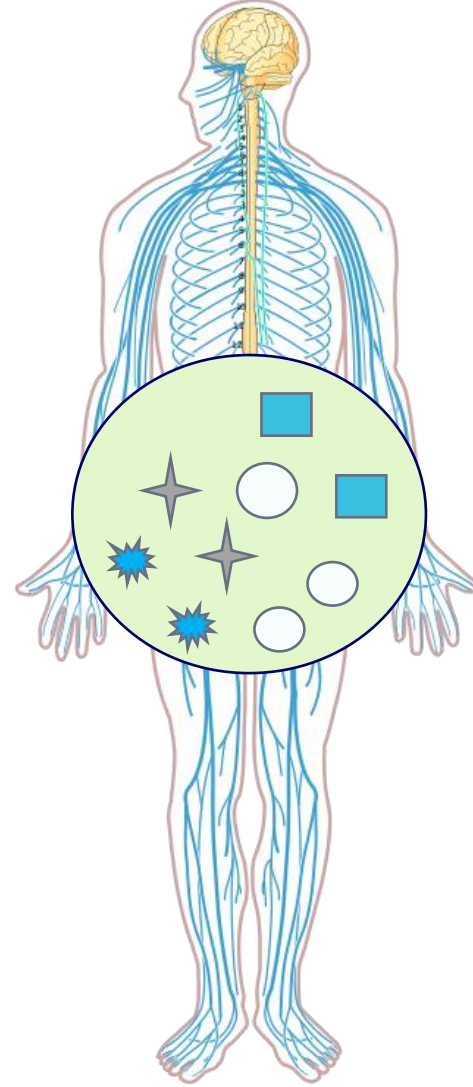Recurrence and / or death

"Disease-free survival"

Byrd DA, et al. *In progress.*

Microbiome Diversity & Colorectal Cancer Outcomes

Alpha diversity = 2

Alpha diversity = 4

Higher alpha diversity → improved disease-free survival

Shannon Index:
HR (95% CI) = 0.40 (0.19, 0.86)

Byrd DA, et al. *In progress.*

Microbiome Diversity & Colorectal Cancer Outcomes

Multiple bacteria → improved disease-free survival

HR (95% CIs):

Coprococcus: 0.51 (0.34, 0.76)
Proteus: 0.05 (0.01, 0.36)
Roseburia: 0.76 (0.61, 0.93)

- Many are involved in regulating immunity and inflammation
- Many also produce bioactive products
  - May be targetable

Byrd DA, et al. *In progress.*

Diet & Colorectal Cancer Outcomes

Yogurt & fiber → improved disease-free survival

Byrd DA, et al. *In progress.*

Future Directions: The Gut Microbiome & Colorectal Cancer

- Larger studies w/in ColoCare

  - Tumor immunity

  - Diet patterns

  - Early-onset CRC

  - Address disparities
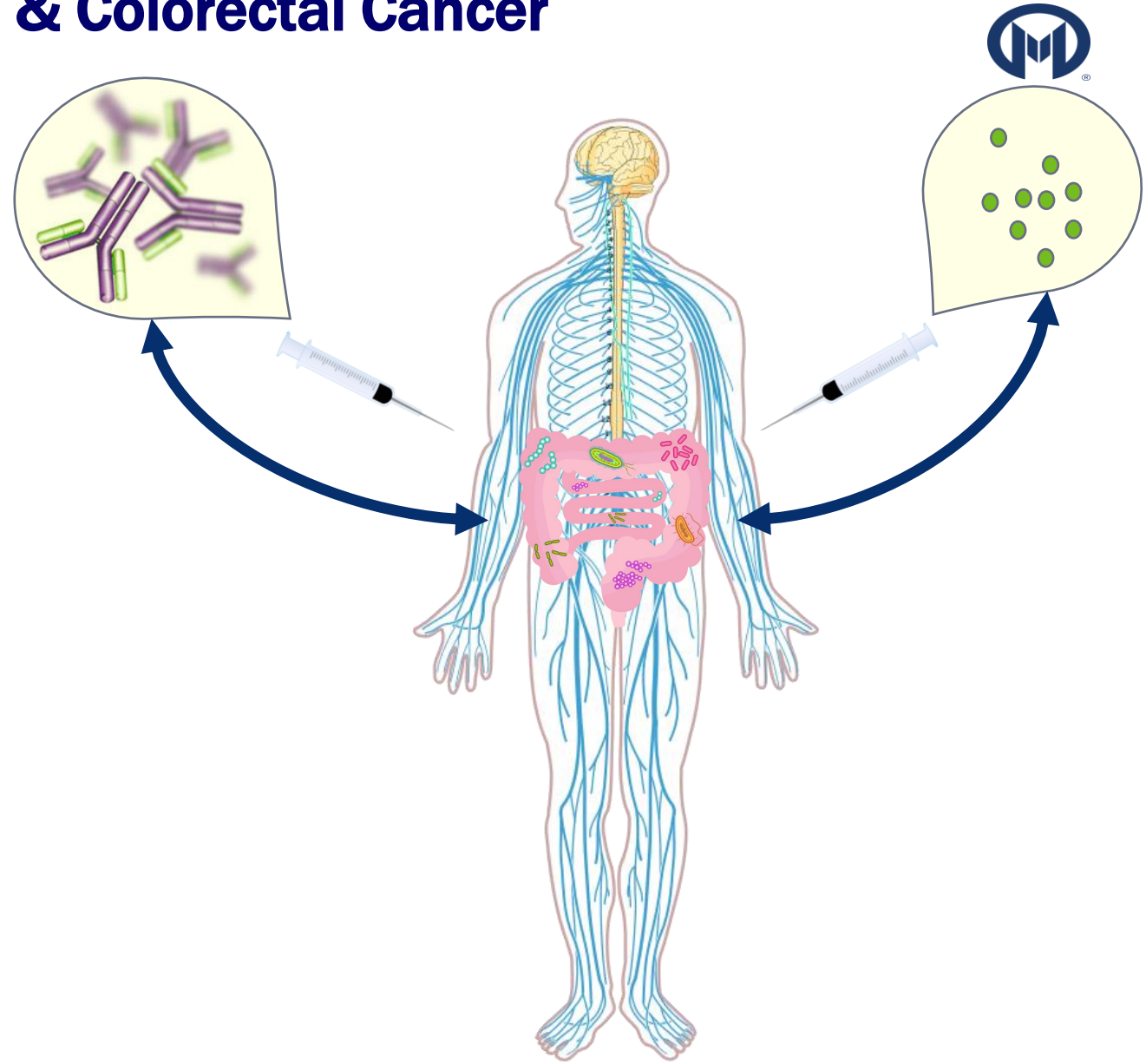
The Microbiome & Colorectal Cancer Disparities
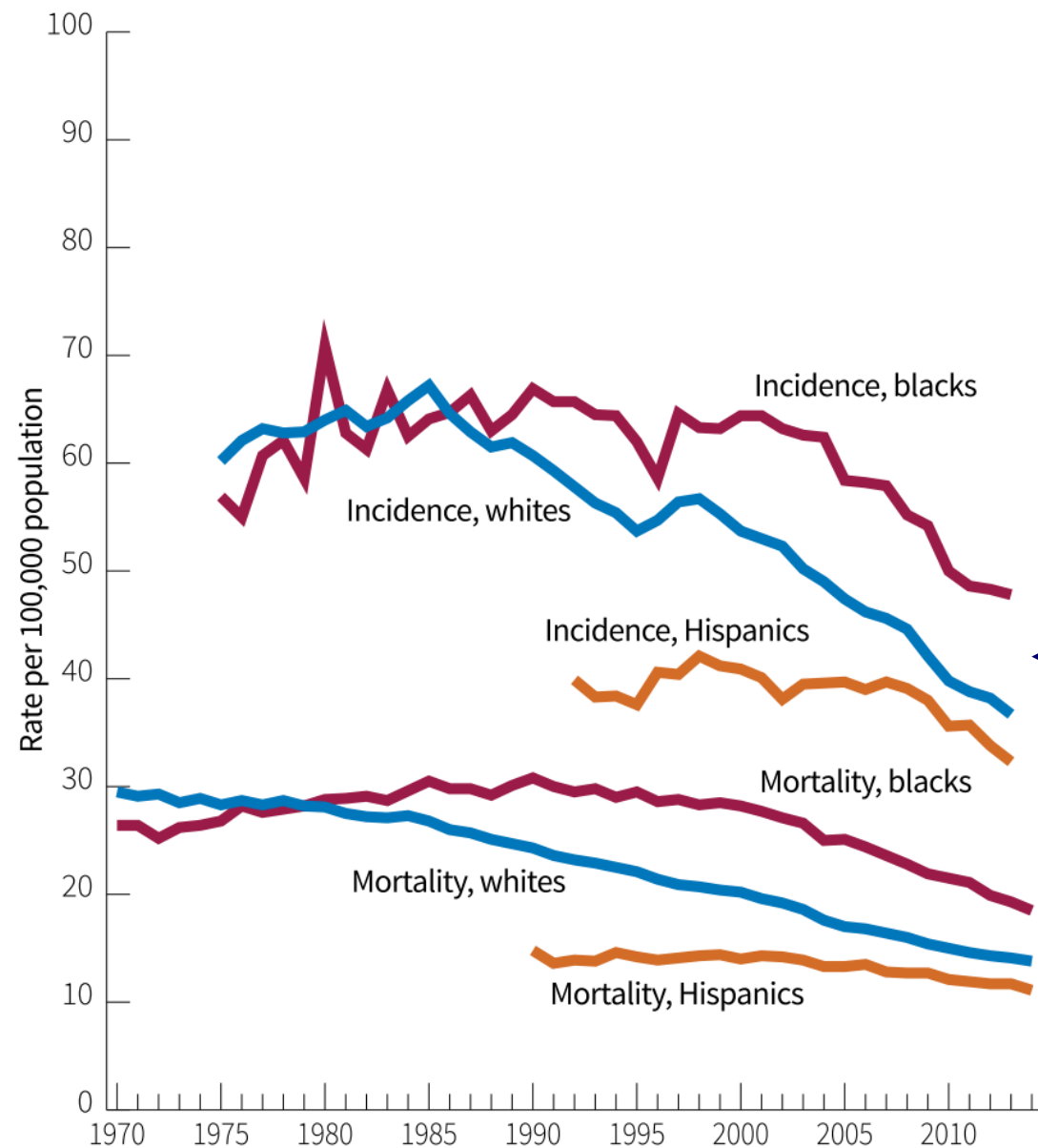
Colorectal cancer incidence rate in Black Americans is

20% ↑ than in White Americans

Colorectal cancer mortality rate in Black Americans is
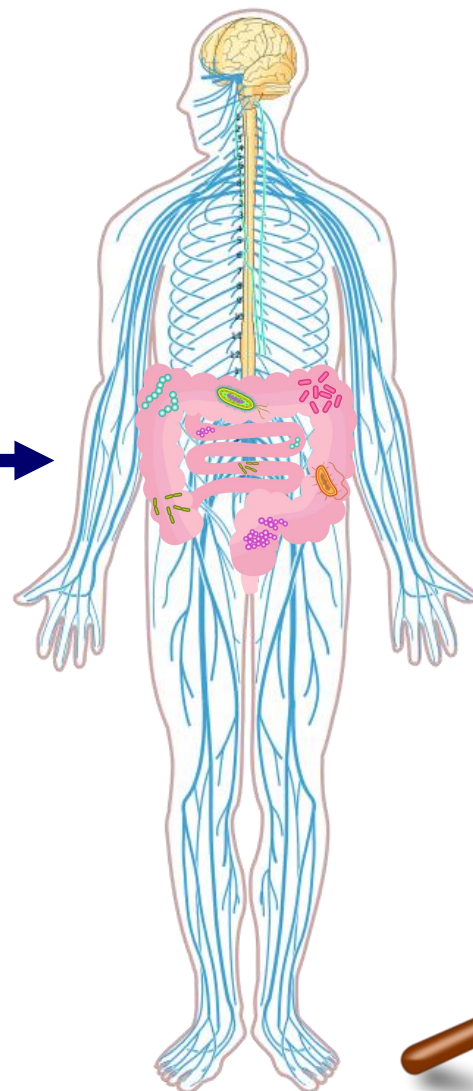
40% ↑ than in White Americans

The Gut Microbiome & Disparities

- Exposures associated w/ "race" & "ethnicity":
  - Racism
  - Psychosocial factors
  - Diet / lifestyle
  - Healthcare- / policy-related factors
  - Environmental factors

Complex & sometimes difficult to measure

Byrd DA, et al (2020) *Genome Biology*

Racial / ethnic microbiome differences

Cross-sectional study in Southern Community Cohort:

- Oral microbiome:
  - N = 1058 African Americans
  - N = 558 European Americans
- African Americans had ↑ alpha diversity
- Differences in overall microbiome composition & taxa abundance

Limitation:

Lack of detailed investigations into other exposures associated w/ self-reported race / ethnicity

E.g., of periodontal disease

Yang (2019) *mSystems*

Racial / ethnic microbiome differences

Cross-sectional study in Amsterdam, Netherlands:

- Fecal microbiome:

  - N = 439 Dutch, 367 Ghanaian, 280 Moroccan, 197 Turk, 443 African Surinamese, & 358 South-Asian Surinamese participants

- Differences in alpha diversity, beta diversity, & certain microbes

- After adjustment for ethnicity-related factors → differences remained

Beta diversity = 2

Deschasaux (2018) *Nat Med*
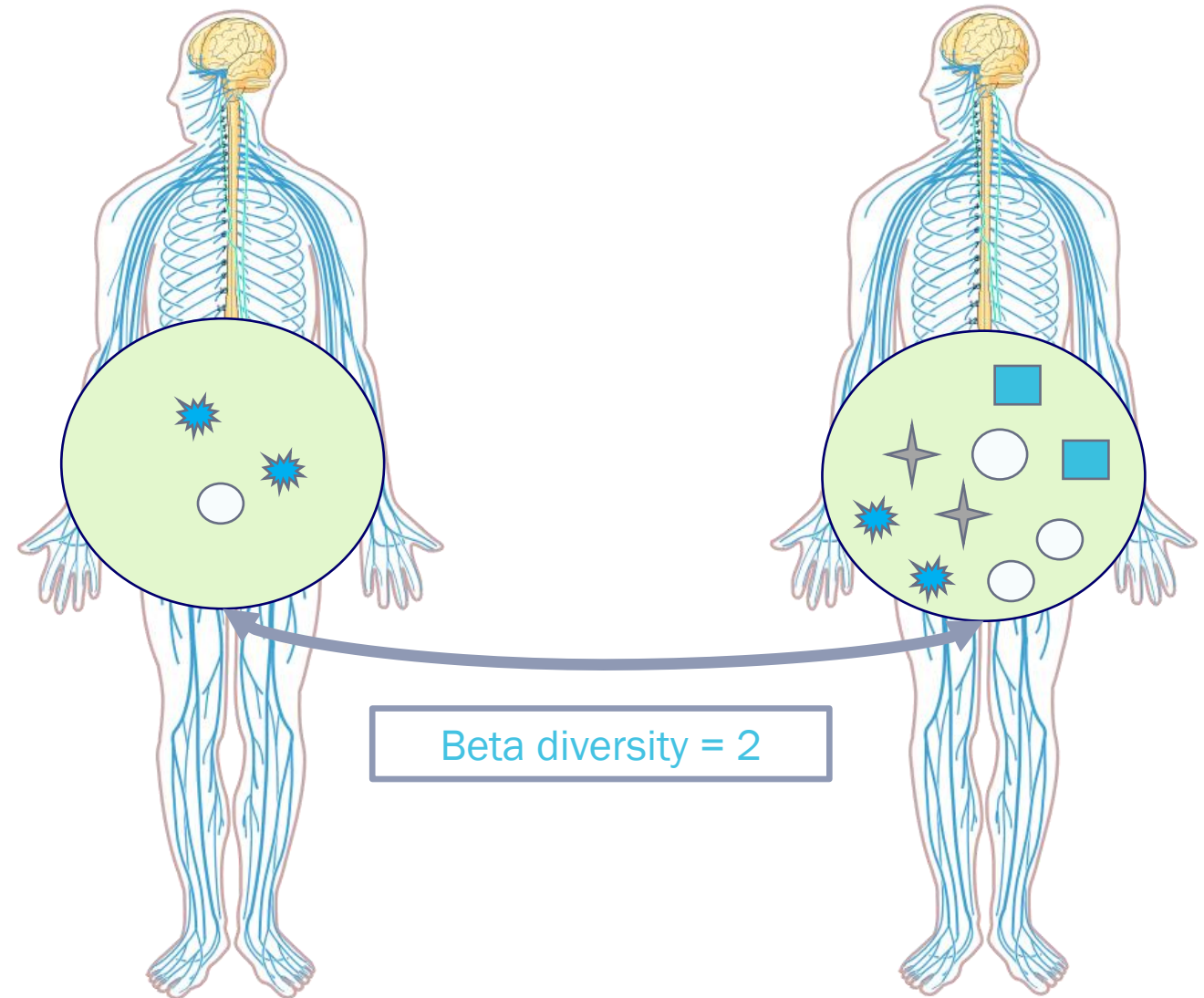
Example: The gut microbiome & cancer disparities
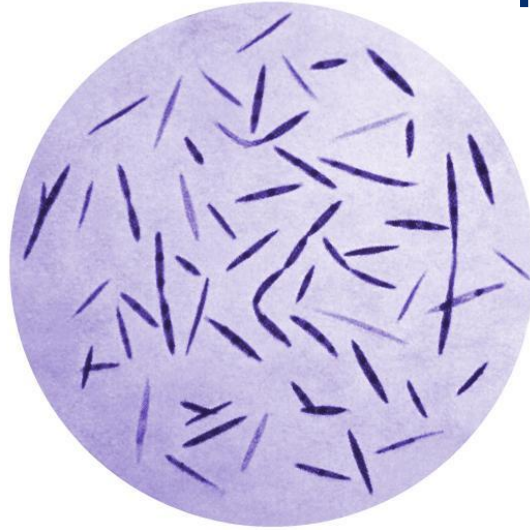
- *Fusobacterium nucleatum* →
  ↑ colorectal cancer progression

  - Primarily studied among homogenous populations

Women with & without colorectal cancer

Non-Hispanic White women

Non-Hispanic Black women

↑ associations with colorectal cancer

No association

Carson T, **Byrd DA**, et al. *In progress.*
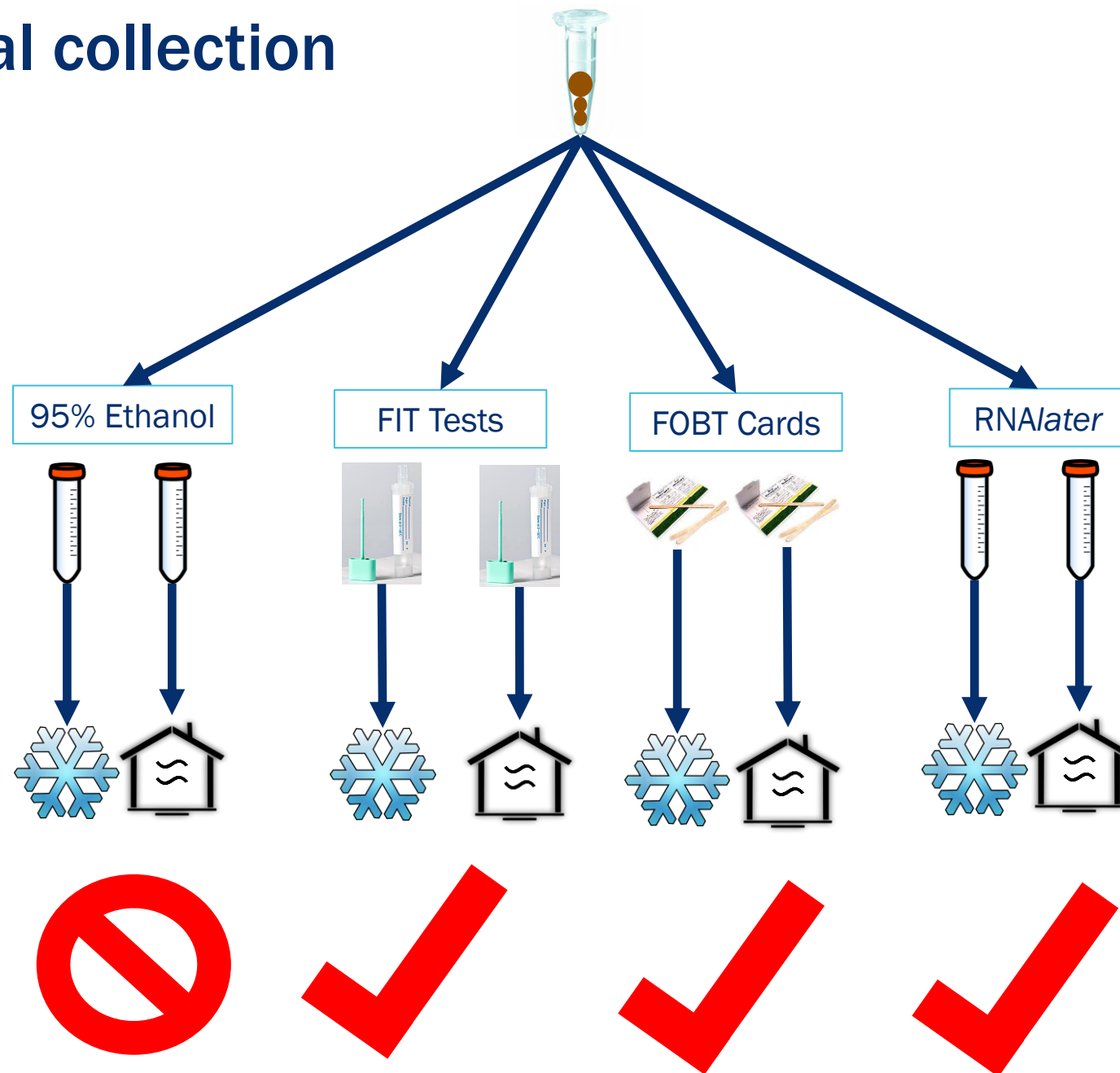
Long-term goal:

Characterizing the gut microbiome across large, diverse racial / ethnic groups & geographic locations

Stability of fecal collection methods

95% Ethanol   FIT Tests   FOBT Cards   RNA*later*

Byrd DA, et al (2020) *mSphere*

Fecal Sample Collection Methods

FIT tests = opportunities for establishing **diverse** prospective fecal microbiome cohorts in CRC screening populations

Future Directions: The Microbiome & Cancer Disparities

"FIT test"

- Tests for blood in stool to screen for colorectal cancer & its precursor

- Often provided to patients without access to colonoscopy screening (age 45 – 75)

- Normally discarded after testing

- Goal: Establish a biobank of discarded FIT tests from diverse participants in the clinical screening population in Florida &, eventually, nationally

- Leverage ongoing interventions at Moffitt to improve community uptake of FIT screening

Impact: Florida FIT Biobank
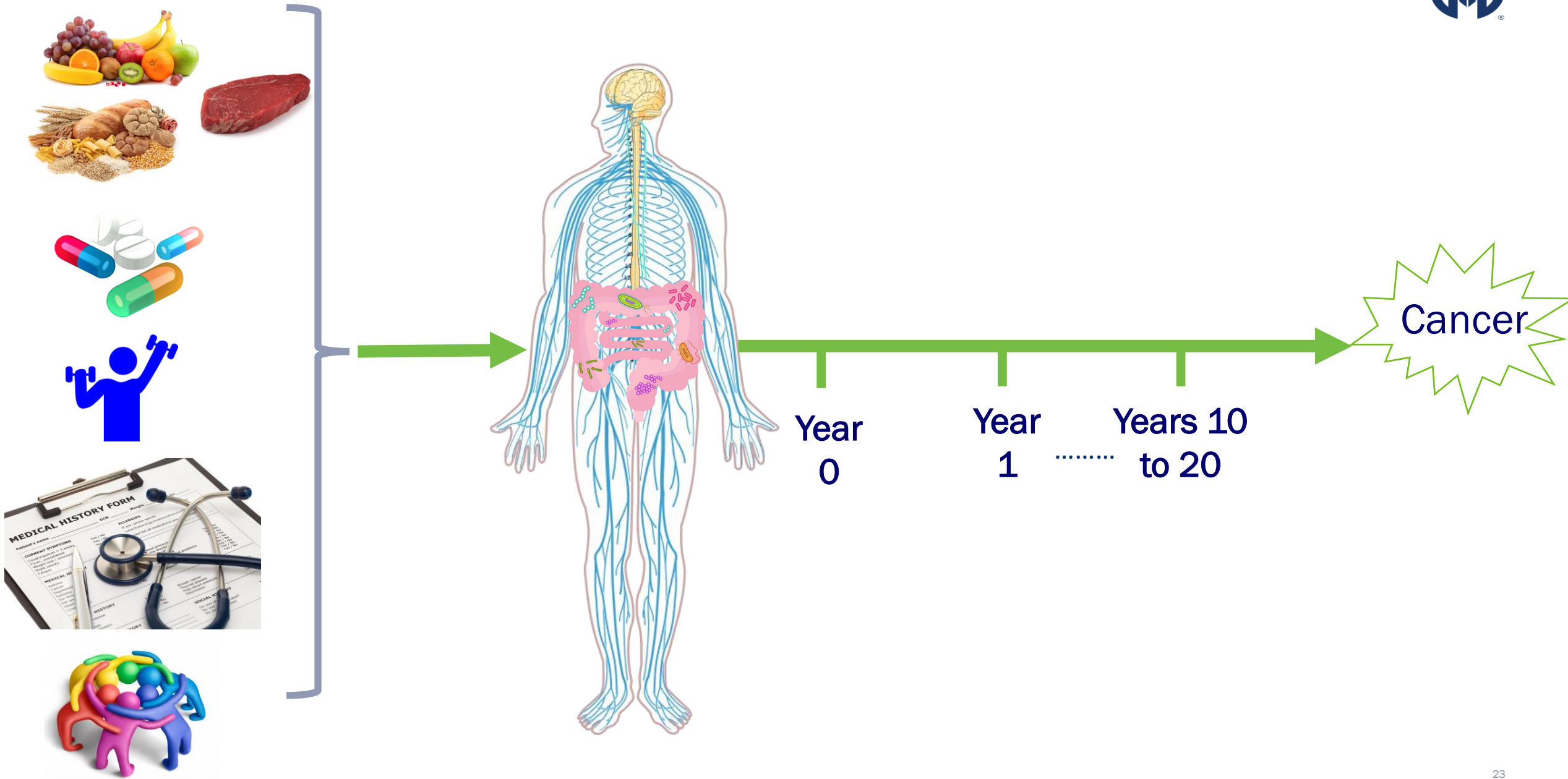
Includes a diverse, understudied population
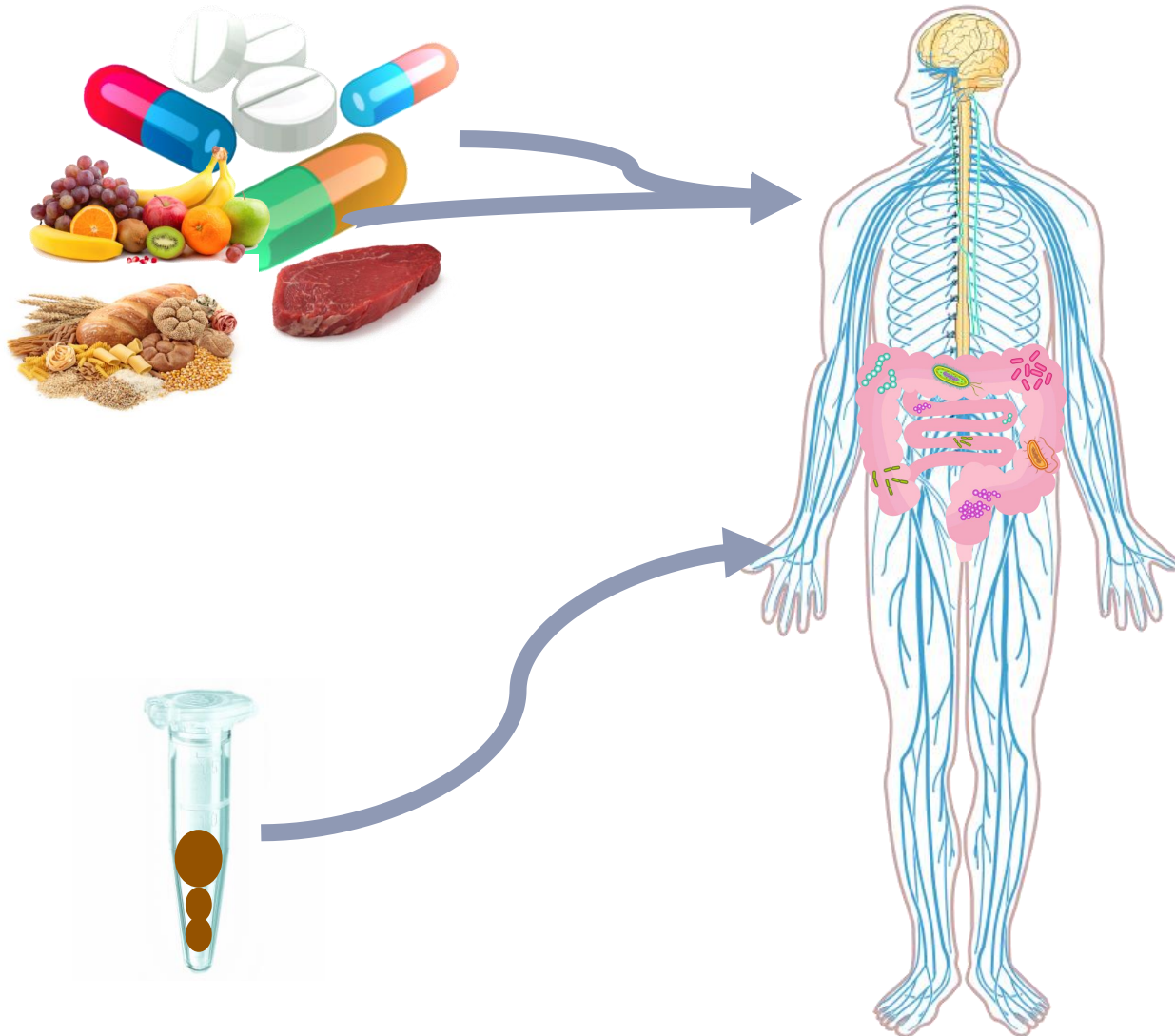
Collaborating clinics serve:
- Anyone regardless of ability to afford care
- Many migrant workers
- Residents of rural areas
- Diverse racial / ethnic backgrounds

Impact: Florida FIT Biobank

Year 0

Year 1 ········ Years 10 to 20
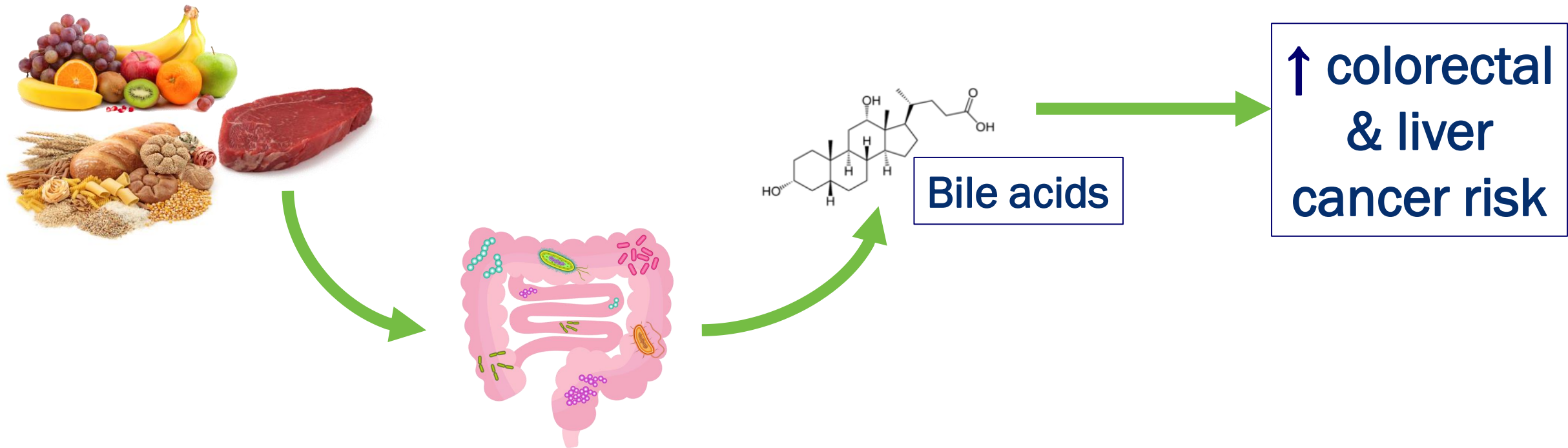
Cancer

The Gut Microbiome: Next Steps
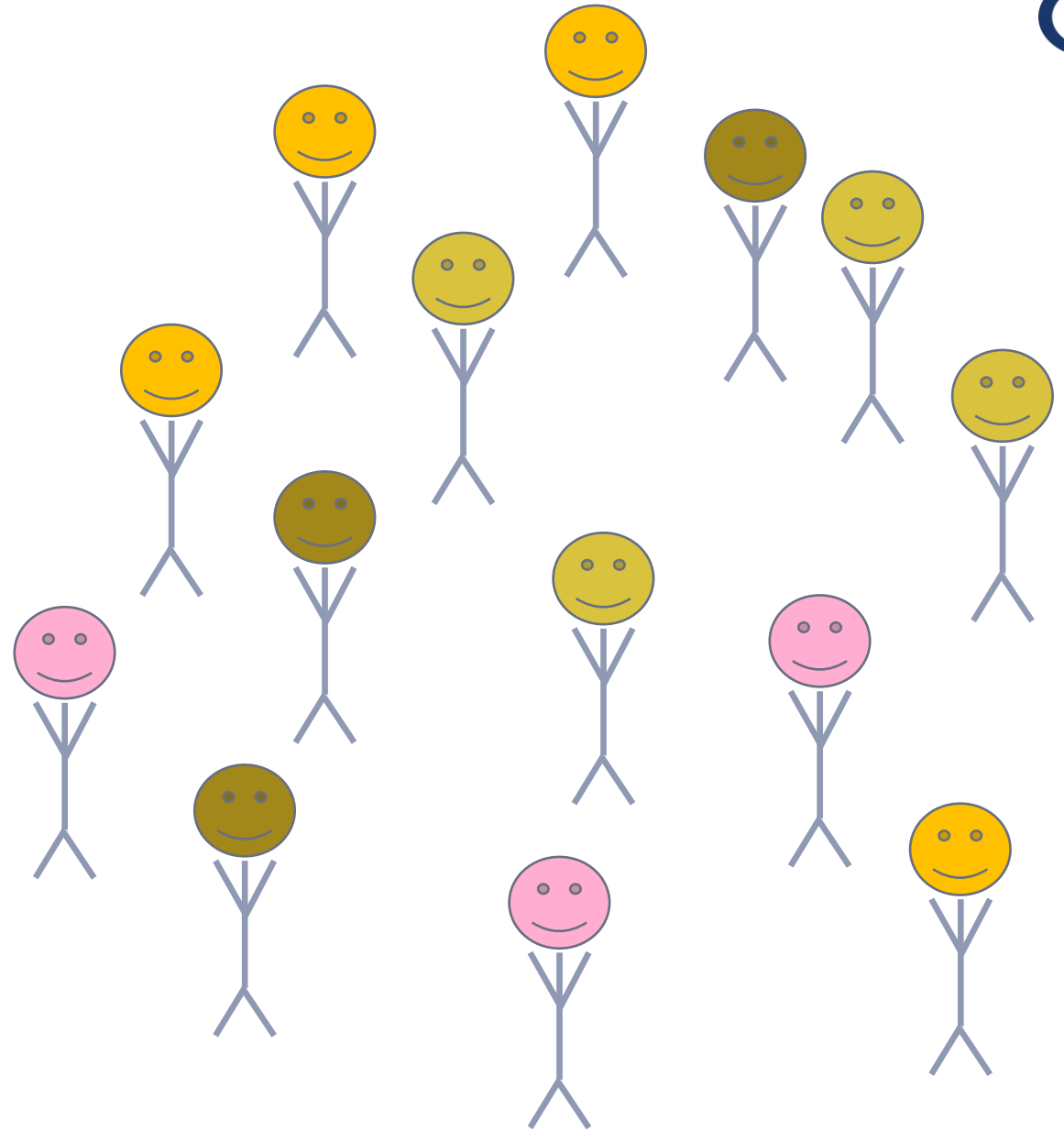
Continued investigation of associations of the microbiome with cancer development & progression

Identify 'high-risk' microbiome characteristics

Intervene to change the gut microbiome from 'high-risk' to 'low-risk' to prevent or better treat cancer

Diet & the microbiome

Bile acids

↑ colorectal & liver cancer risk

Diet & Bile Acids

Bile acids

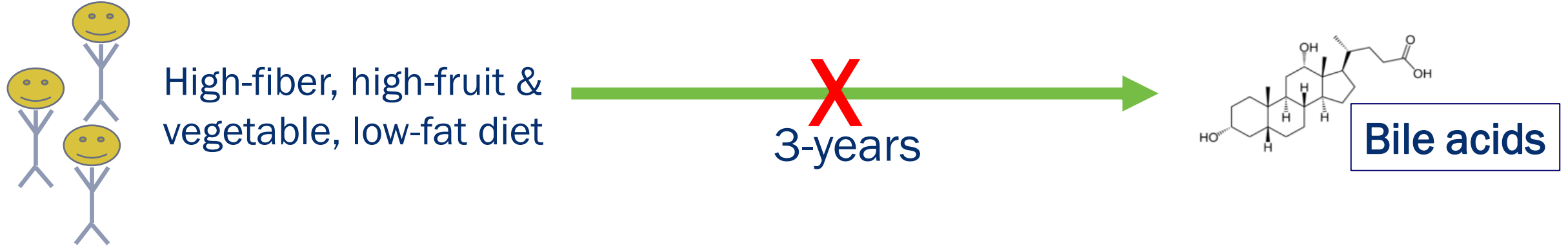In a study among Finnish male smokers:

Fiber & coffee → ↓ cancer-associated bile acids

Alcohol & certain fats → ↑ cancer-associated bile acids
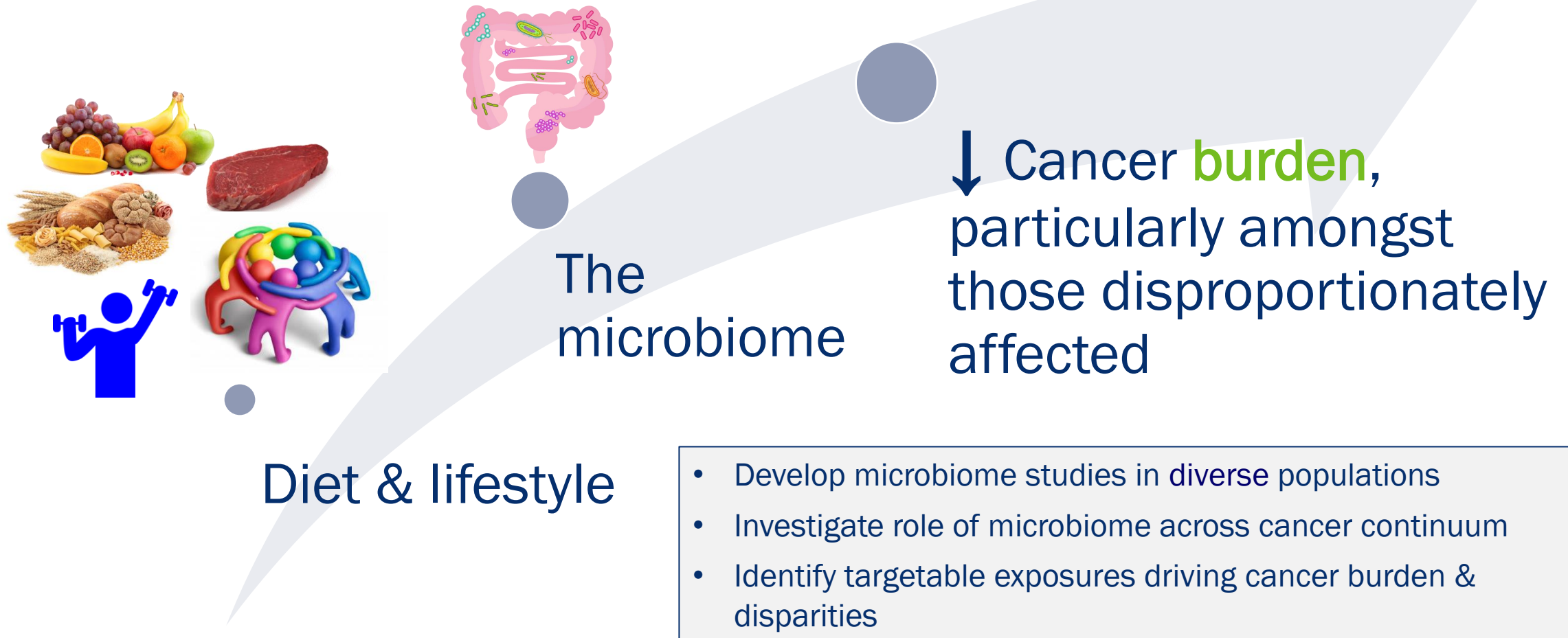
In a study among US men & women :

Fiber → ↓ cancer-associated bile acids

Byrd DA et al., Am J Clin Nutr

Diet & Bile Acids

Long-term high-fiber diet → ↓ levels of cancer-associated bile acids

Byrd DA et al., In progess

Conclusions

Diet & lifestyle

The microbiome

↓ Cancer burden, particularly amongst those disproportionately affected

- Develop microbiome studies in diverse populations
- Investigate role of microbiome across cancer continuum
- Identify targetable exposures driving cancer burden & disparities

Thank you!

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Demetrius Albanes

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Jennie Ose
Erin Siegel
Adetunji Toriola
And many others…