

The Impact of Gut Health on Ageing and Wellbeing

Dr Nila Dharan | 23 May 2025

In The Know - Research and Treatments Evening

Overview

- Gut health and the gut microbiome
- Gut health and ageing
- Impact of HIV on gut health
- Knowledge gaps
- Research in HIV and ageing/comorbidities
 - ARCHIVE Study
- Future directions

What is gut health?

- Balance of gastrointestinal tract (stomach, intestines, other digestive organs) for effective function and overall well-being
- A healthy gut is important for:
 - Breakdown of food, absorbing nutrients, lipid metabolism, eliminating waste
 - Metabolism
 - Immune system
 - Disease prevention

Gut microbiome

- Community of trillions of microorganisms (bacteria, fungi and viruses) living in gastrointestinal tract
- Healthy gut microbiome crucial for overall health
 - Promotes longevity, healthy ageing
- Healthy gut supported by maintaining diverse diet, environmental exposures, genetics/age, antibiotics, lifestyle (stress, exercise, sleep)

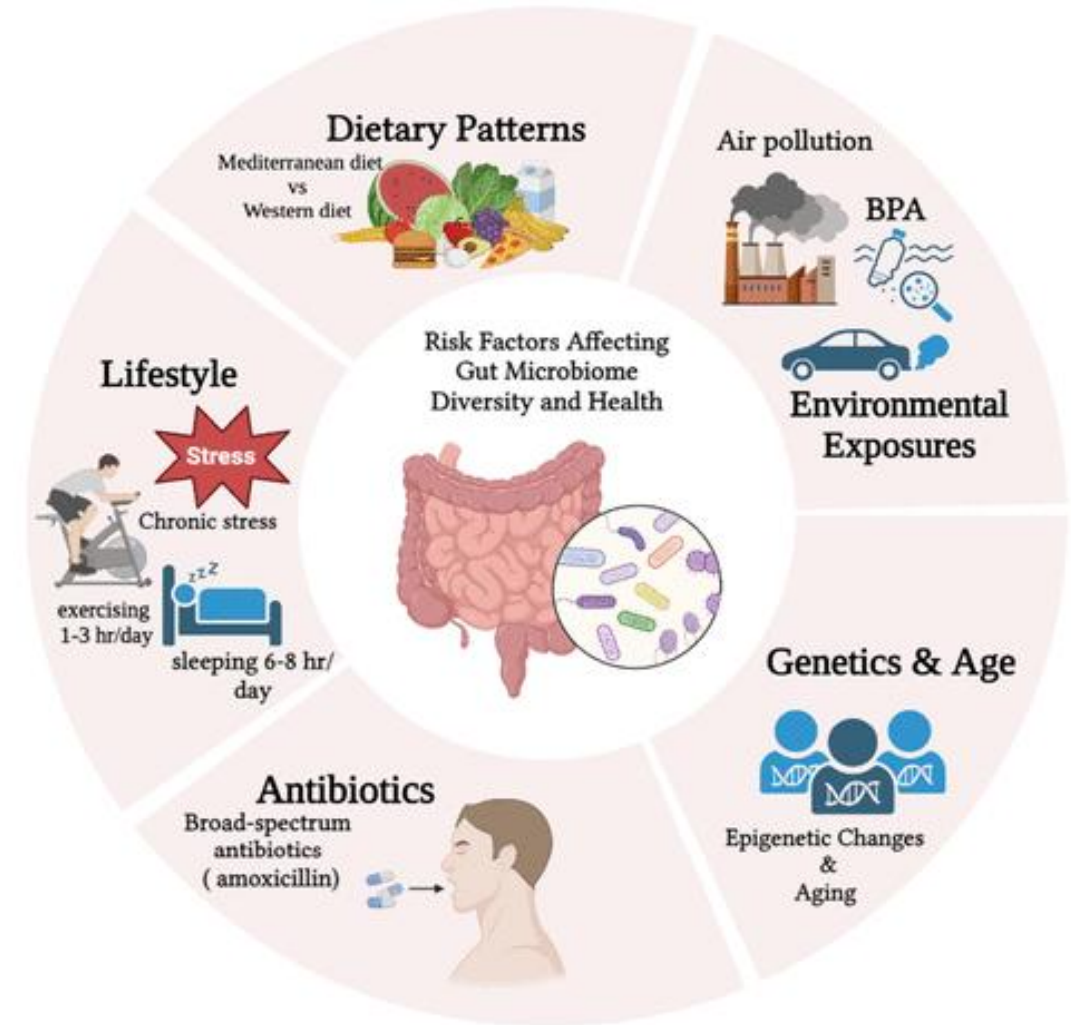
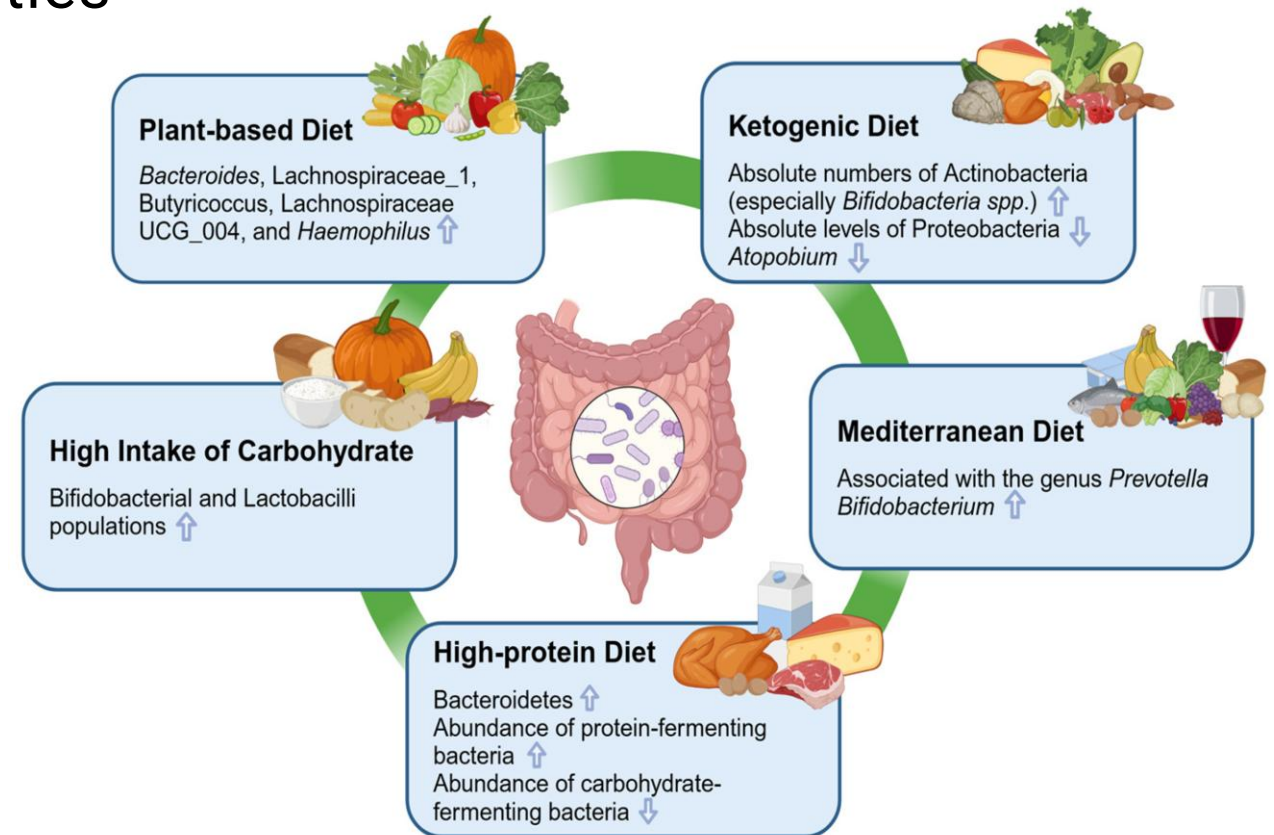


Figure. Almahal ZH, et al. *ACS Chem Neurosci*. 2025

Diet, microbiome and comorbidities

- Dietary patterns → changes to microbiome → systemic inflammation
- Drives development of comorbidities
 - Heart disease
 - Diabetes
 - Obesity
 - Arthritis
 - Depression, Anxiety
 - Neurocognition
 - Frailty
 - Autoimmune



Impact of gut health on ageing

- Gut microbiome of centenarians similar to young adults¹
 - Types of species
 - Species evenness
- Gut microbiota in centenarians associated with high antioxidant activities²
- Gut **virome** in centenarians is diverse with potential to modulate metabolism and promote healthy lifespan³
- Bile acid pathway metabolism in centenarians can reduce risk of infection and maintain intestinal balance⁴

Impact of HIV on the gut

- HIV infection leads to depletion of CD4+ T cells
- Disruption of gut-associated lymphoid tissue (GALT) → permeable intestinal barrier wall = microbial gut translocation
 - Bacterial products move from inside the intestine into the blood¹
 - Causes systemic inflammation²
- Can persist in those effectively treated with ART³

Impact of HIV on the gut microbiome

- People with HIV also have altered gut microbiome¹
 - Increase harmful bacteria and decrease beneficial bacteria
- Reasons for this include:
 - Translocation and systemic immune activation
 - Intestinal environment less hospitable to beneficial microbes
 - ART and other medications
 - Co-infections, e.g. hepatitis (gut-liver axis)

Knowledge gaps – ageing and the gut

- What role does gut health play in the link between HIV and biological ageing, and ageing-related comorbidities?
- Further research needed to establish how gut health affect:
 - Accelerated biological ageing
 - Related to systemic inflammation
 - Clinical ageing-related comorbidities
 - Cardiovascular disease, neurocognitive impairment, frailty
- Research in links between gut health and outcomes will help us:
 - Validate gut health and inflammatory biomarkers to **identify** individuals at higher risk of these outcomes
 - Identify new non-pharmaceutical **interventions** to reduce these diseases

Our research – current focus

- Ageing and comorbidities in PLHIV
 - Biological markers (e.g. cellular, molecular)
 - Inflammatory markers
 - Ageing outcomes (comorbidities, frailty, neurocognitive etc)
 - Context of wide-spread use of effective ART with shifting side effects
- Established ARCHIVE study
 - Age-related Clonal Haematopoiesis in an HIV Evaluation Cohort
 - 220 people with HIV, 226 people without HIV in Australia aged ≥ 55 years
 - Blood collected for genomic and inflammatory analysis
 - Self-reported questionnaire on health and lifestyle

Clonal haematopoiesis (CH)

- Expansion of clonal populations of blood cells derived from a single stem cell
 - When a blood cell gains a genetic mutation that causes it to grow more than other blood cells – grows into a population of cells with the same genetic mutation
- Driven by non-heritable mutations
- Occurs in ~10% of adults over 60 years

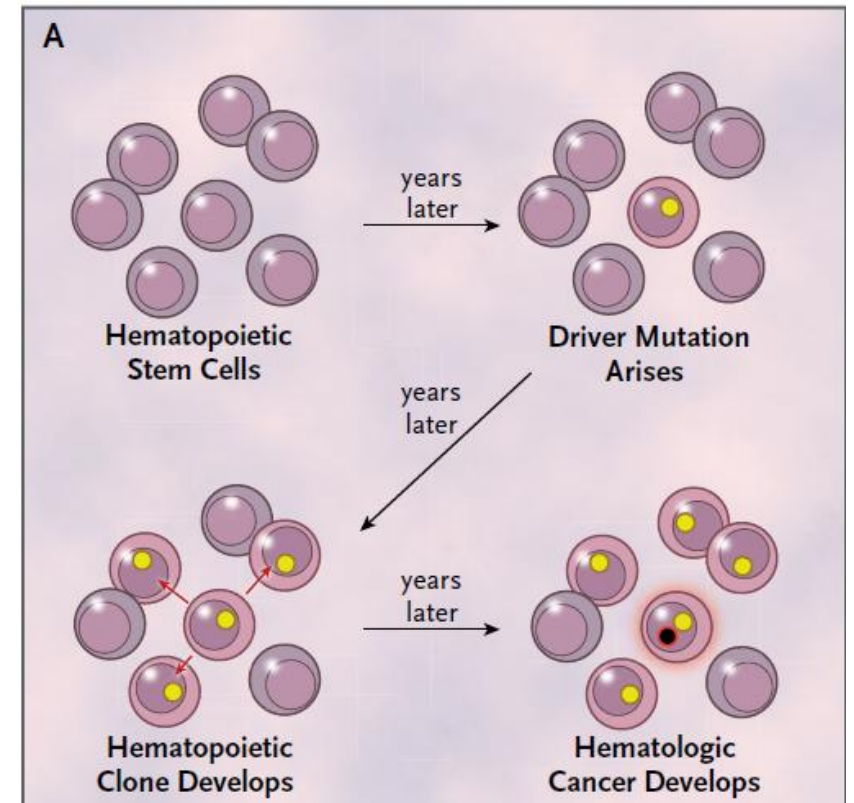
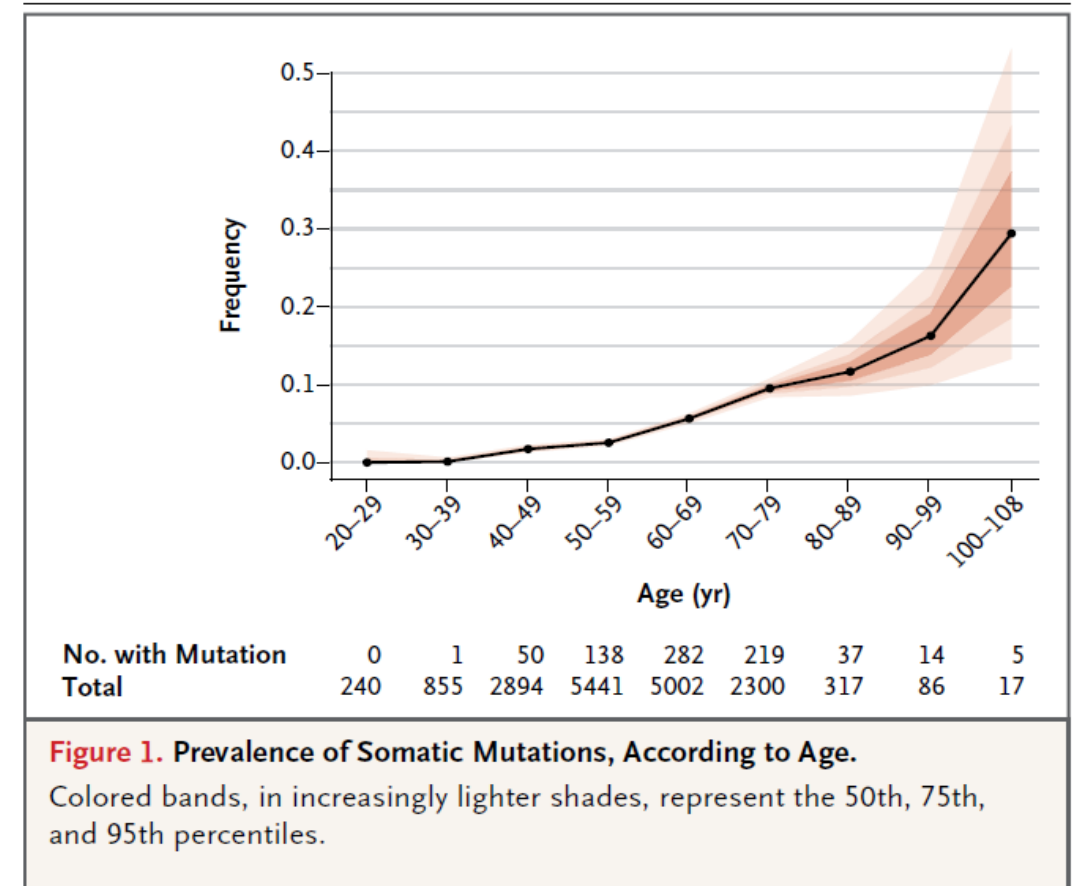


Figure. Genovese et al. *NEJM*. 2014;371:2477-87.

Clonal haematopoiesis (CH)

- Studies on CH the general population:
 - Increases with age
 - Associated with¹:
 - Blood cancers (11x)
 - Cardiovascular events (2x)
 - Stroke (2x)
 - All-cause mortality (1.4x)
 - Related to inflammatory marker dysregulation^{2,3}



Our research findings

- HIV is associated with increased risk of CH (2x)¹
- Associated with increased inflammatory biomarkers¹
- CH associated with frailty and reduced quality of life²

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HIV is associated with an increased risk of age-related clonal hematopoiesis among older adults

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Report

Age-related clonal hematopoiesis and HIV infection are associated with geriatric outcomes: The ARCHIVE study

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ARCHIVE Study Group

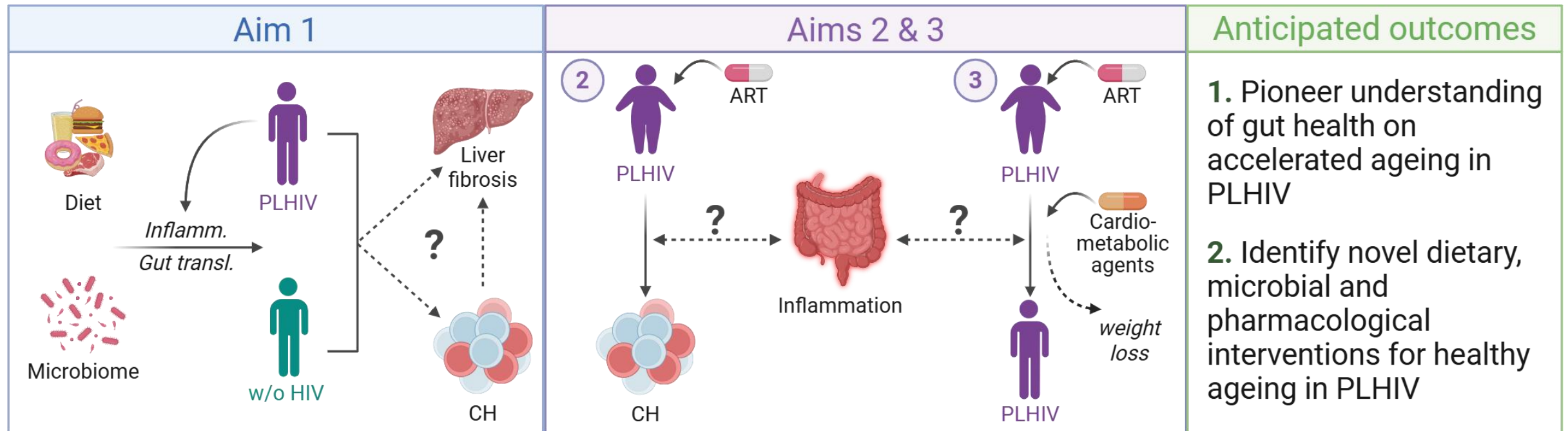
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Our research – additional findings

- Poor diet associated with CH
 - Increased red meat and processed foods
 - Very basic diet data collected
 - Non-significant trend
- CH associated with gut translocation markers
- CH associated with increased liver fibrosis
 - Measured by FIB-4 (calculated by blood markers)

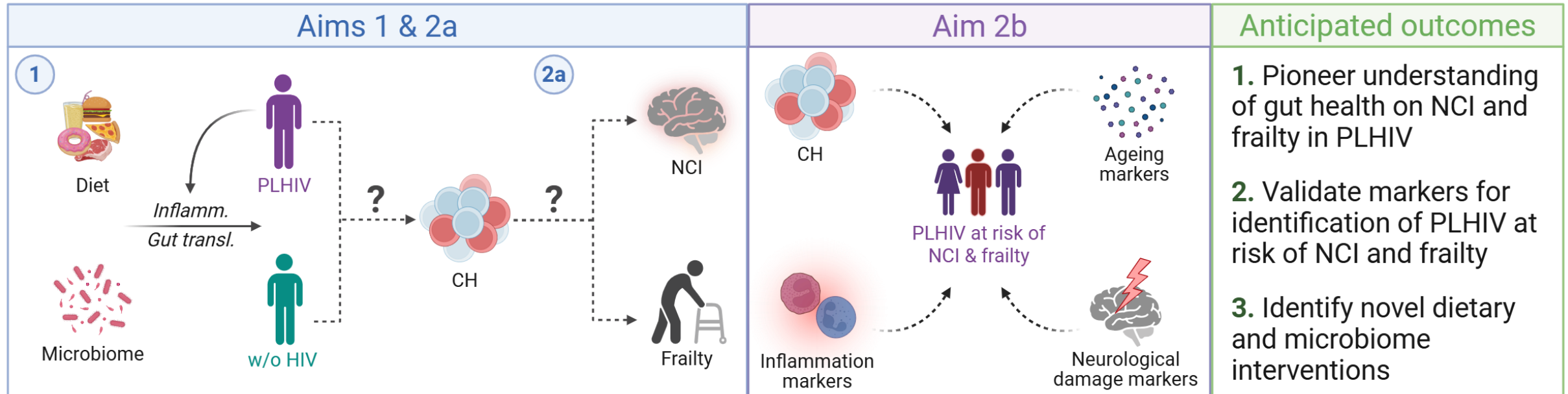
Our research – upcoming focus

- How does diet quality, gut inflammation and weight gain affect systemic inflammation and accelerated ageing in PLHIV?



Our research – upcoming focus

- How does diet quality and gut inflammation affect neurocognition and frailty in PLHIV?



Potential interventions to reduce gut inflammation and improve microbiome diversity

Lifestyle/behavioural

Diverse diet
Hydration
Exercise
Stress management

Supplements

Prebiotics
Probiotics
Synbiotics
Postbiotics
Antibiotics

Microbiota transplant

Colonoscopy
Enema
Capsule

Potential interventions to reduce gut inflammation and improve microbiome diversity

- FMT proven effective to treat persistent *C. diff* infection¹
- Further research exploring application of FMT on range of diseases
 - Autoimmune, e.g. IBD, IBS, MS, diabetes
 - Allergies
 - Depression and anxiety
 - + many more

Summary

- What we know about the impact of poor gut health in PLHIV:
 - Impacted by diet, microbiome, medications, lifestyle
 - Drives gut translocation leading to systemic inflammation
 - Associated with comorbidities
 - In PLHIV, it can persist despite effective treatment
- What we know about clonal haematopoiesis
 - Increased in PLHIV
 - Associated with inflammation and comorbidities
 - Gut health may be an important driver

Summary

- Where we plan to go next
 - Characterise diet, microbiome and gut translocation
 - Links to CH and other systemic inflammatory markers
 - Links to ageing-related clinical outcomes
 - Neurocognitive impairment
 - Frailty
 - Mental health
- Overall aim – slow biological ageing and reduce clinical comorbidities; improve quality of life through healthy ageing

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- Sarah-Jane Dawson

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Impact of poor gut health – biological measures

