



Alimentary Pharmabiotic Centre  
Interfacing Food and Medicine

# Diet-Microbiota Interactions and The Elderly

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<http://apc.ucc.ie>

<http://eldermet.ucc.ie>

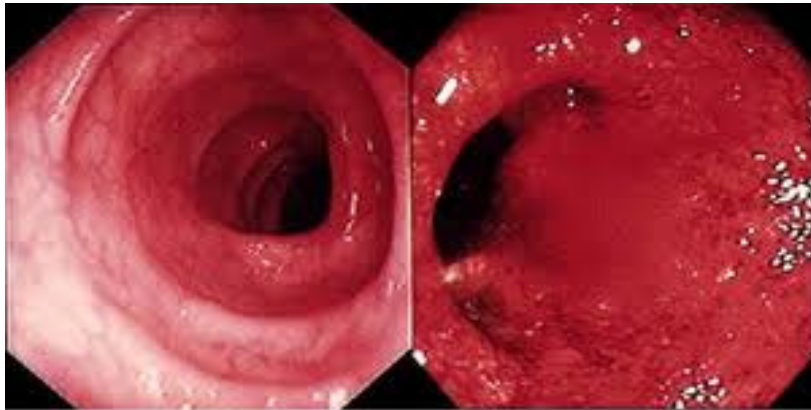


<http://apc.ucc.ie>

# The human gut microbiota

- *~10 times more bacterial cells in GIT than human cells in body*
- *~ 150 times more bacterial genes than human genes*
- *Perform a number of beneficial functions*
- *Variations in the gut microbiota in disease*

# Diseases with microbiota linkages



Healthy Colon

Ulcerative Colon



Irritable Bowel Syndrome



Obesity



## ***“Gut microbiota as an indicator and agent for nutritional health in elderly Irish subjects”***

### ***Why elderly?***

- Increasing proportion in population
- Increased susceptibility to infection
- Increased inflammatory status (Inflamm-aging)
- Changes in microbiota composition and activity
- Prospect of dietary modulation



# Eldermet dataset

- Data:
  - 178 elderly ( $\geq 65$  yrs) Irish subjects
    - 83 *Community-dwelling*
    - 20 *Day hospital (out-patient)*
    - 15 *Rehabilitation ( $\leq 6$  weeks)*
    - 60 *Long-stay ( $> 6$  weeks)*
    - (13 Young healthy controls)
  - Metabolomics (NMR)
  - 16S rDNA amplicons (454) & shotgun (Illumina) sequencing
  - Clinical Variables
    - BMI, frailty
    - malnourishment,
    - depression
    - cognitive function
    - dementia
  - No antibiotics treatment  $\leq 1$  month prior sampling
  - Dietary data
    - 168 elderly subjects
    - food frequency questionnaire (FFQ), 147-item, weighted by 10 consumption frequencies

## Gut microbiota composition correlates with diet and health in the elderly

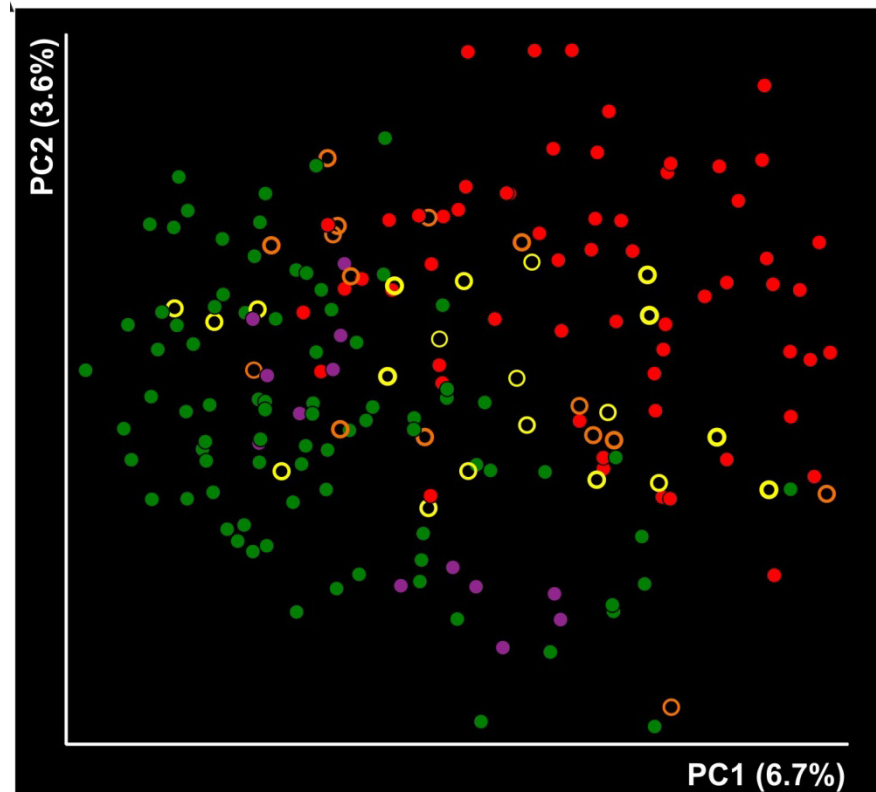
Marcus J. Claesson<sup>1,2\*</sup>, Ian B. Jeffery<sup>1,2\*</sup>, Susana Conde<sup>3</sup>, Susan E. Power<sup>4</sup>, Eibhlís M. O'Connor<sup>1,2</sup>, Siobhán Cusack<sup>1</sup>, Hugh M. B. Harris<sup>1</sup>, Mairead Coakley<sup>4</sup>, Bhuvaneshwari Lakshminarayanan<sup>4</sup>, Orla O'Sullivan<sup>4</sup>, Gerald F. Fitzgerald<sup>1,2</sup>, Jennifer Deane<sup>1</sup>, Michael O'Connor<sup>5,6</sup>, Norma Harnedy<sup>5,6</sup>, Kieran O'Connor<sup>6,7,8</sup>, Denis O'Mahony<sup>5,6,8</sup>, Douwe van Sinderen<sup>1,2</sup>, Martina Wallace<sup>9</sup>, Lorraine Brennan<sup>9</sup>, Catherine Stanton<sup>2,4</sup>, Julian R. Marchesi<sup>10</sup>, Anthony P. Fitzgerald<sup>3,11</sup>, Fergus Shanahan<sup>2,12</sup>, Colin Hill<sup>1,2</sup>, R. Paul Ross<sup>2,4</sup> & Paul W. O'Toole<sup>1,2</sup>



# Subjects separate by community location

5.4 million 16S rDNA reads => 47,500 OTUs

## Unweighted UniFrac OTU PCoA



Community

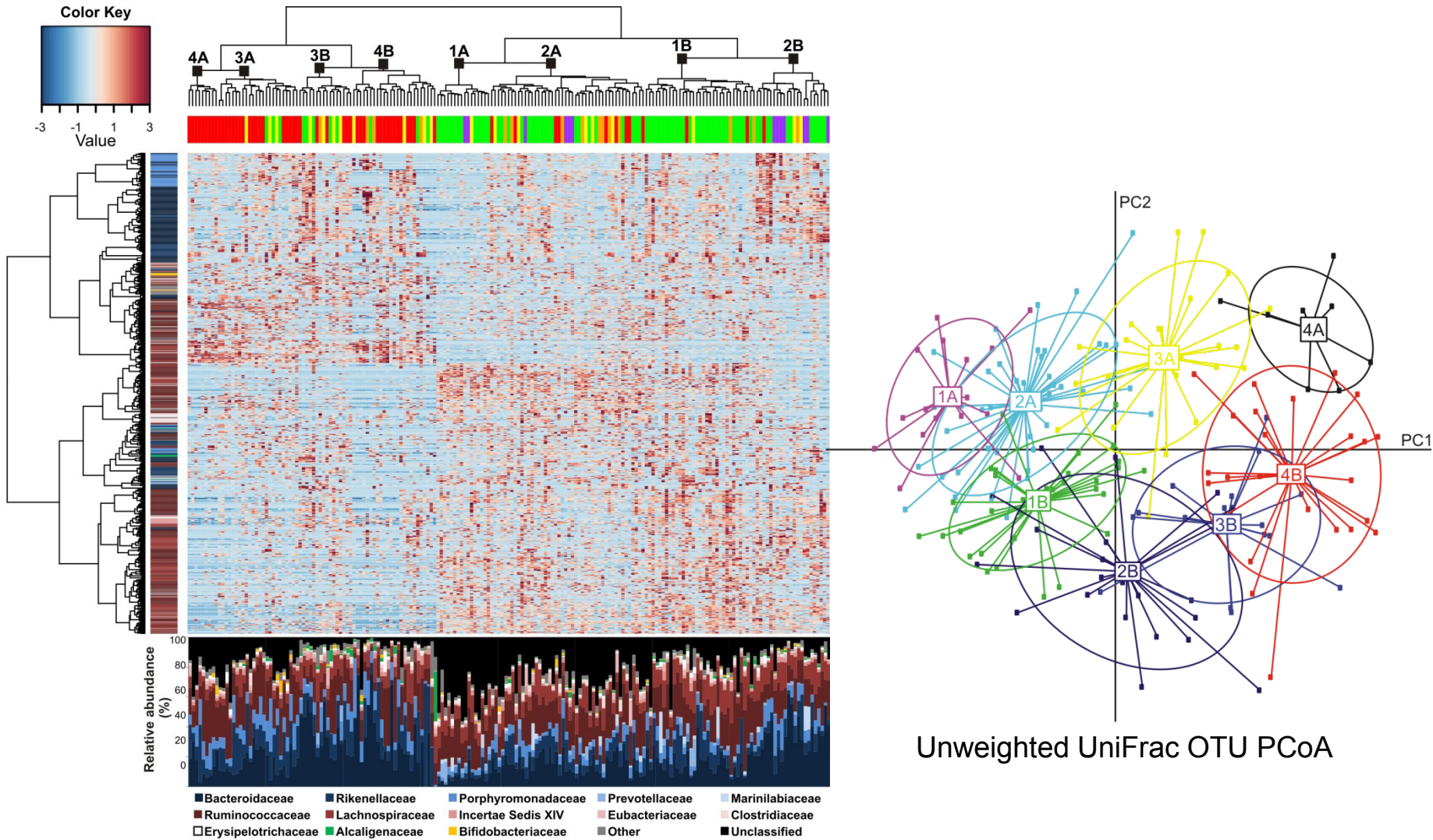
Day Hospital

Rehab

Long-stay

Young control

# Subjects separated by community location



Unweighted UniFrac OTU PCoA

Hierarchical Ward-linkage clustering based on Spearman correlation coefficients of the proportion of OTUs for each subject

# What impact has diet on microbiota?

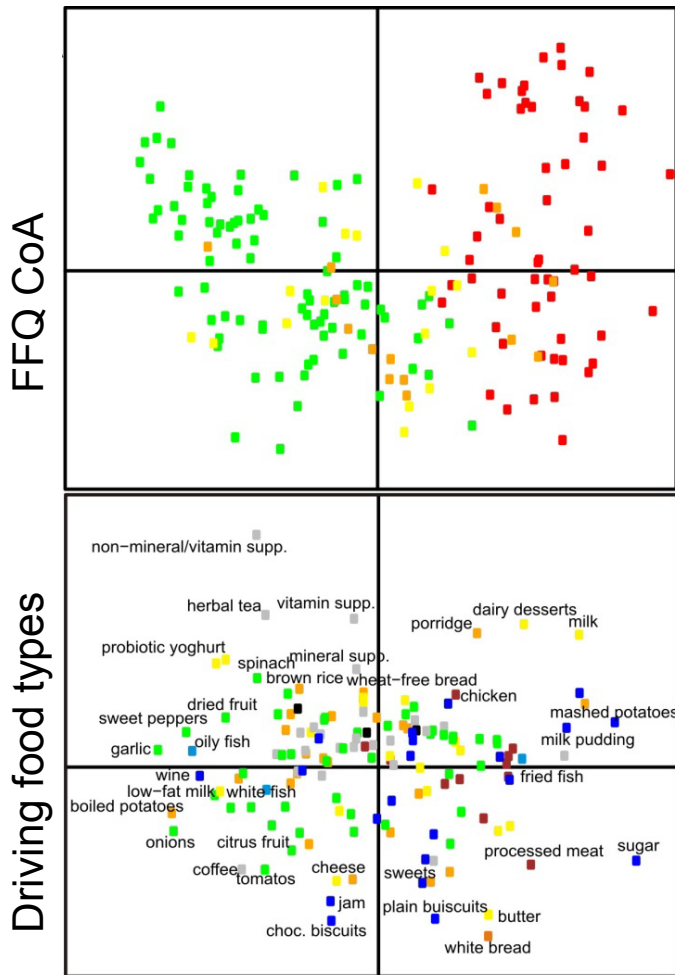
## *Food Frequency Questionnaire (FFQ)*

- *Long-term dietary habits*
- *FFQ data for 96% elderly subjects*
- *147 food types (beef/apples/white rice/potatoes/milk/porridge etc)*
- *Healthy Food Diversity (HFD): how diverse AND healthy a diet is*

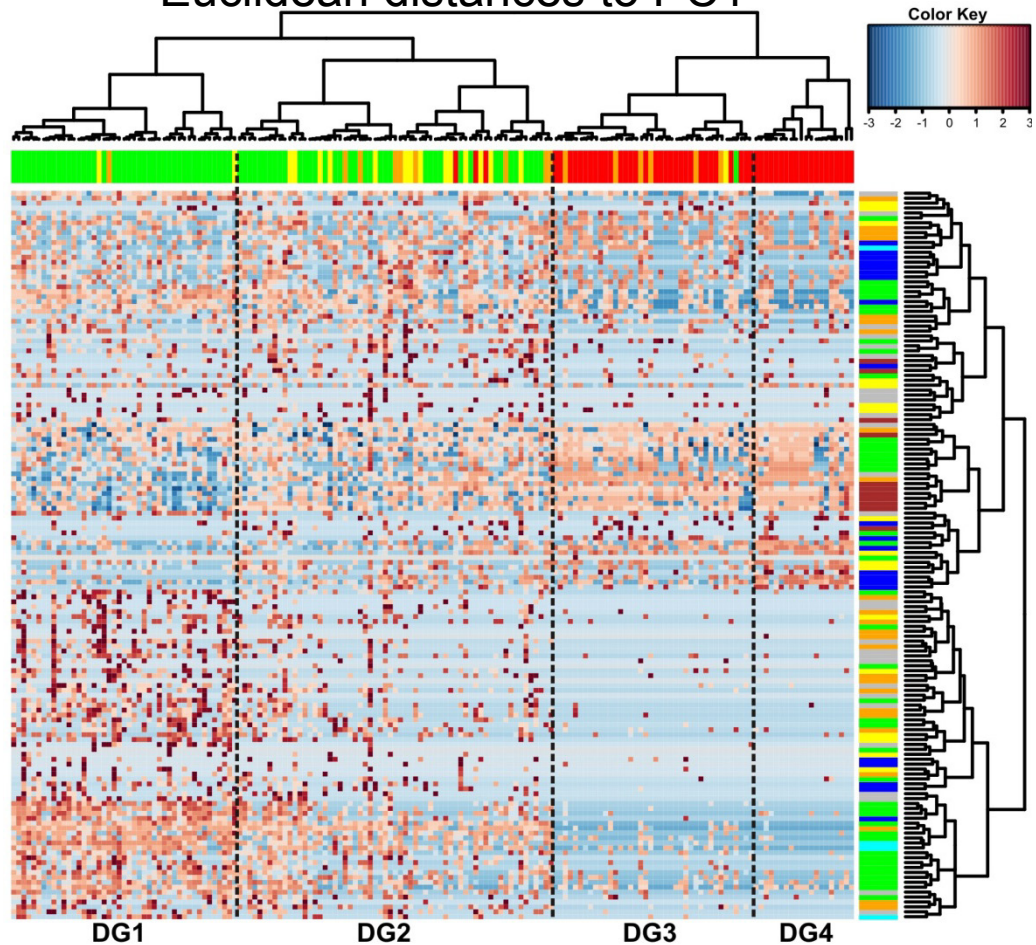


# FFQ multivariate analysis

Correspondence analysis



Complete-linkage clustering based on Euclidean distances to PC1

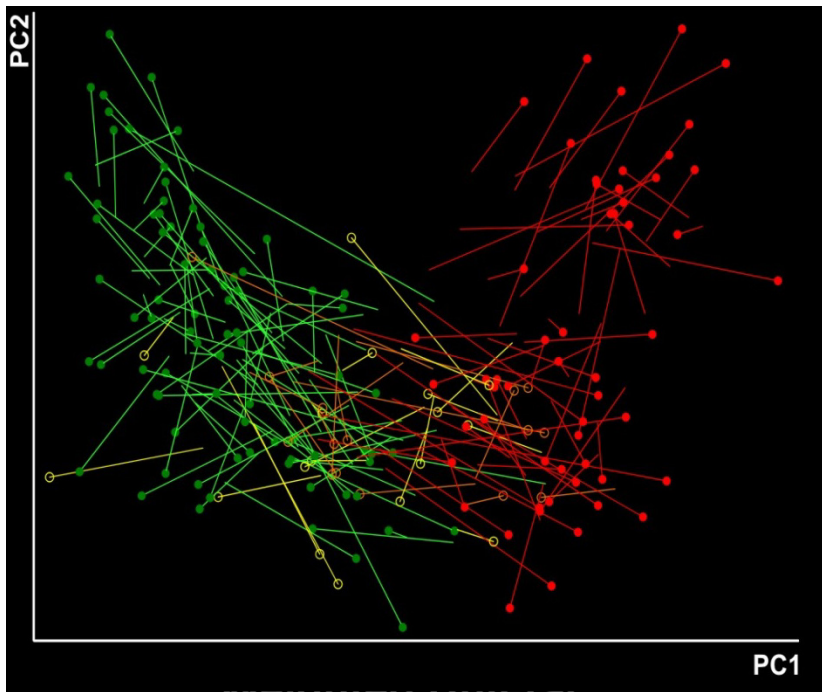


DG1: “low fat / high fibre”  
 DG2: “moderate fat and fibre”

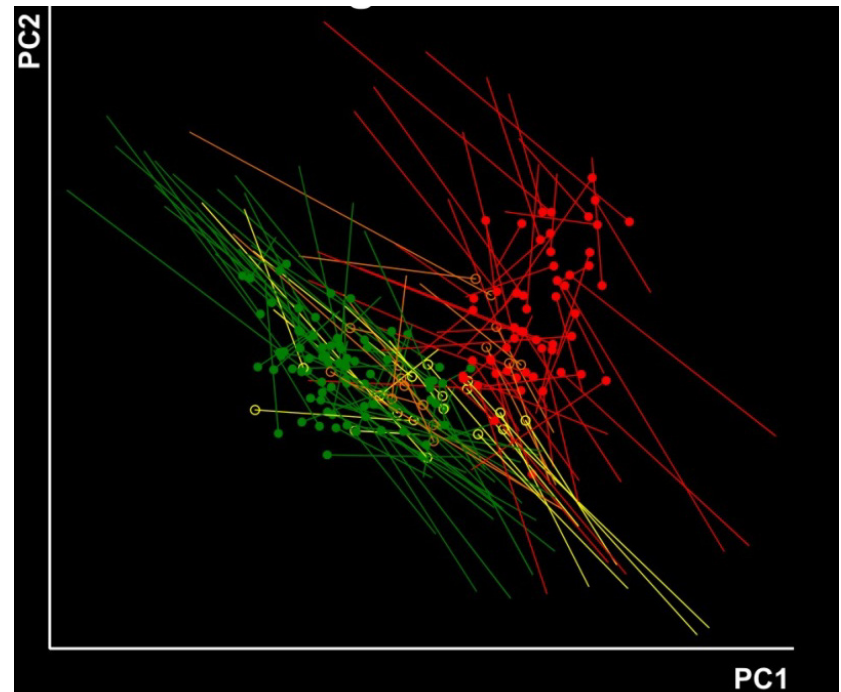
DG3: “moderate fat / low fibre”  
 DG4: “high fat / moderate fibre”

# Microbiota & diet by community location

Unweighted UniFrac PCoA vs. FFQ PCA



Weighted UniFrac PCoA vs. FFQ PCA



Diet

Microbiota

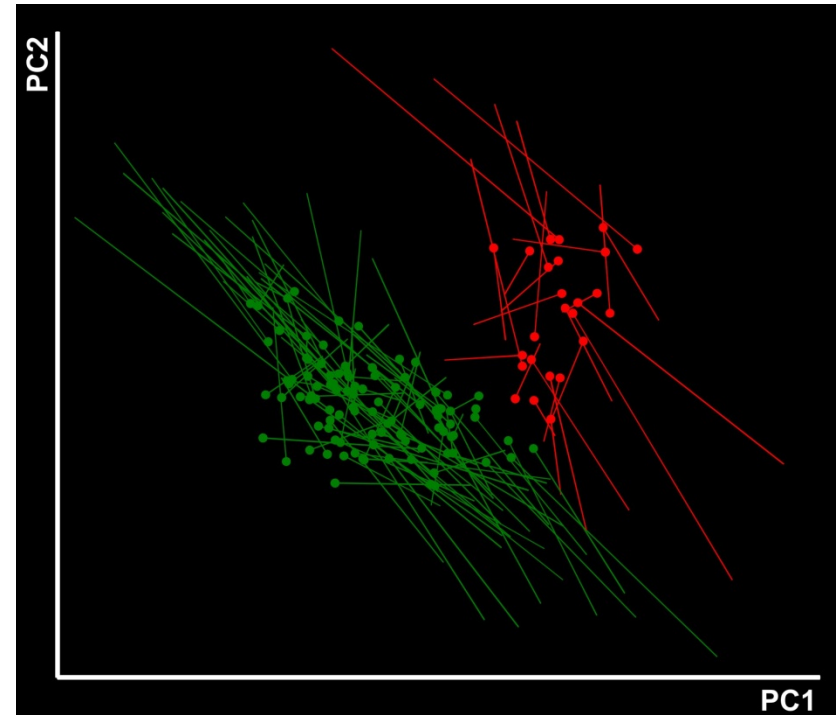
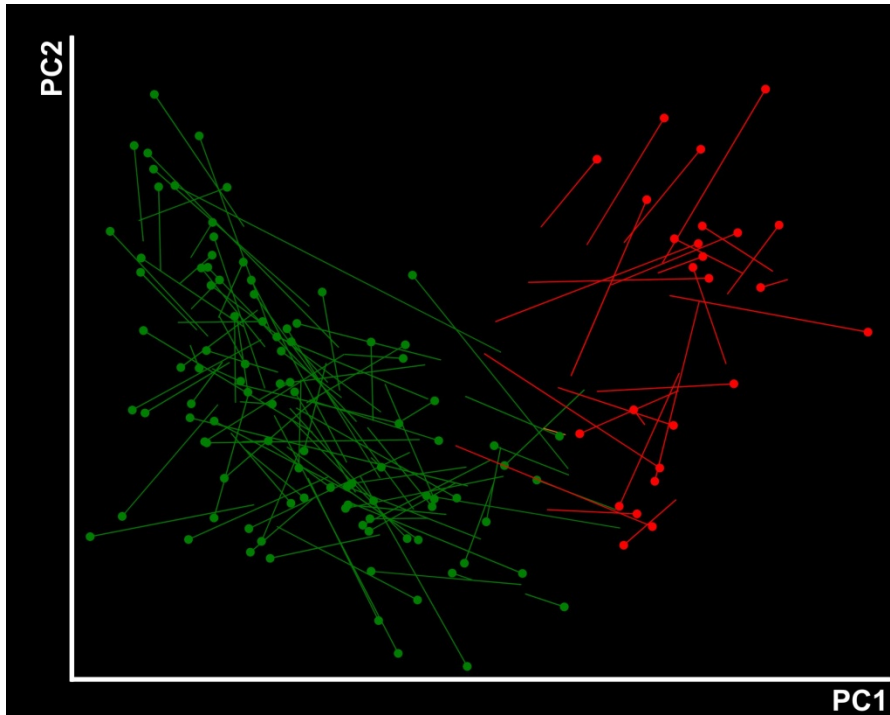
Community

Day Hospital

Rehab

Long-stay

# Microbiota & diet by duration in long-stay care



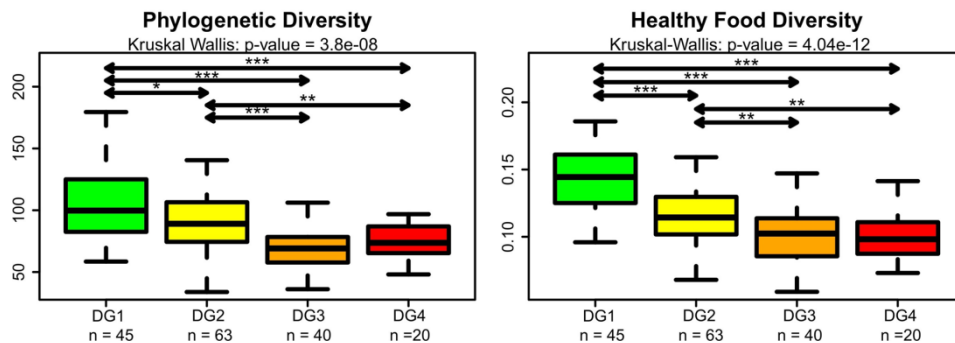
Diet ————— Microbiota

N/A (C+DH)

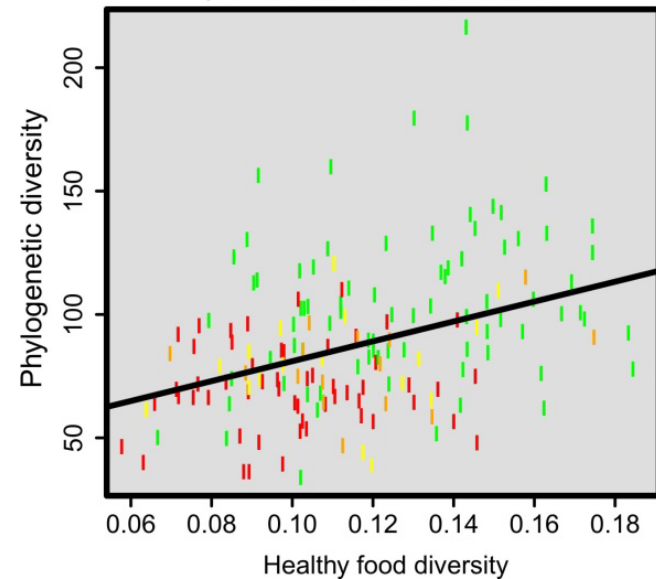
Year 1+

# Diversity of microbiota and diet

- Healthy Food Diversity index (HFD) showed that it positively correlated with microbial diversity indices

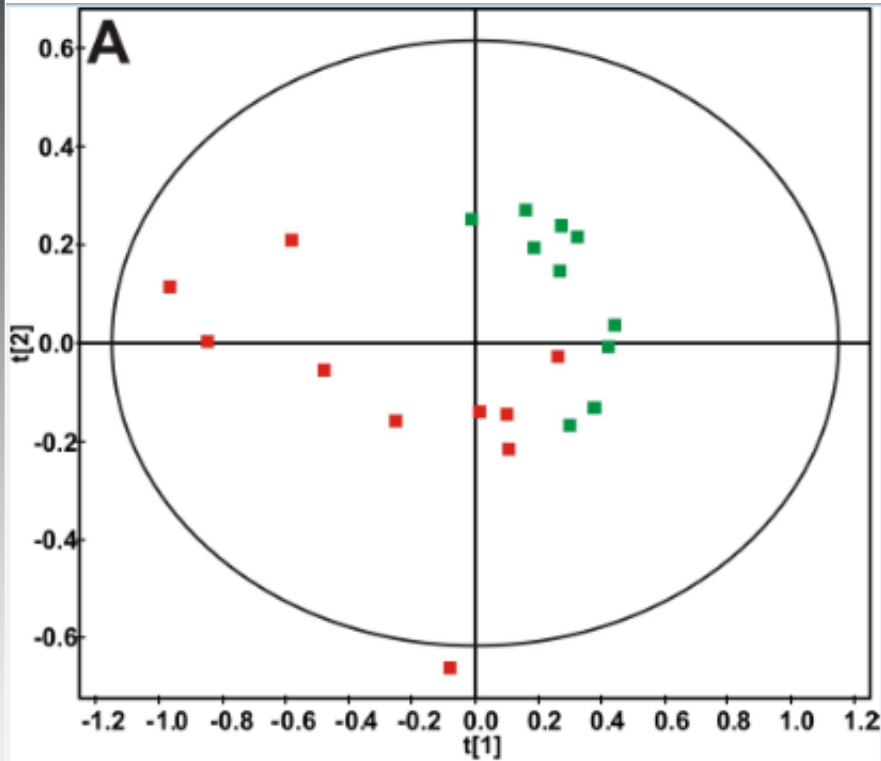


Phylogenetic Diversity vs. Healthy Food Diversity  
p-value = 3.46e-07 R = 0.381



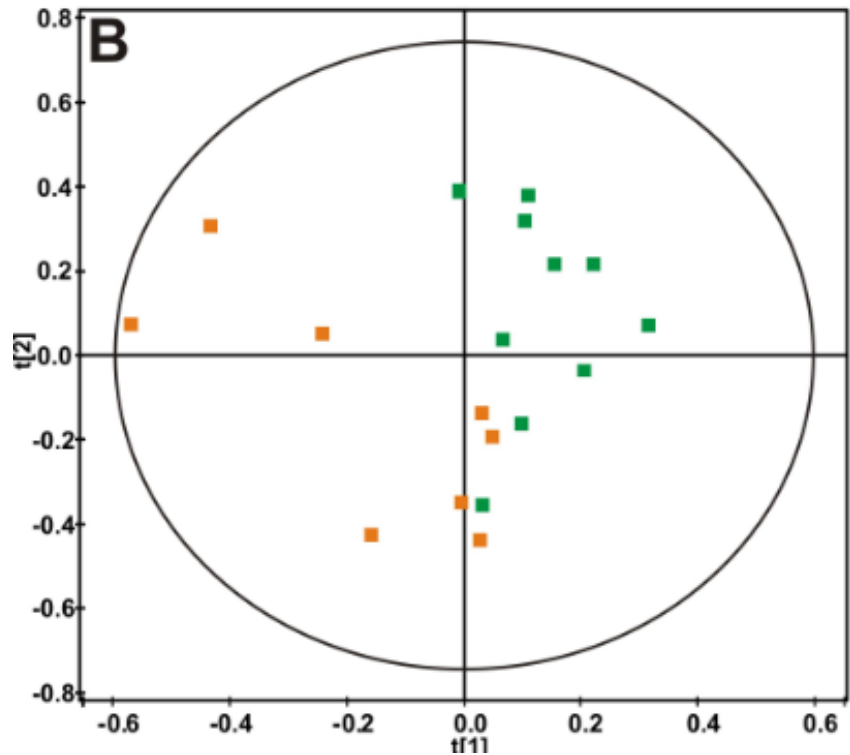
- Significant differences across the four groups, suggest that a healthy diverse diet promotes a more diverse gut microbiota.

# Separation of residence location by faecal water NMR metabolome



Long-stay

Community

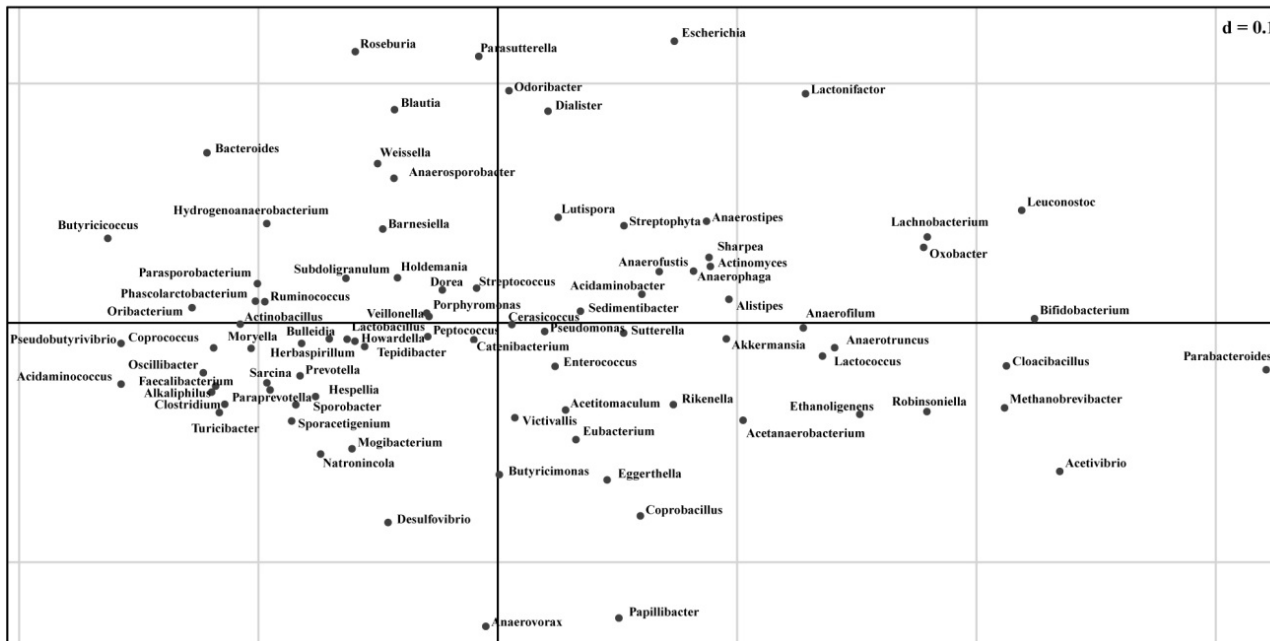
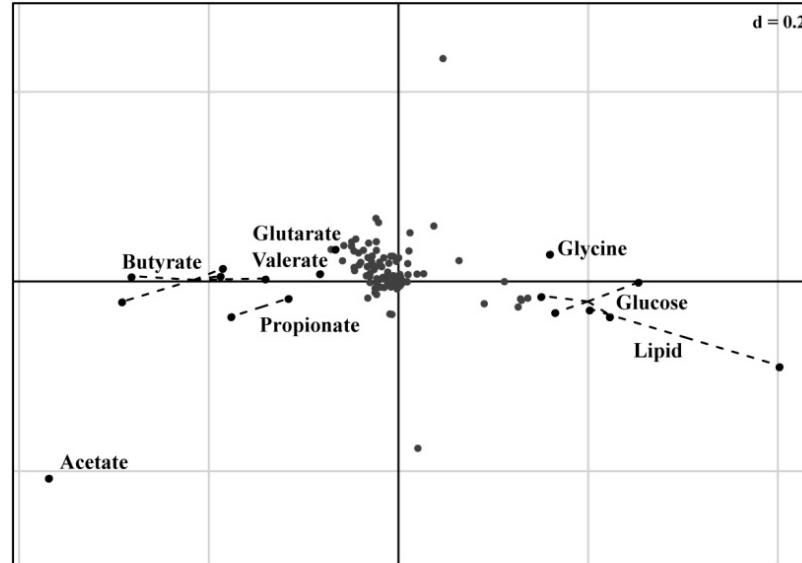
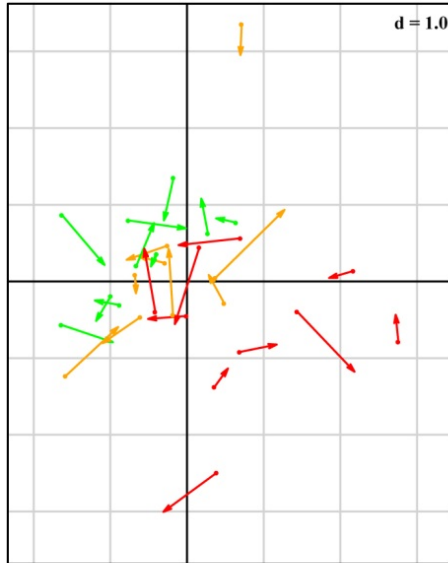


Rehab

Community



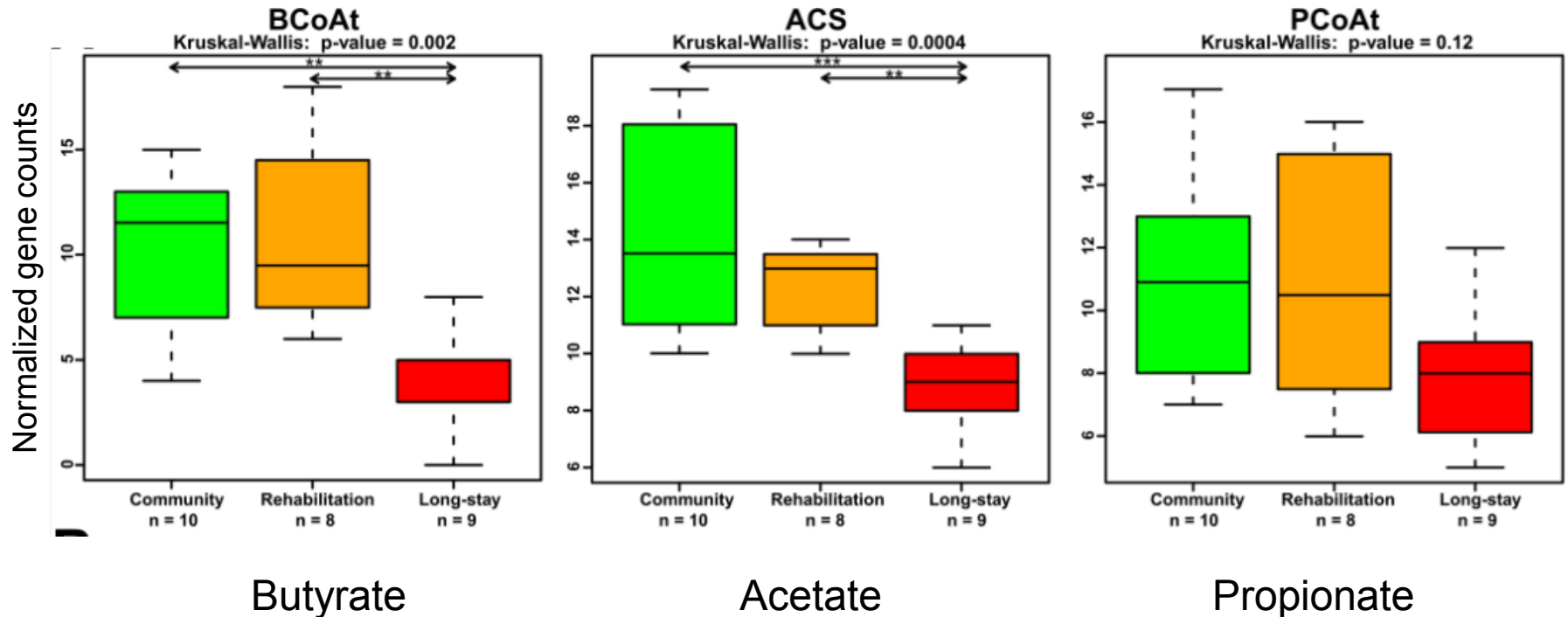
# Integrating metabolome, metabolites & genus-level microbiota



Co-inertia of  
microbiota &  
metabolome →  
by location

NMR spectrum  
metabolite PCA

# Shotgun metagenome: differentially abundant SCFA genes



- BCoAt: Butyryl-CoA transferase/Acetyl-CoA hydrolase
- ACS: Acetate-formyltetrahydrofolate synthetase/Formate-tetrahydrofolate ligase
- PCoAt: Propionyl-CoA:succinate-CoA transferase/Propionate CoA-transferase

# Microbiota-health correlations

## *Health/clinical markers*

- *BMI: Body Mass Index*
- *CC: Calf Circumference*
- *MAC: Mid-Arm Circumference*
- *SBP: Systolic Blood Pressure*
- *DBP: Diastolic Blood Pressure*
- *CCI: Charlson Index of Comorbidity*
- *Barthel Index of Activities of Daily Living*
- *FIM: Functional Independence Measure*
- *MMSE: Mini-Mental State Exam*
- *MNA: Mini-Nutritional Assessment*

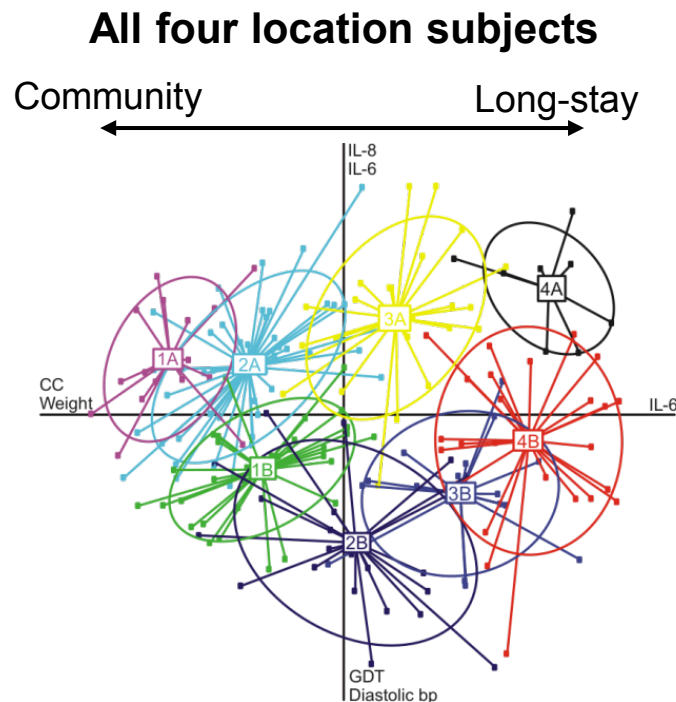
## *Possible confounders*

- *Antibiotics:*
  - *Exclude <1 mo*
  - *>1 mo had no sign. effect on  $\mu$ -biota ( $\alpha$ - or  $\beta$ -diversity)*
- *Quantile regression model adjusted for:*
  - *Age*
  - *Gender*
  - *Location*
  - *Medication*



# Microbiota separation correlates with health measures

## Location-specific unweighted UniFrac PCoAs



*Following adjustment for age/gender/location/medication, microbiota correlates significantly with e.g. frailty and inflammation. Prospective studies needed to establish causality.*

# Microbiota separation correlates with health measures

## Location-specific unweighted UniFrac PCoAs

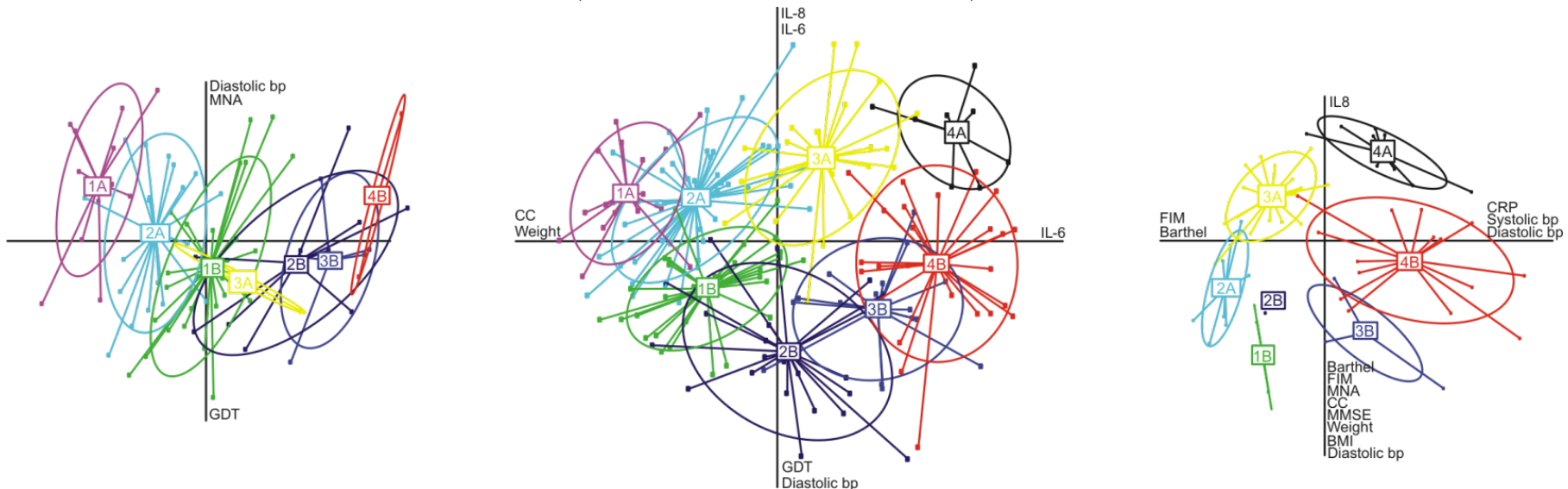
All four location subjects

Community-only subjects

Community

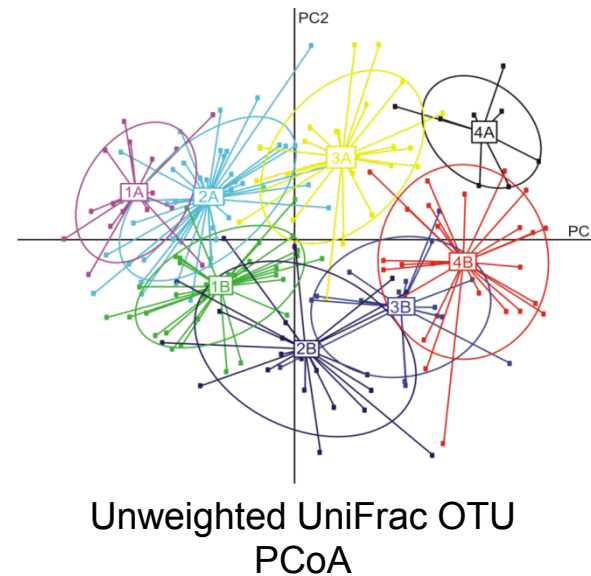
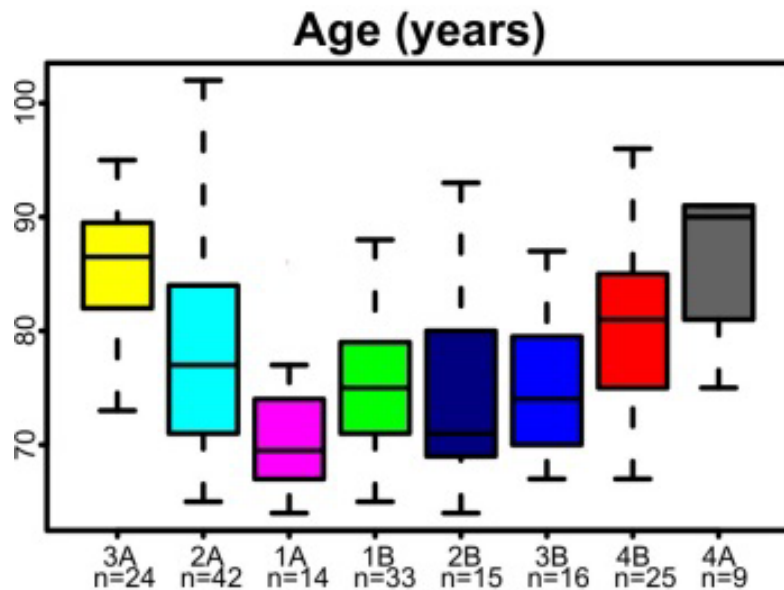
Long-stay

Long-stay-only subjects

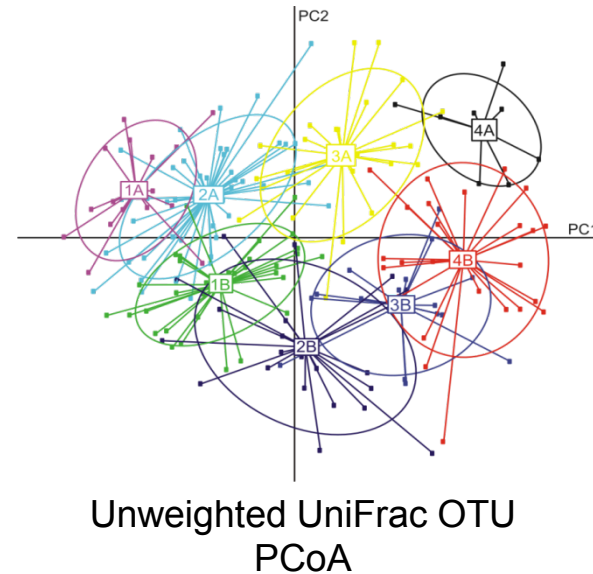
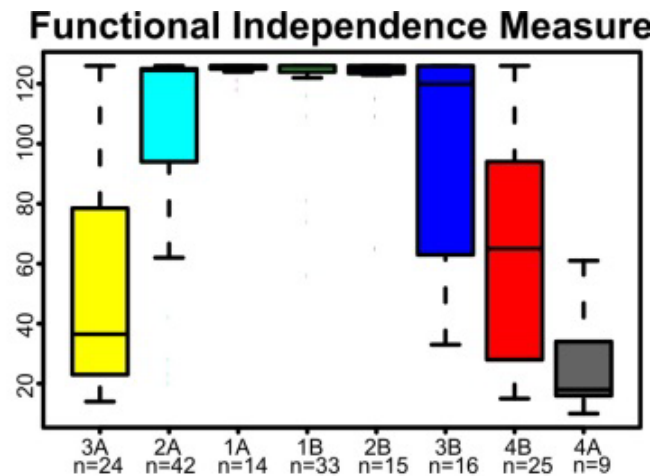
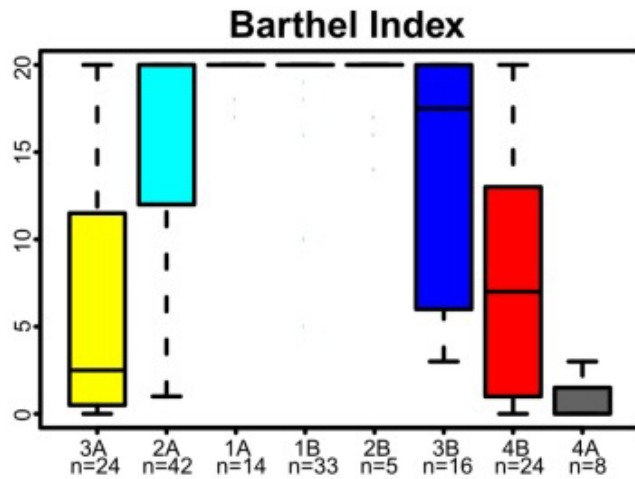


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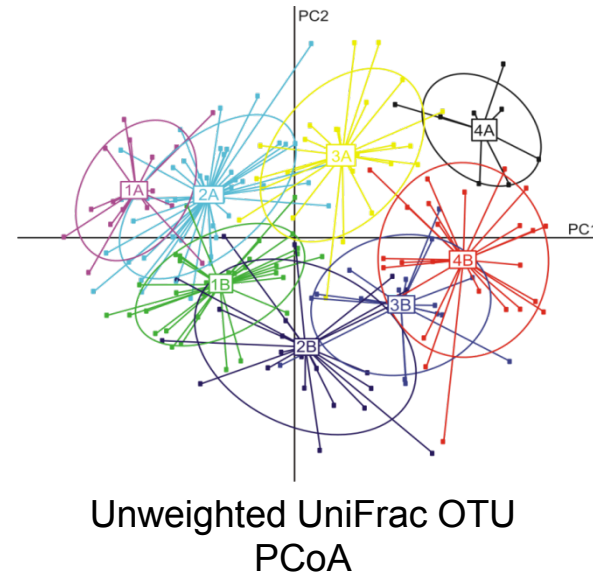
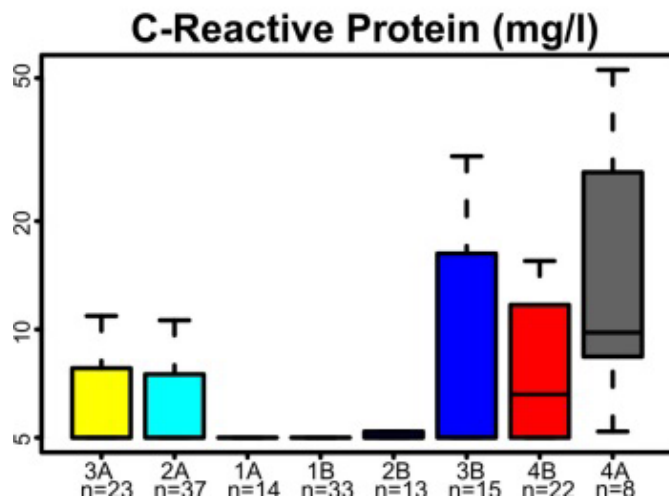
# Microbiota clustering correlates with health measures



# Microbiota clustering correlates with health measures



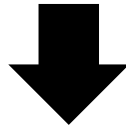
# Microbiota clustering correlates with health measures



# Summary

*(Claesson, Jeffery et al., 2012 Nature)*

- *Microbiota in elderly is different depending on community location*
- *Driven by habitual diet*
- *Microbiota alterations correlate with health changes especially in long-stay*



***Diet shapes gut microbiota, which may impact on health in elderly people***

*May lead to carefully designed dietary interventions to promote healthier aging*



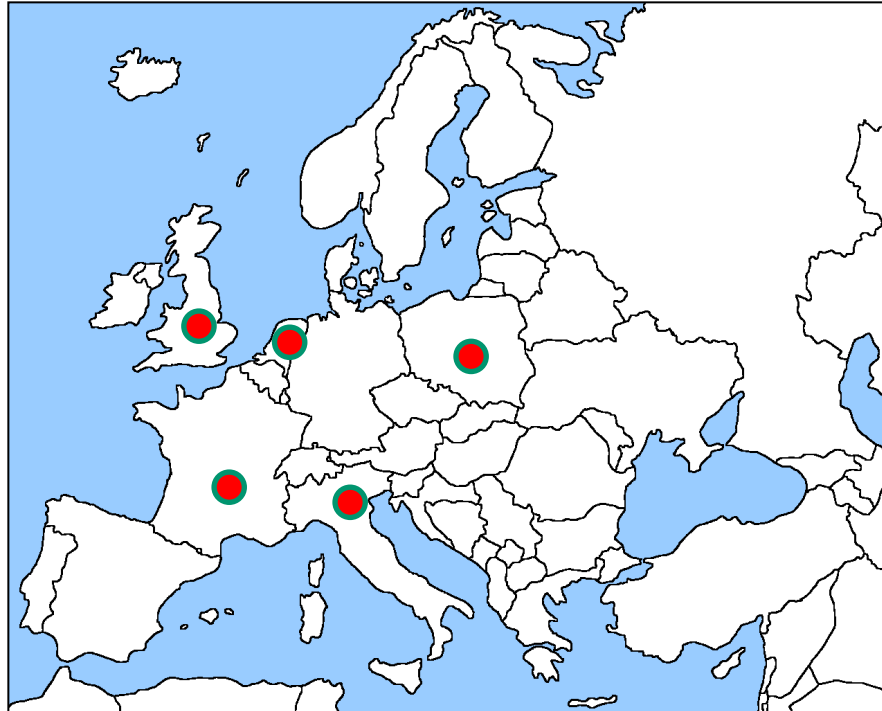
NU-AGE



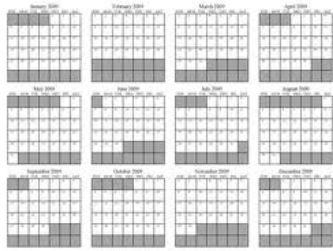
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UNIVERSITÀ DI BOLOGNA

n = 1,250

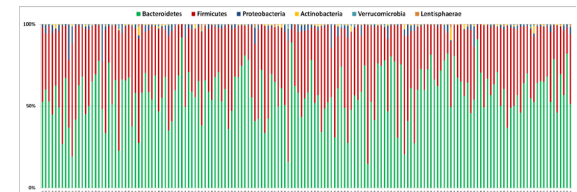
UK, NL, FR,  
IT, PL



T<sub>0</sub>



12 mo.'s



5 x 25 subjects

# Challenges

- *Microbiota modulation / restoration*
  - *Prospective / longitudinal studies*
  - *Interventions*
- *Intergrated metabolomics, nutritional and microbial datasets*
- *Dietary guidelines informed by microbiota needs*



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Interfacing Food and Medicine



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Bhuna Laks  
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# Microbiota clustering correlates with health measures

