Akkermansia muciniphila and its association with obesity in Australian men

Jessica A Davis[1], Fiona Collier[2,3] Amanda L Stuart[4], Mohammadreza Mohebbi[5], Amy Loughman[1], Julie A Pasco[3,4,6,7] & Felice N Jacka[1]

[1]Deakin University, Food & Mood Centre, IMPACT Strategic Research Centre, School of Medicine, Barwon Health, Geelong, Australia, [2]Deakin University, Geelong, Australia, [3]Barwon Health, Geelong, Australia,
[4] IMPACT Strategic Research Centre, School of Medicine Deakin University, Geelong, Australia, [5]Biostatistics Unit, Faculty of Health, Deakin University, Geelong, Australia, [6]Department of Clinical Epidemiology, Monash University, Prahran, Australia,
[7]Melbourne Medical School-Western Campus, The University of Melbourne, Melbourne, Australia

INTRODUCTION

Obesity represents one of Australia's leading risk factors for burden of disease and is associated with various chronic health conditions including type 2 diabetes mellitus (T2DM), cancers, and cardiovascular disease, which is the leading cause of death worldwide. Increasing evidence suggests differences in the gut microbiota of lean and obese individuals. *Akkermansia muciniphila (A. muciniphila)* is a mucin-degrading bacterium from the *Verrucomicrobia* phylum found in the intestinal lining, and accounts for 1-3% of total intestinal microbiota in healthy adults. Animal and human studies have found that lower relative abundance of *A. muciniphila* correlates with obesity and unhealthy metabolic markers including fasting glucose, insulin sensitivity, and low-density lipoprotein cholesterol. One explanation for this association may be that increased *A. muciniphila* improves integrity of the intestinal lining and reduces permeability of endotoxins which have been associated with the chronic inflammation copresent in obesity **(Fig. 1)**.

While previous literature has assessed the relationship between body composition and *A. muciniphila*, no human research has considered diet quality despite the the clear relevance of diet quality to metabolic health and gut microbiome composition.

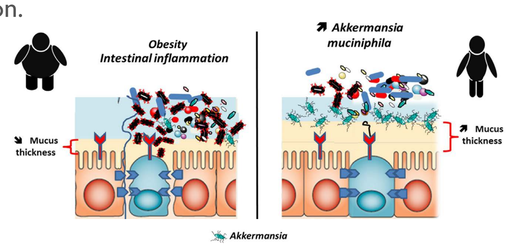

Figure 1. Effects of *A. muciniphila* on host intestinal barrier. Adapted from Cani et al. 2017.

AIM

This study aimed to investigate relative abundance of *A. muciniphila* in relation to body composition in Australian men, taking into account measures of diet quality.

METHODS

Design: This cross-sectional study was conducted within the ongoing Geelong Osteoporosis Study where clinical and lifestyle data were collected from the most recent male follow-up, and from this a sample of 159 men was compiled.

Microbiota profiling: 16S rRNA diversity profile sequencing was performed on DNA extracted from stool samples to determine the relative abundance of *A. muciniphila*.

Outcome measures: Android and gynoid fat percentage from dual-energy X-ray absorptiometry scans and body mass index (BMI) were used as outcome measures in regression analyses.

Covariates: Potential confounders/effect modifiers included but were not limited to measures of diet, medication use, physical activity levels, and smoking status.

RESULTS

- Of participants (mean age 65.9yr, range 34.2-92.2yr), 126 (79%) were overweight/obese and 33 (21%) were non-overweight/obese.
- 95% of men had some *A. muciniphila* in their stool and the distribution of the log transformed relative abundance was bimodal **(Fig. 2)**. Based on this distribution two categories were developed: 1) low abundance < 0.1% *A. muciniphila* and 2) high abundance ≥ 0.1%.
- Reflux medication was identified as a confounder for *A. muciniphila* and gynoid fat, however no other correlations were observed with *A. muciniphila* **(Table 1)**.
- A significant, inverse relationship was observed between *A. muciniphila* and BMI (-1.73 (95% CI -3.03, -0.42), p=0.010)) **(Fig. 3a)**, android fat (-3.84% (95% CI -6.97, -0.72), p=0.016)) **(Fig. 3b)**, and gynoid fat (-0.02% (95% CI -0.04, 0.00), p=0.047)) **(Fig. 3c)** adjusted for age. However, the association between *A. muciniphila* and gynoid fat was not statistically significant when also adjusted for reflux medications (p=0.065).

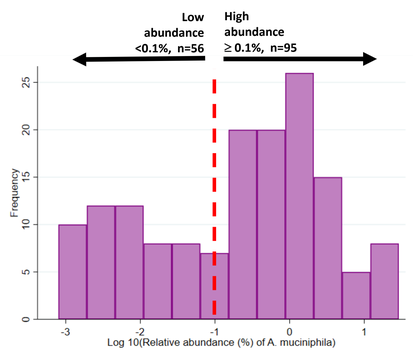

Figure 2. Bimodal distribution of $\log^{10}$ transformed relative abundance of *A. muciniphila* generated a clear cut-off for low and high abundance

Table 1. Spearman rank-order correlation of potential confounders and relative abundance of *A. muciniphila*, BMI, android fat, and gynoid fat

Potential confounders	Relative abundance of *A. muciniphila* (r_s)	p value	BMI (r_s)	p value	Android fat (r_s)	p value	Gynoid fat (r_s)	p value
Age	0.063	NS	0.078	NS	0.115	NS	0.119	NS
Energy	-0.100	NS	0.007	NS	-0.018	NS	0.024	NS
DQS	0.038	NS	-0.016	NS	**-0.181**	**0.023***	-0.071	NS
Physical activity	-0.030	NS	0.028	NS	0.238	NS	**0.286**	**<0.001****
Smoker	0.021	NS	-0.121	NS	**-0.180**	**0.023***	**-0.165**	**0.038**
Med. T2DM	-0.068	NS	0.097	NS	0.066	NS	0.097	NS
Med. antibiotics	0.091	NS	0.083	NS	-0.025	NS	0.083	NS
Med. reflux	**-0.182**	**0.021***	0.140	NS	0.211	NS	**0.171**	**0.031***
Med. bowel	-0.026	NS	0.072	NS	0.050	NS	-0.004	NS
Fibre	-0.033	NS	-0.083	NS	-0.121	NS	-0.083	NS
SFA	-0.148	NS	0.037	NS	-0.003	NS	0.014	NS
PUFA	-0.061	NS	-0.013	NS	-0.083	NS	-0.013	NS
MUFA	-0.100	NS	-0.023	NS	-0.056	NS	-0.023	NS
Protein	-0.076	NS	-0.007	NS	-0.084	NS	-0.066	NS
Fruit and veg	0.080	NS	-0.078	NS	-0.080	NS	-0.106	NS

* p<0.05. **p<0.001

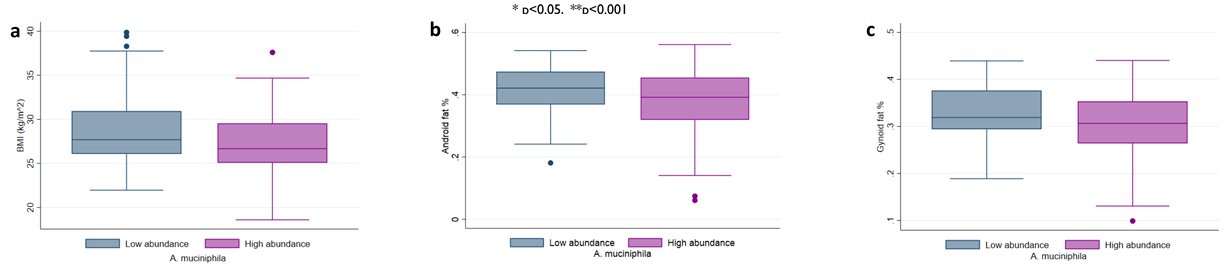

Figure 3. Box plot graph displaying the association between categorised *A. muciniphila* (negligible and detectable) and obesity measures. **a.** Association between relative abundance of *A. muciniphila* and BMI. **b.** Association between relative abundance of *A. muciniphila* and android fat **c.** Association between relative abundance of *A. muciniphila* and gynoid fat

CONCLUSIONS

Results from the current study suggest that the relative abundance of *A. muciniphila* was significantly, inversely associated with BMI and android fat percentage in our sample of Australian men when adjusted for age. While no dietary associations were evident, reflux medication was identified as a confounder in the relationship between *A. muciniphila* and gynoid fat which supports previous research suggesting that use of protein pump inhibitors may impact the microbiome. Further research is required to establish whether this association between *A. muciniphila* and body composition is causal. If so, the use of *A. muciniphila* as a therapeutic, or lifestyle and dietary adjustments to encourage increased relative abundance of *A. muciniphila*, may provide a potential non-invasive intervention for obesity. Future research addressing obesity prevention and treatment strategies may benefit from more in-depth analysis of *A. muciniphila*'s role in gut microbiota composition, inflammation and obesity-related endotoxemia.

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