



# An estimate of the causal influence of body mass index on gut microbiome variation

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Poster link



SCAN ME

## Introduction

Variation in the accumulation of body fat, body composition, and obesity can all be proxied by body mass index (BMI) which itself is a recognized risk factor for numerous health outcomes. What remains unclear is the complete picture of factors influencing BMI. One possible factor is gut microbiome variation, which previous research has demonstrated to be strongly correlated with BMI. Critically, whilst it may be the case that human gut flora variation influences BMI, it remains at least equally – if not more – likely that the opposite effect is true. Here, we use data from the Flemish Gut Flora Project to estimate causal effect estimates between BMI (exposure) and gut flora (outcome).

## Methods

### 1. Estimate linear effect estimates

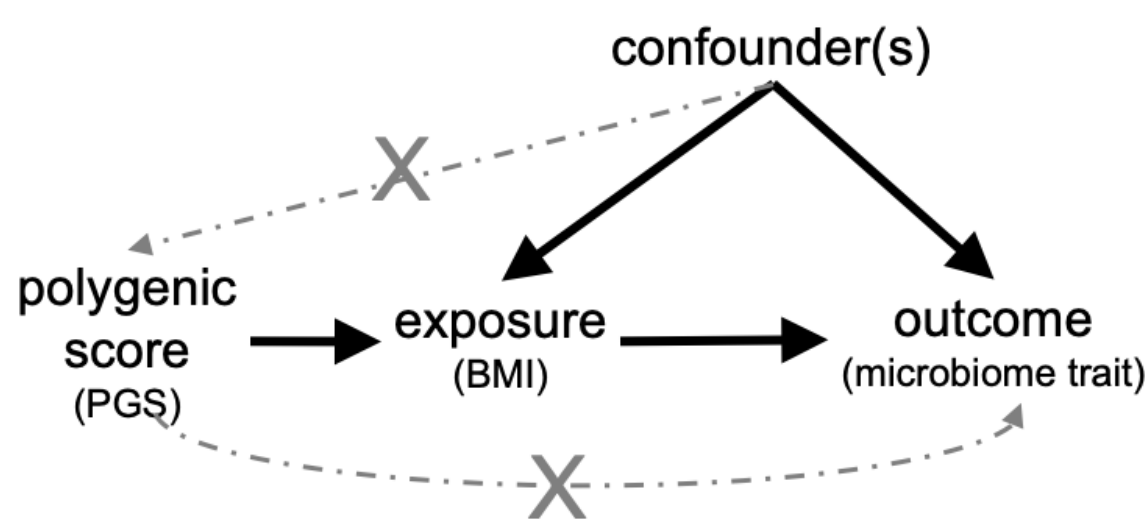
- (generalized) multivariable linear model
- exposure = BMI
- outcome = MT

### 2. Estimate the causal effect by one-sample MR (see Figure below)

- exposure = BMI
- outcome = MT
- instrumental variable or genetic proxy was a PGS composed of 670 SNPs associated to BMI by Pulit et al HMG 2019.

### 3. Compare linear sex-specific estimates

### 4. Compare linear and MR estimates



A directed acyclic graph (DAG) of Mendelian randomization (MR) illustrating the assumptions of the methodology. Namely, the instrument or PGS here, is associated with the exposure, but independent of the outcome and there is no confounding between the instrument and outcome.

## Population Description

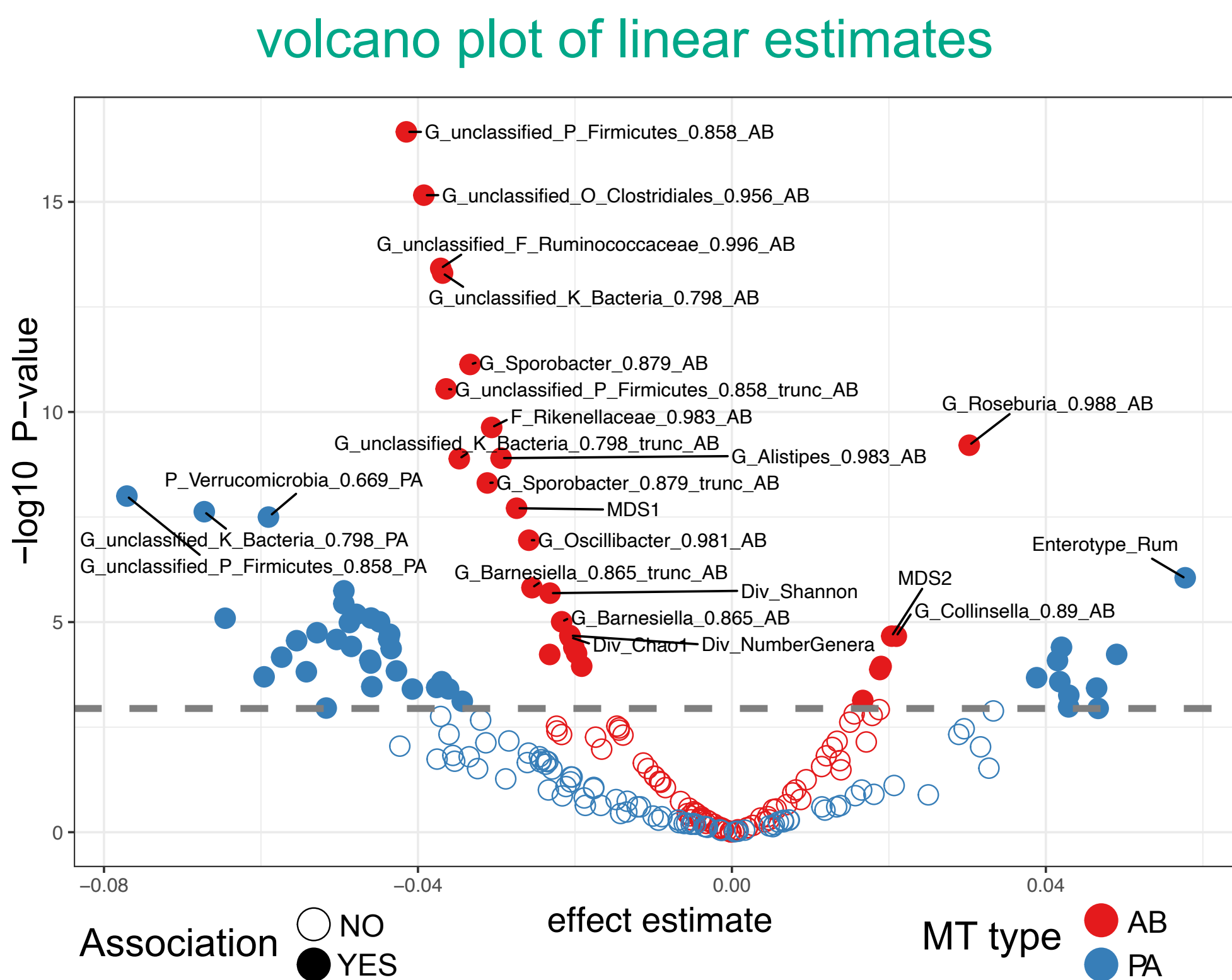
	total pop.	females	males
N (obs.   imputed)	2257	1330   1343	897   913
age in years (95 CI)	52.29 (24-73)	50.48 (23-71.77)	54.93 (27-74)
height in cm (95 CI)	170.1 (154-188)	165.49 (153-178)	176.91 (163-190)
weight in kg (95 CI)	72.72 (49.71-107)	66.85 (48.8-96.5)	81.39 (58.17-114)
BMI kg/cm <sup>2</sup> (95 CI)	25.06 (18.2-35.16)	24.42 (18-34.68)	25.99 (19.16-35.31)
smoking (Never   Ever   Current)	1040   803   172	700   409   90	327   387   79
PGS SNP count (study   matched   filtered)	670   665   656	281   281   279	221   104   103
BMI var. exp. by PGS (%)	4.40	1.79	3.00

### Abbreviation Key

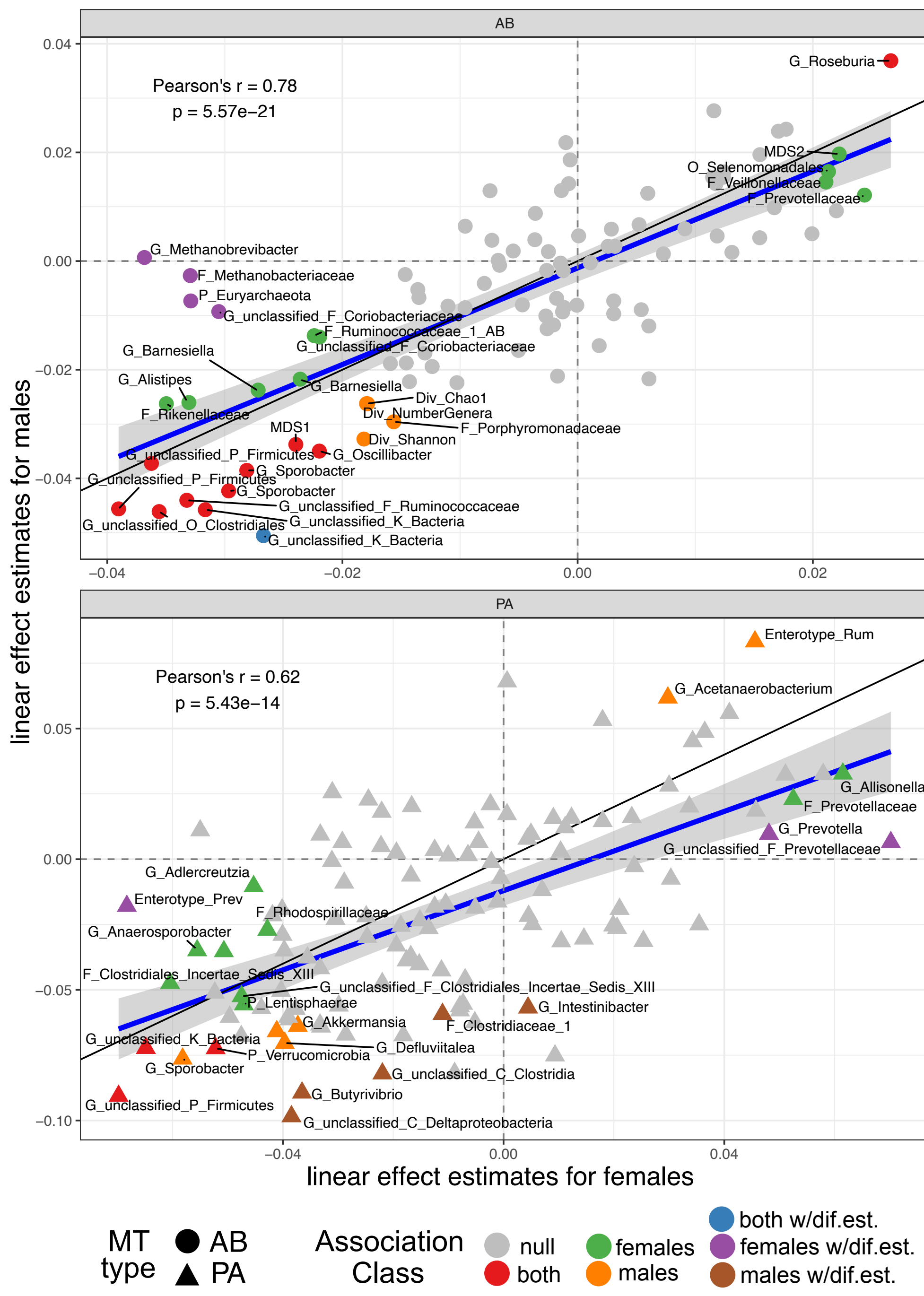
MR: Mendelian randomization  
MT: microbial traits  
PGS: polygenic score

AB: abundance MT  
PA: presence | absence MT

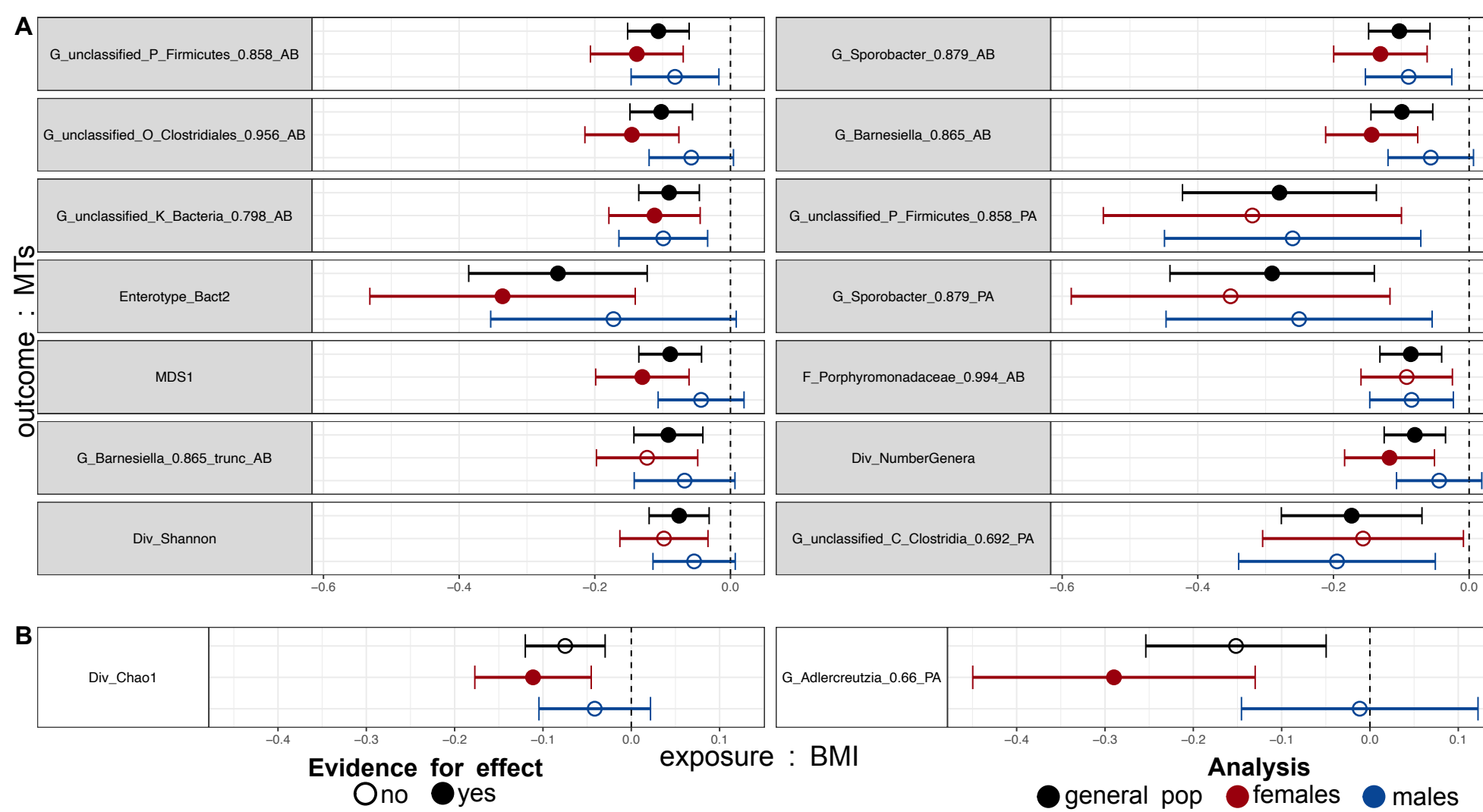
## Linear Model Estimates



### Comparison of linear effect estimates between males and females



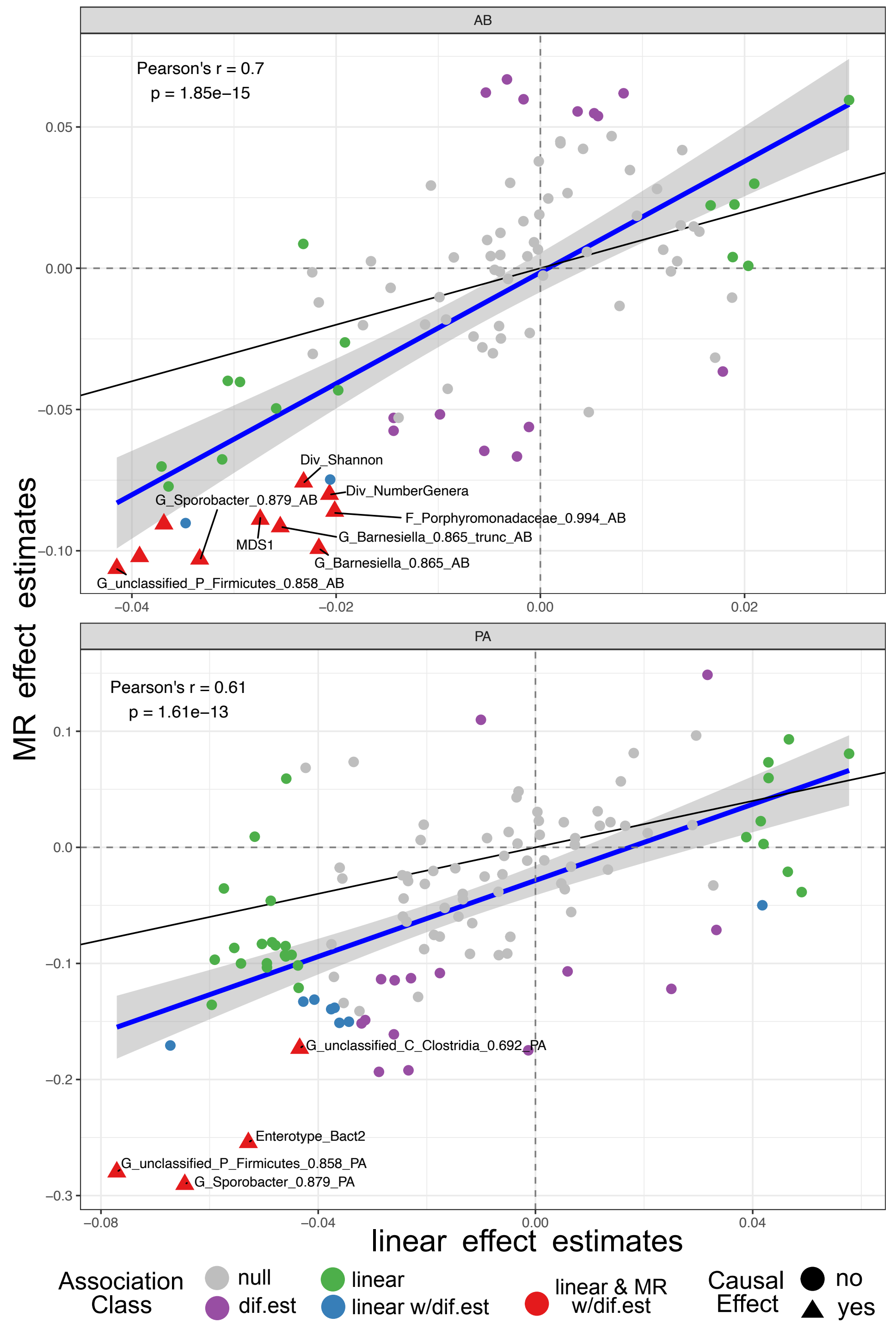
## Forest Plot of MTs with Evidence of a BMI Effect



(A) 14 MTs with evidence of being causally influenced by BMI in the general population (black points), alongside estimates in females (red) and males (blue).  
(B) Two MTs with evidence of being causally influenced by BMI in females, but not in the general population or males.

## Linear and MR Estimate

### Comparison of MR and linear effect estimates



## Results & Conclusion

Overall, results support a conclusion that gut microbiome variation can be causally influenced by variation in BMI and not the reverse.

- 215 MTs tested
- 67 MTs associated with BMI in linear models
- 14 MTs causally affected by BMI in the general population
- 10 MTs causally affected by BMI in females
  - 2 of 10 are novel to females
  - including the phytoestrogen metabolizing genera *Adlercreutzia*
- Conventional linear estimates and MR estimates are correlated providing evidence that:
  - linear effect estimates are reasonable predictors of MR estimates
  - BMI has a broad causal effect on MTs

## Acknowledgements

We are grateful to all the participants of the Flemish Gut Flora Project. This work would be impossible without their participation.

**Contact:** <https://teamtimpson.github.io>