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# #269 UTILITY OF MULTIVARIATE DATA ANALYSIS AND PENALIZED META-REGRESSION TO EXPLORE SOURCES OF HETEROGENEITY IN MICROBIOME META-ANALYSES

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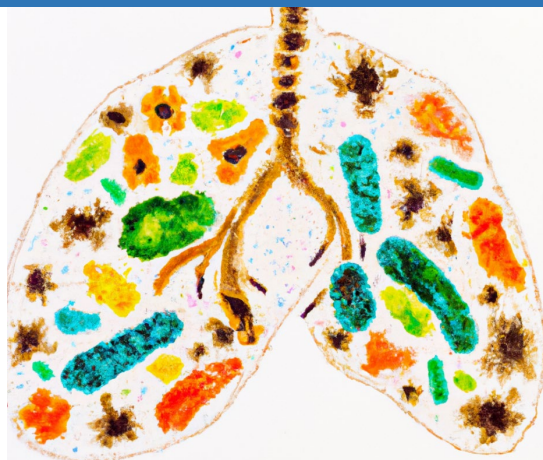
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## Background and Aims

**Meta-analysis** combines study results to boost statistical power through appropriate data pooling. Ensuring accurate conclusions includes examining potential biases and heterogeneity. **Random effects meta-regression** is typically used to explore heterogeneity and understand sources of variability.

Bioinformatics and NGS advances have improved our understanding of the microbiota's role in health. However, considerable **variability** exists due to differences in study methodologies, such as pipelines, sequencing techniques, and sample collection.

In human microbiota studies beyond the gut, a limited number of studies  $n$  addressing the same research question and numerous differing characteristics  $d$  create a **high-dimensional** problem, necessitating adapted statistical analysis.



## Methods

### Data from Ake et al. WoM 23:

- Mean-SD differences in the Shannon index between cases and controls
- Technics: sampling, sequencing, rarefaction, taxonomy, ASV
- Population: age, continent, disease, group status

### Exploring sources of variability :

- Weighted Lasso regression with stability selection (glmnet, stabs)
- Separate random effects meta-regressions (R package metaphor)

## Results

Characteristic	$\hat{\beta}$	$p$	$P$
Sampling: Up vs BAL	-	0.6	13%
Continent: AS vs AM	-	0.7	19%
EU vs AM	-		24%
Sequencing: PCR vs Illum	+	0.5	<b>46%</b>
Rarefaction: Y vs N	-	0.4	<b>51%</b>
Taxonomy: OTU vs G	+	0.8	14%
ASV: Y vs N	+	<b>0.3</b>	30%
Disease: Wheez-Rh vs Lung	-	0.5	33%
Status: H-D vs D-D	-	0.8	23%
Age: 4-8 vs 0-4	+	0.8	38%
8-14 vs 0-4	+		15%

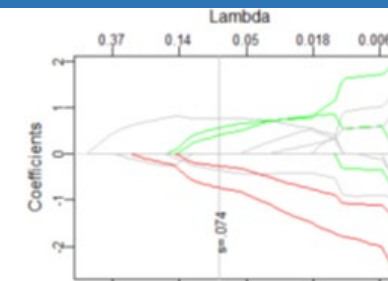
$Y$  = standardized mean difference in the Shannon index (Controls-Cases),  $w$  = SD

$\hat{\beta}$  = regression coefficient estimate (only sign)

$p$  = ANOVA p-value, separate random effects

$P$  = probability selection, Lasso regression

$n = 25, d = 11$



## Conclusion

Method choice significantly impacts source variability identification. Lasso lacks study heterogeneity control, separate models lacks adjustment. **Futur**: Lasso random effects meta-regression (dependencies: glmnet and metaphor).

## (Some) References

- Ake et al. The respiratory microbiome  $\alpha$ -diversity and chronic respiratory diseases in children: systematic review. *WoM*, 2023
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