

Foregut Microbiome in Development of Esophageal Adenocarcinoma

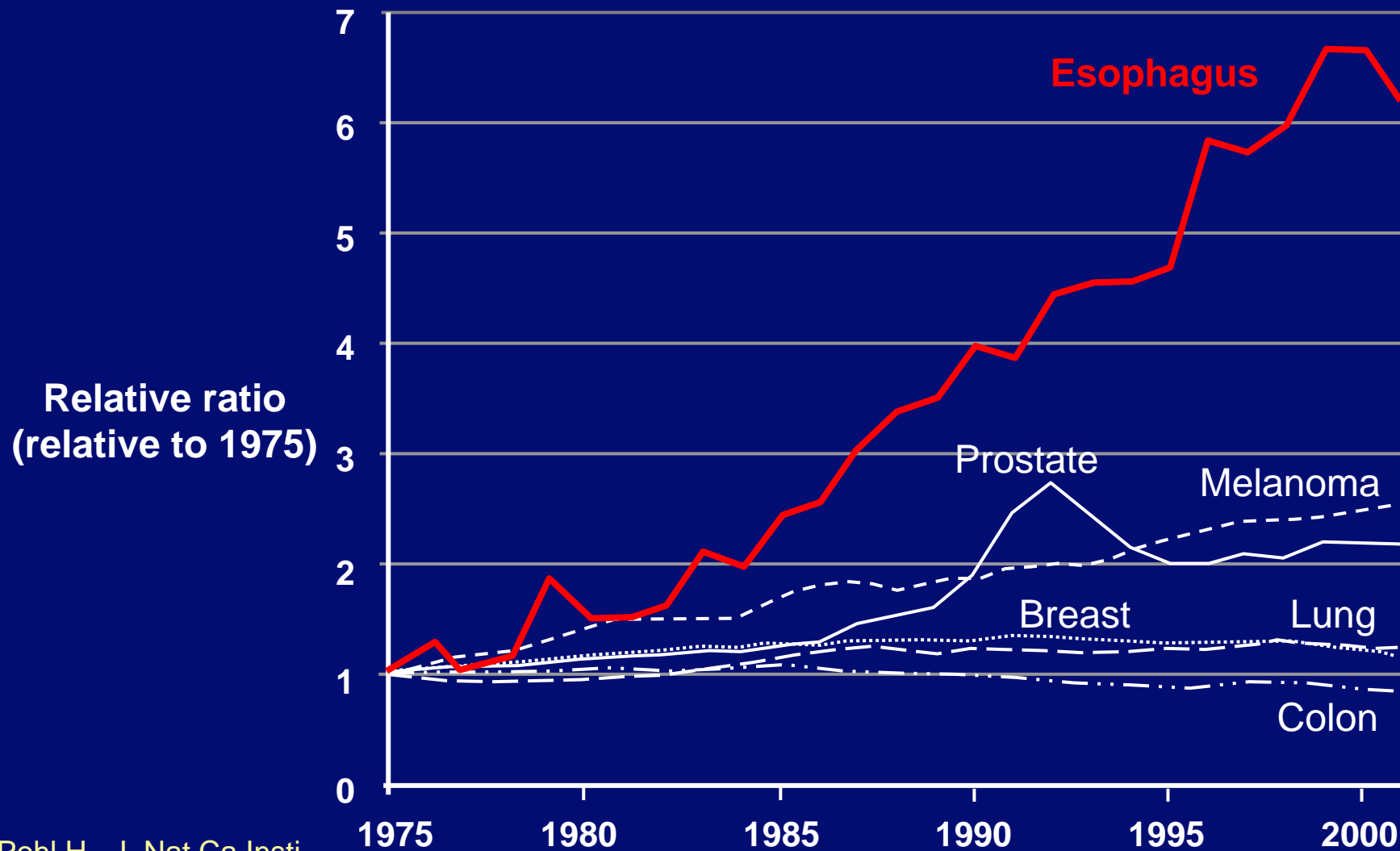
UH3CA140233

Zhiheng Pei, MD, PhD

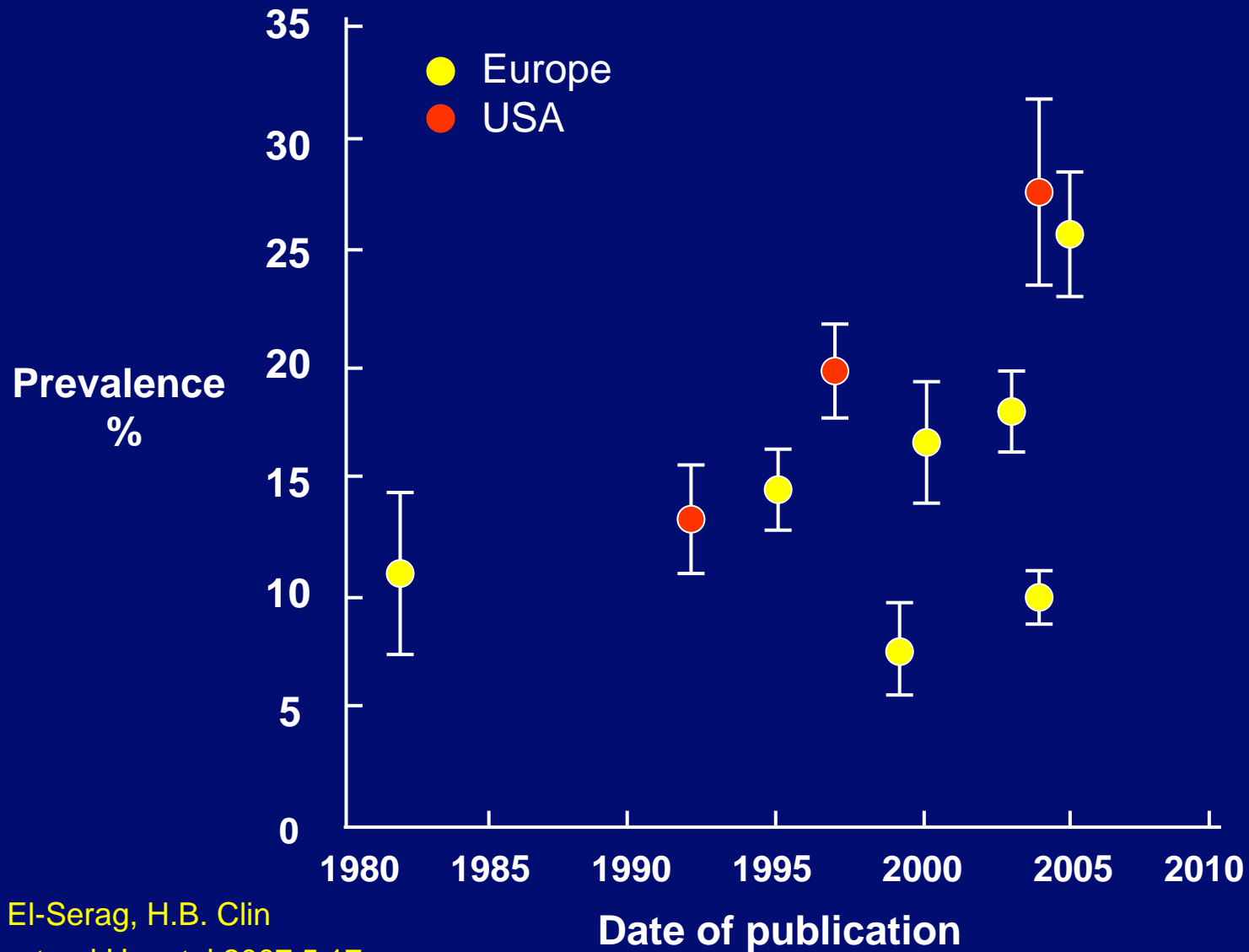
New York University School of Medicine

Karen Nelson, PhD
The J. Craig Venter Institute

Relative change in incidence of common cancers in USA



Time trend in prevalence of at least weekly heartburn/acid regurgitation



El-Serag, H.B. Clin

Gastroenterol Hepatol 2007;5:17.

Working hypothesis

Foregut microbiome is altered in esophageal adenocarcinoma (EA) and its precursors, reflux esophagitis (RE) and Barrett's esophagus (BE).

Long term hypothesis

Chronic exposure to an abnormal microbiome is carcinogenic.

Goals

Post-UH3

Causation

UH3

Correlation

UH2

Feasibility

UH2

Feasibility

UH2 findings

**Case-control study
Interim analysis**

Case group 1: Reflux esophagitis (n=17)

Case group 2: Barrett's esophagus (n=11)

Case group 3: Esophageal adenocarcinoma (n=1)

Control group: normal (n=7)

Age 50-79

UH2 biological milestone

16S rRNA gene survey

Taxonomic assignment

Classification of samples into microbiome types

Association between phenotypes and microbiome types, by Fisher Exact

Outcomes

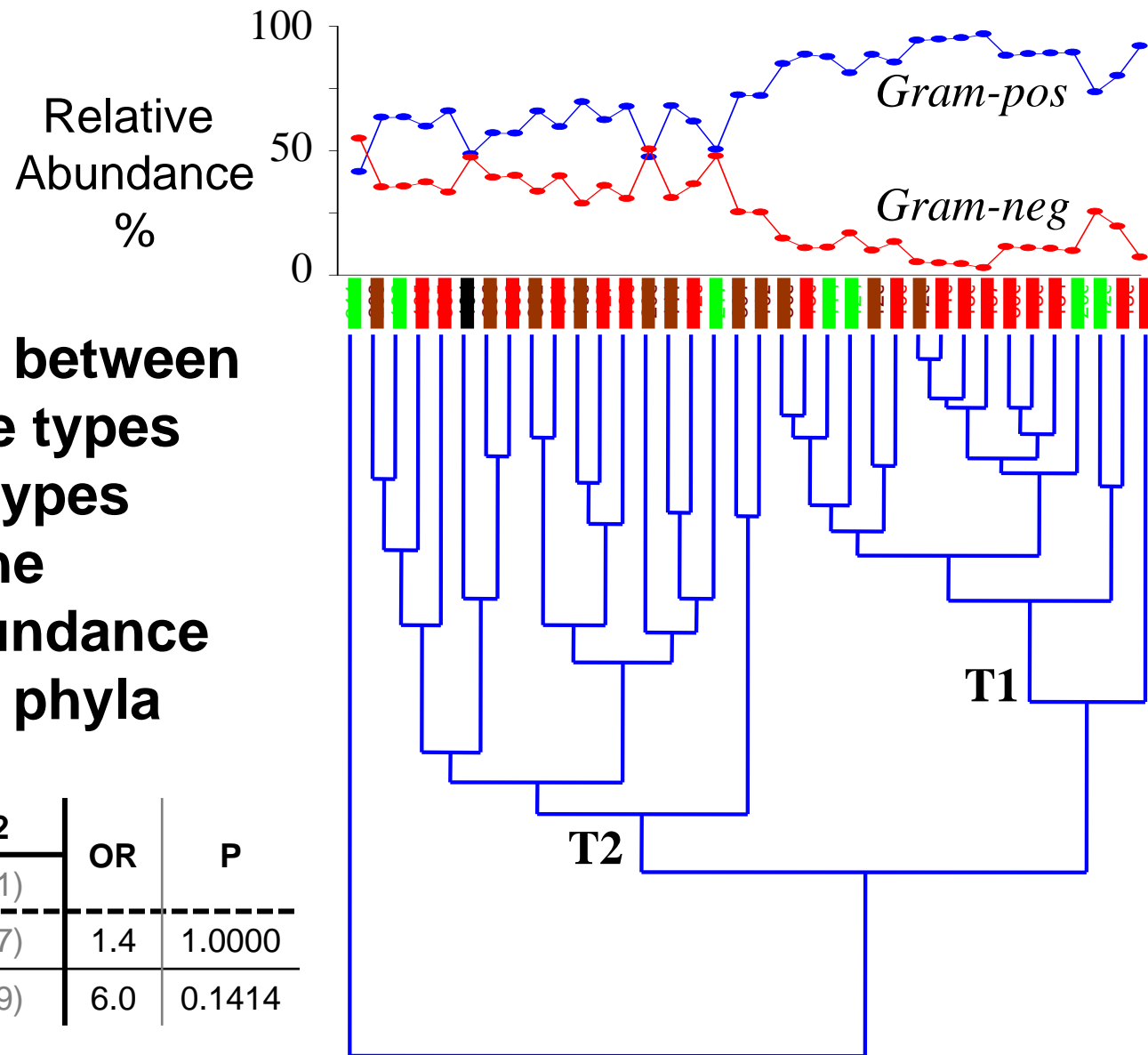
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graph TD; Outcomes[Outcomes] --> NoAssociation[No association]; Outcomes --> InadequateSampleSize[Inadequate sample size (Type I error)]; Outcomes --> SignificantAssociation[Significant association];
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No
association

Inadequate
sample size
(Type I error)

Significant
association

Correlation between microbiome types and phenotypes based on the relative abundance of all major phyla



	T1	T2	OR	P
NL	4 (11)	2 (1)		
RE	10 (5)	7 (7)	1.4	1.0000
BE/EA	3 (4)	9 (9)	6.0	0.1414

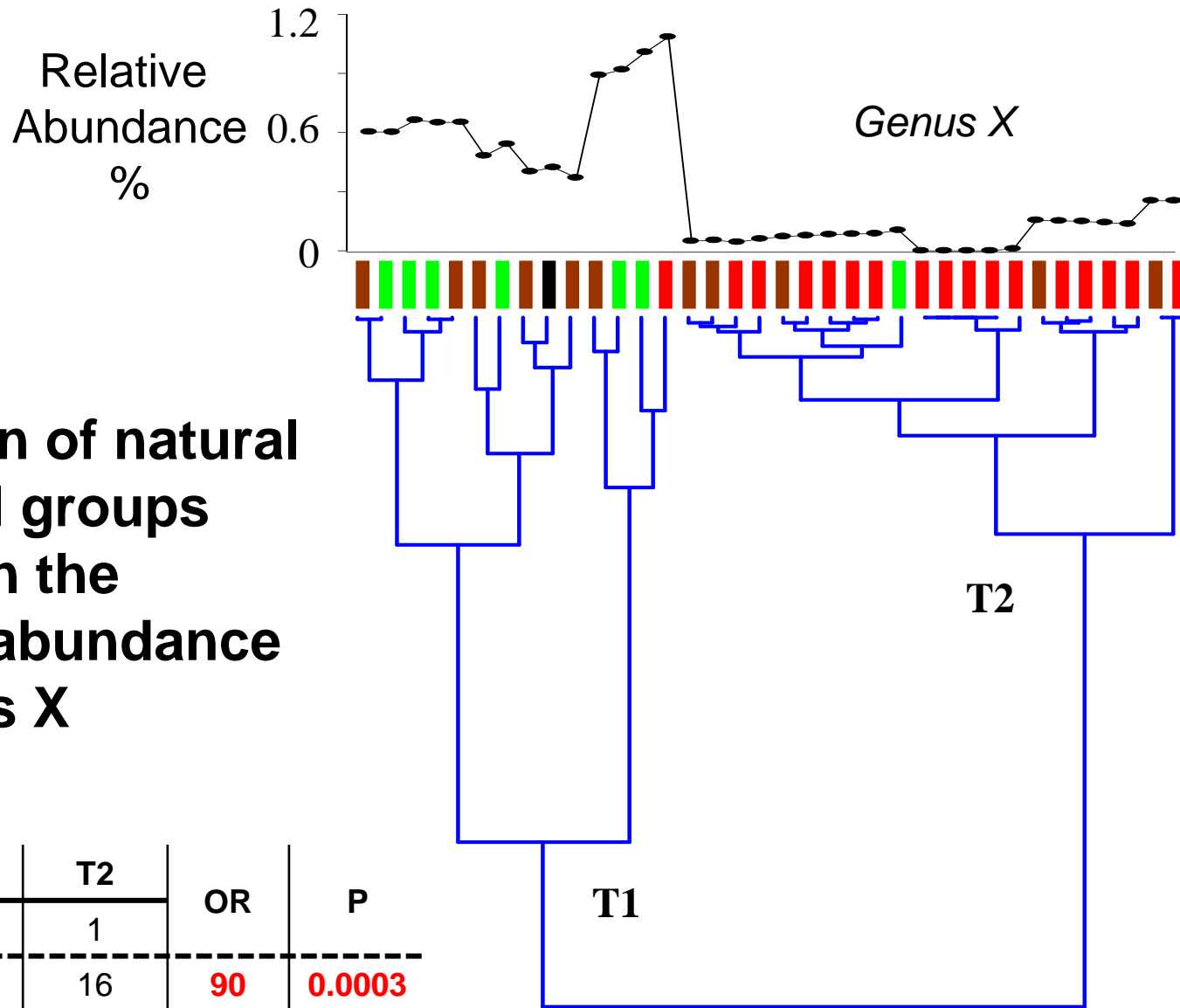
Sample size estimation based on major phyla

Power	Reflux	Barrett's	Cancer
80%	621	25	10
90%	822	32	12
95%	1,010	39	14
99%	1,417	52	17

Comparison of 2 types of microbiomes by relative abundance (%) of phylum

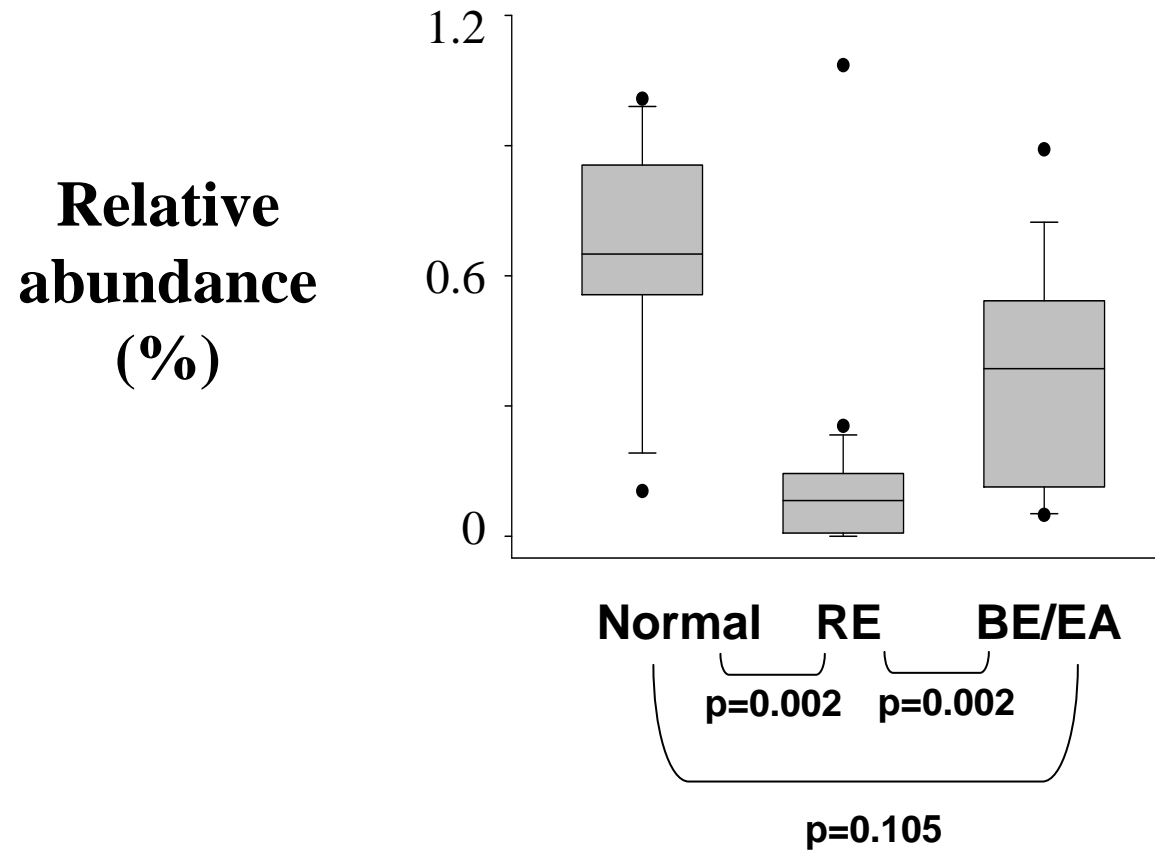
Phylum	Type 1 (n=18)	Type 2 (n=18)	P value
Actinobacterium	3.84	4.94	0.3262
Firmicutes	84.30	56.79	<0.0001
Bacteroidetes	3.58	11.17	<0.0001
Fusobacterium	1.26	3.56	0.0007
Proteobacterium	6.23	21.50	<0.0001
“Gram positive”	88.14	61.73	<0.0001
“Gram negative”	11.07	36.24	<0.0001

Detection of natural bacterial groups based on the relative abundance of Genus X



	T1	T2	OR	P
NL	6	1		
RE	1	16	90	0.0003
BE/EA	6	5	5.0	0.3156

Comparison of the relative abundance of genus X among normal, RE and BE/EA phenotypes



Summary of feasibility study

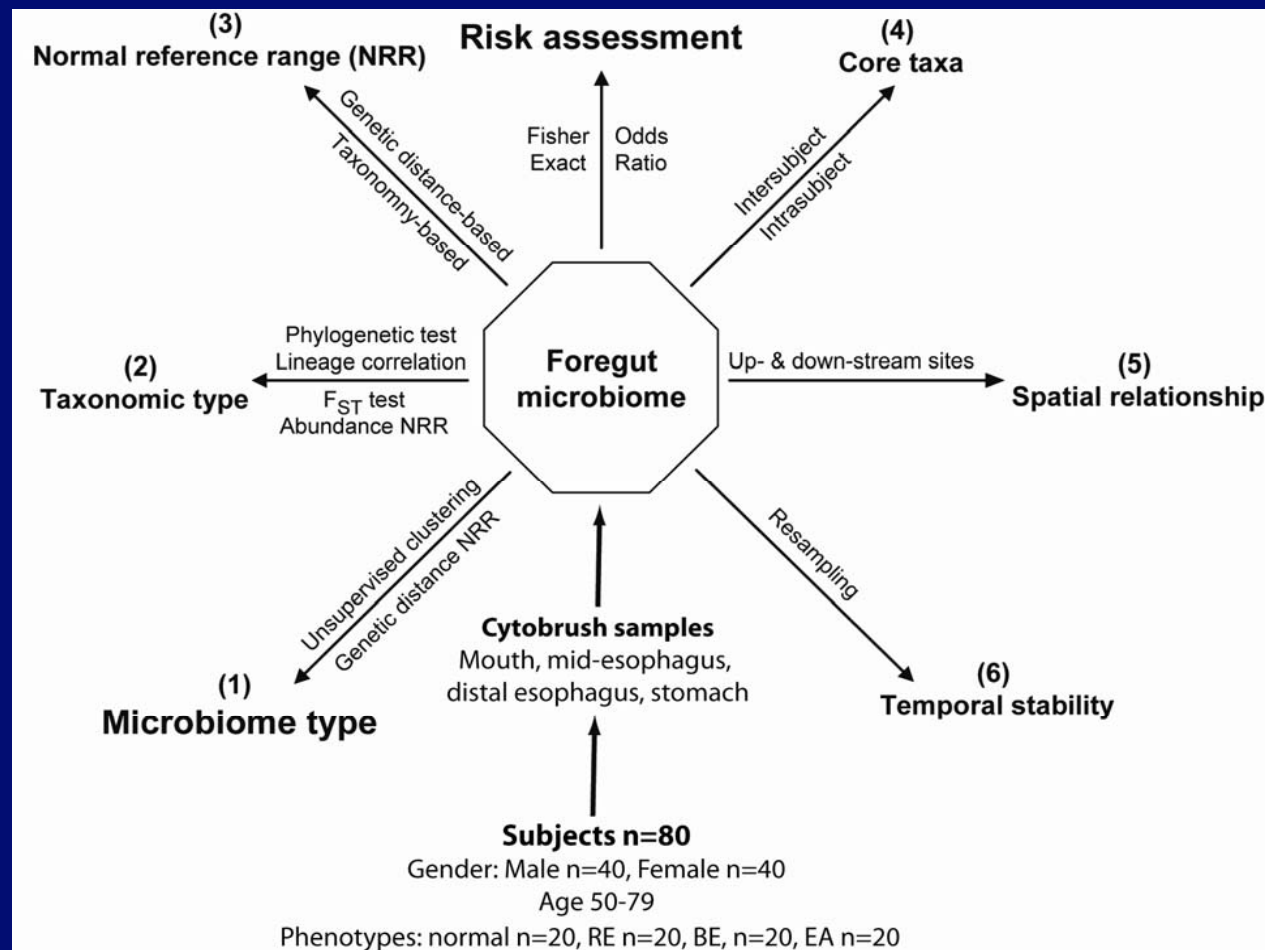
At the phylum level, there were general trends of decreasing Firmicutes and increasing Gram-negative bacteria in Barrett's esophagus and esophageal adenocarcinoma. Statistical difference could be reached by increasing the samples sizes.

At the genus level, there was a strong decrease of Genus X in reflux esophagitis and Barrett's esophagus. In depth 16S rRNA gene survey could reveal changes in other genera in the reflux disorders.

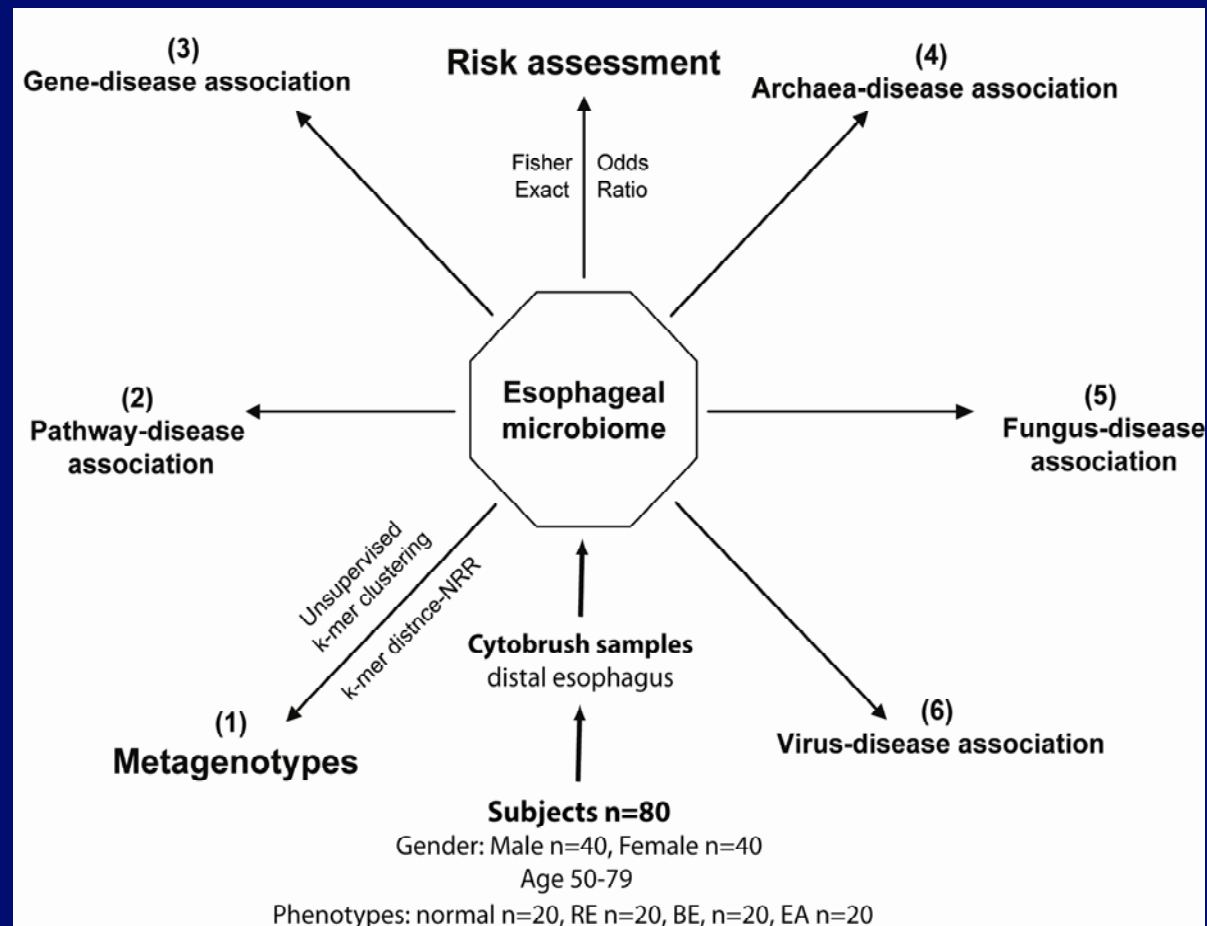
UH3 Aims

Correlation

Specific aim 1: 16S rRNA gene survey



Specific aim 2: metagenomic shotgun analysis



Post-UH3

Causation

Causation

Antibiotics

Probiotics

Pathogenic mechanisms

Acknowledgement

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