LUNG MICROBIOME IN HEALTH AND DISEASE

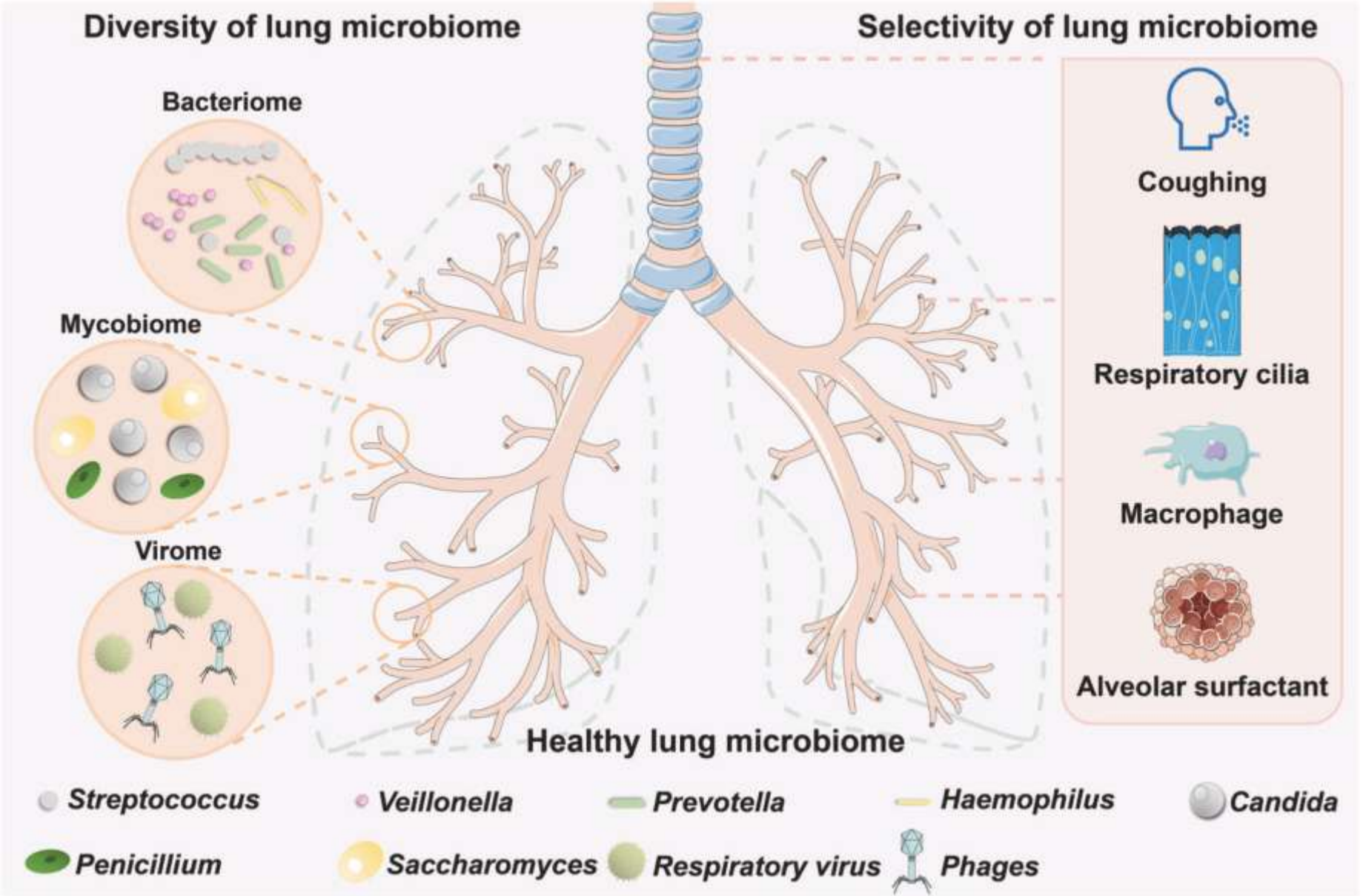
RASHMI S PILLAI

- Microbiome in Healthy Lung
- Microbiome detection methods
- Lung Microbiome in Diseases

Microbiome of Healthy Lung

- The healthy lungs host a **low-biomass, diverse microbial community**.
- We inhale from a non-sterile environment.
- Healthy lung defence mechanisms: keep effective balance of immigration, elimination and regional growth.
- Maintains **immune tolerance**, prevents pathogen overgrowth, and contributes to mucosal homeostasis.
- Influenced by **oral micro aspiration**, host immunity, and environmental exposures.

COMPOSITION OF LUNG MICROBIOME



Li R. et al. *Sig Transduct Target Ther*. 2024;9:19

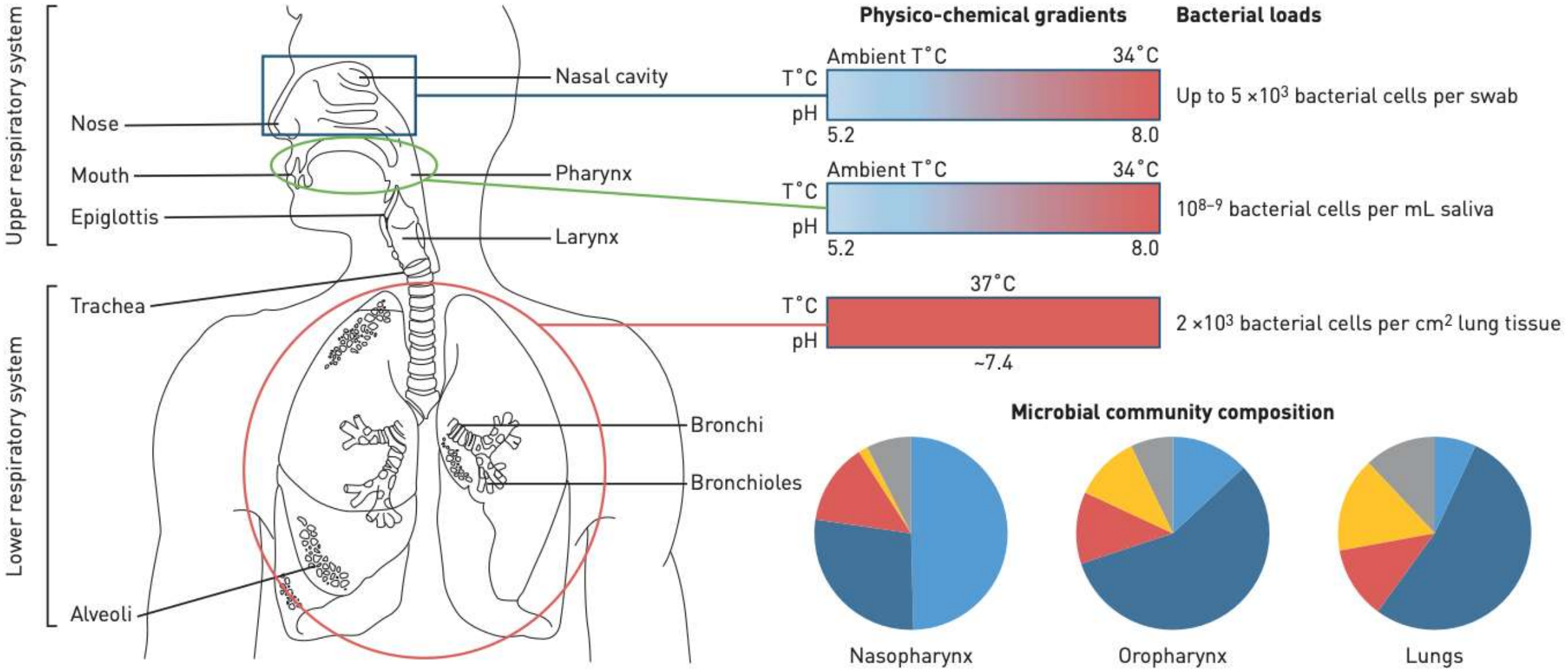
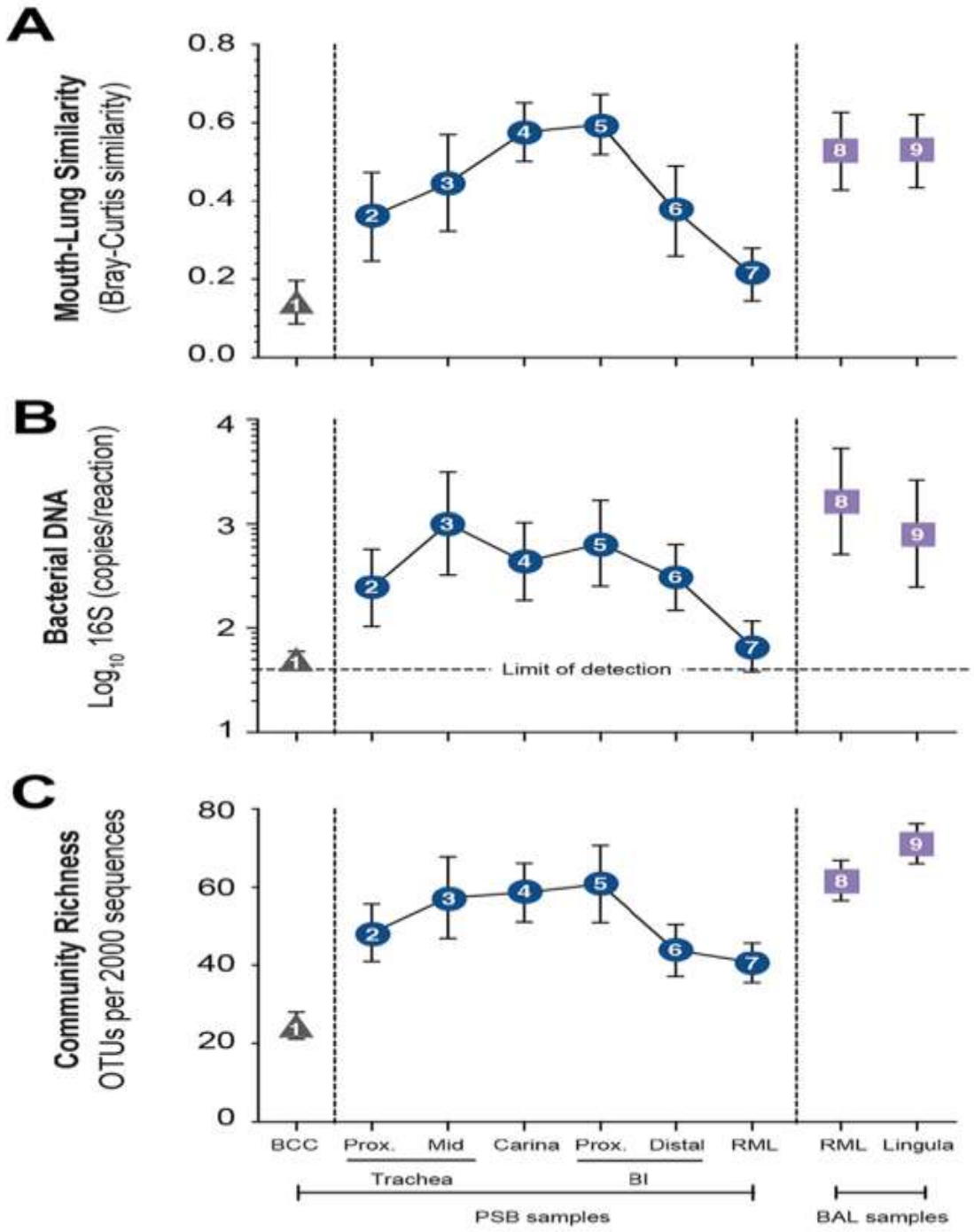


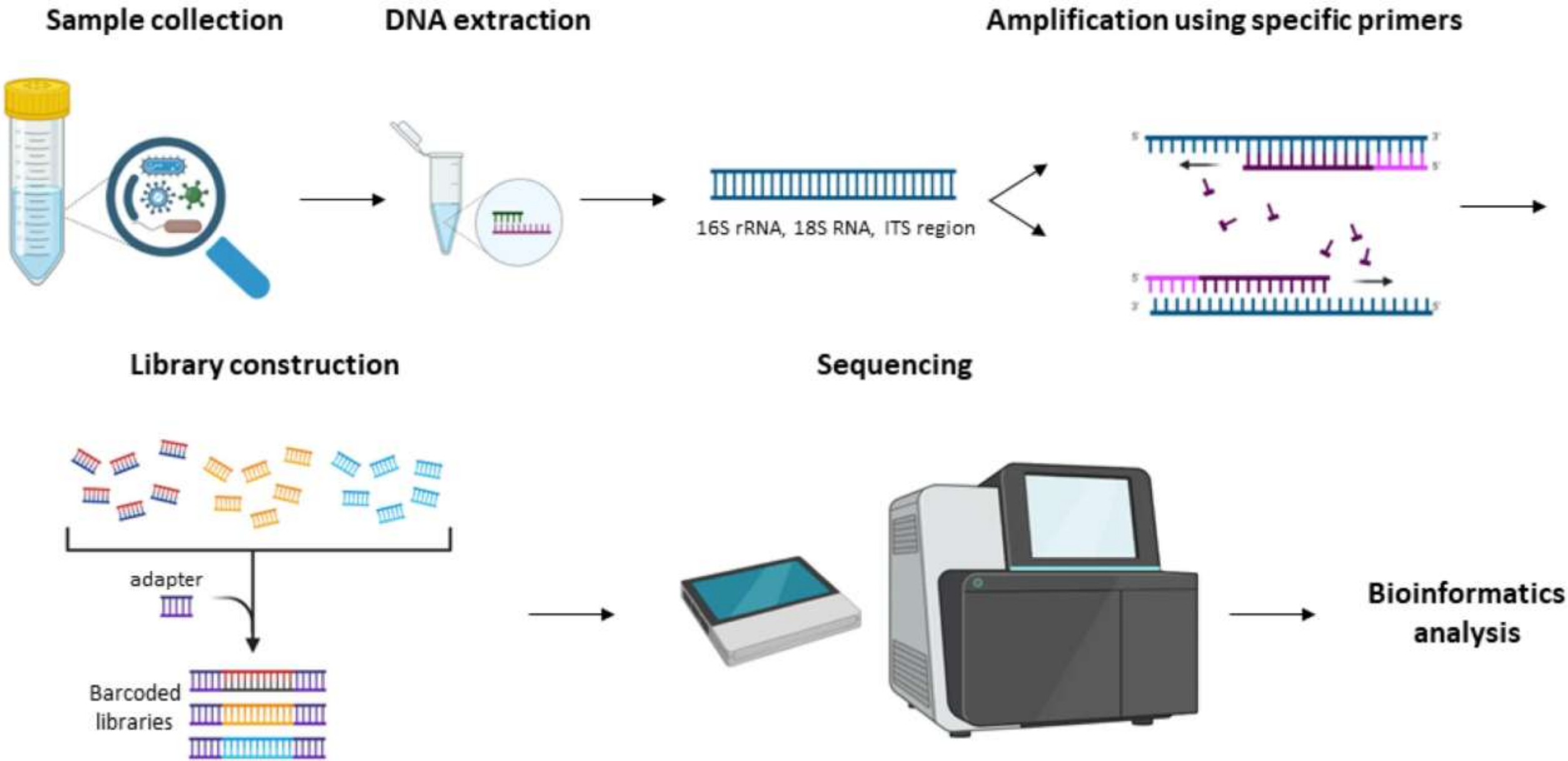
Figure 1. The upper and lower respiratory systems as microbial habitats for micro-organisms. Three major compartments are shown comprising the nasopharynx, the oropharynx and the lungs, with prevailing physico-chemical conditions, bacterial loads and composition of the bacterial community in each compartment. The bacterial phyla in the microbial community composition comprise *Actinobacteria* (light blue), *Firmicutes* (dark blue), *Proteobacteria* (red), *Bacteroides* (yellow) and others (grey). Information from [29, 48–52].

Type of Study	Prospective experimental bronchoscopy study
Study Population	8 healthy adults without respiratory disease (age 26–71 years)
What was done?	• Serial sampling of the LRT using 6 protected specimen brushings (PSB) and B/L bronchoalveolar lavage (BAL). • Included extensive contamination controls (bronchoscope contamination control, sterile saline, unused brushes and reagent controls). • 16S rRNA (V4) sequencing performed on all samples to map bacterial topography.
Result	The healthy lower respiratory tract is not sterile. Its microbiome is primarily derived from the oropharynx through continuous micro-aspiration, and carefully performed bronchoscopy can be used for studying the lung microbiome.

Dickson RP, Erb-Downward JR, Freeman CM, McCloskey L, Falkowski NR, Huffnagle GB, **et al.** Bacterial topography of the healthy human lower respiratory tract. *mBio.* 2017;8(1):e02287-16. doi:10.1128/mBio.02287-16.



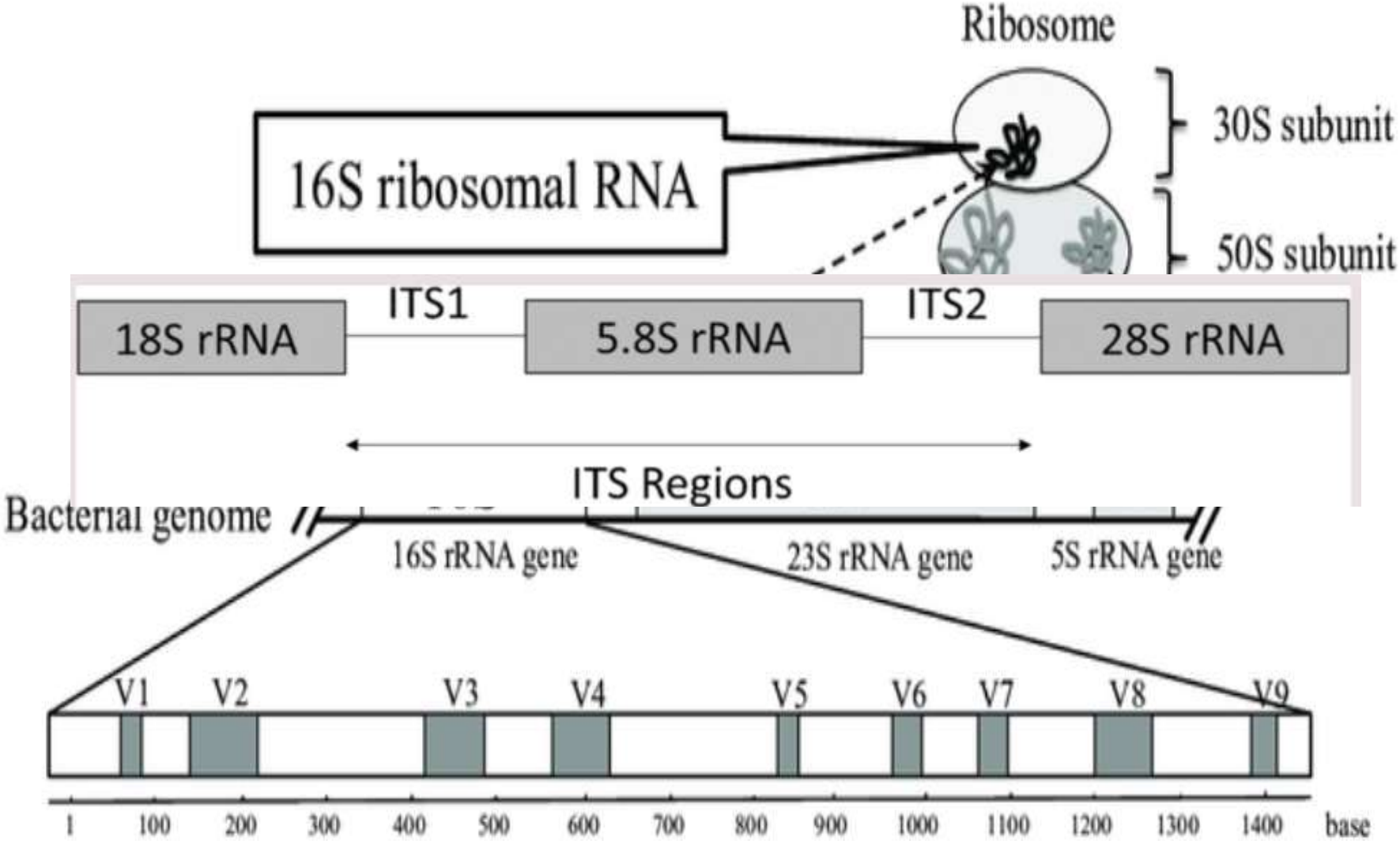
Dickson RP, Erb-Downward JR, Freeman CM, McCloskey L, Falkowski NR, Huffnagle GB, **et al.** Bacterial topography of the healthy human lower respiratory tract. *mBio.* 2017;8(1):e02287-16. doi:10.1128/mBio.02287-16.



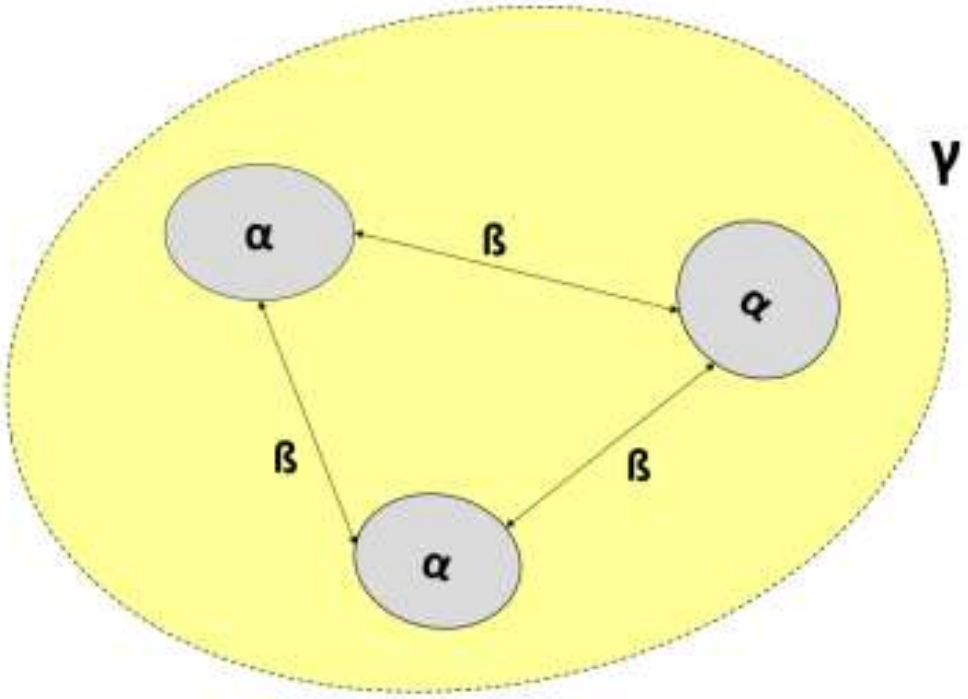
Athanasopoulou, K. et al. Biomedicines. 2023.

DETECTION METHODS

16S rRNA	ITS	Shotgun metagenomics	Whole Genome Sequencing
• Molecular fingerprint → bacterial taxonomic profiling • 16Sr RNA subunit in 30S • Inability to differentiate live and dead microbes	• Internal transcribed spacer → fungal microbiome studies	• Entire mixed DNA extract sequenced. • All functional genes of each organism in the sample • Antimicrobial resistance or virulence genes or metabolism of the organism present.	• Isolate microorganisms and sequence them individually


Ribosome
16S ribosomal RNA
30S subunit
50S subunit
18S rRNA
ITS1
5.8S rRNA
ITS2
28S rRNA
ITS Regions
Bacterial genome
16S rRNA gene
23S rRNA gene
5S rRNA gene
V1
V2
V3
V4
V5
V6
V7
V8
V9
1
100
200
300
400
500
600
700
800
900
1000
1100
1200
1300
1400
base

Feature	Culture	16S rRNA Sequencing	Shotgun Metagenomic Sequencing
Detection	Viable, culturable bacteria	Bacterial DNA	Total DNA (bacteria, fungi, viruses, archaea)
Sensitivity	Lowest	High	Highest
Detects viable organisms only?	**Yes**	**No (DNA from live and dead bacteria)**	**No (DNA from live and dead organisms)**
Anaerobes	Frequently missed	Detected	Detected
Taxonomic resolution	Species (if cultured)	Usually genus (occasionally species)	Species/strain level
Functional information	Phenotypic only	Not available	Functional genes, metabolic pathways and resistome
Turnaround time	24–72 h	24–48 h	48–72 h
Major limitation	Misses unculturable organisms	Cannot detect fungi/viruses and cannot distinguish live from dead bacteria	Expensive, computationally intensive, host DNA contamination



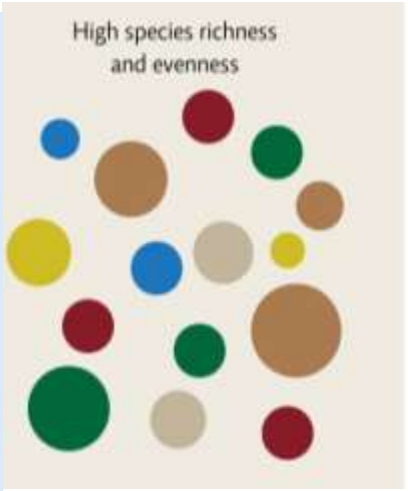
Alpha Diversity: Within sample diversity

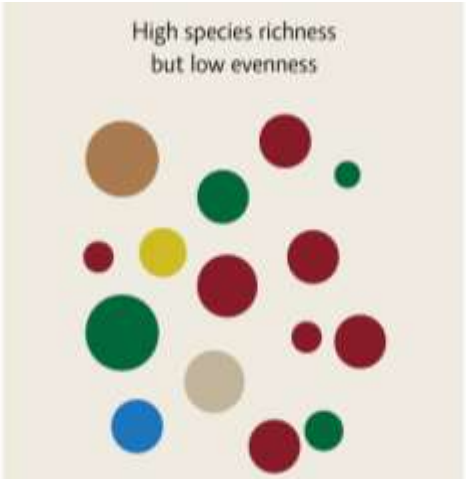
Beta Diversity: Between sample diversity

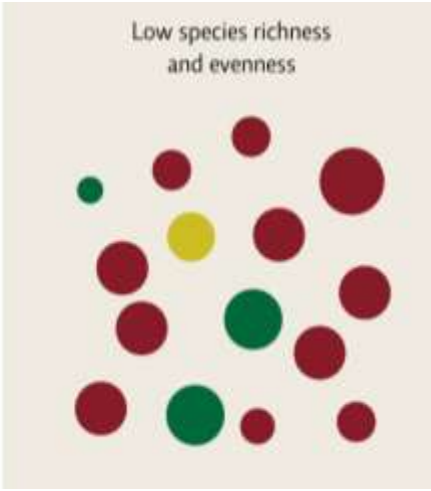
Gamma diversity: Total diversity in a larger region

Species richness: The total number of species in the area (species diversity)

Species evenness: How evenly individuals are distributed among the species (population size of each species)







ALPHA DIVERSITY

CHAO 1	• Estimates unseen taxa
SHANNON INDEX	• Richness + evenness
SIMPSON INDEX	• More weight on dominant taxa.

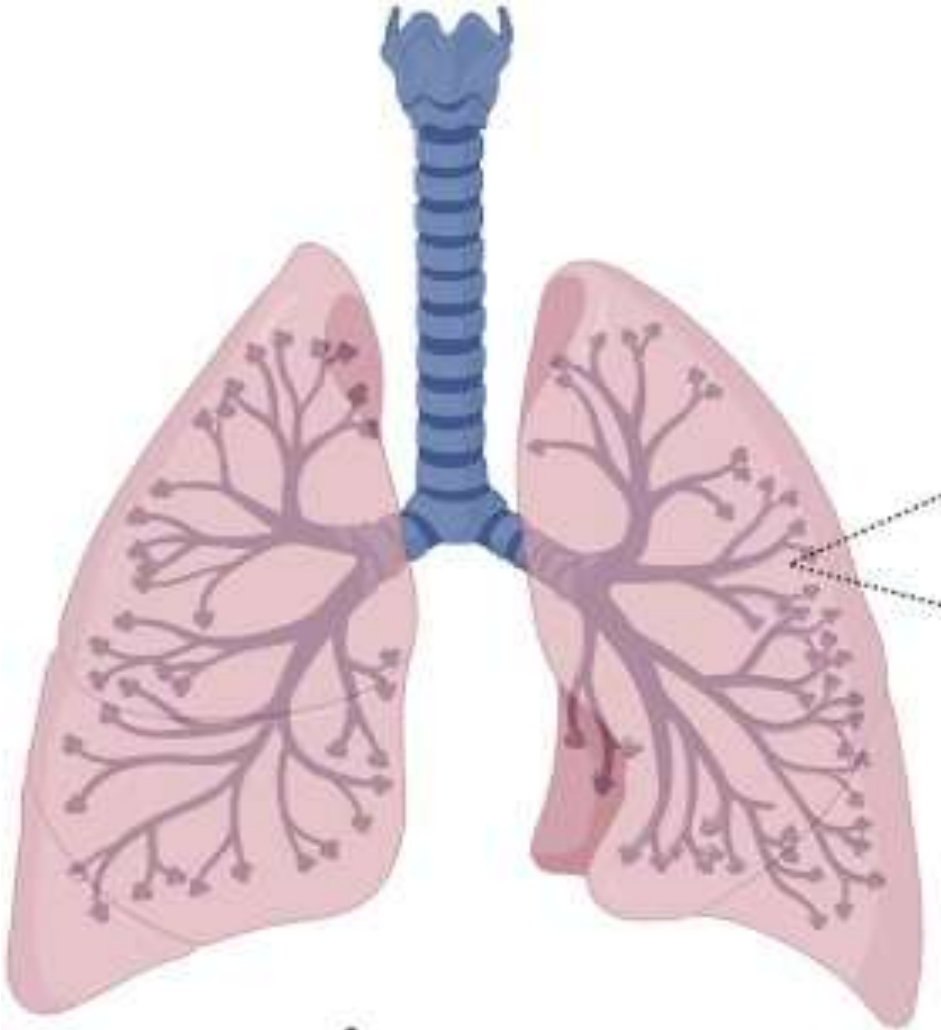
Cassol I et al; *Sci Rep* 15,622 (2025)

BETA DIVERSITY

Researchers compare microbial composition using distance/similarity metrics such as:

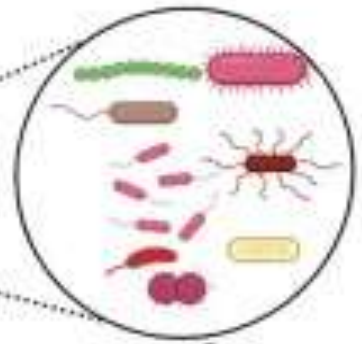
- **Bray-Curtis dissimilarity** – considers abundance of species
- **Unweighted UniFrac** – based on presence/absence and evolutionary relationships
- **Weighted UniFrac** – includes both phylogeny and abundance

These metrics are often visualized using methods like **Principal Coordinates Analysis (PCoA)** plots.



Lungs

Microbiome



Lung disease

- High microbial density
- Low microbial diversity

(↓ species richness)

Healthy lung

- Low microbial density
- High microbial diversity

(↑ species richness)

Microbiome roles

- Prevents from infection/inflammation
- Immunity development
- Activates immune cells

Saroj Khatiwada et al; *Human Microbiome Journal*; 2020

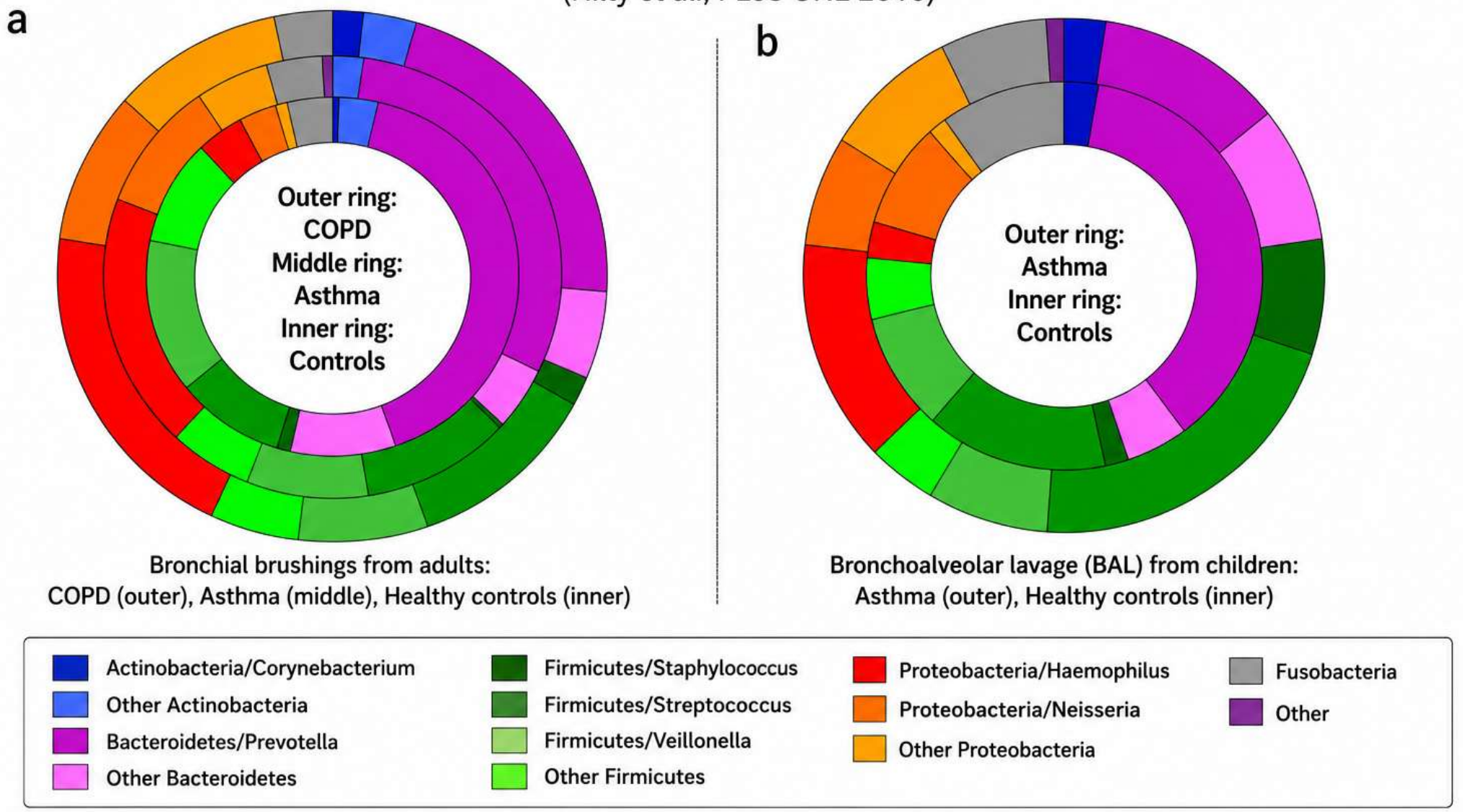
LUNG MICROBIOME AND COPD

Type of Study	• Cross-sectional • 16S rRNA gene sequencing
Study Population	**44 subjects** (24 adults: 11 asthma, 5 COPD, 8 controls; 20 children: 13 difficult asthma, 7 controls). Microbiome sequencing completed in **43 subjects**.
Methodology	• N**ose, oropharynx, bronchial brushings (adults)** and **BAL (children)**. • **5,054 bacterial sequences** →16S rRNA sequencing and OTU-based community analysis.
Key Findings	• **Lower airways are not sterile** (≈2×10^3 bacterial genomes/cm^2). • ↑ **Proteobacteria** (especially Haemophilus) in asthma/COPD. • ↓ **Bacteroidetes** (particularly Prevotella) in disease. • Similar dysbiosis observed in **children with difficult asthma**.
Clinical Significance	First study to demonstrate a **resident lung microbiome** and identify **airway dysbiosis** in asthma, establishing the foundation for lung microbiome research.

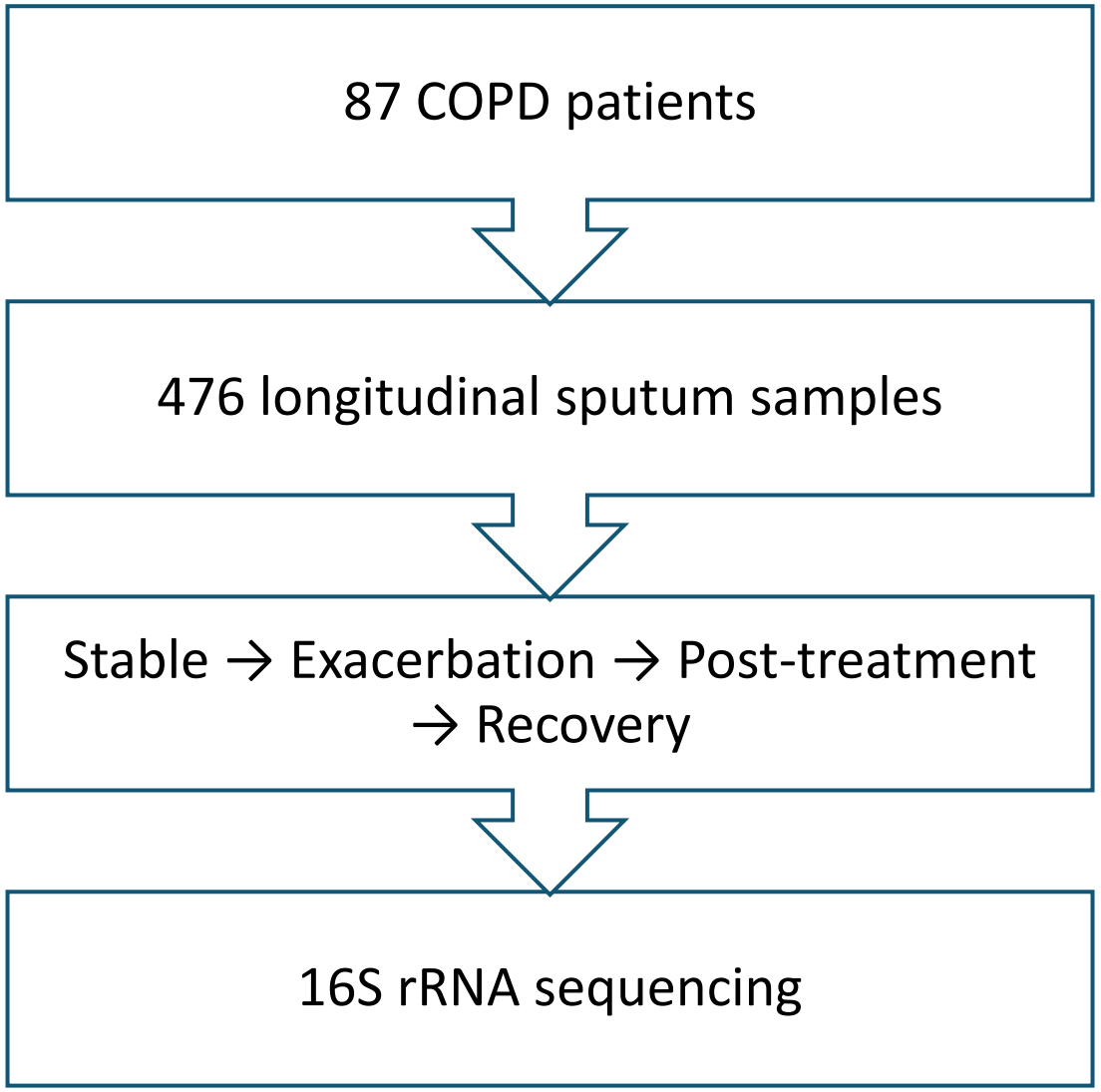
Hilty M, Burke C, Pedro H, Cardenas P, Bush A, et al. (2010) PLoS ONE 5(1): e8578. doi:10.1371/journal.pone.0008578

Airway Microbiota Composition in COPD, Asthma and Healthy Controls

(Hilty et al., PLoS ONE 2010)

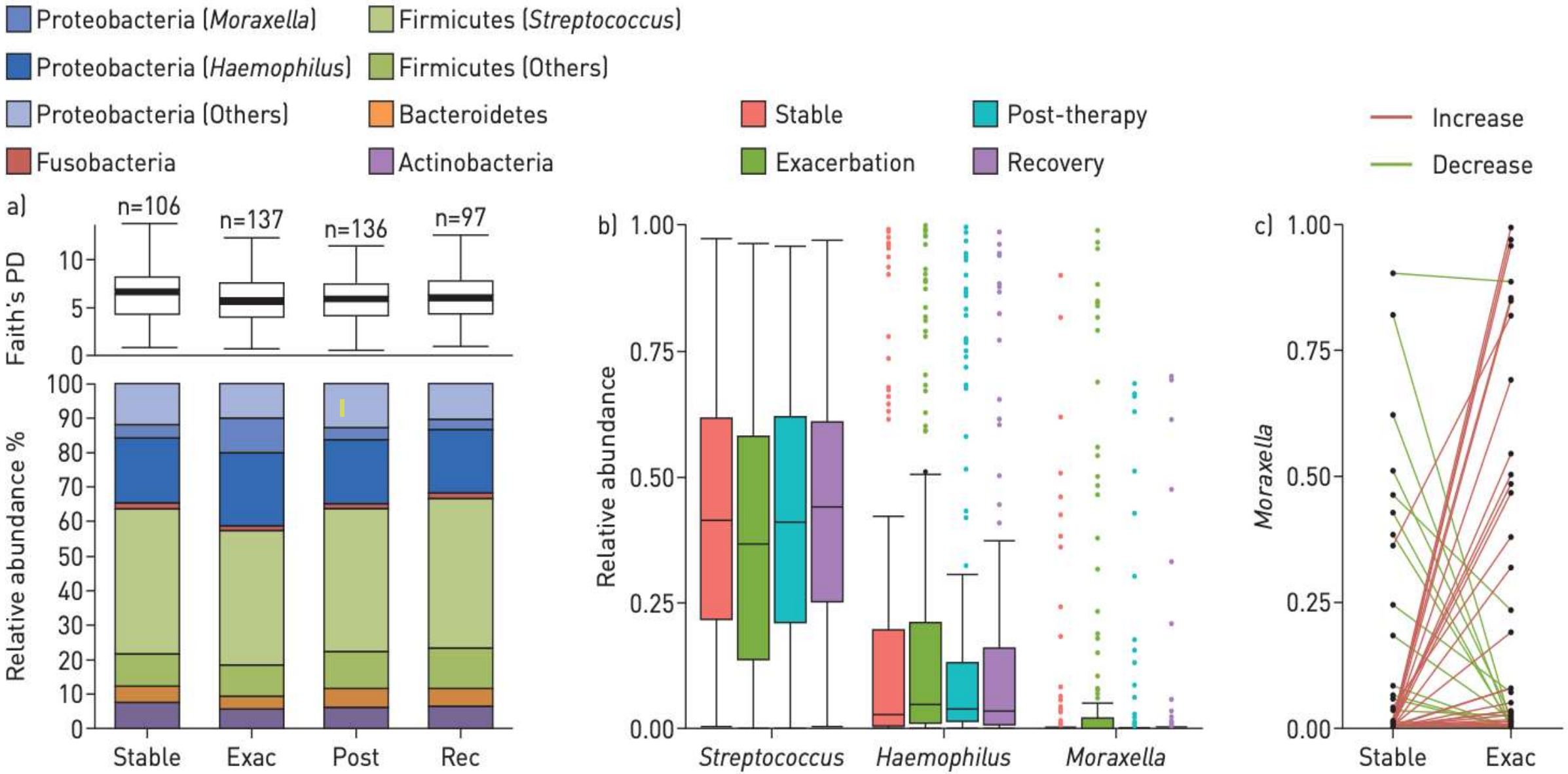


Hilty M, Burke C, Pedro H, Cardenas P, Bush A, et al. (2010) PLoS ONE 5(1): e8578. doi:10.1371/journal.pone.0008578

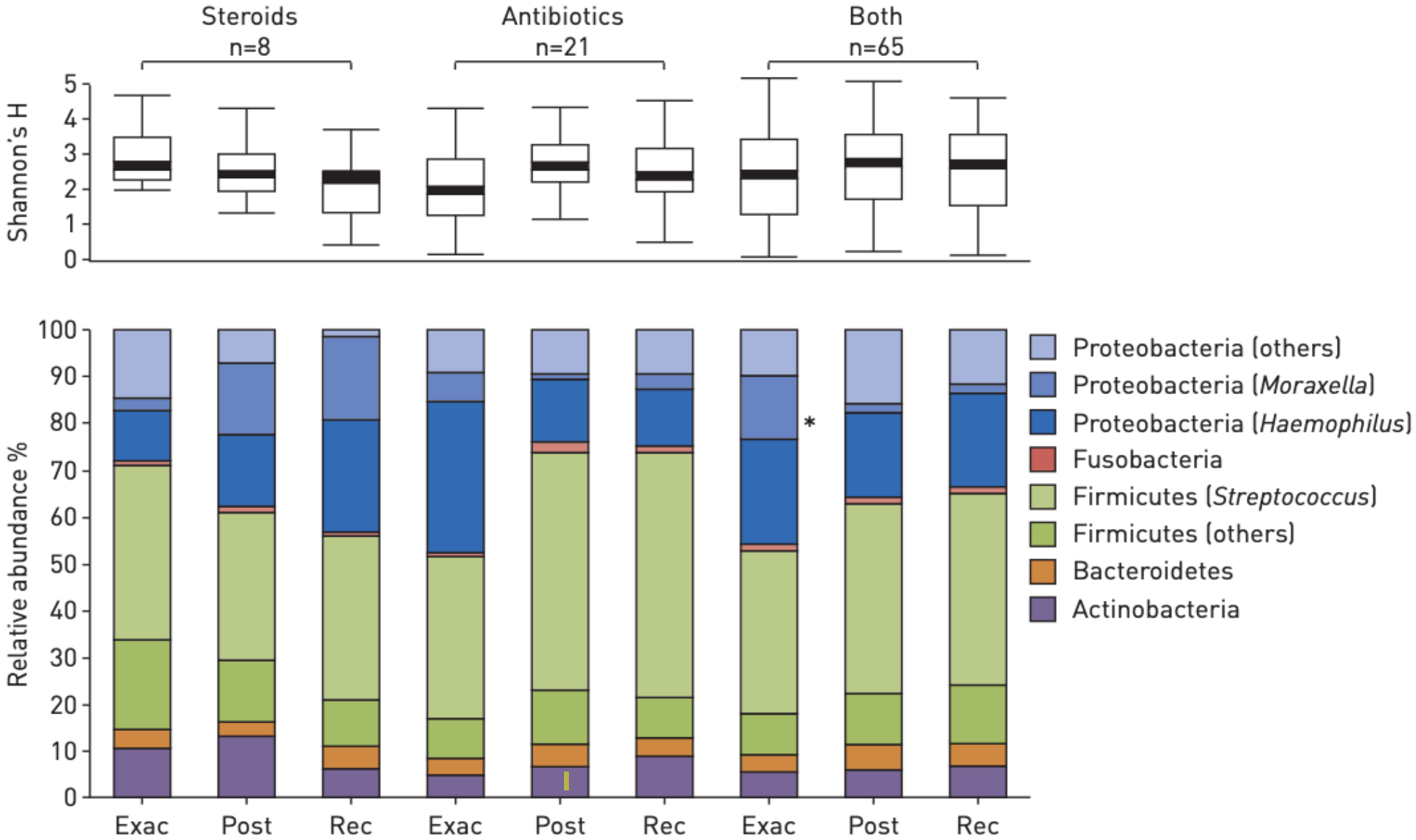


Across the whole cohort, exacerbations showed small, non-significant average shifts, but clinically meaningful dysbiosis occurred in specific phenotypes and patient subgroups.

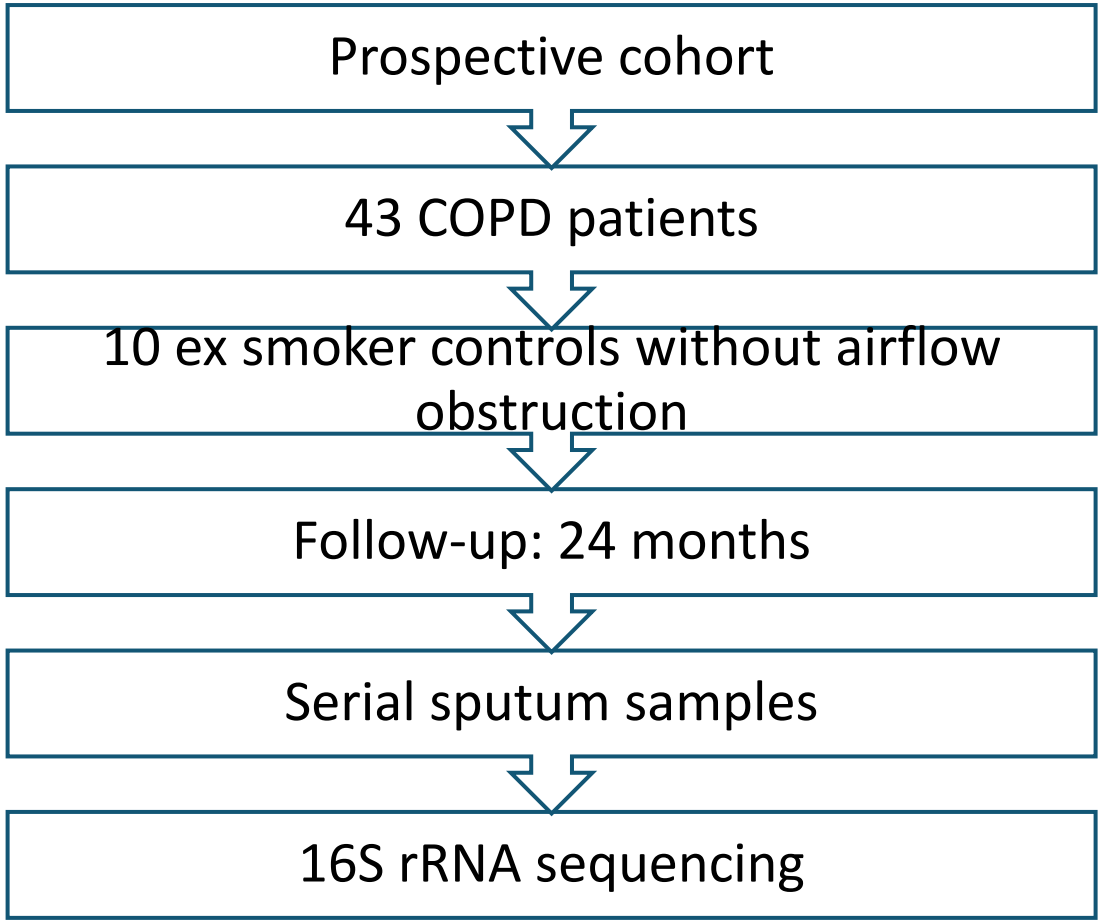
Wang Z et al; Lung microbiome dynamics in COPD exacerbations. Eur Respir J. 2016 Apr



Wang Z et al; Lung microbiome dynamics in COPD exacerbations. Eur Respir J. 2016 Apr



Wang Z et al; Lung microbiome dynamics in COPD exacerbations. Eur Respir J. 2016 Apr



- *Streptococcus* remained the dominant genus.
- Overall microbial diversity remained stable over two years.
- Long-term inhaled corticosteroids reduced:

➢ *Veillonella*

➢ *Catonella*

➢ *Saccharimonas*

- Continued smoking increased:

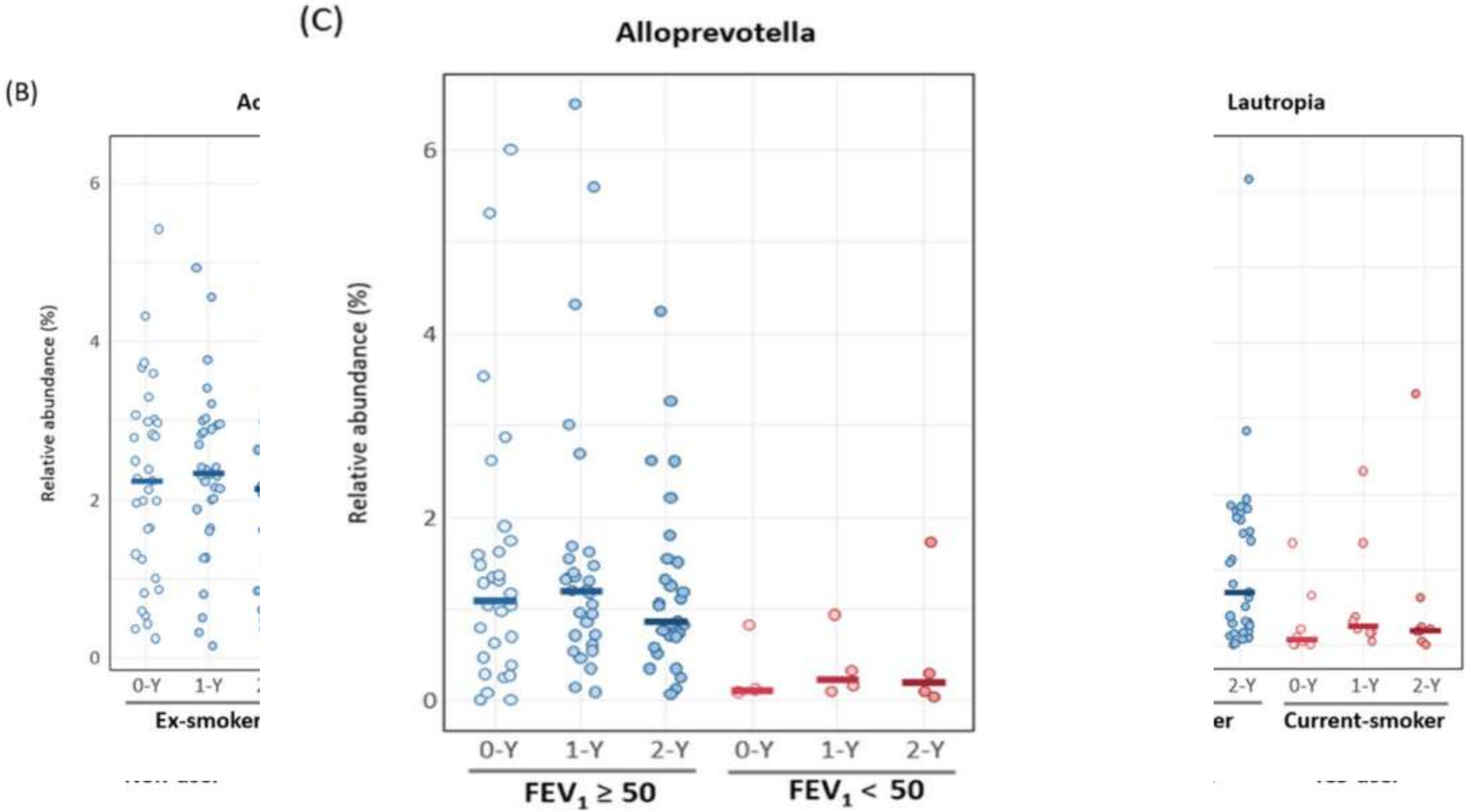
➢ *Actinomyces*

➢ *Bulleidia*

and reduced:

➢ *Lautropia*

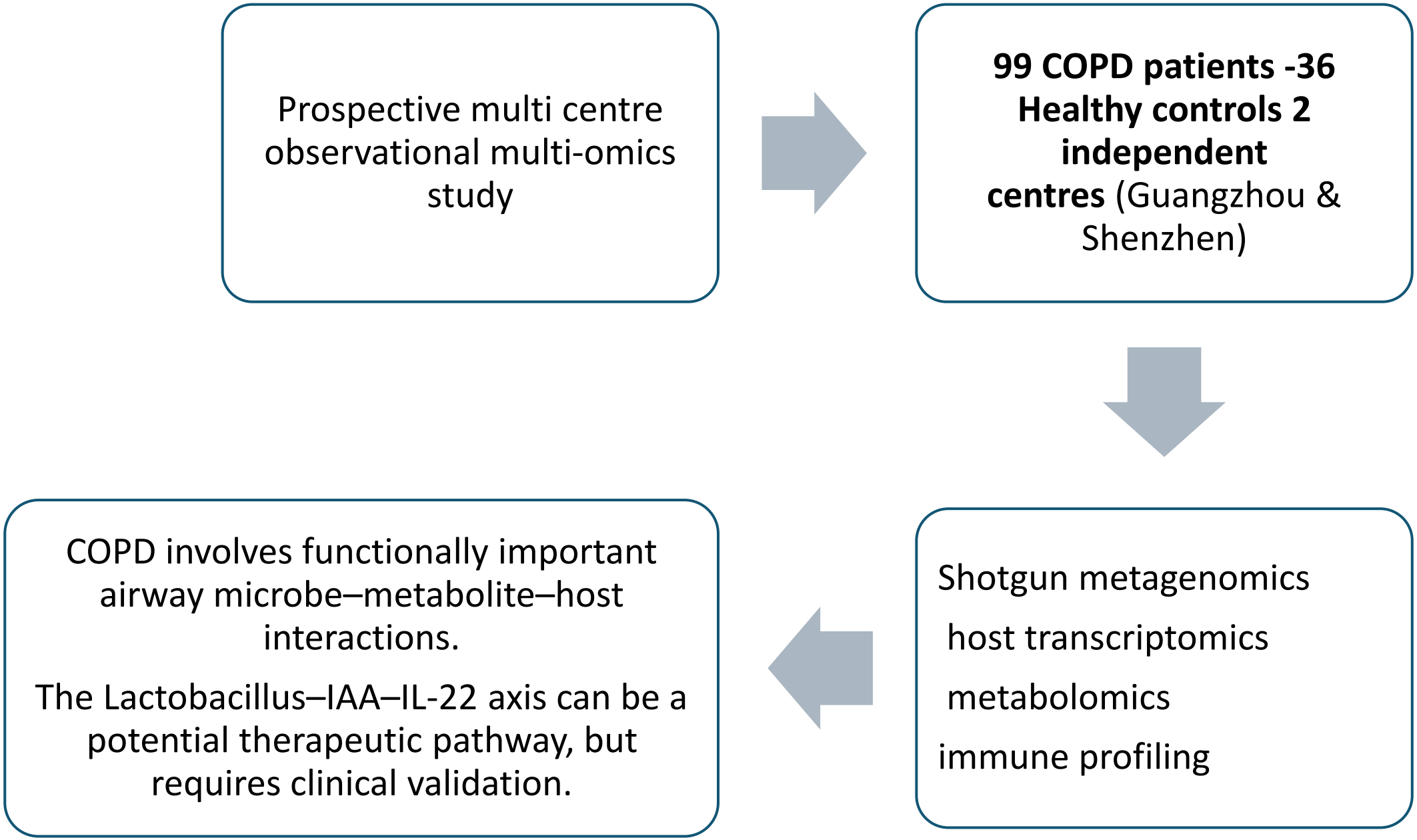
Moon SW et al; Longitudinal change of lung microbiome in chronic obstructive pulmonary disease: a prospective cohort study; Respir Res. 2026 Feb 25



Moon SW et al; Longitudinal change of lung microbiome in chronic obstructive pulmonary disease: a prospective cohort study; Respir Res. 2026 Feb 25

Type of study	Systematic review and meta-analysis
Evidence base	21 → COPD (COPD; 1,273 patients and 6,718 healthy controls) 6→ asthma. (559 patients and 5,310 HCs), 1→ COPD and asthma combined, 1→pulmonary cystic fibrosis
Main findings in COPD	• ↓ **Bifidobacterium**. • ↓ **Lactobacillus**
Asthma findings	No significant difference in gut α-diversity versus healthy controls

Pan J, Zhang Y, Qiu S, Peng S, Kang H, Tung TH, et al. Gut microbiome dysbiosis in chronic lung disease: a systematic review and meta-analysis. *Front Cell Infect Microbiol.* 2025;15:1554846. doi:10.3389/fcimb.2025.1554846.

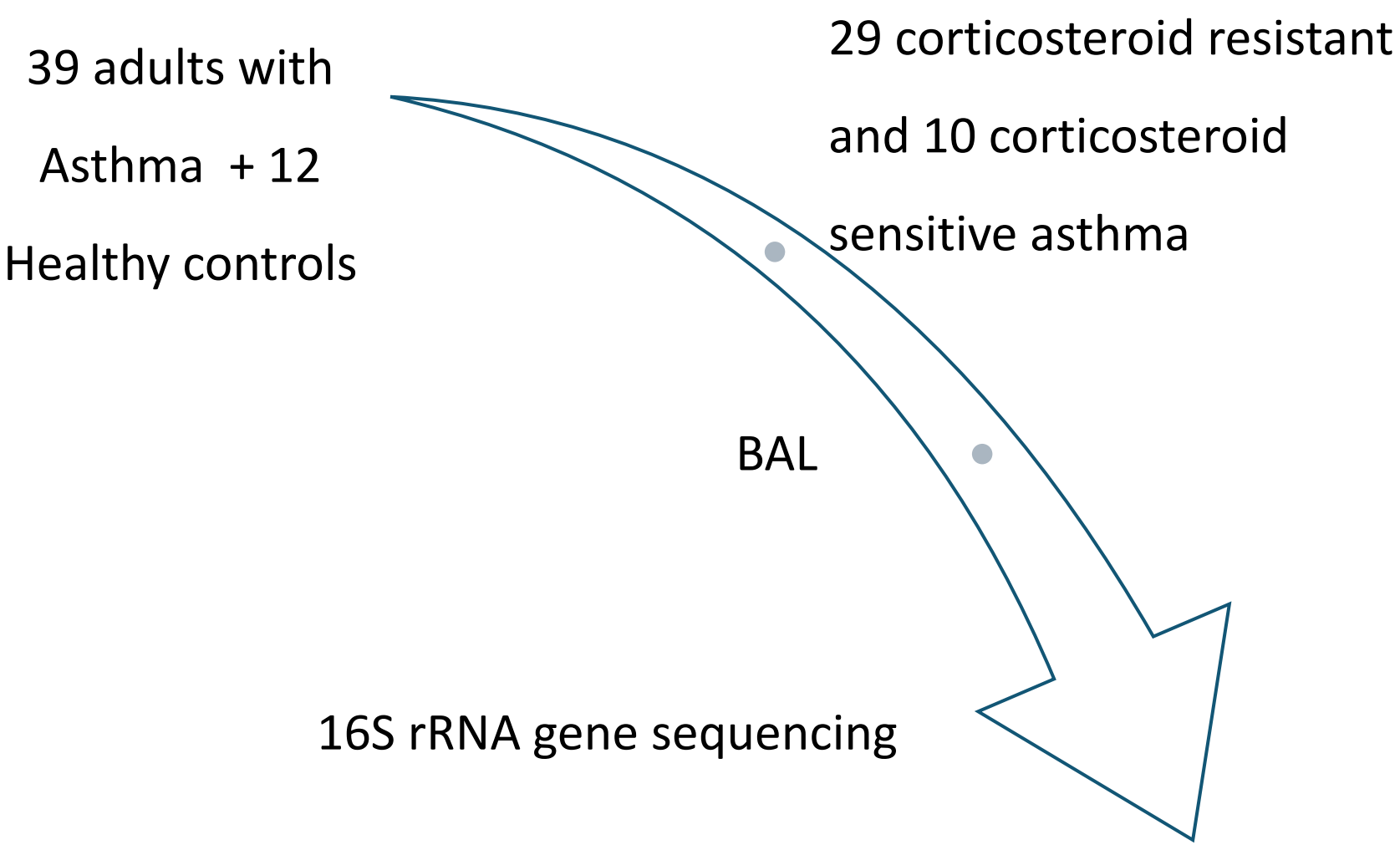


Yan Z et al; Multi-omics analyses of airway host-microbe interactions in chronic obstructive pulmonary disease identify potential therapeutic interventions; Nat Microbiol. 2022 Sep;7

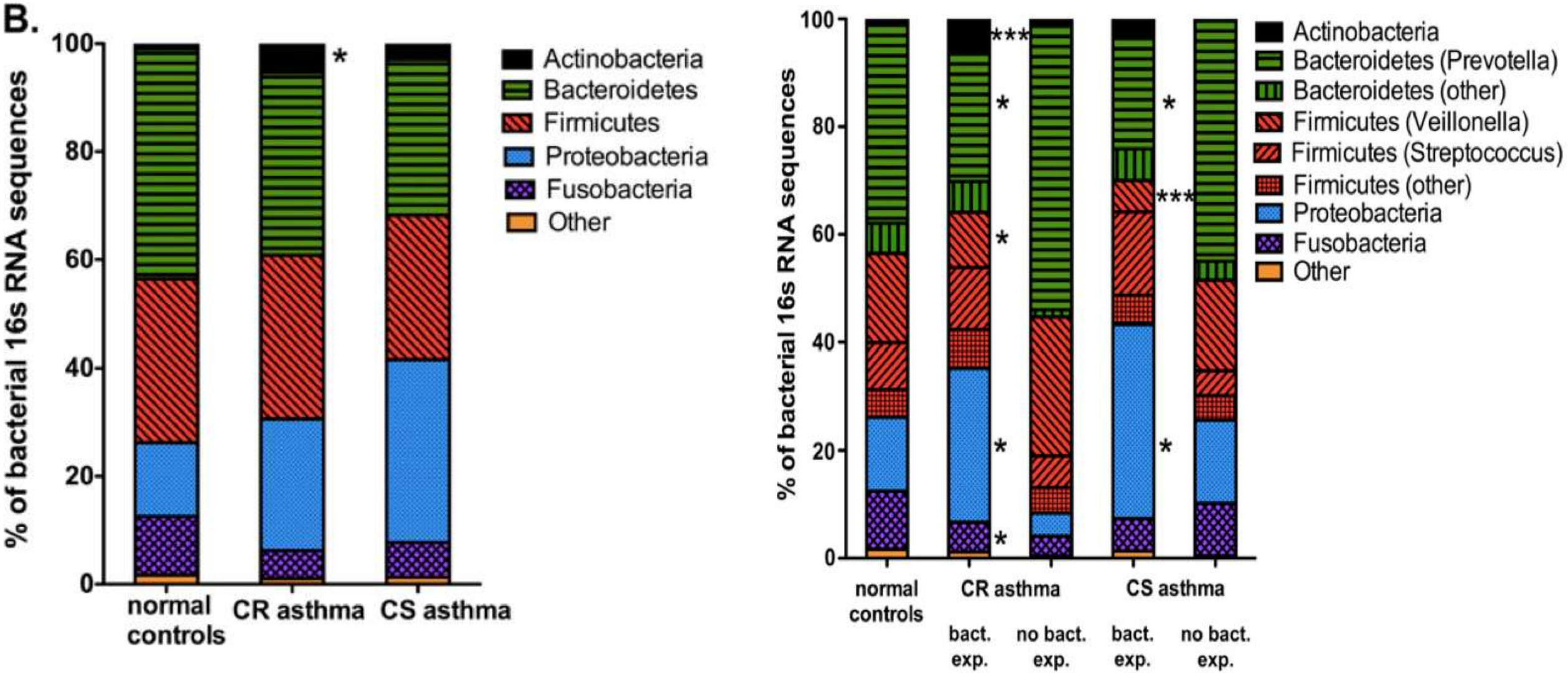
LUNG MICROBIOME AND BRONCHIAL ASTHMA

Type of study	Prospective birth cohort study – KOALA cohort
Follow up	From birth to 6-7 years
Methodology	• Questionnaire • Infant fecal sample at 1 month • Determination of atopic sensitization – specific IgE
Results	→Clostridium difficile colonization at 1 month was linked to later wheeze, eczema and asthma. →Vaginal home delivery had lower risk of asthma and food sensitization than vaginal hospital delivery, mainly in children with atopic parents.

van Nimwegen FA, et al. *J Allergy Clin Immunol.* 2011;128:948–955.e3. doi:10.1016/j.jaci.2011.07.027.



Goleva E, Jackson LP, Harris JK, et al. The effects of airway microbiome on corticosteroid responsiveness in asthma. *Am J Respir Crit Care Med*. 2013;188:1193–1201.



Goleva E, Jackson LP, Harris JK, et al. The effects of airway microbiome on corticosteroid responsiveness in asthma. *Am J Respir Crit Care Med*. 2013;188:1193–1201.

Prospective Longitudinal cohort study

Serial nasopharyngeal swabs every **2–4 weeks** over autumn–winter. 16S rRNA sequencing was used to study microbiome changes during stable asthma and exacerbation.

33 asthmatic schoolchildren + 20 non-asthmatic controls

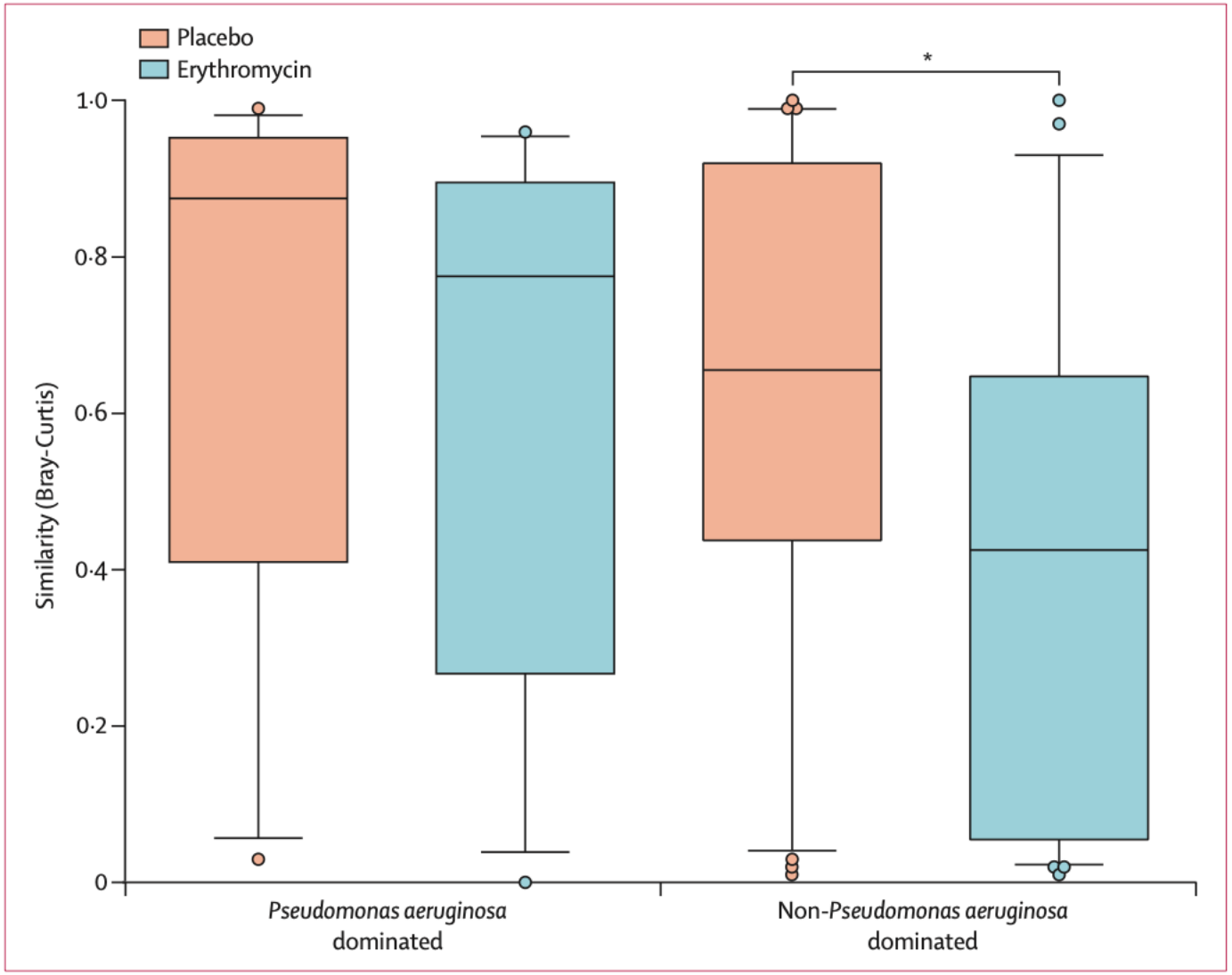
144 nasopharyngeal swabs successfully sequenced: 135 asthma samples + 9 controls

Hou J, et al. Temporal dynamics of the nasopharyngeal microbiome and its relationship with childhood asthma exacerbation. *Microbiol Spectr.* 2022;10:e00129-22.

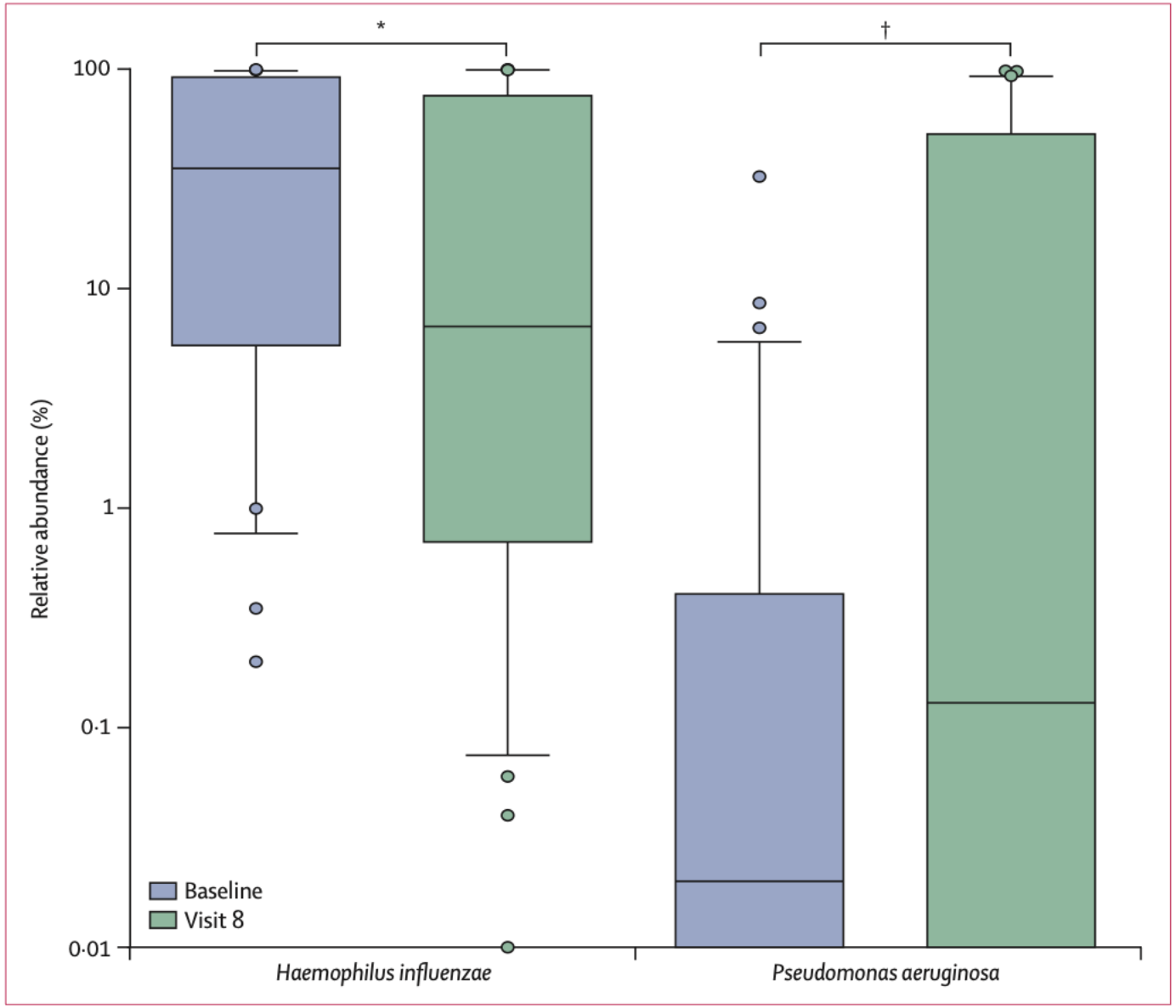
LUNG MICROBIOME AND BRONCHIECTASIS

Type of study	**Microbiome analysis from the randomized, double blind, placebo-controlled BLESS trial**
Study population	Adults with non- CF bronchiectasis and ≥2 infective exacerbations in previous year
Intervention	Erythromycin 400mg BD x 12 months
Samples analyzed	Paired sputum sample → 86 patients : placebo (42) and Erythromycin (44)
Method	16S rRNA sequencing of sputum microbiota

Rogers GB, Bruce KD, Martin ML, Burr LD, Serisier DJ. *Lancet Respir Med*. 2014;2:988–996. doi:10.1016/S2213-2600(14)70213-9.



Rogers GB, Bruce KD, Martin ML, Burr LD, Serisier DJ. *Lancet Respir Med*. 2014;2:988–996. doi:10.1016/S2213-2600(14)70213-9.



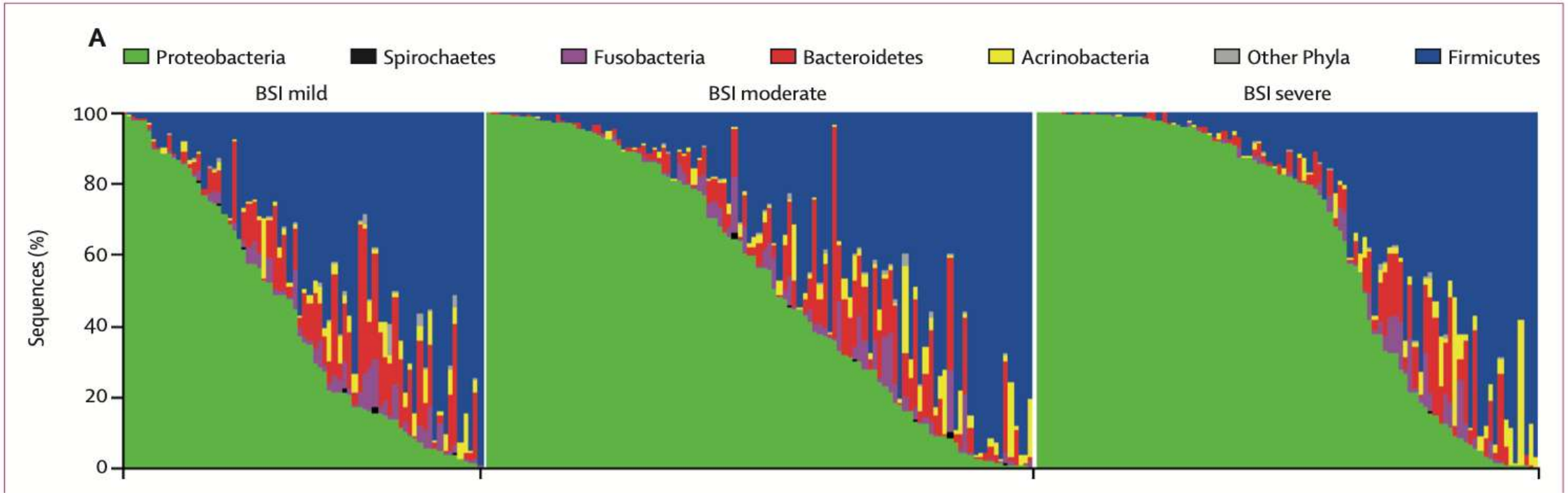
Rogers GB, Bruce KD, Martin ML, Burr LD, Serisier DJ. *Lancet Respir Med*. 2014;2:988–996. doi:10.1016/S2213-2600(14)70213-9.

Type of Study	**International multicentre cross sectional cohort**
Study population	238 stable bronchiectasis patients from Asian and European centres
Methodology	• Sputum fungal profiling using ITS1/ITS2 sequencing • Aspergillus qPCR and conidial quantification • Measured sputum galactomannan, Aspergillus-specific IgE/IgG and TARC • Linked mycobiome profiles with clinical outcomes

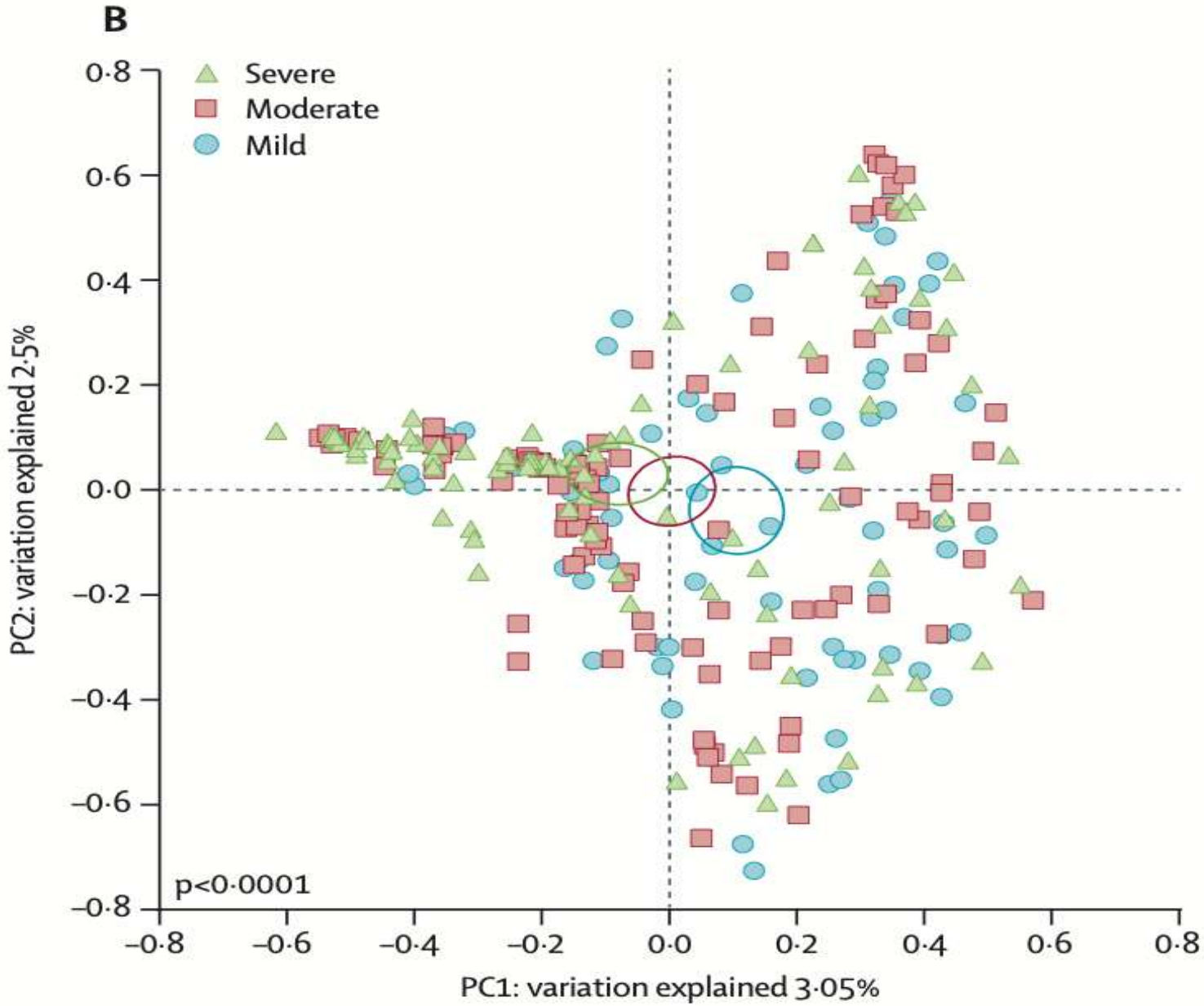
Mac Aogáin M, Chandrasekaran R, Lim AYH, *et al*. *Eur Respir J*. 2018;52:1800766. doi:10.1183/13993003.00766-2018.

Type of study	Longitudinal cohort study
Study population	281 adults with stable non – CF Bronchiectasis Sequencing data → sputum samples of 281 → stable baseline cohort. 49 (17%) → >1 sample when clinically stable →longitudinal analysis. 64 (23%) patients → stable and exacerbation samples.
Follow up	5 years
Method	• Baseline sputum collected during clinical stability • 16S rRNA gene sequencing performed • Patients followed for exacerbations, hospitalisation, lung function decline and mortality

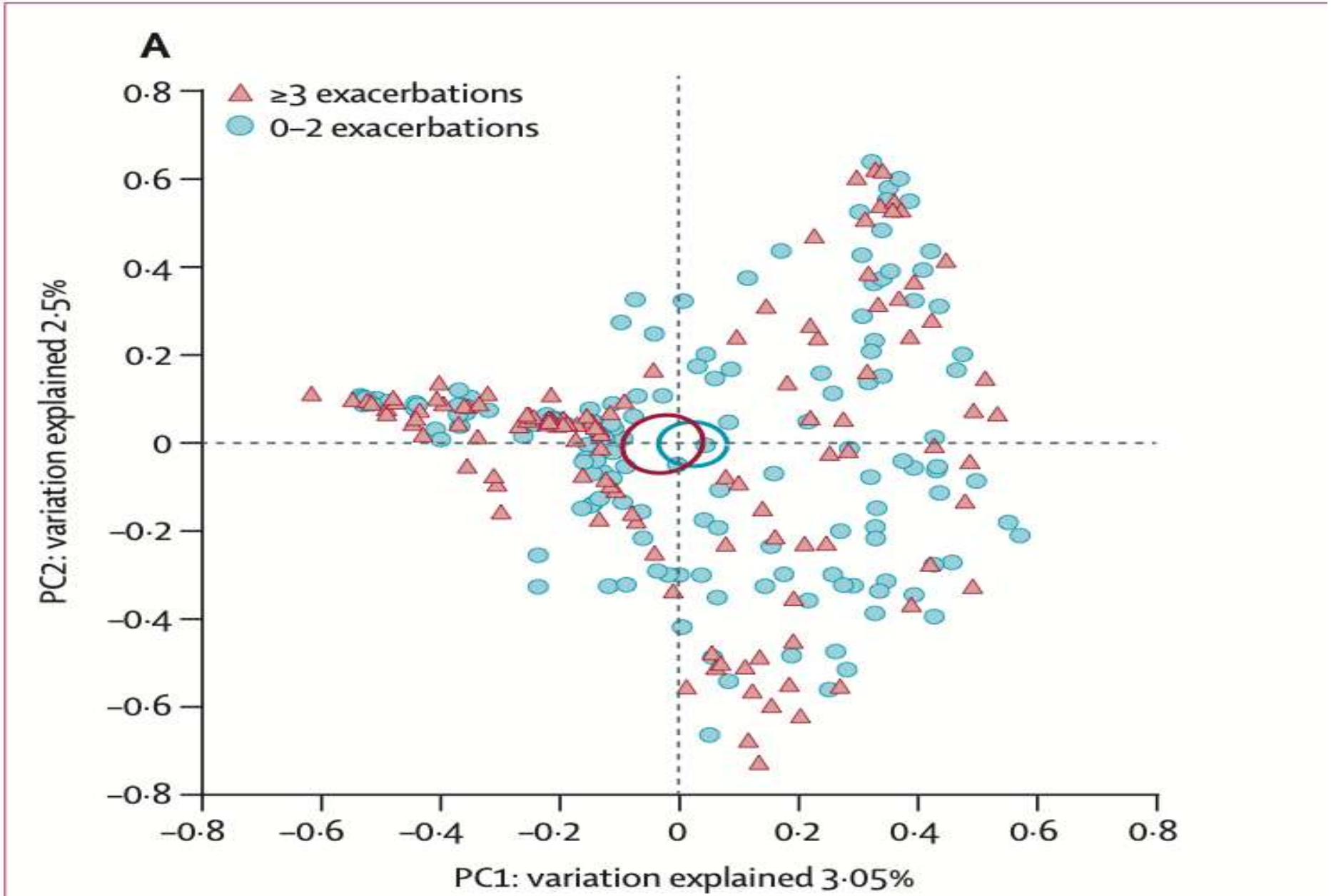
Dicker AJ, Lonergan M, Keir HR, *et al*. The sputum microbiome and clinical outcomes in patients with bronchiectasis: a prospective observational study. *Lancet Respir Med*. 2021;9:885–896.



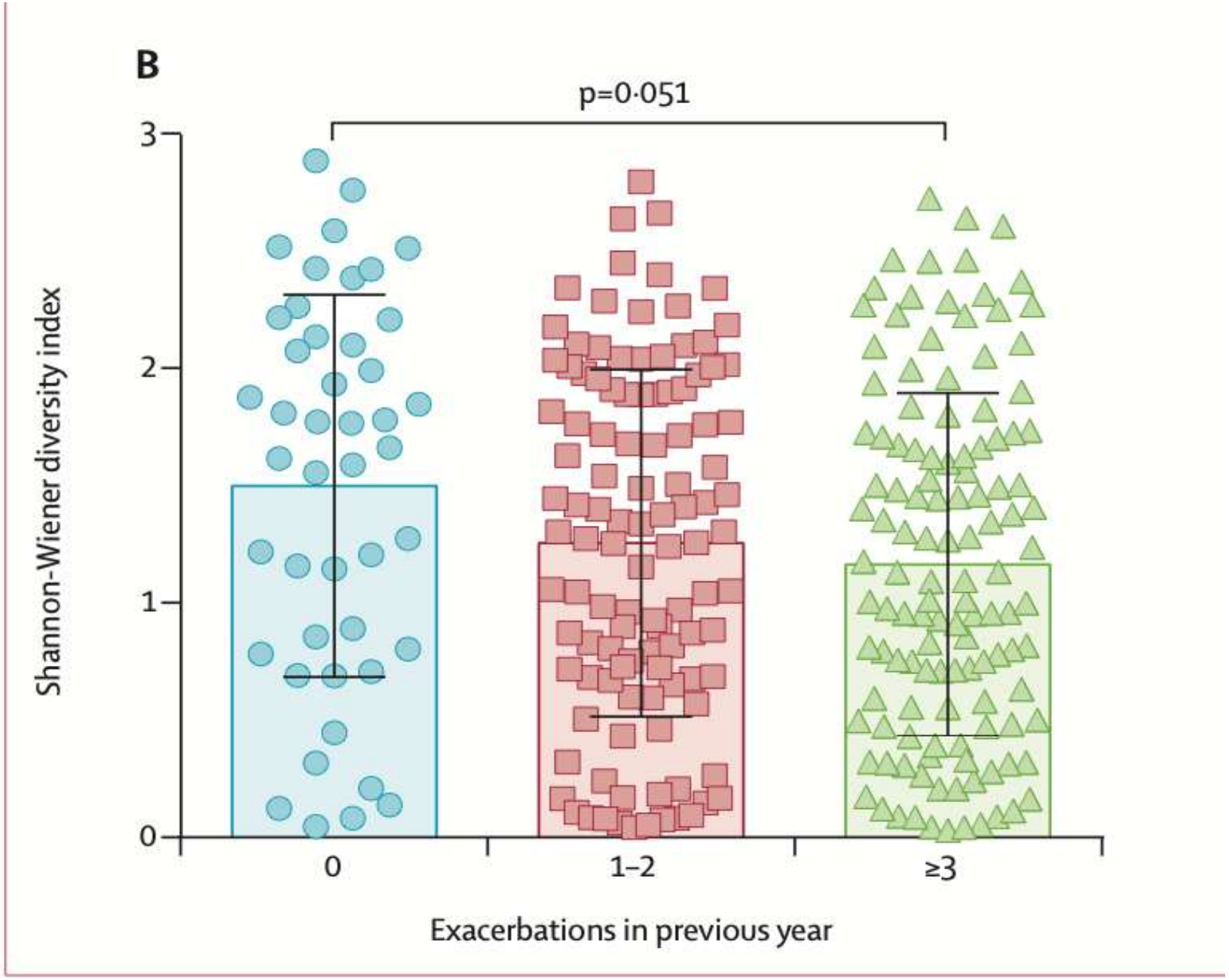
Dicker AJ, Lonergan M, Keir HR, *et al*. **The sputum microbiome and clinical outcomes in patients with bronchiectasis: a prospective observational study.** *Lancet Respir Med*. 2021;9:885–896.



Dicker AJ, Lonergan M, Keir HR, *et al*. **The sputum microbiome and clinical outcomes in patients with bronchiectasis: a prospective observational study.** *Lancet Respir Med*. 2021;9:885–896.



Dicker AJ, Lonergan M, Keir HR, *et al*. **The sputum microbiome and clinical outcomes in patients with bronchiectasis: a prospective observational study.** *Lancet Respir Med*. 2021;9:885–896.



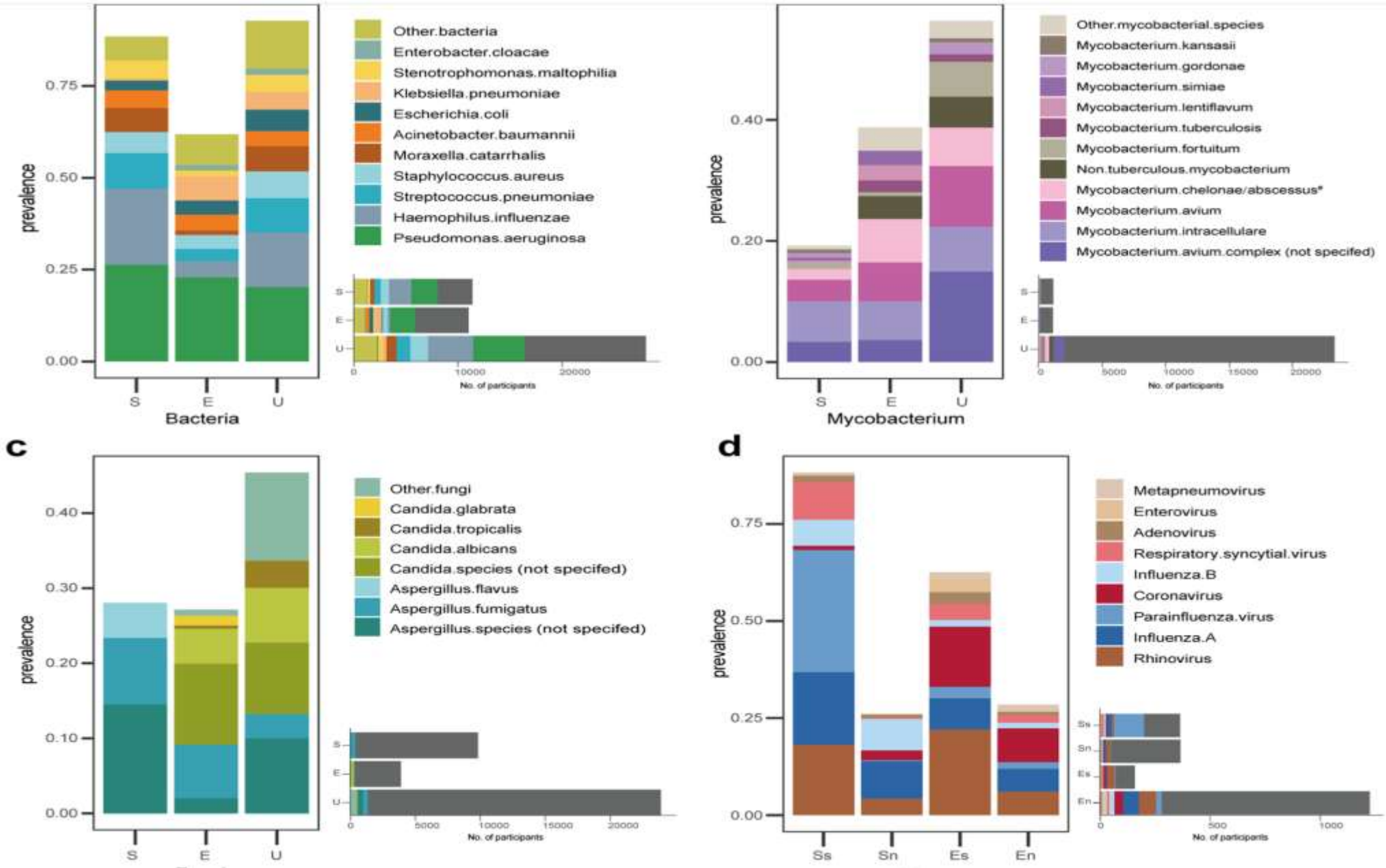
Dicker AJ, Lonergan M, Keir HR, *et al*. **The sputum microbiome and clinical outcomes in patients with bronchiectasis: a prospective observational study.** *Lancet Respir Med*. 2021;9:885–896.

Type of study	Systematic review and meta-analysis
Databases searched	PubMed, Embase, Cochrane + 3 Chinese databases
Period	Jan 2000 – Aug 2023
Included studies	98 studies
Total participants	54,384 adults
Population	Adults with CT-confirmed non-CF bronchiectasis
Analysis groups	Stable, Exacerbation, Undetermined

Wang Y, Xiao J, Yang X, *et al*. *Respir Res*. 2025;26:77.
doi:10.1186/s12931-025-03140-w.

Microbe group	Key findings
Bacteria	Pseudomonas aeruginosa most common across stages
Stable state	P. aeruginosa 26%, H. influenzae 21%
Exacerbation	P. aeruginosa 23%, K. pneumoniae higher at 7%
Mycobacteria	MAC/NTM detected; often underreported
Fungi	Aspergillus more in stable state; Candida more in exacerbation
Viruses	Rhinovirus most common; detection depended more on sample type than disease stage

Wang Y, Xiao J, Yang X, *et al*. *Respir Res*. 2025;26:77.
doi:10.1186/s12931-025-03140-w.

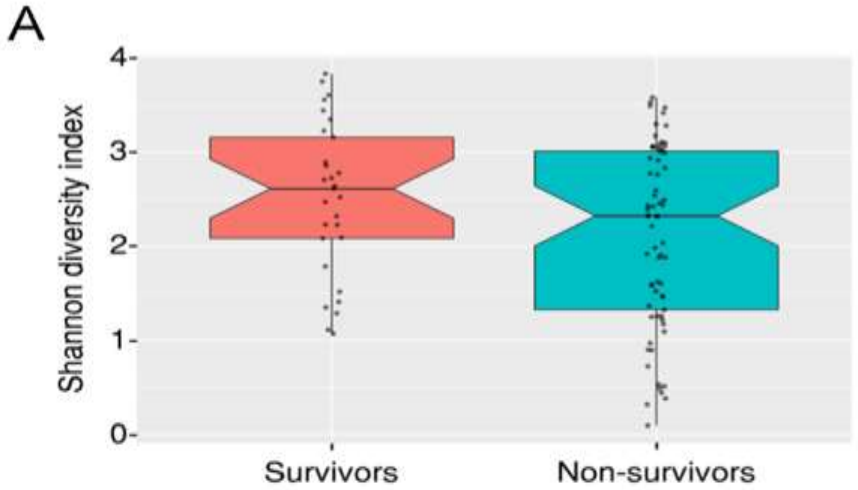


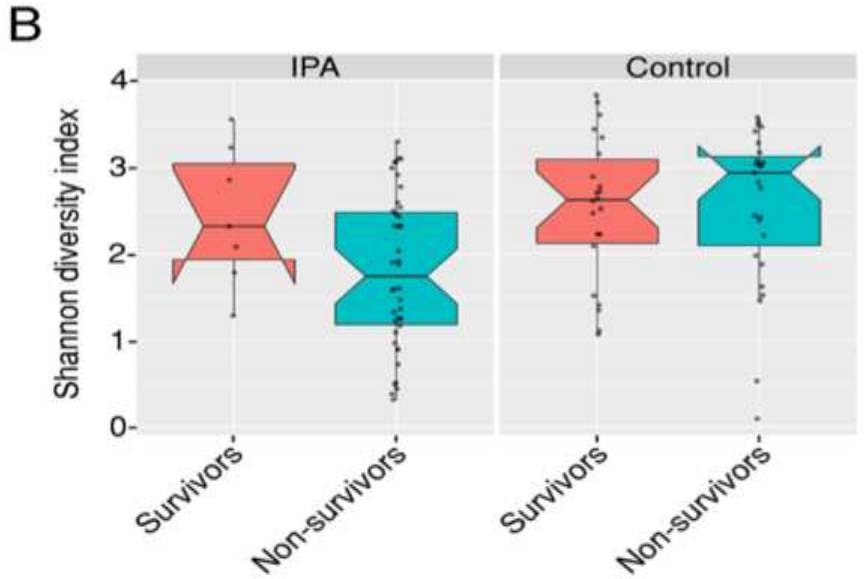
Wang Y, Xiao J, Yang X, *et al*. *Respir Res*. 2025;26:77. doi:10.1186/s12931-025-03140-w.

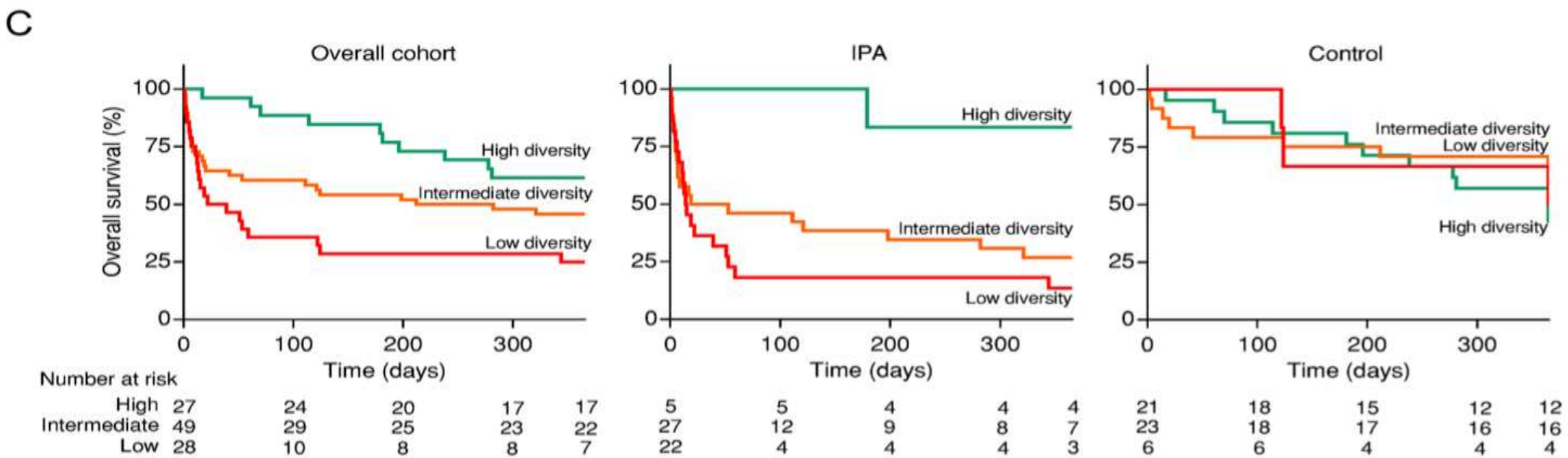
LUNG MICROBIOME IN ASPERGILLOSIS

Type of study	Observational cohort study
Study population	104 immunocompromised adults
Groups	IPA: 54; Controls: 50
Sample	Bronchoalveolar lavage
Method	16S rRNA sequencing + BAL immune profiling
Key clinical differences	IPA group had more ICU admission: 51.9% vs 24%, and more mechanical ventilation: 33.3% vs 10%
Microbiome findings	IPA had reduced alpha diversity and enrichment of Staphylococcus, Escherichia, Paraclostridium, Finegoldia
Depleted in IPA	Prevotella and Veillonella

Hérivaux A, Willis JR, Mercier T, *et al*. *Thorax*. 2022;77:283–291. doi:10.1136/thoraxjnl-2020-216179.







Hérivaux A, Willis JR, Mercier T, *et al*. *Thorax*. 2022;77:283–291. doi:10.1136/thoraxjnl-2020-216179.

Type of Study	Prospective observational study
Study Population	**111 hospitalized CAP patients** undergoing bronchoscopy

What was done?

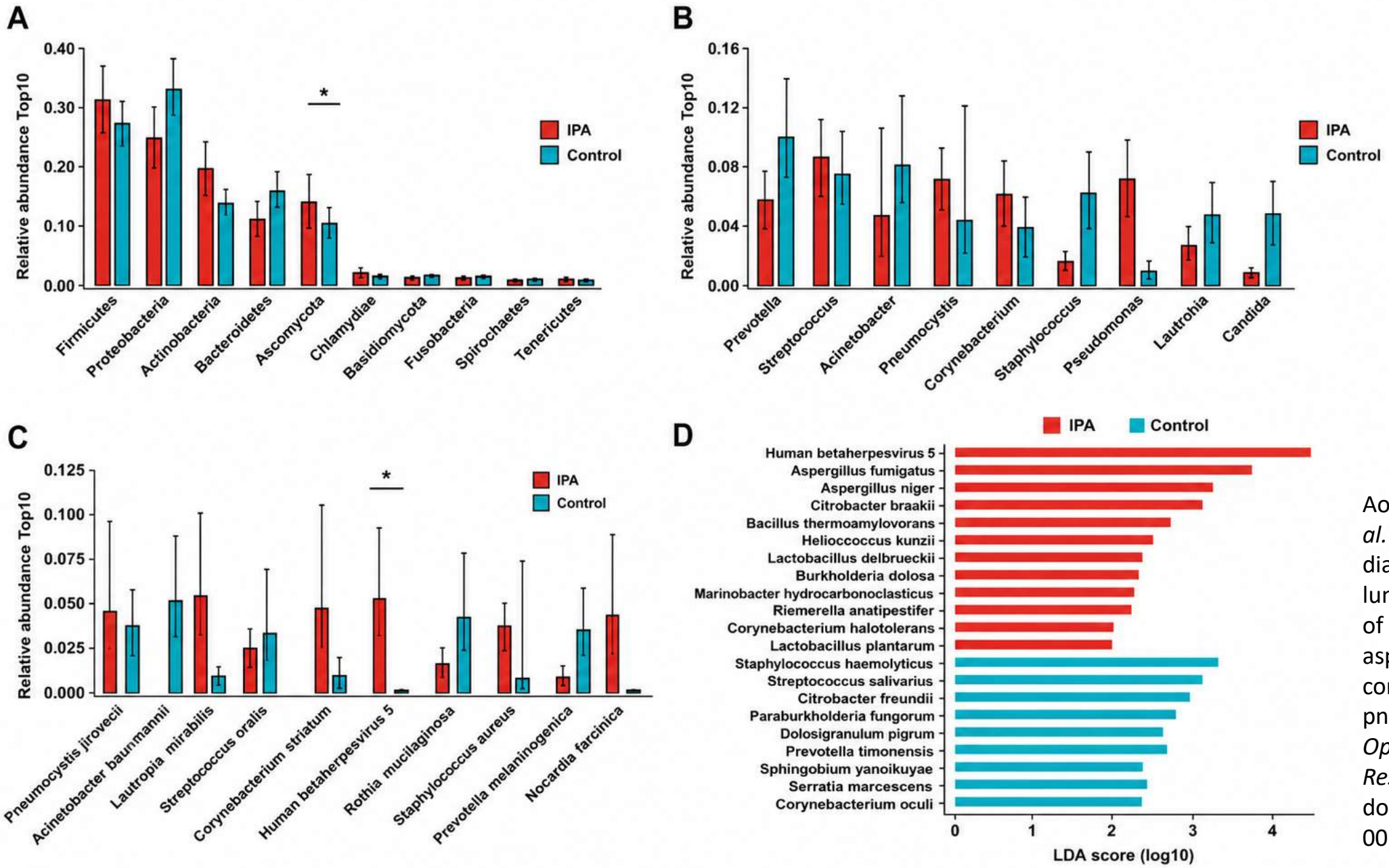
- Bronchoalveolar lavage (BAL) collected for microbiological evaluation.
- BAL microbiome analysed using **16S rRNA sequencing**.
- Clinical outcomes compared between IPA and non-IPA patients.

Ao Z, Xu H, Li M, *et al*. Clinical characteristics, diagnosis, outcomes and lung microbiome analysis of invasive pulmonary aspergillosis in the community-acquired pneumonia patients. *BMJ Open Respir Res*. 2023;10:e001358. doi:10.1136/bmjresp-2022-001358.

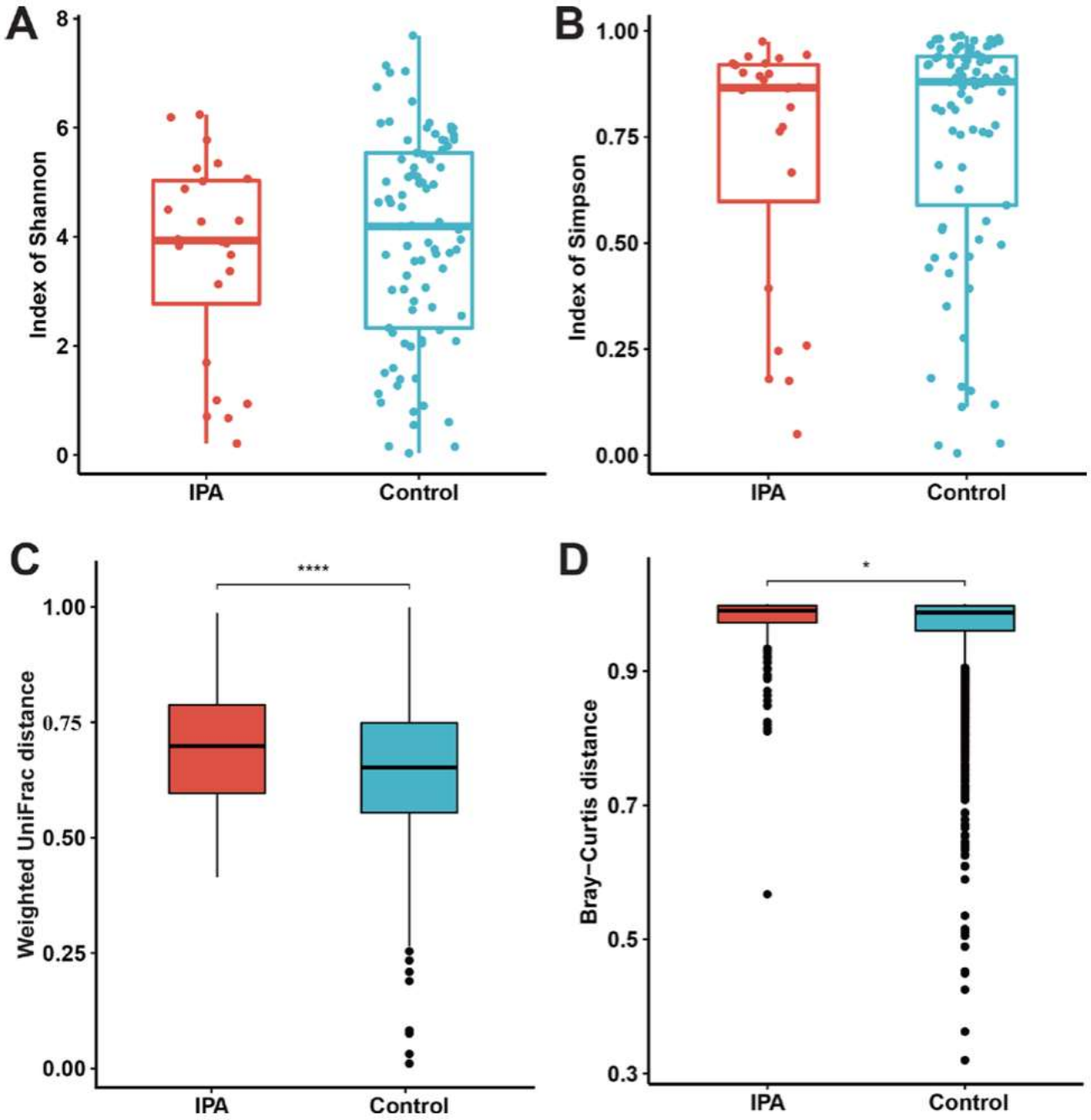
Results

- Microbiome analysis available in 109 patients (24 IPA, 85 controls)
- β-diversity differed significantly between IPA and controls ($P<0.001$).
- α-diversity (Shannon and Simpson) was lower in IPA but not statistically significant.

Ao Z, Xu H, Li M, *et al.* Clinical characteristics, diagnosis, outcomes and lung microbiome analysis of invasive pulmonary aspergillosis in the community-acquired pneumonia patients. *BMJ Open Respir Res.* 2023;10:e001358. doi:10.1136/bmjresp-2022-001358.



Ao Z, Xu H, Li M, *et al.* Clinical characteristics, diagnosis, outcomes and lung microbiome analysis of invasive pulmonary aspergillosis in the community-acquired pneumonia patients. *BMJ Open Respir Res.* 2023;10:e001358. doi:10.1136/bmjresp-2022-001358.

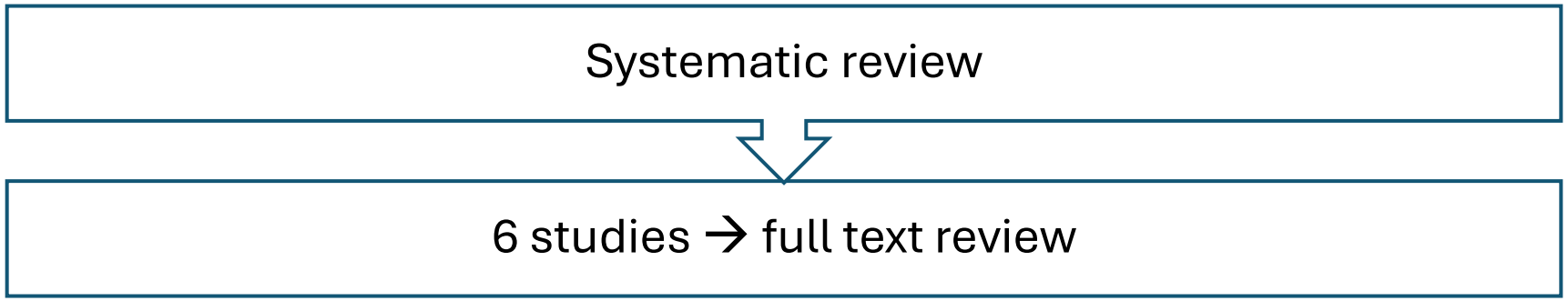


Ao Z, Xu H, Li M, *et al.* Clinical characteristics, diagnosis, outcomes and lung microbiome analysis of invasive pulmonary aspergillosis in the community-acquired pneumonia patients. *BMJ Open Respir Res.* 2023;10:e001358. doi:10.1136/bmjresp-2022-001358.

LUNG MICROBIOME IN ILD

Type of Study	Prospective multicentre cohort study (COMET)
Study Population	55 patients with idiopathic pulmonary fibrosis (IPF) enrolled in the COMET study
Methods	• Bronchoalveolar lavage (BAL) → 16S rRNA qPCR → prospective follow up.
Primary Outcome	Disease progression, defined as death, acute exacerbation, lung transplantation, or ≥10% decline in FVC within 48 weeks.

Han MK et al.; COMET Investigators. Lung microbiome and disease progression in idiopathic pulmonary fibrosis: an analysis of the COMET study. *Lancet Respir Med.* 2014



Key findings

- IPF showed altered lung microbiome and reduced diversity.
- IPF patients may carry higher bacterial burden than controls.
- Increased bacterial load was linked to faster IPF progression and higher mortality.
- Streptococcus and Staphylococcus were associated with poorer IPF outcomes.
- AE-IPF showed higher bacterial burden and enrichment of Proteobacteria such as Campylobacter and Stenotrophomonas.
- Evidence in HP and sarcoidosis remains limited.

Puiu R, Motoc NS, Lucaciu S, *et al*. *Biomolecules*. 2024;14:247.
doi:10.3390/biom14030247

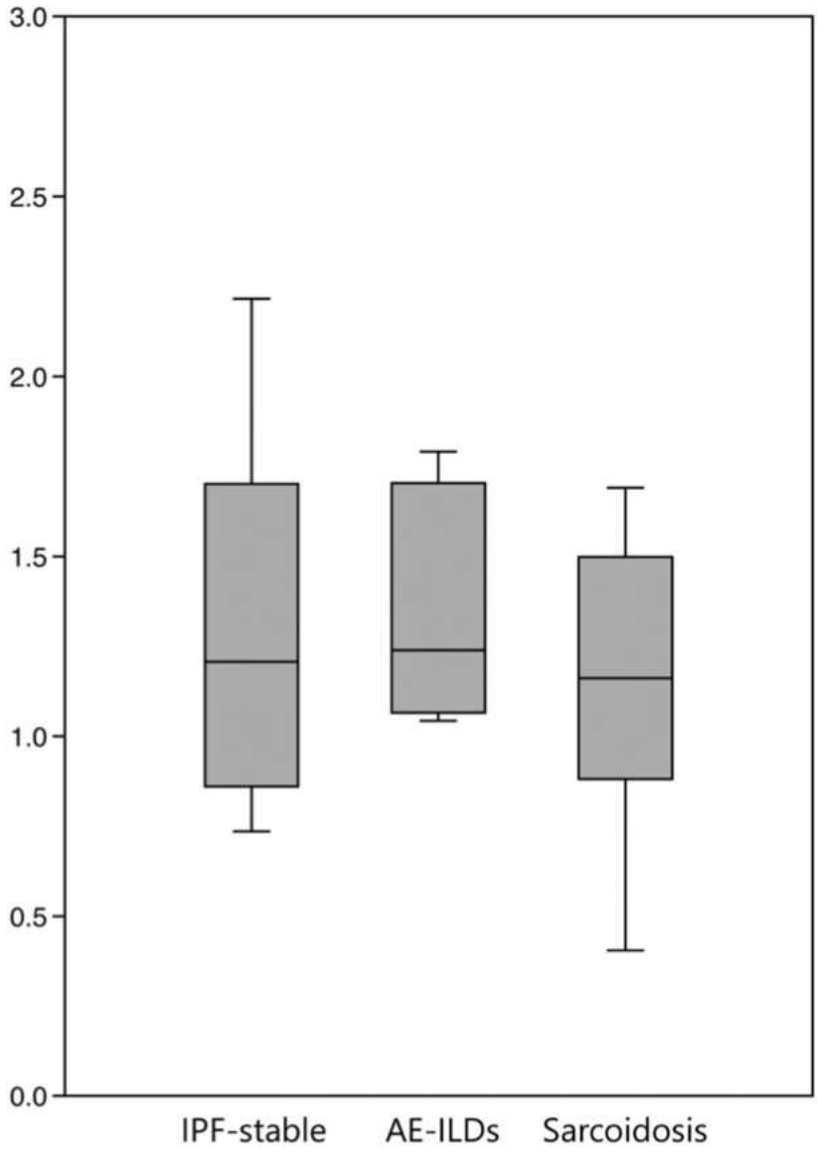
Type of study	Experimental observational study
Study population	**31 patients**
Groups	**IPF-stable: n=12**; **AE-ILDs: n=6**; **Sarcoidosis: n=13**
Sample	Bronchoalveolar lavage fluid
Method	**RNA-based metagenomic NGS** on Illumina platform
What was done?	Compared BALF microbial reads and lung microbiome structure across stable IPF, acute exacerbation of ILD, and sarcoidosis.

Takeuchi S, Kawada JI, Suzuki A, et al. *Health Sci Rep.* 2025;8(2):e70328. doi:10.1002/hsr2.70328.

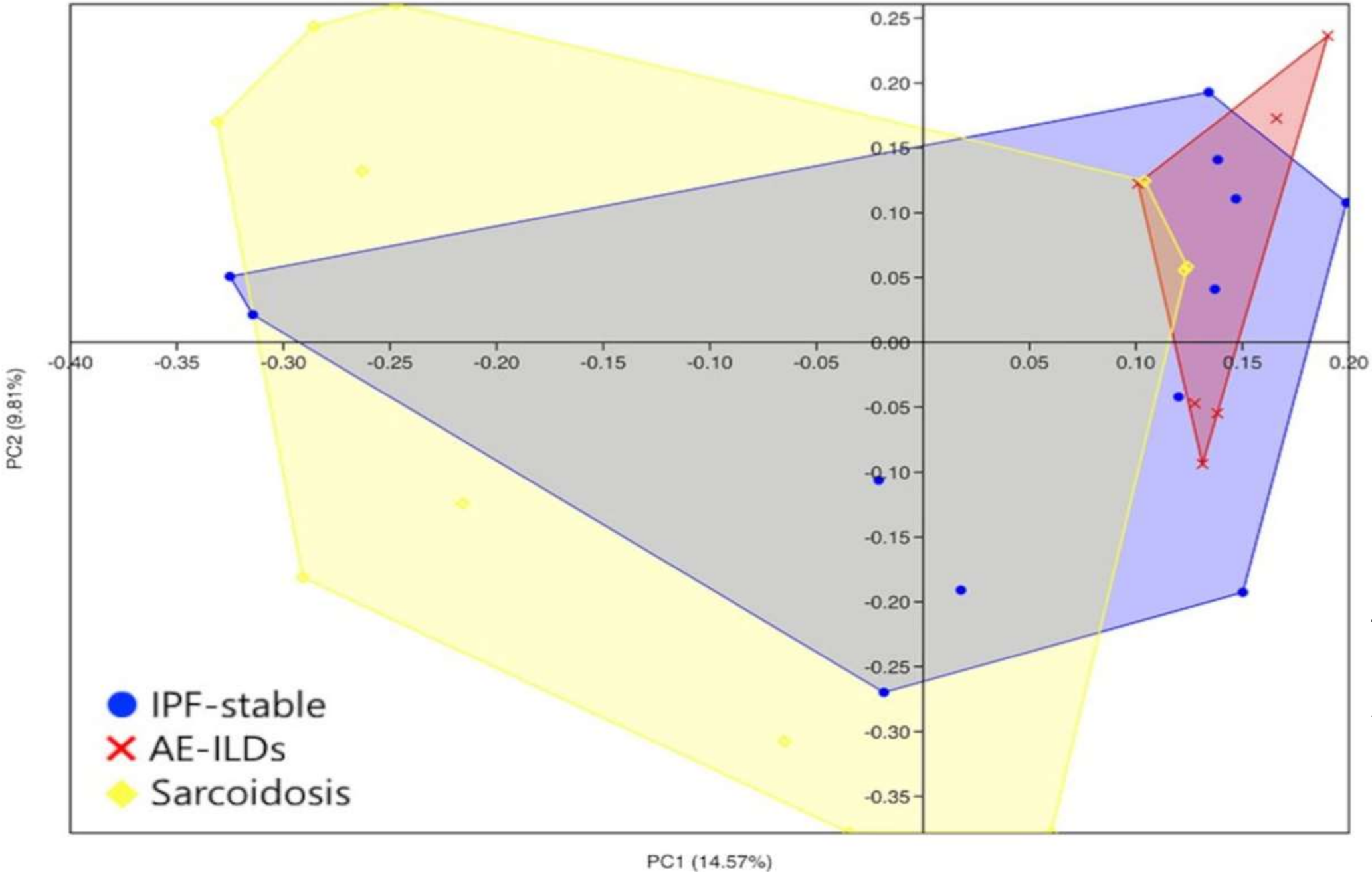
Key findings

- 87 pathogens detected at genus level.
- Dominant genera: Prevotella, Streptococcus, Veillonella.
- These reads were most abundant in sarcoidosis.
- AE-ILDs had only small numbers of bacterial reads.
- α-diversity: no significant difference among groups .
- β-diversity: significantly different between AE-ILDs and sarcoidosis.

Takeuchi S, Kawada JI, Suzuki A, et al. *Health Sci Rep*. 2025;8(2):e70328. doi:10.1002/hsr2.70328.



Takeuchi S, Kawada JI, Suzuki A, et al. *Health Sci Rep*. 2025;8(2):e70328. doi:10.1002/hsr2.70328.

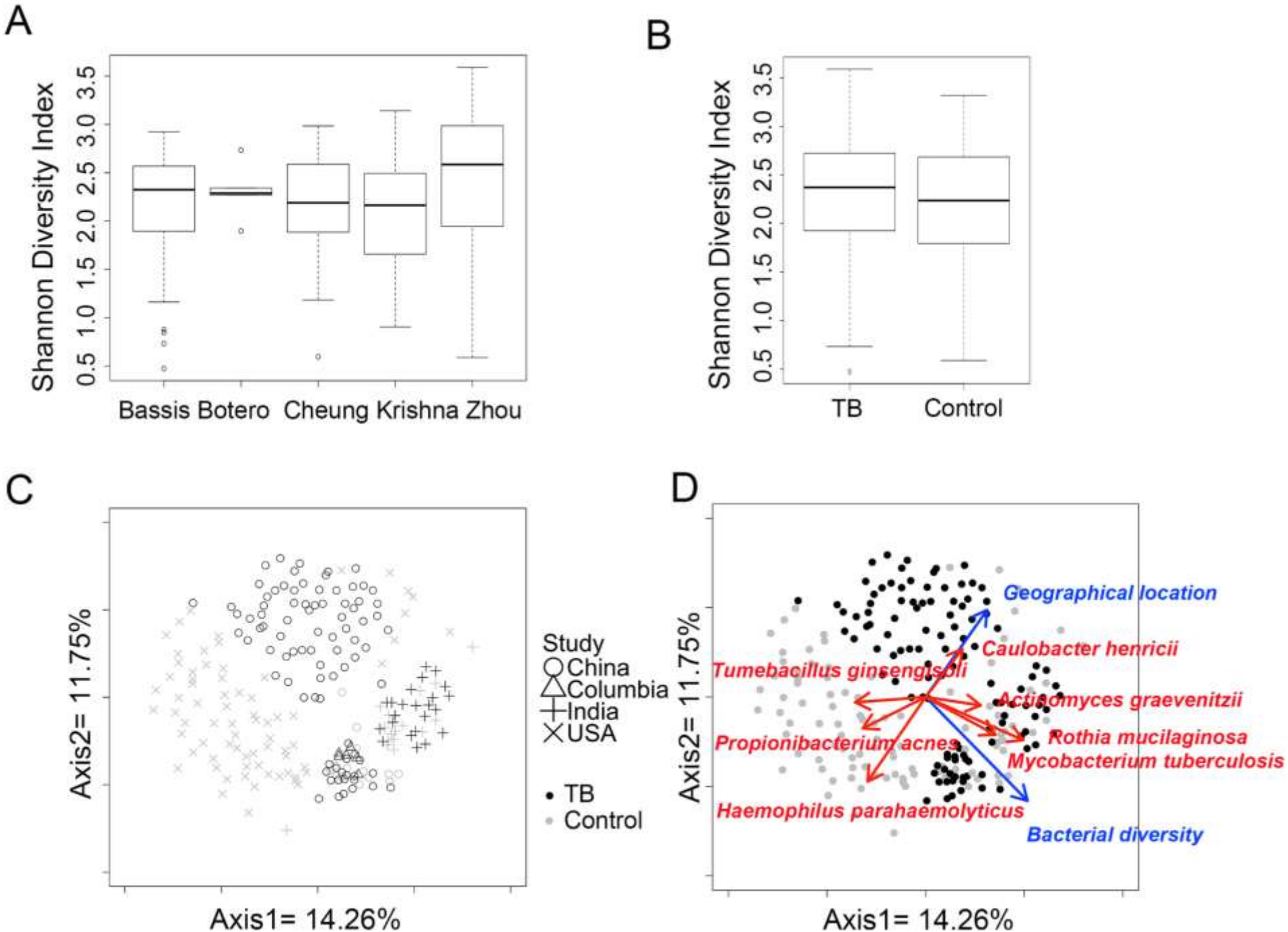


Takeuchi S, Kawada JI, Suzuki A, et al. *Health Sci Rep*. 2025;8(2):e70328. doi:10.1002/hsr2.70328.

LUNG MICROBIOME IN TUBERCULOSIS AND NTM

Type of study	Meta-analysis and standardized re-analysis of published 16S rRNA lung microbiome datasets in pulmonary tuberculosis.
Methodology	Integrated raw sequencing data from PTB patients and healthy controls using a uniform bioinformatics pipeline; performed taxonomic and microbial network analyses.
Key findings	• PTB showed a distinct lung microbiome compared with controls. • PTB enriched with M. tuberculosis, Rothia mucilaginosa, Actinomyces graevenitzii. • Controls enriched with Cutibacterium acnes and Haemophilus parahaemolyticus.

Hong BY, Paulson JN, Stine OC, Weinstock GM, Cervantes JL. Meta-analysis of the lung microbiota in pulmonary tuberculosis. *Tuberculosis (Edinb).* 2018;109:102–108. doi:10.1016/j.tube.2018.02.006.



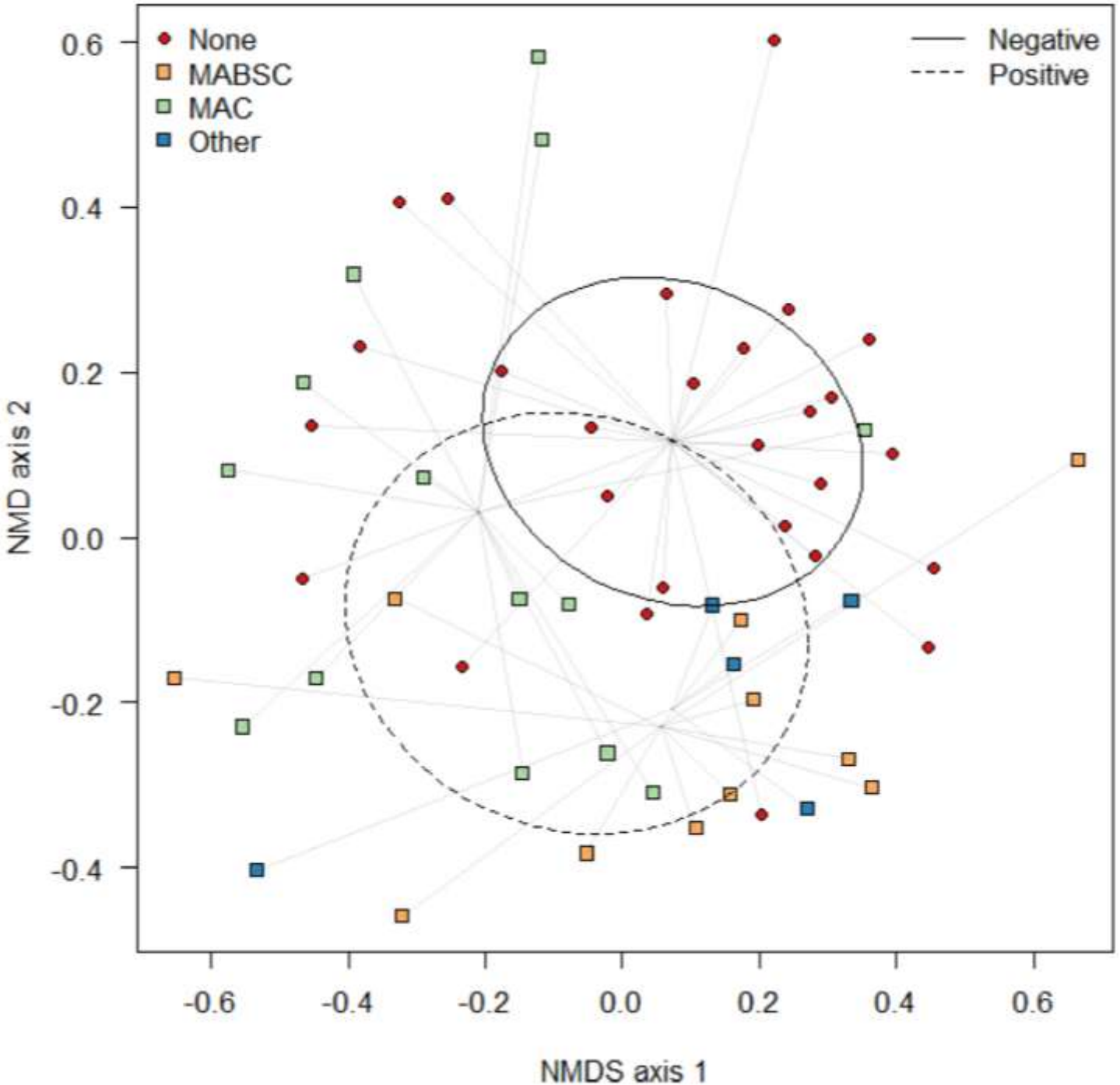
Hong BY, et al. *Tuberculosis (Edinb)*. 2018;109:102–108.

Type of study	Global systematic review, meta-analysis, and patient-level amplicon metagenomic meta-analysis (AMMA) of lung and gut microbiota in tuberculosis.
Methodology	38 studies (3,394 participants) →4 continents.
Key findings	• No universal microbial signature of TB; geography dependent • TB → reduced lung microbial diversity, whereas gut diversity → higher; ATT→ consistently reduced diversity in both lung and gut. • TB depleted core commensal genera

Mbabazi M, Kateete DP, Nakazzi F, Wandera JN, Mutesi N, Ocan M, et al. The impact of tuberculosis and its treatment on the lung and gut microbiota: a global systematic review, meta-analysis, and amplicon-based metagenomic meta-analysis. *BMC Infect Dis.* 2025;26(1):219. doi:10.1186/s12879-025-12369-1.

Type of study	• Prospective observational microbiome study • **shotgun metagenomic sequencing** of sputum • Adults with cystic fibrosis, comparing patients with and without **nontuberculous mycobacterial pulmonary disease (NTM-PD)**.
Key findings	• **NTM infection significantly remodeled the CF airway microbiome**, producing a distinct microbial community structure. •NTM-positive patients showed **reduced microbial network complexity and altered microbial interactions**, indicating ecological disruption

Hardman M, Higgi S, Hanson L, Schutz K, Wargo MJ, Teneback CC, et al. Nontuberculous mycobacteria remodel lung microbiota in cystic fibrosis-associated respiratory infections. *Microbiol Spectr.* 2025;13(9):e0038225. doi:10.1128/spectrum.00382-25.



Hardman M, et al. *Microbiol Spectr.* 2025;13(9):e0038225.

LUNG MICROBIOME IN ARDS

Type of study	Systematic review of pulmonary microbiome alterations in ARDS
Methodology	• 11 observational studies comprising 660 patients (466 with ARDS). • 16S rRNA sequencing, shotgun metagenomics, and culture-independent techniques
Key findings	• ARDS a/w pulmonary microbial dysbiosis, with frequent enrichment of Enterobacteriaceae and other opportunistic pathogens. • Several studies → reduced α-diversity and altered community composition, although findings were heterogeneous. • Gut-associated organisms in the lung were a/w fewer ventilator-free days and higher mortality.

Schneider K, Ulrichsen JU, Westphal AN, Iepsen UW, Ronit A, Plovsing RR, et al. Composition and diversity of the pulmonary microbiome in acute respiratory distress syndrome: a systematic review. *Crit Care.* 2025;29(1):361. doi:10.1186/s13054-025-05548-8.

LUNG TRANSPLANTATION

- Studies post transplant

→higher microbial mass and dysbiosis

→Lower α diversity and altered composition

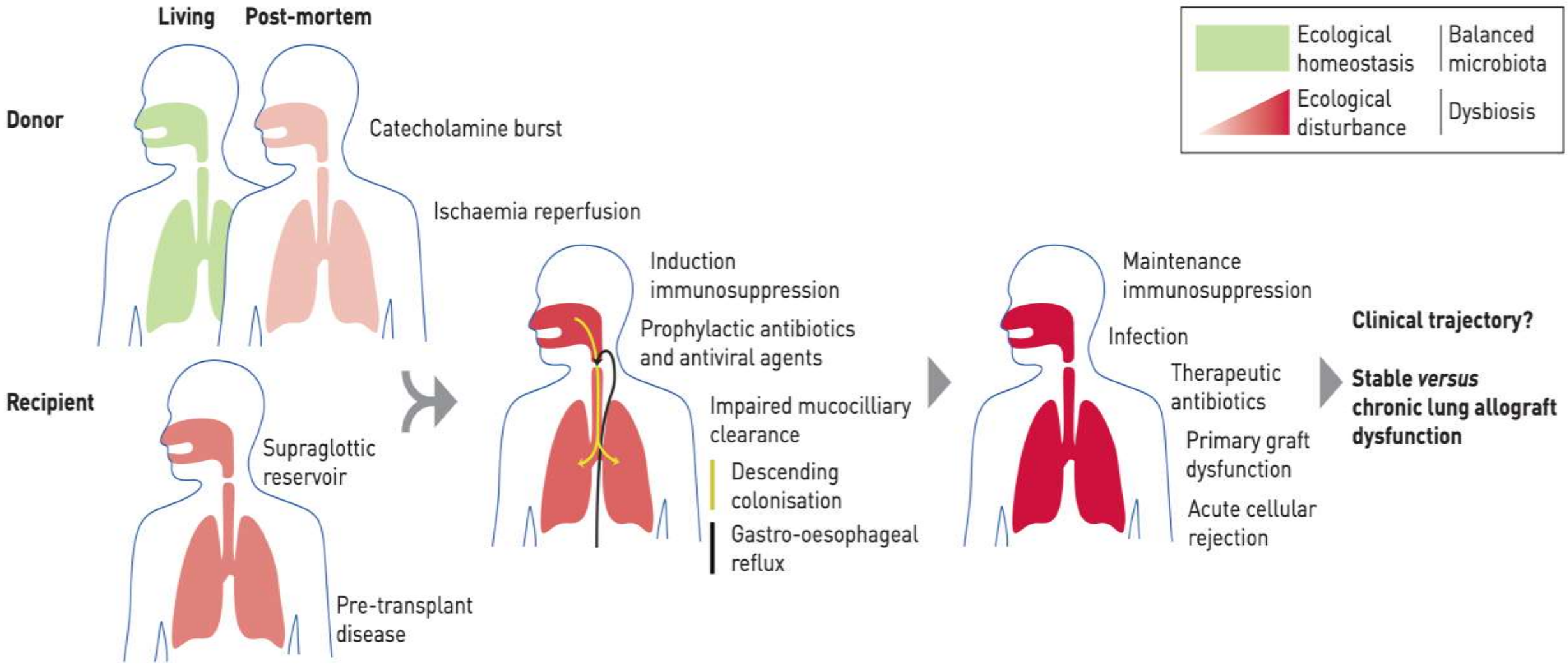
A number of studies have shown that an increase in bacterial biomass in the allograft, and enrichment with the genera Proteobacteria, or more specifically, Pseudomonas species, is associated with CLAD.

→Donor dependent

→Recipient specific

→Transplantation related

John E McGiniss et al; *J Heart Lung Transplant;* 2021 August


Living
Post-mortem
Donor
Catecholamine burst
Ischaemia reperfusion
Recipient
Supraglottic reservoir
Pre-transplant disease
Induction immunosuppression
Prophylactic antibiotics and antiviral agents
Impaired mucocilliary clearance
Descending colonisation
Gastro-oesophageal reflux
Maintenance immunosuppression
Infection
Therapeutic antibiotics
Primary graft dysfunction
Acute cellular rejection
Clinical trajectory?
Stable *versus* chronic lung allograft dysfunction
Ecological homeostasis
Balanced microbiota
Ecological disturbance
Dysbiosis

Comparison of the Respiratory Microbiome in Healthy Nonsmokers and Smokers

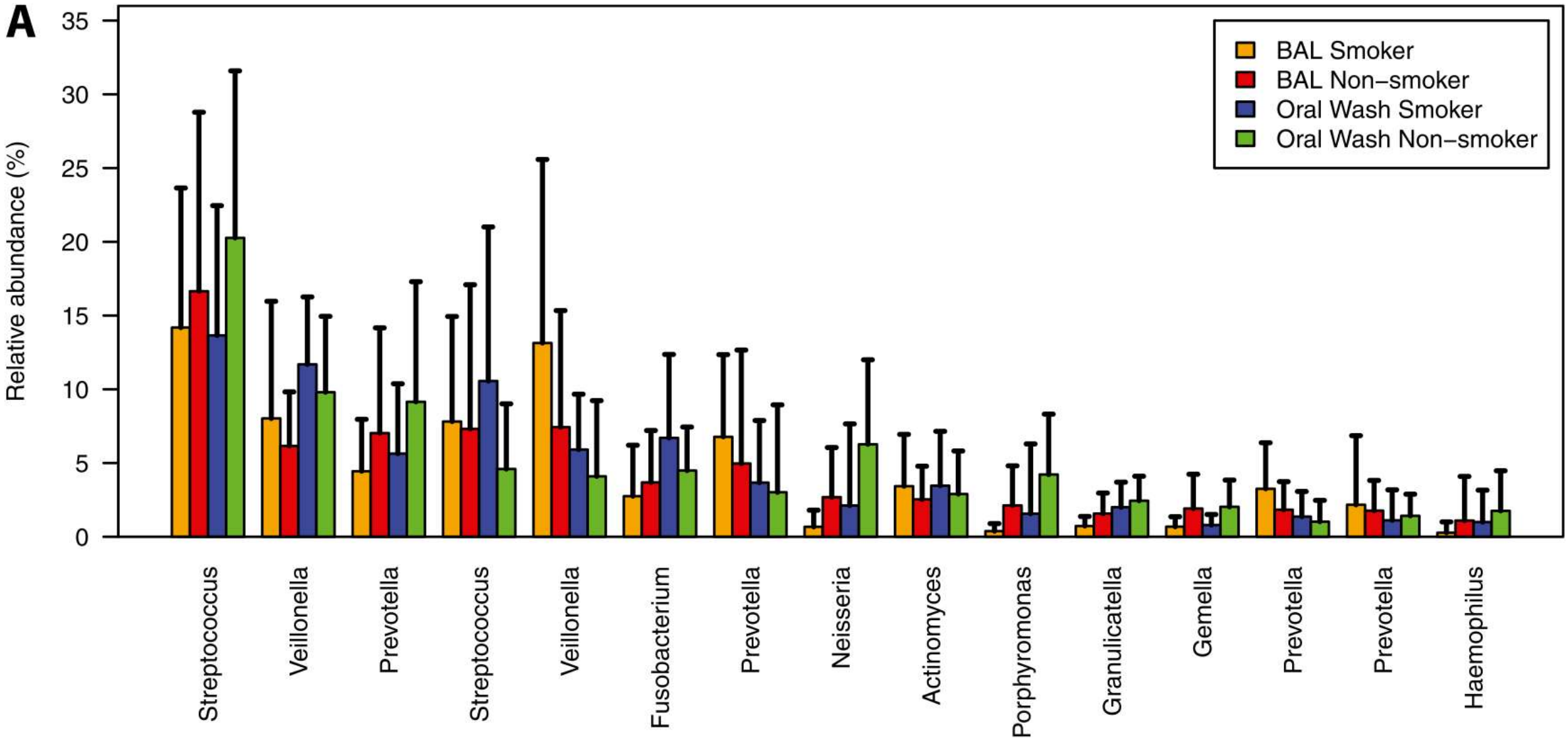
Alison Morris[1,2], James M. Beck[3,4,5], Patrick D. Schloss[3], Thomas B. Campbell[5], Kristina Crothers[6], Jeffrey L. Curtis[3,4], Sonia C. Flores[5], Andrew P. Fontenot[5], Elodie Ghedin[7,8], Laurence Huang[9], Kathleen Jablonski[10], Eric Kleerup[11], Susan V. Lynch[9], Erica Sodergren[12], Homer Twigg[13], Vincent B. Young[3,14], Christine M. Bassis[3,4], Arvind Venkataraman[15], Thomas M. Schmidt[15], and George M. Weinstock[12]; on behalf of the Lung HIV Microbiome Project

Prospective, multisite, observational cohort study

Healthy smokers and nonsmokers from 8 cities → 64 (45 non smokers and 19 current smokers)

→lung bacterial populations are similar to those in the oropharynx, but the lung also contains distinctive populations of organisms

→The mouth microbiome differs in nonsmokers and smokers, but lung communities were not significantly altered by smoking.



Morris A, Beck JM, Schloss PD, et al. *Am J Respir Crit Care Med*. 2013;187(10):1067-1075. doi:10.1164/rccm.201210-1913OC

TAKE HOME POINTS

- The healthy lung is not sterile, it harbors a low-biomass, diverse microbiome maintained by balanced microbial immigration, elimination, and host immunity.
- Respiratory diseases are consistently associated with microbial dysbiosis, characterized by altered community composition, reduced diversity, and enrichment of opportunistic pathogens.
- Disease-specific microbial signatures exist, but no universal microbiome profile has been identified across respiratory disorders.
- The gut–lung axis plays an important immunological role, influencing susceptibility, inflammation, and disease progression through microbial metabolites and immune signaling.

TAKE HOME POINTS

- Microbiome composition influences clinically important outcomes, including corticosteroid responsiveness, exacerbation risk, disease progression, survival, and transplant outcomes.
- Advances from 16S rRNA sequencing to shotgun metagenomics and multi-omics can lead to deeper insights into microbial function and host–microbe interactions.
- Standardization of sampling techniques, sequencing methods, and bioinformatic analysis is essential before microbiome findings can be translated into routine clinical practice.
- The future lies in precision respiratory medicine, where microbiome-based biomarkers and microbiome-targeted therapies may complement conventional treatment strategies.

THANK YOU