The Gut Microbiome in Chronic Obstructive Pulmonary Disease (COPD), Results From a Large Population-Based Cohort

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Rationale: The gut-lung axis represents a bidirectional communication system between the gastrointestinal and respiratory tracts, with growing evidence linking the gut microbiome to lung health. However, human studies conducted so far have been limited by small cohorts or lack of spirometry data, leading to inconsistent findings. This highlights the need for larger, well-characterized cohort studies to better understand the relationship between the gut microbiome, lung function, and chronic obstructive pulmonary disease (COPD). In this study, we investigate these associations in a large population-based cohort, the Lifelines Dutch Microbiome Project.
Methods: Gut microbiome data from 5,445 individuals was analyzed using shotgun metagenomics and extensive clinical data including spirometry. From the total cohort, a subset of 3,515 participants was selected for COPD-specific analyses by excluding those with asthma/other respiratory conditions or age<40. Among these, 632 had COPD (FEV1/FVC <0.7), and 2,883 were classified as non-COPD.
Microbial profiles were analyzed in both the total cohort in relation to lung function (FEV1% predicted) and the subset cohort for the presence of COPD. All linear regression analyses were adjusted for age, sex, smoking status, BMI, antibiotic usage, proton pump inhibitor usage, and technical factors and an FDR<0.05 was considered significant after correcting for multiple testing.
Results: In the total cohort (n=5,445), alpha diversity ($p<0.05$) was positively associated with lung function (FEV1% predicted), indicating that individuals with higher lung function had greater microbiome diversity. Differential abundance analyses revealed 23 bacterial species significant associated with lung function (FEV1% predicted).
In the COPD-specific cohort (n=3,515), we found no significant difference in alpha diversity metrics between COPD and non-COPD participants, but three bacterial species were significantly less abundant in individuals with the prevalence of COPD (FDR<0.05). Notably, two of these bacteria, *Rothia mucilaginosa* and *Dorea longicatena*, were also more abundant in the individuals with better lung function (n=5,445), potentially indicating beneficial properties for lung health in general. *Rothia mucilaginosa* has been reported to exhibit anti-inflammatory properties via inactivation of the NF-κB pathway, and *Dorea longicatena* is known to produce short-chain fatty acids, particularly butyrate, which modulates immune responses and reduce inflammation.
Conclusions: This study demonstrates that gut microbiome composition is associated with lung function and COPD in a population-based cohort. The findings suggest that certain gut bacteria may contribute to maintaining lung health, potentially through anti-inflammatory mechanisms. These results highlight the gut microbiome as a potential target for novel therapeutic interventions aimed at improving lung function and managing COPD.

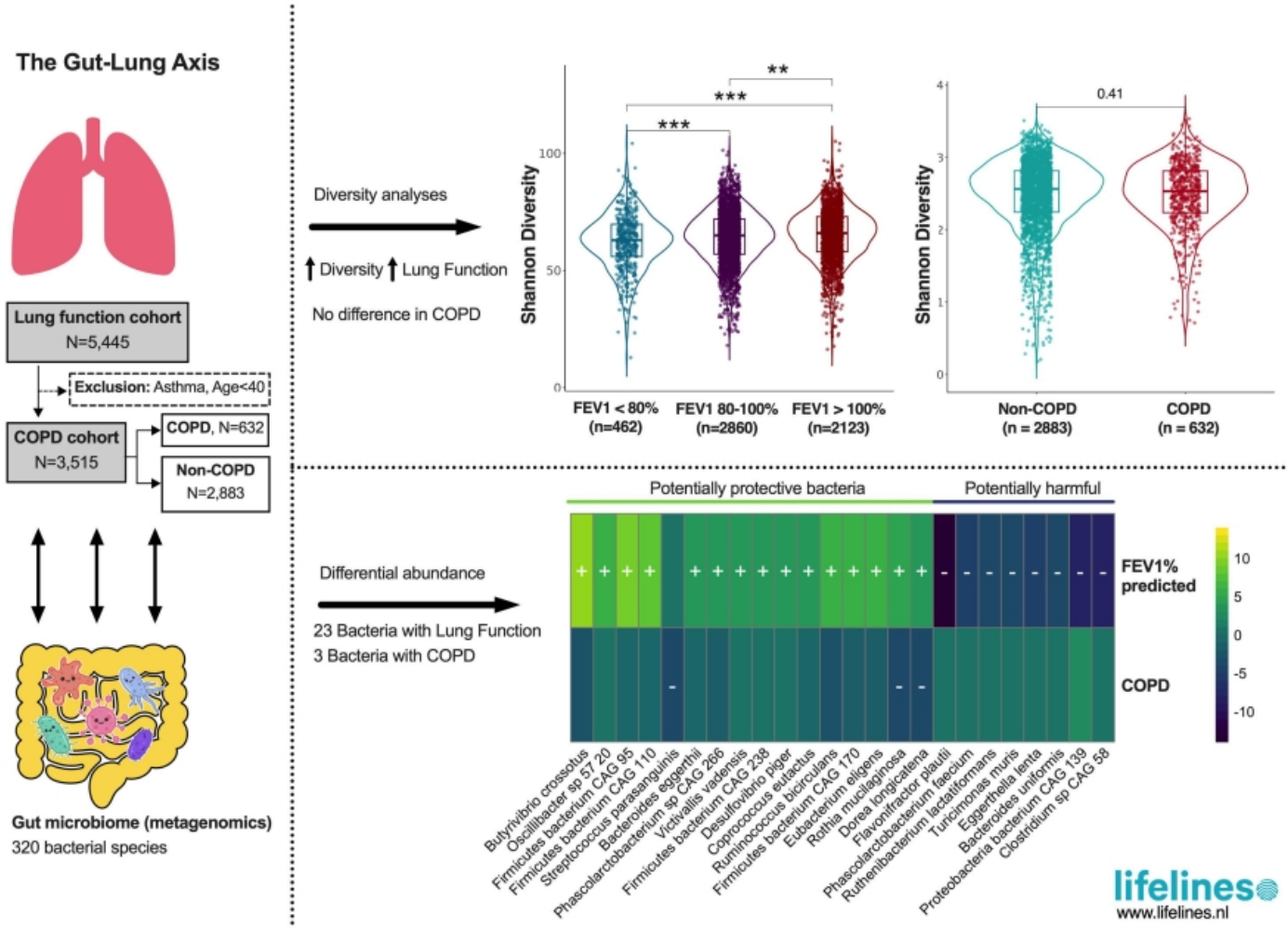

Figure 1: Overview of the gut-lung axis study, illustrating the association between the gut microbiome and lung function or COPD. Left panel shows a schematic representation of the study cohort. Top-right panel shows the diversity analyses showing relationship between alpha diversity (Shannon index) and lung function (FEV1% predicted) or COPD. The bottom-right panel shows differential abundance analysis of gut bacterial species in relation to lung function or COPD.

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