Supplementary Table 1. Summary of studies investigating the microbiome in sputum samples of COPD participants

Author (Year)	Sequencing technique	Participants characteristics	Summary findings
Cabrera-Rubio, et al. (2012)[1]	16S rRNA	8 participants in stable phase	-Microbiome profiling in sputum, bronchial aspirate, BAL and bronchial mucosal biopsy revealed lower diversity in sputum samples compared to the other 3 sample types
Molyneaux, et al. (2013)[2]	16S rRNA, qPCR	14 participants in stable phase, 17 healthy controls	-After rhinovirus infection, there was a rise in bacterial burden and outgrowth of *Haemophilus influenza* from pre-existing microbiota in COPD participants. This was not observed in healthy controls.
Garcia-Nunez, et al. (2014)[3]	16S rRNA	17 participants in stable phase	-Most prevalent phyla were Proteobacteria, Firmicutes, and Actinobacteria -Patients with moderate disease showed greater microbial diversity than patients with advanced disease - Alpha diversity was decreased in patients with advanced disease
Galiana, et al. (2014)[4]	16S rRNA, qPCR	19 participants in stable phase	-Bacterial diversity was higher in patients with moderate COPD than with severe COPD -Bacterial load was higher in severe COPD -In severe COPD patients, the composition of bacterial genera differed more among themselves, than samples from the mild/moderate group
Huang, et al. (2014)[5]	16S rRNA, qPCR	12 participants; sample collection before, during and after AECOPD	-Abundance of several bacterial phyla differed between stable phase and AECOPD, where Proteobacteria abundance was increased during AECOPD - Steroid and antibiotic therapy showed opposite effects on the microbiome, whereby steroid therapy increased Proteobacteria abundance - *Haemophilus influenza* abundance was positively correlated to the abundance of phylogenetically related bacteria, whereas the abundance of other bacteria was negatively correlated
Barker, et al. (2015)[6]	16S rRNA, qPCR	120 participants in stable phase, 55 paired stable and AECOPD data	- *Haemophilus influenza* bacterial load was an independent predictor of sputum TNF-alpha and IL-1beta levels in stable state - at AECOPD, change of *Moraxella catarrhalis* bacterial load compared to

			stable state correlated with change in sputum TNF-alpha and IL-1beta concentration; this was not observed in *Haemophilus influenza*
Millares, et al. (2015)[7]	16S rRNA, metagenomics	8 participants with severe COPD; sample collection during stable phase and AECOPD	- The relative abundance of bacterial phyla and genera were consistent between stable phase and AECOPD -Functional pathways changed at AECOPD events, indicating a shift of the metabolic functionality of the microbiome towards AECOPD
Brill, et al. (2015)[8]	Sputum culture;16S rRNA, qPCR	99 participants in stable phase, 86 completed follow up,	-A randomized controlled trial investigating different antibiotic classes (moxifloxacin, doxycycline, azithromycin, placebo) -Total airway bacterial load did not decrease after 3 months of antibiotic therapy -Increases in antibiotic resistance in all treatment groups
Wang, et al. (2016)[9]	16S rRNA, qPCR	87 participants; sample collection during stable state, AECOPD, 2 weeks post-therapy and 6 weeks recovery	-Sputum microbiome profiles were dynamic from stable state towards AECOPD, involving the change of microbial diversities, abundances of bacterial communities and the outgrowth of "keystone bacteria", such as *Haemophilus* or *Moraxella* spp. -Microbiome structure and diversity were correlated with serum and sputum biomarkers -Steroid and antibiotic therapy showed opposite effects on the microbiome with respect to diversity and outgrowth of individual bacteria and bacterial communities
Wang, et al. (2017)[10]	16S rRNA	281 participants; sample collection at baseline and AECOPD	- Microbiome composition shifted from highly diverse to less diverse during AECOPD, where few bacterial genera become predominant abundant -Bacterial dysbiosis was associated with increased exacerbation severity, indicated by higher CAT scores and decrease of lung capacity -Microbial dysbiosis, in concert with eosinophilic inflammation, was associated with even higher exacerbation severity
Leitao Filho, et al. (2018)[11]	16S rRNA	102 participants hospitalized due to AECOPD, followed for one year after discharge	- Microbiome profile in hospitalized AECOPD patients is significantly associated with 1-year mortality -Reduced microbial diversity indicated poorer survival prognosis -The combined absence of Veillonella/presence of Staphylococcus

			was associated with an increased risk of 1-year mortality by 85-fold
Ghebre, et al. (2018)[12]	16S rRNA, RT-PCR panel for common respiratory viruses	73 participants with AECOPD, 32 asthmatic patients with exacerbation	-Asthma and COPD patients share 3 exacerbation biological clusters after integrating microbiome profiles and host-inflammatory profiles -Cluster 1: increased pro-inflammatory mediators, evidence of neutrophilic inflammation, bacteria-associated with increased proportions of Proteobacteria and Proteobacteria/Firmicutes ratio -Cluster 2: increased blood and sputum eosinophils, type 2 mediators and increased proportions of Bacteroidetes -Cluster 3: increased type 1 mediators and proportions of Actinobacteria and Firmicutes
Sinha, et al. (2018)[13]	16S rRNA	4 participants; sample collection during stable phase (two-days, 2-9 months)	-Alpha diversity is similar over a two-day period -Microbiome variability was increased over a 9-months period -Firmicutes was the most prevalent phylum, followed by Bacteroidetes
Mayhew et al. (2018)[14]	16S rRNA	101 participants, 584 (spontaneous and induced) sputum samples from stable and exacerbation time points over 1 year	-Subtypes of COPD have distinct bacterial compositions and stabilities over time - Microbiome profiles show less variation within an individual than between individuals, however, some individuals exhibited high variability over time - With increasing disease severity, the abundance of Proteobacteria increases, whereas diversity overall decreases -No significant changes of diversity or taxa relative abundance between stable and exacerbation phase (with the exception of *Moraxella* spp.) -COPD patients with higher exacerbation frequencies exhibit less stable lung microbiome over time - Microbiome composition of bacterial exacerbations differs from viral and eosinophilic
Wang et al. (2019)[15]	16S rRNA, qPCR, host RNA microarray, Proteomic assay	16 healthy controls, 43 participants with COPD, sample collection during stable state, AECOPD, 2 weeks post-therapy and 6 weeks recovery, 6 months from	- stable COPD patients showed a significantly increased relative abundance of the genera *Moraxella*, *Streptococcus* and Actinobacteria, as well as decreased alpha diversity, compared to healthy controls -the relative abundance of *Moraxella* was increased at stable state in GOLD III versus II patients and in ICS versus non-ICS exposed patients - During AECOPD, the relative abundance of *Moraxella* was increased and alpha

		the first stable visit	diversity decreased compared to the stable state, along with significantly increased neutrophil and decreased macrophage percentage. - the trend of increased *Moraxella* and decreased alpha diversity was reversed at post- exacerbation time points - significant associations between *Moraxella* and *Haemophilus* with host transcriptome and proteome profiles of host interferon and pro-inflammatory signaling pathways and neutrophilic inflammation

qPCR=quantitative PCR; AECOPD= acute exacerbations of COPD

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