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| **The influence of the gut microbiome and metabolome in chronic obstructive pulmonary disease (COPD): a systematic review** |
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| **Introduction/Aim:**Chronic Obstructive Pulmonary Disease (COPD) is a heterogeneous lung condition affecting 1-in-7 Australians ≥40 years, and the third leading cause of death worldwide. Current inhaled corticosteroid treatment relieves symptoms, however, predisposes to respiratory infections. COPD is driven by local and systemic inflammation, and infectious and immune crosstalk is established between the gut and lungs. Modification of gut bacteria positively influences lung health, and microbial metabolites are immunomodulatory. Therefore, we aimed to identify and synthesise the literature describing the gut microbiome and metabolome’s role in COPD pathogenesis.**Methods:** Relevant English language studies were identified via online databases. Interventional and observational studies were included. Eligible studies examined the effect of oral interventions that modify gut microbiome or metabolome in COPD or described the differences in gut microbiome or metabolome in COPD. Two independent reviewers performed title and abstract screening, full-text review of eligible articles and qualitative assessment. Meta-analyses will be performed where possible.**Results:** 5052 studies were screened by title and abstract, with 41 articles eligible for full-text screening. Twenty original research articles were included for quality assessment and data extraction. 83% of intervention studies were animal models and 78% of observational studies were human cohorts. Preliminary review of identified articles has revealed that COPD was associated with altered gut microbial diversity and composition, and depleted metabolome. Most studies utilised 16S amplicon sequencing, which does not provide functional insight. However, increased abundance of *Firmicutes* was evident in murine and human COPD and was associated with lung function decline. One study indicated COPD-associated metabolites of which 46% were lipid-related, indicating lipid metabolism may be altered.**Conclusion:** The gut microbiome is a promising therapeutic target for COPD. We have identified a paucity of human randomised control studies; however observational studies suggest potential therapeutic targets or faecal biomarkers. These targets require clinical and experimental validation.**Grant Support:** This research is supported by an Australian Government Research Training Program Scholarship. |