Conclusions: We found that digestion of powdered milk and CF meconium by pancreatic enzymes was faster with lower salt concentrations. Endogenous pancreatic enzymes are insufficient in patients with MI, and hyperosmolar solutions could slow meconium digestion. Future studies are needed to establish ideal conditions for dissolving obstructive meconium in animal models, with the goal of relieving intestinal obstruction in newborns with MI.

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Cystic fibrosis transmembrane conductance regulator potentiator (ivacaftor) has minimal effects on gut microbiome composition in people with cystic fibrosis and gating mutations

R. Bass[1], C. Tanes[1], E. Friedman[2], K. Bittinger[1], G. Wu[2], V. Stallings[1,3].
[1]*Division of Gastroenterology, Hepatology and Nutrition, Children's Hospital of Philadelphia, Philadelphia, PA;* [2]*Division of Gastroenterology and Hepatology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA;* [3]*Department of Pediatrics, University of Pennsylvania, Philadelphia, PA*

Background: Cystic fibrosis (CF) is associated with gut microbiota dysbiosis. It is likely that the etiology of microbiota differences in CF is multifactorial and includes impaired bicarbonate secretion, low pH, abnormal gastrointestinal motility, inspissated intestinal stool and mucous, fat malabsorption, lack of endogenous pancreatic enzymes, high fat diet, and frequent antibiotic use. Prior studies have demonstrated altered microbiota composition in individuals with CF. The impact of highly effective CF transmembrane conductance regulator (CFTR) modulator therapy on the microbiota is largely unknown. We compare microbiota composition in individuals with CF and gating mutations at baseline and 3 months after initiation of the CFTR potentiator ivacaftor with that in healthy controls.
Methods: Subjects with gating mutations were recruited from CF centers in the United States and Italy. Stool samples were collected at baseline and 3 months after initiation of ivacaftor treatment. Age-matched healthy subjects were included from two previously published cohorts [1,2]. Microbiome composition was assessed using shotgun metagenomic sequencing with the DNeasy PowerSoil Kit (Qiagen, Germantown, MD) for extraction, the NexteraXT DNA Library Preparation Kit (Illumina, San Diego, CA), and an Illumina HiSeq 2500 using 2 × 125 base pair chemistry. Data were processed using the Sunbeam, abundance of bacteria was estimated using Kraken, and analysis was conducted in R. Dysbiosis score was calculated as the median Bray-Curtis distance to healthy participants.
Results: Eighteen individuals with CF (7 male, 11 female, median age 15.3), 13 of whom had exocrine pancreatic insufficiency and five of whom had pancreatic sufficiency, completed the study. There were no differences in alpha diversity between healthy and CF subjects using richness or Shannon's index, but CF subjects had higher dysbiosis scores ($p < 0.001$) and a different microbiota composition (beta diversity) than healthy controls (Figure 1, permutational multivariate analysis of variance $p < 0.01$). These differences in composition corresponded to a greater relative abundance of *Enterobacteriaceae*, *Escherichia coli*, and *Veillonella parvula* in subjects with CF and a smaller relative abundance in ten *Bacteroidetes* taxa, *Eubacterium rectale, Faecalibacterium prausnitzii,* and *Akkermansia muciniphila* (all false discovery rate < 0.05). By contrast, treatment with ivacaftor for 3 months did not lead to statistically significant differences in alpha diversity (richness or Shannon's diversity index), beta diversity (Bray-Curtis distances), or relative abundance of specific bacterial taxa.
Conclusions: Different microbiome composition was found in subjects with CF than in healthy participants, consistent with previously reported results. We observed no statistically significant effects of ivacaftor treatment on gut microbiota composition, although this was a small cohort with multiple confounders, including antibiotics use and differences in exocrine pancreatic function.

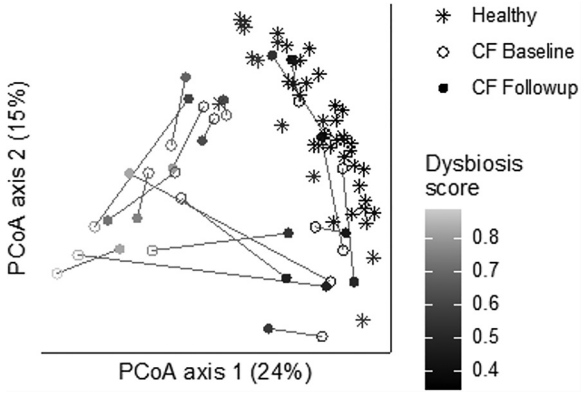

Figure 1. Principal coordinate analysis plot of microbiome composition (Bray-Curtis distance) in people with cystic fibrosis (CF) and healthy controls

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Gastrointestinal symptoms in a cystic fibrosis transmembrane conductance regulator modulator era—an international survey

R. Calthorpe[1], B. Hayee[2], L. Howells[3], Z. Elliott[4], A. Horsley[5,6], N. Goodchild[7], N. Rowbotham[1], S. Smith[1], K. Thomas[3], D. Peckham[8], S. Carr[9], H. Barr[10], I. Stewart[11], A. Smyth[12,13]. [1]*Evidence Based Child Health Group, Lifespan and Population Health, School of Medicine, University of Nottingham, Nottingham, UK;* [2]*King's College Hospital NHS Foundation Trust, London, UK;* [3]*Centre of Evidence Based Dermatology, School of Medicine, University of Nottingham, Nottingham, UK;* [4]*Parent of Children with Cystic Fibrosis, Nottingham, UK;* [5]*Division of Infection, Immunity and Respiratory Medicine, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK;* [6]*Manchester University NHS Foundation Trust, Manchester, UK;* [7]*Patient and Public Involvement Representative and Person with Cystic Fibrosis, Suffolk, UK;* [8]*Leeds Teaching Hospitals NHS Trust, Leeds, UK;* [9]*Royal Brompton Hospital, London, UK;* [10]*Nottingham University Hospitals NHS Trust, Nottingham, UK;* [11]*National Heart and Lung Institute, Imperial College London, London, UK;* [12]*Evidence Based Child Health Group, Lifespan and Population Health, University of Nottingham, Nottingham, UK;* [13]*Nottingham University Hospitals NHS Trust and University of Nottingham, National Institute for Health and Care Research Nottingham Biomedical Research Centre, Nottingham, UK*

Background: How to relieve gastrointestinal (GI) symptoms in people with cystic fibrosis (CF) was identified as a research priority and explored through an international qualitative survey in the CF community in 2018 [1]. After introduction of elexacaftor/tezacaftor/ivacaftor (ELX/TEZ/IVA) in 2019, many more people with CF (PwCF) are able to access CF transmembrane conductance regulator (CFTR) modulator therapy. Although the respiratory benefits of ELX/TEZ/IVA are well documented, effects on the GI tract are not well understood. The aim of this study was to characterize GI symptoms in the CF population and ascertain whether the introduction of modulators affected them.
Methods: PwCF, families, and health care professionals (HCPs) completed electronic surveys over a 1-month period. The survey was promoted