the CRMS and CF groups ($p = 0.32$). Similarly, there was insufficient evidence to conclude that mean percent predicted (FEV$_1$)pp differed between the CRMS (102.2 ± 6.4%) and CF (96.6 ± 11.6%) groups ($p = 0.23$).

**Conclusions:** There were no significant differences in LCI or FEV$_1$pp between the CF and CRMS groups, although we identified one child with CRMS with an abnormal LCI, suggesting the potential utility of MBW to stratify children with CRMS at risk of developing CF. Ongoing EBC analysis and correlation with lung function tests may be an additional way to assess lower airway inflammation in children with CRMS and risk of progression to CF.

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Oxygen-enhanced magnetic resonance imaging and multiple-breath washout with or without short extension as novel assessments of cystic fibrosis lung health

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**Background:** Poor sensitivity of spirometry and forced expiratory volume in 1 second (FEV$_1$) means that the gold standard for lung function testing in cystic fibrosis (CF) is suboptimal. The lung clearance index (LCI$_{2.5}$) derived from multiple-breath washout (MBW) is considered a good alternative but also has limitations. We recently developed an extension to MBW (MBW$_{ShX}$) to capture signal from previously overlooked under- and upper-airways (UVLU) [1], although any MBW protocol will lack spatial information. Oxygen-enhanced magnetic resonance imaging (OE-MRI) provides a functional assessment of the lung on a spatial level, without the use of hyperpolarized gas or ionizing radiation. The parameter reported here, R$_{2}^*$ enhancement, originates from the influence on the proton MRI signal of oxygen in the airways and dissolved within alveolar water and capillary blood. It thus represents a surrogate outcome combining ventilation, gas exchange, and perfusion, with lower enhancement indicative of worse disease. We are conducting a longitudinal study to establish clinimetrics of these techniques; early cross-sectional data are reported here.

**Methods:** Twenty people with CF underwent spirometry, MBW$_{ShX}$ (Ecomedics Exhaler D, Spiroware software 3.3.1) and OE-MRI on one day. MBW$_{ShX}$ protocol: After the standard MBW end of test, subjects performed a slow vital capacity (VC), followed by tidal breathing until end-of-test criteria were re-met. Quantification of UVLU is calculated by change in percentage of nitrogen resulting from the SVC, standardized for lung size. LCI$_{2.5}$ (LCI$_{2.5}$ + UVLU) is a measure of global lung health, whereas UVLU is a standalone marker. The MRI protocol consisted of a dynamic series of multislice two-dimensional dual-echo radio frequency–spoiled T$_1$-fast field echo sequence acquired with a temporal resolution of approximately 1.5 seconds during free breathing using a Siemens Aera 1.5 T scanner. The initial 60 acquisitions were obtained with medical air; the gas supply was then switched to 100% oxygen for 150 acquisitions and then returned to medical air for a final 150 acquisitions. Dynamic quantitative R$_2^*$ maps were calculated, and the lung parenchyma, excluding central major vasculature, was manually segmented. Normally distributed parameters are presented as mean ± SD and nonparametric parameters as median (range). Pearson (R) and Spearman ($\rho$) tests were used to assess correlations. $p < 0.05$ was considered significant.

**Results:** All 20 participants completed MBW$_{ShX}$ and the OE-MRI protocol. Subjects were aged 13 ± 5.3, with FEV$_1$pp of 92.2 ± 12.3%, percent predicted forced vital capacity (FVCcpp) of 98.8 ± 11.2%, LCI$_{2.5}$ of 7.5 (6.3–15.6), LCI$_{ShX}$ of 9.0 (6.1–31.0), and UVLU of 1.2 (0.3–15.3). R$_{2}^*$ enhancement ($0.087 ± 0.017$ms) did not correlate with FEV$_1$pp or FVCcpp, but significant negative correlations were seen with LCI$_{2.5}$ ($r = −0.47$, $p < 0.05$), LCI$_{ShX}$ ($r = −0.64$, $p = 0.01$), and UVLU ($r = −0.67$, $p = 0.001$).

**Conclusions:** OE-MRI is feasible and tolerated by children as young as 7. Unlike spirometric values, LCI$_{2.5}$ correlated significantly with OE-MRI R$_{2}^*$, again highlighting the superior sensitivity of MBW over FEV$_1$ in mild to moderate CF lung disease. Novel MBW$_{ShX}$ values also performed well; correlations with OE-MRI were numerically greater than with LCI$_{2.5}$ although at this stage, we are not powered for statistical comparison. This ongoing project will assess short- and long-term repeatability of these novel assays, create a normative range, assess spatial heterogeneity, and optimize MBW and OE-MRI parameters for use as future clinical and research outcomes.

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The Streamlined Treatment of Pulmonary exacerbations in Pediatrics pilot study of oral antibiotic timing in pediatric cystic fibrosis pulmonary exacerbations

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**Background:** Optimizing pulmonary exacerbations (PEX) management is a top research priority for the cystic fibrosis (CF) community. Several reports support more aggressive use of oral antibiotics for the treatment of PEX symptoms, although particularly in children with relatively preserved lung health, milder exacerbations are frequently virally driven and self-limiting and may not always require oral antibiotics, particularly in the era of highly effective modulator therapy. Streamlined Treatment of Pulmonary exacerbations in Pediatrics (STOP PENDS) was a multicenter, pilot study evaluating feasibility and acceptability of randomization to one of two arms for management of mild PEX within 1 to 7 days of symptom onset: early oral antibiotics (initiation at randomization plus airway clearance) versus tailored therapy (airway clearance alone at randomization, with oral antibiotics initiated for worsening cough, cough not improving within 7 days, or cough not resolved by 14 days).

**Methods:** STOP PENDS was a prospective, multicenter, randomized, unblinded study that enrolled children with CF aged 6 to 18 at a time of clinical stability and followed them through one randomized PEX or up to 18 months. Parents received a text message weekly to report new cough. For mild PEX meeting prespecified criteria, children were eligible for randomization to the early antibiotics or tailored therapy arm. Participants with a randomized PEX were followed for 28 days and then exited the study. The study team contacted the participant at defined intervals following randomization, and treatment was escalated (i.e. antibiotics were started for the “tailored therapy” arm, and participants returned to clinical care in the “early antibiotic” arm) for prespecified criteria or upon request of the participant or family. All study procedures could be conducted remotely. The primary objective was to estimate the proportion of participants randomized to the tailored therapy arm that avoided antibiotics during the 28-day PEX period.

**Results:** One hundred twenty-one children were enrolled at 10 study sites between November 2020 and December 2021; 65% were on highly effective modulators, 55% were aged 12 to 18, 48% were male, and 50% had grown methicillin-susceptible Staphylococcus aureus (MSSA) and 12% Pseudomonas aeruginosa isolated from their most recent culture. The mean (SD) baseline FEV$_1$ at enrollment was 98 (16%). Ninety-four participants had reported at least one PEX, and 63 (goal 80) PEXs were randomized after a mean (SD) of 102 (87) days of enrollment. All but 3 were reported remotely, unrelated to a clinic visit. Thirteen participants reported only PEX that met criteria for being too severe that were not randomized. Eighteen