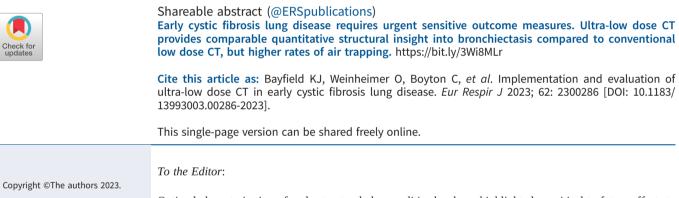


## Implementation and evaluation of ultra-low dose CT in early cystic fibrosis lung disease

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Optimal characterisation of early structural abnormalities has been highlighted as critical to future efforts to detect and prevent cystic fibrosis (CF) lung disease progression [1]. Computed tomography (CT) is currently the gold standard, detecting structural disease at an earlier stage than radiography or lung function testing, with predictive value for subsequent progression and later forced expiratory volume in 1 s (FEV<sub>1</sub>) decline [1]. Compared to other emerging radiological modalities for early disease detection, such as magnetic resonance imaging (MRI), CT is more widely accessible and MRI at present is not able to directly quantify the extent of bronchiectasis due to its limitations in spatial resolution. Current US CF Foundation clinical guidelines state that CT should be "considered every 2-3 years, using the lowest possible radiation dose" [2]. Early lung disease is identified on CT by air trapping, increase in airway wall thickness and airway diameter, and potentially irreversible bronchiectasis [3]. Spirometer-directed CT has standardised lung volume acquisition and outlined the importance of both inspiratory and expiratory image acquisition [4]. Consensus recommendations for "low dose" CT scanning were published in 2016 [5], but radiation exposure remains a concern, given the six-fold increase in CT use and ongoing increase in cumulative radiation exposure for CF patients [6]. Imaging requires optimal structural information at the lowest possible radiation dose [5]. Given the increased vulnerability of children to ionising radiation, "low dose" CT protocols have already been incorporated in paediatric clinical trials using CT-based primary outcome measures [7], and use of ultra-low dose (ULD) CT has emerged in adult CF research and in isolated paediatric patients [6]. However, formal validation of the effects on quantitative measures of structural disease has not been performed. Low dose (LD) CT shows limitations compared to standard dose CT because of known drifts in CT lung density dependent on dose [8]. We hypothesised that ULD implementation would not detrimentally affect structural disease detection in early CF lung disease, and specifically targeted an age range to explore this where volume variation during spirometry-directed CT could be minimised between imaging modalities. Thus, the primary aims in this study were to 1) implement spirometer-directed novel ULD CT in school-aged children with CF, and 2) validate its

outcomes against same-session LD CT using visual as well as fully automated quantitative CT analysis for structural airway disease.