Methods We did a causal mediation analysis using data from the UK CF registry, which captures 99% of all people with CF in the UK and records clinical information including weight and infection status at annual review visits. The exposure of interest was SEC in the first year of life measured by the index of multiple deprivation; the outcome was first lung function measure between ages 6 and 9. We were interested in mediation by weight trajectory during the first six years of life. Potential confounders were sex, year of birth, genotype and infection.

All children born between 2000 and 2010 and diagnosed by newborn screening were included in the analysis if they had at least one lung function measure between ages 6 and 9, at least one weight and infection measure between birth and age 6, and complete data on SECs and baseline confounders. We imputed missing data using multiple imputation by chained equations.

We used the parametric mediational g-formula to estimate the total effect of SECs on lung function, and the indirect effect mediated by weight trajectories in the first six years of life, accounting for potential time-varying confounding by infection. Confidence intervals were estimated using non-parametric bootstrap.

Results Using data from 853 children, we found a total effect of deprivation on lung function, measured by percent of predicted FEV1, of 4.53 percentage points (95% CI 3.44 to 5.77). Our results showed that if we could improve the weight of the most disadvantaged children to have the same distribution as that of the least disadvantaged children, their lung function would improve on average by 0.74 percentage points (95% CI 0.36 – 1.1).

Conclusion Only 16% (95% CI 8%-25%) of the inequalities in early lung function for people with CF were explained by weight trajectories in the first 6 years of life, suggesting that other important pathways to inequalities need exploration.