

Reply to letter by Huls et al. (ERJ-01465-2015.R2)

“Inclusion of children with airway disease for the development of spirometry reference data”

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Inclusion of children with airway disease for the development of spirometry reference data

Reply to letter by Hüls et al.

Dear Sir

We wish to thank Dr Hüls and colleagues for their interest in our recent paper[1], and the opportunity to clarify the rationale behind the conclusions we reached, which differ from their own. Despite the title of their letter, it is important to emphasise that we did not recommend inclusion of symptomatic children, those with a prior history of adverse exposures, or those with current respiratory illness such as asthma, when establishing spirometric reference equations, where international standards regarding definition of health may need to be adhered to. Indeed we state clearly in the discussion that under such circumstances, the target sample size may have to be increased by at least 30% to account for such exclusions, a proportion not dissimilar to that reported by Hüls et al. What was demonstrated by our results is that when carrying out epidemiological studies such as the Size and Lung function In Children (SLIC) study[2], the primary aim of which was to ascertain the extent to which ethnic differences in lung function can be attributed to differences in physique and socioeconomic factors, inclusion criteria can be broader without biasing results. This not only renders the results more generalisable but has considerable practical and economic benefits.

Although the authors compared their data from the LUNOKID study with our results, there are differences regarding the definition of 'current asthma' between the two studies. Thus, whereas 'current asthma' was apparently categorised according to current medication in the LUNOKID study, within the SLIC study 'current asthma' was defined as those with 'either doctor-diagnosis or asthma medication in the past 12 months, with or without current symptoms/wheeze', ensuring that any child with a prior history of asthma was only included if asymptomatic and without treatment for at least 12 months. Despite these differences in asthma classification, it is reassuring to know that "no relevant mean differences were found for the other subgroups or for the total study population when all subgroups were included" within the LUNOKID study, thereby confirming our findings from the SLIC study. Both studies also agree on the higher failure rate due to technically unsatisfactory data when including children with respiratory symptoms. However, while the LUNOKID authors argue that due to potential difficulties in separating upper and lower respiratory tract

infections, 'strict criteria to define a healthy population should be adhered to', our experience suggests that any naïve child (i.e. one unfamiliar with spirometric assessments) with significant respiratory symptoms is likely to be self-excluded provided strict quality control is applied, and that exclusion of a high proportion of the population on 'health grounds' could result in over-estimation of abnormalities and potential mismanagement of lung disease.

In conclusion, while we completely agree that inclusion and exclusion criteria applied to subjects must vary according to the underlying question and study design, we would like to confirm that we excluded results from any children with current asthma or who were on asthma medication. For the purposes of data collection in population-based studies of lung function such as the SLIC study, we stand by our conclusion that with exception of clear-cut factors such as current and chronic respiratory disease, paediatric reference samples for spirometry can be relatively inclusive and hence more generalisable to the general population.

References

1. Lum S, Bountziouka V, Sonnappa S, Cole TJ, Bonner R, et al. (2015) How "healthy" should children be when selecting reference samples for spirometry? *Eur Respir J* 45: 1576-1581.
2. Lum S, Bountziouka V, Sonnappa S, Wade A, Cole TJ, et al. (2015) Lung function in children in relation to ethnicity, physique and socioeconomic factors. *Eur Respir J* 46: 1662-1671.