
Authors’ response

We read with great interest the comment by Salome and coworkers on our recently published article.1 We are grateful for their interest in our work, although they attribute to us a conclusion that does not appear in our paper. We conclude that bronchial reactivity indices are independent predictors for the health-related quality of life of patients with asthma and we propose that they might be of use in clinical practice. In our conclusion, however, no comparison is established between bronchial reactivity and sensitivity.

We agree that the analysed indices of bronchial reactivity represent different expressions of the slope of the dose–response curve. Certainly, the differences in their relationship with the Asthma Quality of Life Questionnaire are attributable to changes in shape or linearity due to the mathematical transformation applied in their calculation.

Nevertheless, we do not agree with the assimilation between the provocative dose causing a 20% fall in forced expiratory volume in 1 s (FEV1) (PD20a) and dose–response slope (DRS). Both parameters seem to be qualitatively different since the dose–response curves plotted in their determination are also different. PD20a is obtained from curves plotted on a semilogarithmic scale whereas DRS is obtained from a linear dose axis. Moreover, the calculation of PD20 uses the fall in FEV1 between the last and penultimate doses while, for DRS determination, the fall in FEV1 is considered that between the last dose and the post-diluent baseline value. These different approaches provide necessarily different values. In fact, and in contrast to Salome and coworkers, in our patients with asthma the relationship between PD20 and DRS is slight (r=-0.416, r=0.042).

We therefore believe that DRS and PD20 are not completely equivalent. DRS allows for airway responsiveness to be assessed in all individuals, including those who do not reach the threshold PD20. Several studies, including some of their own group,2 have already shown that DRS to methacholine or histamine is associated with asthma diagnosis and symptoms. Moreover, DRS allows for a better separation of patients with and without asthma than PD20.3 It has recently been shown that adolescents with asthma remission had a significant decrease in speed of bronchial constriction (bronchial reactivity) whereas the threshold of methacholine (bronchial sensitivity) was not altered.4

Finally, and in agreement with Porsbjerg et al.,5 we consider that the differences in the estimation procedure and the non-censored character of the DRS, continuous index of responsiveness and bronchial reactivity index should justify their stronger relationship with health-related quality of life than PD20.

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Outcome after bronchitis depends on disease definition

Sigurs et al recently published their 18-year prospective controlled follow-up study of 47 subjects hospitalised for respiratory syncytial virus (RSV) bronchitis at age <12 months.1 In the cohort the prevalence of wheezing and asthma was higher than in population-based controls at 3, 7 and 13 years of age.

Asthma was present, depending on definition, in 39–59% of 46 study subjects and in 7–9% of 92 controls,1 in line with an asthma prevalence of 9.5% in Swedish young adults. The risk of adulthood asthma after
RSV bronchiolitis was therefore 3.5–4.1-fold compared with the population.

Lung function by forced expiratory volume in 1 s (FEV1), ratio of FEV1 to forced vital capacity (FVC) and mid forced expiratory flow (FEF25–75) was reduced in the former patients with RSV bronchiolitis with and without current asthma but not in asthmatic controls. The differences were significant in both pre- and post-bronchodilator measurements, suggesting the permanence of the changes. Instead, no evidence was found for permanent small airway dysfunction by lung clearance calculation.1

In our study, 100 infants aged <24 months were hospitalised with bronchiolitis in 1992–5. Eighty-one attended the control visit at age 12 years; asthma was present in 20% of former patients with RSV and in 52% of former non-RSV patients (OR 0.27, 95% CI 0.89 to 2.82), and in 5% of former patients with rhinovirus and in 34% of former non-rhinovirus patients (OR 2.6, 95% CI 0.89 to 7.94). RSV bronchiolitis was associated with a restrictive pattern of lung function documented by reduced FVC.4

A post-questionnaire study including population-based controls was performed in 2008 when the study subjects were 17–18 years of age (unpublished). Sixty-seven former patients with bronchiolitis and 155 controls attended, and current asthma was present in 30% and 5%, respectively (OR 7.9, 95% CI 3.3 to 19.3). Asthma was present in 30% and 5%, respectively (OR 7.9, 95% CI 3.3 to 19.3). Asthma was common after early life bronchiolitis but a viral aetiology of bronchiolitis was present in 25% of the cases.1

In future studies of bronchiolitis and wheezing illnesses, whether a true causative role of viral infection in early life bronchiolitis during the first year of life1 and for their contribution of as yet unpublished findings from their 24-month follow-up of the Finnish cohort.2 Their data, obtained in subjects previously hospitalised with bronchiolitis in the first 2 years of life (25/81 cases tested for RSV were positive and 19/66 were positive for rhinovirus), confirm our findings of increased asthma rates up to early adulthood. The Finnish study extends these findings by including severe bronchiolitis due to other viral agents, most notably rhinovirus, which is today a well-recognised risk factor for later wheezing illness.8 Interests. In the Finnish cohort of hospitalised subjects aged <24 months, RSV predominated in those aged <6 months (‘European bronchiolitis’) and rhinovirus in those aged ≥6–24 months (‘American bronchiolitis’).3 4 In future studies of bronchiolitis, stratified analyses by age and viral findings are mandatory.

**Authors’ response**

We thank Dr Hyvärinen and colleagues for their insightful comments on our recent paper on asthma and allergy outcome at age 18 years after severe respiratory syncytial virus (RSV) bronchiolitis during the first year of life1 and for their contribution of as yet unpublished findings from their 18-year follow-up of the Finnish cohort.2 Their data, obtained in subjects previously hospitalised with bronchiolitis in the first 2 years of life (25/81 cases tested for RSV were positive and 19/66 were positive for rhinovirus), confirm our findings of increased asthma rates up to early adulthood. The Finnish study extends these findings by including severe bronchiolitis due to other viral agents, most notably rhinovirus, which is today a well-recognised risk factor for later wheezing illness.8 Interestingly, in the Finnish cohort of hospitalised subjects aged <24 months, RSV predominated in those aged <6 months and rhinovirus in those aged 6–24 months. While rhinovirus carried the greatest risk of asthma at age 12 years, the increased rates of asthma at age 18 were similar in former RSV- and rhinovirus-infected subjects. What remains unclear, regardless of the underlying viral aetiology, is whether these episodes of severe bronchiolitis are simply identifying those infants already at a predisposed risk of subsequent wheezing illness in later childhood or whether a true causative role of viral infection exists. In our cohort only one of the infants had a previous episode of wheezing, and we are therefore confident that their RSV bronchiolitis represents their first lower respiratory tract illness.

If stratification by age and viral type are incorporated in future studies, it would be important to ensure that the confounding effects of previous viral infections are taken into account if a causal relationship is to be investigated. Ideally, such studies should also include premorbid assessment of lung function and allergic sensitisation, and identified genetic risk factors.

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