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 (FEF_{25–75}) was reduced in the former patients with RSV bronchiolitis with and without current asthma but not in asthmatic controls.¹ 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 1992–3. 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 0.09 to 0.82), and in 58% of former patients with rhinovirus and in 34% of former non-rhinovirus patients (OR 2.6, 95% CI 0.89 to 7.94).³ 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study including population-based controls was performed in 2008 when the study subjects were 17–18 years of age (unpublished).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 25% of the former patients with RSV and in 26% of the former patients with rhinovirus. As in the study of Sigurs *et al*,¹ asthma was common after early life bronchiolitis but a viral aetiology of bronchiolitis no longer had a predictive value.

Sigurs *et al* enrolled only RSV-positive patients with bronchiolitis aged <12 months treated in hospital, and >90% of the cases were aged ≤6 months.¹ In the Tucson birth cohort study from which our current concept about childhood wheezing phenotypes originates, patients with bronchiolitis were aged <24 months with parent-reported wheezing treated usually at home.⁵ In the Finnish post-bronchiolitis studies highlighting the role of rhinovirus aetiology, RSV predominated in infants 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.

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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.³ 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 insult.

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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Longitudinal change of prebronchodilator spirometric obstruction

We read with interest the article by Probst-Hensch *et al* about longitudinal changes of prebronchodilator spirometric values.¹ They reported a non-persistent obstruction rate of 20.9% and concluded that prebronchodilator spirometry values only might misclassify chronic obstructive pulmonary disease (COPD). We are surprised by this high non-persistence rate and we believe that there are some issues that have to be taken into account regarding the obtained lung function values, irrespective of the quality control.²

First, we noticed that ~40% of the non-persistent subjects were never-smokers and

that the age range of subjects included was large: 18–62 years. COPD screening is not efficient in never-smokers and subjects under 40 years of age. In such subjects normal age-related decline is expected, and non-persistent obstruction could indicate erroneously lowered baseline forced expiratory volume in 1 s (FEV₁) or follow-up forced vital capacity (FVC). We wonder whether exclusion of never-smokers would have given a lower rate. Secondly, there is no explanation provided for the high number of never-smokers that develop airflow obstruction during follow-up. In incident stages I and II, 44.7% and 35.3%, respectively, are never-smokers. We acknowledge that both in smokers and never-smokers lung function decreases with age; however, these numbers seem unusually high. Thirdly, no correction for intraindividual measurement errors was applied. An intraindividual error will be present when measuring FEV₁/FVC over time. When ~94% of the non-persistent cases were mildly obstructive, we wonder whether correction for intraindividual measurement errors would have produced lower non-persistent rates. Fourthly, it would seem that the interindividual SD values of both FVC and FEV₁/FVC (% predicted) are very low; in non-persistent cases even 0.0. In a random sample from the population one would suspect a stronger variability in lung function values.

We calculated prebronchodilator non-persistence rate in subjects participating in the NELSON study, a lung cancer screening trial; see table 1.³ We found a non-persistence rate of 7.0% (52/741) which is far less than the 20.9% reported by Probst-Hensch *et al.* We believe this rate is of more interest because it is based on high-risk subjects all heavily exposed to tobacco smoking and

Table 1 Demographics of subjects in the NELSON study

	n=2253
Age (SD)	59.8 (5.3)
Follow-up years*	3.0 (2.9–3.1)
Pack-years (SD)	40.2 (17.6)
FEV ₁ /FVC <0.70 (%)	33
Smoking status	
Current smoker (%)	1253 (55.6)
Former smoker (%)	1000 (44.4)

*Median (IQR).

FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity.

subsequently at risk to develop COPD. The 3-year follow-up time was shorter than the 11 years in the SAPALDIA study, but in theory this should have led to higher non-persistence rates in our cohort.

Finally, if one treats the results as correct, it remains unknown whether post-bronchodilator values would have led to lower non-persistence rates because this was not formally investigated in the study, nor supported by previous studies.

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Authors' response

We appreciate the issues raised by Dr Hoessein regarding our paper¹ and respond as follows.

First, the NELSON study is a randomised screening trial for lung cancer and therefore targets subjects at high risk. The focus of our paper is different. We evaluated the prognostic meaning of a change in prebronchodilation spirometry—a common outcome in environmental epidemiology—in terms of respiratory health, not specifically bound to chronic obstructive pulmonary disease (COPD). We showed that this outcome has value in epidemiological research, but that understanding of the early stages of airflow obstruction, where non-persistence seems highest, remains poor. These early stages are a commonly affected outcome by inhaled

Table 1 Baseline characteristics according to change in severity of obstruction* during follow-up

	Persistently normal n=4181	Incident stage I n=683	Incident stage II n=85	Persistent stage I n=294	Stage I progressing n=56	Persistent stage II n=61	Non-persistent n=113
Female sex (%)	54.7	54.2	44.7	39.1	33.9	32.8	40.7
Age in years (mean/SD)	39.2/11.2	45.3/10.3	44.5/11.9	48.8/9.6	48.5/9.2	49.5/9.1	47.0/9.1
No professional education (%)	12.1	16.4	23.5	15.6	21.4	19.7	8.8
FEV ₁ % of predicted value (mean/SD)	109.9/13.6	107.4/12.5	91.3/12.5	101.3/10.9	89.1/7.0	67.4/10.4	99.6/13.5
FVC % of predicted value (mean/SD)	114.0/15.1	119.2/14.4	100.6/13.4	125.9/13.2	116.0/10.0	96.0/12.4	122.4/15.2
FEV ₁ /FVC % of predicted value (mean/SD)	100.9/6.3	94.6/5.1	94.9/6.7	84.1/4.1	80.2/5.3	73.3/9.9	84.8/4.6
Never smoker (%)	49.9	44.7	35.3	36.7	19.6	31.1	38.9
Light smoker at baseline (<15 PY)† (%)	28.7	19.3	13.6	20.9	9.3	11.8	24.5
Heavy smoker at baseline (≥15 PY)† (%)	18.2	31.8	42.4	38.4	62.5	52.5	29.2
Shortness of breath at baseline (%)	21.7	25.0	42.4	25.5	44.6	47.5	14.2
Chronic bronchitis at baseline (%)	7.3	11.6	20.0	13.3	19.6	27.9	9.7
Wheezing in last 12 months at baseline (%)	4.8	7.8	22.4	9.9	28.6	20.0	8.0
Non-current asthma at baseline (%)	5.6	10.5	17.6	12.2	21.4	27.9	9.7
Current asthma at baseline (%)	1.8	3.4	11.8	4.4	16.1	16.4	4.4
Health service use for respiratory problems at baseline (%)	18.0	22.0	27.1	26.9	33.9	42.6	23.0

*Obstruction was defined as FEV₁/FVC<0.70 based on prebronchodilation spirometry.

†Numbers do not add up to 100.0% due to smokers with missing pack-year information.
FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity; PY, pack-years.