with no third-year wheezing and with no aeroallergen sensitisation) [8]. Nearly 90% of children who wheezed with HRV in year 3 had asthma at age 6 yrs. In the same study, aeroallergen sensitisation during infancy and at age 3 yrs only modestly increased the risk for asthma at age 6 yrs (odds ratio 3.6, 95% CI 1.7–7.7, and odds ratio 3.4, 95% CI 1.7–6.9, *versus* those with no wheezing and those with no aeroallergen sensitisation, respectively) [8]. In another study on a high-risk cohort, wheezing with HRV during the first year of life was associated with wheezing at age 5 yrs (odds ratio 3.2, 95% CI 1.1–9.5) [7]. Comparable findings were made for current asthma. Strikingly, these associations were restricted to children who displayed early sensitisation (age $\leqslant$2 yrs). Two other studies have also reported an association between HRV-induced early wheezing and atopy/atopic characteristic [9, 10].

Thirdly, systemic corticosteroids as short 1–5-day courses are one of the cornerstones of the management of acute asthma in children, but their efficacy among young wheezing children has thus far remained obscure. RSV bronchiolitis does not respond to systemic corticosteroids, but most of the previous studies have not tried to identify other potential responders. Only one study has studied the efficacy of systemic corticosteroids in relation to HRV aetiology among young first-time wheezers [6, 10]. A 3-day course of oral prednisolone decreased the probability of recurrent wheezing ($\geqslant$3 physician-confirmed episodes) in children with eczema (hazard ratio 0.2, 95% CI 0.0–0.6) and HRV (hazard ratio 0.2, 95% CI 0.1–0.7). Prednisolone decreased recurrent wheezing by 48% over a 12-month study period in these first-time wheezers affected by HRV.

Taken together, many studies have consistently shown that HRV infections are common among early wheezers and they are markedly associated with recurrent wheezing and the development of asthma up to school-age. In addition, there are preliminary data that first-time wheezers affected by human rhinovirus are likely respond to prednisolone in terms of less recurrent wheezing at least for the subsequent 12 months. Clinically, a rapid respiratory syncytial virus detection test is useful in placing patients at ward, but for the assessment of long-term prognosis human rhinovirus PCR is needed. Considering that aeroallergen sensitisation develops usually after 2–3 yrs of life, human rhinovirus detection seems already to give clinically highly relevant information during infancy.

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STATEMENT OF INTEREST
None declared.

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From the authors:

We thank T. Jartti and colleagues for their interesting and useful comments on our previously published Task Force Report [1]. Accumulating evidence indeed suggests that human rhinovirus infections are common triggers of wheezing in young children. Observations from two cohorts in the US and Finland indicate that human rhinovirus infections may also be of prognostic importance, and this was mentioned in our paper. In agreement with T. Jartti and colleagues, it was the opinion of the Task Force, however, that this data was preliminary, and that identification of rhinovirus as the culprit in acute wheezing episodes in preschool children at present would not change the clinical management of such patients at the present time. The *post hoc* observation that prednisolone may reduce recurrent wheezing in preschool children initially hospitalised with a rhinovirus-associated acute wheezing episode [2] requires confirmation in a randomised trial before such treatment can be advised for clinical use. At present, therefore, because identifying the specific virus that causes acute wheeze in preschool children does not influence their clinical management, routine viral studies are not indicated in

such patients. However, we would welcome further research data in this area.

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STATEMENT OF INTEREST

A statement of interest for P.L.P. Brand can be found at www.erj.ersjournals.com/misc/statements.shtml

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Lung function decline in COPD trials

To the Editors:

In his recent editorial, SUISSA [1] has again expressed criticism of the TORCH (Toward a Revolution in Chronic Obstructive Pulmonary Disease (COPD) Health) trial [2]. The focus this time is the analysis of rate of decline in lung function [3], and in particular he questions whether the reduction in rate of decline in forced expiratory volume in one second (FEV_1) observed with the active treatments (salmeterol, fluticasone or the combination of both treatments) compared with placebo is due to ''regression to the mean'' caused by missing data.

Missing data for lung function and exacerbations are unfortunately inevitable in any long-term trial in COPD. SUISSA [1] states that ''… measurements were missing so that the pure intent-to-treat analysis was not possible''. Such a ''pure intent-to-treat'' analysis of lung function or exacerbation data is not possible for any long-term COPD trial, as this would require complete data.

In fact, the quantity of missing data for lung function in TORCH is similar to the UPLIFT (Understanding Potential Long-term Impacts on Function with Tiotropium) [4] and OPTIMAL [5] trials quoted in the article by SUISSA [1]. In TORCH, 4,857 (79%) patients provided lung function data at 48 weeks, OPTIMAL had complete 1-yr lung function data for 322 (72%) patients and, in UPLIFT, 4,970 (83%) patients were included in the rate of decline analysis. To suggest that TORCH is different from either UPLIFT or OPTIMAL in terms of the impact of missing data is misleading.

SUISSA [1] claims that the treatment comparisons for rate of decline in TORCH may be influenced by regression to the mean. Regression to the mean is a phenomenon commonly associated with comparisons where data collected at a given time-point are compared with baseline or historical data. Randomised trials, such as TORCH, where active interventions are compared with placebo, are generally viewed as avoiding this problem, since any regression to the mean should affect all groups equally [6].

The data generated by SUISSA [1] for his ''illustration'' of the problem are questionable. He has selected only those 322 patients from OPTIMAL who completed the study, in order to make inferences about patients who did not complete (*e.g.* any patient who died during the OPTIMAL study was not included). The problem is then compounded by the false assumption that only patients with the worst lung function withdrew from the study. Removing those with the worst values on the first visit is not the same as removing those who drop out early. Table 1 shows the actual withdrawal pattern from TORCH compared with that assumed by SUISSA [1].

The SUISSA [1] illustration assumes that the 263 placebo patients with no data beyond baseline all came from the lowest 18% according to baseline FEV_1. In fact, only 75 came from this group and the majority of the subjects with no data beyond baseline had higher FEV_1 values. Similarly, for the combination therapy, his assumption is that all 141 patients with no data beyond baseline correspond to the lowest 9% according to baseline FEV_1, while in contrast only 17 patients belonged to this group. The illustration

TABLE 1 Comparison of actual TORCH data and the SUISSA [1] illustration

Stratification according to FEV_1 at baseline	SUISSA [1] assumed withdrawals	Actual withdrawals
Placebo		
Lowest 18%	263	75
Highest 82%	0	188
Combination therapy		
Lowest 91%	141	17
Highest 9%	0	124

Data are presented as n. TORCH: Toward a Revolution in Chronic Obstructive Pulmonary Disease Health; FEV_1: forced expiratory volume in one second.