Reply: The Western Diet: A Smoking Gun for Chronic Obstructive Pulmonary Disease and Asthma?

From the Authors:

We thank Dr. Kerley for his thoughtful comments in response to our editorial and bringing to our attention published dietary interventional studies in asthma. Our editorial focused almost exclusively on studies in chronic obstructive pulmonary disease (COPD), which reflected in part the positive result in the study by Brigham and colleagues (i.e., a positive relationship between diet and COPD [1]), but not asthma [2]) and in part the literature, where numerous epidemiological studies have reported significant associations between healthy diets and a reduced risk for COPD [1].

Dr. Kerley is quite correct that healthy diets have been associated with better outcomes in those with asthma, but it is not clear whether they are also associated with a lower risk of asthma [1, 3]. This distinction is important in the setting of prevention through better dietary preferences. Dr. Kerley cites two studies: a small pilot study of seven individuals with asthma, which showed no effect on asthma outcomes after 4 weeks of a diet high in unsaturated fats [4], and a larger, randomized study in which 46 subjects with well-defined asthma were randomized to the high-antioxidant-intervention arm over 14 weeks, and clinically meaningful reductions in inflammatory markers (interleukin-6, C-reactive protein, and tumor necrosis factor α) were found along with reductions in asthma exacerbations [5]. We note that between 40% and 50% of these subjects with asthma had smoking histories consistent with possible asthma–COPD overlap or neutrophilic asthma, in which the above inflammatory mediators have been implicated [6, 7]. This behooves researchers to think carefully about the type of individual with asthma they include in their studies and the generalizability of any results.

Although we would not discourage researchers from undertaking randomized dietary intervention trials to better support clinical recommendations for COPD and asthma, we believe considerable resources would be required along with careful thought to patient recruitment to answer the important questions posed by Dr. Kerley. We would not rule out the possibility that comparable benefits can be achieved in subtypes of COPD and asthma by reducing systemic inflammation with the use of existing pharmacological interventions such as statins [8, 9].

Author disclosures are available with the text of this letter at www.atsjournals.org.

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References


Childhood Exposures, Asthma, Smoking, Interactions, and the Catch-Up Hypothesis

To the Editor:

We welcome the interesting insights provided by Bui et al [1], which support the previously reported concept that personal smoking alters the effect of childhood factors on adult lung function and chronic obstructive pulmonary disease (COPD) development [2]. The authors present highly valuable longitudinal data illustrating the complex interactions potentially underlying COPD development across life. However, we disagree with the authors’ suggestion that data from the Tasmanian Longitudinal Health Study (TLHS) contradict recently published findings from the National Survey of Health and Development (NSHD) regarding the effect of childhood experience on adult lung function among never-smokers [1].

Both studies show that patients with childhood asthma have lower adult lung function, whether they go on to smoke or not. Among never-smokers in the NSHD, childhood asthma (recorded at 6–15 years) was associated with forced expiratory volume in 1 second (FEV1) deficits of 294.4 ml (95% confidence interval [CI], 136.3–452.4 ml; P < 0.001) at age 43 years (Figure E3) [2]. Among TLHS never-smokers, frequent childhood asthma/bronchitis (recorded at 7 years) was associated with an FEV1 deficit of 166 ml (95% CI, 65–268 ml; P < 0.01) at age 53 years (Table E10) [1].

However, data from the NSHD also show that some adverse exposures, recorded earlier in childhood, influenced adult lung function predominantly among those who subsequently became smokers [2]. These findings lead us to advocate the “catch-up hypothesis”: that lung growth and development between childhood and adulthood may permit recovery from early life insults if that recovery remains unimpeded by further or ongoing adverse

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exposures, such as personal smoking, adverse environmental exposures, or conditions such as asthma (Figure 1) (2). We believe this hypothesis goes some way in explaining the historically disproportionate occurrence of COPD among smokers affected by poverty, yet without evidence of accelerated adult FEV₁ decline.

We would argue that the purportedly different exposure–outcome relationships between the TLHS and NSHD studies (1) simply reflect differences in both the timing and nature of the exposures examined, which in turn determines opportunity for recovery. First, the NSHD examined exposures during the first few years of life. This particularly vulnerable developmental period (3) precedes that studied by the THLS, perhaps affording NSHD members more time for recovery during subsequent childhood. Second, the NSHD studied early life exposures, such as lower respiratory infections, home overcrowding, and social class, which seem less likely to have consistently persisted into adulthood than asthma. Recovery from a previous but subsequently inactive event, such as a respiratory infection during infancy, seems more likely than recovery from an ongoing adverse exposure, such as persisting asthma. The TLHS provides the very useful insight that within their study, up to 82% of the effect of childhood "frequent asthma, bronchitis" on adult COPD was mediated by active adult asthma. Clearly, childhood asthma can influence future COPD development, especially if individuals do not "grow out of" their childhood asthma, but instead their asthma persists into adulthood.

Further recent support for the catch-up hypothesis may be drawn from data highlighting considerable variation in lung function trajectories between 8 to 16 years of age (4) and data, from the TLHS, suggesting the existence of a trajectory compatible with recovery from low function between childhood and adulthood (5).

These are exciting times, perhaps allowing great strides in understanding how, why, and when COPD develops. Unfortunately, there is not and will not be a single perfect study. However, the wealth of recently published life-course data (1, 2, 4, 5) can help us piece together the jigsaw of COPD development across life, but only if the pieces are assembled correctly.

Author disclosures are available with the text of this letter at www.atsjournals.org.

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References


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Reply: Childhood Exposures, Asthma, Smoking, Interactions and the Catch-Up Hypothesis

From the Authors:

We welcome discussion about apparent differences between findings reported by the two longitudinal cohorts: the Tasmanian Longitudinal Health Study (TAHS) (1) and the British National Survey of Health and Development (NSHD) (2). These relate to the influence of early-life factors on lung function measured in midadulthood, and the implications for the “catch-up” phenomenon in the
absence of smoking in later life (2). Relevant comparisons between the study designs of the NSHD and TAHS are summarized in Table 1.

It should be noted that the differences between these two studies in the early-life exposures examined and how these factors were grouped precludes clear and direct comparisons. Both manuscripts examine the role of early-life factors on adult lung function, and their interactions with personal smoking, but how this was explored was quite different. We agree that the discrepancy in the main finding might also be explained by differences in the nature and timing of the early-life exposures. Similarly, it is relevant that the NSHD examined the influence of individual environmental factors on lung function, and this contrasts with the latent class of risk factors in the TAHS, which might represent a more complex interplay between environmental exposures and the host responses.

Both papers consistently reported that early-life insults contributed to reduced lung function in middle age, and that personal smoking in later life commonly augmented these lung function deficits. In the NSHD, early-life factors (respiratory infection and home overcrowding) had a significant adverse effect on adult lung function among ever smokers, but not among never-smokers. Similarly, in the TAHS, the effect of parental smoking class on adult lung function was only significant among ever-smokers, but not among never-smokers. Where the results from the two studies start to diverge is the effect of personal smoking on the effect of early-life asthma. In the TAHS, the “frequent asthma, bronchitis, allergy” class was significantly associated with lower adult lung function in both never- and ever-smokers, and the effect was further augmented in ever-smokers. In the NSHD, although childhood asthma was associated with adult lung function impairments, this effect was not augmented by personal smoking. This apparent difference may be a result of the “frequent asthma, bronchitis, allergy” class in the TAHS having captured severe asthma as well as multiple allergies, thus representing the allergic/severe asthma phenotype rather than just asthma in the NSHD.

A related TAHS paper that examined lung function trajectories spanning the first to sixth decade of life identified an “early low, accelerated growth, normal decline” trajectory for 8% of our participants (3). This individual pattern resembles the catch-up hypothesis suggested by Allinson and colleagues, as children with early lung function impairment were observed to have subsequent acceleration of lung function growth to attain normal peak levels by late adolescence. This trajectory was characterized by low current smoking rates (9%) and minimal personal smoking history (median, 0; interquartile range, 0–10 pack-years). Although exposures including infections, home overcrowding (in NSHD), and parental smoking (in TAHS) suggested the catch-up among never-smokers, the catch-up was not seen for asthma (in both NSHD and TAHS) (2, 3). This suggests that although some childhood exposures, in the absence of personal smoking, may lead to catch-up growth in lung function, other (host related) factors such as asthma may not allow such catch-up.

Together, these two studies provide complementary information clarifying different aspects of the link between early-life exposures and their long-term effects on lung function. They highlight the importance of understanding which factors may be associated with the potential to “catch-up” lung function that is compromised by early-life insults. This phenomenon is potentially good news for parents/physicians whose children/patients have lung function impairment, as smoking abstinence may avert additional harm from taking up the smoking habit, albeit only relevant to a subgroup. Ultimately, the rigorous comparison and potential pooling of findings from studies such as the NSHD and TAHS is necessary to gain the greatest insight into the complexities that link childhood factors to the development of chronic obstructive pulmonary disease.

**Table 1. Comparisons between the British National Survey of Health and Development and the Tasmanian Longitudinal Health Study**

<table>
<thead>
<tr>
<th>Feature</th>
<th>TAHS</th>
<th>NSHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of early-life exposure</td>
<td>Six distinct profiles of 11 respiratory risk factors</td>
<td>Early-life disadvantage including respiratory infection, paternal occupation, home overcrowding, air pollution</td>
</tr>
<tr>
<td>Type of variable</td>
<td>Latent class (statistically different from other classes)</td>
<td>Standard variable</td>
</tr>
<tr>
<td>Initial lung function measure</td>
<td>Pre- and post-BD spirometry at age 53 years Investigated using pre-BD FEV₁ trajectories between age 7 and 53 years in a related paper (3)</td>
<td>Pre-BD spirometry at age 43 years Pre-BD spirometry at baseline and at age 60–64 years</td>
</tr>
<tr>
<td>Serial lung function</td>
<td>Interactions for both post-and pre-BD spirometry</td>
<td>Interaction for pre-BD spirometry</td>
</tr>
<tr>
<td>Reported interaction with smoking</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Definition of abbreviations: BD = bronchodilator; FEV₁ = forced expiratory volume in 1 second; NSHD = National Survey of Health and Development; TAHS = Tasmanian Longitudinal Health Study.*

**Author disclosures** are available with the text of this letter at www.atsjournals.org.

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References


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