Childhood exposures, asthma, smoking, interactions and the catch-up hypothesis

James P Allinson[1], Rebecca Hardy[2], Gavin C Donaldson[1], Jadwiga A Wedzicha[1]

1. Airways Disease Section, National Heart and Lung Institute, Imperial College London, United Kingdom
2. MRC Unit for Lifelong Health and Ageing at UCL, London, United Kingdom

Address correspondence to:

Dr J.P. Allinson

COPD Research Group, Airways Disease Section, National Heart and Lung Institute, Guy Scadding Building, Dovehouse Street, Imperial College London, United Kingdom, SW3 6LY

Phone: +44 207 5945665; E-mail: j.allinson@imperial.ac.uk

Running Title: Childhood exposures and the catch-up hypothesis

Descriptor: COPD, poverty, growth & development

Manuscript word count: 565

Childhood exposures, asthma, smoking, interactions and the catch-up hypothesis

James P Allinson, Rebecca Hardy, Gavin C Donaldson, Jadwiga A Wedzicha

To the editors,

We welcome the interesting insights provided by Bui et al[1] which support the previously reported concept that personal smoking alters the impact of childhood factors upon adult lung function and 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 (NHSD) regarding the impact of childhood experience on adult lung function among never-smokers.[1]

Both studies show that childhood asthmatics have lower adult lung function whether they go on to smoke or not. Among never-smokers in the NSHD, childhood asthma (recorded at 6 to 15 years) was associated with FEV_1 deficits of 294.4ml (95% Confidence Interval (95%CI): 136.3 to 452.4; 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 FEV_1 deficit of 166ml (95%CI: 65 to 268; 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 exposures, such as personal smoking, adverse environmental exposures or conditions like asthma (See Figure 1).[2] We believe this

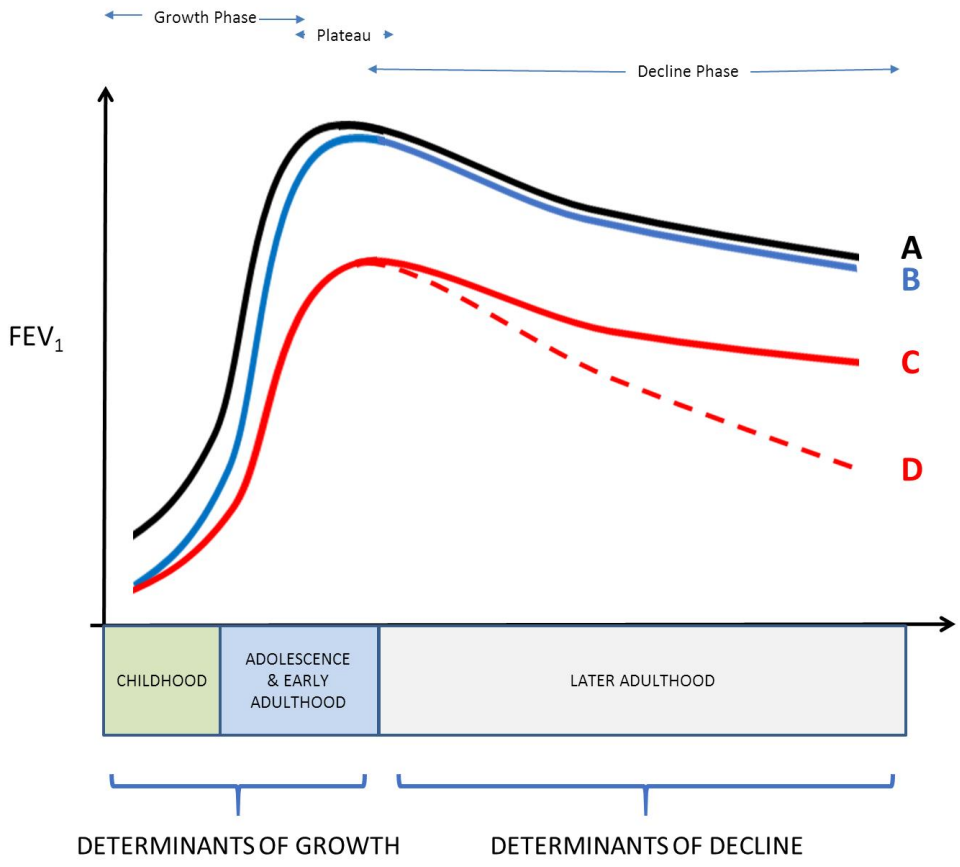
hypothesis goes someway in explaining the historically disproportionate occurrence of COPD among smokers affected by poverty yet without evidence of accelerated adult FEV_1 decline.

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. Firstly, 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. Secondly, 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.

FIGURE 1: FEV_1 trajectories across life illustrating the catch-up hypothesis (see main text):
A (Black): Normal childhood FEV_1, normal adult peak and then normal decline;
B (Blue): Low childhood FEV_1 followed by catch-up growth, normal peak adult and then normal decline;
C (Solid Red): Low childhood FEV_1 without catch-up growth, low adult peak and then normal decline;
D (Dashed Red): Low childhood FEV_1 without catch-up growth, low adult peak and then accelerated adult decline (accelerated decline may affect members of any trajectory but only shown here as a variant of trajectory C for simplicity).



1. Bui DS, Walters HE, Burgess JA, et al. Childhood Respiratory Risk Factor Profiles, Their Interactions and Mediators, and Middle-age Lung Function: A Prospective Cohort Study from the 1st to 6th Decade. Annals of the American Thoracic Society 2018.

2. Allinson JP, Hardy R, Donaldson GC, Shaheen SO, Kuh D, Wedzicha JA. Combined Impact of Smoking and Early-Life Exposures on Adult Lung Function Trajectories. American journal of respiratory and critical care medicine 2017;196:1021-30.

3. Shaheen SO, Sterne JA, Tucker JS, Florey CD. Birth weight, childhood lower respiratory tract infection, and adult lung function. Thorax 1998;53:549-53.

4. Schultz ES, Hallberg J, Andersson N, et al. Early life determinants of lung function change from childhood to adolescence. Respiratory medicine 2018;139:48-54.

5. Bui DS, Lodge CJ, Burgess JA, et al. Childhood predictors of lung function trajectories and future COPD risk: a prospective cohort study from the first to the sixth decade of life. The lancet Respiratory medicine 2018.