



Transitioning from infancy to adulthood: a black box full of opportunities

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A better understanding of the factors that modulate the transition of lung function from infancy to adulthood is key to understanding adult respiratory health <https://bit.ly/3k1mXA0>

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During pregnancy, an obstetrician takes care of both mother's and child's health. After birth, a paediatrician continues to care for the child and, if nothing serious and unexpected happens, most adolescents will be on their own without sanitary control until about their 5th–6th decade of age, where prevalent cardiovascular, respiratory and/or metabolic chronic diseases begin to emerge. This has been described as a “black box” period [1] which, interestingly, may be full of opportunities for prevention, early diagnosis, careful monitoring and, eventually, early intervention. Two recent observations support this possibility. First, between 4 and 12% of young adults (~25 years of age) in the general population have low lung function and, importantly, they are at a higher risk of respiratory, cardiovascular and metabolic diseases later in life, and die prematurely [2, 3]. Second, there are many different environmental risk factors that influence lung function through life and, as shown in figure 1, these factors change with age and interact between them in an increasingly complex fashion [4]. Eventually, it is this dynamic set of gene–environment interactions which modulates the lung function trajectory (figure 2) that any individual follows from birth until death [3, 5–8]. Collectively, these observations indicate that early life events are critically important in determining the health expectancy of the individual through life [7], and open new opportunities for disease understanding, disease prevention, early treatment, therapeutic optimisation and, eventually, prognosis improvement [9, 10]. For instance, if, as discussed above, not achieving a normal lung function peak in early adulthood identifies a group of young individuals at risk of respiratory, cardiovascular and/or metabolic diseases later in life, as well as of premature death [2], then spirometry should be routinely measured in this young population, perhaps when they apply for a driving licence, when they enter the army and/or begin university studies [7, 9]. Likewise, we now know that some children born with low lung function can “catch-up” and regain a normal lung function trajectory, whereas others cannot (figure 2) [7]. The precise mechanisms underlying this “catch-up” are currently unclear and possibly involve both environmental and genetic factors [7], but their better understanding may open possibilities for better prevention [11], as well as to stimulate lung growth in infancy and, perhaps, later in life too [7].

In this context, the study published in this issue of the *European Respiratory Journal* by WANG *et al.* [12] in young adults should be welcome. Specifically, these investigators explored in the BAMSE cohort the

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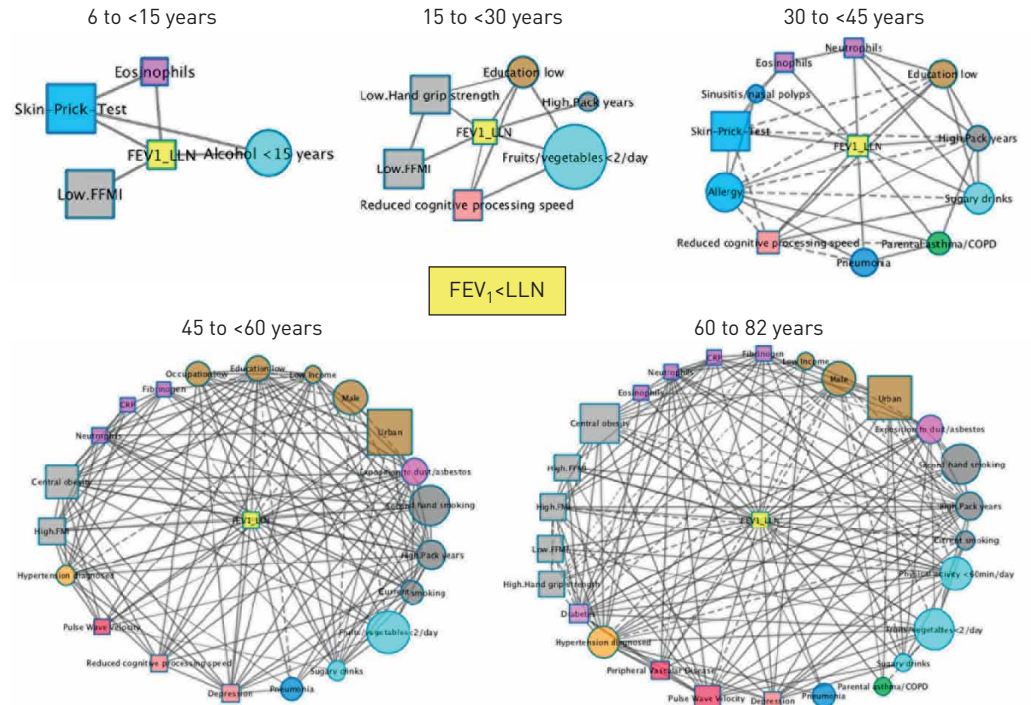


FIGURE 1 First-neighbour networks for forced expiratory volume in 1 s (FEV_1) less than lower limit of normal (LLN) (centre yellow node) in different age bins. Each node represents one variable, node size is proportional to the prevalence of that variable in that specific age bin, and node colour indicates variable category. Links between nodes indicate the existence of a significant ($p < 0.05$) relationship between them, thicker edges indicate lower p-values, and the line type indicates whether the odds ratio is < 1 (continuous) or > 1 (dashed). Note that the different factors significantly associated with $FEV_1 < LLN$ change and increase with age, and that many of them are preventable. Reproduced with permission from reference [4].

prevalence and early life risk factors for chronic bronchitis in young adults. BAMSE (Swedish abbreviation for Children, Allergy, Milieu, Stockholm, Epidemiology) is an ongoing longitudinal, population-based prospective birth cohort that included 4089 children born between 1994 and 1996 in Stockholm, Sweden, originally designed to study risk factors for asthma, allergic diseases and lung function in childhood, as well as prognostic factors of already established disease [13]. The current analysis corresponds to data obtained between 2017 and 2019, when participants were 22–24 years old [12]. WANG *et al.* [12] showed that, in this population of young adults: 1) the prevalence of “chronic bronchitis”, defined as the combination of cough and mucus production in the morning during winter, was 5.5%, without sex

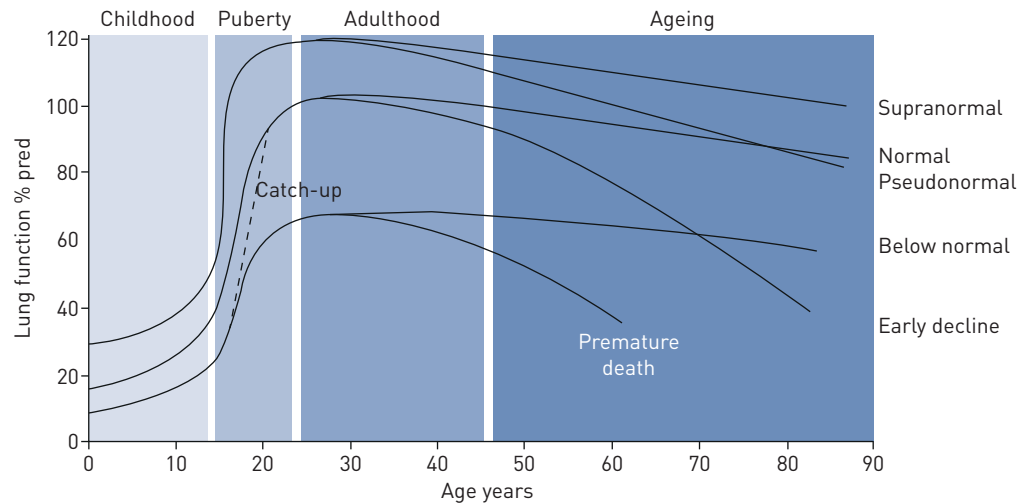


FIGURE 2 Different lung function trajectories from birth to death. Reproduced with permission from reference [8].

differences, a figure that is not dissimilar to that reported in older age bins in the general population; and 2) recurrent respiratory infections, a diagnosis of “asthma” in childhood, current and former smoking, and exposure to air pollution were associated risk factors for chronic bronchitis, whereas breastfeeding was protective [12].

As any other study, this one in particular also has some limitations, as actually acknowledged by authors, including that: 1) the authors did not use the “standard definition” of chronic bronchitis (*i.e.* cough and/or sputum production for 3 months, irrespective of winter time, during two consecutive years, after excluding other causes); 2) “respiratory infections” were self-reported, which can clearly be biased by recall, and there is no “evidence” that these acute episodes do really correspond to a viral/bacterial “infection”; and 3) the term “asthma” may be misleading, particularly in children, since other conditions such as abnormal lung development can mimic the symptoms of “asthma” [8]. On the other hand, a “diagnosis of asthma” may well indicate the presence of some respiratory problem, being it “true” asthma or not [8].

Despite these limitations, the main message from this analysis is that chronic bronchitis does indeed occur in early adulthood [12]. Whether this represents a response to environmental injuries (such as infections, smoking and/or ambient pollution), and/or it is the end result of abnormal lung development and/or changes in the pulmonary microbiome, is unknown. In this context, however, the observation that maternal breastfeeding protects from chronic bronchitis in early adulthood is in keeping with a systematic review and meta-analysis that found a positive association of breastfeeding with reduced asthma/wheezing [14]. Furthermore, some of the authors of the study have also recently published another analysis of the BAMSE cohort, showing that breastfeeding for 4 months or more seems to reduce the risk of asthma up to 8 years and has a beneficial effect on lung function [15]. Human milk contains high amounts of IgA, cytokines, and long-chain fatty acids and oligosaccharides, and has a specific microbiome (breastmilk microbiome) that can influence the gut (and lung?) microbiome, as well as help the child immune system to mature [15, 16]. On the other hand, whether chronic bronchitis in this young population represents a form of “pre-COPD” [17, 18] is unclear, but this possibility is supported by some previous observations showing that a proportion of individuals with chronic bronchitis do eventually develop COPD [19]. Finally, the observation that food, but not airborne allergens, influence chronic bronchitis in this young adult population deserves further research that integrates similar molecular approaches in both paediatric and adult populations and in longitudinal studies [1]. Collectively, these observations confirm that early life events are important risk factors for lung health later in life [3, 5–7, 20] and, importantly, that many of them can be prevented (figure 1) [4]. Furthermore, understanding the biological basis of these observations, as well as diagnosing and intervening earlier, may be of great relevance of respiratory health through life [10]. To achieve these goals, a year ago the European Respiratory Society launched a Clinical Research Collaboration named CADSET (Chronic Airway DiSeases Early sTratification) that now includes 30 research institutes and has access to data different 45 cohorts that involve almost 300 000 individuals through Europe (<https://cadset.org>), including the group of investigators in Stockholm that signed the paper editorialised here [12]. Stay tuned!

Conflict of interest: None declared.

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