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Editorial Office Notes:
RES-19-431
COMMENTARY

Publication Fee Waiver: YES
Volume number: 24

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/resp.13652

Major contributions by and the future scope of cohort studies to advance Respiratory and Sleep medicine

Key words: longitudinal, cohort, respiratory, sleep

Prospective cohort studies are valuable in establishing the aetiology and prognosis of diseases. These studies can provide the best evidence on potential interventions that can either be trialled in randomised controlled trials or inform prevention strategies, when it is not feasible or ethical to conduct trials. Alternatively, retrospective cohort studies can be conducted either when the cohort has already been recruited or is identified retrospectively. This approach has been particularly helpful in occupational health, which can draw upon workplace records for data. This editorial briefly outlines the contributions made by prospective cohort studies to the fields of Respiratory and Sleep Medicine.

While there are a number of population based and clinical cohort studies in respiratory health, few span early childhood to adulthood with three (Tasmanian Longitudinal Health Study (TAHS), Melbourne Epidemiology Study of Childhood Asthma (MESCA), National Child Development Study (NCDS)) reaching well into the 6th decade of life(1-3). Together, these studies have changed multiple paradigms in asthma, chronic obstructive pulmonary disease (COPD) and lung function trajectories. They have shown that there are multiple early life longitudinal wheeze phenotypes, with some affecting lung growth (4), and that lung function deficits in COPD are partly established in early life. Not only is the aetiology of COPD related to multiple risk factors, but early life and adult risk factors also interact with each other to increase the risk of COPD(5, 6). While a majority of childhood asthma resolves by adulthood, asthma that persists from childhood is the major contributor to severe asthma burden in adults. Severity of asthma, female sex, parental history of asthma, and atopic disorders (in particular eczema and allergic rhinitis) are risk factors for the persistence of childhood asthma into adult life(1, 7).

As studies that started in childhood have matured in the past five years, establishing how lifetime lung function trajectories deviate from the normal trajectory has received increasing interest. Six population-based FEV_1 trajectories from the TAHS have now been described (Figure 1) and 75% of COPD by age 53 years arises from three trajectories that demonstrated lung function deficits from childhood(3). It has also been shown that half of those with COPD at age 62 years had normal FEV_1 before 40 years of age and a rapid decline in FEV_1 thereafter, while the other half had low FEV_1 in early adulthood and a subsequently normal decline. Early life risk factors that increase the risk of COPD as well as low lung function trajectories include early life asthma and bronchitis, and early life exposures to infection and smoking(6). The discrepancy between these two studies in the contribution made by early life lung function deficits to the overall COPD burden (75% vs 50%) may reflect the relative increase made by accelerated lung function decline to COPD developed by age 62 years(8).

There is increasing evidence that early life risk factors interact with adult asthma, smoking and occupational exposures to increase the risk of COPD in a multiplicative fashion. Given the current evidence on the interactions between lifetime risk factors, these risk profiles could be used to identify those who are at risk of developing COPD. These risk profiles could also be used to diagnose COPD in combination with symptoms, lung function measurements and smoking history, approaches which are commonly used in clinical practice. To use such complex information practically in busy clinical settings, the development of risk prediction tools would be essential.

Longitudinal cohort studies in sleep medicine have also played a key role in establishing the high prevalence of disorders, key aetiological risk factors and associated co-morbidity risks. The Wisconsin Sleep cohort was established over 30 years ago and performed gold standard laboratory polysomnography at four yearly intervals in 1,500 State employees. It established

the high prevalence of sleep disordered breathing in the middle-aged population – affecting 24% of men and 9% of women(9). It has also confirmed the aetiological role played by weight gain and obesity in the development of obstructive sleep apnoea (OSA)(10). As well as causing a symptom burden including fatigue and excessive daytime sleepiness, OSA has been strongly associated with depression, hypertension, cardiovascular disease, cerebrovascular disease and increased mortality. The Wisconsin Sleep cohort was the first to demonstrate that the incidence of depression and hypertension was increased over long term follow up in subjects with OSA(11). These data formed the basis for subsequent intervention trials showing that continuous positive airway pressure (CPAP) could lead to improvements in blood pressure.

The association between OSA, cardio- and cerebro-vascular disease and mortality was further strengthened by data from the Sleep Heart Health Study (SHHS), a sub-study of the well-known Framingham cohort. The SHHS has shown that severe OSA (where the Apnoea Hypopnoea Index [AHI] is ≥ 30 events/hour) is associated with an increased risk of incident stroke and all-cause mortality, adjusted for known confounders(12). Although in the SHHS the association between OSA and mortality was only significant for males < 70 years of age, the Wisconsin Sleep cohort has demonstrated that subjects with severe OSA also have increased mortality over an 18 year follow up period(13).

Using such longitudinal studies, risk prediction tools have already been established for other major non-communicable diseases such as cardiovascular and cancer, but the field of respiratory and sleep medicine is lagging far behind in this regard. There is already enough evidence to utilise longitudinal studies to develop and validate risk prediction tools for respiratory diseases, however more longitudinal research is needed to consider such an approach for sleep health. To understand lifetime risk profiles of sleep disorders, whole of life cohort studies spanning early childhood to adult life, or data from adult cohorts which include knowledge of early life risk factors are needed. Embedding sleep assessments into

current and future follow ups of active cohort studies would further delineate the role of sleep disorders as major public health problems. Given that multimorbidity has been identified as the new public health challenge in 21st century(14), respiratory cohort studies that span childhood to adulthood also provide an opportunity to longitudinally investigate comorbidities of COPD, which carries the highest burden of multiple morbidities.

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Disclosure statement: Shyamali Dharmage is supported by the National Health & Medical Research Council. Garun Hamilton has received equipment for research from Resmed, Philips Respironics and Air Liquide Healthcare. Michael Abramson holds investigator initiated grants for unrelated research from Pfizer and Boehringer-Ingelheim. He has also undertaken an unrelated consultancy for Sanofi.

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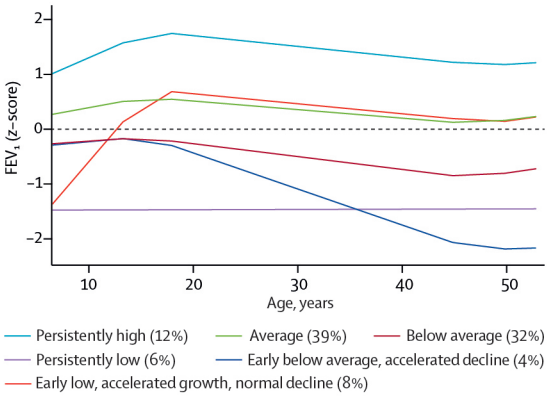
Figure legend

Figure 1: Trajectories of lung function (FEV_1 z-score) from 7 to 53 years of age. The six trajectories represent the latent growth patterns of lung function. The group prevalences do not add up to 100% because of rounding. (Reproduced with permission from Bui et al.[3])



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Title:
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Date:
2019-07-26

Citation:
Dharmage, S. C., Hamilton, G. S. & Abramson, M. J. (2019). Major contributions by and the future scope of cohort studies to advance respiratory and sleep medicine. RESPIROLOGY, 24 (11), pp.1049-1050. https://doi.org/10.1111/resp.13652.

Persistent Link:
http://hdl.handle.net/11343/286208

File Description:
Accepted version