Concept Plan

Provisional Paper Title: Sarcopenia and lung function decline – Do breathing difficulties lead to muscle weakness?

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Please describe your proposal in 2-3 pages with sufficient detail for helpful review.

Objective of the study:

Sarcopenia is the degenerative loss of skeletal muscle mass, quality, and strength commonly associated with aging and it is one of the most important causes of frailty (1). Patients with chronic respiratory disease often have advanced features of sarcopenia including impaired grip strength, reduced walking speed, and loss of skeletal muscle (2-4). However, it is unclear why people with impaired lung function develop sarcopenia and only few cross-sectional studies (mostly Korean) have investigated this association in the general population (5-6). In this project, I will investigate the longitudinal associations between an accelerated decline in lung function and skeletal muscle mass, grip strength, and gait speed, and what risk factors might explain these associations at age 45 in the Dunedin Multidisciplinary Health and Development Study (Dunedin Study).

Data analysis methods:

As part of my PhD, I am analysing trajectories of lung function decline among participants in the Dunedin Study, which is a longitudinal investigation of health and behaviour in an unselected population-based cohort (n=1,037) born in Dunedin in 1972/1973. The cohort has been assessed at multiple ages through childhood and up to age 45 years, with a very high rate of follow-up. In the Dunedin Study, lung function has been measured (by spirometry) at every assessment since age 9 and grip strength (by dynamometer), gait speed (by 4 meter walking test), and body composition (by dual-energy x-ray

absorptiometry, DXA and bioelectrical impedance analysis, BIA) were measured at age 45.

Although only age 45, many participants have experienced significant loss of lung function, which is just one marker of accelerated aging. In this project, I will first establish whether there are longitudinal associations between an accelerated decline in lung function between age 21 and age 45, measured using FEV1, FVC, and their ratio, and skeletal muscle mass, grip strength, and gait speed at age 45. Then I will investigate whether the associations can be explained by known risk factors such as tobacco smoking, systemic inflammation (high sensitivity CRP), obesity, or lack of physical activity.

Multiple linear regression (for continuous outcome variables) and multiple logistic regression (for outcomes categorised into levels) will be used for statistical modelling. Latent profile analysis will be performed to identify distinct trajectories of lung function decline between age 21 and age 45. Standard model diagnostics will be used. Subgroup analyses will be performed for men and women with interactions used to assess evidence for effect modification. All analyses will be conducted using Stata 15.1 and/or R 3.5.3 (or later versions).

Variables needed at which ages:

Skeletal muscle mass, grip strength, and gait speed at age 45.

Significance of the Study (for theory, research methods or clinical practice):

Sarcopenia and frailty are key research areas in geriatrics. We know that these are major contributors to mortality and morbidity in chronic lung diseases, such as COPD, and it is suspected that lung disease accelerates loss of muscle mass and strength. The mechanisms behind this are not well understood. My research will address this by providing deeper understanding of a common and debilitating cause of frailty.

This research will also establish decline in lung function as a marker of accelerated ageing, thereby raising the profile of ageing research at Otago through the Dunedin Multidisciplinary Health and Development Study.

References:

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4. Schols AM, Broekhuizen R, Weling-Scheepers CA, Wouters EF. Body composition and mortality in chronic obstructive pulmonary disease. The American journal of clinical nutrition. 2005;82(1):53-9.
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6. Park CH, Yi Y, Do JG, Lee YT, Yoon KJ. Relationship between skeletal muscle mass and lung function in Korean adults without clinically apparent lung disease. Medicine. 2018;97(37):e12281.