

Appendix Section B(2): CONCEPT PAPER TEMPLATE

**DUNEDIN MULTIDISCIPLINARY HEALTH AND DEVELOPMENT
STUDY**
(The Dunedin Study)

CONCEPT PAPER TEMPLATE
(July 2024)



DUNEDIN STUDY CONCEPT PAPER

Provisional Paper Title: The natural history of Preserved Ratio Impaired Spirometry (PRISm)

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P.I. Sponsor:

(if the proposing author is a student or colleague of an original PI)

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Please describe your proposal in 2-3 pages with sufficient detail for helpful review by addressing all areas outlined below.

Objective of the study:

- To describe the prevalence and changes in PRISm across adult phases of the Dunedin Study.
- To correlate the presence of PRISm with restrictive spirometry and restrictive lung function (body box).
- To assess the respiratory symptom burden associated with PRISm
- To assess potential risk-factors for PRISm, including childhood asthma, smoking, body weight, and height.

Data analysis methods¹:

PRISm will be defined according to age-specific cut-points for %-predicted FEV₁/FVC and FEV₁, based on the values for non-asthma non-smoking participants in the study. The primary definition of PRISm uses post-bronchodilator spirometry, although in keeping with many studies, we will also define pre-bronchodilator PRISm.

The prevalence of PRISm as well as airflow obstruction, will be documented at each age. Changes in category (Normal, Obstructive, PRISm) between ages will be shown using alluvial plots. This will be done for post-bronchodilator spirometry (ages 18, 26, 32, 38 and 45) (primary analysis).

We will compare lung volumes (TLC, RV, FRC) at age 45 among those with PRISm, normal, and obstructive lung function (ANOVA).

Logistic regression analyses will assess the associations between smoking,

¹ A key concern for the Dunedin Study is superficial analyses of data that simply identify differences or deficits between ethnic groups or other communities where inequities exist (e.g. persons with disabilities, Pasifika peoples, members of migrant and SOGIESC (Sexual Orientation, Gender Identify and Expression and Sexual Characteristics) communities). The cumulative effect of these types of studies is stigmatising and not of benefit. Any research that identifies differences must (a) incorporate information on the broader context (e.g. historical or political factors); (b) where possible undertake additional analyses to examine the source of the difference/s, and (c) include policy recommendations for its resolution.

obesity, cannabis use, height, and childhood asthma and PRISm at age 45 (dependent variable).

Logistic regression analyses will assess the associations between PRISm at age 45 (independent variable) and the respiratory symptoms or wheeze, dyspnea, cough, and sputum production with adjustment for sex and with and without further adjustments for smoking, asthma, cannabis use, and asthma.

Variables needed at which ages:

Spirometry – all ages (pre and post)

Respiratory questionnaires

Height, weight

Smoking history including current smoking status and pack-years

Cannabis history (current use and joint-years)

Body-box measurements ages 26 – 45.

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

The term “Preserved Ratio Impaired Spirometry” (PRISm) “was introduced in 2014 to refer to a pattern of lung function in which individuals have low lung function with proportionate reductions in FEV₁ and FVC (i.e. a low FEV₁, but a normal FEV₁/FVC ratio).[1] It is reported to occur in between 6 and 24% of the global population.[2] As expected, it overlaps with the traditional definition of “restrictive” spirometry, which is defined as a low FVC but a normal FEV₁/FVC ratio. Restrictive spirometry has been described for many years and is found in a number of conditions in which the lungs are made smaller by intrinsic lung disease (such as fibrosis) or by chest wall disease restricting expansion. However, restriction seen on spirometry can be misleading and should be confirmed by other measurement of lung volume (such as using a body plethysmograph or gas dilution techniques).[3] The same caveat can be applied to PRISm – this does not necessarily imply restriction and one of the reasons for introducing the term was to avoid implying a diagnosis of any of these diseases.

It is likely that people with PRISm may have one of several different conditions: First, some will have true restrictive lung disease (causing low FVC and FEV₁, with a preserved ratio and a low Total Lung Capacity), Second, they may be developing COPD with a low FEV₁, but the ratio has not yet met the criterion for obstruction. Third, they may have just done an inadequate FVC (a common error in spirometry), which falsely elevates the FEV₁/FVC ratio, Forth, they may simply have smaller than average lungs (since “normal” values are designed to exclude the 5% of healthy people with the lowest lung function).

Despite these uncertainties, there has been a proliferation of publications about PRISm. It has been shown that it can be related to respiratory symptoms and is associated with higher respiratory, cardiovascular, and overall mortality.[4-6] It has been included in recent international guidelines as a form of “pre-COPD” to indicate a high risk of developing COPD.[7, 8] However, there is much that is not yet understood. Although some studies have investigated the consistency of PRISm on follow-up, no studies have described this across the lifecourse.[2, 6] Few population-based studies have described the transition from PRISm to COPD over a long-follow-up. Furthermore, few studies have the data to explore the

overlap between PRISm and restrictive lung disease using body-box measurements of Total Lung Capacity.

The Dunedin Study has the potential to make an important contribution to our understanding of PRISm: We can describe the consistency of this lung function pattern across the lifecourse, identify the proportion that transition to COPD, explore associations with symptoms and risk factors, and document the overlap with restrictive lung disease.

How the paper will contribute to Māori health advancement and/or equitable health outcomes²

Māori suffer a disproportionate burden of chronic lung disease: this is well-documented for COPD.[9] If PRISm is found to be a precursor of COPD as has been suggested, this would indicate that simple spirometry in high risk populations could identify people who are likely to develop COPD and provide an opportunity to intervene. PRISm is also associated with a higher risk of cardiovascular and other diseases, which also disproportionately affect Māori. Understanding the relationship between PRISm and overall health has the potential to alleviate some of this excess burden.

References:

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² Helpful information can be found here: https://www.hrc.govt.nz/sites/default/files/2020-01/NZ%20Prioritisation-Framework-FA-web_0.pdf