# Cardiopulmonary outcomes in people with impaired lung function: the role of metabolic syndrome

Roham Sadeghimakki[a] and Abd A. Tahrani[b,*]

[a]Public Health Nutrition Research Group, London Metropolitan University, London, UK
[b]Institue of Metabolism and Systems Research (IMSR), University of Birmingham, Birmingham, UK

The Lancet Regional Health - Europe 2023;35: 100796
Published Online xxx
https://doi.org/10.1016/j.lanepe.2023.100796

Impaired lung function, either with airflow limitation or with preserved ratio impaired spirometry (PRISm), is common globally and associated with increased cardiorespiratory morbidity, cause-specific mortality and overall mortality.[1,2] In this context, understanding the impact of metabolic syndrome on cardiopulmonary outcomes is clinically important, given the growing global prevalence of metabolic syndrome, driven in part by the increasing obesity rates, and its associations with major adverse cardiovascular events and all-cause mortality.[3,4]

In this issue of *The Lancet Regional Health – Europe*, Marott et al. examined the contribution of metabolic syndrome to increased cardiopulmonary morbidity and mortality observed in adults with impaired lung function.[5] For this purpose, the authors utilised the data from well-characterised 106,845 adults aged 44–75 years, from the prospective Copenhagen General Population Study, who were followed up for 15 years. Metabolic syndrome was defined based on the presence of 3 out of 5 criteria related to dyslipidaemia, hyperglycaemia, hypertension and central obesity per American Heart Association recommendations. Baseline lung function was classified as normal, PRISm and airflow limitation based on the forced expiratory volume during the first second ($FEV_1$), forced vital capacity (FVC) and $FEV_1$/FVC ratio. Study outcomes were based on real-world data from the national registries.

Overall, 14% and 6% of the study population were categorised as having airflow limitation and PRISm, respectively. Metabolic syndrome was common in the study population (23%), with a higher prevalence in the PRISm group (39%) compared with the airflow limitation and normal-lung-function groups (23% and 22%, respectively). This increased prevalence of metabolic syndrome in individuals with PRISm is not surprising given the well-described mechanical and inflammatory links between abdominal obesity, as a major component of metabolic syndrome, and the "restrictive" spirometric pattern.[6]

In the study by Marott et al., people with versus without metabolic syndrome had higher absolute 5-year risks of all-cause mortality, cardiac/respiratory mortality, and hospital admissions for ischaemic heart disease and/or heart failure and respiratory disease across the three lung function phenotypes (normal, PRISm and airflow limitation), regardless of the severity of PRISm or airflow limitation. The risk of these outcomes was also increased in individuals with PRISm/airflow limitation with or without metabolic syndrome relative to those with normal lung function and no metabolic syndrome. Notably, individuals with severe PRISm and metabolic syndrome had the highest hazard ratio (95% confidence interval) of 5.32 (3.76–7.54) for all-cause mortality. Furthermore, metabolic syndrome explained 13% and 27% of the influence of lung function impairment (PRISm or airflow limitation) on hospitalisation with ischaemic heart disease and/or heart failure and all-cause mortality, respectively.

These results clearly demonstrate that metabolic syndrome was associated with increased cardiopulmonary morbidity and mortality among individuals with lung function impairment in the Danish population. Interestingly, high-sensitivity C-reactive protein and fibrinogen explained a higher proportion of the influence of lung function impairment on all-cause mortality compared with metabolic syndrome, suggesting the contribution of multiple additional factors to the observed findings.

The study has several strengths and limitations, as discussed by the authors. There are, however, additionally important aspects to consider. Denmark is a high-income country with lower daily smoking rates and social inequalities compared with other European and developed countries,[7,8] limiting the generalisability of the findings. It is also noteworthy that there are two different waist circumference cutoffs to define central adiposity, and the authors used the criteria requiring higher waist circumference values, potentially including individuals with more advanced metabolic disease in their analyses. Whether using lower cutoffs could change the findings needs to be explored.

The findings of the current study have important public health and clinical implications because metabolic syndrome is preventable and treatable. Addressing metabolic syndrome, as a part of a wider multifactorial lifestyle intervention, can be potentially effective in reducing the burden of impaired lung function.[9]

DOI of original article: https://doi.org/10.1016/j.lanepe.2023.100759
*Corresponding author. Institute of Metabolism and Systems Research (IMSR), University of Birmingham, Edgbaston, Birmingham B15 2TT, UK.
*E-mail address:* a.a.tahrani@bham.ac.uk (A.A. Tahrani).

The current analysis does not provide details about the contribution of the individual components of metabolic syndrome to the observed associations with adverse outcomes to guide policy and treatment strategies. However, it is likely that addressing these individual components will have favourable impacts on cardiovascular disease and mortality in people with impaired lung function. Currently, there are a variety of pharmacological and non-pharmacological interventions for hypertension, hyperglycaemia, dyslipidaemia and obesity that have been shown to reduce the risk of cardiovascular disease and mortality.[10]

There is a need for studies to assess the current findings in other populations with wider demographic, socioeconomic and geographic representation. There is also a need for studies to explore the mechanistic links between metabolic syndrome and adverse outcomes in people with impaired lung function and evaluate the impact of metabolic syndrome treatment on the cardiopulmonary burden in this population. This can help develop risk-stratified strategies for effective multidisciplinary management and improved patient outcomes in this complex setting.

#### Contributors

Writing – original draft: RS. Writing – review & editing: RS and AAT. Both authors approved the final version submitted to the journal.

#### Declaration of interests

RS declares no conflict of interest.

AAT is currently an employee of and has shares in Novo Nordisk. The views expressed in this manuscript are those of the author and not Novo Nordisk. Novo Nordisk had no role in this manuscript.

#### References


1 Wijnant SRA, De Roos E, Kavousi M, et al. Trajectory and mortality of preserved ratio impaired spirometry: the Rotterdam Study. *Eur Respir J*. 2020;55. https://doi.org/10.1183/13993003.01217-2019.

2 Duong M, Islam S, Rangarajan S, et al. Mortality and cardiovascular and respiratory morbidity in individuals with impaired FEV1 (PURE): an international, community-based cohort study. *Lancet Glob Health*. 2019;7:e613–e623.

3 Noubiap JJ, Nansseu JR, Lontchi-Yimagou E, et al. Geographic distribution of metabolic syndrome and its components in the general adult population: a meta-analysis of global data from 28 million individuals. *Diabetes Res Clin Pract*. 2022;188:109924.

4 Mottillo S, Filion KB, Genest J, et al. The metabolic syndrome and cardiovascular risk: a systematic review and meta-analysis. *J Am Coll Cardiol*. 2010;56:1113–1132.

5 Marott JL, Ingebrigtsen TS, Çolak Y, et al. Impact of the metabolic syndrome on cardiopulmonary morbidity and mortality in individuals with lung function impairment: a prospective cohort study of the Danish general population. *Lancet Reg Heal Eur*. 2023. https://doi.org/10.1016/j.lanepe.2023.100759.

6 Leone N, Courbon D, Thomas F, et al. Lung function impairment and metabolic syndrome: the critical role of abdominal obesity. *Am J Respir Crit Care Med*. 2009;179:509–516.

7 Eurostat. Tobacco consumption statistics. https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Tobacco_consumption_statistics; 2023.

8 Organisation for Economic Co-operation and Development. *Does Inequality Matter?*. 2021. https://doi.org/10.1787/3023ed40-en.

9 Mahadzir MDA, Quek KF, Ramadas A. Group-based lifestyle intervention strategies for metabolic syndrome: a scoping review and strategic framework for future research. *Medicina (B Aires)*. 2021;57:1169.

10 Joseph JJ, Deedwania P, Acharya T, et al. Comprehensive management of cardiovascular risk factors for adults with type 2 diabetes: a scientific statement from the American Heart Association. *Circulation*. 2022;145:e722–e759.