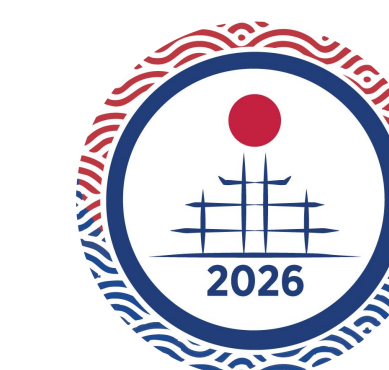




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INTRODUCTION

- Preserved-ratio impaired spirometry (PRISm) and restrictive spirometric pattern (RSP) represent distinct phenotypes within the preserved-ratio category.
- However, definitions based solely on FEV1 or FVC may result in phenotypic overlap and misclassification.
- Although previous studies have reported different mortality profiles, the differential associations of PRISm and RSP with lung cancer (LC) risk remain unclear.
- This study aimed to compare the associations of PRISm and RSP with LC incidence.

METHODS

- Participants from the UK Biobank underwent standardized baseline spirometry. Percent-predicted FEV1 and FVC were calculated using the GLI 2012 reference equations.
- Participants were classified into six spirometric patterns: normal spirometry, PRISm only, RSP only, PRISm+RSP, mild COPD, and moderate-to-severe COPD based on FEV1/FVC, FEV1, and FVC thresholds.
- Associations between spirometric patterns and LC risk were evaluated using multivariable Cox proportional hazards models. Smoking-stratified analyses and multiplicative interaction tests were performed to assess effect modification.

CONCLUSIONS

- PRISm and RSP represent distinct spirometric phenotypes with divergent lung cancer risk profiles: PRISm is significantly associated with an increased risk of lung cancer, whereas RSP shows no such association.
- Distinguishing these phenotypes in clinical spirometry may improve lung cancer risk stratification and inform early detection strategies.

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RESULTS

- Among 306,443 included participants (mean age 55.9 years; 46.0% men), spirometry pattern prevalence was: normal (73.4%), RSP only (1.0%), PRISm only (3.1%), PRISm + RSP (7.4%), mild COPD (7.3%), and moderate-to-severe COPD (7.9%) (Figure B).
- During a median follow-up period of 13.7 years, 2,474 lung cancer cases were documented.
- Compared with normal spirometry, PRISm only was significantly associated with increased LC risk (HR 1.54; 95% CI, 1.23–1.94). In contrast, RSP only showed no significant association with incident lung cancer (HR 0.94; 95% CI, 0.52–1.70; $P=0.832$) (Figure C).
- Among ever smokers, PRISm only was significantly associated with incident LC: former smokers (HR=1.78, 95% CI, 1.30–2.45) and current smokers (HR=1.71, 95% CI, 1.22–2.40), with no association in never smokers (Figure C).
- A significant multiplicative interaction between PRISm only and ever smoking was observed ($P=0.034$). In contrast, RSP only demonstrated no association with LC across any smoking stratum.

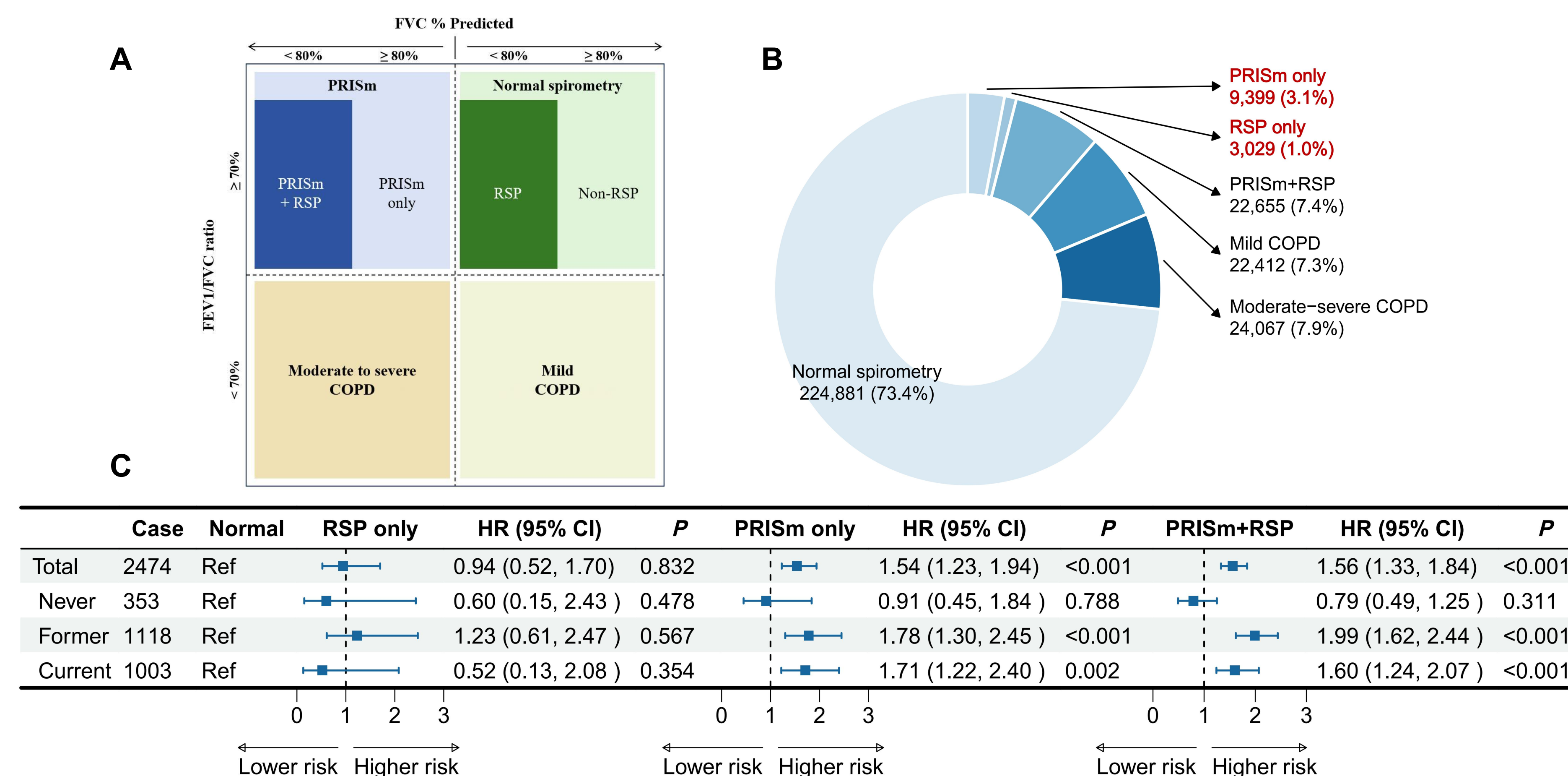


Figure A. Classification of spirometric patterns; **Figure B.** Distribution of spirometric patterns; **Figure C.** Associations with lung cancer by smoking status. The overall model was adjusted for age, sex, BMI, smoking status, Townsend deprivation index, and family history of lung cancer; smoking-stratified models were adjusted for the same covariates except smoking status.