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## BACKGROUND AND AIM

Activity-related breathlessness is twice as prevalent among women as men in the general population and is associated with adverse health outcomes. The cause of the gender difference is unknown and not related to level of lung function impairment measured as forced expiratory volume in 1 second (FEV<sub>1</sub>) or forced vital capacity (FVC) in percent of predicted.

We aimed to test the hypothesis that the higher activity-related breathlessness in women is explained by their smaller mean absolute lung volume (FEV<sub>1</sub>).

## METHODS

This was a cross-sectional analysis of the population-based multicenter third European Community Respiratory Health Survey (ECRHS III). The analysis included people in the random population sample with data on activity-related breathlessness measured using the Modified Medical Research Council (mMRC) scale. Exclusion criterion was disability to walk for other reason than cardiopulmonary disease.

Associations with mMRC were analyzed using multivariate ordered logistic regression clustering on center. The variance in mMRC scores explained by gender was measured using McKelvey & Zavoina's R<sup>2</sup>.

The model was adjusted for age, BMI, chronic bronchitis, chronic airflow limitation (CAL, defined as FEV<sub>1</sub>/FVC < lower limit of normality using the GLI 2012 reference data), pack-years smoking, exercise, ischemic heart disease (IHD), and a history of depression.

## RESULTS

We included 3,250 people (51% women) aged 38 to 67 years across 12 countries (Europe and Australia).

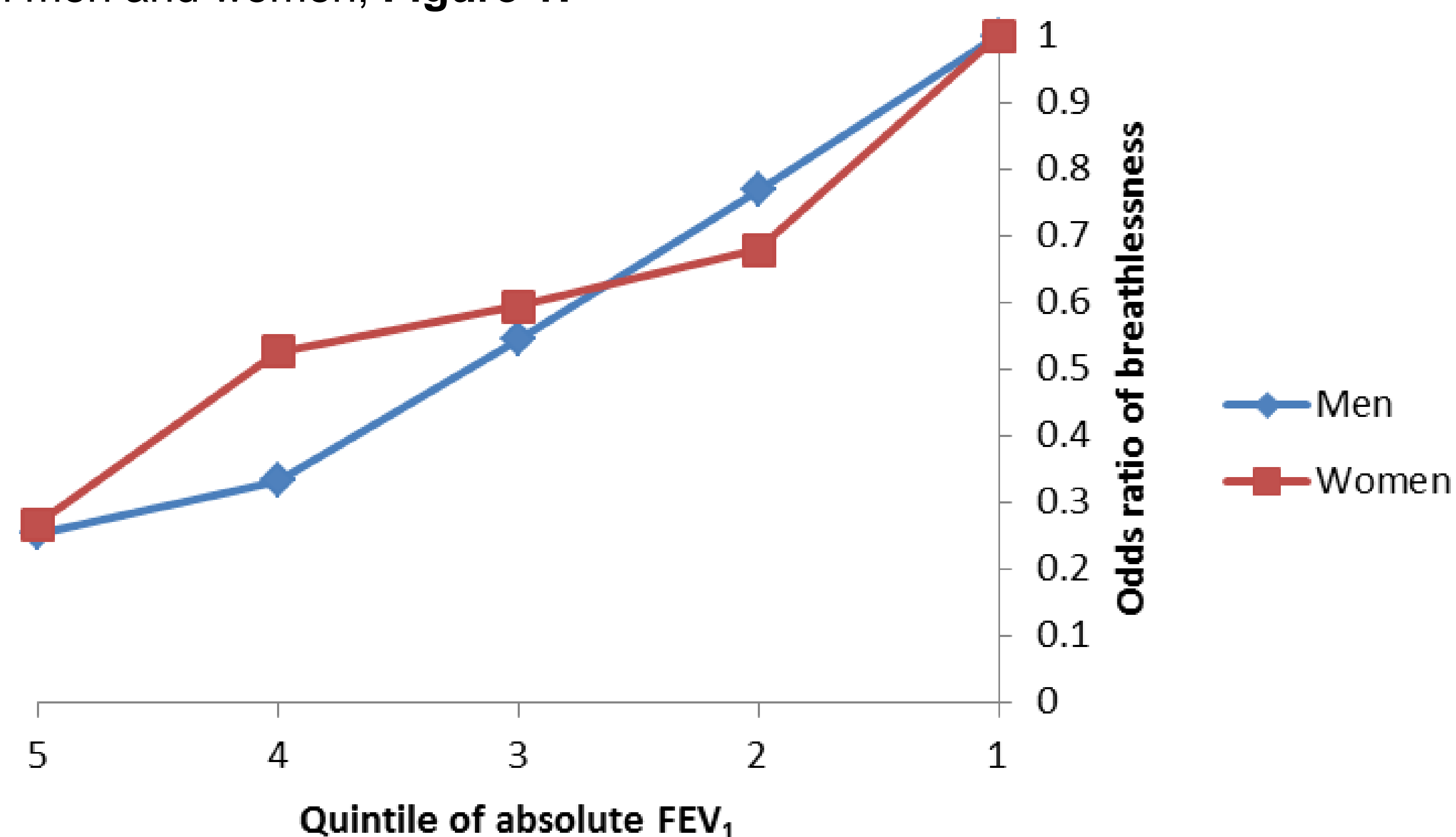
Compared with men, women had lower absolute FEV<sub>1</sub> (2.7±0.5 vs. 3.7±0.7 l) and similar FEV<sub>1</sub>%pred (100±14 vs 99±15 %).

Characteristics of the population sample is shown in **Table 1**:

Characteristic	Women N = 1,673 (51%)	Men N = 1,577 (49%)	All N = 3,250
Age	53.7 ± 7.0	54.2 ± 7.0	54.0 ± 7.0
mMRC breathlessness score			
0	1,226 (73)	1,349 (86)	2,575 (79)
1	343 (21)	203 (13)	546 (17)
2	95 (6)	22 (1)	117 (4)
3-4	9 (1)	3 (0)	12 (0)
FEV <sub>1</sub> , L	2.67 ± 0.46	3.68 ± 0.66	3.16 ± 0.76
FEV <sub>1</sub> , % of predicted	98.8 ± 13.8	98.5 ± 14.5	98.7 ± 14.1
FVC, L	3.39 ± 0.56	4.74 ± 0.80	4.04 ± 0.96
FVC, % of predicted	99.6 ± 12.9	99.2 ± 13.5	99.4 ± 13.2
FEV <sub>1</sub> /FVC	0.79 ± 0.06	0.78 ± 0.06	0.78 ± 0.06
Body mass index (kg/m <sup>2</sup> )	26.3 ± 5.0	27.2 ± 4.1	26.7 ± 4.6
Pack-years smoking, median (IQR)	1.3 (0 to 19.2)	7.0 (0 to 30.5)	3.9 (0 to 24.3)
Exercise (hours per week)			
≥ 2	688 (41)	763 (48)	1,451 (45)
0.5 to 1	437 (26)	366 (23)	803 (25)
None	548 (33)	448 (28)	996 (31)
CAL (FEV <sub>1</sub> /FVC < LLN)	73 (4)	87 (6)	160 (5)

## RESULTS continued

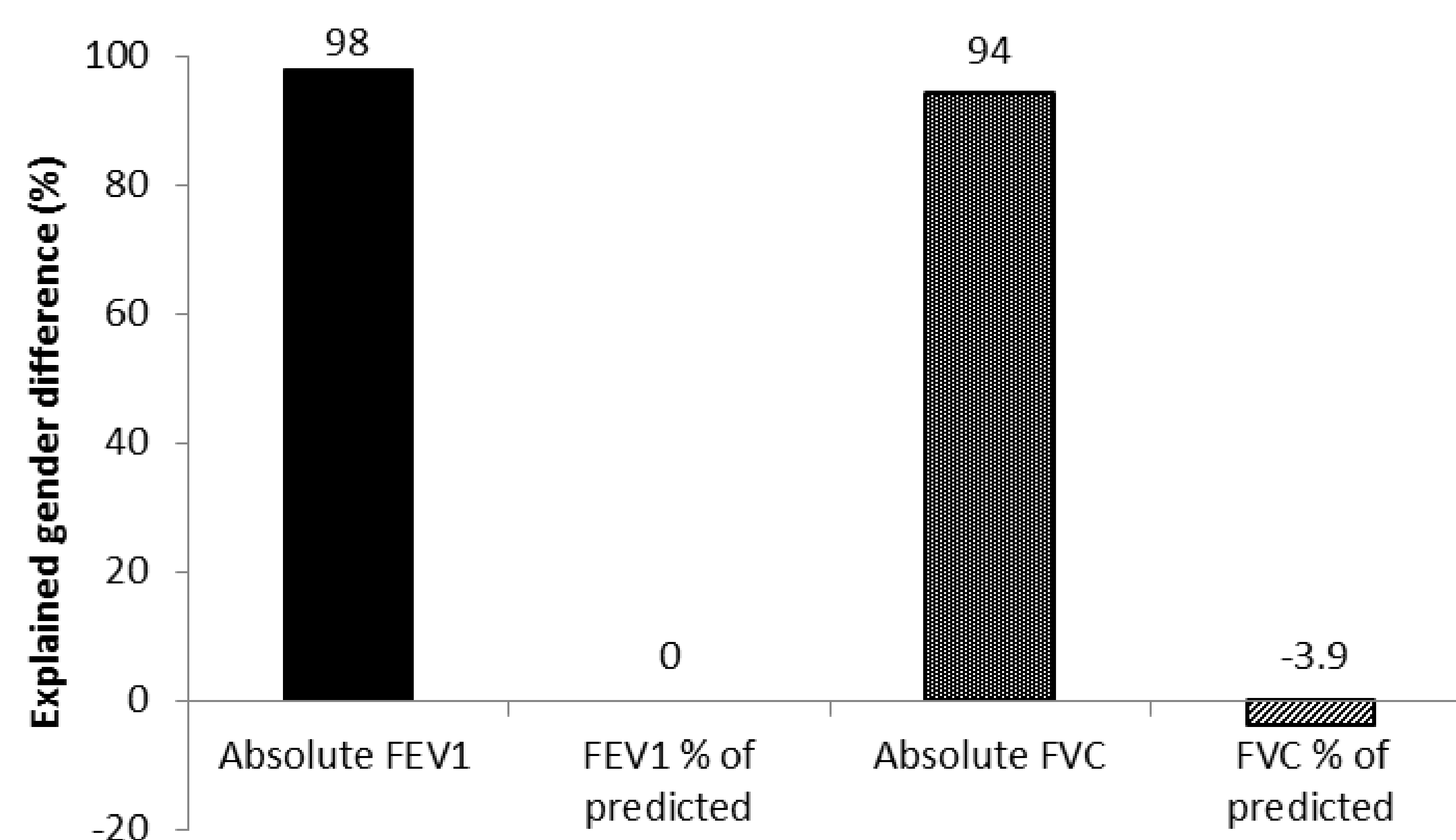
Lower absolute FEV<sub>1</sub> was associated with increased adjusted breathlessness in both men and women; **Figure 1**:



Activity-related breathlessness (mMRC ≥ 1) was twice as common in women (27%) as in men (14%).

The increased breathlessness in women compared with men, odds ratio (OR) 2.21 (95% CI, 1.79 to 2.72) was not reduced when controlling for FEV<sub>1</sub> % of predicted (OR 2.33) but **disappeared when controlling for absolute FEV<sub>1</sub>, OR 0.89 (95% CI, 0.69 to 1.14)**.

Absolute FEV<sub>1</sub> explained 98–100% of the gender difference controlling for potential confounders (Figure 2). Findings were similar when using FVC instead of FEV<sub>1</sub> and in healthy never-smokers.



**Figure 2.** Percent of the gender difference in activity-related breathlessness explained by FEV<sub>1</sub> and FVC

## CONCLUSION

The markedly higher activity-related breathlessness among women in the general population was largely explained by smaller absolute lung volumes (FEV<sub>1</sub> or FVC).

Matching on FEV<sub>1</sub>%predicted puts women at an disadvantage in relation to breathlessness. This gender bias is removed by accounting for absolute lung volume.

**Conflicts of interest:** None.