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Relationship between FEV1 reduction and respiratory symptoms in the general population

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ABSTRACT: Obstructive airways diseases typically present with dyspnoea, cough and wheeze, and are defined by a reduced forced expiratory volume in one second (FEV1)/forced vital capacity (FVC) ratio. Traditionally, however, the severity of chronic obstructive pulmonary disease is graded by the FEV1 % predicted rather than the FEV1/FVC ratio, whilst other potentially valid measures of FEV1 impairment, such as the absolute difference of FEV1 from predicted or the absolute level of FEV1, tend not to be used. The authors have therefore explored the relationship between these different measures of FEV1 impairment and chronic respiratory symptoms in a general population sample.

FEV1 and FVC were measured and questionnaire data were obtained on cough, wheeze, shortness of breath and general self-reported breathing trouble in a cross-sectional survey of 2,633 adults aged 18–70 yrs from a district of Nottingham, UK. Odds ratios for each symptom were calculated for declining levels of absolute FEV1, FEV1 % pred, absolute difference of FEV1 from predicted, and FEV1/FVC ratio. They were plotted to display the shape and strength of these relationships before and after adjustment for each other measure.

The odds of symptoms increased with declining levels of all FEV1 measures, particularly for wheeze and general breathing trouble. Although this study was not sufficiently powerful to detect significant differences between measures, these relationships were consistently strongest, before and after adjustment, for FEV1 % pred, particularly below a threshold of ~75%.

The authors conclude that forced expiratory volume in one second % predicted appears to be the measure of airflow impairment most closely associated with chronic respiratory symptoms in the general population.

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The common diseases of airflow obstruction, chronic obstructive pulmonary disease (COPD), and asthma, are major worldwide causes of morbidity and mortality [1–7]. However, although the obstructive airways diseases are defined in terms of a reduced ratio of forced expiratory volume in one second (FEV1) to forced vital capacity (FVC), this lung function measure is not generally used to grade the severity of these diseases. For COPD in particular, most published clinical guidelines have elected to define disease severity in terms of the FEV1 as a percentage of the predicted value (% pred) [8–11], but the use of this measure to define severity, although theoretically justifiable, has never been validated. Indeed, since both variation and longitudinal change in FEV1 are absolute rather than relative functions [12–15], there are *a priori* grounds to believe that the absolute difference in FEV1 from predicted, or even the unadjusted absolute FEV1 value, may be more valid determinants of disease severity than either FEV1/FVC ratio or FEV1 % pred. However, the relationship between these indices and the occurrence of symptoms has never been clearly defined.

Therefore, in this study, the shape and strength of the relationships between the above four measures of FEV1 reduction and common respiratory symptoms were investigated in a cross-sectional survey of a random sample of adults, in an exploratory analysis intended to determine whether any one or more measures has an obviously stronger relationship with the presence of symptoms of airflow obstruction and cough. The authors also looked for evidence of a threshold of increased risk of symptoms that might be of value in defining disease severity and screening for individuals at high risk of developing respiratory symptoms in the future.

Methods

Data were obtained from a previously reported study of the relationship between diet and lung function in a community population sample carried out in 1991 [16]. Briefly, 7,106

Table 1. – Prevalence (%) of reported respiratory symptoms

Symptom question	Prevalence
Have you had an attack of shortness of breath that came on following strenuous activity at any time during the last 12 months?	25.7
Do you ever have trouble with breathing?	19.5
Have you had wheeze or whistling in your chest at any time in the last 12 months?	24.0
Do you usually cough during the day, or at night, during the winter, and do you usually cough like this for as much as 3 months of the year?	9.3

Table 2. – Number of individuals in each measurement category

Absolute FEV1 L	N	Absolute difference from predicted L	n	% pred	n	FEV1/FVC %	n
>4.50	204	>0	1368	>100.0	1371	>85	842
>4.25	138	>-0.2	464	>95.0	355	>80	691
>4.00	152	>-0.4	312	>90.0	313	>75	566
>3.75	187	>-0.6	186	>85.0	176	>70	293
>3.50	215	>-0.8	119	>80.0	137	>65	112
>3.25	281	>-1.0	65	>75.0	87	>59	68
>3.00	296	>-1.4	56	>70.0	60	⩽59	61
>2.75	269	⩽-1.4	63	>54.5	71		
>2.50	259			⩽54.5	63		
>2.25	225						
>2.00	155						
>1.75	125						
>1.40	67						
⩽1.40	60						

FEV1: forced expiratory volume in one second; % pred: % predicted; FVC: forced vital capacity.

adults aged ⩾18 yrs were selected by systematic sampling from a random starting point in the electoral register for a population of ~87,000 living in a local authority area of Nottingham, UK. Subjects were invited to attend a local surgery or health centre where, as part of a more extensive protocol [16], they completed a questionnaire on current respiratory symptoms and smoking history, and had FEV1 and FVC measured in the sitting position using a dry bellows spirometer (Vitalograph, Buckingham, UK), recording the highest of three maximal expiratory manoeuvres. The respiratory questionnaire elicited symptoms including cough for ⩾3 months of the year, shortness of breath following strenuous activity in

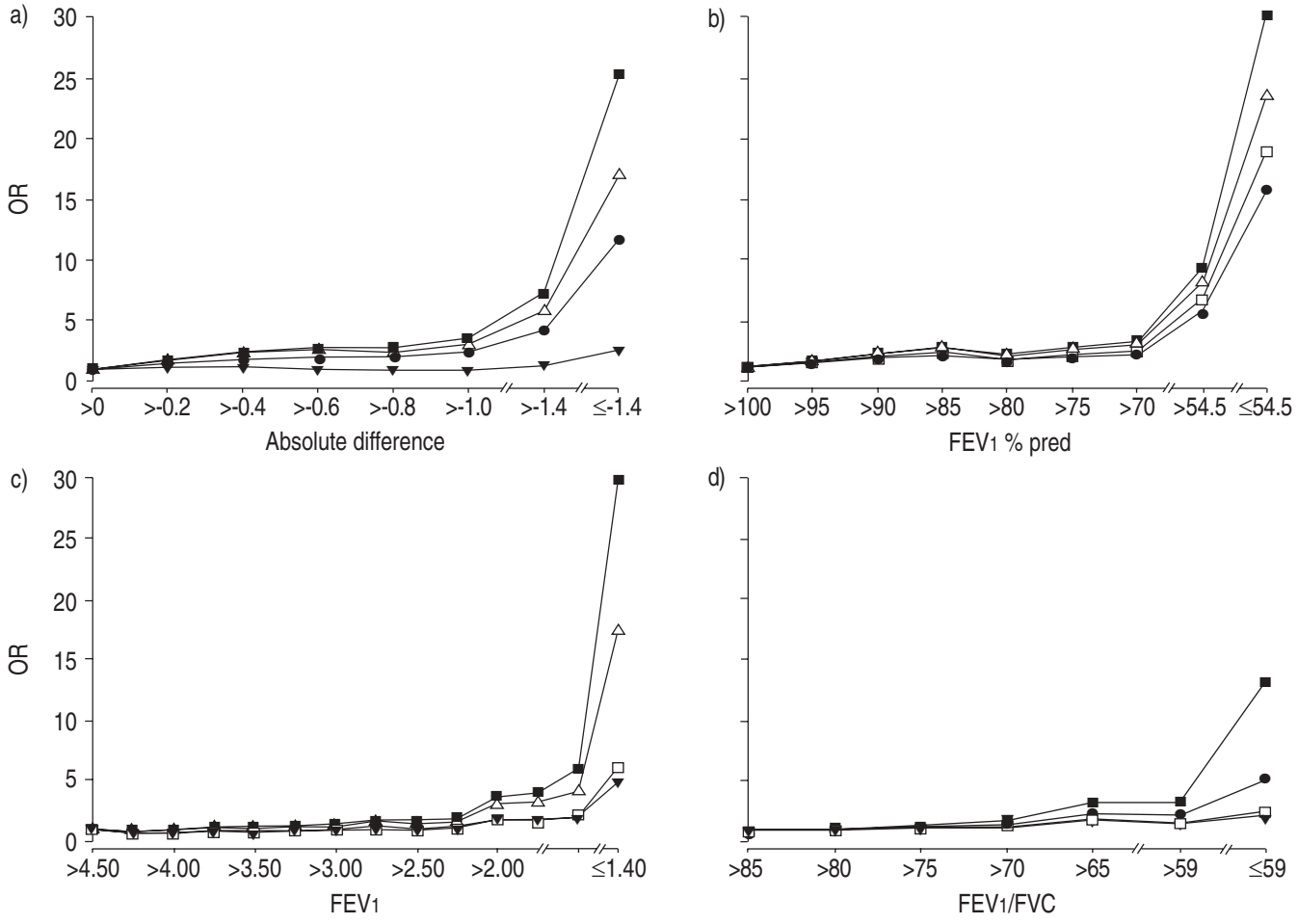

Fig. 1. – Odds ratios (ORs) of answering "yes" to the question: "Do you ever have trouble with your breathing?" ■: unadjusted; ●: adjusted forced expiratory volume in one second (FEV1); △: adjusted FEV1/forced vital capacity (FVC); ▼: adjusted % predicted (% pred); □: adjusted absolute difference.

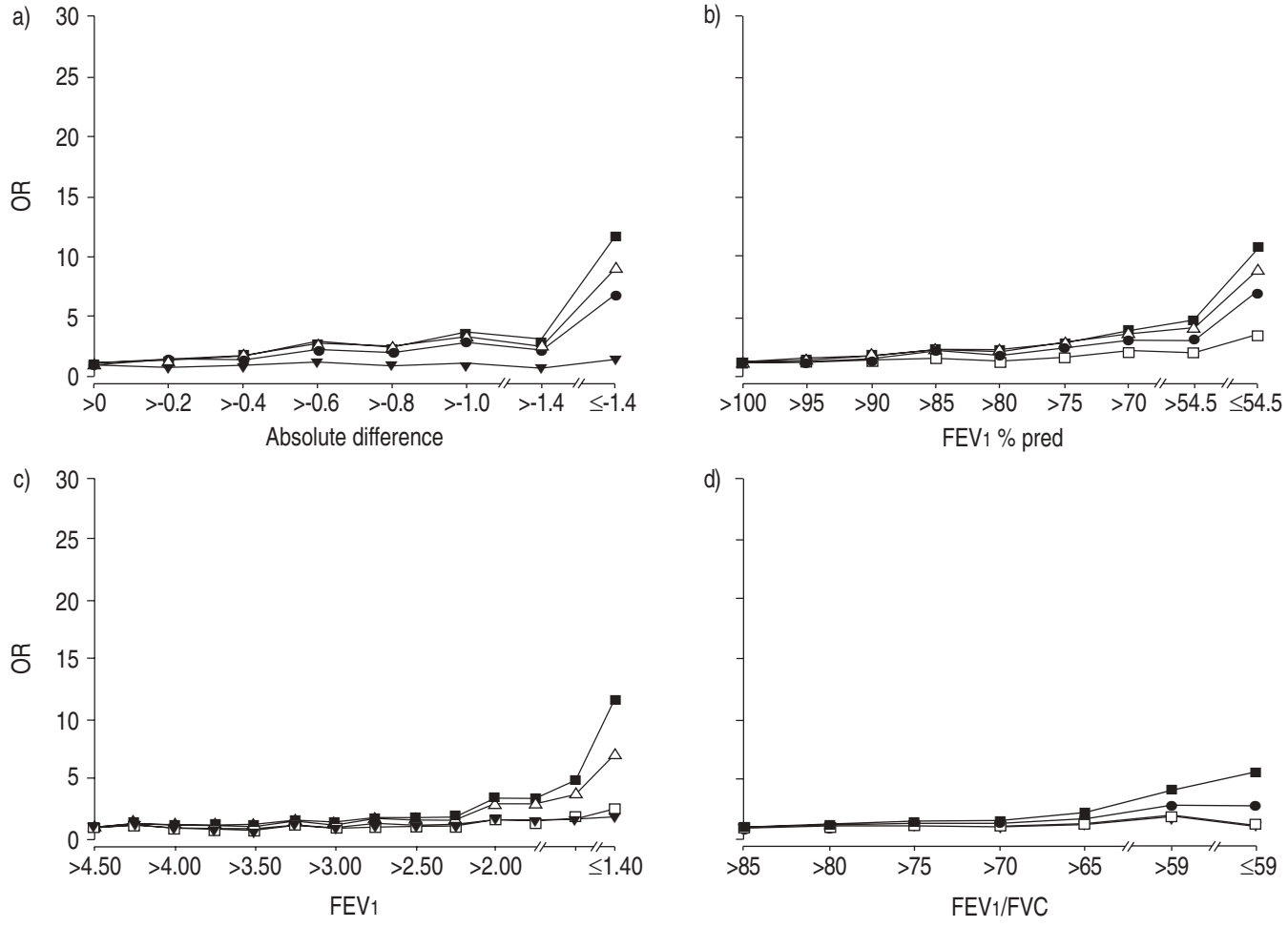

Fig. 2. – Odds ratios (ORs) of answering "yes" to the question: "Have you had shortness of breath following strenuous activity in the last year?" ■: unadjusted; ●: adjusted forced expiratory volume in one second (FEV_1); △: adjusted FEV_1/forced vital capacity (FVC); ▼: adjusted % predicted (% pred); □: adjusted absolute difference.

the past year, wheezing or whistling in the chest in the past year, and "ever had trouble with my breathing" (table 1). The study was approved by the Nottingham City Hospital and Nottingham University Ethics Committees.

Standard predicted FEV_1 values [17] were used to derive the FEV_1 % pred and the absolute difference between observed and predicted FEV_1 for each individual, to use in addition to the observed absolute FEV_1 and the FEV_1/FVC ratio, as measures of FEV_1 abnormality in the present study. To determine the relative odds of experiencing symptoms in relation to decreasing levels of these measures, the range of each FEV_1 measure was initially divided into equal arithmetic categories, defining the reference groups arbitrarily as values above 4.5 L for absolute FEV_1, greater than predicted for % pred and absolute difference from predicted FEV_1, and above 85% for the FEV_1/FVC ratio. To ensure that odds ratios (ORs) for the lowest categories were not biased by inclusion of different proportions of the population, the lowest lung function category boundaries were manipulated to ensure that the lowest category of each measure included a similar number of individuals.

The ORs for each symptom in each lung function category relative to the reference range were estimated by logistic regression, at first, analysing each lung function measure alone and then with adjustment for each of the other measures. Plots of these ORs across the range of lung function measures were then prepared and assessed visually to identify the measure or measures most strongly related to symptoms in univariate and multivariate analyses, and to look for evidence of a threshold level below which symptoms tend to become more common.

Results

A total of 2,633 individuals, estimated to represent 48–59% of those sampled from the electoral register and potentially eligible for participation [16], took part in the study. Full demographical details on the participants have been published previously [16]. In summary, they comprised 50% females, 50% never-smokers, 28% exsmokers and 23% current smokers, and had a mean age of 40 yrs, range 18–70 yrs. Mean±SD FEV_1 was 3.2±0.92 L and ranged 0.55–6.45 L. The proportion of participants reporting positive responses to the respiratory symptom questions are shown in table 1. The arithmetic categories of the four measures of FEV_1 and the numbers of individuals in each category are shown in table 2. The numbers in the higher range categories vary considerably but the lowest categories all contain 60–63 individuals.

The relative odds of reporting each symptom in relation to each measure of FEV_1 before and after adjustment for other measures are plotted in figures 1–4. In general, the unadjusted odds of reporting symptoms increased as lung function decreased for all FEV_1 measures, although to a lesser extent for cough, and particularly below a level of between 2.0–2.5 L for absolute

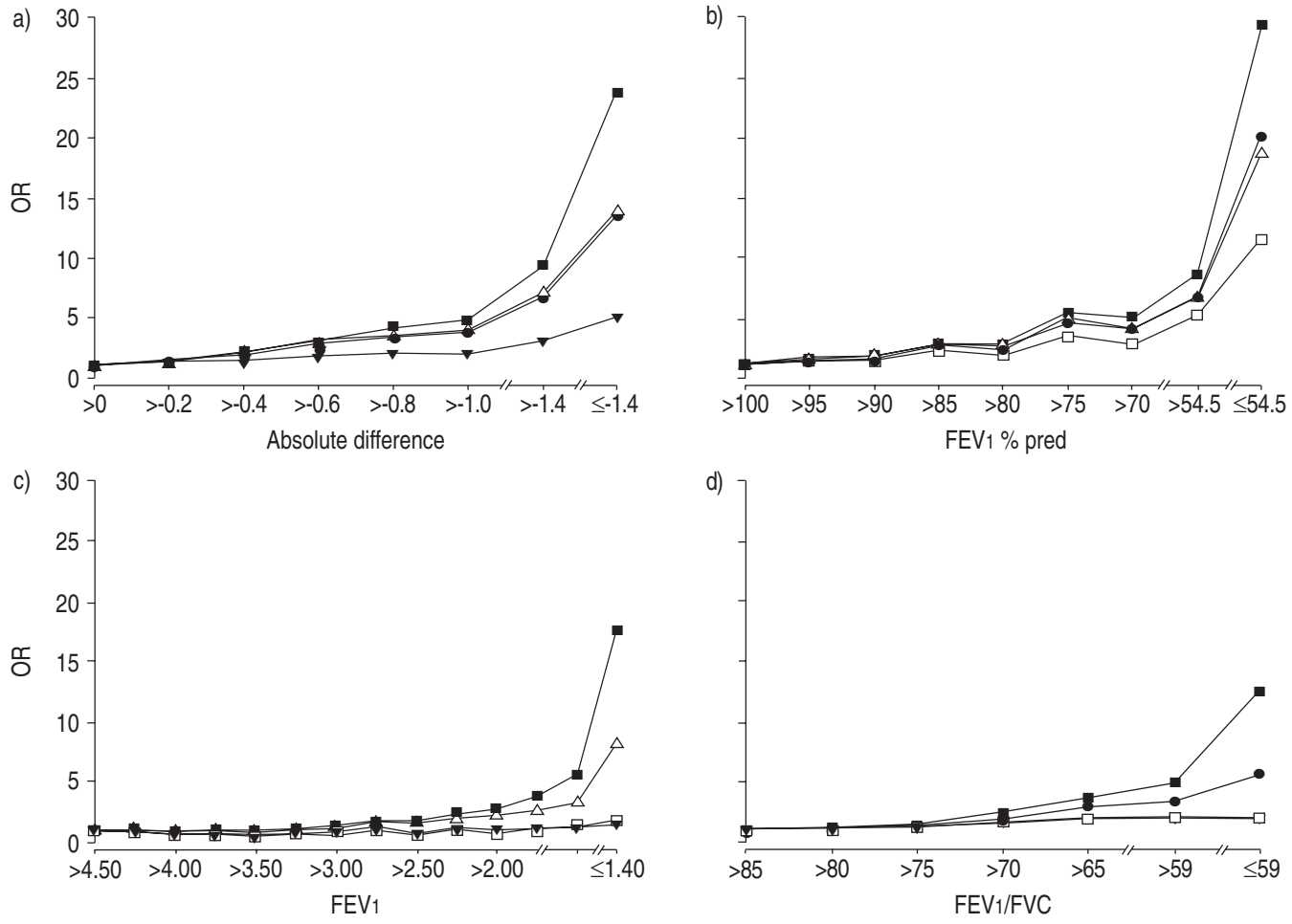

Fig. 3. – Odds ratios (ORs) of answering "yes" to the question: "Have you had wheezing or whistling in your chest at any time in the last 12 months?" ■: unadjusted; ●: adjusted forced expiratory volume in one second (FEV1); △: adjusted FEV1/forced vital capacity (FVC); ▼: adjusted % predicted (% pred); □: adjusted absolute difference.

FEV1, 0.8–1.2 L for absolute difference from predicted, 80–75% for % pred, and 65–59% for FEV1/FVC ratio. Although there was no statistically significant difference between the different measures in this respect, the lowest category of FEV1% pred was consistently associated with the highest odds of symptoms and FEV1/FVC with the lowest. For example, the OR for wheeze in the lowest category of FEV1% pred was 29.3 (95% confidence interval (CI) 14.7–58.5), for absolute difference from predicted 23.5 (12.4–55.0), for absolute FEV1 7.7 (8.7–35.9), and for the FEV1/FVC ratio 12.5 (6.7–22.6, fig. 3). Similar trends were observed for "ever having had trouble with breathing" and for "shortness of breath following strenuous activity" (figs 1 and 2). However, the ORs for having a cough each day for $\geqslant$3 months of the year in the lowest compared with the highest lung function categories were weaker, being 8.5 (4.9–15.0) for FEV1 % pred, 8.5 (4.8–15.0) for the absolute difference of FEV1 from predicted, 12.1 (5.3–27.4) for absolute level of FEV1, and 6.3 (3.3–11.7) for the FEV1/FVC ratio (fig. 4).

When each measurement was adjusted for any of the other three measures, the resultant ORs for each measure generally decreased, particularly after adjustment for the absolute difference of FEV1 from predicted and for the FEV1 % pred. However, the adjusted relative odds for respiratory symptoms remained consistently higher for the FEV1 % pred measure, and the threshold below which symptoms became markedly more frequent remained similar at ~75% of predicted.

Discussion

This study has shown that of four simple available measures of FEV1 impairment, the ORs for the typical symptoms of COPD and asthma tended to be higher in the general population in association with extreme values of the FEV1 % pred, than with other measures. This study also demonstrates that the risk of symptoms increases relatively modestly with declining lung function across the majority of the range of all of the measures studied, but then increases more substantially at lower levels. For FEV1 % pred, this threshold of increased symptom risk was at ~75%.

This study was an exploratory analysis of data from an existing survey intended to look at the shape and strengths of the relationships between different lung function measures and symptoms, and was not intended or indeed suitably powered to carry out formal statistical comparisons between measures. In addition, the study was not designed to compare relationships between symptoms and lung function in individuals with different clinical diagnoses. However, inspection of the curves plotted for each symptom provides a fairly consistent theme in that relative order shows the relationship tendency to be strongest for FEV1 % pred, followed by absolute difference of FEV1 from predicted, absolute FEV1, and FEV1/FVC ratio. This in turn implies that symptoms arise in any individual in relation to a relative loss of FEV1, rather than to the absolute FEV1 *per se*. This finding was

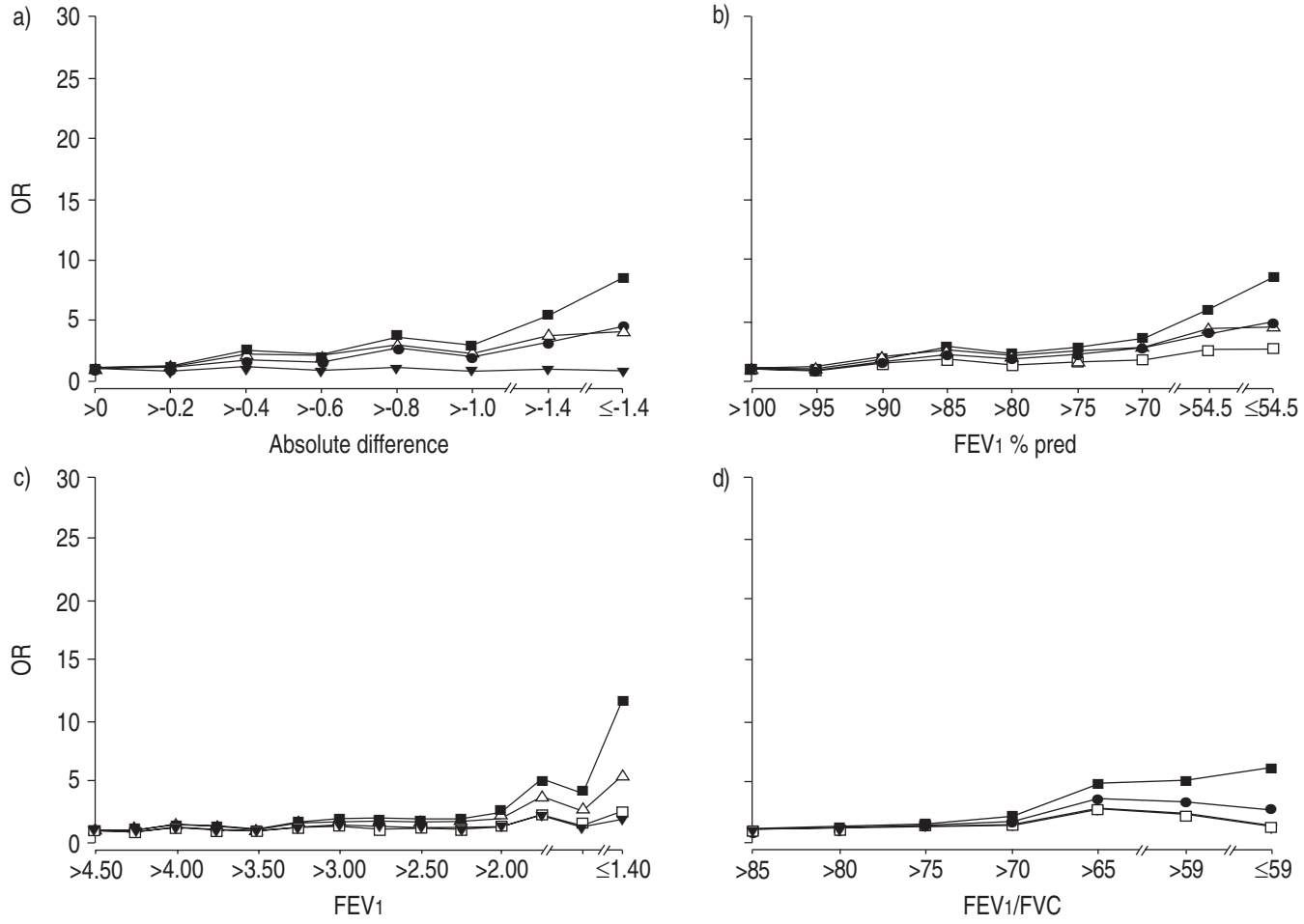

Fig. 4. – Odds ratios (ORs) of reporting a cough for ⩾3 months of the year. ■: unadjusted; ●: adjusted forced expiratory volume in one second (FEV1); △: adjusted FEV1/forced vital capacity (FVC); ▼: adjusted % predicted (% pred); □: adjusted absolute difference.

unexpected in view of the fact that obstructive airways diseases are defined in terms of a reduced FEV1/FVC ratio, and also in the light of what is known of the distribution of errors in FEV1 measurement and the pattern of longitudinal decline in FEV1 with age. Studies of the repeatability of FEV1 demonstrate that errors in FEV1 measurement are unrelated to the magnitude of the FEV1 [14, 15], whilst longitudinal data indicate that decline in FEV1 occurs at a fixed rate of $mL \cdot yr^{-1}$ [12, 13], rather than as a proportion of the FEV1 level. These observations suggest that the absolute difference of reduction in FEV1 relative to the predicted value, or simply the absolute FEV1, might have initially been expected to be more valid measures of the risk of symptoms than a relative measure such as FEV1% pred.

The relative strengths of the relationships observed differed between symptoms, being much less strong for cough. This may reflect the fact that cough and airflow obstruction are manifestations of two different pathological processes, cough arising from mucosal inflammation and mucus hypersecretion and airflow obstruction from emphysematous change [18–22], and that although these processes frequently coexist in the lungs of smokers, cough and sputum production are not necessarily associated with airflow obstruction [12, 23]. Others have reported that chronic cough [24] and breathlessness [25, 26] are associated with a low level of FEV1, while TAGER *et al.* [27] and KRZYZANOWSKI *et al.* [28] found that symptoms including cough, wheeze, chest illness and breathlessness were related to an increased decline of FEV1 over time. However, no previous study has, to the authors′ knowledge, attempted to compare the relative relationships of these symptoms with different measures of lung function impairment.

These findings are of particular potential importance for standardising the classification of COPD severity and for the use of lung function measures to screen individuals at high risk of developing chronic respiratory symptoms. Current guidelines are consistent in using FEV1 % pred to measure severity but differ in the thresholds they use to grade severity [8–10]. Although the relationship between symptoms and functional impairment is likely to vary substantially between and within individuals over time (particularly as a result of temporal adaptation), these findings support the continued use of FEV1 % pred as the marker of severity that best indicates both functional and symptomatic impairment, and suggest 75% as the threshold value that best identifies individuals at increased risk of symptoms. For the purposes of screening high-risk individuals it would also appear from the data that the 75–80% level is one at which interventions to reduce further loss of FEV1 are likely to be particularly valuable.

The present data arise from a population studied for other purposes, according to a protocol that involved a relatively extensive protocol of dietary and other assessments. As a consequence, the participation rate was not as high as might have been achieved with a simpler protocol that could have been administered in the participant′s home, but it seems unlikely that the relative strengths of the relationships described could have been markedly biased by selective response. It is likely that this sample, by virtue of the protocol

requirement to attend a local health centre, systematically excludes those with extreme low lung function values and those who are infirm for other reasons. Again, however, this should not affect the qualitative comparison of the relationships between symptoms and lung function. In methodological terms, an alternative approach to categorising the range of lung function values would have been to use deciles or other equal frequency categories rather than the arithmetic categories chosen here. The latter was adopted to give clearer and more disparate intervals on the lung function scale, but analysis using equal frequency categories did not, in practice, influence the shapes of the curves at the lower range of each measure. The categorisation made no difference to the multivariate analysis since the adjustment was made using the original individual rather than categorised observations. The range of lung function measures available for analysis was also inevitably restricted to those collected at the time of the study, so we are unable to comment on relationships with other potentially informative measures, such as ventilatory capacity or gas transfer.

Therefore, although these findings need to be explored independently in different populations, this study suggests that at least in relation to symptoms, FEV1 % pred is more closely related to the occurrence of chronic respiratory symptoms in the general population than other measures of lung function impairment.

The validity of this observation now needs to be tested in other data sets to look at validity within clinically diagnosed asthma and chronic obstructive pulmonary disease, and also in relation to other disease markers and outcomes, such as mortality and natural history, to provide a more complete picture of the relationship between lung function and disease severity. For the present, however, this study provides support for the current convention of using forced expiratory volume in one second per cent predicted to grade severity and to guide management in chronic obstructive pulmonary disease.

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