

# COPD Assessment Test (CAT) Score is Associated With Risk of Future Exacerbation: An Analysis From the IMPACT Trial

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## Introduction

- The COPD Assessment Test (CAT) is a validated, disease-specific, patient-completed questionnaire that is simple and quick to complete, comprised of eight items (cough, phlegm, chest tightness, breathlessness when going uphill or upstairs, any activity limitation at home, confidence leaving home, sleep and energy), each of which is scored 0–5 (total: 0–40).<sup>1</sup> Higher CAT scores indicate increased disease burden and poorer health status.<sup>2</sup>
- The CAT score is used in the Global initiative for chronic Obstructive Lung Disease (GOLD) strategy document to inform initiation of COPD therapy.<sup>3</sup> There is a paucity of data evaluating the association between CAT scores and risk of exacerbations.
- In the InforMing the PATHway of COPD Treatment (IMPACT) trial, single-inhaler triple therapy with fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) resulted in a significantly lower rate of moderate/severe exacerbations than dual therapy with FF/VI or UMEC/VI.<sup>4</sup> This analysis was undertaken to assess the relationship between health status as indicated by CAT score and the risk of exacerbations in patients participating in the IMPACT trial.

## Methods

- IMPACT (GSK study CTT116855; NCT02164513) was a Phase III, 52-week, double-blind, multicenter trial in which patients ≥40 years of age with symptomatic COPD (CAT score ≥10) and ≥1 moderate/severe exacerbations in the previous 12 months were randomized 2:2:1 to receive FF/UMEC/VI 100/62.5/25 mcg, FF/VI 100/25 mcg, or UMEC/VI 62.5/25 mcg.<sup>4</sup>
- The primary endpoint was the annual rate of on-treatment moderate/severe exacerbations with FF/UMEC/VI versus FF/VI and UMEC/VI.<sup>4</sup> Other endpoints included the annual rate of on-treatment moderate exacerbations and on-treatment severe exacerbations.

- In the current analysis the rate of moderate/severe exacerbations, moderate exacerbations (post hoc), and severe exacerbations (post hoc) with FF/UMEC/VI versus FF/VI and UMEC/VI were evaluated in patients with a baseline CAT score (defined as CAT score at Day 1) <20 and ≥20. As all patients in IMPACT were symptomatic (inclusion criterion: CAT score ≥10), this CAT threshold was chosen to represent lower and higher symptom levels. Among the 10,355 patients in the IMPACT intent-to-treat (ITT) population, the mean (standard deviation [SD]) CAT score was 20.1 (6.1).<sup>5</sup>

- Moderate exacerbations were defined as requiring treatment with antibiotics and/or oral/systemic corticosteroids. Severe exacerbations were defined as resulting in hospitalization or death.

- Exacerbation rates and percentage reductions in exacerbation rates (based on pairwise treatment rate ratios) with 95% confidence intervals (CI) were estimated for the ITT population using a generalized linear model assuming a negative binomial distribution and the following covariates: treatment group, sex, exacerbation history (≤1 and ≥2 moderate/severe), smoking status, geographic region, and post bronchodilator % predicted forced expiratory volume in 1 second (FEV<sub>1</sub>).

## Results

### Patients

- Of the 10,355 patients in the IMPACT ITT population, 10,157 patients had baseline CAT score data available and were included in this analysis; 41% had a CAT score ≥20 (indicating poorer health-related quality of life [HRQL]) and 59% had a CAT score <20 at baseline.
- The baseline demographics and disease characteristics of patients with a CAT score ≥20 were similar across the treatment groups, as were those of patients with a CAT score <20 (Table 1).
  - Patients with a CAT score ≥20 were slightly younger, had worse lung function, and more were current smokers than patients with a CAT score <20.

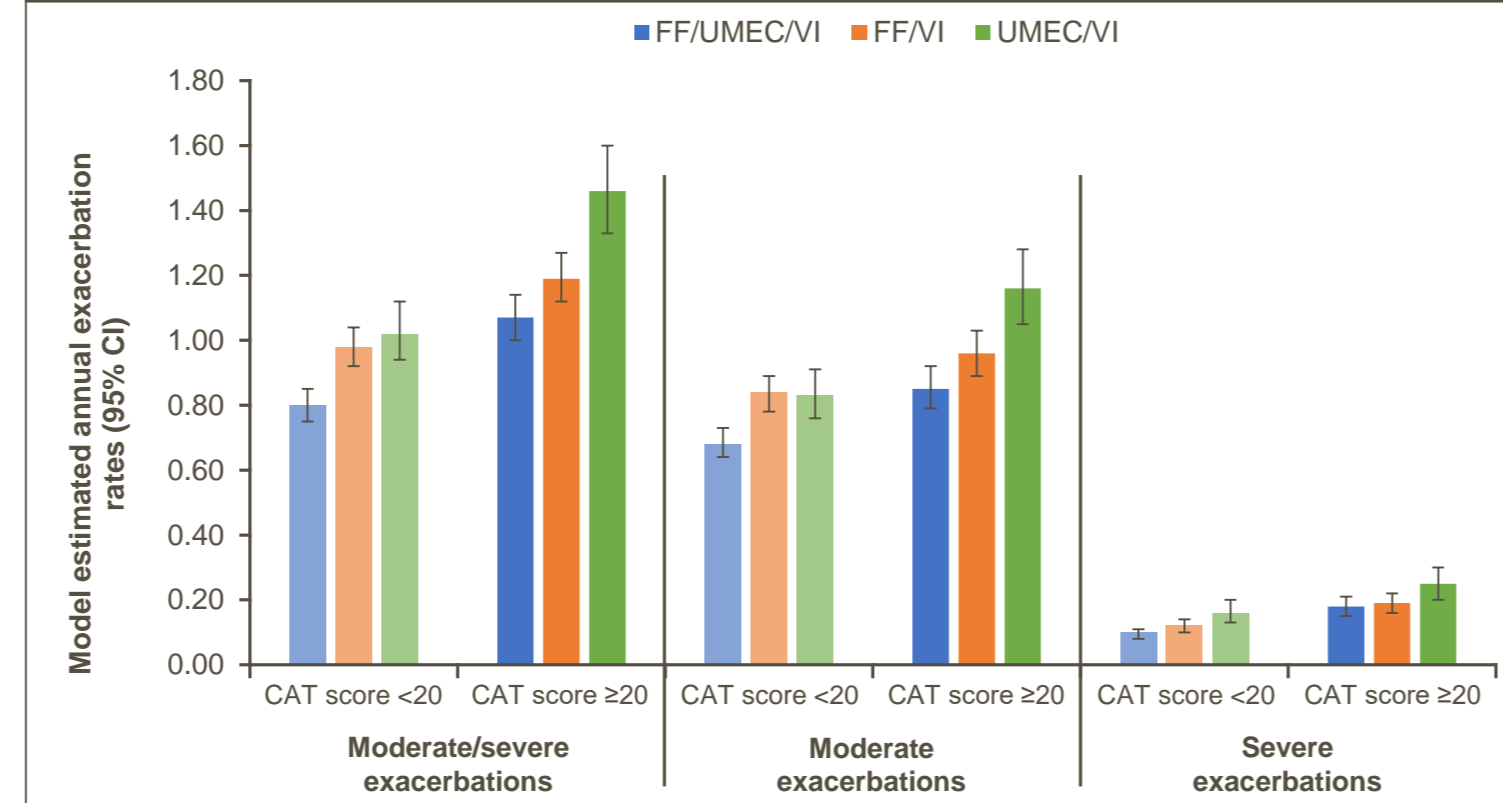
**Table 1. Baseline demographics and disease characteristics by CAT score subgroups (ITT population)**

	CAT score <20			CAT score ≥20		
	FF/UMEC/VI (N=2429)	FF/VI (N=2327)	UMEC/VI (N=1196)	FF/UMEC/VI (N=1647)	FF/VI (N=1720)	UMEC/VI (N=838)
Age, mean (SD) years	66.2 (8.1)	66.0 (8.1)	66.1 (8.2)	64.0 (8.3)	64.4 (8.5)	64.1 (8.2)
Male, %	69	70	68	64	63	62
BMI (kg/m <sup>2</sup> ), mean (SD)	26.3 (5.6)	26.4 (5.7)	26.2 (5.5)	27.1 (6.9)	27.0 (6.5)	27.1 (6.3)
Smoking status, %						
Current	30	30	30	41	40	42
Former	70	70	70	59	60	58
COPD exacerbation history, n (%)						
Moderate						
0	434 (18)	417 (18)	197 (16)	314 (19)	356 (21)	172 (21)
1	810 (33)	792 (34)	399 (33)	579 (35)	603 (35)	290 (35)
≥2	1185 (49)	1118 (48)	600 (50)	754 (46)	761 (44)	376 (45)
Severe						
0	1815 (75)	1768 (76)	913 (76)	1203 (73)	1234 (72)	619 (74)
1	549 (23)	485 (21)	250 (21)	369 (22)	416 (24)	179 (21)
≥2	65 (3)	74 (3)	33 (3)	75 (5)	70 (4)	40 (5)
Moderate/severe						
0	0 (0)	5 (<1)	1 (<1)	2 (<1)	0 (0)	1 (<1)
1	1070 (44)	1045 (45)	523 (44)	749 (45)	823 (48)	389 (46)
≥2	1359 (56)	1277 (55)	672 (56)	896 (54)	897 (52)	448 (53)
Post-bronchodilator FEV <sub>1</sub> % predicted, mean (SD)	47.2 (14.9)	47.3 (14.7)	47.0 (14.6)	43.5 (14.9)	42.9 (14.5)	43.3 (14.6)

### COPD exacerbation rates

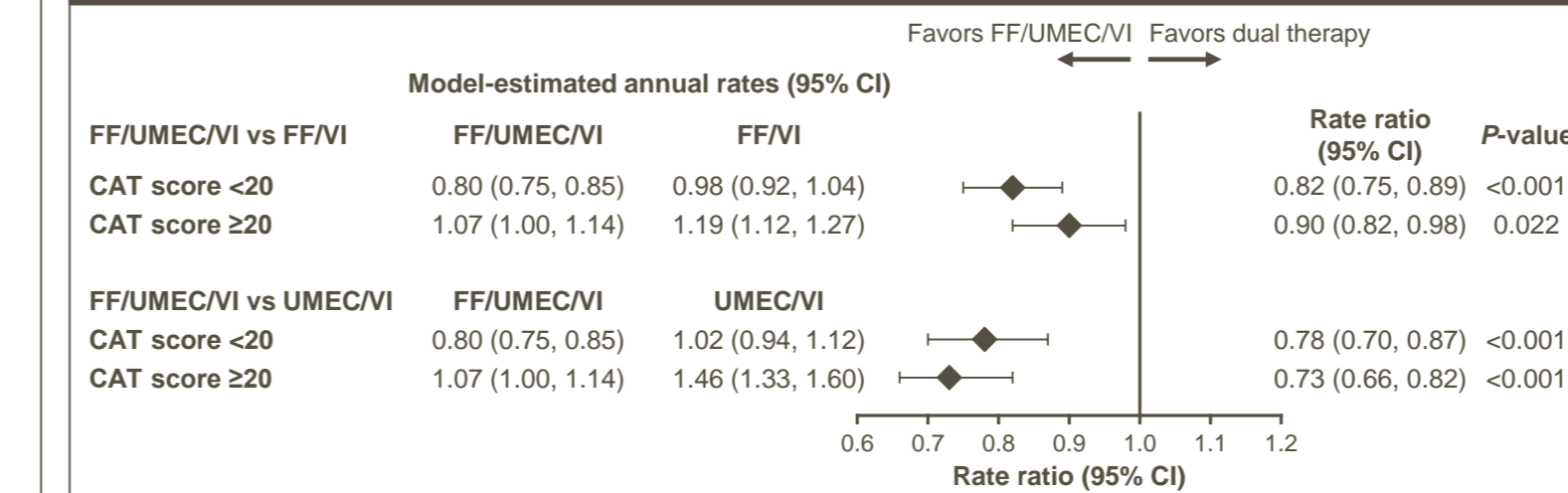
- The annual rates of on-treatment moderate/severe, moderate and severe exacerbations were higher in patients with a CAT score ≥20 than in patients with a CAT score <20 in all treatment groups (Figure 1).
  - In the FF/UMEC/VI group the annual rate of moderate/severe exacerbations was 0.80 (95% CI: 0.75, 0.85) in patients with CAT score <20 and 1.07 (95% CI: 1.00, 1.14) in patients with CAT score ≥20. A similar pattern was observed in the two dual therapy groups.

**Figure 1: Annual rates of on-treatment exacerbations by CAT score subgroup**

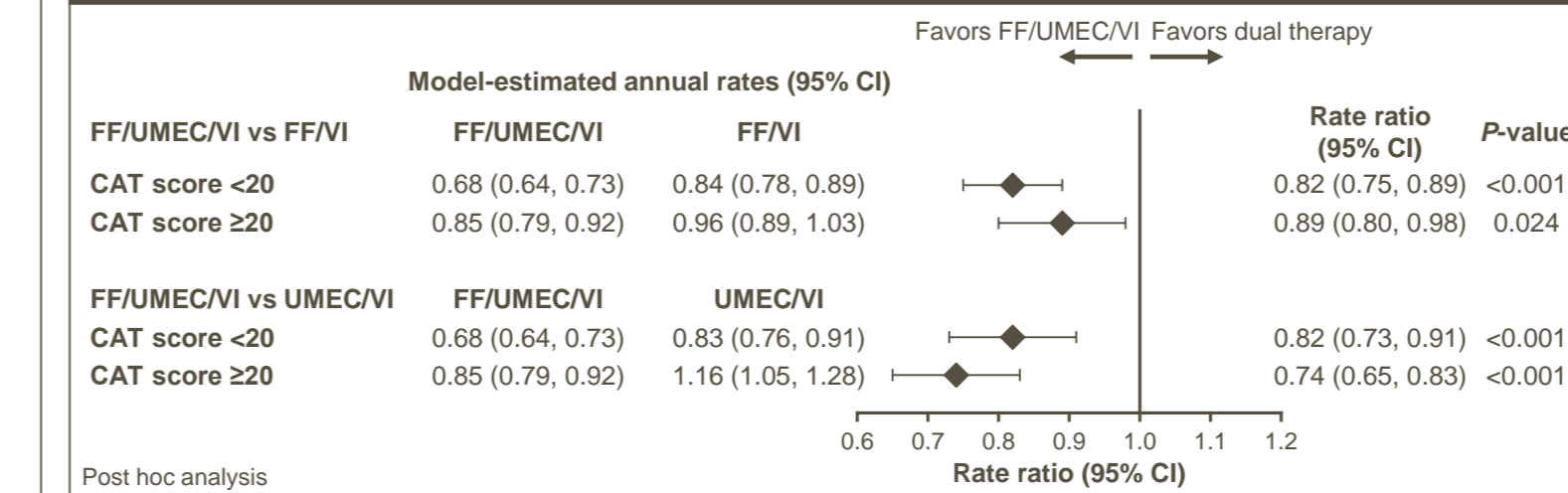


- FF/UMEC/VI significantly reduced annual rates of moderate/severe exacerbations versus FF/VI and UMEC/VI in all patients, regardless of baseline CAT score (Figure 2).
  - FF/UMEC/VI reduced the annual rates of moderate/severe exacerbations versus FF/VI by 18% (95% CI: 11, 25;  $P < 0.001$ ) in patients with CAT score <20 and 10% (95% CI: 2, 18;  $P = 0.022$ ) in patients with CAT score ≥20.
  - FF/UMEC/VI reduced the annual rates of moderate/severe exacerbations versus UMEC/VI by 22% (95% CI: 13, 30;  $P < 0.001$ ) in patients with CAT score <20 and 27% (95% CI: 18, 34;  $P < 0.001$ ) in patients with CAT score ≥20.
- FF/UMEC/VI significantly reduced annual rates of moderate and severe exacerbations versus UMEC/VI, regardless of baseline CAT score (Figure 3 and 4). FF/UMEC/VI significantly reduced annual moderate exacerbation rates versus FF/VI (Figure 3); point estimates for the reduction in annual rates of severe exacerbations were in favor of FF/UMEC/VI over FF/VI but were not significant (Figure 4).

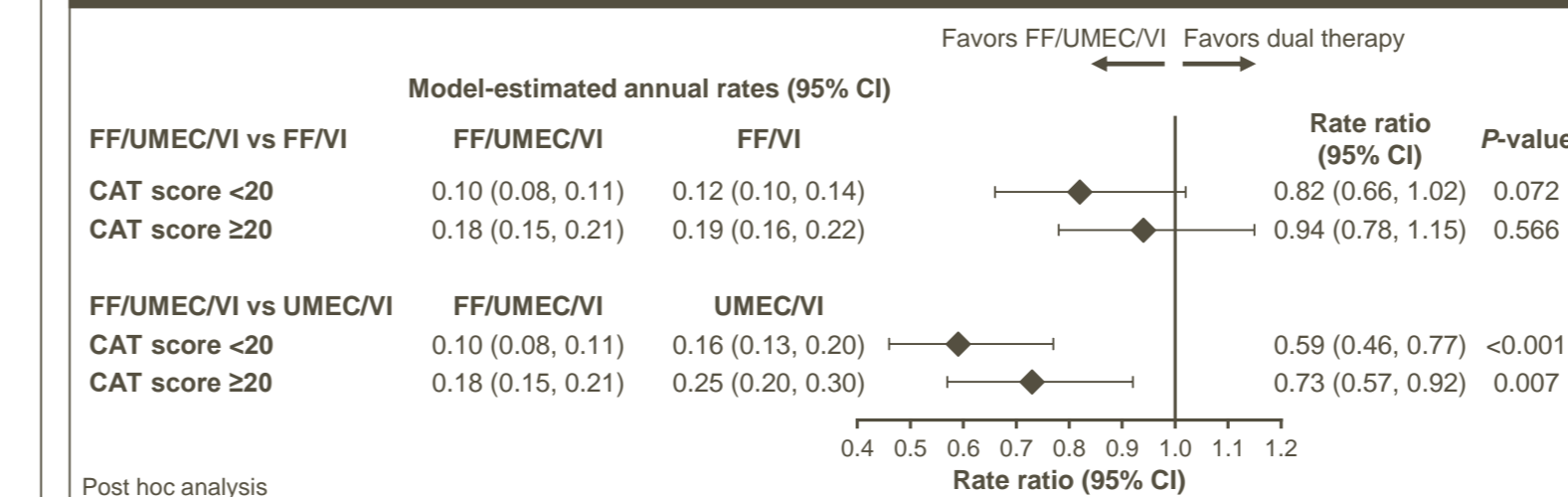
**Figure 2. Annual rates of on-treatment moderate/severe exacerbations by CAT score subgroups**



**Figure 3. Annual rates of on-treatment moderate exacerbations by CAT score subgroups**



**Figure 4. Annual rates of on-treatment severe exacerbations by CAT score subgroups**



## Safety

- No relevant difference in the number of patients experiencing adverse events of special interest (AESIs) was observed based on baseline CAT score across all treatment arms (Table 2).

**Table 2: Incidence of on-treatment AESIs by CAT score subgroups**

AESI, n (%)	FF/UMEC/VI		FF/VI		UMEC/VI	
	CAT score <20 (n=2429)	CAT score ≥20 (n=1647)	CAT score <20 (n=2327)	CAT score ≥20 (n=1720)	CAT score <20 (n=1196)	CAT score ≥20 (n=838)
Anticholinergic syndrome (SMQ)	100 (4)	76 (5)	78 (3)	57 (3)	37 (3)	33 (4)
Asthma/bronchospasm (SMQ)	8 (<1)	19 (1)	21 (<1)	13 (<1)	13 (1)	3 (<1)
CV effects	246 (10)	198 (12)	222 (10)	200 (12)	114 (10)	109 (13)
LRTI excluding pneumonia	104 (4)	95 (6)	106 (5)	90 (5)	59 (5)	48 (6)
Pneumonia	175 (7)	138 (8)	170 (7)	120 (7)	55 (5)	40 (5)
Urinary retention	4 (<1)	4 (<1)	7 (<1)	5 (<1)	6 (<1)	3 (<1)

AESI (AEs which have specified areas of interest for FF, UMEC or VI or for patients with COPD); CV, cardiovascular; LRTI, lower respiratory tract infection; MedDRA, Medical Dictionary for Regulatory Activities; SMQ, Standardized MedDRA Query.

## Conclusions

- Patients with worse health status (CAT score ≥20) at baseline experienced higher rate of exacerbations in the IMPACT trial.
- FF/UMEC/VI reduced exacerbation rates versus FF/VI and UMEC/VI in both CAT score subgroups as described in the results, consistent with the overall ITT population. There were no safety differences observed between the CAT score subgroups.
- These results underscore the importance of the relationship between health status and exacerbation risk.<sup>5</sup> The CAT offers a practical way to assess health status in clinical settings.

## References

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