

The EXACT-PRO Initiative: Development and Validation of a Single Patient-Reported Outcome Measure for Evaluating Exacerbations of Chronic Obstructive Pulmonary Disease

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Objective: To develop and validate a patient-reported outcome (PRO) instrument for measuring frequency, severity, and duration of COPD exacerbations in international trials.

Methods: Multi-sponsor initiative involving experts and the FDA. **Phase I:** Instrument development informed by literature and qualitative data from focus groups and interviews with U.S. COPD patients. International experts addressed concept relevance, transferability, translation ease. **Phase II:** Prospective, 2-group, observational study of patients with 1) confirmed exacerbation (PDA diary Days 1–28 and 60–67) or 2) stable COPD (PDA for 7 days). Item analyses and Rasch IRT were used to reduce the items from 23 to 14. Validity testing included known-group differences and relationship to clinical history, SGRQ-C, and clinician and patient assessment of exacerbation severity.

Results: **Phase I:** N= 83; 45% male; 16% African American; 13% Hispanic; mean age = 65 (± 10); stable FEV-1 = 44% pred (± 16). **Phase II:** N=410 (222 acute; 188 stable); 48% male; mean age = 65 (± 10); stable FEV-1 = 51% pred (± 20). Factor analyses supported a unidimensional structure suitable for Rasch analysis. Overall chi-square=149.3 df=84; person-separation index=0.92. Three respiratory domains (breathlessness (5 items), cough-sputum (2 items), chest symptoms (3 items)) account for 68% of the variance; 4 items address systemic manifestations. Internal consistency (Day 1, N=410) total = 0.91; domains = 0.87; 0.69; 0.87. Reproducibility (ICC) in stable patients (n=171) Day 1 to 7 = 0.77; 0.71; 0.66; 0.64. Correlation with SGRQ-C Day 1 (N=395): r = 0.64; 0.66; 0.35; 0.46 ($p < 0.0001$). Significant differences in scores were found across exacerbation severity Day 1 ($p < 0.001$) and between responders and non-responders Days 1 to 10 ($p < 0.0001$).

Conclusions: The EXacerbations of Chronic Pulmonary Disease Tool (EXACT) is a 14-item diary for evaluating exacerbation outcomes of COPD with measurement properties demonstrated to be adequate for use in clinical trials with a similar population.

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