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**Title:** Characteristics of GOLD 2011 grading system in the COPDGene cohort

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**Body:** Background: The 2011 GOLD summary report outlines a new COPD grading system based on symptoms, exacerbation history and FEV1. Here we use the COPDGene patient cohort to better understand how well this grading system describes a large, general COPD cohort. Methods: All COPD subjects from the 10,000 subject COPDGene cohort were grouped per the GOLD 2011 grading system: "A" MMRC  $\leq 1$ , FEV1  $\geq 50\%$  and  $\leq 1$  exacerbation in the prior year; "B" MMRC  $\geq 2$ , FEV1  $\geq 50\%$  and  $\leq 1$  exacerbation; "C" MMRC  $\leq 1$ , FEV1  $< 50\%$  and  $\geq 2$  exacerbations; and "D" MMRC  $\geq 2$ , FEV1  $< 50\%$  and  $\geq 2$  exacerbations. Per guidelines, subjects not meeting these criteria were classified as C or D based on MMRC and the worse of FEV1 or exacerbation history categories. Results: Of 4,475 subjects, 33.8%, 20.9%, 8.3% and 41.0% were classified as GOLD A, B, C and D respectively. FEV1 was lowest (37.1%), BODE index highest (4.7), SGRQ highest (54.0) and walk distance lowest (960 ft) in grade D. Grade D subjects were most frequently on a recommended medication regimen (93.1%), followed by C (68.1%), B (61.0%) and A (24.2%). As grades C and D are defined by MMRC,  $\leq 1$  and  $\geq 2$  respectively, and either FEV1  $< 50$  or  $\geq 2$  exacerbations in the prior year, significant heterogeneity in disease severity range is seen: FEV1%, C (18-103) and D (9-103); exacerbations in prior year, C (0-6) and D (0-6); SGRQ C (0-83) and D (2-98); and emphysema C (0.1-52.3%) and D (0.02-61.2%). Conclusions: A relatively small proportion of subjects met criteria for grade C suggesting patients with low FEV1 and frequent exacerbations but mild dyspnea are less common. While subjects within grades C and D have similar dyspnea severity, they are quite dissimilar with respect to other markers of disease severity.