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Title: Correlates of dyspnea in the BOLD study

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Body: Background: To our knowledge, no study has assessed the worldwide variation in dyspnea prevalence or correlates of dyspnea. Aim: We used cross-sectional data from population-based samples in 15 countries of the BOLD study to estimate prevalence of dyspnea in the full sample and in an a priori defined low-risk group (few risk factors or dyspnea-associated diseases). Methods: Dyspnea was defined by the modified Medical Research Council questions. We used ordered logistic regression analysis to study the association of dyspnea with site, sex, age, education, smoking habits, low/high BMI, self-reported disease, and spirometry results. Results: Of the 9,484 participants, 27% reported any dyspnea. In the low-risk subsample (N=4,329), 16% reported any dyspnea. All covariates were significantly associated with changes in dyspnea. In particular the odds ratio for increased dyspnea (95% confidence interval) was 2.16 (1.94-2.42) for being female, 1.92 (1.71-2.15) for obesity, 2.26 (1.94-2.63) for heart disease and 2.94 (1.58-5.48) for having gone through lung surgery. When forced vital capacity (FVC) fell below 60% of predicted, the increase in dyspnea accelerated. Through all models the site variables remained significant, although a declining Wald chi-square test indicated that up to 53% of the site effects might be explained by the included covariates. Conclusions: Site differences in dyspnea prevalence persisted even after covariate adjustments. This might indicate cultural and language differences in the expression of symptoms. A curvilinear relation between FVC and dyspnea might suggest a threshold effect on dyspnea. Finally, dyspnea in low-risk subjects could be interpreted as an effect of physical deconditioning, rather than

disease.