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| BACKGROUND Chronic obstructive pulmonary disease (COPD) is thought to result from an |
| accelerated decline in forced expiratory volume in 1 second (FEV1) over time. Yet it is possible that |
| a normal decline in FEV1 could also lead to COPD in persons whose maximally attained FEV1 is |
| less than population norms. METHODS We stratified participants in three independent cohorts (the |

Framingham Offspring Cohort, the Copenhagen City Heart Study, and the Lovelace Smokers

Cohort) according to lung function (FEV1 ?80% or <80% of the predicted value) at cohort inception

Lung-function trajectories leading to chronic obstructive pulmonary disease

(mean age of patients, approximately 40 years) and the presence or absence of COPD at the last study visit. We then determined the rate of decline in FEV1 over time among the participants according to their FEV1 at cohort inception and COPD status at study end. RESULTS Among 657 persons who had an FEV1 of less than 80% of the predicted value before 40 years of age, 174 (26%) had COPD after 22 years of observation, whereas among 2207 persons who had a baseline FEV1 of at least 80% of the predicted value before 40 years of age, 158 (7%) had COPD after 22 years of observation (P<0.001). Approximately half the 332 persons with COPD at the end of the observation period had had a normal FEV1 before 40 years of age and had a rapid decline in FEV1 thereafter, with a mean (±SD) decline of 53±21 ml per year. The remaining half had had a low FEV1 in early adulthood and a subsequent mean decline in FEV1 of 27±18 ml per year (P<0.001), despite similar smoking exposure. CONCLUSIONS Our study suggests that low FEV1 in early adulthood is important in the genesis of COPD and that accelerated decline in FEV1 is not an obligate feature of COPD. Copyright © 2015 Massachusetts Medical Society.