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ABSTRACT

Background We aimed to disentangle genetic and environmental causes in lung cancer while considering smoking status.

Methods Four Nordic twin cohorts (43 512 monozygotic (MZ) and 71 895 same sex dizygotic (DZ) twin individuals) had smoking data before cancer diagnosis. We used time-to-event analyses accounting for censoring and competing risk of death to estimate incidence, concordance risk and heritability of liability to develop lung cancer by smoking status.

Results During a median of 28.5 years of follow-up, we recorded 1508 incident lung cancers. Of the 30 MZ and 28 DZ pairs concordant for lung cancer, nearly all were current smokers at baseline and only one concordant pair was seen among never smokers. Among ever smokers, the case-wise concordance of lung cancer, that is the risk before a certain age conditional on lung cancer in the co-twin before that age, was significantly increased compared with the

cumulative incidence for both MZ and DZ pairs. This ratio, the relative recurrence risk, significantly decreased by age for MZ but was constant for DZ pairs. Heritability of lung cancer was 0.41 (95% CI 0.26 to 0.56) for currently smoking and 0.37 (95% CI 0.25 to 0.49) for ever smoking pairs. Among smoking discordant pairs, the pairwise HR for lung cancer of the ever smoker twin compared to the never smoker co-twin was 5.4 (95% CI 2.1 to 14.0) in MZ pairs and 5.0 (95% CI 3.2 to 7.9) in DZ pairs.

Conclusions The contribution of familial effects appears to decrease by age. The discordant pair analysis confirms that smoking causes lung cancer.