



Prenatal and prepubertal exposures to tobacco smoke in men may cause lower lung function in future offspring: a three-generation study using a causal modelling approach

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Fathers' prepuberty and paternal grandmothers' pregnancy are vulnerable periods to the adverse effects of smoking on offspring's lung function. Preventing smoking in these susceptibility time windows might improve the next generation's health. <https://bit.ly/3vvgjsN>

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Abstract

Mechanistic research suggests that lifestyle and environmental factors impact respiratory health across generations by epigenetic changes transmitted through male germ cells. Evidence from studies on humans is very limited.

We investigated multigeneration causal associations to estimate the causal effects of tobacco smoking on lung function within the paternal line. We analysed data from 383 adult offspring (age 18–47 years; 52.0% female) and their 274 fathers, who had participated in the European Community Respiratory Health Survey (ECRHS)/Respiratory Health in Northern Europe, Spain and Australia (RHINESSA) generation study and had provided valid measures of pre-bronchodilator lung function. Two counterfactual-based, multilevel mediation models were developed with: paternal grandmothers' smoking in pregnancy and fathers' smoking initiation in prepuberty as exposures; fathers' forced expiratory volume in 1 s (FEV₁) and forced vital capacity (FVC), or FEV₁/FVC z-scores as potential mediators (proxies of unobserved biological mechanisms that are true mediators); and offspring's FEV₁ and FVC, or FEV₁/FVC z-scores as outcomes. All effects were summarised as differences (Δ) in expected z-scores related to fathers' and grandmothers' smoking history.

Fathers' smoking initiation in prepuberty had a negative direct effect on both offspring's FEV₁ (Δz -score -0.36 , 95% CI -0.63 – -0.10) and FVC (-0.50 , 95% CI -0.80 – -0.20) compared with fathers' never smoking. Paternal grandmothers' smoking in pregnancy had a negative direct effect on fathers' FEV₁/FVC (-0.57 , 95% CI -1.09 – -0.05) and a negative indirect effect on offspring's FEV₁/FVC (-0.12 , 95% CI -0.21 – -0.03) compared with grandmothers' not smoking before fathers' birth nor during fathers' childhood.

Fathers' smoking in prepuberty and paternal grandmothers' smoking in pregnancy may cause lower lung function in offspring. Our results support the concept that lifestyle-related exposures during these susceptibility periods influence the health of future generations.