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| **Parental pre-pubertal passive smoke exposure is associated with Early-Onset Adult-Remitting asthma trajectory in offspring: a two-generational cohort study** |
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| **Introduction/Aim:**  Paternal pre-pubertal passive smoke exposure is associated with childhood asthma in offspring, potentially through germ line effects. However, the impact of such exposure in parents on the lifetime risk of asthma remained uncertain.  **Methods:**  We investigated 1,059 father-offspring and 1,492 mother-offspring pairs of the Tasmanian Longitudinal Health Study (TAHS). Parents self-reported their passive smoke exposure before age 15 years. Offspring’s asthma was assessed at ages 7, 13, 18, 30, 43, 50, and 53 years and life-course asthma trajectories were developed using group-based trajectory modelling. Multinomial logistic regressions were conducted to examine associations between paternal or maternal pre-pubertal passive smoke exposure and life-course asthma trajectories in their offspring separately. Potential mediating and interactive effects were evaluated for parental active smoking, offspring sex, their respiratory conditions during childhood and active smoking by midlife.  **Results:**  Paternal pre-pubertal passive smoke exposure was associated with their offspring’s Early-Onset Adult-Remitting asthma trajectory (adjusted multinomial odds ratio [aMOR]=2.50 [95%CI: 1.08-5.79]), but not Persistent asthma into mid-adult life trajectory. Maternal pre-pubertal passive smoke exposure also demonstrated an association with offspring’s Early-Onset Adult-Remitting asthma trajectory (aMOR=2.21 [0.97-5.03]), which was stronger in offspring who were additionally exposed to childhood passive smoke (aMOR=4.38 [1.02-18.76]; p-interaction=0.026). The observed associations were minimally (<11%) mediated through factors related to familial smoking history and other respiratory conditions during offspring childhood.  **Conclusion:**  Any parental pre-pubertal passive smoke exposure is likely to increase the risk of asthma in future generations. This risk is greater when offspring is additionally exposed to passive smoke during childhood. It is likely that the stronger paternal effect was at least partly mediated by germ line epigenetic changes in sperm atogenesis; the weaker maternal effect on offspring would have to be somatic and related likely to passive smoke effects in utero and infancy/childhood, because all gametes (eggs) are fully formed before birth.  **Grant Support:**  National Health and Medical Research Council; JL is supported by the China Scholarship Council - University of Melbourne PhD Scholarship and “Population Health Investing in Research Students’ Training”. |