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Title: Which children have the strongest longitudinal associations between early exposure to environmental tobacco smoke and age of asthma development?

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Body: Objective: We sought to understand the effects of risk factors such as atopy on the longitudinal association between early-life exposure to environmental tobacco smoke (ETS) and age of physician-diagnosed asthma (PDA) development in childhood. Methods: In the Toronto Child Health Evaluation Questionnaire, parents of 5619 grades 1-2 students reported age of PDA development, exposure to ETS during pregnancy and the first year of life, history and family history of atopy and demographic information. Using Cox proportional hazard models, we conducted stratified analyses by potential effect modifiers. Results: Household ETS exposure prevalence was 8.3% during pregnancy and 10.6% in the first year of life; 15.5% of children developed PDA, 31.2% had a history of atopy and 9.8% had a history of maternal asthma. Children exposed to ETS during pregnancy developed asthma sooner [adjusted hazard ratio (aHR) 1.27, 95% confidence interval (CI): 1.00-1.61]. Stronger associations were seen among children without a history of atopy (aHR 1.92, 95% CI: 1.42-2.61) and without maternal asthma (aHR 1.74, 95% CI: 1.34-2.25); these relationships persisted for ETS exposure in the first year of life (aHR 1.52, 95% CI: 1.12-2.07 and 1.39, 95% CI: 1.08-1.79, respectively). Conclusions: Longitudinal associations between ETS exposure during pregnancy or the first year of life and age of PDA development are stronger in children without a history of atopy and without maternal asthma. Greater understanding of these associations may guide hypotheses regarding possible mechanisms of association and suggest strategies for exposure reduction in higher-risk children.