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Title: Febrile and gynaecological infections in pregnancy increase the risk of childhood respiratory disorders in the offspring

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Body: Emerging evidence suggests that foetal and early life environmental factors are critical for determining the susceptibility to allergic and respiratory diseases. In the present study, we investigated whether maternal febrile infections (FI) or gynaecological infections (GI) during pregnancy are associated with allergic respiratory diseases in the offspring, and whether specific pregnancy trimesters are involved. We enrolled 4,577 children, aged 3-14yr. Their parents filled in a standardized questionnaire about children's respiratory health and the events occurred during pregnancy and at birth. We evaluated the incidence of wheezing, asthma and rhinitis, and the occurrence of five respiratory symptoms in the last 12 months. Children born to mothers who reported FI and GI had more respiratory symptoms in the last 12 months (IRR:1.40, 95%CI:1.12-1.74 and IRR:1.60, 95%CI:1.24-2.06, respectively). This association was stronger when FI occurred in the 1st trimester of pregnancy (IRR:2.12, 95%CI:1.37-3.28). The incidence of asthma was significantly higher in the children whose mothers reported FI or GI in the 1st trimester of pregnancy (HR:2.61, 95%CI:1.01-6.76 and HR:3.50, 95%CI:1.24-9.91, respectively). GI in the 3rd trimester were associated with higher risk of wheezing (HR:1.55, 95%CI:1.11-2.17) and rhinitis (HR:1.82; 95%CI:1.02-3.26). FI and GI might increase the risk of developing respiratory symptoms and diseases, especially when occurring in specific trimesters of pregnancy. These findings suggest that FI and GI might interfere with foetal programming of respiratory and immune system through different mechanisms.