

# Early-life antibiotic exposure increases the risk of asthma, allergic rhinitis and eczema

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## **ABSTRACT (340 words)**

**Introduction:** Studies have linked the use of antibiotics in early childhood to a range of childhood disorders such as asthma. However, for asthma it has been difficult to disentangle the directionality between antibiotics and disease. While most previous studies have focused on a single disease, we now utilize the vast health databases available in Denmark to investigate if antibiotics given in a critical developmental period in infancy are associated with several disease outcomes related to the immune system.

**Methods:** In a nationwide registry study of all children born in Denmark between 1998 and 2006 (N = 511,990) we investigated the association between antibiotics before one year of age and the outcomes asthma, allergic rhinitis and eczema. Cases were defined from data on hospitalisations or prescription medications in the Danish national registries. Using cox regression analyses, the study population was followed for up to 12 years of age.

**Results:** Preliminary results showed that antibiotic use in the first year of life was associated with an increased risk of being hospitalized with asthma: adjusted hazard ratio (HR) 1.54 (95% CI 1.48 - 1.57) and allergic rhinitis HR 1.34 (95% CI 1.21 - 1.48). Likewise, the risk was significantly increased for cases defined by medication prescriptions: asthma HR 1.50 (95% CI 1.47 - 1.52), allergic rhinitis HR 1.28 (95% CI 1.25 - 1.30), and eczema HR 1.18 (95% CI 1.16 - 1.20). Further, for every added course of antibiotics, the risk increased in a dose-response manner for all outcomes.

**Conclusions:** Early-life antibiotic use was associated with later asthma, allergic rhinitis and eczema. The results showed a stepwise increase in risk with every new course of antibiotics. These results suggest that antibiotics in early life can influence the developing microbiome and perhaps an improper maturation of the immune system and later disease. While the asthma association could be a case of reverse causation, it is unlikely that the development of allergic rhinitis or eczema would lead to more antibiotics. Further studies on causation is warranted.