Title: Exposure to farming environments in childhood and asthma and wheeze in rural populations: A systematic review with meta-analysis

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Body: Background: Particularly strong associations with asthma and allergic diseases have been described for exposure to farming environments in childhood. The aim of this systematic review was to update and extend existing narrative reviews, test for heterogeneity across studies, and conduct a meta-analysis.

Methods: Published literature was searched through PubMed including all articles added before September 1, 2011. Articles were included if they reported an epidemiological study on the exposure to a farming environment in childhood and subsequent wheeze or asthma. Heterogeneity of effect measures was evaluated using Cochran's Q and I². Effect measures were summarized by random-effects meta-analysis for various outcome definitions. Results: In total, 357 retrieved abstracts revealed 52 articles from 39 studies with data considered for the meta-analysis. Most studies were conducted among children or on childhood onset of disease. Most data was on doctor diagnosed asthma or current wheeze. The meta-analysis showed substantial heterogeneity across studies with similar outcome definitions. Nonetheless, the combined effects were statistically significant and showed an approximate 25% lower asthma prevalence among exposed subjects compared to unexposed subjects. Conclusions: The protective 'farm-effect' on asthma was reported in numerous studies. Its underlying factors ought to be studied and promising efforts have been already made. However, the heterogeneity of the effect across studies should also be investigated because whatever causes it is a potential threat to valid synthesis of evidence and to the detection of specific protective factors.