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Title: Maternal complications and conditions in pregnancy and wheezing in early childhood: A combined analysis of 14 European birth cohorts

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Body: Aims.We assessed the relationship of maternal complications including hypertensive disorders and diabetes in pregnancy, and pre-pregnancy body mass index (BMI) with wheezing symptoms in infants, combining data from birth cohorts participating in the CHICOS (Developing a Child Cohort Research Strategy for Europe) project. Methods. Eligible cohorts met the following criteria: recruitment from 1990 onwards, maternal complications recorded at any time during pregnancy, and wheezing recorded in the first

12-24 months of life. Associations of maternal complications and ever (≥ one episode), and recurrent (≥4 episodes) wheezing were assessed for each cohort, adjusting for maternal country of birth, education, asthma, smoking in pregnancy, parity, and age. Crude, adjusted and mutually adjusted risks ratios (aRR) were pooled using a random-effects meta-analysis. Results. The analysis included 93245 subjects. Ever wheezing ranged from 20 to 47 %, and recurrent wheezing from 3 to 14%. Pre-eclampsia and obesity (BMI≥ 30; ref: BMI: 18.5-24) were associated with an increased risk of ever wheezing (aRR, 1.09; 95% CI: 1.02, 1.17 and 1.12; 95% CI: 1.07, 1.18, respectively). Both estimates increased slightly for recurrent wheezing. Maternal pre-pregnancy overweight (BMI: 25-29) was associated with an increased risk of wheezing, both ever and recurrent (aRR: 1.09, 95% CI: 1.06, 1.11 and 1.20: 1.13, 1.26, respectively). Neither hypertension nor diabetes were found to be associated with ever or recurrent wheezing. Conclusions. Pre-pregnancy overweight, obesity and pre-eclampsia are associated with a slightly increased risk of wheezing in infants.