

Kallen BAJ et al. Is erythromycin therapy teratogenic in humans? *Reproductive Toxicology* 20: 209-214, 2005

Type of study	Population-based retrospective cohort
Where	Sweden
When	1995-2002
Characteristics of the cohort	Newborns whose mothers reported use of erythromycin (or penicillin V) in early pregnancy, identified in the Swedish Medical Birth Register
Characteristics of the treated diseases	Not indicated
Exposure definition	Intake in early pregnancy
Ascertainment of drug exposure	Nation-wide medical birth registry. Information on drug use reported by the pregnant women (midwife interviews at the first visit of the pregnant woman to the antenatal care centers, usually in weeks 10-12 and for more than 90% before the end of the first trimester). The registry also contains information on drugs prescribed in pregnancy by the antenatal care services. All drug information collected prospectively in relation to delivery
Size of the studied cohort	Exposed to the studied drug: 1844 infants (1813 deliveries) exposed in utero to erythromycin before the first antenatal care visit Exposed to other drugs: 9110 infants (8980 deliveries) exposed in utero to penicillin V before the first antenatal care visit Reference group for malformation rate: total number of infants born in the general population during the study period
Exposed cohort	Newborns exposed to the studied drug
Control cohort	Newborns not exposed to the studied drug: - exposed to penicillin V - all infants, born in the general population during the study period
Malformations definition	Not indicated (in discussion: this includes a number of mild and variable conditions)
Malformations ascertainment	Identified from three sources: the Medical Birth Register (neonatal period), the Swedish Register of Congenital Malformations (neonatal period), the Hospital Discharge Register (discharge diagnoses at any hospitalization up to the end of 2002)
Prevalence of malformations among control offspring	Exposed to penicillin V: 4.7% (cardiovascular malformations 0.9%, pyloric stenosis 0.06%) All infants: 4.6% (cardiovascular malformations 1.0%, pyloric stenosis 0.06%)
Analysis	Mantel-Haenszel OR and 95% CI were estimated (according to year of birth, maternal age, parity, smoking, number of previous miscarriages). When expected numbers were low, risk ratios as observed/expected numbers were calculated instead and 95% CI determined from Poisson models
Strengths	- Nation-wide population based study - The drug information was retrieved prospectively, data not affected by delivery outcome - Multiple sources for malformation identification reduced the risk of ascertainment bias - Information on other concomitant drugs use
Weaknesses	- Drug use reported by the pregnant women - No information on the number of abortions, stillbirths or drug dosage - Not indicated if information on maternal drug use was available at the time of paediatrician's examination - Analysis: multiple testing (there was no prior hypothesis)

	- Possibility of confounding by indication
Main results	The risk for any congenital malformation after erythromycin therapy was increased (OR 1.24, 95% CI 1.0-1.5) and this was due to an effect on cardiovascular malformations (OR 1.92, 95% CI 1.4-2.7). There was also an indicated increased risk for pyloric stenosis (risk ratio 3.0, 95% CI 1.1-8.5 after exposure in early pregnancy)