

28 Laegreid L et al. Congenital malformations and maternal consumption of benzodiazepines: a case-control study. *Dev Med Child Neurol* 32, 432-441, 1990

Type of study	Case-control
Where	Sweden
When	1985-1986
Cases	<ul style="list-style-type: none"> - 18 cases: 25 infants identified as born alive with one or more of the four selected diagnoses from the International Statistical Classification of Diseases of congenital minor and major malformations: a) embryopathy and fetopathy, unspecified; b) unspecified congenital malformations of the nervous system; c) cleft palate and cleft lip; d) congenital malformations of the urinary tract - The paediatric diagnostic register at the East Hospital and the files of dead neonates reviewed (diagnoses made in the neonatal period, or in the case of neonatal death, found at autopsy, by the paediatrician in charge of the neonatal unit or by the clinical pathologist)
Case prevalence among the population	2.3 per 1,000 liveborn infants
Controls	- 60 controls: 109 infants discharged from the delivery or neonatal units as healthy, selected using paired sampling
Exposure definition	Intake benzodiazepines (BZD) in early pregnancy: diazepam, desmethyl-diazepam, flunitrazepam, oxazepam, clonazepam, nitrazepam, lorazepam
Ascertainment of drug exposure	23 of the 25 cases blood-tested in early pregnancy (drug analysis in 18 (78%)); 91 of the 109 controls blood-tested (drug analysis in 60 (66%))
Prevalence of exposure among controls	3.3%
Analysis	OR and low 95% CI were estimated (Wald test w^2 for OR, Fisher exact test for fourfold tables used)
Strengths	<ul style="list-style-type: none"> - Good characterization of cases: diagnoses made independently before the study started - Thorough information about drug exposure (blood-tested) - Analyses of maternal serum were blind - Information on other drugs used
Weaknesses	<ul style="list-style-type: none"> - Small number of subjects - Drug analysis was possible for 78% of cases and 66% of controls - Possibility of some undetected confounding factors
Main results	The association between one or more of the particular malformations and BZD-positive maternal serum samples in early pregnancy was highly significant (OR 23, $p=0.00006$, low CI 8)