

Sabers A et al. Epilepsy and pregnancy: lamotrigine as main drug used. *Acta Neurol Scand* 109, 9-13, 2004

Type of study	Prospective cohort (multicentre registry: six centres) without controls
Where	Denmark
When	1996-2000
Characteristics of the starting cohort	Pregnant women with epilepsy with or without AED during pregnancy (voluntary participation, included as soon as possible in pregnancy)
Characteristics of the disease	The epilepsy syndrome was idiopathic in 46% of the patients, symptomatic/cryptogenic in 49%, not classified in 5%
Ascertainment of drug exposure	Data collected prospectively from the epileptologist/neurologist responsible for the neurological care of the woman (data: aetiology of epilepsy, classification of seizures, occurrence of seizures during first trimester and AED doses and plasma levels, co-medications including supplementation of folic acid during the pregnancy). Tests of plasma levels of relevant AEDs taken at each visit before the morning dose of AED
Exposure definition	Women with epilepsy treated with AED during the first trimester
Size of the studied cohort	Pregnant women with epilepsy: 151 pregnancies recruited, 147 in follow up, 137 liveborn infants (138 (94%) treated with AED during the first trimester, 9 (6%) untreated: 109 (74%) on monotherapy, two, three and four AEDs given in 25 (17%), 3 (2%) and 1 (1%) cases, respectively)
Exposed cohort	Newborns exposed to a group of drugs
Control cohort	Not considered
Malformations ascertainment	Paediatrician examined the newborns within the first 5 days of life. In case of any suspected or demonstrated malformation all relevant hospital and delivery records were examined. No fetal malformations were detected prenatally
Malformations definition	Abnormality of an essential embryonic structure present at birth or discovered during the neonatal period
Analysis	Chi-square test corrected with Yates corrections, 95% CI
Strengths	<ul style="list-style-type: none"> - Thorough information about drug exposure (data collected prospectively from the epileptologist/neurologist) - Most of the outcomes ascertained prospectively - Information about characteristics of the disease and supplementation of folic acid during pregnancy
Weaknesses	<ul style="list-style-type: none"> - Small number of cases (a possible explanation for the low proportion of malformations) - No information about women who refused to participate (voluntary participation, risk of selection bias) - Patients might be included after the end of first trimester: the design of this study was not optimal for registration of spontaneous abortions - Not indicated if the paediatrician was aware of the drug use - Possibility of confounding by indication - Some birth defects may not be included because they appear later after birth
Main results	The overall risk of malformations among newborns in the AED-exposed group was 3.1% (two infants were born with multiple malformations (valproate monotherapy), two infants had ventricular septal defects (one oxcarbazepine monotherapy, one

oxcarbazepine and lamotrigine)). The risk of malformations was 2.0% in women treated with lamotrigine and 6.7% in women treated with valproate (NS). The most frequent AEDs used were lamotrigine 35%, oxcarbazepine 25%, valproate 20%. 74%

received monotherapy. Folic acid supplementation was taken during first trimester by 80% of patients.