

**Wilton LV et al.** The outcomes of pregnancy in women exposed to newly marketed drugs in general practice in England. *Br J Obstet Gynaecol* 105, 882-889, 1998

Type of study	Retrospective cohort (34 prescription-event monitoring studies)
Where	England
When	Not indicated
Characteristics of the cohort	Newborns whose mothers exposed to 34 newly marketed drugs during the first trimester, identified by the Prescription Pricing Authority (PPA)
Characteristics of the treated diseases	Not indicated
Exposure definition	Intake during the first trimester of pregnancy
Ascertainment of drug exposure	Women identified from the first National Health Service prescriptions written by general practitioners (prescription information/ exposure data provided by the PPA). Simple questionnaires (green forms) posted to the prescribing doctors at least six months following the first prescription for each patient and provided information on drugs: indication, reason for stopping, duration of therapy, events during/after treatment
Size of the studied cohort	Exposed to the studied drugs: 831 pregnancies (first trimester, excluded: 74 second/third trimester); 557 newborns (10 twins, 1 stillborn), (outcome not ascertained in 51 pregnancies (6%): 16 patients moved, in 35: incomplete follow-up)
Exposed cohort	Newborns exposed to the studied drugs
Control cohort	External Liveborn infants in England/Wales
Malformations definition	Congenital anomalies classified according to the Office of Population Censuses and Surveys (OPCS) monitoring groups. Minor congenital anomalies which are not required to be transmitted to the OPCS, classified separately
Malformations ascertainment/outcome of pregnancy	The doctor was sent a questionnaire to determine clinical events, including pregnancy, occurring after the drug was dispensed. A supplementary questionnaire determined the outcome of each reported pregnancy (patient's medical record). A separate questionnaire was sent for abortions
Prevalence of malformations among control offspring	2% of liveborn infants in England/Wales
Analysis	- Results of individual studies
Strengths	- Nation-wide population based study - Exposure data not dependent on patient recall - The drug information retrieved prospectively, data not affected by delivery outcome - Information on reproductive end points, other drugs, lost to follow up
Weaknesses	- The response rate of prescription-event monitoring studies may underestimate the total number of pregnancies in exposed women (under/selective reporting) - Not control for potential confounders - The general practitioner was aware of the exposure status of the women - Possibility of confounding by indication - Not indicated if information on maternal drug use was available at the time of paediatrician's examination - Some birth defects may not be included because they appear later after birth - No information on drug dosage, compliance
Main results	The outcome ascertained for 780 (94%) of 831 pregnancies: 547

(66%) births, 10 (1%) ectopic pregnancies, 94 (11%) spontaneous miscarriages, 5 (<1%) missed abortions, 120 (14%) legal abortions, 4 (<1%) intrauterine deaths. Of 557 infants born, 14 (2.5%) had congenital anomalies, similar to the percentage of congenital anomalies estimated by the Office for National Statistics (abortions/intrauterine deaths: 0.9% (2) congenital anomalies; 3 minor congenital anomalies in liveborn single babies not reported to the OPCS)