

Mastroiacovo P et al: Prospective assessment of pregnancy outcomes after first-trimester exposure to fluconazole. *Am J Obstet Gynecol*, 1996, 175, 1645-50

Type of study	Prospective cohort
Where	Italy
When	1992-1994
Characteristics of the starting cohort	Women who contacted three Italian Teratogen Information Services, exposed to low-dosage regimens of fluconazole during the first 12 weeks of pregnancy
Ascertainment of drug exposure	Structured interview few days after the exposure (with detailed history of prescription and non prescription drug use, information on the commercial preparation, dosage, indication, and time of use during pregnancy)
Exposure definition	Intake during the first 12 weeks of pregnancy
Size of the studied cohort	Exposed women: 228 recruited, 226 in follow-up, 177 newborns Unexposed reference group women: 452 in follow up, 409 newborns
Exposed cohort	Newborns exposed to a specific drug
Control cohort	Newborns not exposed to the studied drug (exposed to agents that are known not to be teratogenic or embryotoxic); frequency-matched by region of residence; pregnant women had contacted the three Services during the same period, women with a family history of birth defects or with chronic diseases were excluded
Malformations ascertainment	Prospective ascertainment with follow-up interview, similar in both the exposed and nonexposed groups: women were contacted by phone after 6-7 weeks of the expected date of delivery In the presence of congenital anomaly, neonatal problems, prolonged hospital stay, additional information from the attending physician was requested
Malformations definition	Recorded only those congenital anomalies that warranted medical or surgical treatment
Prevalence of malformations among control offspring	4.2%
Analysis	Adjusted OR and 95%CI (logistic regression to control for potential confounders: gestational age at the first contact with the Teratology Information Service, maternal age, parity, previous miscarriages, previous infants with congenital anomalies, maternal education, smoking, alcohol use)
Strengths	<ul style="list-style-type: none"> - Internal reference group - Exposures were ascertained few days after the intake and outcomes were ascertained prospectively - All Centers used similar operating procedures for data collection and exposure assessment - No differentiated recall bias between the exposed and non exposed groups - The staff at the follow-up interview was unaware of the exposure status of the women - The time of the interview after delivery was similar in the two groups - Completeness of follow-up
Weaknesses	<ul style="list-style-type: none"> - Women were self-selected by calling the Service for counselling - Self-reported outcome by women (as written on the children's neonatal discharge report) - Some birth defects may not be included because they appear later after birth
Main results	First-trimester exposure to fluconazole does not appear to increase the

prevalence of congenital anomalies (OR 1.07, CI95% 0.4-2.8)
Women in the exposed group had a fivefold increased occurrence of induced abortions, because the fear of malformations induced by at least one health care provider