

REFLUX NEPHROPATHY AND THE RISK OF ADVERSE PREGNANCY RELATED OUTCOMES

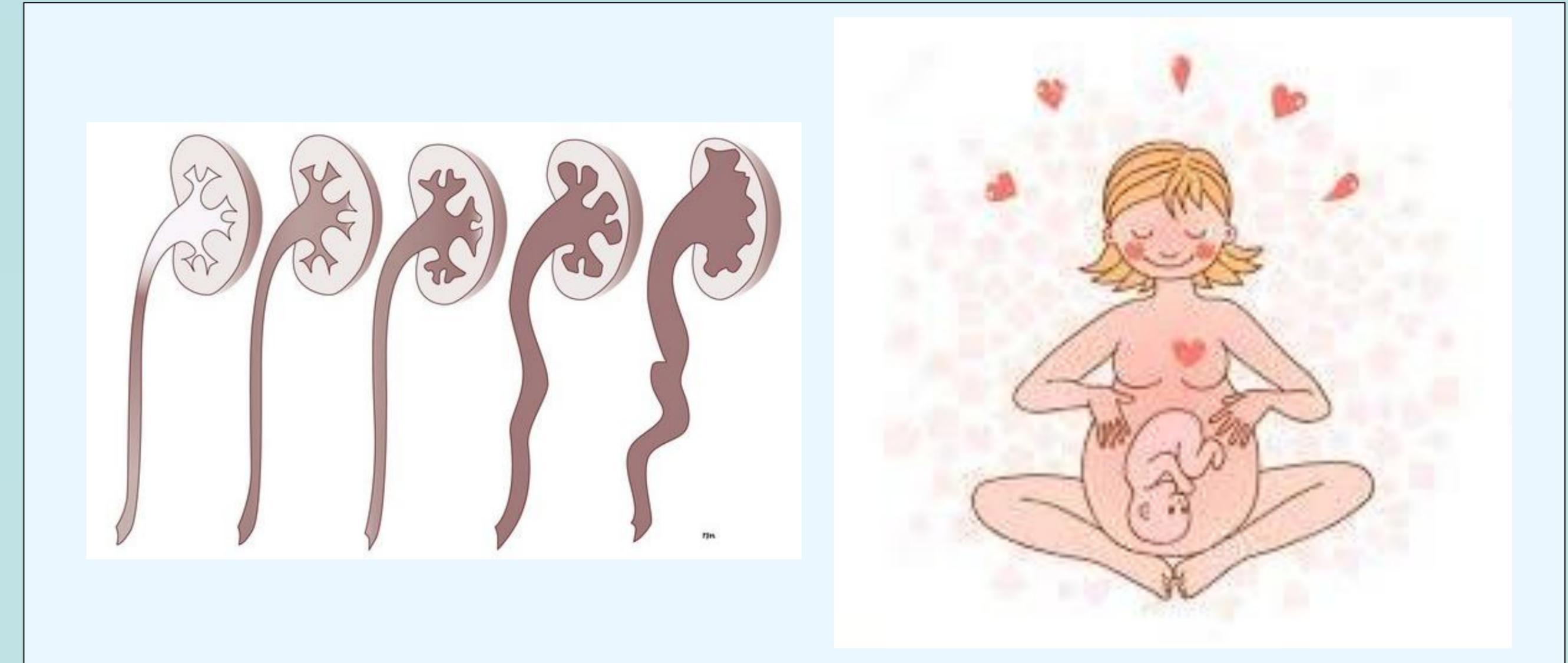
A systematic review and meta-analysis of case series and reports in the new millennium

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Introduction and objectives:

Reflux nephropathy is a common urinary tract malformation, and a substantial cause of morbidity in women of childbearing age. While recent studies provide information on pregnancy-related outcomes, a systematic, meta-analytic review is not yet available and may help interpreting their heterogeneous results. The aim of the present study is to **analyze pregnancy-related outcomes in literature on reflux nephropathy**, to perfect the estimation of the risks, and to identify specific research needs.



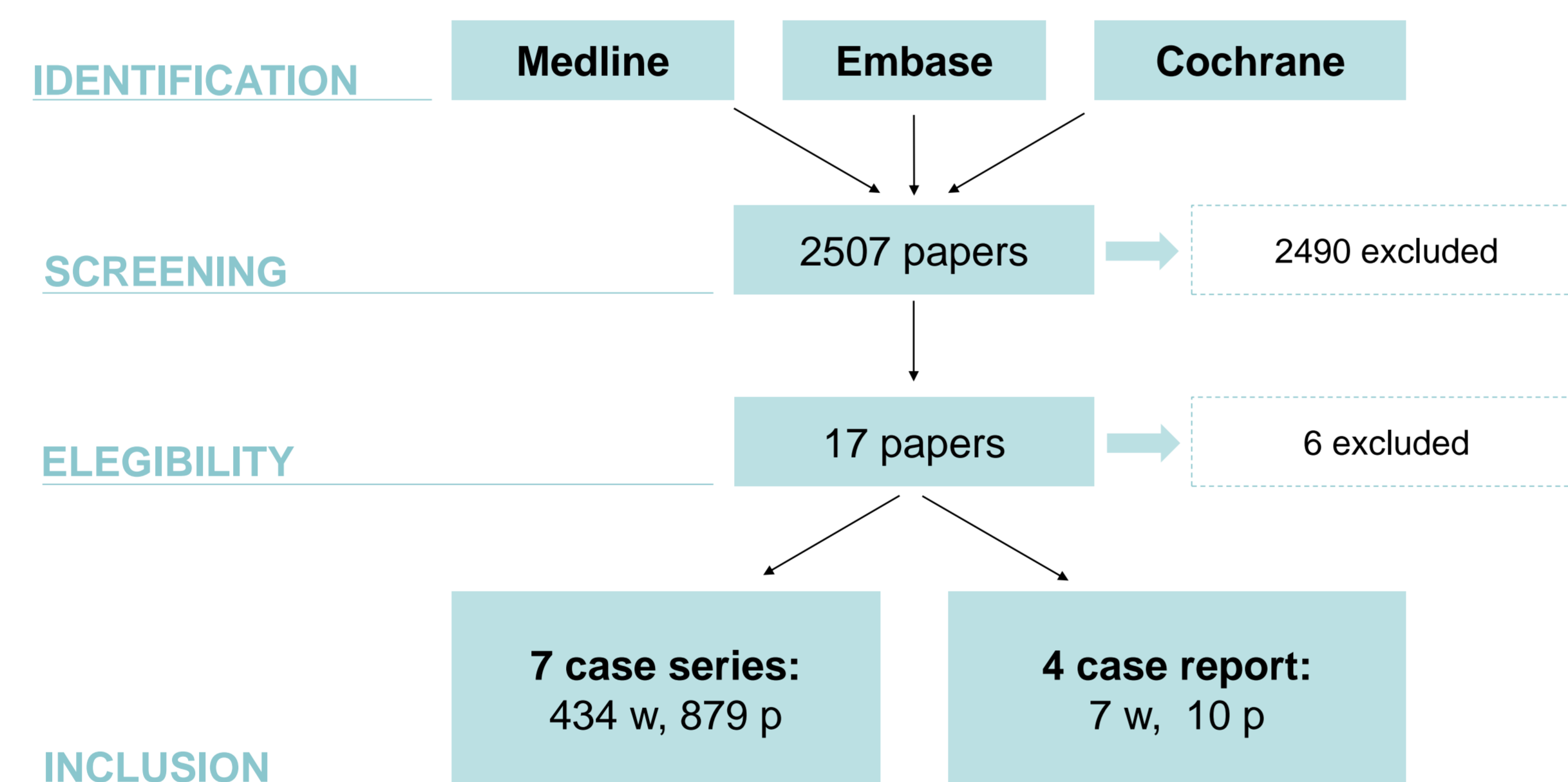
Methods:

Medline, EMBASE and the Cochrane review databases were searched from January 2000 to May 31st 2016. Anticipating the retrieval of low number of series, and of heterogeneous designs and definitions, eligibility criteria were kept broad. Thus, we included all published studies that discussed reflux nephropathy in pregnancy and that reported on at least one pregnancy-related outcome. Data was extracted of eligible case series (≥ 6 cases). No study had a control group, not allowing for contextualization of results. For the outcomes preeclampsia (PE), pregnancy-induced hypertension (PIH), preterm birth, and newborns small for gestational age, we therefore employed as a control group the low-risk pregnancies from a multicenter Italian database (TOCOS) including 1418 live born singletons gathered in two Italian Centers (Torino and Cagliari). Case reports were analyzed narratively.

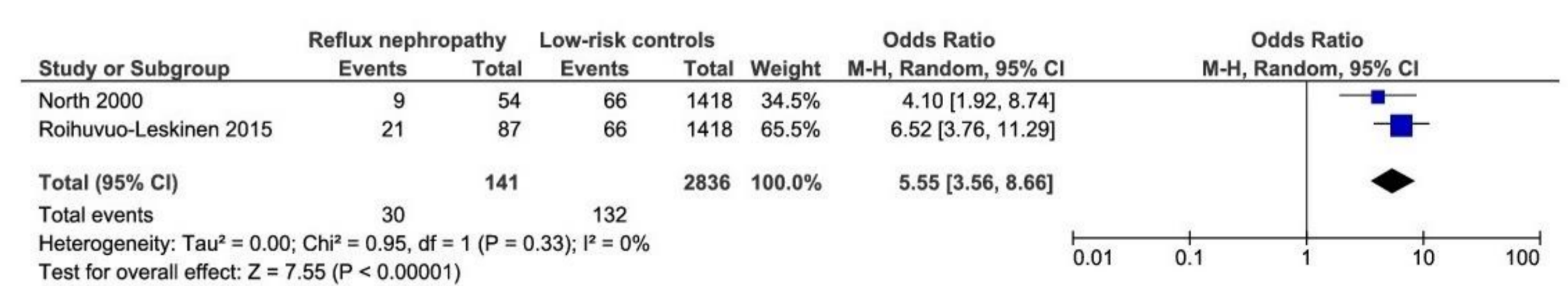
Results:

The search retrieved 2507 papers, of which 7 case series and 4 case reports were included. The series report on 434 women with 879 pregnancies, no study reported on controls. There is high heterogeneity for the study designs, number of pregnancies (26 to 242), setting of the study and study aim. Compared to the low-risk control cohort, the meta-analysis showed an **increased risk of PIH (OR 5.55; CI 3.56- 8.66)**, **PE (OR 6.04; CI 2.41-15.13)**, and a **ten-fold increased risk of all hypertensive disorders combined (OR 10.43; CI 6.90-15.75)**. **No difference was observed in preterm delivery and caesarean sections.** A higher incidence of stillbirth was reported in one paper. The case reports warn against a severe complication, hydro(uretero)nephrosis with or without infection, reported in all 10 patients. In spite of the complications described in the mothers, all reported foetal outcomes were good, even if details are missing in most papers.

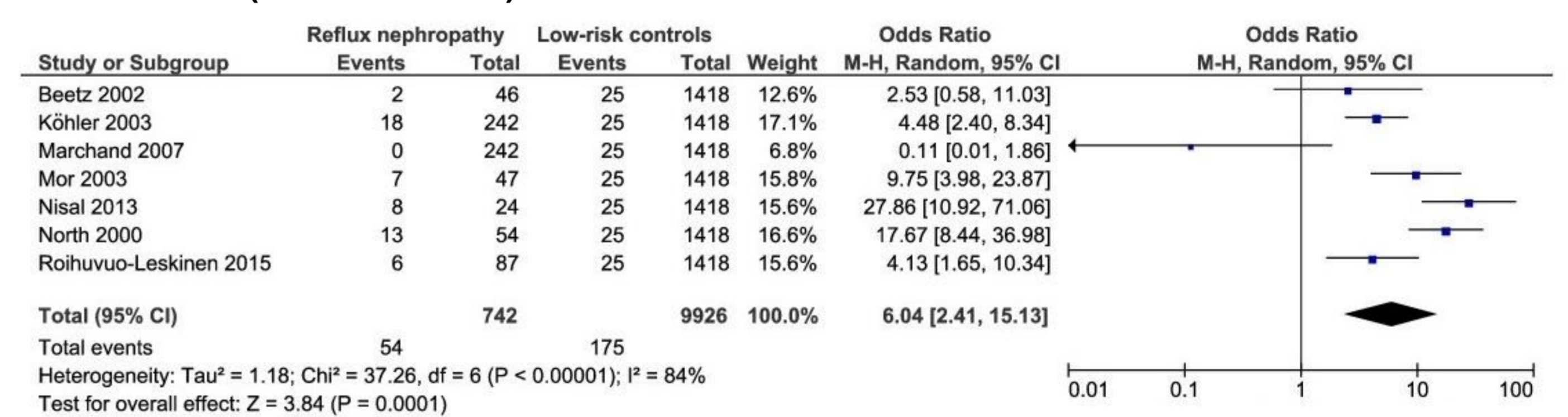
REFLUX NEPHROPATHY AND PREGNANCY OUTCOMES: SYSTEMATIC REVIEW



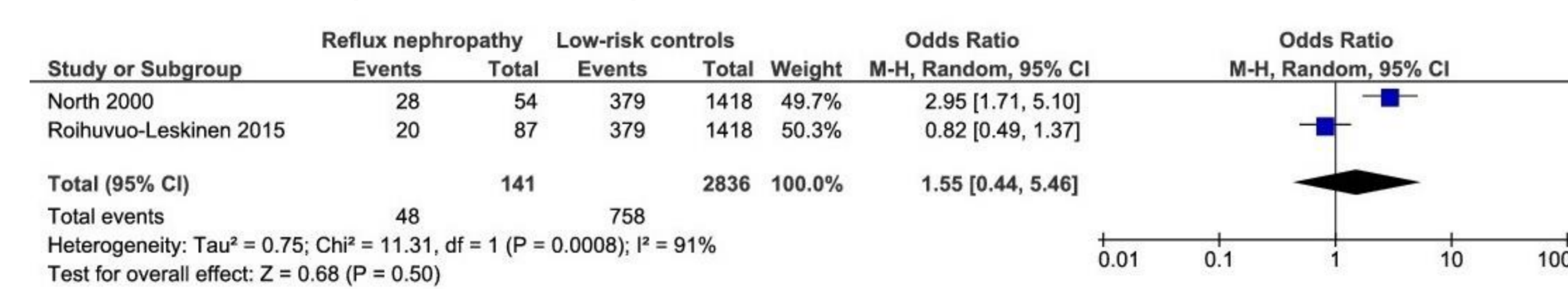
ODDS RATIO FOR PREGNANCY-INDUCED HYPERTENSION IN REFLUX NEPHROPATHY VERSUS LOW RISK CONTROLS (TOCOS STUDY)



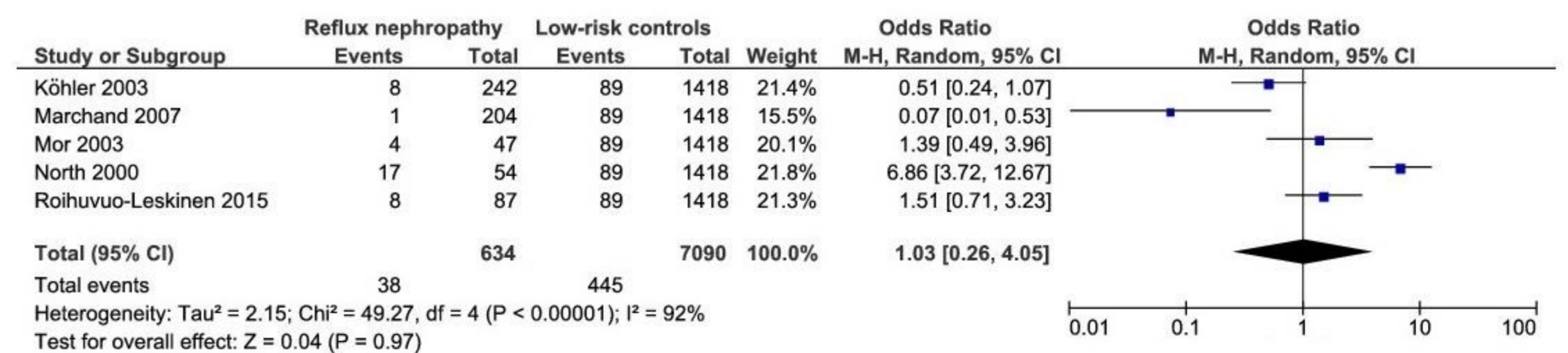
ODDS RATIO FOR PREECLAMPSIA IN REFLUX NEPHROPATHY VERSUS LOW RISK CONTROLS (TOCOS STUDY)



ODDS RATIO FOR CAESAREAN SECTION IN REFLUX NEPHROPATHY VERSUS LOW RISK CONTROLS (TOCOS STUDY)



ODDS RATIO FOR PRETERM DELIVERY IN REFLUX NEPHROPATHY VERSUS LOW RISK CONTROLS (TOCOS STUDY)



Conclusions:

Reflux nephropathy is associated with an **increased risk of PIH and PE, but not of preterm delivery, suggesting the occurrence of late 'maternal' PE**, that affect foetal growth and pregnancy outcomes less severely than early 'placental' PE. The finding of a higher incidence of stillbirth in one series demands further analysis. The case reports focused on severe to extreme hydronephrosis, thereby suggesting that regular ultrasounds may be useful in pregnancy. These results suggest the **need for focusing follow-up in particular on the last phases of pregnancy, due to the clustering of most of the adverse events (late PE and PIH, stillbirth and possible also hydronephrosis) in these periods.**

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