

Introduction

- Stillbirth is a type of fetal loss in the mid-late 2nd trimester (1-3)
- Reported in >2,500,000 women annually, mostly in low and middle-income households (4)
- Evidence suggests correlation between stillbirth and future maternal disease (cardiovascular, metabolic, malignant) and increase risk of mortality. (5-7)
- Results are controversial with differences in size and population groups.

Objective

- To quantify the correlation between stillbirth and long-term maternal morbidity and mortality

Methodology

- Design: Systematic review (SR) and meta-analysis (MA)
- Databases: MEDLINE, EMBASE, AMED, BNI, CINAHL, Cochrane Library and grey literature search
- Study selection: 2 independent reviewers
- Data Extraction: study design, participant and comparator demographic characteristics, definition of fetal loss, incidence of morbidity and mortality outcomes
- Risk of Bias: Newcastle Ottawa Scale (NOS) by 2 independent reviewers
- Statistical analysis:
 - Outcomes: Ischaemic Heart Disease (IHD), Cerebrovascular Disease (CVD), All circulatory disease, Renal disease, Malignant disease, Type 2 Diabetes Mellitus (T2DM), Depression
 - Dichotomous outcomes using random effects model, presented as pooled risk ratios (RR) with 95% confidence intervals (CI)
 - Heterogeneity: I² statistics

Inclusion criteria

- Studies examining the incidence of all types of morbidities and mortality in the women with stillbirth
- Outcomes ≥1 year after stillbirth
- All study types except for study except case reports or letters

Exclusion criteria

- No exposure to stillbirth
- History of disease unrelated to stillbirth
- Pregnancy termination for any indication
- Long-term mortality and morbidity in offspring
- Maternal morbidity or mortality as a direct pregnancy complication (<1 year after pregnancy).

Table 1: Study Inclusion and Exclusion criteria

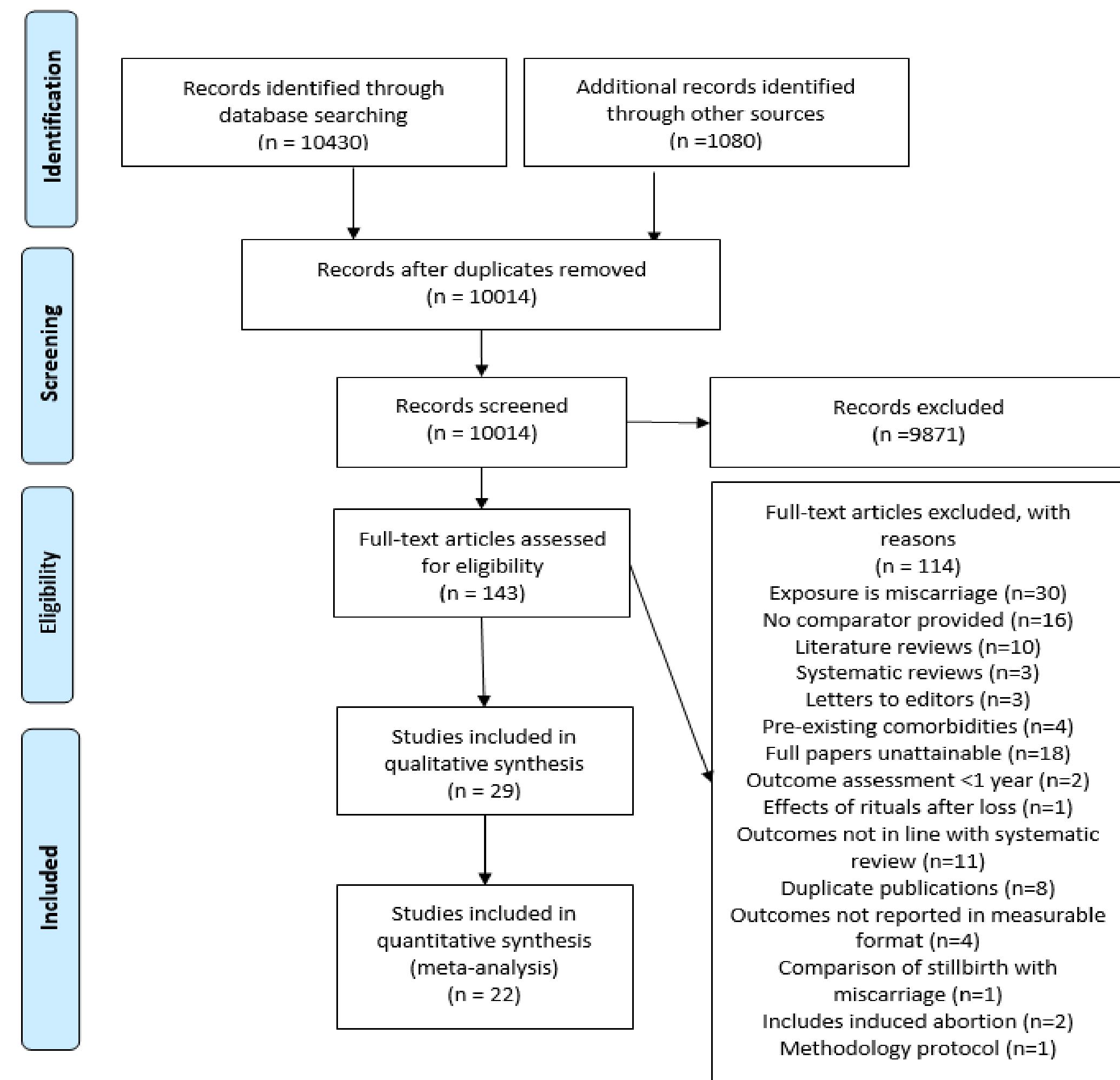


Figure 1: PRISMA Flowchart of study inclusion and exclusion

Results

General Characteristics

- 29 studies included in SR and 22 in MA (PRISMA chart in figure 1)
- Total Exposed: 168,557 vs Total Controls: 8,547,276
- Mean follow-up 16.4 years
- Risk of bias: 18/29 studies low risk (NOS 7-9/9) and 1 high risk (NOS 5-9)

Outcomes

- IHD: RR 1.74 (95% CI [1.39-2.19, p<0.001])**
- Cerebrovascular Disease: RR 1.71 (95% CI [1.44-2.04; p<0.001])**
- Circulatory Disease: RR 1.86 (95% CI [1.01-3.45]; p=0.05)**
- Renal disease: RR 1.97 (95% CI [1.51-2.57], p<0.001)**
- T2DM: RR 1.34 (95% CI [0.95-1.89];p =0.09)
- Malignant disease:
 - Breast cancer: **RR 0.83 (95% CI [0.69-0.99]; p=0.04)**
 - Endometrial & ovarian cancer: no meta-analysis; no association
 - All cancer mortality: RR 1.17 (95% CI [0.95-1.45]; p=0.15, I²: 0%)
- Depression: RR 1.90 (95% CI [0.96-3.88]; p=0.08)

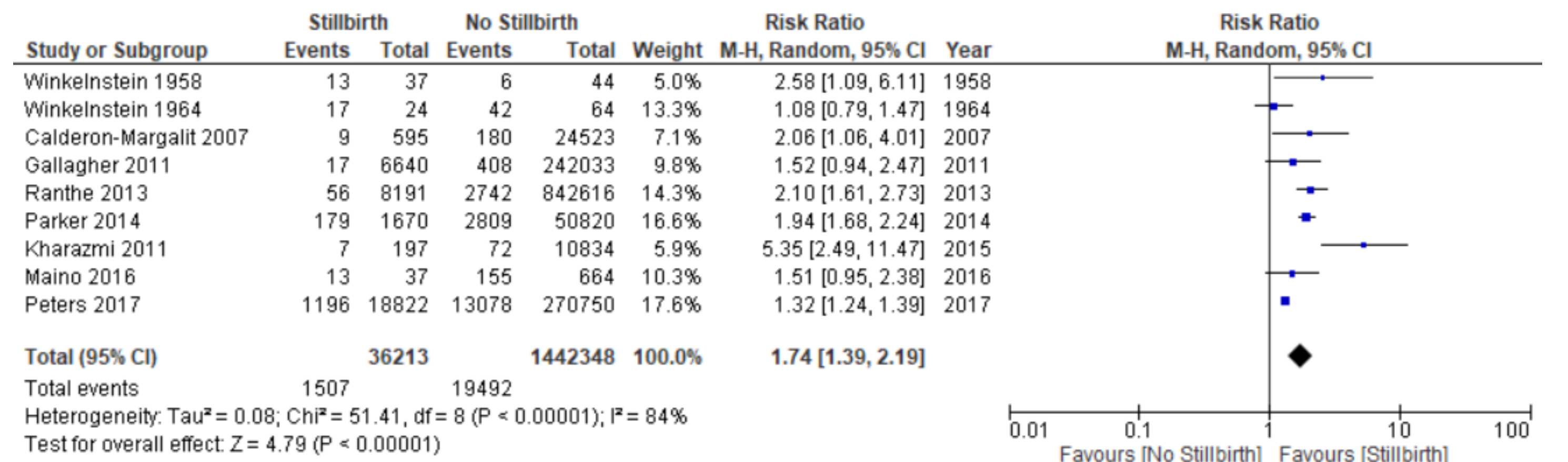


Figure 2: Forest plots with RR and 95% CI comparing IHD in women with and without stillbirth

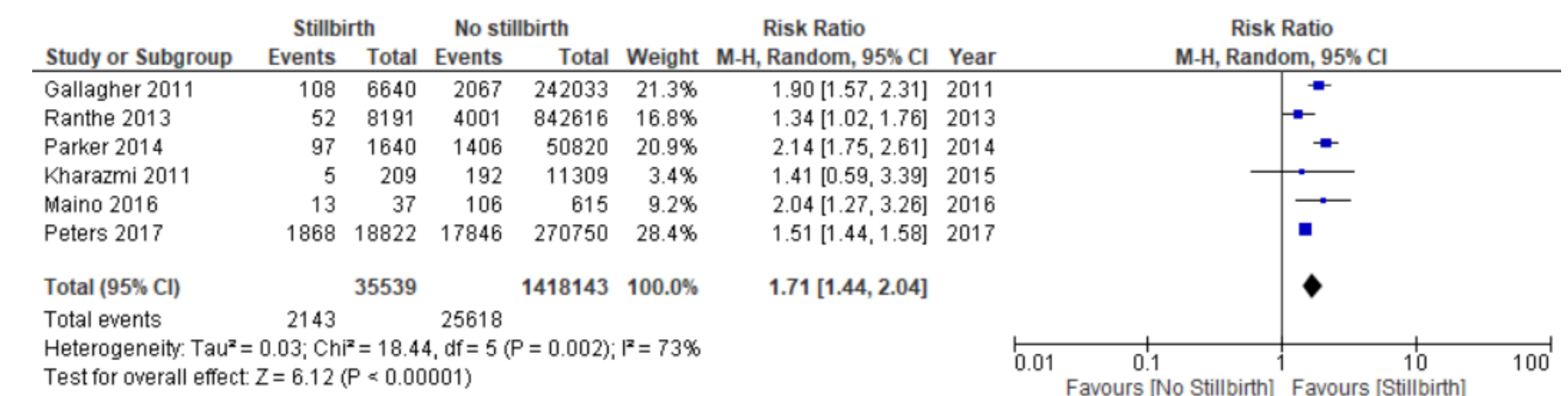


Figure 3: Forest plots with RR and 95% CI comparing CVD in women with and without stillbirth

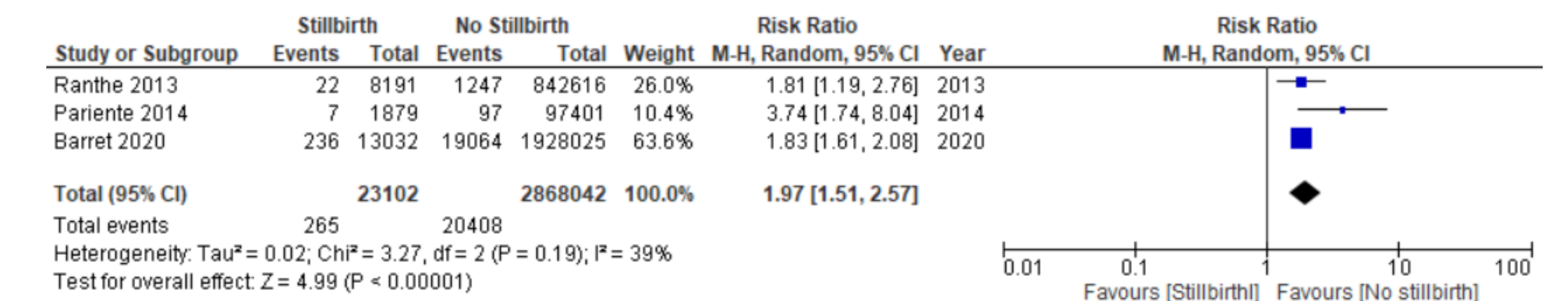


Figure 4: Forest plots with RR and 95% CI comparing renal disease in women with and without stillbirth

Conclusion and future work

- Women exposed to stillbirth have an increased risk of IHD, cerebrovascular and renal disease compared to those without previous history.
- We suggest follow up of women with stillbirth with focus on early lifestyle modifications aiming to prevent or diagnose such conditions early.
- However, the small number of studies in some analysis and the potential contributing confounders such as diet, exercise, and socioeconomic background require further research.

