Systematic Review: Therapies to Prevent Preterm Prelabour Rupture of Membranes

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Background

Preterm prelabour rupture of membranes (PPRoM) is a common cause of preterm delivery affecting up to 3% of pregnancies. It is associated with high rates of mortality and morbidity due to the impact on pulmonary development and concurrent infection. We aimed to systematically investigate whether any intervention used, either in relation to PPRoM or for other pregnancy disorders, have been shown to reduce the prevalence of PPRoM.

Methods

We performed a systematic review and meta-analysis of RCTs that evaluated the use of various interventions in pregnancy. The primary measure was the prevalence of PPRoM. We completed a literature search through Medline, Embase, PubMed and Cochrane Library, identifying RCTs that compared a therapy to standard care (no therapy or placebo) in pregnancy. It was conducted according to the Cochrane Handbook. Odds ratios with 95% CI were calculated. Quality of evidence was assessed using GRADE methodology. Risk of bias was assessed according to the Version 2 of the Cochrane risk-of-bias tool for randomised trials (RoB 2).

Results

29 studies met the inclusion criteria

Intervention	Number of Papers
Docosahexaenoic acid (DHA)	4
Aspirin	1
Rofecoxib	1
Vitamin C and Vitamin E	6
Vitamin C alone	2
Folic acid (alone, with iron, with iron and zinc, and with multiple micronutrients)	1
Zinc	2
Calcium	3
Copper	1
Treatment of Bacterial Vaginosis	7

There was no significant difference in the prevalence of PPRoM in the treatment groups compared to placebo, except for:

Rofecoxib showed an increased risk of PPRoM (RR 2.46, 95% CI 1.28 – 4.73, p = 0.007, 1 trial, 98 women; very low quality of evidence)

Folic acid with a multiple micronutrient supplement showed a reduction in PPRoM (RR 0.40, 95% CI 0.19 – 0.84, p = 0.01, 1 trial, 1671 women; very low quality of evidence).
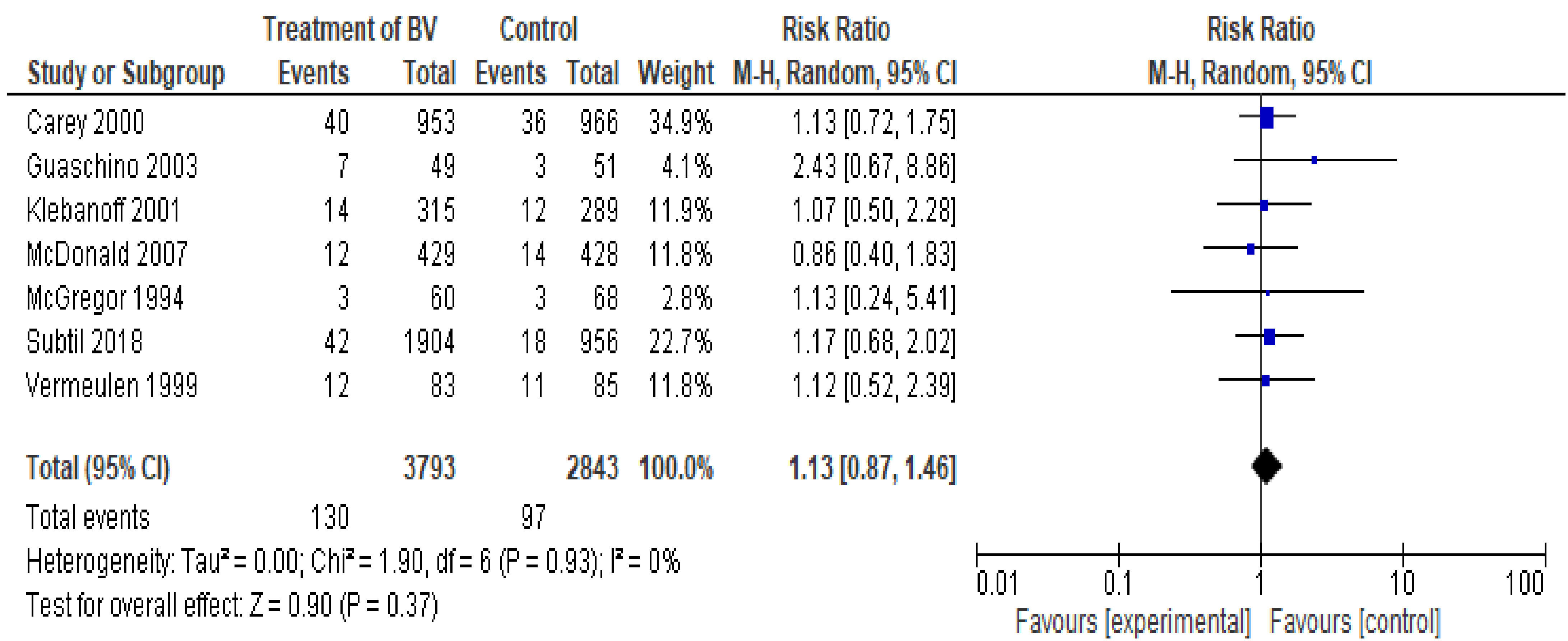
Results for Treatment of Bacterial Vaginosis

Study or Subgroup	Treatment of BV Events	Treatment of BV Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Carey 2000	40	953	36	966	34.9%	1.13 [0.72, 1.75]
Guaschino 2003	7	49	3	51	4.1%	2.43 [0.67, 8.86]
Klebanoff 2001	14	315	12	289	11.9%	1.07 [0.50, 2.28]
McDonald 2007	12	429	14	428	11.8%	0.86 [0.40, 1.83]
McGregor 1994	3	60	3	68	2.8%	1.13 [0.24, 5.41]
Subtil 2018	42	1904	18	956	22.7%	1.17 [0.68, 2.02]
Vermeulen 1999	12	83	11	85	11.8%	1.12 [0.52, 2.39]
Total (95% CI)		3793		2843	100.0%	1.13 [0.87, 1.46]
Total events	130		97			

Heterogeneity: Tau² = 0.00; Chi² = 1.90, df = 6 (P = 0.93); I² = 0%
Test for overall effect: Z = 0.90 (P = 0.37)

Figure 1: Forest plot of comparison of treatment of bacterial vaginosis versus control on PPRoM
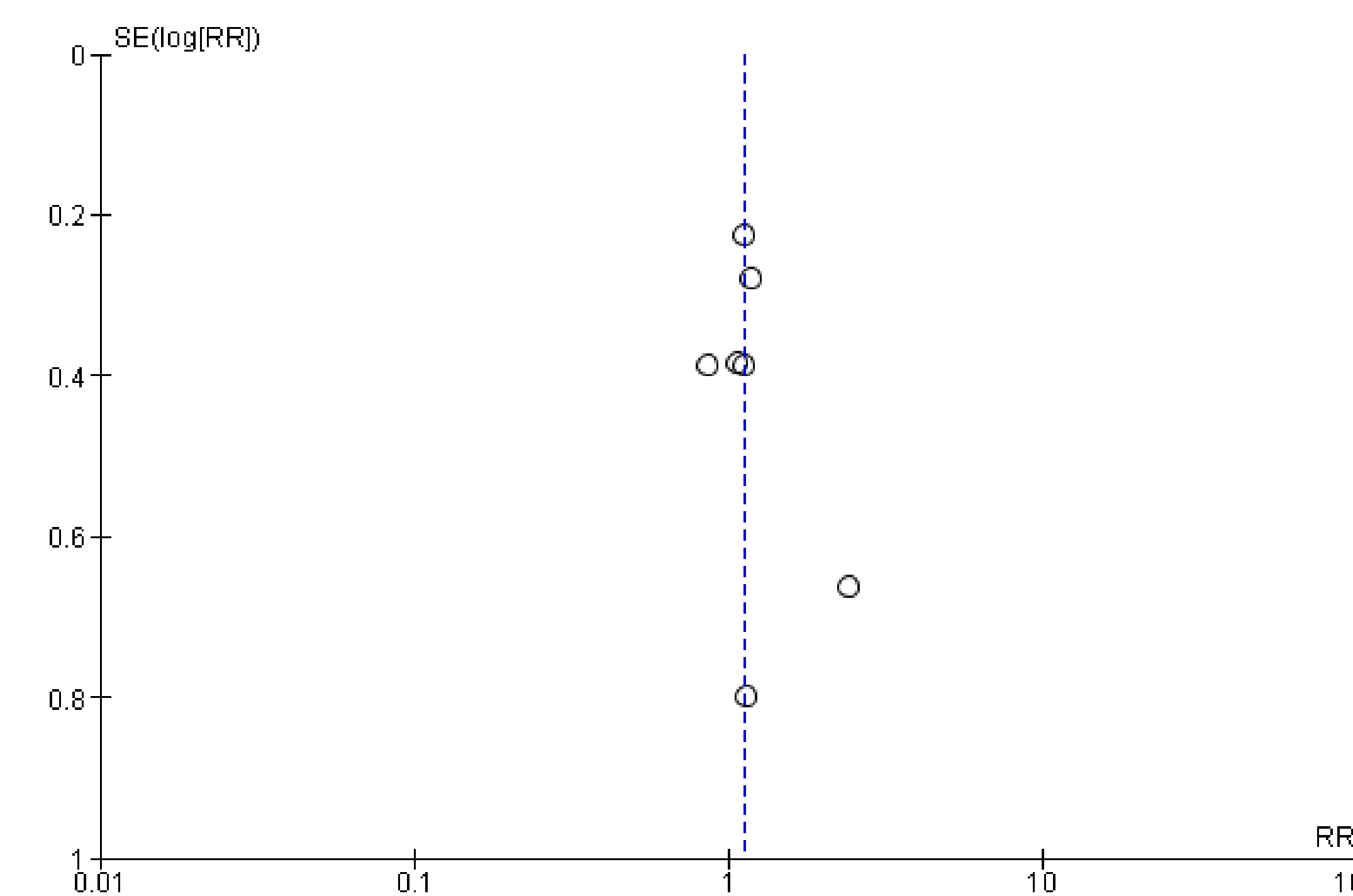

Figure 2: Funnel plot of comparison of treatment of bacterial vaginosis versus control on PPRoM
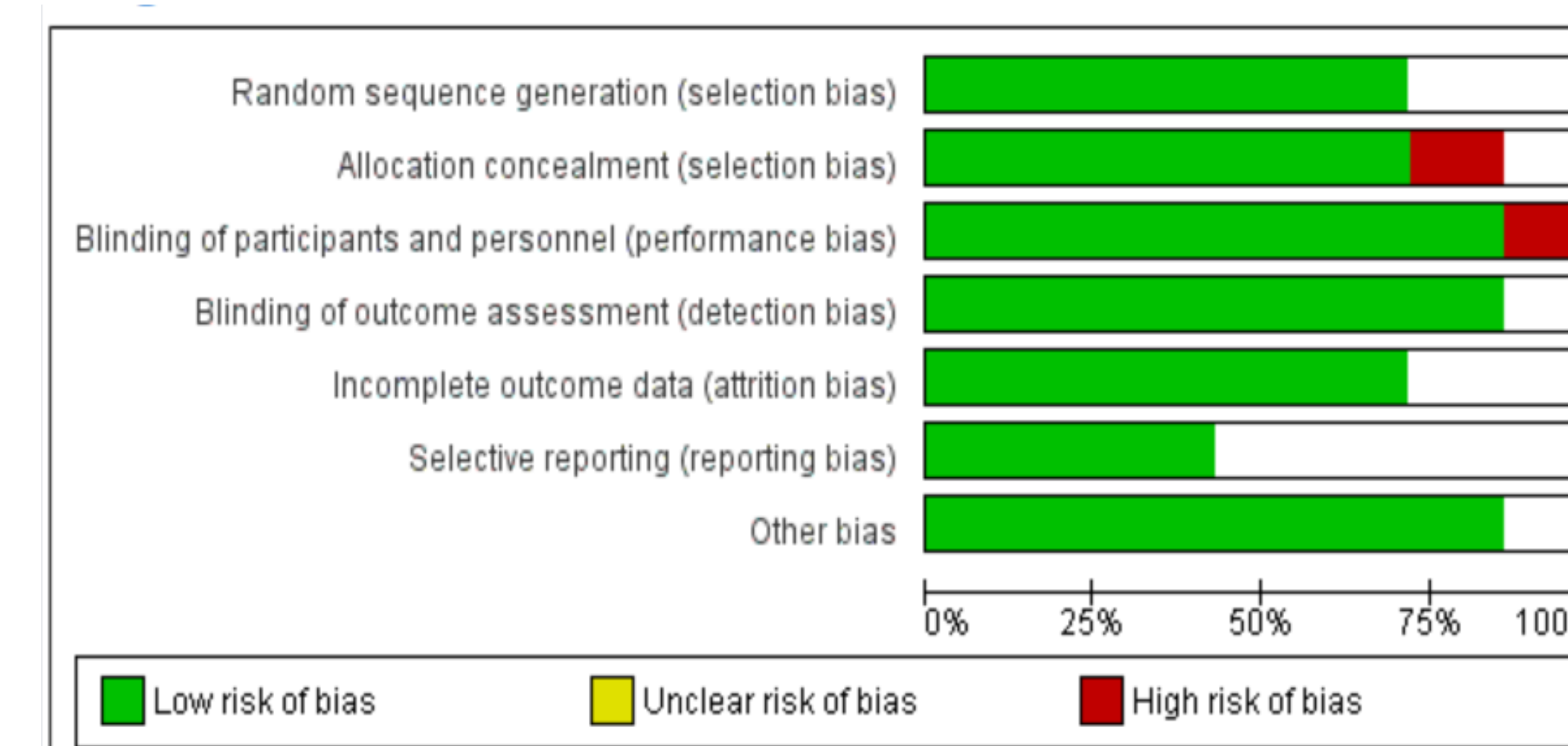

Figure 3: Risk of bias graph

Summary and Conclusions

- This systematic review and meta-analysis was unable to convincingly identify any interventions with evidence that they reduce the prevalence of PPRoM, with the exception of a multiple micronutrient supplement that may have some benefit in a very specific population.
- Given that preterm infants are at the highest risk of poor outcomes, future obstetric research should include the development of preventative interventions.

Disclosures: Nil