

Hormonal contraceptive use in sickle cell disease: A systematic review and meta-analysis

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INTRODUCTION

Pregnancy planning is imperative for women with SCD. During pregnancy, there is a high risk of adverse obstetric and perinatal complications. It is important that women seek preconception care so that any additional risk factors can be identified and modified. Despite this, in 2010 the rate of unintended pregnancy in women with SCD was 53%. This demonstrates an unmet need for contraception advice in these women. However, the safest method of contraception for use in women with sickle cell disease has not yet been fully elucidated. There is a lack of robust evidence surrounding the safety of contraceptive use in women with SCD, particularly regarding the use of combined hormonal contraceptive methods and intrauterine devices (IUDs).

OBJECTIVE

To determine which method of contraception is safest for women with sickle cell disease. We hope that our results will be useful in aiding practitioners to synthesis the existing evidence thereby helping women to reach informed decisions about their reproductive health during counselling and to help women with Sickle Cell Disease safely plan the timing of their pregnancies or avoid unplanned-pregnancies.

METHOD

A systematic review and meta-analysis of English articles using CENTRAL, Embase, Medline, Popline, Web-of-Science (1974 - 2019). Additional studies were identified by searching reference lists of papers. All pooled-analyses were based on fixed-effects models. The outcome measured in the meta-analysis was the risk of increased crisis frequency. Five studies met our inclusion criteria.

Identification	•The search was performed independently by two reviewers •Databases searched: Medline, Embase, Popline, CENTRAL and Web of Science •Additional papers were found by scanning reference lists of relevant articles
Eligibility	Studies comparing the effects of all contraceptive methods to each other or to a control group Primary outcomes: thrombosis, frequency of sickle cell crisis
Risk of bias	• Risk of bias of each individual study was assessed using the Newcastle Ottawa Scale
Quantitative analysis	The primary outcome measure was the frequency of sickle cell crises We used statistical meta-analysis with a random effects model to assess the association between hormonal contraception and frequency of sickle cell crisis. The level of heterogeneity is expressed using I²

RESULTS

Progestogen only contraception

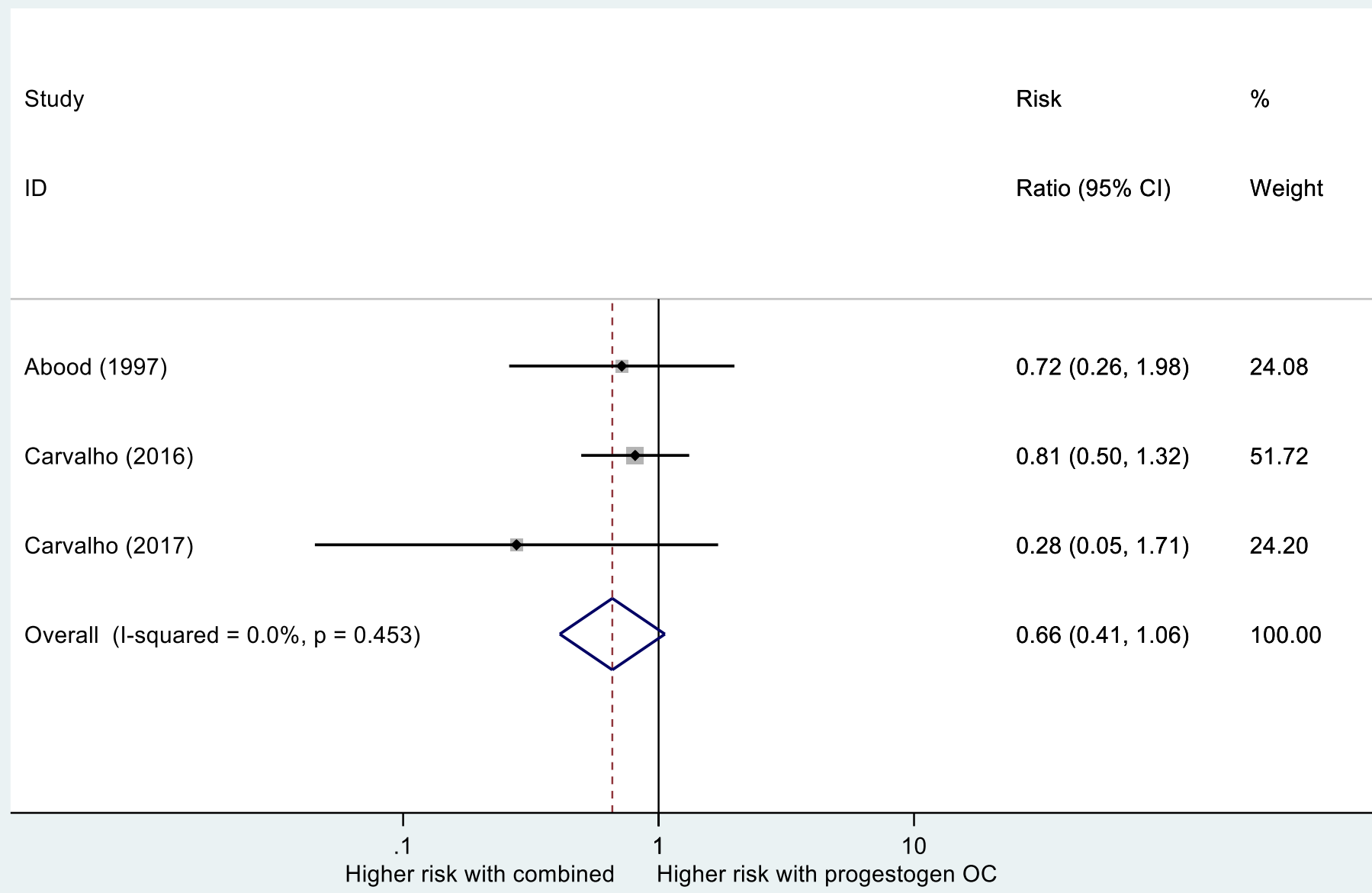
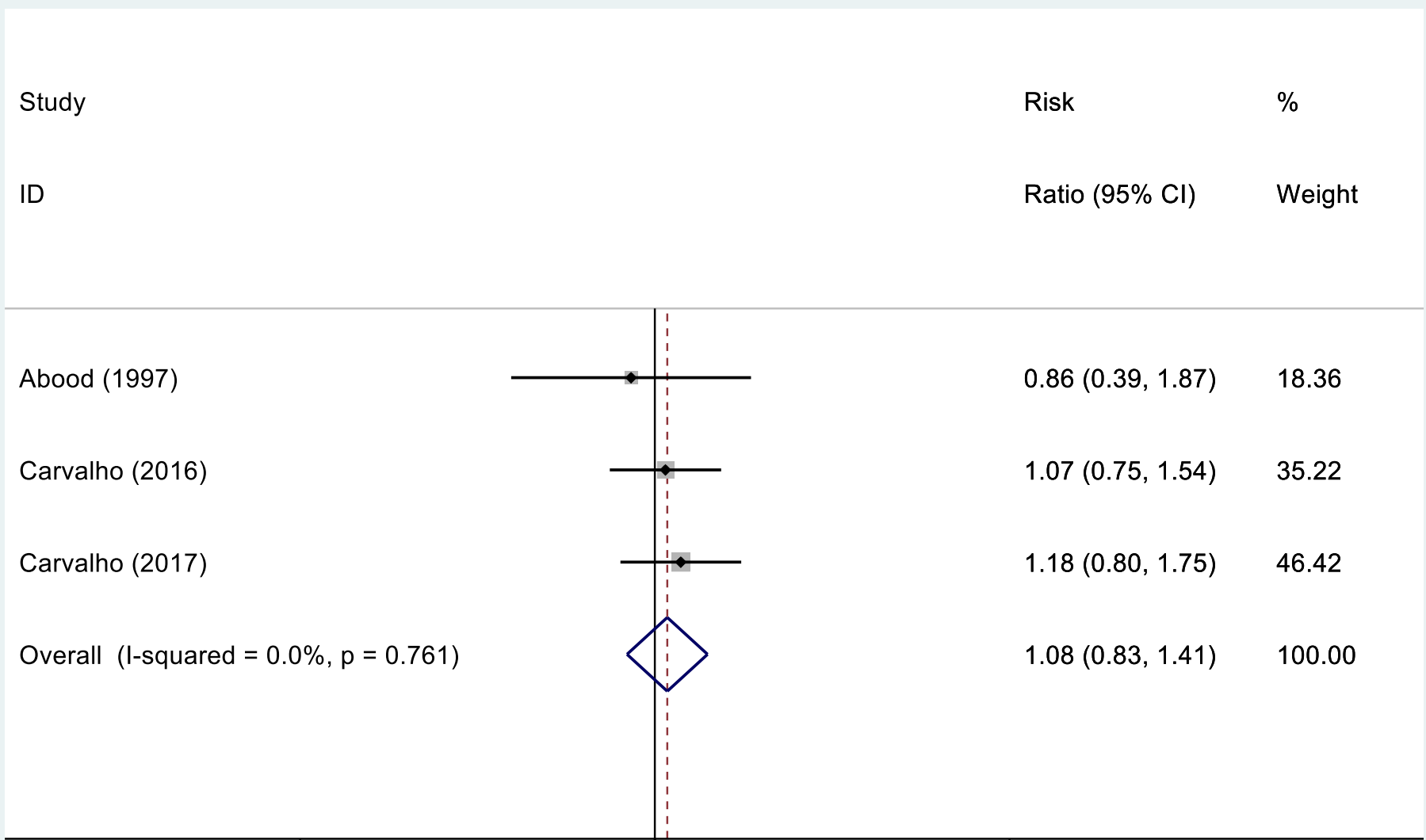
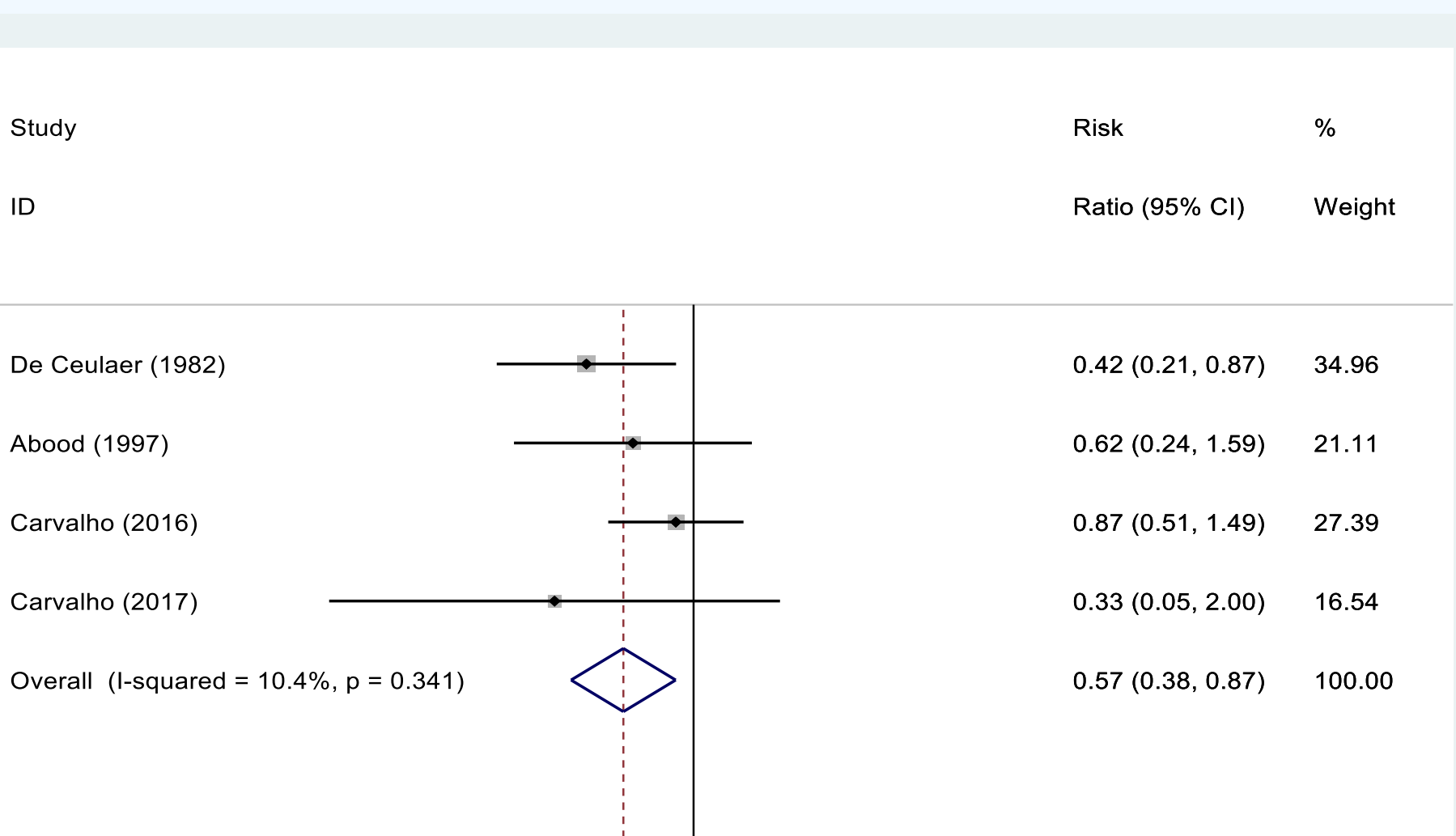
The first forest plot compared women who used progestogen only methods to a control group i.e. women receiving placebo or using non-hormonal methods. This estimate was based on four studies. There is a significant association between progestogen only method and a reduced frequency of crisis (RR = 0.57, 95% CI = 0.38-0.87). Those who used progestogen only methods had a 57% reduction in risk of increased crisis frequency compared to control groups. There was some evidence of heterogeneity (I² = 10.4%).

Combined hormonal contraception

We then compared women using combined hormonal contraception to a control group (see Figure 3). This was based on three studies²²⁻²⁴. The meta-analysis showed that combined hormonal contraception was not associated with an increased crisis frequency (RR = 1.08, CI = 0.83 - 1.41). There was no evidence of heterogeneity (I² = 0%).

Progestogen only vs Combined hormonal contraception

When comparing progestogen only and combined oral contraceptive methods, the meta-analysis suggested there may be a higher risk of increased crisis frequency when using combined hormonal contraception. However this was not statistically significant (RR = 0.66, CI = 0.41 - 1.06). There was no evidence of heterogeneity (I² = 0%).



DISCUSSION

The findings of our meta-analysis provide further evidence that no contraception should be contra-indicated in patients with SCD and progesterone may be protective against sickle cell crisis. It has been postulated that administration of progesterone results in a reduction in sickle crises due to stabilization of the red cell membrane with improved red cell survival²⁵. The findings of our systematic review and meta-analysis support this hypothesis. This suggests that in addition to being an effective form of contraception, progestogen only methods may have additional therapeutic benefits for women with SCD. The use of progestogen only methods was not associated with the development or increased risk of thrombosis.

From our review of the literature, specific adverse effects of the combined hormonal contraception in women with SCD were less clear. However, our meta-analysis showed no increase in sickle cell crisis with the use of combined hormonal contraception compared to control groups (95% CI, 0.83 - 1.41). Only six women reported VTE incidence with the use of combined hormonal contraception and any changes in haematological parameters did not reach significance

The use of an intrauterine device was not associated with any of the primary outcomes studied in this paper.

CONCLUSION

We report the use of hormonal contraception, including those containing oestrogen, is not associated with an increase in adverse effects in women with sickle cell compared to the background rate. Furthermore, progestogen-only contraceptives appear protective with regards to sickle cell crises.