

## Evidence Assessment: Summary of a Systematic Review

### Who is this summary for?

For Doctors and Health Personnel, Administrators and Managers of health facilities and partners involved in mother and child health.

## Vitamin E supplementation in pregnancy

### Key findings

- There was a reduction in the number of placentas coming away early (placental abruption) in women given vitamin E supplements in combination with other agents.
- Routine supplementation with vitamin E in combination with other supplements during pregnancy did not improve outcomes for babies or women.
- There may be harms associated with vitamin E supplements in pregnancy, as there was an increased risk of abdominal pain and term prelabour rupture of foetal membranes in women supplemented with vitamin E in combination with other supplements.

### Background

Does giving vitamin E supplementation, alone or in combination with other vitamins, given to women during pregnancy improve outcomes for their babies by reducing the incidence of pre-eclampsia and the number of babies born too early? Or does it cause harm?

Although vitamin E deficiency is rarely seen in healthy adults, for pregnant women, insufficient dietary vitamin E (found in vegetable oils, nuts, cereals and some leafy green vegetables) may lead to complications such as pre-eclampsia and the baby being born small. In addition, vitamin E deficiency can be made worse by too much iron and so it is important to investigate the optimum amounts for pregnancy.

### Questions

What are the effect of vitamin E supplementation, alone or in combination with other separate supplements, on pregnancy outcomes, adverse events, side effects and use of health services?

**Vitamin E supplementation in pregnancy in Cameroon.** According to the demographic and health survey the 2011, maternal mortality has doubled in Cameroon between 2002 and 2011 from 430 to 782 deaths per 100,000 live births. Vitamin E is not systematically used to prevent hypertension in pregnant women in Cameroon. This intervention could improve pregnancy outcomes in Cameroon.

**Table 1: Summary of the systematic review**

	<b>What the review authors searched for</b>	<b>What the review authors found</b>
<b>Studies</b>	Randomised or quasi-randomised controlled trials	Twenty one randomised or quasi-randomised controlled trials met the inclusion criteria
<b>Participants</b>	Pregnant women receiving vitamin E supplementation or control, living in areas where there is either inadequate dietary intake of vitamin E or where there is presumed adequate intake.	Pregnant women receiving vitamin E supplementation or control, living in areas where there is either inadequate dietary intake of vitamin E or where there is presumed adequate intake.
<b>Interventions</b>	Vitamin E supplementation, alone or in combination with other separate supplements.	Three trials supplemented women with vitamin E alone. Seventeen trials gave women supplements with vitamin E in addition to vitamin C. Of these, two trials supplemented women with additional supplements to vitamin E and vitamin C, either allopurinol or aspirin and fish oil (Rivas 2000). A further trial supplemented women with a vitamin E rich fraction of palm oil, however no further information was provided. Fifteen trials used the same dose of daily 400 international units (IU) vitamin E or 800 IU vitamin E. The dose of vitamin E was unknown for three trials.
<b>Controls</b>	Placebo, no placebo or other supplements	Placebo, no placebo or other supplements
<b>Outcomes</b>	<p><b>Primary outcomes :</b></p> <p><b>Maternal</b></p> <ol style="list-style-type: none"> <li>1. Development of clinical pre-eclampsia</li> <li>2. Maternal haematological measures: haemolytic anaemia, reticulocytosis, hyperbilirubinaemia and haemoglobin concentrations</li> <li>3. Preterm birth (defined as less than 37 weeks' gestation)</li> </ol> <p><b>Neonatal</b></p> <ol style="list-style-type: none"> <li>1. Stillbirth, neonatal death, perinatal death</li> <li>2. Infant haematological measures: haemolytic anaemia, reticulocytosis, hyperbilirubinaemia and haemoglobin concentrations</li> <li>3. Intrauterine growth restriction (defined as birthweight less than third centile or the most extreme centile reported)</li> </ol> <p><b>Secondary outcomes</b></p> <p><b>Maternal</b></p> <ol style="list-style-type: none"> <li>1. Prelabour rupture of membranes (PROM), preterm and at term</li> <li>2. Death up to six weeks postpartum</li> <li>3. Elective delivery (induction of labour or elective caesarean section)</li> <li>4. Caesarean section (emergency plus elective)</li> <li>5. Bleeding episodes (such as placental abruption, antepartum hemorrhage, postpartum hemorrhage, complications of epidural anaesthesia, need for transfusion)</li> </ol> <p><b>Neonatal</b></p> <ol style="list-style-type: none"> <li>1. Birthweight</li> <li>2. Infant death</li> <li>3. Gestational age at birth</li> <li>4. Congenital malformations</li> <li>5. Apgar score less than seven at five minutes</li> </ol>	For maternal primary outcomes, development of clinical preeclampsia was, bleeding episodes was reported in seven trials. For neonatal primary outcomes, stillbirth was reported in nine trials, neonatal deaths for nine trials, perinatal deaths. For secondary outcomes, birthweight was, PROM and maternal death was reported in seven trials.

**Date of the most recent search:** 31 March 2015.

**Limitations:** This is a high quality systematic review, **AMSTAR =11/11**

**Citation:** Rumbold A, Ota E, Hori H, Miyazaki C, Crowther CA. Vitamin E supplementation in pregnancy. Cochrane Database of Systematic Reviews 2015, Issue 9. Art. No.: CD004069. DOI: 10.1002/14651858.CD004069.pub3.

## Table 2: Summary of findings

<b>Any vitamin E supplementation versus placebo, no placebo or other supplements</b>			
<b>Population:</b> pregnant women receiving vitamin E supplement at ion or control, living in areas where there is either inadequate dietary intake of vitamin E or where there is presumed adequate intake.			
<b>Settings:</b> Australia, Brazil, Canada, Holland, India, Iran, Malaysia, Mexico, Peru, South Africa, Turkey, UK, USA, Vietnam, Venezuela.			
<b>Intervention:</b> any vitamin E supplement at ion versus placebo, no placebo or other supplements			
<b>Outcomes</b>	<b>Relative effect (95% CI)</b>	<b>No of Participants (studies)</b>	<b>Quality of the evidence (GRADE)</b>
<b>Stillbirth</b>	1.17 [0.88-1.56]	19023 (9)	Moderate
<b>Preterm birth (less than 37 weeks' gestation)</b>	0.98 [0.88-1.09]	20565 (11)	High
<b>Clinical pre- eclampsia (random- effects model)</b>	0.91 [0.79-1.06]	20878 (14)	Moderate
<b>Intrauterine growth restriction (various definitions)</b>	0.98 [0.91-1.06]	20202 (11)	High
<b>Prelabour rupture of fetal membranes - preterm</b>	1.27 [0.11-1.75]	1999 (12)	Low
<b>Bleeding episodes (placental abruption)</b>	0.64 [0.44-0.93]	14922 (7)	High

### Applicability

The 21 trials were from 15 countries including low- to high-income countries such as Australia, Brazil, Canada, Holland, India, Iran, Malaysia, Mexico, Peru, South Africa, Turkey, UK, USA, Vietnam, and Venezuela. These interventions are not resource intensive and may be applied in other low resources settings such as Cameroon.

### Conclusions

The large body of evidence does not support taking vitamin E supplements, alone or in combination, during pregnancy. This is because taking vitamin E in combination with other supplements during pregnancy does not help to prevent problems in pregnancy including stillbirth, baby death, preterm birth, pre-eclampsia or low birthweight babies.

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