Topical preparations for preventing stretch marks in pregnancy (Review)

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[Intervention Review]

Topical preparations for preventing stretch marks in pregnancy

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ABSTRACT

Background

Striae gravidarum (stretch marks developing during pregnancy) occur in 50% to 90% of women. They appear as red or purple lines or streaks that fade slowly to leave pale lines or marks on the skin. The abdomen, breasts and thighs are commonly affected. The exact cause of stretch marks is unclear and no preparation has yet been shown to be effective in preventing the development of stretch marks. They are a source of significant anxiety for women, impacting on their quality of life.

Objectives

To assess the effects of topical preparations on the prevention of stretch marks in pregnancy.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (31 October 2011) and reference lists of retrieved reports.

Selection criteria

We included randomised controlled trials and quasi-randomised controlled trials comparing topical preparations (with active ingredients) with other topical preparations (with active ingredients), with a placebo (that is, preparations without active ingredients) or with no treatment for the prevention of stretch marks in pregnant women.

Data collection and analysis

Three review authors independently assessed trial eligibility and trial quality, and extracted data. Data were checked for accuracy. The primary outcome was the presence of stretch marks and the secondary outcome was the severity of stretch marks.

Main results

We included six trials involving 800 women. Of the six trials, we judged the risk of bias for three as 'low risk' for random sequence generation, blinding of participants and personnel, blinding of outcome assessment, completeness of outcome data and selective reporting.

There was no statistically significant average difference in the development of stretch marks in women who received topical preparations with active ingredients compared to women who received a placebo or no treatment (average risk ratio (RR) 0.74; 95% confidence interval (CI) 0.53 to 1.03; five trials, 474 women; random-effects model, $Tau^2 = 0.09$, $I^2 = 65\%$) (Analysis 1.1).

Results were consistent with the main effects when we performed a sensitivity analysis excluding studies judged to be at high risk of bias for random sequence generation, allocation concealment or more than 20% missing data for a given outcome (average RR 0.81; 95% CI 0.60 to 1.10; four trials, 424 women; random-effects model, $Tau^2 = 0.05$, $I^2 = 57\%$).

The was no statistically significant average mean difference in the severity of stretch marks (standardised mean difference (SMD) -0.31; 95% CI -1.06 to 0.44; two trials, 255 women; $Tau^2 = 0.26$, $I^2 = 87\%$).

There was no statistically significant difference in the development of stretch marks in women who received topical preparations with active ingredients compared to women who received other topical preparations with active ingredients (average RR 0.51; 95% CI 0.16 to 1.60; two trials, 305 women; $Tau^2 = 0.53$, $I^2 = 74\%$). There was no statistically significant difference in the severity of stretch marks (mean difference (MD) -0.20; 95% CI -0.53 to 0.13; one trial, 206 women; heterogeneity not applicable).

Authors' conclusions

We found no high-quality evidence to support the use of any of the topical preparations in the prevention of stretch marks during pregnancy. There is a clear need for robust, methodologically rigorous randomised trials involving larger sample sizes to evaluate the effects of topical preparations on the development of stretch marks in pregnancy. In addition, it is important that preparations commonly used by women to prevent and treat stretch marks are evaluated within the context of robust, methodologically rigorous and adequately powered randomised trials.

PLAIN LANGUAGE SUMMARY

Topical preparations for preventing stretch marks in pregnancy

Stretch marks commonly develop during pregnancy, particularly in the third trimester. They affect 50% to 90% of women. They appear as red lines or streaks that fade slowly after the pregnancy to leave pale lines on the skin. The abdomen, breasts and thighs are most often affected. They do not disappear entirely, therefore any treatment which prevents them would be welcomed by many women. In this review, we identified randomised controlled trials and quasi-randomised controlled trials that compared topical creams, lotions and ointments containing active ingredients with placebo or no treatment, and topical preparations with active ingredients versus other topical preparations.

We included six trials (involving 800 women) in this review. We found that the application of a skin preparation to the areas affected by stretch marks during pregnancy did not prevent the development of stretch marks in the women during pregnancy. Only three trials (involving 461 women) looked at the severity of the stretch marks and did not show a clear difference. The preparations used included Alphastria, Trofolastin, Verum, olive oil and cocoa butter, which all contain vitamin E; Alphastria and Verum also have hyaluronic acid. Of the six trials, we judged three to be at low risk of bias. All trials were relatively small, with four of the six trials each including less than 100 women. The trials were also different in terms of when the women first started to use the topical applications, ranging from the first trimester to the first 20 weeks.

BACKGROUND

The following review is an update of the review 'Creams for preventing stretch marks in pregnancy' (Young 1996).

Description of the condition

Striae distensae (stretch marks), or striae gravidarum as they are known in pregnancy (Cunningham 2010), are considered to be the most common connective tissue change in pregnancy (Lawley 1999). Rates of occurrence of striae gravidarum vary (Salter 2006),

with reported rates ranging between 50% and 90% (Osman 2007). In primiparous women incidences of 52% (Atwal 2006), 61% (Osman 2007) and 87.7% (Ghasemi 2007) have been reported, while a rate of 71.1% was found in a study involving both primigravidae and multigravidae (Muzaffar 1998). Striae gravidarum seem to affect all racial groups (Buchanan 2010). Although once considered to be more common in white than in black or Asian women (Wong 1984; Wong 1989), more recently non-white women were seen to be at greater risk (Chang 2004). Striae gravidarum are common during the first pregnancy (Salter 2006) and usually present during the third trimester (Atwal 2006; Cunningham 2010). However, there have been reports in women under 24 weeks' gestation and of women first developing them in a second pregnancy (Chang 2004).

Striae have been defined as 'visible linear scars' (Burrows 2004: 46.6) that have evolved through recognised stages (Kang 1996) similar to the stages of tissue healing (Kang 1998; Salter 2006) or scar formation (Elson 1990). They manifest as 'reddish slightly depressed streaks' (Cunningham 2010: 111) or 'reddish purple linear macules' (Horn 2007: 947). They often fade gradually (Kang 1996; Kang 1998; Papoutsis 2007; Salter 2006) leaving glistening (Cunningham 2010), white depressed (Elson 1990) or pale wrinkled lines (Watson 1998) on the skin, from about six months following birth (Murray 2009). These glistening lines are commonly seen on multiparous women in addition to the reddish striae of the current pregnancy (Cunningham 2010). These benign skin changes (Atwal 2006) commonly occur on the abdomen but are also seen on the breasts and thighs (Cunningham 2010; Horn 2007; Osman 2008; Salter 2006; Thomas 2004), hips and buttocks (Horn 2007; Osman 2008) and groin and axillae (Papoutsis 2007). Striae have been reported as ranging in severity and have been graded as mild, moderate or severe by some authors (Atwal 2006; Osman 2007; Osman 2008). Atwal 2006: 966 developed and used a numerical system that captured the severity of striae, focusing on the number of striae present and the degree of erythema, or redness. A score of zero to three represented no striae or 'no significant striae', four to nine was considered 'mild', 10 to 15 as 'moderate' and greater than 16 represented 'severe striae'. Other criteria for assessing the severity of striae gravidarum include degrees of 'scaling, burning or stinging, or pruritus' (Kang 1996:520).

While attracting much discussion and debate over the years (Nigam 1989), the exact cause or origin of striae gravidarum remains in doubt (Ghasemi 2007; Lawley 1999; Osman 2007; Osman 2008; Wong 1984) and is understood poorly (Burrows 2010), with researchers disagreeing about their histopathological origins (Zheng 1985). Nevertheless, several risk factors have been identified. Early researchers attributed the development of striae to stretching (Wilks, 1861 cited by Poidevin 1959) and the stretch theory was accepted widely as the cause of striae gravidarum up until the middle of the last century (Poidevin 1959) when it became evident that other factors such as increased adrenal cortical activity may be involved (Poidevin 1959).

From his study of 116 primigravid women, Poidevin 1959 concluded that striae development was not solely reliant on stretching and that striae gravidarum should not be referred to as stretch marks. Poidevin 1959 proposed the existence of a 'striae factor' for each woman and while not identifying what this 'striae factor' may be, he found a clear relationship between the reduced glucose tolerance in pregnancy, a sign of adrenocortical hyperactivity, and the development of striae. This link between increased adrenocortical hormonal activity and striae gravidarum has been suggested by others (Liu 1974; McKenzie 1971). Liu 1974 asserts that striae gravidarum only develop in oestrogen and relaxin primed connective tissue, in response to stretching. Further, increased corticosteroid levels in pregnancy (Venning 1946) are thought to be a contributing factor. Oestrogen, relaxin and corticosteroids are thought to promote the formation of a type of mucopolysaccharide ground substance which promotes separation of the collagen fibrils (Bryant 1968) and the formation of striae gravidarum in response to stretch (Liu 1974). Collagen is responsible for the tensile strength of the skin (Waugh 2010) and under normal conditions the interfibrillar substance is highly viscous and there is no slipping or separation of collagen fibrils (Archer 2004). In pregnancy, the collagen mechanism is disrupted and irreversible sliding and separation of fibres occurs (Archer 2004). Liu 1974's position on the development of striae gravidarum is challenged by Shuster 1979, who contends that while the hormones of pregnancy may alter the collagen fibrils, there is no evidence to support this. Instead, Shuster 1979 suggests that striae are always due to stretching and, furthermore, only occur in immature connective tissue characterised by a "critical titre of rigid cross-linked collagen and elastic unlinked collagen" (Shuster 1979: 161), which may be a factor in the higher risk of striae in younger women identified in some studies (Atwal 2006; Murphy 1992; Thomas 2004). The stretching factor is supported by Thomas 2004 who suggest that the degree of stretch applied is also influential.

Further insight into the pathogenesis of striae is given by Watson 1998 who suggests that the development of striae is related to changes in the dermal elastic fibres rather than the collagen. They hypothesised that striae may occur in individuals where there is a deficiency in 'cutaneous fibrillin' and can arise in conditions like pregnancy where there is extra stretching on the skin. The extra strain or stretching could be sufficient to tear the elastic fibre network, resulting in the formation of striae (Watson 1998). Perhaps corticosteroids may also be influential here as they are thought to weaken the 'dermal elastic fibres' leading to their tearing (McKenzie 1971: 774). However, it is far from conclusive, as Zheng 1985 suggest that striae are scars and are not due to rupture of the connective tissue in response to stress. They found that the elastic fibres and collagen arrangement were in keeping with a scar. Furthermore, they are characterised by absent rete ridges and a thinning and flattening of the overlying epidermis (Zheng 1985) and are devoid of sweat glands or hair follicles.

While hormonal influences and stress or stretching factors continue to be considered important in the development of striae (Lawley 1999), other risk factors have been associated with the development of striae gravidarum (Salter 2006). Identified risk factors include family history, race, skin type, birthweight, baseline body mass index, weight gain and inadequate nutrition (Osman 2007), younger maternal age, increased pregnancy weight gain, use of corticosteroids and a genetic susceptibility (Papoutsis 2007). A number of researchers identified younger maternal age as a risk factor for the development of striae (Atwal 2006; Murphy 1992; Thomas 2004) while others found no association with age (Ghasemi 2007). Greater weight gain (Atwal 2006; Murphy 1992) and higher body mass (Thomas 2004) have been identified as significant factors in the development of striae by some researchers while Chang 2004 indicated that weight gain and changes in weight during pregnancy were less predictive of the development of striae than were genetic factors. A personal history of breast or thigh striae and genetic factors were thought to be the most predictive for the development of striae (Chang 2004). Family history was also identified by Osman 2007, where women with a family history of striae gravidarum were more likely to have moderate to severe striae gravidarum compared to those with no family history. Finally, a number of researchers have identified a significant relationship between the development of striae gravidarum and an increased infant birthweight (Atwal 2006; Ghasemi 2007; Murphy 1992).

Striae have been a significant anxiety for women since early times (Salter 2006). They are an aesthetic concern for many women (Atwal 2006; Chang 2004; Ghasemi 2007; Osman 2007; Osman 2008; Rangel 2001) and can also be a source of stress (Chang 2004; Mallol 1991; Salter 2006). They may also cause itching (Horn 2007; Lawley 1999; Martius 1973; Muzaffar 1998; Papoutsis 2007; Salter 2006) or a burning sensation (Salter 2006) for some women. Authors differ in their evaluation of how symptomatic or not they are; some see them as often symptomatic (Salter 2006) while others report them as usually asymptomatic (Papoutsis 2007).

Description of the intervention and how the intervention might work

Many writers refer to the challenges of treating striae (Alster 1997; Elsaie 2009; Papoutsis 2007), while their prevention has attracted somewhat less attention. Some argue that it may not be possible to prevent striae (Cunningham 2010). Yet, there are an abundance of products on the market claiming to prevent striae (Summers 2009). Consequently, over the years women have used many approaches and preparations to either prevent or treat striae gravidarum, and often at great expense (Salter 2006). It appears that there are no specific treatments for striae (Elsaie 2009; Errickson 1994; Salter 2006) and no preparation has yet been found to be effective in preventing or healing the lines that remain (Papoutsis 2007). Approaches or preparations used in the prevention and treatment include topical preparations, lasers or pulsed light (Elsaie 2009). However, only topical preparations are considered safe to use in pregnancy and the theoretical reasoning for how they are thought to work include:

- stimulation of fibroblastic activity leading to increased production of collagen and fibronectin (Brinkhaus 2000; Elsaie 2009);
- increased blood perfusion through massaging of the area and potential anti-inflammatory effects (Wierrani 1992);
- Increased skin hydration (Elsaie 2009).

Why it is important to do this review

Striae gravidarum affect between 50% and 90% of women (Osman 2007) during pregnancy and usually remain as silvery scar lines on the skin. They are an unwanted consequence of pregnancy, impacting on women's perception of themselves (Osman 2008) and their quality of life (Salter 2006), and are thus of significant concern to women of child bearing age.

There are many unproven products on the market (Burrows 2010) tried by many women. Consequently, many women incur great expense (Salter 2006) trying to prevent or treat striae (Osman 2008). It is important, therefore, to systematically assess the evidence on the effectiveness of these creams and preparations in the prevention of striae. The findings of this review will benefit both women and healthcare professionals. The review will assist women to make informed decisions about their choice of treatment to prevent striae gravidarum and inform healthcare practitioners when advising women on the effectiveness of topical preparation for the prevention of striae gravidarum.

OBJECTIVES

To assess the effects of topical preparations on the prevention of stretch marks in pregnancy.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised and quasi-randomised controlled trials comparing topical preparations (with active ingredients) with other topical preparations (with active ingredients), with a placebo (that is, preparations without active ingredients) or with no treatment.

Types of participants

Pregnant women prior to 20 weeks' gestation, including women expecting their first or subsequent babies and women experiencing multiple pregnancies.

Types of interventions

For the purpose of this review topical preparations are categorised as follows.

1. Creams or lotions with active ingredients

Creams and lotions are defined as emulsions with moisturising and emollient effects. They can be either be an 'oil-in-water' or a 'water-in-oil' emulsion (Hunter 1973). Viscosity determines whether an emulsion is categorised as a lotion or a cream.
Examples include:

- Trofolastin cream (containing Centella asiatica extract, alpha tocopherol and collagen-elastin hydrolysates) (Mallol 1991);
- Alphastria cream (containing hyaluronic acid, vitamins A and E, allantoin and calcium pantothenate) (de Buman 1987);
- cocoa butter lotion (containing cocoa butter and tocopheryl acetate (vitamin E) (Osman 2008).

2. Ointments with active ingredients

Ointments are defined as semi-solid preparations and can be of three types: those that are 'water soluble', those that 'emulsify with water', or those that 'repel water' (Hunter 1973: 412).
Examples include:

- Verum ointment (containing vitamin E, essential free fatty acids, panthenol, hyaluronic acid, elastin and menthol) (Wierrani 1992).

For the purpose of this review, a placebo is a topical preparation without active ingredients, or 'no treatment'.

Comparisons

1. Topical preparations with active ingredients compared with placebo or no treatment
2. Topical preparations with active ingredients compared with other topical preparations with active ingredients

Types of outcome measures

Primary outcomes

1. Presence of stretch marks

Secondary outcomes

1. Severity of stretch marks

Search methods for identification of studies

Electronic searches

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting the Trials Search Co-ordinator (31 October 2011). The Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

1. quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE;
3. weekly searches of EMBASE;
4. handsearches of 30 journals and the proceedings of major conferences;
5. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL, MEDLINE and EMBASE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Specialized Register' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.
Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Co-ordinator searches the register for each review using the topic list rather than keywords.

Searching other resources

We searched the reference lists of all the identified studies and retrieved one trial (Msika 2002).
We did not apply any language restrictions.

Data collection and analysis

For methods used in previous versions of this review, please see Appendix 1.
Methods for this update of the review are informed by the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Selection of studies

Three review authors (M Brennan, D Devane, and G Young (MB, DD and GY) independently assessed all potential studies identified for inclusion as a result of the search strategy. We would have resolved any disagreements through discussion but this was not necessary.

Data extraction and management

We designed a form to extract data. For eligible studies, three review authors (MB, DD and GY) extracted the data using the agreed form. We resolved discrepancies through discussion. We contacted authors from two trials (Horace Fletcher for Buchanan 2010; P Msika for Msika, unknown year) for further information (see notes in Characteristics of included studies). All data were entered into the Review Manager software (RevMan 2011) and checked for accuracy by the three review authors (MB, DD and GY).

Assessment of risk of bias in included studies

Three review authors (MB, DD and GY) independently assessed the risk of bias for each study using criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). If there had been any discrepancies we would have resolved them through discussion, but this was not necessary.

(1) Random sequence generation (checking for possible selection bias)

We described for each included study the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.
We assessed the method as:

- low risk (any truly random process, e.g. random number table; computer random number generator);
- high risk (any non-random process, e.g. odd or even date of birth; hospital or clinic record number);
- unclear risk (insufficient information to permit judgment).

(2) Allocation concealment (checking for possible selection bias)

We described for each included study the method used to conceal the allocation sequence and determined whether intervention allocation could have been foreseen in advance of or during recruitment, or changed after assignment.
We assessed the methods as:

- low risk (e.g. telephone or central randomisation; consecutively numbered sealed opaque envelopes);
- high risk (open random allocation; unsealed or non-opaque envelopes; alternation; date of birth);
- unclear risk (insufficient information to permit judgment).

(3) Blinding of participants and personnel (checking for possible performance bias)

We described for each included study the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We considered that studies were at low risk of bias if they were blinded or if we judged that the lack of blinding could not have affected the results.
We assessed the methods as:

- low risk, high risk or unclear risk for participants;
- low risk, high risk or unclear risk for personnel.

(4) Blinding of outcome assessment (checking for possible detection bias)

We described for each included study the methods used, if any, to blind outcome assessors from knowledge of which intervention a participant received. We considered that studies were at low risk of bias if they were blinded, or if we judged that the lack of blinding could not have affected the results.
We assessed the methods as:·

- low risk (no blinding of outcome assessment but the authors judged that the outcome was not likely to be influenced by this);
- high risk (no blinding of outcome assessment and the outcome measurement was likely to have been influenced by this);
- unclear risk (insufficient information to permit judgment; the study did not address this).

(5) Incomplete outcome data (checking for possible attrition bias through withdrawals, dropouts, protocol deviations)

We described for each included study, and for each outcome or class of outcomes, the completeness of data including attrition and exclusions from the analysis. We stated whether attrition and exclusions were reported, the numbers included in the analysis at each stage (compared with the total number of randomised participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information was reported, or was supplied by the trial authors, we re-included the missing data in the analyses we undertook.
We assessed the methods as:

- low risk (20% or less of missing data);
- high risk (more than 20% of missing data);
- unclear risk (insufficient reporting to permit judgment; the study did not address this).

(6) Selective reporting (checking for reporting bias)

We investigated the possibility of selective outcome reporting bias by identifying the outcomes in the study protocol (if available) and in the methods section of the publication, and by cross-checking to see if these outcomes were reported in the results section of the trial publication(s). PubMed and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (http://www.who.int/ictrp/en/) were searched for the study protocols.
We assessed the methods as:

- low risk (where it was clear that all of the study's pre-specified outcomes as identified in the study protocol (where available) and in the method's section were reported on; that all expected outcomes of interest to the review were reported on);
- high risk (where it was clear that not all of the study's pre-specified outcomes as identified in the study protocol (where available) and in the method's section were reported on; failure to include a key outcome that would have been expected to have been included);
- unclear risk (insufficient information to permit judgment).

(7) Other bias (checking for other biases)

We described for each included study any important concerns we had about other possible sources of bias. We assessed whether each study was free of other problems that could put it at risk of bias as follows:

- low risk (study appeared to be free of bias);
- high risk (had at least one important risk of bias, for example related to study design);
- unclear risk (insufficient information to permit judgment).

Measures of treatment effect

Dichotomous data

For dichotomous data, we presented the results as summary risk ratio (RR) with 95% confidence interval (CI).

Continuous data

For continuous data, we used the mean difference for outcomes measured in the same way between trials. We used the standardised mean difference to combine trials that measured the same outcome but used different scales.

Unit of analysis issues

Cluster-randomised trials

We did not identify any cluster-randomised trials in our search. In future updates of this review, if we identify any cluster-randomised trials we will include them along with individually randomised trials. We will adjust their sample sizes using the methods described in the *Handbook for Systematic Reviews of Interventions* (Higgins 2011) using an estimate of the intracluster correlation co-efficient (ICC) derived from the trial (if possible), from a similar trial, or from a study of a similar population. If we use ICCs from other sources we will report this and conduct sensitivity analyses to investigate the effect of variation in the ICC. If we identify cluster-randomised trials and individually-randomised trials we will synthesise the relevant information. We will consider it reasonable to combine the results from both where there is little heterogeneity between the study designs and where we consider that there is unlikely to be an interaction between the effect of the intervention and the choice of randomisation unit. We will acknowledge heterogeneity in the unit of randomisation and perform a sensitivity analysis to investigate the effects of this heterogeneity on the review findings.

Dealing with missing data

For included studies, we noted the levels of attrition.
For all outcomes we carried out analyses, as far as possible, on an intention-to-treat basis, that is we attempted to include all participants randomised to each group in the analyses, and all participants were analysed in the group to which they were allocated regardless of whether or not they received the allocated intervention. The denominator for each outcome in each trial was the number randomised minus any participants whose outcomes were known to be missing.

Assessment of heterogeneity

We assessed statistical heterogeneity in each meta-analysis using the Tau² (tau-squared), I², and X² (Chi²) statistics. We regarded heterogeneity as substantial if:
(a) the I² value was high (exceeding 30%); and
either
(b) there was inconsistency between trials in direction or magnitude of effects (judged visually), or a low (< 0.10) P value in the Chi² test for heterogeneity;
or
(c) the estimate of between-study heterogeneity (Tau²) was above zero.

Assessment of reporting biases

As there were less than 10 studies included in the meta-analysis we did not investigate publication bias using funnel plots. In future updates of this review, if there are 10 or more studies included in the meta-analysis, we will assess funnel plot asymmetry visually and use formal tests for funnel plot asymmetry. For continuous outcomes, we will use the test proposed by Egger 1997, and for dichotomous outcomes we will use the test proposed by Harbord 2006. If asymmetry is detected in any of these tests or is suggested by a visual assessment, we will performed exploratory analyses to investigate it.

Data synthesis

We carried out statistical analysis using the Review Manager software (RevMan 2011). As there was clinical diversity in respect of

the interventions, that is each trial used a different topical preparation with different active ingredients, we used a random-effects model meta-analysis to produce an overall summary of the average treatment effect across the six included trials. This random-effects summary is treated as the average range of possible treatment effects and therefore the true effect differs in the different trials or varies '...across studies about an overall pooled value' (Riley 2011). For each outcome reported, we presented the results of the random-effects model analyses as the average treatment effect with its 95% confidence interval, and the estimates of Tau^2 and I^2.

Subgroup analysis and investigation of heterogeneity

We neither planned nor conducted any subgroup analyses.
In future updates of this review, if we identify substantial heterogeneity we will investigate it using subgroup analyses and sensitivity analyses. We will consider whether an overall summary is meaningful and, if it is, use random-effects model analysis to produce it.
We plan to carry out the following subgroup analysis.

1. Parity (nulliparous versus multiparous women).

Subgroup analysis will be restricted to primary outcomes.
We will assess subgroup differences by the interaction tests available within RevMan (RevMan 2011). We will report the results of subgroup analyses quoting the χ^2 statistic and P value, and the interaction statistic I^2 value.

Sensitivity analysis

The previous version of this review (Young 1996) did not include any a priori sensitivity analysis. In this update we undertook a sensitivity analysis by trial quality, by removing from the analysis those studies judged to be at high risk of bias for random sequence generation, allocation concealment, or with more than 20% missing data for a given outcome. In future updates of this review, the criteria for sensitivity analysis will broaden to determine the effect of also excluding trials judged to be at high risk of bias for blinding.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of studies awaiting classification.

Results of the search

Our updated search identified a total of 13 reports relating to 12 trials (Buchanan 2010; de Buman 1987; Lachmann 2011; Mallol 1991; Martius 1973; Mendez Velarde 2010; Msika 2002; Ortega 1985; Osman 2008; Puder 1965; Taavoni 2011; Wierrani 1992). Eight new potential trials for inclusion were identified (Buchanan 2010; de Buman 1987; Lachmann 2011; Mendez Velarde 2010; Msika 2002; Ortega 1985; Osman 2008; Taavoni 2011) in addition to the four studies (Mallol 1991; Martius 1973; Puder 1965; Wierrani 1992) included in the previous version of this review (Young 1996). All of the trials were retrieved via the search of the Cochrane Pregnancy and Childbirth Group Trials Register with the exception of two studies (Lachmann 2011; Msika 2002). Msika 2002 was found from searching reference lists of retrieved studies and Lachmann 2011 via communication with Expanscience Laboratories in France during our attempts to get more information on Msika 2002. Other searches did not yield any further potentially eligible studies.
This updated review includes six studies (involving 800 women). Two additional trials (Lachmann 2011; Ortega 1985) are awaiting classification. Despite translating the paper, there was insufficient information on the randomisation process to judge if the study by Ortega 1985 was eligible for inclusion and attempts to contact the authors have been unsuccessful (see Studies awaiting classification). We are awaiting the translated report of Lachmann 2011 from Expanscience Laboratories (France).

Included studies

This update includes four (Buchanan 2010; de Buman 1987; Osman 2008; Taavoni 2011) new studies bringing the total number of included studies to six (involving a total of 800 women) (Buchanan 2010; de Buman 1987; Mallol 1991; Osman 2008; Taavoni 2011; Wierrani 1992) (see Characteristics of included studies).
Included studies were undertaken in Germany (de Buman 1987), Spain (Mallol 1991), Austria (Wierrani 1992), West Indies (Buchanan 2010), Lebanon (Osman 2008) and Iran (Taavoni 2011) and were conducted mainly in antenatal clinics and medical centres.
Two studies compared topical preparations with active ingredients with placebo, that is Trofolastin (which contains Centella asiatica extract, alpha tocopherol and collagen-elastin hydrolysates) versus placebo cream (Mallol 1991) and cocoa butter lotion versus placebo lotion (Osman 2008). Two studies compared topical preparations with active ingredients with no treatment, that is olive oil versus no treatment (Taavoni 2011) and Verum ointment (which contains vitamin E, essential free fatty acids (vitamin F), panthenol, hyaluronic acid, elastin and menthol) versus no treatment (Wierrani 1992). One study compared topical preparations with active ingredients with other topical preparations with active ingredients, that is cocoa butter cream versus a similar cream

with vitamin E and other constituents but without cocoa butter (Buchanan 2010). Finally, one study included two intervention groups and a placebo group; topical preparations with active ingredients were compared with other topical preparations with active ingredients, and topical preparations with active ingredients were compared with placebo, that is Alphastria cream (which contains hyaluronic acid, vitamin A, vitamin E, allantoine, calcium pantothenate) versus a cream with vitamins and excipients, and Alphastria cream and cream with vitamins and excipients versus a cream with excipients only (de Buman 1987).

Excluded studies

For this update, we have added two new excluded studies (Mendez Velarde 2010; Msika 2002) bringing the total number of excluded studies to four (Martius 1973; Mendez Velarde 2010; Msika 2002; Puder 1965) (see Characteristics of excluded studies).

Risk of bias in included studies

We assessed the risk of bias in the included studies (Figure 1; Figure 2). Overall, the studies were at low or unclear risk of bias across most domains (Figure 1). No study was at low risk of bias across all seven domains, while three studies (Buchanan 2010; Mallol 1991; Osman 2008) were at low risk of bias across five of the seven domains and one study (Taavoni 2011) was at low risk of bias across four of the seven domains. All of the included studies were at unclear risk of bias for allocation concealment except for Wierrani 1992, which was at high risk of bias (Figure 2). Details of risk of bias within domains and across studies are given below.

Figure 1. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

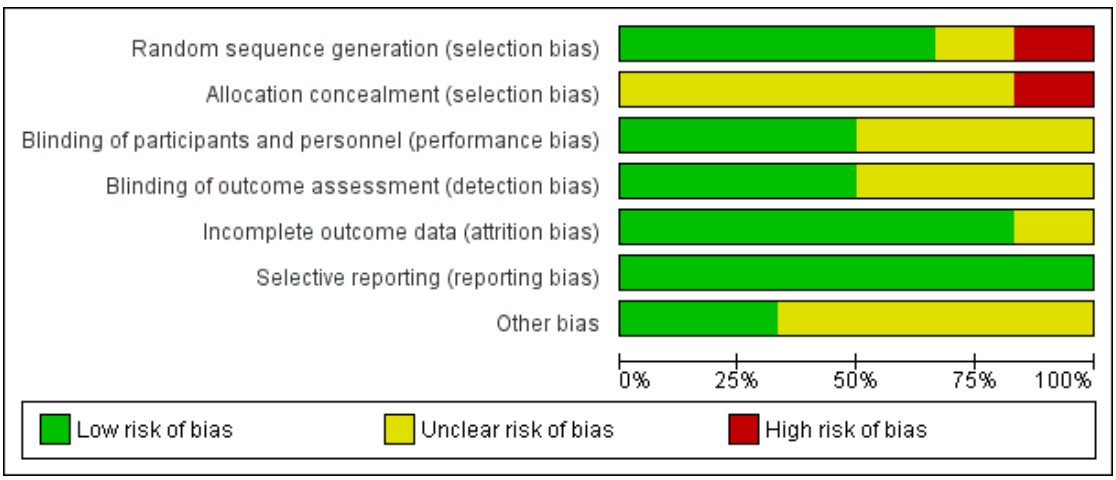
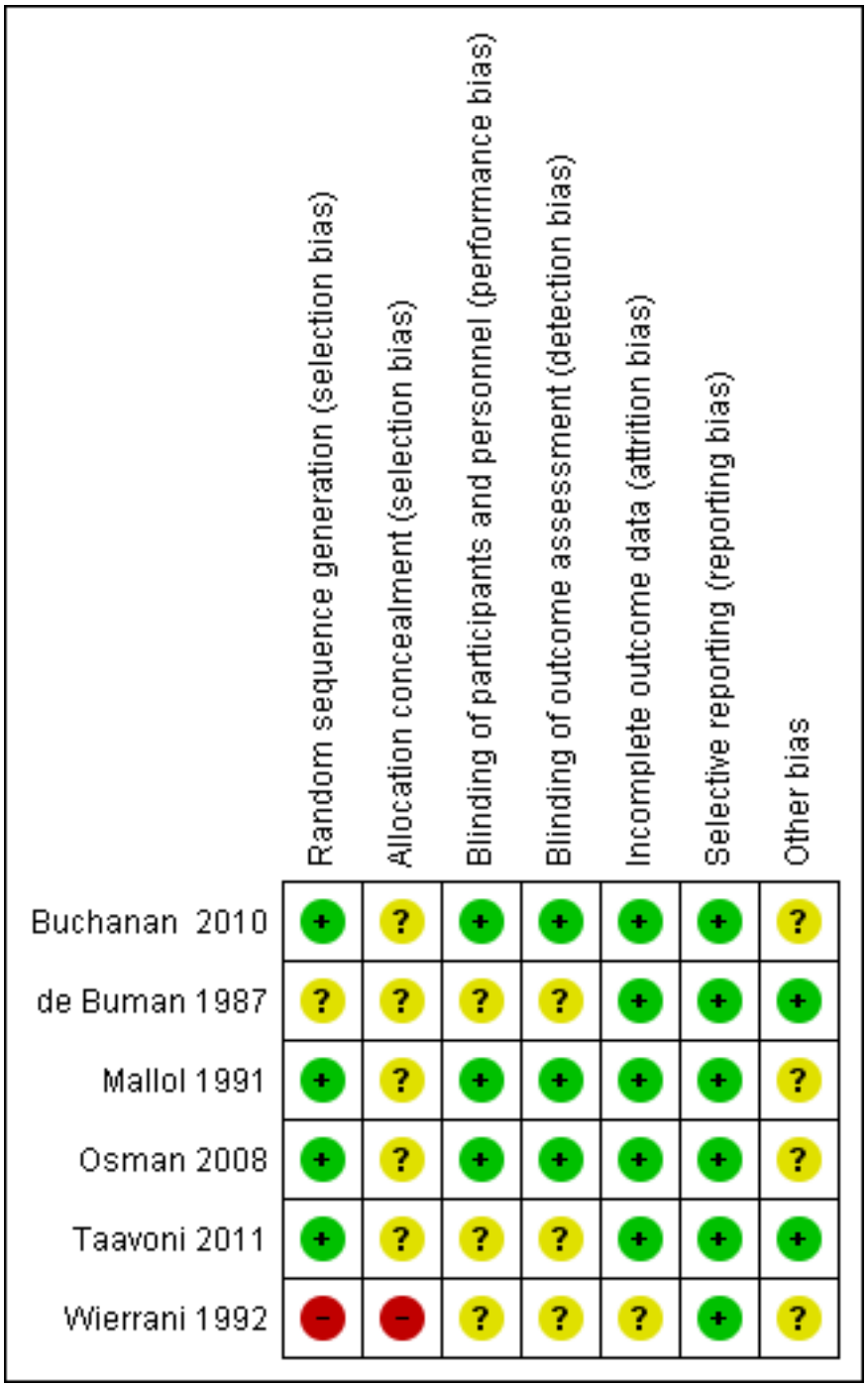


Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

Four of the six included studies (Buchanan 2010; Mallol 1991; Osman 2008; Taavoni 2011) were at low risk of bias in random sequence generation, one was at unclear risk (de Buman 1987) and one was at high risk (Wierrani 1992). de Buman 1987 was at unclear risk due to insufficient information to judge the risk of bias, while Wierrani 1992 was at high risk of bias as alternate day allocation was used to enrol women in the treatment groups. On uneven dates women were included in the treatment group and on even dates women were enrolled in the no treatment group.

Five of the six included studies (Buchanan 2010; de Buman 1987; Mallol 1991; Osman 2008; Taavoni 2011) were at unclear risk of bias in allocation concealment and Wierrani 1992 was at high risk of bias. Two of the six studies, with unclear risk of bias for allocation concealment (Buchanan 2010; de Buman 1987), had insufficient information to judge the risk of bias while three of the other four (Mallol 1991; Osman 2008; Taavoni 2011) reported insufficient information on how women were allocated to the study groups. In Wierrani 1992 randomisation was performed according to day of treatment (that is, alternate days).

Blinding

Three of the six included studies (Buchanan 2010; Mallol 1991; Osman 2008) were at low risk of bias in blinding of participants and personnel and in blinding of outcome assessment. Three of the six included studies were at unclear risk (de Buman 1987; Taavoni 2011; Wierrani 1992) due to insufficient or no information reported to permit judgement of risk of bias for performance or detection bias.

Incomplete outcome data

Five of the six included studies (Buchanan 2010; de Buman 1987; Mallol 1991; Osman 2008; Taavoni 2011) were at low risk of bias for incomplete outcome data and one study was at unclear risk (Wierrani 1992). In the study by Wierrani 1992 the number of women randomised was not given, only the number of women included in the analysis. In the Mallol 1991 trial report it was not stated explicitly how many women were randomised, but it was stated that 'The assay was carried out on 100 pregnant women'. They reported total 'valid' cases as 41 for intervention (active cream) and 39 for placebo. Assuming 100 women were randomised, then 20 women were excluded from the analysis overall, giving 20% incomplete outcome data (low risk) (see Characteristics of included studies).

Selective reporting

All of the six included studies (Buchanan 2010; de Buman 1987; Mallol 1991; Osman 2008; Taavoni 2011; Wierrani 1992) were at low risk of bias in selective reporting.

Other potential sources of bias

We judged two of the six included studies (de Buman 1987; Taavoni 2011) to be at low risk of other biases, and four studies (Buchanan 2010; Mallol 1991; Osman 2008; Wierrani 1992) at unclear risk of other biases. In the studies by Mallol 1991 and Wierrani 1992, the number of women randomised to each group were not stated explicitly, while in the studies by Buchanan 2010; and Osman 2008 the researchers raised concerns regarding intervention fidelity. Buchanan 2010: 68 stated '...that it was not possible to verify that the patients were using the cream as instructed or whether they were sharing the cream or using other creams', while Osman 2008: 1142 stated that 'Reports of compliance varied greatly for each patient and assessors reported that women may have been telling them what they wanted to hear when they asked about compliance'. They acknowledged that compliance may have been an issue in the study but that use of the study lotion reflected general population use (Osman 2008: 1142). Therefore, we judged Buchanan 2010 and Osman 2008 to be at unclear risk of other biases.

The source of funding was not identified for all but two of the included studies, Osman 2008 where both intervention and placebo lotions were provided by ET Browne Drug Company, Inc and Taavoni 2011 where the authors declared no funding source.

Effects of interventions

This updated review now includes data from six studies involving 800 women.

1. Topical preparations with active ingredients compared with placebo or no treatment (five trials and 474 women)

This comparison includes data from the following studies: de Buman 1987; Mallol 1991; Osman 2008; Taavoni 2011; Wierrani 1992.

Primary outcome (five trials and 474 women)

There was no statistically significant average difference in the development of stretch marks in women who received topical preparations with active ingredients compared to women who received a placebo or no treatment (average risk ratio (RR) 0.74; 95% confidence interval (CI) 0.53 to 1.03; five trials, 474 women; random-effects model, $Tau^2 = 0.09$, $I^2 = 65\%$) (Analysis 1.1).

Results were consistent with the main effects when we performed a sensitivity analysis, excluding the Wierrani 1992 study which was at high risk of bias for random sequence generation and allocation concealment (average RR 0.81; 95% CI 0.60 to 1.10; four trials, 424 women; random-effects model, $Tau^2 = 0.05$, $I^2 = 57\%$).

Secondary outcome (two trials and 255 women)

There was no statistically significant average mean difference in the severity of stretch marks in women who received topical preparations with active ingredients compared to women who received a placebo or no treatment (standardised mean difference (SMD) -0.31; 95% CI -1.06 to 0.44; two trials, 255 women; random-effects model, $Tau^2 = 0.26$, $I^2 = 87\%$) (Analysis 1.2). The heterogeneity between the two trials was large and therefore the average result may not be meaningful, that is it is unlikely that such an average effect would be found in real life (the effect could be similar to one or other of the trials, but unlikely to be an 'average' of both).

2. Topical preparations with active ingredients compared with other topical preparations with active ingredients (two trials and 305 women)

This comparison included two studies with 305 women (Buchanan 2010; de Buman 1987). Buchanan 2010 compared cocoa butter cream, which contained a variety of constituents for example 25% cocoa butter, glycerin, isopropyl palmitate, hydrolysed collagen, hydrolysed elastin and tocopheryl acetate (vitamin E) with a cream identical to the intervention cream but without the 25% cocoa butter. In the second trial (de Buman 1987), Alphastria cream (containing hyaluronic acid, vitamin A, vitamin E, allantoine, calcium pantothenate) was compared with a cream with vitamins and excipients.

Primary outcome

There was no statistically significant average difference in the development of stretch marks in women who received topical preparations with active ingredients compared to women who received other topical preparations with active ingredients (average RR 0.51; 95% CI 0.16 to 1.60; two trials, 305 women; random-effects model, $Tau^2 = 0.53$, $I^2 = 74\%$) (Analysis 2.1).

Secondary outcome (one trial and 206 women)

The was no statistically significant mean difference in the severity of stretch marks in women who received topical preparations with active ingredients compared to women who received other topical preparations with active ingredients (mean difference (MD) -0.20; 95% CI -0.53 to 0.13; one trial, 206 women; heterogeneity not applicable) (Analysis 2.2).

DISCUSSION

Stretch marks are a very common connective tissue change that can occur in pregnancy (Lawley 1999), affecting between 50% and 90% (Osman 2007) of women and remaining as silvery scar lines on the skin. They are an unwanted consequence of pregnancy, impacting on women's perception of themselves (Osman 2008) and their quality of life (Salter 2006), and are thus of significant concern to women of child bearing age. There are many products of unproven effectiveness on the market (Burrows 2010), which are tried by many women. This review assessed the effects of topical preparations on the prevention of stretch marks in pregnancy.

The review includes six trials (involving a total of 800 women) conducted mainly in antenatal clinics and medical centres in varied geographical locations. It should be noted that the random-effects model summaries presented are the average effects found for both the development and severity of stretch marks. The use of the random-effects model is based on the assumption that the treatment effect will be different across the studies due to heterogeneity between the studies. It therefore calculates the average of all the treatment effects across the trials (Riley 2011) and thus may not be the actual effect in any of the included studies.

Summary of main results

Topical preparations with active ingredients compared with placebo or no treatment

This review found that there was no statistically significant average difference in the development of stretch marks in women who received topical preparations with active ingredients compared to women who received a placebo or no treatment. All studies were relatively small, with four of the five trials including less than 100 women (de Buman 1987; Mallol 1991; Taavoni 2011; Wierrani 1992) and one trial by Osman 2008 including less than 200 women as reflected in the narrower confidence interval.

Trials differed in relation to the timing of commencement of the topical applications. Three of the five studies included women presenting in trimester one (de Buman 1987; Mallol 1991; Osman 2008) while Taavoni 2011 and Wierrani 1992 recruited women at 18 to 20 weeks and 20 weeks' gestation, respectively. All trials recruited women prior to the third trimester when stretch marks usually occur (Atwal 2006; Cunningham 2010).

Parity of the women participating in the included trials also differed. Mallol 1991 included both multigravidae and primigravidae, while Taavoni 2011 and Osman 2008 included primigravidae women only in their studies. The study by de Buman 1987 identifies that one case of stretch marks occurred in a twin pregnancy in the intervention group receiving with active ingredients (Group A). No information on parity was given for the other included study (Wierrani 1992). It is likely, therefore, that some of

the women in some trials had stretch marks from an earlier pregnancy, while the inclusion of some women with a multiple pregnancy may have increased the likelihood of those women developing stretch marks. In a multiple pregnancy there may be extra strain and, as suggested by Watson 1998, extra strain or stretching could be sufficient to tear the elastic fibre network, resulting in the formation of striae.

While topical preparations varied, many of them included some common ingredients. For example, two trials (de Buman 1987; Wierrani 1992) included hyaluronic acid in the active topical preparation (that is Alphastria cream and Verum ointment, respectively). Hyaluronic acid has been identified as stimulating fibroblastic activity (de Buman 1987), and fibroblasts are key cells in maintaining tissue structure and tone. A number of the preparations also contained vitamin E (de Buman 1987; Mallol 1991; Osman 2008; Taavoni 2011; Wierrani 1992), which promotes the development of the intracellular substance (Wierrani 1992) and is a known antioxidant used in many skin products. However, it is not evident which, if any, of these ingredients could exert a possible preventative action for the formation of striae.

We found no statistically significant average difference in the severity of stretch marks in women who received topical preparations with active ingredients compared to women who received a placebo or no treatment. Data on the severity of stretch marks were only available in two of the five included studies (Mallol 1991; Osman 2008). In the study by Osman 2008, severity was assessed by trained assessors using a validated tool, while Mallol 1991 refers to using 'an arbitrary score 0 = no striae, 1 = few and thin striae, 2 = many thin striae or few thick striae, and 3 = many thick striae'. Neither study refers to inter-rater reliability and therefore it is unclear how errors in measurement were minimised.

From a clinical perspective while none of the topical products in the included trials (Alphastria cream, Trofolastin, cocoa butter lotion, olive oil, and Verum), with the exception of cocoa butter lotion (Osman 2008) and olive oil (Taavoni 2011), appear to be widely available, some women may indeed be applying cocoa butter lotion or olive oil in the hope of preventing the development of stretch marks. However, this review found no statistically significant average difference in the development of stretch marks in women who received topical preparations with active ingredients compared to women who received a placebo or no treatment. Therefore, based on this review it is not possible to recommend any of the preparations.

Topical preparations with active ingredients compared with other topical preparations with active ingredients

This review found no statistically significant average difference in the development of stretch marks or in the severity of stretch marks in women who received topical preparations with active ingredients compared with other topical preparations with active ingredients in trials (Buchanan 2010; de Buman 1987) involving small numbers of participants. In the trial by Buchanan 2010, the topical preparations contained multiple ingredients including isopropyl palmitate (emollient), propylene glycol isostearate (emollient), PPG-15 stearyl ether (1-octadecoxypropan-2-ol) (emollient), hydrolysed collagen, hydrolysed elastin and tocopheryl acetate (vitamin E). Preparations differed only in the addition of cocoa butter (25%). In the study by de Buman 1987, the intervention preparation contained several ingredients (hyaluronic acid, vitamin A, vitamin E, allantoine, calcium pantothenate) while the comparison preparation contained vitamins in addition to the excipient.

Data on the severity of stretch marks were only available in one of the two included studies (Buchanan 2010). In this study, Buchanan 2010 assessed the severity of stretch marks using the '4 quadrant technique of Davey (1972) with a simplification by Fletcher (unpublished)'. The researchers outline the process of ensuring that assessments were reliable and state that checking of researchers' assessments was undertaken with the aid of digital photographs until such time as 'a consensus of the striae scoring system by different observers' was achieved.

Overall completeness and applicability of evidence

Based on the findings of this review, which included six small trials, it is not possible to recommend any of the preparations for the prevention of stretch marks in pregnancy .

Quality of the evidence

We assessed the risk of bias of included trials as 'low risk' for random sequence generation, blinding of participants and personnel, and in blinding of outcome assessment, complete outcome data and selective reporting in only three of the six trials (Buchanan 2010; Mallol 1991; Osman 2008). We assessed one study (Wierrani 1992) as at high risk of bias for random sequence generation and allocation concealment. Overall findings are not sensitive to exclusion of this study.

The quality of evidence is also impacted on by the possible imprecision of the study results due to the small numbers of participants and events, and their wide confidence intervals. This is particularly evident in some of the trials (Taavoni 2011; Wierrani 1992).

Potential biases in the review process

We have taken every step to ensure that there are no potential biases in the review processes. We undertook a systematic and comprehensive search without language restrictions and adhered to best practice in undertaking the review. Three authors (MB, DD and GY) independently assessed each study and agreed the studies that

were for inclusion in the review and those that were for exclusion. Data extraction was also completed independently and checked for accuracy by three authors (MB, DD and GY). We contacted authors from two trials (Horace Fletcher for Buchanan 2010; P Msika for Msika 2002) for further information (see notes in Characteristics of included studies and Characteristics of excluded studies). All data were entered into the Review Manager software (RevMan 2011) and checked for accuracy by three authors (MB, DD and GG). Consequently, biases in the review processes are unlikely.

Preparations possibly worth pursuing might include Trofolastin (Mallol 1991), Alphastria (de Buman 1987), and Verum (Wierrani 1992). The latter two preparations contain hyaluronic acid, which has been identified as stimulating fibroblastic activity (de Buman 1987) and therefore maintaining tissue structure and tone. In addition, it is important that preparations commonly used by women to prevent and treat stretch marks are evaluated within the context of robust, methodologically rigorous and adequately powered randomised trials.

AUTHORS' CONCLUSIONS

Implications for practice

We found no high-quality evidence to support the use of any of the topical preparations in the prevention of stretch marks during pregnancy.

Implications for research

There is a clear need for robust, methodologically rigorous randomised trials involving larger sample sizes to evaluate the effects of topical preparations on the development of stretch marks in pregnancy.

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As part of the pre-publication editorial process, this review has been commented on by four peers (an editor and three referees who are external to the editorial team), a member of the Pregnancy and Childbirth Group's international panel of consumers and the Group's Statistical Adviser.

REFERENCES

References to studies included in this review

Buchanan 2010 *{published data only}*

Buchanan K, Fletcher HM, Reid M. Prevention of striae gravidarum with cocoa butter cream. *International Journal of Gynecology and Obstetrics* 2010;**108**(1):65–8.

de Buman 1987 *{published data only}*

de Buman M, Walther M, de Weck R. Effectiveness of Alphastria cream in the prevention of pregnancy stretch marks (striae distensae). Results of a double-blind study [Wirksamkeit der Alphastria–Creme bei der Vorbeugung von Schwangerschaftsstreifen (Striae distensae). Ergebnisse einer Doppelblind–Studie]. *Gynakologische Rundschau* 1987;**27**:79–84.

Mallol 1991 *{published data only}*

Belda MA, Costa D, Noval A, Sola M, Mallol J. Prophylaxis of striae gravidarum with a topical formulation - a double blind study. Proceedings of 22nd International Congress of Confederation of Midwives; 1990 October 7-12; Kobe, Japan. 1991.

Mallol J, Belda MA, Costa D, Noval A, Sola M. Prophylaxis of striae gravidarum with a topical formulation. A double blind trial. *International Journal of Cosmetic Science* 1991;**3**: 51–7.

Osman 2008 *{published data only}*

Osman H. Cocoa butter for prevention of stretch marks. ClinicalTrials.gov (http://clinicaltrials.gov/ct2/show/NCT00114660) (accessed 21 March 2006).

Osman H, Usta IM, Rubeiz N, Abu-Rustum R, Charara I, Nassar AH. Cocoa butter lotion for prevention of striae gravidarum: a double-blind, randomised and placebo-controlled trial. *BJOG: an international journal of obstetrics and gynaecology* 2008;**115**(9):1138–42.

Taavoni 2011 *{published data only}*

Taavoni S, Soltanipour F, Haghani H, Ansarian H, Kheirkhah M. Effects of olive oil on striae gravidarum in the second trimester of pregnancy. *Complementary Therapies in Clinical Practice* 2011;**17**(3):167–9.

Wierrani 1992 *{published data only}*

Wierrani F, Kozak W, Schramm W, Grunberger W. Attempt of preventive treatment of striae gravidarum using preventive massage ointment administration. *Wiener Klinische Wochenschrift* 1992;**104**:42–4.

References to studies excluded from this review

Martius 1973 *{published data only}*
Martius G. Prevention of striae gravidarum. *Medizinische Welt* 1973;**24**:799–800.

Mendez Velarde 2010 *{published data only}*
Méndez Velarde FA, Salceda Pérez MA, Moya CB, Azpeitia De La O CM, Vázquez Coronado DP, Ore Colio L. Effect of a moisturizing cream in the prevention of striae gravidarum [Efecto de una crema hidratante para prevenir las estrias del embarazo]. *Dermatologia Revista Mexicana* 2010;**54**(5):273–8.

Msika 2002 *{published data only}*
Msika P, Gavaud-Kennedy C, Pitiot M, Camel E, Arnaud-Boissel L, Guillot JP. Prevention of stretch marks: A randomized double bind clinical study versus placebo. *Journal of European Academy of Dermatology and Venereology* 2002;**16 Suppl 1**:154.
Msika P, Gavaud-Kennedy C, Pitiot M, Camel E, Arnaud-Boissel L, Guillot JP. Prevention of stretch marks: a randomized double blind clinical study versus placebo. http://www.mustelausa.com/professional/˙images/pdfs/M9.pdf (accessed 5 October 2011) 2002.

Puder 1965 *{published data only}*
Puder H. Treatment of striae gravidarum. *Medizinische Welt* 1965;**16**:650–3.

References to studies awaiting assessment

Lachmann 2011 *{published data only}*
Lachmann N, Biassette M, Boy E, Chadoutaud B, Msika P. Assessment of the preventive effect of a topical treatment on striae gravidarum during pregnancy: a multicenter open study on primiparae. Journal of Investigative Dermatology September 2011; Vol. 131, issue Issue S2, Abstract 275: S46.

Ortega 1985 *{published data only}*
Ortega A. Clinical and experimental study of the prevention of stretch marks in pregnancy [Estudio clínico experimental de la prevención de las estrías en el embarazo]. *Acta Ginecologica* 1985;**42**(1):29–36.

Additional references

Alster 1997
Alster TS. Laser treatment of hypertrophic scars, keloids, and striae. *Dermatologic Clinics* 1997;**15**(3):419–29.

Archer 2004
Archer CB. Functions of the skin. In: Burns T, Breathnach S, Cox N, Griffiths C editor(s). *Rook's Textbook of Dermatology*. 7th Edition. Vol. **1**, Malden Massachusetts: Blackwell Science, 2004:4.1–4.12.

Atwal 2006
Atwal GSS, Manku LK, Griffiths CEM, Polson DW. Striae gravidarum in primiparae. *British Association of Dermatology* 2006;**55**(5):965–9.

Brinkhaus 2000
Brinkhaus B, Lindner M, Schuppan D, Hahn EG. Chemical, pharmacological and clinical profile of the East Asian medical plant Centella asiatica. *Phytomedicine* 2000;**7**(5):427–48.

Bryant 1968
Bryant WM, Greenwell JE, Weeks PM. Alterations in collagen organization during dilatation of the cervix uteri. *Surgery, Gynecology & Obstetrics* 1968;**126**(1):27–39.

Burrows 2004
Burrows NP, Lovell CR. Disorders of connective tissue. In: Burns T, Breathnach S, Cox N, Griffiths C editor(s). *Rook's Textbook of Dermatology*. 7th Edition. Vol. **3**, Malden Massachusetts: Blackwell Science, 2004:46.1–46.71.

Burrows 2010
Burrows NP, Lovell CR. Disorders of connective tissue. In: Burns T, Breathnach S, Cox N, Griffiths C editor(s). *Rook's Textbook of Dermatology*. 8th Edition. Vol. **3**, Malden Massachusetts: Blackwell Science, 2010:45.1–45.70.

Chang 2004
Chang ALS, Agredano YZ, Kimball AB. Risk factors associated with striae gravidarum. *Journal of the American Academy of Dermatology* 2004;**51**(6):881–5.

Clarke 2000
Clarke M, Oxman AD, editors. Cochrane Reviewers' Handbook 4.2 [updated February 2003]. In: The Cochrane Library [database on CDROM]. The Cochrane Collaboration. Oxford: Update Software; 2003, Issue 2.

Cunningham 2010
Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY. *Williams Obstetrics*. 23rd Edition. New York: McGraw Hill, 2010.

Egger 1997
Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;**315**(7109):629–34.

Elsaie 2009
Elsaie ML, Baumann LS, Elsaaiee LT. Striae distensae (stretch marks) and different modalities of therapy: an update. *Dermatologic Surgery* 2009;**35**(4):563–73.

Elson 1990
Elson ML. Treatment of striae distensae with topical tretinoin. *Journal of Dermatological Surgical Oncology* 1990; **16**(3):267–70.

Errickson 1994
Errickson CV, Matus NR. Skin disorders of pregnancy. *American Family Physician* 1994;**49**(3):605–10.

Ghasemi 2007
Ghasemi A, Gorouhi F, Rashighi-Firoozabadi M, Jafarian S, Firooz A. Striae gravidarum: associated factors. *Journal of the European Academy of Dermatology and Venereology* 2007; **21**(6):743–6.

Harbord 2006
Harbord RM, Egger M, Sterne JA. A modified test for small-study effects in meta-analyses of controlled trials with binary endpoints. *Statistics in Medicine* 2006;**25**(20): 3443–57.

Higgins 2011
Higgins JPT, Green S, editors. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Horn 2007
Horn TD, Hoskyn J. Dermatologic disorders during pregnancy. In: Reece A, Hobbins JC editor(s). *Clinical Obstetrics. The Fetus & Mother*. 3rd Edition. Malden Massachusetts: Blackwell Publishing, 2007:947–60.

Hunter 1973
Hunter JAA. Diseases of the skin. The basis of skin therapy. *British Medical Journal* 1973;**4**(5889):411–3.

Kang 1996
Kang S, Kim KJ, Griffith CEM, Wong TY, Talwar HS, Fisher GJ, et al.Topical Tretinoin (retinoic acid) improves early stretch marks. *Archives of Dermatology* 1996;**132**(5): 519–26.

Kang 1998
Kang S. Topical tretinoin therapy for management of early striae. *Journal of the American Academy of Dermatology* 1998;**39**(2 Pt 3):s90–s92.

Lawley 1999
Lawley TJ, Yancey KB. Skin changes and diseases in pregnancy. In: Freedberg IM, Eisen AZ, Wolf K, Austen KF, Goldsmith LA, Katz SI, et al. editor(s). *Fitzpatrick's Dermatology in General Medicine*. 5th Edition. Vol. **Vol II**, New York: McGraw Hill, 1999:1963–9.

Liu 1974
Liu DTY. Letter: Striae gravidarum. *Lancet* 1974;**1**(7858): 625.

McKenzie 1971
McKenzie AW. Skin disorders in pregnancy. *The Practitioner* 1971;**206**(236):773–80.

Murphy 1992
Murphy KW, Dunphy B, O'Herlihy C. Increased maternal age protects against striae gravidarum. *Journal of Obstetrics and Gynaecology* 1992;**12**(5):297–300.

Murray 2009
Murray I, Hassall J. Change and adaptation in pregnancy. In: Fraser DM, Cooper MA editor(s). *Myles Textbook for Midwives*. 15th Edition. Edinburgh: Churchill Livingstone Elsevier, 2009:189–225.

Muzaffar 1998
Muzaffar F, Hussain I, Haroon TS. Physiologic skin changes during pregnancy: a study of 140 cases. *International Journal of Dermatology* 1998;**37**(6):429–31.

Nigam 1989
Nigam PK. Striae cutis distensae. *International Journal of Dermatology* 1989;**28**(7):426–8.

Osman 2007
Osman H, Rubeiz N, Tamim H, Nassar AH. Risk factors for the development of striae gravidarum. *American Journal of Obstetrics and Gynecology* 2007;**196**(1):62.e1–62.e5.

Papoutsis 2007
Papoutsis J, Kroumpouzos G. Dermatologic disorders of pregnancy. In: Gabbe SG, Niebyl JR, Simpson JL editor (s). *Obstetrics. Normal and Problem Pregnancies*. 5th Edition. Philadelphia: Churchill Livingstone Elsevier, 2007:1178–92.

Poidevin 1959
Poidevin LOS. Striae gravidarum. Their relation to adrenal cortical hyperfunction. *Lancet* 1959;**2**(7100):436–9.

Rangel 2001
Rangel O, Arias I, Garcia E, Lopez-Padilla S. Topical tretinoin 0.1% for pregnancy-related abdominal striae: An open-label, multicenter, prospective study. *Advances in Therapy* 2001;**18**(4):181–6.

RevMan 2011
The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). 5.1. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2011.

Riley 2011
Riley D, Gates S, Neilson J, Alfirevic Z. Statistical methods can be improved within Cochrane pregnancy and childbirth reviews. *Journal of Clinical Epidemiology* 2011;**64**(6): 608–18.

Salter 2006
Salter SA, Kimball AB. Striae gravidarum. *Clinics in Dermatology* 2006;**24**(2):97–100.

Shuster 1979
Shuster S. The cause of striae distensae. *Acta Dermato-Venereologica. Supplementum* 1979;**59**(85):161–9.

Summers 2009
Summers B, Lategan M. The effect of a topically-applied cosmetic oil formulation on striae distensae. *South African Family Practice* 2009;**51**(4):332–6.

Thomas 2004
Thomas RGR, Liston WA. Clinical associations of striae gravidarum. *Journal of Obstetrics and Gynaecology* 2004;**24** (3):270–1.

Venning 1946
Venning EH. Adrenal function in pregnancy. *Endocrinology* 1946;**39**:203–20.

Watson 1998
Watson REB, Parry EJ, Humphries JD, Jones CJP, Polson DP, Kielty CM, et al.Fibrillin microfibrils are reduced in skin exhibiting striae distensae. *British Journal of Dermatology* 1998;**138**(6):931–7.

Waugh 2010
Waugh A, Grant A. *Ross and Wilson Anatomy and Physiology in Health and Illness*. 11th Edition. Edinburgh: Churchill Livingstone, 2010.

Wong 1984
Wong RC, Ellis CN. Continuing medical education. Physiologic skin changes in pregnancy. *Journal of the American Academy of Dermatology* 1984;**10**(6):929–40.

Wong 1989
Wong RC, Ellis CN. Physiologic skin changes in pregnancy. *Seminars in Dermatology* 1989;**8**(1):7–11.

Zheng 1985
Zheng P, Lavker RM, Kligman AM. Anatomy of striae. *British Journal of Dermatology* 1985;**112**(2):185–93.

References to other published versions of this review

Young 1995
Young GL. A cream to prevent striae gravidarum. [revised 12 May 1993]. In: Enkin MW, Keirse MJNC, Renfrew MJ, Neilson JP, Crowther C (eds.) Pregnancy and Childbirth Module. In: The Cochrane Pregnancy and Childbirth Database [database on disk and CDROM] The Cochrane Collaboration; Issue 2, Oxford: Update Software, 1995.

Young 1996
Young G, Jewell D. Creams for preventing stretch marks in pregnancy. *Cochrane Database of Systematic Reviews* 1996, Issue 1. [DOI: 10.1002/14651858.CD000066]

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Buchanan 2010

Methods	**Study design:** randomised controlled trial. **Duration of study:** not stated.
Participants	**Setting:** antenatal clinic in the University Hospital, of the West Indies, Mona, Kingston, Jamaica **Inclusion criteria:** '...primigravidas and multigravidas with no stretch marks' enrolled before 16 weeks' gestation **Exclusion criteria:** 'Women who were taking steroids and women with medical illnesses that caused stretch marks...'; 'Women with a twin pregnancy or polyhydramnios...' **Participants randomised:** 150 women were randomly assigned to the intervention (cocoa butter group) and 150 women to the comparison group
Interventions	**Experimental:** application of 473 ml of cocoa butter cream containing cocoa butter cream (25%), water, glycerin (skin conditioner), distearyldimonium chloride (skin conditioner), isopropyl palmitate (emollient), cetearyl alcohol (stabilizer), propylene glycol isostearate (emollient), PPG-15 stearyl ether (1-octadecoxypropan-2-ol) emollient, hydrolysed collagen, hydrolysed elastin, tocopheryl acetate (vitamin E), dimethicone (skin conditioner). Half a cap full of cream was applied to the 4 abdominal quadrants daily (until used up) **Control:** cream which was identical to the intervention cream with the exception of addition of the 25% cocoa butter We did not consider this a true placebo as it contains other active ingredients like vitamin E
Outcomes	**Outcomes considered in the review:** • presence of stretch marks; • severity of stretch marks.
Notes	'...number of stretch marks was assessed using the 4 quadrant technique of Davey (1972) with a simplification by Fletcher (unpublished), which involved using a pictorial chart to aid the providers in using Davey's technique. Digital photographs were taken of the abdomen of some women...' 1 of the study authors Horace Fletcher confirmed that the percentage of women who developed striae was erroneously included in the enrolment data and that none of the woman had striae at enrolment

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	'The women were assigned cocoa butter cream or placebo using a table of random numbers...'

Allocation concealment (selection bias)	Unclear risk	Insufficient information on which to judge risk of bias.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	'The women and the researchers were blinded to the allocation'
Blinding of outcome assessment (detection bias) All outcomes	Low risk	'...The researchers were blinded to the allocation'.
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Development of striae** In the intervention arm, 30 women were excluded from analysis (lost to follow up n = 28, discontinued intervention due to rash n =2). The 2 women who discontinued treatment were returned to group denominator (n = 122). 18.7% incomplete outcome data. In the control arm 28 women were excluded from analysis (lost to follow up n = 27, discontinued intervention due to skin rash n = 1). The 1 woman who discontinued due to skin rash (n = 1) was restored to the group denominator (n = 123). 18% incomplete outcome data. **Severity of striae** Intervention group: data available for 101 of the 120 women. Missing data = 15.8% Control group: data available for 105 of the 122 women. Missing data = 13.9%
Selective reporting (reporting bias)	Low risk	The protocol was not available and following clarification from the authors all the outcomes stated in the methods section were reported adequately in the results.
Other bias	Unclear risk	**Intervention integrity** Authors state '...that it was not possible to verify that the patients were using the cream as instructed or whether they were sharing the cream or using other creams' **Funding source** No funding source identified.

de Buman 1987

Methods	**Study design:** randomised controlled trial. **Duration of study:** not stated (states women were monitored over 10 months).
Participants	**Setting:** Obstetrical and Gynecological Clinic in a Hospital in Cantonal, Fribourg **Inclusion criteria:** women at the beginning of the third month of pregnancy. **Exclusion criteria:** not stated. **Participants randomised:** 90 women randomised: 30 women to each group (group A - Alphastria cream n = 30; group B - cream with vitamins and excipients n = 30; group C - placebo with just excipient n = 30)
Interventions	**Experimental:** 'Application of 10cm (3g) Alphastria cream (contains hyaluronic acid, Vitamin A, Vitamin E, allantoine, calcium pantothenate)...' daily to the thighs, abdomen and chest. 'The cream was massaged gently into each area for a few minutes each' **Control:** application of 1 of 2 creams : 1 containing vitamins and excipients, and 1 containing excipients only
Outcomes	**Outcomes considered in the review:** • presence of stretch marks.
Notes	As group B contains vitamins and excipients we compared group A (Alphastria cream) with group B (vitamins and excipients) and then group A and B with group C (excipients only) [MB]

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	States that a randomised 'predetermined code system' was used. Insufficient Information on which to judge risk of bias.
Allocation concealment (selection bias)	Unclear risk	Treatments were administered anonymously. Insufficient information on which to judge risk of bias
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	While treatments were administered anonymously and the study is reported as a double blind study no detail is given on who was blinded. Insufficient detail on which to judge risk of bias.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information on which to judge risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	In the control arm (group C) (n = 30) , 3 women were excluded from the analysis (withdrawals due to intolerance, allergy, and miscarriage). We restored these 3

de Buman 1987 (*Continued*)

		women to the group denominator (n = 30) .
Selective reporting (reporting bias)	Low risk	The protocol was not available but all the outcomes stated in the methods section were reported adequately in the results
Other bias	Low risk	None identified. **Funding source** No funding source identified.

Mallol 1991

Methods	**Study design:** randomised controlled trial. **Duration of study:** 30 months.
Participants	**Setting:** antenatal clinic in Barcelona. **Inclusion criteria:** women in the first 12 weeks of pregnancy. **Exclusion criteria:** none stated. **Participants randomised:** not stated, study does not state how many were randomised to the intervention and control group. Total valid cases are reported as 41 in the active cream group and 39 in the placebo group
Interventions	**Experimental:** application of active cream (Trofolastin) (n = 41) which '...was a marketed product...' containing Centella asiatica extract and alpha- tocopherol and collagen - elastin hydrolysates. Application of active cream (Trofolastin) (n = 41) containing Centella asiatica extract and alpha- tocopherol and collagen - elastin hydrolysates. 'Product applied daily from the end of the 12^{th} week of pregnancy to the day of labour on abdomen, breasts, buttocks and hips'. **Control/Comparison intervention:** placebo cream containing only the excipient part of the active cream and '...identical in colour, flavour and texture'. 'Product applied daily from the end of the 12^{th} week of pregnancy to the day of labour on abdomen, breasts, buttocks and hips'
Outcomes	**Outcomes considered in the review:** • presence of stretch marks; • severity of stretch marks.
Notes	Striae were evaluated using '...an arbitrary score 0 = no striae, 1 = few and thin striae, 2 = many thin striae or few thick striae, and 3 = many thick striae'

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Probably adequate as 'randomised code numbers' were used.

Mallol 1991 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	No details given as to how women were allocated to the 2 groups
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Both intervention and control '...creams were identical in colour, flavour and texture' and were '...marked with a randomised code number'. Codes were not opened until the data collection was complete
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Codes were not opened until the data collection was complete
Incomplete outcome data (attrition bias) All outcomes	Low risk	States 'The assay was carried out on 100 pregnant women' but does not state explicitly how many women were randomised. Total 'valid' cases are noted as 41 for intervention (active cream) and 39 for placebo. Assuming 100 women randomised, then 20 women were excluded from the analysis overall, due to abortion (n = 1) and 'several address changes' (n = 19). 20% incomplete outcome data.
Selective reporting (reporting bias)	Low risk	The protocol was not available but all the outcomes stated in the methods section were reported in the results
Other bias	Unclear risk	Number of women randomised into each group is not given. States 'The assay was carried out on 100 pregnant women' but does not state explicitly how many women were randomised' **Funding source** No funding source identified.

Osman 2008

Methods	**Study design:** randomised controlled trial. **Duration of study:** November 2004 to July 2006 (from study protocol).
Participants	**Setting:** 4 medical centres in Lebanon. **Inclusion criteria:** nulliparous women with a singleton pregnancy presenting to the clinic in trimester 1, '...between November 2004 and December 2005 **Exclusion criteria:** women with a '...known hypersensitivity to cocoa butter...' or the lotion components **Participants randomised:** 105 women were randomised to the intervention group (co-

	coa butter lotion) and 105 to the placebo lotion group
Interventions	**Experimental:** application of a thin layer of a commercially available lotion containing cocoa butter and tocopheryl acetate (vitamin E) to the abdomen, breasts and thighs once daily, from '...between 12 and 18 completed weeks of gestation...' to delivery **Control:** placebo lotion with no active ingredients, which '...was made to look, smell, and feel the same as the study lotion...'
Outcomes	**Outcomes considered in the review:** • presence of stretch marks; • severity of stretch marks.
Notes	Trained assessors (n = 5) completed '... the data collection tools and...' assessed '...the severity of SG based on a scale developed and previously validated by the authors (Osman et al 2007). 'The scale took ...consideration the density and width of striae to estimate the surface area of the body part affected' '...funding by the Center for Research on Population and Health at the American University of Beirut, Lebanon, with generous support from the Wellcome Trust' '...and the University Research Board (URB) at the American University of Beirut, Beirut, Lebanon'

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	'Randomization was conducted using a computer-generated random number table'
Allocation concealment (selection bias)	Unclear risk	Not stated how participants were allocated to each of the 2 groups
Blinding of participants and personnel (performance bias) All outcomes	Low risk	'...researchers, study participants and their physicians were blinded to the lotion assignment'. '...Codes for the study and placebo lotions were opened after the final assessment of the last randomised woman'
Blinding of outcome assessment (detection bias) All outcomes	Low risk	'Assessors... were blinded as to the lotion assignment'. '...Codes for the study and placebo lotions were opened after the final assessment of the last randomised woman'
Incomplete outcome data (attrition bias) All outcomes	Low risk	In the intervention arm (n = 105), 14 women were excluded from analysis (remaining n = 91) due to abortion n = 3, withdrew n = 2, lost to follow up n = 9. We restored n = 3 (abortion) to the group denominator (n = 94). Equates to 10.5% incomplete outcome data in the interven-

Osman 2008 (*Continued*)

		tion group. In the control arm (n = 105), 21 women were excluded from analysis (remaining n = 84) due to abortion n = 5, withdrew n = 6, lost to follow up n = 9, allergic reaction n = 1). We restored n = 6 (abortion, and allergic reaction) to the group denominator (n = 90). Equates to 14.3% incomplete outcome data in the control arm
Selective reporting (reporting bias)	Low risk	Study protocol is available and all outcomes have been reported as planned. However a secondary outcome (severity of striae) is reported in the study which is not identified as such in the protocol. Study protocol reports that women will be asked to give their assessment of the presence or absence of striae and their severity'. Trained assessors assessed the severity of striae in the study.
Other bias	Unclear risk	**Intervention integrity** Authors state that 'Reports of compliance varied greatly for each patient and assessors reported that women may have been telling them what they wanted to hear when they asked about compliance' **Funding source** Both study and placebo lotions were provided by ET Browne Drug Company, Inc

Taavoni 2011

Methods	**Study design:** randomised controlled trial. **Duration of study:** not stated.
Participants	**Setting:** Department of Obstetrics and Gynaecology, Lolagar Hospital and Shahid Akbarabadi Hospital, Iran University of Medical Sciences, Tehran, Iran **Inclusion criteria:** '**...**nulliparous women aged between 20 and 30 years old, in their 18th to 20th week of gestation with body mass indices ranging between BMI 18.5--25'. **Exclusion criteria:** '**...**included: [polyhydramnios], occurrence of dermal discuses, administration of corticosteroids, application of other ointments on the abdominal area, lack of compliance with the study protocol' **Participants randomised:** 35 women were randomised to the intervention group and 35 women to the control group
Interventions	**Experimental:** application of '...olive oil topically onto...' the '... abdominal skin ...twice a day...for eight weeks, ...without massaging'. Application continued until week 28. **Control:** no treatment.

Taavoni 2011 (*Continued*)

Outcomes	**Outcomes considered in this review:** • presence of stretch marks.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	'Subjects were randomised using a computer-generated randomization table to either the control or intervention group'
Allocation concealment (selection bias)	Unclear risk	No detail given as to how women were allocated to the 2 groups
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information given on blinding in the study.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information given on blinding of outcome assessment.
Incomplete outcome data (attrition bias) All outcomes	Low risk	None (percentages in Table 2, p. 168 suggest no losses to follow up)
Selective reporting (reporting bias)	Low risk	The protocol was not available but the outcome stated in the methods section was reported adequately in the results
Other bias	Low risk	None identified. **Funding source** Authors declared no funding source.

Wierrani 1992

Methods	**Study design:** quasi-randomised controlled trial. **Duration of study:** not stated.
Participants	**Setting:** antenatal clinic in Vienna. **Inclusion criteria:** pregnant women > 18 and < 35 years. **Exclusion criteria:** history of metabolic disorders; long term medication use for example corticosteroid use; alcohol abuse; history suggestive of a complicated pregnancy **Participants randomised:** not stated. States that '24 participants in the Verum group and 26 in the control group could be included in the final evaluation'.

Wierrani 1992 (*Continued*)

Interventions	**Experimental:** application of an ointment (Verum, which contained: vitamin E, essential free fatty acids (vitamin F), panthenol, hyaluronic acid, elastin and menthol. Frequency of application not stated **Control:** no treatment.
Outcomes	**Outcomes considered in the review:** • presence of stretch marks.
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	Alternate day allocation. 'On days with uneven dates the pregnant women were included in the Verum (treatment) group'. Women enrolled on even dates were given no treatment
Allocation concealment (selection bias)	High risk	Allocation was performed according to day of treatment (see above)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information to judge risk of bias.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to judge risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number of women randomised not given. States that '24 participants in the Verum group and 26 in the control group could be included in the final evaluation'.
Selective reporting (reporting bias)	Low risk	The protocol was not available but all the outcomes stated in the methods section were reported adequately in the results.
Other bias	Unclear risk	Number of women randomised into each group is not given. States that '24 participants in the Verum group and 26 in the control group could be included in the final evaluation' **Funding source** No funding source identified.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Martius 1973	Not stated whether this study was randomised. Review authors believe it was not and attempts to contact the author have failed
Mendez Velarde 2010	The study does not fit the criteria for inclusion in the review. It compared the application of a topical cream on wet skin versus its application on dry skin. Nor did it have a placebo or a no treatment group
Msika 2002	The study is at unclear risk of bias in five of the seven domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment and selective reporting. While initial attempts to contact the authors were unsuccessful, eventual contact was made with Expanscience Laboratories. However, it was not possible to get further information on the trial
Puder 1965	Not randomised.

Characteristics of studies awaiting assessment *[ordered by study ID]*

Lachmann 2011

Methods	**Study design:** unclear. **Duration of study:** not stated.
Participants	**Setting:** not stated. **Inclusion criteria:** women between '16-19 weeks of amenorrhea...'. 'Primipare were selected according [to] factors which have been associated with the SG occurrence' **Exclusion criteria:** not stated. **Participants randomised:** unclear.
Interventions	**Experimental:** unclear. **Control:** unclear. Study involved the application of a cream which 'contains patented ingredients: lupeol, natural biopeptides and arabinogalactane which counteract tissue inflammation and stimulate extracellular matrix (ECM) remodelling' 'The cream was applied twice daily during 5 months'.
Outcomes	**Outcomes considered in the review:** • presence of stretch marks.
Notes	Funded by Expanscience Laboratories.

Ortega 1985

Methods	**Study design:** unclear. **Duration of study:** not stated.
Participants	**Setting:** Obstetrics and Gynaecology Department, Mother-Infant Hospital, Palma de Mallorca **Inclusion criteria:** women in the second trimester of pregnancy who were 'not obese (more than 10% overweight)' **Exclusion criteria:** not stated. **Participants randomised:** it is unclear if the women were randomised to the different groups It states that 146 women were 'distributed into groups': Group I (n = 61) was assigned to the cream with excipients only (placebo), group II (n = 55) was assigned the cream with the active ingredients while group III (n = 30) was assigned to the control arm ['neither instructed to massage nor use a cream']
Interventions	**Experimental:** application of an 'L. anti-striae cream', containing 'fitelenos (simulating factors of neo-elastogenesis and transcutaneous penetrating factors)' ...'once or twice a day' ...'on the abdomen, legs and breasts, in a down-up direction following the skin's traction lines' from the 'second trimester' until the puerperium. 'They were advised to undergo a massage once or twice a day each lasting from 5 to 10 minutes'. Participation in exercise is also referred to but no details are given. **Control:** application of a cream containing excipients only 'once or twice a day', 'on the abdomen, legs and breasts, in a down-up direction following the skin's traction lines' from the 'second trimester' until the puerperium. 'They were advised to undergo a massage once or twice a day each lasting from 5 to 10 minutes'. Participation in exercise is also referred to but no details are given Or no treatment [no massage or cream].
Outcomes	**Outcomes considered in the review:** • presence of stretch marks; • severity of stretch marks.
Notes	

DATA AND ANALYSES

Comparison 1. Topical preparations with active ingredients compared with placebo or no treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Presence of stretch marks	5	474	Risk Ratio (M-H, Random, 95% CI)	0.74 [0.53, 1.03]
2 Severity of stretch marks	2	255	Std. Mean Difference (IV, Random, 95% CI)	-0.31 [-1.06, 0.44]

Comparison 2. Topical preparations with active ingredients compared with other topical preparations with active ingredient

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Presence of stretch marks	2	305	Risk Ratio (M-H, Random, 95% CI)	0.51 [0.16, 1.60]
2 Severity of stretch marks	1	206	Mean Difference (IV, Random, 95% CI)	-0.20 [-0.53, 0.13]

Analysis 1.1. Comparison 1 Topical preparations with active ingredients compared with placebo or no treatment, Outcome 1 Presence of stretch marks.

Review: Topical preparations for preventing stretch marks in pregnancy

Comparison: 1 Topical preparations with active ingredients compared with placebo or no treatment

Outcome: 1 Presence of stretch marks

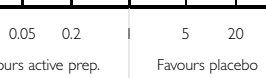
Study or subgroup	Active preparations n/N	Placebo or no treatment n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
de Buman 1987	15/60	10/30		14.4 %	0.75 [0.38, 1.46]
Mallol 1991	14/41	22/39		19.0 %	0.61 [0.36, 1.00]
Osman 2008	75/94	71/90		31.6 %	1.01 [0.87, 1.17]
Taavoni 2011	16/35	22/35		21.2 %	0.73 [0.47, 1.13]
Wierrani 1992	7/24	16/26		13.8 %	0.47 [0.24, 0.95]
Total (95% CI)	**254**	**220**		**100.0 %**	**0.74 [0.53, 1.03]**

Total events: 127 (Active preparations), 141 (Placebo or no treatment)

Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 11.59$, df = 4 (P = 0.02); $I^2 = 65\%$

Test for overall effect: Z = 1.78 (P = 0.075)

Test for subgroup differences: Not applicable



Analysis 1.2. Comparison 1 Topical preparations with active ingredients compared with placebo or no treatment, Outcome 2 Severity of stretch marks.

Review: Topical preparations for preventing stretch marks in pregnancy

Comparison: 1 Topical preparations with active ingredients compared with placebo or no treatment

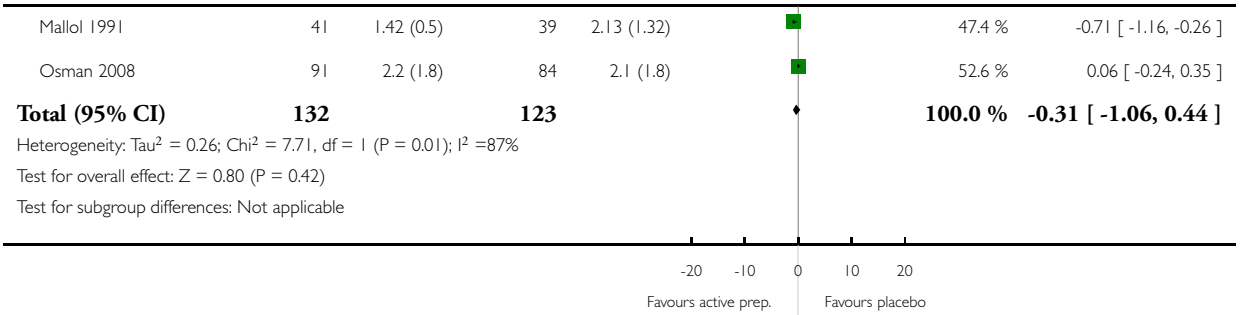
Outcome: 2 Severity of stretch marks

Study or subgroup	Active preparations		Placebo or no treatment		Std. Mean Difference	Weight	Std. Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
Mallol 1991	41	1.42 (0.5)	39	2.13 (1.32)		47.4 %	-0.71 [-1.16, -0.26]
Osman 2008	91	2.2 (1.8)	84	2.1 (1.8)		52.6 %	0.06 [-0.24, 0.35]
Total (95% CI)	**132**		**123**			**100.0 %**	**-0.31 [-1.06, 0.44]**

Heterogeneity: $Tau^2 = 0.26$; $Chi^2 = 7.71$, df = 1 (P = 0.01); $I^2 = 87\%$

Test for overall effect: Z = 0.80 (P = 0.42)

Test for subgroup differences: Not applicable



Analysis 2.1. Comparison 2 Topical preparations with active ingredients compared with other topical preparations with active ingredient, Outcome 1 Presence of stretch marks.

Review: Topical preparations for preventing stretch marks in pregnancy

Comparison: 2 Topical preparations with active ingredients compared with other topical preparations with active ingredient

Outcome: 1 Presence of stretch marks

Study or subgroup	Active preparations n/N	Other active preparations n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Buchanan 2010	54/122	68/123		61.7 %	0.80 [0.62, 1.03]
de Buman 1987	3/30	12/30		38.3 %	0.25 [0.08, 0.80]
Total (95% CI)	**152**	**153**		**100.0 %**	**0.51 [0.16, 1.60]**

Total events: 57 (Active preparations), 80 (Other active preparations)

Heterogeneity: $Tau^2 = 0.53$; $Chi^2 = 3.88$, df = 1 (P = 0.05); $I^2 = 74\%$

Test for overall effect: Z = 1.15 (P = 0.25)

Test for subgroup differences: Not applicable

Analysis 2.2. Comparison 2 Topical preparations with active ingredients compared with other topical preparations with active ingredient, Outcome 2 Severity of stretch marks.

Review: Topical preparations for preventing stretch marks in pregnancy

Comparison: 2 Topical preparations with active ingredients compared with other topical preparations with active ingredient

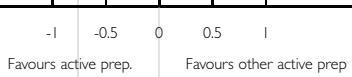
Outcome: 2 Severity of stretch marks

Study or subgroup	Active preparations N	Mean(SD)	Other active preparations N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Buchanan 2010	101	1 (1.2)	105	1.2 (1.2)		100.0 %	-0.20 [-0.53, 0.13]
Total (95% CI)	**101**		**105**			**100.0 %**	**-0.20 [-0.53, 0.13]**

Heterogeneity: not applicable

Test for overall effect: Z = 1.20 (P = 0.23)

Test for subgroup differences: Not applicable



APPENDICES

Appendix 1. Methods used to assess trials included in previous versions of this review

The following methods were used to assess Mallol 1991, Wierrani 1992 in previous versions of this review (Young 1996).
We evaluated trials under consideration for methodological quality and appropriateness for inclusion, without consideration of their results. We processed trial data as described in Clarke 2000.

WHAT'S NEW

Last assessed as up-to-date: 6 March 2012.

Date	Event	Description
31 October 2011	New citation required and conclusions have changed	Two new authors helped prepare this updated review. After restructuring the review's comparisons the review found no high-quality evidence to support the use of any of the topical preparations in the prevention of stretch marks during pregnancy
31 October 2011	New search has been performed	Two studies (three reports) identified in an earlier search have now been included in the review (de Buman 1987; Osman 2008). An updated search identified a further six trials: two studies have been included (Buchanan 2010; Taavoni 2011) ; two have been excluded (Mendez Velarde 2010; Msika 2002) and two are awaiting classification (Lachmann 2011; Ortega 1985). This review is now comprised of six included studies, four excluded studies and two studies that are awaiting classification The title has changed from 'Creams for preventing stretch marks in pregnancy' and the methods have been updated

HISTORY

Protocol first published: Issue 2, 1996

Review first published: Issue 2, 1996

Date	Event	Description
1 October 2009	Amended	Search updated. Three reports added to Studies awaiting classification
1 September 2008	Amended	Converted to new review format.
30 April 2004	New search has been performed	Search updated. A second study (Wierrani 1992) has been reviewed. This compares massage using an ointment containing several possibly active ingredients with no treatment.

CONTRIBUTIONS OF AUTHORS

All review authors (MB, GY and DD) prepared this review update.

DECLARATIONS OF INTEREST

None known.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We have separated outcomes into primary and secondary outcomes. The outcome from the previous version of this review (presence of stretch marks) is our primary outcome and we have added a new secondary outcome (severity of stretch marks). The methods have been updated to reflect the latest *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

We have also changed the title of the review from 'Creams for preventing stretch marks in pregnancy' to 'Topical preparations for preventing stretch marks in pregnancy'.

For this update we restructured the review comparisons to compare: (1) topical preparations with active ingredients compared with placebo or no treatment, and (2) topical preparations with active ingredients compared with other topical preparations with active ingredients. This is in contrast to comparing active creams with placebo or with no treatment, as presented in Young 1996.

NOTES

In the next update of this review we will carry out subgroup analysis by parity (nulliparous versus multiparous women), and our criteria for sensitivity analysis will incorporate trials at high risk of bias for blinding. We will also detail how the primary (presence of stretch marks) and secondary (severity of stretch marks) outcomes are measured and by whom. We will include a discussion around if and how included studies have addressed confounding or other risk factors.

INDEX TERMS

Medical Subject Headings (MeSH)

Cosmetics; Dermatologic Agents [*administration & dosage]; Ointments; Randomized Controlled Trials as Topic; Skin; Striae Distensae [*prevention & control]

MeSH check words

Female; Humans; Pregnancy