Treatments for suppression of lactation (Review)

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[Intervention Review]

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ABSTRACT

Background

Various pharmacologic and nonpharmacologic interventions have been used to suppress lactation after childbirth and relieve associated symptoms. Despite the large volume of literature on the subject, there is currently no universal guideline on the most appropriate approach for suppressing lactation in postpartum women.

Objectives

To evaluate the effectiveness and safety of interventions used for suppression of lactation in postpartum women (who have not breastfed or expressed breastmilk) to determine which approach has the greatest comparative benefits with least risk.

Search strategy

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (October 2007).

Selection criteria

Randomised trials evaluating the effectiveness of treatments used for suppression of postpartum lactation.

Data collection and analysis

Two authors independently assessed trial quality and extracted data.

Main results

We included 46 trials (5164 women). The trials were generally small and of limited quality. Five trials (206 women) indicated that bromocriptine significantly reduced the proportion of women lactating compared to no treatment at or within seven days postpartum (three trials, 107 women; relative risk (RR) 0.36, 95% confidence interval (CI) 0.24 to 0.54). Six trials involving oestrogen preparations (diethylstilbestrol, quinestrol, chlorotrianisene, hexestrol) suggested that they significantly reduced the proportion of lactating women compared to no treatment at or within seven days postpartum (RR 0.41, 95% CI 0.29 to 0.59). We found no trials comparing nonpharmacologic methods with no treatment. Trials comparing bromocriptine with other pharmacologic agents suggested similarity in their effectiveness (RR 0.79, 95% CI 0.54 to 1.17). Side effects were poorly reported in the trials and no case of thromboembolism was recorded in the four trials that reported it as an outcome.

Authors' conclusions

There is weak evidence that some pharmacologic treatments (most of which are currently unavailable to the public) are better than no treatment for suppressing lactation symptoms in the first postpartum week. No evidence currently exists to indicate whether nonpharmacologic approaches are more effective than no treatment. Presently, there is insufficient evidence to address the side effects of methods employed for suppressing lactation. When women desire treatment, bromocriptine may be considered where it is registered for lactation suppression in those without predisposition to its major side effects of public concerns. Large randomised trials are needed to compare the effectiveness of pharmacologic (especially bromocriptine) and nonpharmacologic methods to no treatment. Such trials should consider acceptability of the intervention and lactation symptoms of concern to women and be large enough to detect clinically important differences in major side effects between comparison groups.

PLAIN LANGUAGE SUMMARY

Treatments for suppression of lactation

Women cannot always breastfeed after birth. Reasons may be because the infant dies or is adopted, or the mother is too ill, or for the wellbeing of the mother or infant. HIV-positive mothers, particularly those not on antiretroviral drugs during pregnancy, avoid breastfeeding to reduce the risk of passing on the virus to their infants. Some mothers do not breastfeed on personal or social grounds. Without an infant suckling, milk production (lactation) eventually stops of its own accord. In the meantime, women can experience breast engorgement, leakage of milk, discomfort and pain. Clinicians may provide treatment to suppress lactation and reduce these symptoms. Binding the breasts or wearing a tight brassiere, applying an infra-red lamp, fluid and diet restrictions, external application of jasmine flower and ice packs are tried non-drug approaches. Drug treatments include oestrogens and bromocriptine which lowers prolactin levels. However, increased risks of thromboembolism, cerebral accident and myocardial infarction have been reported with their use.

The evidence to support treatments for preventing lactation is limited. The review authors identified 46 controlled trials that randomised a total of 5164 mothers to receive the treatment under investigation, no treatment or another treatment. The trials were generally of limited quality and most were conducted among healthy women who chose not to breastfeed for personal reasons at hospitals in industrialized countries before 1980. Half of the trials involved bromocriptine. Five trials (206 women) reported that taking bromocriptine was better than no treatment in suppressing lactation in the first week after giving birth. The nine trials using oestrogen preparations (diethylstilbestrol, quinestrol, chlorotrianisene, hexestrol) also showed suppression of lactation. A combination of testosterone and oestrogen preparations was of some benefit in reducing symptoms in two trials (346 women). Other pharmacologic agents (clomiphene, tamoxifen, prostaglandins, pyridoxine, oxytocin and homeopathic preparation) were tested in single small trials. Generally, side effects were poorly reported and no case of thromboembolism was recorded among trials that included it as an adverse treatment outcome. Most of the drugs tested are currently not available or registered for suppressing lactation. No trials compared non-drug approaches to no treatment and none of the included trials provided reliable data on women's satisfaction with the treatment.

BACKGROUND

Description of the condition

Indications for lactation suppression

For many years, the importance of breastfeeding to both infants and mothers has been emphasised by healthcare providers and various strategies have been employed to promote it globally. In spite of the well-known advantages of breastfeeding (for example, infant protection against diarrhoeal morbidity and mortality), there are instances when the well being of the mother or infant requires suppression of lactation. Suppression of lactation becomes essential when breastfeeding is no longer required (as in the events of perinatal death and infant adoption) or when the mother is too ill to breastfeed (as in cases of severe obstetric morbidity). Besides medical indications, some mothers in circumstances where alternatives to breastfeeding exist may seek lactation suppression on personal or social grounds. It is estimated that over 30% of women in the United States and United Kingdom do not breastfeed their infants, while a larger proportion discontinue breastfeeding within two weeks of childbirth (Hamlyn 2002; Ryan 2002). Although

physiologic cessation of lactation eventually occurs in the absence of physical stimulus such as infant suckling, a variable proportion of women experience moderate to severe milk leakage and discomfort, before lactation ceases. Up to two-thirds of nonbreastfeeding women experience moderate to severe engorgement and breast pain when no treatment is applied (Spitz 1998). Almeida and Kitay (Almeida 1986) showed that breast engorgement was responsible for puerperal fever in 13.3% of 75 nonbreastfeeding mothers. However, the prevalence, characteristics and health implications of these symptoms have not been well described in the literature.

Lactation suppression and prevention of vertical transmission of HIV

Unlike in the 1970s, when a social reason was the most common indication for lactation suppression (Eastham 1976), the need for complete avoidance of breastfeeding by HIV-positive mothers to reduce the risk of vertical transmission of HIV has offered a more compelling reason in the last decade. Postnatal transmission through breastfeeding accounts for one-third to one-half of all cases of vertical HIV transmission worldwide, with an estimated 16.2% rate of transmission for infants of women untreated with antiretroviral drugs during pregnancy (Nduati 2000). Although breastfed infants of HIV-positive mothers who receive antiretroviral treatment during pregnancy are less likely to be infected with HIV (Wiktor 1999), the risk is further reduced when such infants are fed with substitutes of breast milk (Shaffer 1999). Therefore, as the global prevalence of HIV continues to rise, the need for supervised inhibition of lactation may likely become increasingly relevant, especially in developed countries where safe alternatives of infant feeding are available. The symptoms associated with physiologic cessation of lactation may further compromise the physical and emotional status of the HIV-positive mothers and an effective method of suppressing lactation is desirable to avoid additional morbidity.

Description of the intervention

Nonpharmacologic methods of lactation suppression

Interventions to suppress lactation in nonbreastfeeding women have evolved for centuries. Healthcare providers have used different nonpharmacologic approaches to suppress lactation and relieve the associated symptoms. Before the 20th century, these approaches included breast binding or strapping, emptying of the breast by massage, fluid and diet restrictions and application of external products such as belladonna ointment to the breast and nipples. Later, the avoidance of tactile breast stimulation and application of external agents such as cabbage leaves, jasmine flower and ice packs were included. Although many of these methods are still in use today, data on their efficacy are few and inconclusive. A review by Spitz et al (Spitz 1998) showed that up to one-third of women may experience severe breast pain for most of the first postpartum week when these methods of lactation suppression are employed.

Pharmacologic methods of lactation suppression

In the 1960s, oestrogen preparations given alone or in combination with androgens were demonstrated to be effective in 40% to 100% of women (Llewellyn-Jones 1968; Senior 1969) but their reported association with high rate of rebound lactation (resurgence of lactation following cessation of treatment) and increased risk of thrombosis and pulmonary embolism discouraged their use (Jeffcoate 1968). After it was demonstrated that postpartum lactation depends primarily on pituitary prolactin secretion, the synthetic dopamine agonist and strong prolactin inhibitor bromocriptine was introduced in 1972. Its efficacy in the suppression of postpartum lactation is well documented (Bhardwaj 1979; Dewhurst 1977; Duchesne 1981; Van der Heijden 1991). It is, however, associated with some unpleasant side effects and requires administration for about 10 to 14 days to prevent rebound lactation. It has also been implicated in serious puerperal complications such as cerebral accident and myocardial infarction (Iffy 1996; Ruch 1989). In 1989, the United States Food and Drug Administration recommended against the routine use of bromocriptine for suppression of postpartum lactation, noting that while there was no clear proof of adverse effects, there were also no proven health benefits (US FDA 1989). In spite of this development, bromocriptine is still being used in many countries. Since then, many other drugs have been used for suppression of lactation, including those with recognised prolactin-lowering activity and those with uncertain mechanism of action. These include different preparations of oestrogens, oestrogens in combination with androgens or progestogens, or both, clomiphene, pyridoxine, prostaglandin E_2, other dopamine agonists (cabergoline and lisuride) and serotonin antagonists (cyproheptadine, methysergide and metergoline). All these drugs have demonstrated variable effectiveness in the inhibition of postpartum lactation.

The search for another ergot derivative with clinical efficacy similar to bromocriptine but with better compliance and tolerability profile led to the trials on cabergoline. Various randomised studies in the late 1980s described similar effectiveness and better side effect profile of cabergoline, administered as a single dose compared to the conventional bromocriptine dose in the prevention of postpartum lactation (Anonymous 1991; Giorda 1991). Recent reports suggest that a new drug, which belongs to the sulfhydryl compound, is also an effective inhibitor of lactation and breast engorgement (Akrivis 2000).

Why it is important to do this review

It is clear from this background that the evolution of lactation suppressants is not over. Thus, while the need for specific medical prevention of lactation in non-nursing mothers is being questioned from time to time, many clinicians still apply some kind of treatment. Besides, clinicians appear unclear about the most appropriate method for suppressing lactation when an intervention is indicated. In view of the numerous approaches of lactation inhibition and the continuous search for new drugs, it becomes necessary to synthesise previous research findings to determine the most effective intervention to suppress lactation in nonbreastfeeding mothers. An ideal method would be one that has close to 100% efficacy, with minimal or no side effects and good acceptability profile. A systematic review of the previous studies was therefore conducted to understand whether further trials on new approaches or drugs, or both, are justified.

OBJECTIVES

The objective of this review was to evaluate the effectiveness and safety of interventions used for suppression of lactation in postpartum women (who have not breastfed or expressed breastmilk) to determine which approach has the greatest comparative benefits with least risk.

METHODS

Criteria for considering studies for this review

Types of studies

All published randomised trials evaluating the effectiveness of treatments used for suppression of postpartum lactation. We excluded studies that evaluated the effectiveness of interventions after establishment of lactation (e.g. women who have breastfed or expressed breastmilk). We excluded quasi-randomised trials (e.g. allocation by date of birth or hospital record number).

Types of participants

Postpartum women (who have not breastfed or expressed breastmilk) with indication(s) for suppression of lactation, irrespective of parity and mode of delivery.

Types of interventions

We assessed pharmacologic (drug) and nonpharmacologic (breast binding or strapping, firm breast support, fluid restriction, application of ice packs and external products) interventions specifically aimed at suppressing lactation after childbirth.

We considered the following comparisons in this review:

1. any pharmacologic treatment versus no treatment or placebo;
2. any nonpharmacologic treatment versus no treatment or placebo;
3. comparison of two different nonpharmacologic treatments;
4. comparison of nonpharmacologic versus pharmacologic treatments;
5. comparison of two different pharmacologic treatments;
6. comparison of two different pharmacologic combinations;
7. comparison of different doses of the same agent.

We excluded studies without any of the above comparisons.

Types of outcome measures

Primary outcomes

1. Failure to suppress lactation as indicated by breast pain, engorgement and or milk secretion (or as described by trial authors) at or within seven days postpartum and at or within 14 days postpartum. In trials where data for two or more breast symptoms or signs were reported, data for failure to suppress lactation was derived from the least suppressed of these symptoms or signs.
2. Minor adverse events including nausea, vomiting, headache, dizziness and major adverse events including thromboembolism, myocardial infarction and maternal death.
3. Acceptability of the treatment to the woman.

Secondary outcomes

1. Rebound lactation (resurgence of lactation after cessation of suppressant).
2. Percentage of women who require a second line drug or method, or both, to achieve lactation suppression.
3. Percentage of women who require analgesics to relieve breast pain or discomfort.

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 (October 2007).

The Cochrane Pregnancy and Childbirth Group's 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. handsearches of 30 journals and the proceedings of major conferences;
4. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL and MEDLINE, 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.

We did not apply any language restrictions.

Data collection and analysis

Selection of studies

Two review authors independently assessed for inclusion all the potential studies identified as a result of the search strategy. Disagreements were resolved through discussion.

Data extraction and management

We designed a form to extract data. For eligible studies, both review authors independently extracted the data using the agreed form. We resolved discrepancies through discussion. We entered data into Review Manager software (RevMan 2008) and checked them for accuracy.

When information regarding any of the above was unclear, we attempted to contact authors of the original reports to provide further details. There was no masking of authors or journals.

Assessment of risk of bias in included studies

We independently assessed risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2008). We resolved any disagreements by discussion.

(1) 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 whether allocation sequence was adequately generated and indicated this as:

- Yes (low risk of bias): any truly random process, e.g. random number table; computer random number generator;
- No (high risk of bias): any non random process, e.g. odd or even date of birth; hospital or clinic record number or
- Unclear.

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

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

We assessed whether allocation sequence was adequately concealed and indicated this as:

- Yes (low risk of bias): any adequate allocation concealment method, e.g. telephone or central randomisation; consecutively numbered sealed opaque envelope;
- No (high risk of bias): any inadequate allocation concealment method, e.g. open random allocation; unsealed or non-opaque envelopes, alternation; date of birth;
- Unclear.

(3) Blinding (checking for possible performance and detection 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. Blinding was assessed separately for different classes of outcomes.

We assessed whether knowledge of the allocated intervention was adequately prevented during the study and indicated this as:

- Yes (low risk of bias): blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken; participants and key study personnel not blinded but outcome assessors blinded;
- No (high risk of bias): no blinding or incomplete blinding; likely that blinding of participants and key study personnel could have been broken;
- Unclear.

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

We described for each included study, and for each 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 randomised participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups.

We assessed whether incomplete outcome data were adequately addressed and indicated this as:

- Yes (low risk of bias): no missing data; missing data < 20% of randomised participants; balanced missing outcome data across groups; reason for missing data unrelated to true outcome; appropriate imputing of missing data; intention-to-treat analysis;
- No (high risk of bias): reason for missing data related to true outcome; missing data > 20% of randomised participants; unbalanced missing outcome data across groups; 'as treated' analysis;
- Unclear.

(5) Selective reporting bias

We described for each included study how we investigated the possibility of selective outcome reporting bias and what we found. We assessed whether the reports of study was free of selective outcome reporting and indicated this as:

- Yes (low risk of bias): where it is clear that all of the study's prespecified outcomes and all expected outcomes of interest to the review have been reported;
- No (high risk of bias): where all the study's prespecified outcomes have not been reported; one or more reported primary outcomes were not prespecified; outcomes of interest are reported incompletely and so cannot be used; study fails to include results of a key outcome that would have been expected to have been reported;
- Unclear.

(6) Other sources of bias

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

- Yes (low risk of bias);
- No (high risk of bias);
- Unclear.

Measures of treatment effect

Dichotomous data

For dichotomous data, we presented results as summary risk ratio with 95% confidence intervals.
We carried out statistical analysis using RevMan 2008. We used fixed-effect meta-analysis for combining data in the absence of significant heterogeneity if trials were sufficiently similar. Where there was significant heterogeneity, we used a random-effects model.

Dealing with missing data

For included studies, we noted levels of attrition. We planned but could not explore the impact of including studies with high levels of missing data in the overall assessment of treatment effect using sensitivity analysis as few trials which addressed different interventions had missing data > 20%.
For all outcomes we carried out analyses, as far as possible, on an intention-to-treat basis i.e. we attempted to include all participants randomised to each group in the analyses. The denominator for each outcome in each trial was the number randomised minus any participants whose outcomes are known to be missing.

Assessment of heterogeneity

We used the I^2 statistic to measure heterogeneity among the trials in each analysis. We planned but could not explore substantial heterogeneity (exceeding 50%) by subgroup analysis as few studies reported the criterion (gestational age) that was pre-specified in the protocol.

Data synthesis

We carried out statistical analysis using the Review Manager software (RevMan 2008). We used fixed-effect inverse variance meta-analysis for combining data where trials are examining the same intervention, and the trials' populations and methods are judged sufficiently similar. Where we suspected clinical or methodological heterogeneity between studies sufficient to suggest that treatment effects may differ between trials we used random-effects meta-analysis. For studies with results in formats that cannot be included in meta-analysis, findings were succinctly reported as described by the trialists without attempting to derive a summary effect estimate.
Where substantial heterogeneity was identified in a fixed-effect meta-analysis, we repeated the analysis using a random-effects method.

Subgroup analysis and investigation of heterogeneity

There was no subgroup analysis as few studies reported the criterion (gestational age) that was pre-specified in the protocol.

Sensitivity analysis

We planned but could not conduct sensitivity analyses to explore the effect of trial quality as most of the trials were generally of low and similar methodological quality and in addition addressed different interventions.

RESULTS

Description of studies

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

Out of 112 potentially relevant studies considered for inclusion in this review, 46 trials involving 5164 women met our inclusion criteria, with outcome data on efficacy variables for interventions available for 4935 women. Eight trials (Gerstner 1978; Kaiser 1952; Lo Dico 1980; Martínez 1994; Mizuno 1990; Nisha 2006; Paggi 1975; Polatti 1982) are awaiting further assessment. All of the included trials are relatively small (the largest trial having 800 women) and 28 of them have fewer than 100 participants. The majority (38/46) of the trials were conducted in industrialized countries and all but three trials were single-centre studies conducted in a private, general or university hospital. Twenty-six of the trials were conducted before 1980 and only four after 2000. Four of the trials were published in languages other than English.

Participants

Most of the trials included healthy postpartum women who elected not to breastfeed for personal reasons and a few recruited women who could not breastfeed as a result of stillbirth or child adoption. Participants were women who delivered vaginally at term in most cases. Giorda 1991 randomised only women who were delivered by caesarean section while Piya-Anant 2004 randomised healthy HIV-positive puerperal women. Exclusion criteria were not specified in many of the trials. In the few trials that specified exclusion criteria, these include abnormal findings that are relevant to prolactin secretion, liver disorders, agalactia (inability to lactate), previous breast surgery, tumour of the pituitary gland, use of drugs that might interfere with prolactin secretion and unwillingness to participate in the study. Recruitment of women was not limited to any parity group in any of the trials and parity ranged between one and eight in studies where it was reported.

Interventions

Pharmacologic treatments were compared with placebo in 20 trials and another pharmacologic treatment in 23 trials. Two trials compared nonpharmacologic approaches (Jasmine flower (Shrivastav 1988), tight brassiere with intermittent infrared application (De Gezelle 1979)) with pharmacologic treatments. Only one trial compared two nonpharmacologic treatments (breast binding versus wearing of support bra) (Swift 2002). The classes of pharmacologic agents evaluated in these trials include ergot derivatives (bromocriptine, lisuride, metergoline, cabergoline and terguride), synthetic oestrogen preparations (quinestrol, diethylstilbestrol, ethinyl estradiol, chlorotrianisene and hexestrol), antioestrogenic preparations (tamoxifen, clomiphene and cyclofenil), oxytocics (intranasal oxytocin), androgen preparations (testosterone propionate), combined oestrogen and androgen preparations (testosterone and estradiol esters), prostaglandins and pyridoxine. Twenty-three trials involved bromocriptine. Bromocriptine was compared with placebo in five trials (Dewhurst 1977; Hutchison 1981; Rolland 1973; Walker 1975; Weinstein 1976), other pharmacologic treatments in 16 trials (Anonymous 1991; Boes 1980; Defoort 1987; England 1988; Fischer 1995; Giorda 1991; Kremer 1990; Nilsen 1976; Piya-Anant 2004; Scapin 1982; Steenstrup 1977; Thorbert 1983; Utian 1975; Varga 1972; Venturini 1981; Yuen 1977) and nonpharmacologic methods in two trials (De Gezelle 1979; Shrivastav 1988).

Most of the pharmacologic agents were given orally and a few were given by intramuscular injections. No agent was given intravenously. Dosage varied widely between trials in both amount and duration of treatment. Except in two trials (England 1988, Giorda 1991), treatments were commenced shortly after delivery (less than 12 to 24 hours). Of the drugs tested, only six are currently included in the WHO model list of essential medicines. These are ethinyl estradiol, clomiphene, tamoxifen, pyridoxine, oxytocin and testosterone. None of these drugs was listed for lactation suppression.

Outcomes

The definition of lactation suppression was not consistent among the trials. The primary outcome measures and the descriptions used in most of the trials were suppression of milk secretion or leakage, breast engorgement and/or breast pain. Some trials did not describe what was meant by suppression of lactation and only referred to it as such. For most of the trials, failure to achieve suppression of between one and three breast symptoms or signs (milk secretion or leakage, breast pain, breast engorgement) was presented as a measure of treatment failure. Other outcome measures prespecified for the review such as major and minor side effects, rebound lactation, use of analgesics and need for secondary treatment to achieve suppression were poorly reported in many of the trials. The method of outcome assessments varied widely across studies. In 11 trials, breast symptoms or signs were rated on a visual analogue scale or an ordinal scale of zero to between three and six to describe increasing severity of symptoms or signs (e.g., none, mild, moderate and severe). Most trials used dichotomous variables (or dichotomisable variables) to describe clinical efficacy of treatments while six trials described outcome measures in terms of means of the breast symptom 'scores' or mean change in the degree of breast symptoms. There was no evidence that any of these scoring systems were previously validated. Assessments of clinical efficacy were based on physical examination of the breast by the clinicians or women in the trials, or both, while in the hospital and subsequently by the women at home after hospital discharge. Women were asked to document breast symptoms on a questionnaire or data card that was collected at a specified follow-up period. The duration and the frequency of outcome assessment also varied widely between studies. Follow up varied from 72 hours to eight months postpartum although most assessments were conducted during the first one or two weeks.

As a result of the diversity of the interventions and the method,

duration and frequency of outcome assessments, few trials could be included in meta-analyses for each comparison. It was not possible to conduct sensitivity analyses based on trial quality as most trials are generally at high risk of bias (e.g., allocation concealment was considered adequate in 8.7% of the included trials all of which evaluated different interventions).

Risk of bias in included studies

Overall, the risk of bias for most reports was uncertain as they contained little methodological description (Figure 1 and Figure 2). Details for each trial are given in the 'Characteristics of included studies' table.

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

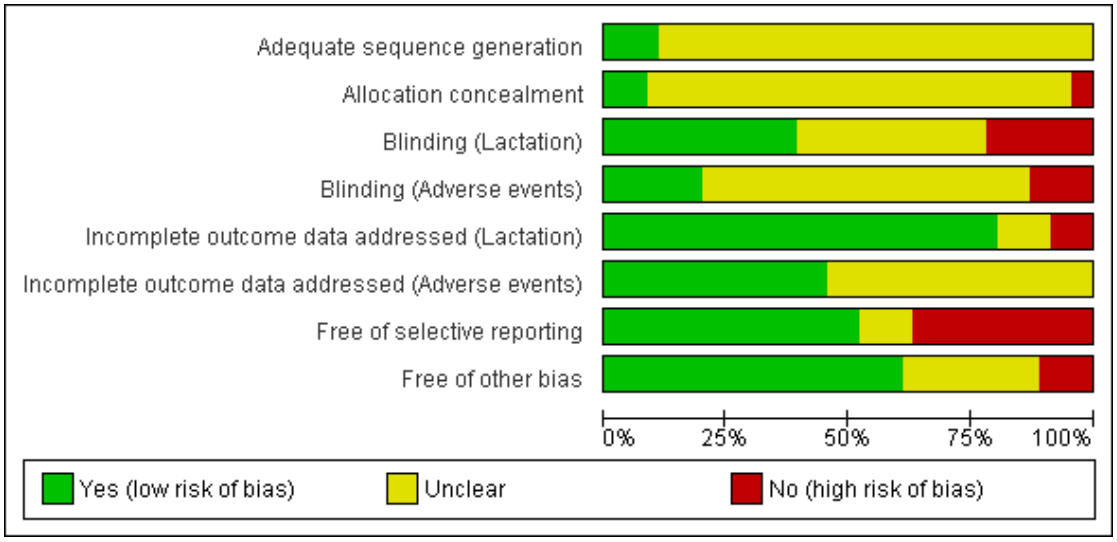
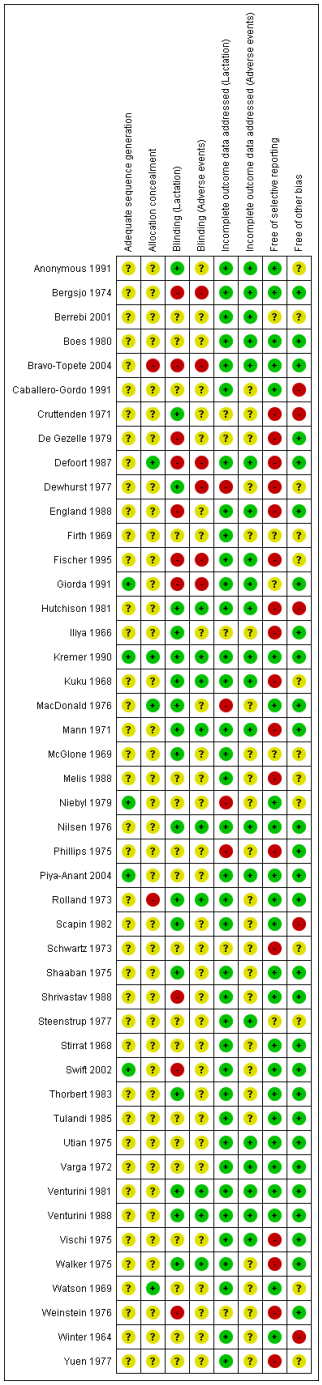


Figure 2. Risk of bias summary: review authors' judgments about each risk of bias item for each included study.



Allocation

The risk of selection bias was uncertain for most trials as generation and concealment of allocation sequence were considered adequate in only a few of the included studies. Generation of allocation sequence was considered adequate in five trials (computer randomisation in two trials (Kremer 1990, Piya-Anant 2004) and use of table of random numbers in three trials (Giorda 1991; Niebyl 1979; Swift 2002). Other studies did not describe the method by which random allocation sequence was generated and only reported that participants were "randomised" or "randomly allocated" into treatment groups. Allocation concealment was considered adequate in only four (8.7%) of the included studies (Defoort 1987; Kremer 1990; MacDonald 1976; Watson 1969). The majority did not provide adequate information to permit appropriate judgement on allocation concealment, while two trials (Bravo-Topete 2004; Rolland 1973) did not conceal their allocation sequences.

Blinding

With regard to blinding of participants, key study personnel and outcome assessors, we considered 18 trials to be at low risk and 10 trials at high risk of bias for the main outcome (lactation) of the review. The risk of bias was uncertain for 18 trials, principally as a result of unclear description of blinding of outcome assessors. Four of these trials only described their blinding method as "double blinded" with no further information to permit appropriate judgements. Of the 23 trials that addressed adverse events as outcome measures, we considered nine to be at low risk of bias, five at high risk of bias and the rest at uncertain risk of bias.

Follow up and exclusions

For the main outcome (lactation), we considered 38 trials to be at low risk of attrition bias, four trials at high risk of bias and four trials of uncertain risk of bias. Loss to follow up or exclusions from the initial cohort entered into the trials varied between 0% and 46.5%. For adverse events, 21 trials adequately addressed incomplete outcome data. It was unclear whether incomplete data were adequately addressed in 25 trials; 23 of these did not address adverse events as outcome measure.

Selective reporting

We considered 24 trials to be at low risk of selective reporting bias, 17 trials at high risk and five at uncertain risk of bias. In most of the reports at high risk of bias, the trialists did not include results for adverse events especially thromboembolism in spite of prior studies implicating oestrogen preparations in this complication.

Other potential sources of bias

Twenty-seven trials were apparently free of other problems that could put them at a risk of bias. We considered five trials to be at high risk of other sources of bias. These sources of bias included extreme imbalance in the number of participants across groups (Caballero-Gordo 1991) statistical analyses by supplier of tested intervention (Cruttenden 1971; Hutchison 1981) and prolonged data collection period involving 25 study personnel and outcome assessors (Winter 1964).

Effects of interventions

Primary outcomes

Pharmacologic treatment versus no treatment or placebo

Ergot derivatives versus no treatment or placebo (comparison 1)

Five trials (206 women) compared bromocriptine with placebo although only three reported data that could be used in meta-analysis. These three trials (107 women) (Dewhurst 1977; Rolland 1973; Weinstein 1976) indicated that bromocriptine reduced the risk of failure of lactation suppression during the first seven days postpartum when compared to placebo (risk ratio (RR) 0.36, 95% confidence interval (CI) 0.24 to 0.54) (comparison 1, outcome 1.1). The two other trials (99 women) excluded from the analysis table (Hutchison 1981; Walker 1975) indicated that bromocriptine resulted in significantly less milk secretion and breast engorgement compared to placebo during the first seven days postpartum. Two trials (76 women) that reported cumulative efficacies of bromocriptine (Dewhurst 1977; Varga 1972) compared to placebo over 14 days postpartum indicated that this ergot derivative was similar to placebo in the suppression of lactation (RR 0.18, 95% CI 0.03 to 1.08; comparison 1, outcome 1.2). Melis 1988 (32 women) indicated that cabergoline reduced the risk of failure to suppress lactation compared to placebo at 14 days postpartum (RR 0.19, 95% CI 0.07 to 0.48; comparison 1, outcome 1.3).

Oestrogen preparations versus no treatment or placebo (comparison 2)

There were nine trials in which oestrogen preparations were compared with placebo. Six of the trials where eight comparisons were made are presented in the data and analysis table. Diethylstilbestrol was compared with placebo in a total of four trials. Three of these trials (288 women) (Schwartz 1973; Stirrat 1968; Weinstein 1976) that are included the analysis table did not indicate any difference in the risk of treatment failure between diethylstilbestrol and placebo at or within seven days postpartum (RR 0.32, 95% CI 0.07 to 1.49; comparison 2, outcome 2.1.1). This analysis table indicates significant heterogeneity among the trials as evident by the very high I^2 statistic. Winter 1964 (800 women) (excluded from the data and analysis table) indicated that milk secretion, breast congestion and breast pain affected fewer women who were treated with diethylstilbestrol compared to those treated with placebo during the first postpartum week.

Three trials (342 women) (Firth 1969; McGlone 1969; Vischi 1975) comparing quinestrol with placebo suggested that it was associated with less risk of treatment failure (RR 0.47, 95% CI 0.30 to 0.73; comparison 2, outcome 2.1.2). I^2 statistic of 93%, however, suggests significant heterogeneity among the trials. Schwartz 1973 (153 women) indicated that chlorotrianisene was associated with less risk of treatment failure when compared with placebo

(RR 0.51, 95% CI 0.36 to 0.73; comparison 2, outcome 2.1.3) in agreement with the report of Phillips 1975 (200 women) (excluded from data and analysis table). Niebyl 1979 (99 women), however, indicated similarity in the risks of treatment failure between chlorotrianisene compared with placebo as at day three postpartum (excluded from data and analysis table). One trial (100 women) (Firth 1969) comparing hexestrol with placebo suggested that it was significantly associated with less risk of treatment failure (RR 0.41, 95% 0.29 to 0.57; comparison 2, outcome 2.1.4) at or within seven days postpartum.

Overall, six trials (833 women) (Firth 1969; McGlone 1969; Schwartz 1973; Stirrat 1968; Vischi 1975; Weinstein 1976) with eight comparisons indicated that oestrogen preparations are associated with reduced risk of failure to suppress lactation when compared with placebo at or less than seven days postpartum (RR 0.41, 95% CI 0.29 to 0.59; comparison 2, outcome 2.1).

Two small trials (Cruttenden 1971; Varga 1972) suggested similarity in the risk of treatment failure between oestrogen preparations (quinestrol and diethylstilbestrol) and placebo up to day 14 postpartum (RR 0.19, 95% CI 0.03 to 1.34; comparison 2, outcome 2.2). Two trials (130 women) (Stirrat 1968; Weinstein 1976) that reported thromboembolism as an outcome measure reported no occurrence of this complication in women treated with diethylstilbestrol and placebo.

Antioestrogens versus no treatment or placebo (comparison 3)

One trial (30 women) (Weinstein 1976) suggested no difference between clomiphene and placebo (RR 1.00, 95% CI 0.51 to 1.95; comparison 3, outcome 3.1.1) when used for lactation suppression in the first postpartum week. The trial also reported no occurrence of thromboembolism in women treated with clomiphene and placebo.

In the Shaaban 1975 trial (140 women), tamoxifen was significantly less likely to be associated with failure to suppress lactation compared to placebo over a period of 14 days postpartum (RR 0.71, 95% CI 0.62 to 0.82; comparison 3, outcome 3.2). The trial reported no occurrence of thromboembolism in women treated with tamoxifen and placebo.

Pyridoxine versus no treatment or placebo (comparison 4)

MacDonald 1976 (175 women) indicated that the risk of failure to achieve lactation suppression at or within seven days postpartum was similar between pyridoxine and placebo (RR 0.95, 95% CI 0.86 to 1.06; comparison 4, outcome 4.1)

Combined oestrogen and androgen preparations versus no treatment or placebo (comparison 5)

Two trials (346 women) (Iliya 1966; Schwartz 1973) compared testosterone enanthate-estradiol valerate combination with placebo for inhibition of lactation. This combination was found to significantly reduce the risk of treatment failure when compared with placebo at or within seven days postpartum (RR 0.10, 95% CI 0.06 to 0.17; comparison 5, outcome 5.1).

Androgen preparations versus no treatment or placebo (comparison 6)

In the comparison of testosterone propionate with placebo, a small trial (30 women) (Weinstein 1976) indicated no evidence of an association between testosterone propionate and risk of treatment failure (RR 1.13 95% 0.60 to 2.11; comparison 6, outcome 6.1). There were no reports of thromboembolism in women who received testosterone propionate and placebo.

Prostaglandins versus no treatment or placebo (not in data and analysis tables)

Tulandi 1985 compared prostaglandin E_2 with placebo in a trial involving 16 women. The trial indicated similarity in the degree of milk leakage, breast engorgement and breast pain between women who received prostaglandin E_2 and those who received placebo.

Oxytocics versus no treatment or placebo (not in data and analysis tables)

One trial (98 women) (Winter 1964) indicated that intranasal oxytocin was similar to placebo in the suppression of lactation symptoms.

Homeopathic preparations versus no treatment or placebo (not in data and analysis tables)

Berrebi 2001 (71 women) suggested a lower risk of treatment failure when homeopathic preparation (with anti-inflammatory and analgesic properties) was compared with placebo on days two and four postpartum.

Pharmacologic treatments versus nonpharmacologic treatments (comparison 7)

Only two trials compared a pharmacologic agent with nonpharmacologic agent. De Gezelle 1979 (90 women) was a five-arm study, which had bendrofluazide (a diuretic), diethylstilbestrol, estradiol/testosterone ester and bromocriptine in the intervention arms and tight brassiere with intermittent application of infra-red lamp as the control arm. The trial suggested that the risks of treatment failure at or within seven days postpartum were significantly reduced by all the studied pharmacologic treatments compared to wearing of tight brassiere and application of infra-red lamp (comparison 7, outcomes 7.1.1 to 7.1.4). Shrivastav 1988 (60 women) indicated that the risk of treatment failure was similar between women who used bromocriptine and those who applied jasmine flowers to the breasts for suppression of postpartum lactation (excluded from data and analysis table).

Comparison of two nonpharmacologic treatments (not in data and analysis tables)

One trial (Swift 2002) indicated that breast binding was associated with higher risk of treatment failure compared to use of a well-fitting support bra.

Comparison of two pharmacologic treatments (comparison 8)

Bromocriptine versus other pharmacologic treatment

Bromocriptine versus oestrogen preparations: bromocriptine was compared with diethylstilbestrol (Nilsen 1976, 38 women; Steenstrup 1977, 41 women), ethinyl estradiol (Piya-Anant 2004; 230 women), and chlorotrianisene (Utian 1975; 31 women). No significant difference was demonstrated in the risks of failure to suppress lactation in any of the trials in the first postpartum week (RR 0.58, 95% CI 0.25 to 1.38; comparison 8, outcome 8.1.1).
Bromocriptine versus other ergot derivatives: Two trials (Scapin 1982, 40 women; Fischer 1995, 150 women) comparing bromocriptine and metergoline and Venturini 1981 (38 women) comparing it with lisuride, did not indicate any difference in the risks of treatment failure in the first postpartum week (RR 1.12, 95% CI 0.37 to 3.42; comparison 8, outcome 8.1.2).
Bromocriptine versus prostaglandins: England 1988 (41 women) compared bromocriptine with prostaglandin E_2 for suppression of lactation. The trial suggested no significant difference between the risks of treatment failure of the two agents at or within seven days postpartum (RR 0.55, 95% CI 0.19 to 1.60; comparison 8, outcomes 8.1.3).

Bromocriptine versus pyridoxine: Boes 1980 (97 women) suggested no difference in the risks of treatment failure between bromocriptine and pyridoxine in the suppression of postpartum lactation at or less than seven days postpartum (RR 0.93, 95% CI 0.75 to 1.15; comparison 8, outcomes 8.1.4).
At day 14 postpartum, bromocriptine has similar risks of treatment failure compared to cabergoline (Anonymous 1991; Giorda 1991, 308 women; RR 1.38, 95% CI 0.93 to 2.05, comparison 8, outcome 8.4.1), diethylstilbestrol (Nilsen 1976; 38 women, RR 0.30, 95% CI 0.07 to 1.30, comparison 8, outcome 8.4.2) and cyclophenil (Thorbert 1983; 24 women, RR 3.50, 95% CI 0.16 to 78.19, comparison 8, outcome 8.4.3). Yuen 1977 (40 women) suggested that bromocriptine was associated with reduced risk of treatment failure compared to chlorotrianisene (RR 0.35, 95% CI 0.19 to 0.66) (comparison 8, outcomes 8.4.4).

Quinestrol versus other oestrogen preparations (comparison 8)

Quinestrol was compared with ethinyl estradiol (Kuku 1968) and diethylstilbestrol (Bergsjo 1974). Both trials (145 women) suggested similarity in the risks of treatment failure between quinestrol and other oestrogen preparations in the first postpartum week (RR 0.91, 95% CI 0.63 to 1.32; comparison 8, outcome 8.1.5).
Watson 1969 (99 women) indicated that quinestrol was associated with increased risk of treatment failure when compared with diethylstilbestrol over a period of one to 10 days (RR 2.84, 95% CI 1.56 to 5.18; comparison 8, outcome 8.4.5).

Comparison of different dosages of the same drugs

High- versus low-dose quinestrol: Vischi 1975 (132 women) suggested that the risk of failure of treatment was significantly lower with 4 mg quinestrol compared to 2 mg quinestrol in lactation suppression (RR 0.51, 95% CI 0.33 to 0.81; comparison 9, outcome 9.1).

Low- versus high-dose terguride: Venturini 1988 (45 women) indicated that terguride 0.5 to 1 mg significantly reduced the risk of failure to suppress postpartum lactation over a period of 15 days when compared with terguride 0.25 mg (RR 0.50, 95% CI 0.29 to 0.88; comparison 10, outcome 10.1). The risks of dizziness following use were similar between women who received a high dose of terguride and those who received low-dose terguride (RR 1.55, 95% 0.07 to 35.89; comparison 10, outcome 10.2).
High- versus low-dose cabergoline: Bravo-Topete 2004 (80 women) indicated that cabergoline 1 mg reduced the risk of failure to suppress lactation when compared to cabergoline 0.5 mg (RR 0.14, 95% CI 0.03, 0.59; comparison 11, outcome 11.1).
Long course versus short course of tamoxifen: Shaaban 1975 (65 women) indicated that long course tamoxifen (14 days administration) reduced the risk of failure to suppress lactation compared to short course tamoxifen (6 days administration) when assessed over two weeks postpartum (RR 0.75, 95% CI 0.61 to 0.92, comparison 12, outcome 12.1).

Secondary outcomes

Rebound lactation

We did not include data from many trials on rebound lactation in the results because of inadequate reporting of data. One trial (40 women) (Rolland 1973) comparing bromocriptine with placebo indicated that bromocriptine insignificantly increased the risk of rebound lactation but the confidence interval was too wide to give a reliable estimate (RR 15.26 95% CI 1.01 to 231.20, comparison 1, outcome 1.4). No other trial comparing pharmacologic agents with placebo provided reliable data on rebound lactation. In the comparison of pharmacologic versus nonpharmacologic treatment, Shrivastav 1988 found no significant difference between the risks of rebound lactation in women treated with bromocriptine compared with those who applied jasmine flower to the breasts (RR 5.00, 95% CI 0.25 to 99.95; comparison 7, outcome 7.2). Stirrat 1968 (100 women) comparing diethylstilbestrol with placebo did not show any difference between the two with respect to rebound lactation (not in data and analysis table). In the comparison of bromocriptine with other pharmacologic agents, four trials (149 women) (England 1988; Steenstrup 1977; Utian 1975; Venturini 1981) suggested similarity in the risks of rebound lactation between the study and control groups in the trials (RR 0.65, 95% CI 0.39 to 1.10, comparison 8, outcome 8.2).

Use of second line drugs or method to achieve lactation suppression

The use of second line drug or methods to achieve suppression was poorly reported in the trials. In the comparison of bromocriptine with any other pharmacologic treatment, there was no statistically significant difference between the risks of using a second line drug or method to achieve lactation suppression when bromocriptine was compared with oestrogen preparations (Utian 1975, 38 women, RR 0.31, 95% CI 0.01 to 7.15, comparison 8, outcome 8.3.1) and other ergot derivatives (Scapin 1982, 40 women, RR

2.67, 95% CI 0.82 to 8.62, comparison 8, outcome 8.3.2). Boes 1980 (97 women) suggested that bromocriptine was associated with reduced proportion of women in need of second line methods to suppress lactation compared to pyridoxine (RR 0.07, 95% CI 0.01 to 0.51; comparison 8, outcomes 8.3.3). Phillips 1975 (196 women) suggested that women who received chlorotrianisene were less likely to use supplemental or concurrent therapy (breast binders, ice bags or analgesics, or both) compared to women who had placebo at or within four days after admission (not in data and analysis table).

DISCUSSION

In spite of the questions on the need to apply treatment for suppressing lactation, a lot of research has gone into finding the most effective treatment. This review indicates that the emphasis for this search has been on pharmacologic treatments (compared with either no treatment or each other). The review included comparisons of orally and intramuscularly administered pharmacologic agents with placebo, other pharmacologic agents and nonpharmacologic methods. In terms of outcome, we used the persistence of one of the three common clinical symptoms or signs of postpartum lactation (i.e., milk secretion, breast engorgement and breast pain) as evidence of failure of lactation suppression. We also explored the consistency of results obtained from this definition with those obtained from separate consideration of each lactation symptom or sign as an indicator of treatment failure. In an attempt to reduce clinical heterogeneity, we extracted results on efficacy of treatment effects within a specified postpartum period.

This review shows that the search for the most effective lactation suppressant has relied on small trials, most of which have low methodological quality. The lack of recent randomised controlled trials on this subject may imply a supposed exhaustiveness and conclusion on this research topic. It may also be attributed to the lack of motivation of potential researchers because of the increasing number of questions on the need for treatments to suppress lactation. The gross variation in the dosage, interventions, duration of treatments and outcome assessments suggests a general lack of a clear understanding of the physiology of lactation and mechanisms of action of the treatments tested among researchers.

This is the first systematic review assessing the effectiveness of all forms of treatments for lactation suppression. Assessment of methodological quality of studies was based on stringent criteria, as evident by the number of relevant trials excluded from the review. In spite of this measure, however, the robustness of the results is diminished by the fact that the majority of included studies are of uncertain methodological quality, as evident in the proportion of trials with adequate allocation concealment (8.7%) and those that blinded their outcome assessments. Blinding of outcome assessment is particularly important for this topic, considering the subjective nature of main outcome measures (secretion, congestion and pain). The extent to which outcome measures are blinded in double-blinded trials where the women served the dual role of participant and outcome assessor is uncertain. Combining data on outcomes assessed by different observers (clinicians and women) is likely to contribute to ascertainment bias in included studies that employed such method. In addition, the validity of the results interpreted by the trialists could not be examined in included trials that reported data that were unsuitable for inclusion in the analyses table. Another major limitation of this review is the fact that a significant proportion of drugs tested in the included trials are currently no longer registered for use in most countries, either as lactation suppressants or otherwise. This may significantly limit the applicability of the findings of the review.

About half of the trials included compared drugs with placebo. In spite of its popularity, only five trials involving 206 women comparing bromocriptine with placebo met the inclusion criteria. All these trials used uncertain methods of generating allocation sequence and allocation concealment, none had outcome assessment blinded and all were conducted over two decades ago. It can thus be concluded that there is weak evidence that bromocriptine is better than nothing for suppressing the symptoms of lactation during the first seven days postpartum. Contrary to a number of case reports, there is insufficient evidence from this review to indicate whether or not bromocriptine is associated with increased risk of major side effects (notably thromboembolism, myocardial infarction and maternal death) in the first postpartum week.

Although there is small evidence that oestrogen preparations may be better than nothing in the first postpartum week, none of the tested agents is presently available in the market. In addition, available data on their risks of major side effects are insufficient to make a reliable conclusion on their safety when used for lactation suppression. Of all the pharmacological agents compared with placebo, only bromocriptine is still registered for use in most countries although not necessarily for lactation suppression. It needs to be stated that bromocriptine appeared to be the gold standard in the 1970s and 1980s as shown by the number of trials where it was tested. The possibility of publication bias therefore exists in the face of seemingly 'overwhelming' evidence. This review did not show sufficient evidence to indicate if other pharmacologic agents (clomiphene, tamoxifen, prostaglandins, pyridoxine, oxytocin and homeopathic preparation) are useful in suppressing the symptoms of lactation postpartum, as they are all based on a single small trial. However, the combination of testosterone and oestrogen preparations appear to be somewhat effective in suppressing the symptoms of lactation.

Evidence on the comparative effectiveness of pharmacologic agents and nonpharmacologic methods is based on two trials, each testing different nonpharmacologic methods (De Gezelle 1979; Shrivastav 1988). It can be concluded from their results that there is not enough evidence to indicate which of the approaches is

better than the other. The comparative effectiveness of jasmine flower with that of bromocriptine can only be useful once there is strong evidence that bromocriptine is better than placebo. There is currently no evidence on whether nonpharmacologic methods are better than placebo in lactation suppression.

There are mixed views on the subject of lactation suppression in most current obstetric textbooks, though the need for applying some kind of treatment is seldom disputed. Most authors refer to research findings indicating the effectiveness of previously tried approaches, many of which were excluded from this review as a result of low methodological quality and high potential for bias (*see* 'Characteristics of excluded studies'). Generally, nonpharmacologic approaches such as use of a well-supporting brassiere and avoidance of nipple stimulation, are often recommended based on the presumed safety and effectiveness of these methods. This policy, however, is not supported by the findings of this review. While the methodological limitations of conducting high-quality trials involving nonpharmacologic methods are understandable, they should not compromise the need to provide evidence-based guidelines on their application.

It is unlikely that the findings from this review would inform any change in the recommendations of the United States Food and Drug Administration on the routine use of bromocriptine for suppression of postpartum lactation, as the evidence indicating its effectiveness is weak even though the review also did not show any clear evidence of adverse effects.

Three issues related to the data and studies included in this review need to be discussed for a better understanding of the implications for practice and research regarding lactation suppression. The review addresses treatments for lactation suppression in postpartum women who do not desire to breastfeed their infant right from birth. Therefore, the findings are not directly applicable to women who had initiated breastfeeding but later wish to discontinue, or to women who lactate due to other pathology (e.g., hyperprolactinaemia). It is possible that the effectiveness as well as the side effect profile of tested agents remote from delivery may be different from that in the immediate postpartum period. Secondly, participants in the included trials were healthy postpartum women (including healthy HIV positive mothers) and it is uncertain if similar results, especially regarding side effects, would be found in postpartum women with a higher baseline risk of morbidity, e.g., those who are ill, or taking medications, or both, including antiretroviral drugs. It is important to note that this category of mothers for whom suppression of lactation may have particular health benefits, is likely to have increased risk of side effects, including drug interactions, which were not explored in the studies included in this review. Lastly, a fundamental question that is yet to be answered is whether postpartum women desire treatment for lactation suppression and, if so, which of the symptoms women are most concerned about. This would definitely go a long way in better interpretation of the effectiveness of the tested approaches.

It is clear from this review that women's views about the treatment received was not a priority, as only four trials with unreliable data explored the acceptability profile of the tested approach.

With respect to side effects, there is insufficient evidence to show that pharmacologic agents are more associated with a higher risk of major adverse effects (notably thromboembolism) compared to no treatment or each other. Several case reports have been published on thromboembolism, myocardial infarction and cerebral angiopathy following the use of bromocriptine, though a causal relationship has not been established. It is interesting to note that, in spite of these concerns, emphasis was not laid on reporting these side effects in trials conducted subsequently. However, these findings should be interpreted against the background of our review of only published data as exploration of unpublished data, especially adverse outcome data from drug company trials, may provide a clearer picture.

AUTHORS' CONCLUSIONS

Implications for practice

There is weak evidence that some pharmacologic treatments (most of which are currently unavailable to the public) are better than no treatment for suppressing the symptoms of lactation in the first week postpartum. There is currently no evidence to show that nonpharmacologic approaches are more effective than no treatment. Presently, there is insufficient evidence to address the issue of side effects of the pharmacologic and nonpharmacologic methods that are employed for suppressing lactation. When women desire treatment for suppressing lactation, consideration may be given to bromocriptine where it is still registered for such use in healthy mothers with no predisposition to major side effects of public concern. In spite of its importance, there is inadequate evidence to comment on the acceptability of approaches for suppressing postpartum lactation to women.

Implications for research

For settings in which application of some forms of treatment for suppressing lactation is the norm, there is a need for well conducted and large randomised controlled trials to compare the effectiveness of pharmacologic treatment, notably, bromocriptine to no treatment. Future research should also focus on comparison of nonpharmacologic approaches with no treatment since they presently do not appear to have any safety concerns for the public. The most important symptom(s) that concern women who desire not to breastfeed should be studied in large observational studies to ensure that effective treatment is sought by researchers on the inclination of clients' needs. Such studies should also be large enough to detect clinically important differences between interventions with respect to major side effects that have been reported through less rigorous research. Priority should be given to studying

fewer dose regimens and cheap approaches in view of women in low-resource countries.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Anonymous 1991

Methods	Randomised trial.
Participants	272 postpartum women who delivered at term and did not wish to lactate for personal or medical reasons. Partipants were expected to be at the hospital for at least three days after delivery and to be visited on day 15 in the hospital or at home. Exclusion criteria: women with history of agalactia or hypogalactia, drug allergy, intrauterine fetal death, pre-eclampsia, liver or kidney impairment and those with concomitant acute diseases. Setting: university or hospital departments of obstetrics and gynaecology in 12 European centres.
Interventions	Cabergoline 1 mg as single dose (n = 136) versus bromocriptine 2.5 mg twice daily for 14 days (n = 136). First treatment dose had to be given within 27 hours after delivery.
Outcomes	Milk secretion, breast engorgement, breast pain, frequency of adverse events and rebound lactation. Women assessed their breasts daily using a self evaluation form. Success of treatment (complete or partial) was evaluated on both day 3 (before hospital discharge) and day 15 postpartum. Adverse events were monitored daily while in hospital and on day 15. Presented data on efficacy refers to day 15 assessment. Presence of breast symptoms from days 16 to 21 in subjects with complete success by day 15 was defined as rebound lactation.
Notes	The drugs were supplied by Farmitalia Carlo Erba, Milan, Italy.

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Method of sequence generation not stated. Participants were "randomised into each treatment arm". Treatments were given according to "a randomised sequence balanced within each centre".
Allocation concealment?	Unclear	Insufficient information about allocation concealment to permit judgement. "The drugs were provided by Farmitalia Carlo Erba in individualised patient kits and assigned by the doctor according to the participant's order of entry". Comment: Unclear whether patients' kits were sequentially numbered and tamper proof.
Blinding? Adverse events	Unclear	Blinding of participants and study personnel ensured. Adverse events outcome included blood pressure and heart rate monitoring. Blinding of outcome assessors uncertain.

Anonymous 1991 (*Continued*)

Blinding? Lactation	Yes	Participants, study personnel and outcome assessors were blinded. Participants also doubled as outcome assessors. Used "double dummy technique" for blinding. Placebo was used to make up the for the difference in the duration of treatments between the two arms of the trial.
Incomplete outcome data addressed? Lactation	Yes	Before day 14: 6/136 missing from cabergoline group (one due to intolerance, two were lost to follow up and three for other reasons); 8/136 missing from the bromocriptine group (three due to intolerance, three were lost to follow up and two had other reasons). Analysis was by intention-to-treat. Efficacy variables were described for all randomised participants regardless of their adherence to study protocol.
Incomplete outcome data addressed? Adverse events	Yes	Four women (three from bromocriptine and one from cabergoline arm) who stopped treatments because of adverse events were included in the result for adverse events.
Free of selective reporting?	Yes	Comparison of outcome measures in the 'Methods' and 'Results' sections of the report indicated no evidence of selective outcome reporting.
Free of other bias?	Unclear	34 women (12.5% of randomised women), 18 taking cabergoline and 16 taking bromocriptine, received concomitant treatment that may have interfered with lactation; ergot derivatives in 28 and oral contraceptives in six, equally dispensed over the two groups. In spite of the similar distribution across both groups, the concurrent use of these classes of drugs could have exaggerated the efficacy and side effects of both interventions.

Bergsjo 1974

Methods	Randomised trial.
Participants	41 women in whom inhibition of lactation was planned. Indications included late abortion or fetal death, missed abortion, previous mastitis and adoption. Women were included in the study if staying in the hospital for at least five days. Exclusion criteria were not specified. Setting: a university hospital in Norway.
Interventions	Quinesterol tablet 4 mg (on day 0) and if necessary, an additional 4 mg tablet on day 4 (n = 23) versus diethylstilbestrol 5 mg tablet thrice daily for five days (n = 18).
Outcomes	Milk secretion, breast pain, additional oestrogen medication, symptoms suggestive of mastitis and thrombosis.

Bergsjo 1974 (*Continued*)

Notes	Quinestrol experimental tablets were supplied by Apothekernes Laboratorium for Special preparater, Oslo, Norway.

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Method of sequence generation not stated. Participants were divided into two groups "by random allocation".
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Lactation	No	No information on blinding of participants, study personnel and outcome assessors. Differences in the dosage regimen between the two interventions suggested no blinding.
Blinding? Adverse events	No	No information on blinding of participants, study personnel and outcome assessors. Differences in the dosage regimen between the two interventions suggested no blinding.
Incomplete outcome data addressed? Adverse events	Yes	Outcome data were available for all participants for the five days in the hospital.
Incomplete outcome data addressed? Lactation	Yes	Two participants (4.9%) were lost to follow up after leaving the hospital (1 from the quinestrol group and the other from the diethylstilbestrol group). Outcome data were available for all participants for the five days in the hospital.
Free of selective reporting?	Yes	Comparison of outcome measures in the 'Methods' and 'Results' sections of the report indicated no evidence of selective outcome reporting.
Free of other bias?	Yes	The study appears free of other sources of bias.

Berrebi 2001

Methods	Randomised trial.
Participants	71 postpartum women who elected not to breastfeed. Setting: Department of Obstetrics and Gynaecology, Federation de Gynecologie-Obstetrique, CHU La Grave, Toulouse Cedex.

Berrebi 2001 (*Continued*)

Interventions	Five homeopathic pills twice daily for 10 days (n = 36) versus placebo (n = 35). All patients received an anti-inflammatory treatment (naproxine-Apranax) for five days.
Outcomes	Milk secretion, breast engorgement and breast pain. Outcome assessment recorded on visual analogue scale.
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Method of sequence generation not stated.
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Adverse events	Unclear	Study described as "double blind trial". No further information to permit judgement on blinding.
Blinding? Lactation	Unclear	Study described as "double blind trial". No further information to permit judgement on blinding.
Incomplete outcome data addressed? Lactation	Yes	No missing outcome data.
Incomplete outcome data addressed? Adverse events	Yes	No missing outcome data.
Free of selective reporting?	Unclear	Insufficient information to permit judgement.
Free of other bias?	Unclear	Insufficient information to assess whether other important risk of bias exists.

Boes 1980

Methods	Randomised trial.
Participants	97 nonbreastfeeding mothers. Indications for suppression included adoption, stillbirth and too small or too ill baby. Setting: a university Hospital in Pretoria, South Africa.
Interventions	Oral bromocriptine 2.5 mg twice daily for 14 days (n=49) versus oral pyridoxine 200 mg thrice daily for 6 days (n=48).

Boes 1980 (*Continued*)

Outcomes	Milk secretion, breast engorgement, and side effects (nausea, dizziness and blood pressure changes). Main outcome measures were graded on scale of 0 to 4; 0 = no secretion or congestion while 4 = profuse secretion or congestion. Outcome assessment were on days 7 and 14.
Notes	Sandoz Products (Pty) Ltd. supplied the materials used in the trial.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation not stated. Participants were "randomly assigned" to treatment groups.
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Lactation	Unclear	Participants and study personnel were blinded to the interventions. Each participant received "identical bubble packs", supplemented with inactive tablets so that each participant took 1 tablet thrice daily for 14 days. Uncertain whether outcome assessors (two doctors) were blinded.
Blinding? Adverse events	Unclear	Uncertain whether outcome assessors (two doctors) were blinded.
Incomplete outcome data addressed? Adverse events	Yes	Outcome data were available for all participants besides three participants excluded after randomisation.
Incomplete outcome data addressed? Lactation	Yes	Three participants were excluded after randomisation (3%): two from the pyridoxine group and one from bromocriptine group. Two patients left the hospital within 24 hours of commencing treatment, while the result of one patient failed to reach the statistician. Outcome data were available for all participants besides those excluded after randomisation.
Free of selective reporting?	Yes	Comparison of outcome measures in the 'Methods' and 'Results' sections of the report indicated no evidence of selective outcome reporting.
Free of other bias?	Yes	The study appears free of other sources of bias.

Bravo-Topete 2004

Methods	Randomised trial.
Participants	80 with indications for inhibition of lactation. Setting: specialist hospital, Mexico.
Interventions	Single dose cabergoline 1 mg (n = 40) versus single dose cabergoline 0.5 mg (n = 40).
Outcomes	Milk secretion, breast engorgement, nausea and headache.
Notes	There was no indication of the day of assessment of breast symptoms.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation not stated. Treatments were given orally "at random".
Allocation concealment?	No	Allocation of intervention was dependent on patient's choice suggesting that no sequence was generated that required concealment.
Blinding? Adverse events	No	Participants, study personnel and outcome assessors were not blinded. Participants had to chose between two bottles containing a label with indication of the dose (either 1 mg or 0.5 mg).
Blinding? Lactation	No	Participants, study personnel and outcome assessors were not blinded. Participants had to chose between two bottles containing a label with indication of the dose (either 1 mg or 0.5 mg).
Incomplete outcome data addressed? Lactation	Yes	No missing outcome data.
Incomplete outcome data addressed? Adverse events	Yes	No missing outcome data.
Free of selective reporting?	Yes	Comparison of outcome measures in the 'Methods' and 'Results' sections of the report indicated no evidence of selective outcome reporting.
Free of other bias?	Yes	The study appears free of other sources of bias.

Caballero-Gordo 1991

Methods	Randomised trial.
Participants	140 healthy postpartum women who did not wish or were unable to breastfeed and who gave informed consent. Exclusion criteria included women with history of agalactia (inability to lactate), intolerance or allergy to drugs, stillbirth, hepatic or renal disorders, those undergoing treatment that might interfere with prolactin secretion and those unwilling to cooperate with study protocol. Setting: a university hospital in Spain.
Interventions	Single cabergoline tablet 1 mg (n = 40); single cabergoline tablet 0.75 mg (n = 40); single cabergoline tablet 0.5 mg (n = 40); placebo were 20 "additional" women.
Outcomes	Milk secretion, breast engorgement and breast pain. Results were described as excellent if there were no breast symptoms (milk secretion, engorgement and pain) "during hospitalisation or up to 14 days". Specific time of outcome assessment uncertain.
Notes	Financial and substantive support by Farmitalia Carlo Erba, Milan, Italy.

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Method of sequence generation not stated. Study was "prospective and randomised".
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Lactation	Unclear	Study described as "double blind trial". No further information to permit judgement on blinding.
Blinding? Adverse events	Unclear	The study did not address this outcome.
Incomplete outcome data addressed? Adverse events	Unclear	The study did not address this outcome.
Incomplete outcome data addressed? Lactation	Yes	9 participants (12.9%) were excluded because of protocol violation, 6 because they did not return for an examination on day 14 and 3 because they used bromocriptine after treatment. Missing data have been imputed using appropriate methods.
Free of selective reporting?	Yes	Comparison of outcome measures in the 'Methods' and 'Results' sections of the report indicated no evidence of selective outcome reporting.

Caballero-Gordo 1991 (*Continued*)

Free of other bias?	No	Had extreme baseline imbalance in the number of participants in intervention arms and the placebo arm (40 versus 20).

Cruttenden 1971

Methods	Randomised trial.
Participants	63 mothers who did not wish to breastfeed. Setting: Cameron Hospital, Hartlepool, United Kingdom.
Interventions	Oral quinestrol 4 mg as single dose (n = 33) versus placebo (n = 30).
Outcomes	Milk secretion and breast discomfort.
Notes	William R. Warner & Co. Ltd. supplied the materials used and helped with statistical analysis of the findings.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation not stated. Treatments were given "randomly".
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Adverse events	Unclear	The study did not address this outcome.
Blinding? Lactation	Yes	Study was conducted in a "double blind manner", neither the medical nor nursing staff knowing the identity of the coded tablets.
Incomplete outcome data addressed? Lactation	Unclear	Outcome data not available for 7 participants (10%) out of the 70 women randomised. Reason for missing data not stated.
Incomplete outcome data addressed? Adverse events	Unclear	The study did not address this outcome.
Free of selective reporting?	No	The trialists did not include results for adverse events especially thromboembolism in spite of published studies implicating oestrogen preparations in this complication before the trial.

Cruttenden 1971 (*Continued*)

Free of other bias?	No	Statistical analysis by the supplier of the tested drug was a potential threat to the validity of results of the study.

De Gezelle 1979

Methods	Randomised trial.
Participants	90 healthy postpartum women (in 5 groups of 18) who chose not to breastfeed. Setting: a university hospital in Belgium.
Interventions	Interventions: oral diethylstilboestrol 5 mg thrice daily for 5 days (n = 18); oral bendroflumethiazide 5 mg thrice daily for 5 days (n = 18); intramuscular single dose of a mixture of estradiol esters (10 mg) and the testosterone esters (200 mg) in olive oil (Estandron Prolongatum ®) (n = 18); oral bromocriptine 5 mg daily for 14 days (n = 18). Control: wearing of tight fitting brassiere night and day with application of infrared lamp thrice daily for 10 minutes each time (n = 18).
Outcomes	Milk secretion, breast engorgement and breast tenderness. Outcome measures were graded as absent, mild, moderate and severe.
Notes	The NIH kit (VLSI) used for determination of serum prolactin in the same study was provided by the National Institute of Health, Bethesda, Md., USA.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation not stated. Treatment regimens were "randomly assigned to five groups of 18 women each".
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Lactation	No	Only the outcome assessors were blinded. Outcome assessor was the same nurse, who had no knowledge of the type of treatment applied.
Blinding? Adverse events	Unclear	The study did not address this outcome.
Incomplete outcome data addressed? Lactation	Unclear	Outcome data for breast engorgement was not provided for two participants in the estandron prolongatum ® group and no reasons for missing data were provided.

De Gezelle 1979 (*Continued*)

Incomplete outcome data addressed? Adverse events	Unclear	The study did not address this outcome.
Free of selective reporting?	No	The study failed to include thromboembolism as an outcome measure in spite of published studies implicating oestrogen preparations in this complication before the trial.
Free of other bias?	Yes	The study appears free of other sources of bias.

Defoort 1987

Methods	Randomised trial.
Participants	54 healthy mothers who delivered at term through uncomplicated vaginal deliveries (except for three women who had caesarean section) and elected not to breastfeed their infants. Exclusion criteria: women with abnormal physical findings or abnormal laboratory results related to vital functions. Setting: a university hospital in Belgium.
Interventions	Single intramuscular injection of long acting bromocriptine 50 mg (n = 26) versus single 3 ml injection of estandrom prolongatum ® (estradiol/testosterone ester combination) (n = 28).
Outcomes	Milk flow, breast engorgement, breast pain, untoward systemic effects, coagulation profile and rebound lactation. Both investigators and patients reported outcomes. Overall efficacy at the end of 28 days was presented. Patient data were extracted.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation was not stated though on "non-alternating" basis.
Allocation concealment?	Yes	Serially numbered closed envelopes provided by the manufacturer were used to conceal allocation of intervention.
Blinding? Adverse events	No	Outcome assessors were not blinded.
Blinding? Lactation	No	Participants were blinded to the intervention, study personnel were not blinded as they had to prepare the injections before administration to the participants. Outcome assessors were not blinded.

Defoort 1987 (*Continued*)

Incomplete outcome data addressed? Adverse events	Yes	Outcome data available for participants that completed the study.
Incomplete outcome data addressed? Lactation	Yes	Three (5.3%) of the 57 participants originally "retained for the study did not complete the study" and their data were not included in the analysis. One of the patients was disqualified after inadvertently taking prohibited drugs (an oral contraceptive and acetylsalicylate) during the observation period while the remaining two were lost to follow up.
Free of selective reporting?	No	The trialists did not include thromboembolism as an outcome measure in spite of published studies implicating oestrogen preparations in this complication before the trial.
Free of other bias?	Yes	The study appears free of other sources of bias.

Dewhurst 1977

Methods	Randomised trial.
Participants	37 participants who did not desire to breastfeed. Setting: Queen Charlotte's Hospital, London.
Interventions	Bromocriptine (2.5 mg) twice daily for 14 days and 1 daily for a further 7 days (n = 20) versus placebo (n = 17).
Outcomes	Milk production, breast engorgement and breast pain reported on data cards over 28 days by participants. Rebound lactation.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation was not stated. Participants were "randomly allocated" treatments.
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Adverse events	No	The study did not address this outcome.

Dewhurst 1977 (*Continued*)

Blinding? Lactation	Yes	Patients were randomly allocated indistinguishable capsules of "active" bromocriptine or pharmacologically inactive placebo. Blinding of participants, study personnel and outcome assessors ensured. Participants also doubled as outcome assessors.
Incomplete outcome data addressed? Adverse events	Unclear	The study did not address this outcome.
Incomplete outcome data addressed? Lactation	No	15/52 (30.7%) of the participants that embarked on the trial did not return sufficient data for analysis. Distribution of missing data across groups and reasons not reported.
Free of selective reporting?	No	The trialists set out to determine the optimum dosage to minimise side effects but did not report side effects of tested interventions.
Free of other bias?	Unclear	The study appears free of other sources of bias.

England 1988

Methods	Randomised trial.
Participants	43 healthy postpartum women who requested lactation suppression. Setting: a university hospital in Johannesburg, South Africa.
Interventions	Oral prostaglandin E_2: 2 mg on puerperal day 3 or 4, then 2 mg 6 hourly at 3 doses, followed after another six hours by a 4 mg dose (n = 21) versus oral bromocriptine 2.5 mg 12 hourly for 14 days (n = 22).
Outcomes	Breast discomfort, congestion and tenderness, volume of breast milk expressed. Severity of breast tenderness were assessed on a linear analogue scale. Record of women after discharge were collected at six weeks postnatal clinic.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation not stated. Women were allocated "by randomised cards".
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.

England 1988 (*Continued*)

Blinding? Lactation	No	No blinding was employed.
Blinding? Adverse events	Unclear	No blinding was employed.
Incomplete outcome data addressed? Lactation	Yes	No missing data.
Incomplete outcome data addressed? Adverse events	Yes	No missing data.
Free of selective reporting?	No	Data on side effects were reported incompletely. Only provided data on two side effects.
Free of other bias?	Yes	The study appears free of other sources of bias.

Firth 1969

Methods	Randomised trial.
Participants	150 postpartum women who elected not to breastfeed. Setting: St George's Hospital, London, United Kingdom.
Interventions	Oral quinestrol 0.8 mg as single dose (n = 50), intramuscular injection 45 mg hexoestrol (n = 50) and oral placebo (n = 50). Treatment was given within two hours of delivery.
Outcomes	Milk secretion and breast congestion.
Notes	Report was presented as correspondence.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation not stated. Participants were "randomly selected" into groups.
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Lactation	Unclear	Study described as "double blind trial". Interventions included both orally and intramuscularly administered drugs. No further information to permit judgement on blinding.

Firth 1969 (*Continued*)

Blinding? Adverse events	Unclear	The study did not address this outcome.
Incomplete outcome data addressed? Lactation	Yes	No missing data.
Incomplete outcome data addressed? Adverse events	Unclear	The study did not address this outcome.
Free of selective reporting?	Unclear	Insufficient information to permit judgement.
Free of other bias?	Unclear	Insufficient information to assess whether other important risk of bias exists.

Fischer 1995

Methods	Randomised trial.
Participants	150 postpartum women who did not nurse their baby. Setting: a university hospital, Nurnberg, Germany.
Interventions	Oral bromocriptine at 2.5 mg twice daily for 14 days (n = 81) and oral metergoline at 4 mg thrice daily for 10 days (n = 69).
Outcomes	Milk secretion, breast tension, minor side effects, acceptability to the woman.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation not stated.
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Lactation	No	No evidence of blinding.
Blinding? Adverse events	No	No evidence of blinding.

Fischer 1995 (*Continued*)

Incomplete outcome data addressed? Lactation	Yes	Data were obtained during the first five days of postpartum admission and seven months later. No missing data for outcomes assessed while on admission.
Incomplete outcome data addressed? Adverse events	Yes	No missing data for outcomes assessed while on admission.
Free of selective reporting?	No	Trialists did not provide data for a key outcome (thromboembolism) that would be expected to have been reported for such a study.
Free of other bias?	Unclear	Insufficient information to assess whether other important risk of bias exists.

Giorda 1991

Methods	Randomised trial.
Participants	36 women who were delivered by caesarean section and elected to suppress postpartum lactation. Setting: Clinics of Obstetrics and Gynaecology, Milan, Italy.
Interventions	Oral cabergoline 1 mg as single dose (n = 18) versus oral bromocriptine 2.5 mg twice daily for 14 days (n = 18).
Outcomes	Milk secretion, breast engorgement and breast pain
Notes	25% per cent of the women had signs of breast engorgement before cabergoline was administered.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Generation of allocation sequence with tables of random numbers.
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Adverse events	No	Only outcome assessors were blinded.
Blinding? Lactation	No	Only outcome assessors were blinded to intervention.

Giorda 1991 (*Continued*)

Incomplete outcome data addressed? Adverse events	Yes	No missing data.
Incomplete outcome data addressed? Lactation	Yes	No missing data.
Free of selective reporting?	Unclear	Specific side effects being evaluated were not stated in the 'Methods' section of the report.
Free of other bias?	Yes	The study appears to be free of other sources of bias.

Hutchison 1981

Methods	Randomised trial.
Participants	40 postpartum women who volunteered. Setting: Women's Hospital, Auckland.
Interventions	Oral bromocriptine 2.5 mg twice daily for 14 days (n = 20) versus oral placebo (n = 20)
Outcomes	Milk secretion, breast engorgement, side effects and acceptability of treatment to the woman. Milk secretion, breast engorgement and side effects were scored daily on a scale of 0 to 3. Milk secretion was expressed as "mean score while in hospital".
Notes	Personnel of Sandoz Pharma Ltd. conducted the statistical analysis and supplied the tablets used in the study.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation not stated.
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Adverse events	Yes	Study participants, personnel and outcome assessors were blinded using active and matching placebo tablets for interventions.
Blinding? Lactation	Yes	Study participants, personnel and outcome assessors were blinded using active and matching placebo tablets for interventions.
Incomplete outcome data addressed? Lactation	Yes	No missing data.

Hutchison 1981 (*Continued*)

Incomplete outcome data addressed? Adverse events	Yes	No missing data.
Free of selective reporting?	No	Although data on acceptability of treatments to the participants was collected as one of the outcome measures, it was not included in the presented result.
Free of other bias?	No	Statistical analysis by the supplier of the tested drug was a potential threat to the validity of results of the study.

Iliya 1966

Methods	Randomised trial.
Participants	192 postpartum women who desired to bottlefeed. Setting: Lying-In Hospital, Boston, MA, USA.
Interventions	Intramuscular deladumone ® (testosterone oenanthate 180 mg/cc plus oestradiol valerate 8mg/cc) given at 2 cc as a single dose (n = 102) versus intramuscular placebo (n = 90).
Outcomes	Breast engorgement and breast pain. Outcome assessments were made on days 2 to 4. All observations were made by the same physician.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation not stated. Treatments were given to the patients "at random".
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Lactation	Yes	Participants, study personnel and outcome assessors were blinded. Treatments were allocated using identical dose vials containing active drug or placebo and coded in random fashion. Contents and the code unknown until the end of the study. Code was broken six months after the completion of the study.
Blinding? Adverse events	Unclear	The study did not address this outcome.

Iliya 1966 (*Continued*)

Incomplete outcome data addressed? Adverse events	Unclear	The study did not address this outcome.
Incomplete outcome data addressed? Lactation	Unclear	Initially, 203 were included in the study, but only 192 were available for satisfactory analysis. Reasons for exclusions not stated.
Free of selective reporting?	No	The trialists did not include thromboembolism as an outcome measure in spite of published studies implicating oestrogen preparations in this complication before the trial.
Free of other bias?	Yes	The study appears to be free of other sources of bias.

Kremer 1990

Methods	Randomised trial.
Participants	61 healthy postpartum women, who were delivered at term and not ready to breastfeed their infants. Exclusion criteria were "relevant abnormal findings on physical examination, abnormal laboratory values and the use of concomitant treatment that would influence the hormonal and metabolic state". Setting: a university hospital in Nijmegen, The Netherlands.
Interventions	Depot bromocriptine injection 40 mg (n = 30) versus depot bromocriptine injection 50 mg (n = 31).
Outcomes	Breast symptoms and side effects.
Notes	Sandoz BV (Uden, The Netherlands) supplied the study medication.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Computerised randomisation was performed.
Allocation concealment?	Yes	The dosages were put in numbered envelopes, which were opened after the formal registration of the participants.
Blinding? Adverse events	Yes	Participants who also doubled as outcome assessors in the trial were blinded.
Blinding? Lactation	Yes	The woman did not know the dosage, but the investigator was aware of it because he prepared the injection just before the injection

Kremer 1990 (*Continued*)

Incomplete outcome data addressed? Lactation	Yes	No missing data.
Incomplete outcome data addressed? Adverse events	Yes	No missing data.
Free of selective reporting?	Yes	Comparison of outcome measures in the 'Methods' and 'Results' sections of the report indicated no evidence of selective outcome reporting.
Free of other bias?	Yes	The study appears free of other sources of bias.

Kuku 1968

Methods	Randomised trial.
Participants	104 women who did not wish to breastfeed or in whom breastfeeding was contraindicated. Setting: Kingston Hospital, United Kingdom.
Interventions	Oral quinestrol 2 mg as single dose (n = 52) versus oral ethinyl estradiol 0.2 mg within six hours, and 0.2 mg twice daily for five days (n = 52).
Outcomes	Milk secretion, breast engorgement and breast pain. The condition of the breast was examined daily for 8 days. Case recorded as successful if the breasts are soft in consistency and without discomfort and no milk, or only a little colostrum expressed on the fifth day.
Notes	William R. Warner and Co. Ltd. supplied the drugs.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation not stated. The preparation were allocated "at random to patients entering the trial".
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Lactation	Yes	Study participants, personnel and outcome assessors were blinded to the interventions. Identical looking capsules were used. Placebo was used to make up the for the difference in the duration of treatments between the two arms of the trial.

Kuku 1968 (*Continued*)

Blinding? Adverse events	Yes	Study participants, personnel and outcome assessors were blinded to the interventions
Incomplete outcome data addressed? Adverse events	Yes	No missing data.
Incomplete outcome data addressed? Lactation	Yes	No missing data.
Free of selective reporting?	No	Report on side effects was only limited to that of the tested drug.
Free of other bias?	Unclear	Insufficient information to assess whether other important risk of bias exists.

MacDonald 1976

Methods	Randomised trial.
Participants	131 postpartum women wishing to bottlefeed their babies. Setting: St. Mary Hospital, Leeds, United Kingdom.
Interventions	Oral pyridoxine 200 mg thrice daily for six days (n = 93) versus oral placebo (lactose) (n = 82).
Outcomes	Milk secretion, breast engorgement and breast discomfort.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation not stated. Interventions were issued "in random order".
Allocation concealment?	Yes	Treatment allocation using identical tablets containing either lactose or pyridoxine in numbered packs dispensed by the hospital pharmacy, which retained the identifying code until completion of the study.
Blinding? Adverse events	Unclear	The study did not address this outcome.
Blinding? Lactation	Yes	Participants, study personnel and outcome assessors were blinded to the interventions.

MacDonald 1976 (*Continued*)

Incomplete outcome data addressed? Lactation	No	Of the 191 women randomised, 14 withdrew as they discharged themselves early from the hospital (nine were on Pyridoxine and 5 were on placebo), one woman decided to breastfeed and another woman was withdrawn for skin rash. Outpatient assessment after discharge on the 9 to10th day was possible for 131 (68.6%) of those randomised. Total exclusion and attrition rate was 31.4%.
Incomplete outcome data addressed? Adverse events	Unclear	The study did not address this outcome.
Free of selective reporting?	Yes	Comparison of outcome measures in the 'Methods' and 'Results' sections of the report indicated no evidence of selective outcome reporting.
Free of other bias?	Yes	The study appears free of other sources of bias.

Mann 1971

Methods	Randomised trial.
Participants	95 postpartum women who desired not to breastfeed. Setting: Lewis Hospital, Isle of Lewis, UK.
Interventions	Oral quinestrol 4 mg single dose (n = 45) versus oral stilbestrol 15 mg per day for seven days (n = 50).
Outcomes	Milk secretion, breast engorgement and rebound lactation.
Notes	A personnel of William R. Warner & Co. Ltd. provided the preparations and helped with the preparation of the report of the study.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation not stated
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Lactation	Yes	Participants, study personnel and outcome assessors were blinded to interventions.

Mann 1971 (*Continued*)

Blinding? Adverse events	Yes	Participants, study personnel and outcome assessors were blinded to interventions.
Incomplete outcome data addressed? Adverse events	Yes	No missing data.
Incomplete outcome data addressed? Lactation	Yes	No missing data.
Free of selective reporting?	No	The trialists did not include thromboembolism as an outcome measure in spite of published studies implicating oestrogen preparations in this complication before the trial.
Free of other bias?	Yes	The study appears free of other sources of bias.

McGlone 1969

Methods	Randomised trial.
Participants	44 mothers who did not wish to breastfeed. Setting: Dryburn Hospital, Durham, United Kingdom.
Interventions	Oral quinestrol 4 mg as single dose (n = 22) versus oral placebo tablets (n = 22).
Outcomes	Milk leakage, breast engorgement and discomfort.
Notes	The Medical Director of William R. Warner & Co. Ltd. supplied the materials and provided advice on the statistical analysis.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation not stated.
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Adverse events	Unclear	The study did not address adverse events related to the interventions.
Blinding? Lactation	Yes	Participants, study personnel and outcome assessors were blinded to the interventions. Coded tablets were assigned randomly and the key to the tablet code was broken after all records had been completed and comparisons made.

McGlone 1969 (*Continued*)

Incomplete outcome data addressed? Lactation	Yes	Six participants (12%) dropped out of the 50 women that entered the trial (3 from each group).
Incomplete outcome data addressed? Adverse events	Unclear	The study did not address adverse events related to the interventions.
Free of selective reporting?	Unclear	The trialists did not include thromboembolism as an outcome measure in spite of published studies implicating oestrogen preparations in this complication before the trial.
Free of other bias?	Unclear	Advice on statistical analysis by the supplier of the tested drug constituted an uncertain threat to the validity of the trial results.

Melis 1988

Methods	Randomised trial.
Participants	32 healthy postpartum women who elected not to breastfeed. All women had an uncomplicated pregnancy and spontaneous delivery at term. Exclusion criteria included use of general anaesthetic agents. Setting: a university hospital in Italy.
Interventions	Oral cabergoline 400 mcg (n = 8), oral cabergoline 600 mcg (n = 8), oral cabergoline 800 mcg (n = 8) and oral placebo (n = 8).
Outcomes	Breast tension, breast tenderness, milk secretion and rebound engorgement.
Notes	Drugs were provided by Farmitalia Carlo Erba, Medical Division, Milan, Italy.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation not stated. Women were "randomly allocated to four treatment groups of eight subjects".
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Lactation	Unclear	Participants and study personnel were blinded to the interventions. Uncertain whether outcome assessors were blinded.
Blinding? Adverse events	Unclear	The study did not address this outcome.

Melis 1988 (*Continued*)

Incomplete outcome data addressed? Adverse events	Unclear	The study did not address this outcome.
Incomplete outcome data addressed? Lactation	Yes	No missing data.
Free of selective reporting?	No	Method of assessment of reported side effects in the cabergoline group was not stated. Non-reporting of side effects in the placebo group did not permit inclusion of result in meta-analysis.
Free of other bias?	Unclear	Women who showed signs of lactation from day 2 of treatment were also given bromocriptine to suppress lactation. The impact of the such additional intervention on the efficacy variables after day 2 of the treatment and its distribution across groups is unclear.

Niebyl 1979

Methods	Randomised trial.
Participants	99 women who had undergone vaginal delivery and who elected lactation suppression. Setting: John Hopkins Hospital, Maryland, U.S.A.
Interventions	Oral chlorotrianisene 72 mg every 12 hours for four doses versus placebo.
Outcomes	Breast congestion, milk secretion, breast pain, haematologic and coagulation factors and satisfaction with drug used.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Used table of random numbers.
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Adverse events	Unclear	The study did not address this outcome.

Niebyl 1979 (*Continued*)

Blinding? Lactation	Unclear	Participants and study personnel were blinded to the interventions. Used identical-appearing capsules containing corn oil as placebo. Uncertain whether outcome assessors were blinded.
Incomplete outcome data addressed? Lactation	No	Loss to follow-up as at day 8 postpartum was 46.5%.
Incomplete outcome data addressed? Adverse events	Unclear	The study did not address this outcome.
Free of selective reporting?	Yes	Comparison of outcome measures in the 'Methods' and 'Results' sections of the report indicated no evidence of selective outcome reporting.
Free of other bias?	Unclear	Fifty participants were initially randomised and an "additional 49 patients were evaluated". Unclear what the initial sample size for the study was.

Nilsen 1976

Methods	Randomised trial.
Participants	38 puerperal women who did not desire to breastfeed. Exclusion criteria included women with severe metabolic disturbance or on concomitant therapy e.g. corticoids, thyroid and antithyroid therapy, diuretics and phenothiazines, which might influence the results of the study. Setting: a university hospital in Oslo, Norway.
Interventions	Oral bromocriptine 2.5 mg twice daily for 14 days (n = 20) versus oral diethylstilbestrol 10 mg twice daily for 7 consecutive days (n = 18).
Outcomes	Milk secretions, breast congestion, side effects, blood pressure changes, clotting profile and rebound lactation. Symptoms were scored on a scale of 0 and 3.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation not stated. "A randomisation list' was employed.

Nilsen 1976 (*Continued*)

Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Adverse events	Yes	Participants, study personnel and outcome assessors were blinded to the interventions.
Blinding? Lactation	Yes	Participants, study personnel and outcome assessors were blinded to the interventions.
Incomplete outcome data addressed? Adverse events	Yes	No missing data for the duration of follow up considered in the review.
Incomplete outcome data addressed? Lactation	Yes	No missing data for the duration of follow up considered in the review.
Free of selective reporting?	Yes	Comparison of outcome measures in the 'Methods' and 'Results' sections of the report indicated no evidence of selective outcome reporting.
Free of other bias?	Yes	The study appears free of other sources of bias.

Phillips 1975

Methods	Randomised trial.
Participants	196 private postpartum women who chose not to breastfeed. Setting: U.S.A.
Interventions	Oral chlorotrianisene 72 mg twice daily for two days for a total dose of four capsules (n = 98) versus placebo (n = 98)
Outcomes	Breast engorgement, milk secretion and discomfort, use of concurrent supplemental therapy - breast binders, ice bags and or analgesics.
Notes	Partly funded by Merrell-National Laboratories, Merrell Inc., Cincinnati, Ohio.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation not stated.
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.

Phillips 1975 (*Continued*)

Blinding? Adverse events	Unclear	The study did not address this outcome.
Blinding? Lactation	Unclear	Women were randomly assigned on a "double blind basis". No further information to permit judgement on blinding.
Incomplete outcome data addressed? Lactation	No	Out of the 200 participants that entered the trial, four were excluded from the analysis as they "took fewer than the specified protocol".
Incomplete outcome data addressed? Adverse events	Unclear	The study did not address this outcome.
Free of selective reporting?	No	The trialists did not include thromboembolism as an outcome measure in spite of published studies implicating oestrogen preparations in this complication before the trial.
Free of other bias?	Yes	The study appears free of other sources of bias.

Piya-Anant 2004

Methods	Randomised trial.
Participants	230 asymptomatic HIV positive mothers aged 18 to 35 years. Normal delivery at 37 to 42 weeks. Exclusion criteria included women at high risk for taking a combined pill with a high dose of oestrogen, women older than 35 years, overweight or with a past history of a thromboembolic episode, women at high risk for taking bromocriptine, those with pregnancy induced hypertension, seizures, stroke and myocardial infarction. Seting: a university hospital in Thailand.
Interventions	Oral ethinyl oestradiol 50 µg twice daily for five days (n = 116) versus Oral bromocriptine dose was not stated (n = 114).
Outcomes	Breast engorgement.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Generation of allocation sequence was by computer randomisation.

Piya-Anant 2004 (*Continued*)

Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Lactation	Unclear	Study participants and personnel were blinded to the interventions. Uncertain whether outcome assessors were blinded to the interventions.
Blinding? Adverse events	Unclear	Study participants and personnel were blinded to the interventions. Uncertain whether outcome assessors were blinded to the interventions.
Incomplete outcome data addressed? Adverse events	Yes	No missing data.
Incomplete outcome data addressed? Lactation	Yes	No missing data.
Free of selective reporting?	Yes	Comparison of outcome measures in the 'Methods' and 'Results' sections of the report indicated no evidence of selective outcome reporting.
Free of other bias?	Yes	The study appears free of other sources of bias.

Rolland 1973

Methods	Randomised trial.
Participants	40 women who had given sufficient proof of lactation in a previous puerperium. Exclusion criteria include women on medication that might influence their hormonal state and patients with hypertension (diastolic pressure more than 100 mmHg). Setting: The Wever Hospital, Heerlen, Netherland.
Interventions	Oral bromocriptine 7.5 mg daily for 7 days (n = 10), oral bromocriptine 5 mg daily for 7 days (n = 10) and oral bromocriptine 2.5 mg daily for 7 days (n = 10), oral placebo (n = 10). First capsule given within the two to six hours after delivery.
Outcomes	Milk secretion, breast engorgement, breast pain, rebound lactation and satisfaction with intervention.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**

Rolland 1973 (*Continued*)

Adequate sequence generation?	Unclear	Method of sequence generation not stated. Participants received treatment "at random".
Allocation concealment?	No	No information about allocation concealment to permit judgement. Participants who had to discontinue medication within the first 72 hours after delivery were excluded and "another patient with the same dosage schedule was admitted into the study". Comment: unlikely that allocation sequence was concealed.
Blinding? Lactation	Yes	Capsules of identical appearance were used for bromocriptine and placebo. Participants, study personnel and outcome assessors were blinded to the interventions.
Blinding? Adverse events	Yes	Participants, study personnel and outcome assessors were blinded to the interventions.
Incomplete outcome data addressed? Adverse events	Unclear	Completeness of data unclear as the result was inadequately presented. "No side effects occurred as a result of CB154 medication; mild symptoms were noted just as frequently in the placebo group as in the treatment groups".
Incomplete outcome data addressed? Lactation	Yes	Analysis was by intention-to-treat. Outcome data for eight participants who stopped treatment due to mammary activity within 90 hours of delivery were included in the analysis
Free of selective reporting?	Yes	Comparison of outcome measures in the 'Methods' and 'Results' sections of the report indicated no evidence of selective outcome reporting.
Free of other bias?	Yes	The study appears free of other sources of bias.

Scapin 1982

Methods	Randomised trial.
Participants	40 healthy postpartum women who did not want to breastfeed for personal reasons. Evidence of adequate mammary activity in the previous pregnancy. Setting: a university hospital in Milan, Italy.
Interventions	Metergoline 4 mg thrice daily for 7 days versus bromocriptine 2.5 mg twice daily for seven days. Additional 7 days treatment when there was evidence of mammary activity. One capsule containing placebo was added to make up similar treatment schedule. All women also had methylergometrine hydrogen maleate 0.2 mg as part of the routine management after delivery and 0.2 mg daily p.o. thrice daily for 7 days.

Scapin 1982 (*Continued*)

Outcomes	Milk excretion, mammary engorgement and pain.
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Method of sequence generation not stated. Participants were randomly allocated to one of the two treatment groups.
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Lactation	Yes	Participants, study personnel and outcome assessors were blinded to the interventions.The two drugs were contained in identical sealed capsule. Capsules were packed in small plastic bags with a label specifying the day and time of administration.
Blinding? Adverse events	Unclear	The study did not address this outcome.
Incomplete outcome data addressed? Lactation	Yes	No missing data.
Incomplete outcome data addressed? Adverse events	Unclear	The study did not address this outcome.
Free of selective reporting?	Yes	Comparison of outcome measures in the 'Methods' and 'Results' sections of the report indicated no evidence of selective outcome reporting.
Free of other bias?	No	There were two periods of treatment, the second depending on the outcome of the first treatment in the first week. The second period of treatment was not consistent across studies.

Schwartz 1973

Methods	Randomised trial.
Participants	346 women who elected not to breastfeed. Setting: a university hospital, Pennsylvania, USA.

Schwartz 1973 (*Continued*)

Interventions	360 mg of intramuscular testosterone oenanthate plus16 mg of oestradiol valerate (n = 89), diethylstilbestrol 5 mg orally thrice daily for three days (n = 89), chlorotrianesene 72 mg orally every 12 hours at four doses (n = 85), injectable and oral placebo (n = 83).
Outcomes	Breast tenderness, consistency and milk leakage.
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Method of sequence generation not stated.
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Lactation	Unclear	Participants and study personnel were blinded to the interventions. Uncertain whether outcome assessors were blinded.
Blinding? Adverse events	Unclear	The study did not address this outcome.
Incomplete outcome data addressed? Lactation	Unclear	Seven participants (1.9%) out of the 353 that entered the trial were excluded from the analysis of outcome data on day 3.
Incomplete outcome data addressed? Adverse events	Unclear	The study did not address this outcome.
Free of selective reporting?	No	The study failed to include results for adverse events directly related to the interventions especially thromboembolism which was associated with oestrogen preparations in published studies before the trial.
Free of other bias?	Unclear	The study appears free of other sources of bias.

Shaaban 1975

Methods	Randomised trial.
Participants	150 postpartum women who elected to bottlefeed their babies and those whose babies were stillborn or were nursed in incubators on account of prematurity. Setting: two tertiary care centres in Egypt.

Shaaban 1975 (*Continued*)

Interventions	Short course tamoxifen 10 mg: 3 tabs twice daily for 2 days, followed by 2 tabs twice daily for two days and 1 tab twice daily for two days, long course tamoxifen 10 mg: 1 tab twice daily for 14 days, placebo equivalent to long course and short course of tamoxifen. Treatments were commenced within two hours of delivery.
Outcomes	Breast milk secretion, engorgement and tenderness, thromboembolic complications.
Notes	The Clinical Research Department of Imperial Chemical Industry supplied tamoxifen.

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Method of sequence generation not stated.
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Adverse events	Unclear	The study did not adequately report this outcome.
Blinding? Lactation	Yes	Participants, study personnel and outcome assessor were blinded to the interventions. The courses of treatment were coded and the code was only broken at the end of the trial.
Incomplete outcome data addressed? Lactation	Yes	Ten women who did not attend for complete follow up were dropped from the trial. Loss to follow up was 6.7%.
Incomplete outcome data addressed? Adverse events	Unclear	The study did not adequately report this outcome.
Free of selective reporting?	Yes	Comparison of outcome measures in the 'Methods' and 'Results' sections of the report indicated no evidence of selective outcome reporting.
Free of other bias?	Yes	The study appears free of other sources of bias.

Shrivastav 1988

Methods	Randomised trial.
Participants	60 women who required suppression of puerperal lactation following a fresh stillbirth or an early neonatal death. Setting: a university hospital in Vellore, India.

Shrivastav 1988 (*Continued*)

Interventions	Jasmine flower: 50 cm of stringed flowers from the same vendor and applied to each breast and replaced every 24 hours for five days (n = 30) versus bromocriptine mesylate 2.5 mg 8 hourly for five days (n = 30).
Outcomes	Serum prolactin, milk secretion and breast engorgement. Milk secretion and engorgement were evaluated by manual pressure on the nipple and observations recorded on a 4-point scale (0, 1, 2 and 3). The two scores were combined to give an aggregate score of 0 to 6. Scores greater than or equal to 4 at the end of 72 hours were considered unsuccessful.
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Method of sequence generation not stated. Women were "randomly divided into groups".
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Adverse events	Unclear	The study did not address this outcome.
Blinding? Lactation	No	Blinding was not possible for participants and study personnel. Uncertain whether outcome assessors were blinded.
Incomplete outcome data addressed? Adverse events	Unclear	The study did not address this outcome.
Incomplete outcome data addressed? Lactation	Yes	No missing data.
Free of selective reporting?	Yes	Comparison of outcome measures in the 'Methods' and 'Results' sections of the report indicated no evidence of selective outcome reporting.
Free of other bias?	Yes	The study appears free of other sources of bias.

Steenstrup 1977

Methods	Randomised trial.
Participants	41 women who wished to prevent postpartum lactation either because of maternal wish, adoption, illness of mother, illness of the child, child death and fetal death in utero. Exclusion criteria: Women with metabolic disturbances and concomitant therapy, e.g. corticoid, thyroid, antithyroid therapy, diuretics, phenothiazines, which might influence the results of the study. Setting: a university hospital in Denmark.
Interventions	Bromocriptine 2.5 mg twice daily for 14 days (n = 20), diethylstilbestrol capsules containing 10 mg of active compound were employed twice daily for 7 days (and made up with placebo to last till 14 days) (n = 21).
Outcomes	Milk secretion, breast engorgement, spotting per vaginam, rebound lactation, failure to suppress lactation at 14 days. Symptoms were scored on a scale of 0 to 3.
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Method of sequence generation not stated. Allocation of patients to two groups was made with the "help of a randomisation list".
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Adverse events	Unclear	Participants and study personnel were blinded to the interventions. Uncertain whether outcome assessors were blinded.
Blinding? Lactation	Unclear	Participants and study personnel were blinded to the interventions. Uncertain whether outcome assessors were blinded.
Incomplete outcome data addressed? Lactation	Yes	Three participants (7.3%) were lost to follow up.
Incomplete outcome data addressed? Adverse events	Yes	Three participants (7.3%) were lost to follow up.
Free of selective reporting?	Unclear	Insufficient information to permit judgement.
Free of other bias?	Unclear	Insufficient information to assess whether other important risk of bias exists.

Stirrat 1968

Methods	Randomised trial.
Participants	100 mothers delivered consecutively and who choose to bottlefeed their babies. Setting: a general hospital in Glasgow, UK.
Interventions	Stilbesterol 5 mg (day 1: 3 tablets thrice daily, day 2: 2 tablets thrice daily, day 3: 1 tablet thrice daily, day 4: 1 tablet twice daily and day 5: 1 tablet statum (n = 50) versus placebo (n = 50).
Outcomes	Milk secretion, breast pain, thromboembolism, number of women who require second line drug or method to achieve suppression.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation not stated. "Patients were randomly assigned to either A or B".
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Adverse events	Unclear	The study did not adequately report this outcome. Only thrombo-embolic episodes were reported in the result.
Blinding? Lactation	Unclear	Participants and outcome assessor were blinded to the interventions. The study personnel were not blinded. The tablets were placed in identical containers labelled A and B, the content being known to one of the authors.
Incomplete outcome data addressed? Adverse events	Unclear	The study did not adequately report this outcome.
Incomplete outcome data addressed? Lactation	Yes	No missing data.
Free of selective reporting?	Yes	Comparison of outcome measures in the 'Methods' and 'Results' sections of the report indicated no evidence of selective outcome reporting.
Free of other bias?	Yes	The study was free of other sources of bias.

Swift 2002

Methods	Randomised trial.
Participants	60 nonbreastfeeding mothers who gave birth to viable newborns of singleton gestations, had an uncomplicated postpartum and had not received hormonal lactation suppressants. Setting: a private hospital in south-central USA.
Interventions	Use of breast binders (n = 30) versus wearing of support bra (n = 30) for the first 10 days postpartum.
Outcomes	Breast engorgement, breast tenderness, breast leakage and use of pain relief measures. Outcomes were rated on a scale of 1 to 4 for each of the 5 data collection periods (postpartum days 1, 3, 4, 9 and 10. Assessments were recorded through telephone on days 3, 4, 9 and 10.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	A table of random numbers was used to determine group assignment before the first contact.
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Lactation	No	Impossible to blind participants and study personnel. Outcome assessors (woman herself) were not blinded.
Blinding? Adverse events	Unclear	The study did not report this outcome.
Incomplete outcome data addressed? Adverse events	Unclear	The study did not report this outcome.
Incomplete outcome data addressed? Lactation	Yes	No missing data.
Free of selective reporting?	Yes	Comparison of outcome measures in the 'Methods' and 'Results' sections of the report indicated no evidence of selective outcome reporting.
Free of other bias?	Yes	The study was free of other sources of bias

Thorbert 1983

Methods	Randomised trial.
Participants	24 women who wished to inhibit lactation after childbirth. Setting: Central Hospital, Kalmar and University Hospital, Lund, Sweden.
Interventions	Cyclofenil 300 mg twice daily for 14 days (n = 13) versus bromocriptine 2.5 mg twice daily for 14 days (n = 11).
Outcomes	Breast engorgement, rebound lactation, number of women who require second line drug or method to achieve suppression.
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Method of sequence generation not stated. "Allocation of treatment was randomised".
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Adverse events	Unclear	The study did not adequately report this outcome.
Blinding? Lactation	Yes	Participants, study personnel and outcome assessors were blinded to interventions. Double blind conditions were achieved by double dummy technique
Incomplete outcome data addressed? Lactation	Yes	No missing data.
Incomplete outcome data addressed? Adverse events	Unclear	The study did not adequately report this outcome.
Free of selective reporting?	Yes	Comparison of outcome measures in the 'Methods' and 'Results' sections of the report indicated no evidence of selective outcome reporting.
Free of other bias?	Yes	The study appears free of other sources of bias.

Tulandi 1985

Methods	Randomised trial.
Participants	16 postpartum women between 20 and 28 years of age, who had normal deliveries and decided not to breastfeed. Setting: a university and a general hospital in Canada.
Interventions	Prostaglandin E_2 at 2 mg daily for four days (n = 8) versus placebo (n = 6).
Outcomes	Breast leakage, breast swelling and pain, serum prolactin. Symptoms were scored on a scale of 0 to 3.
Notes	Upjohn Company of Canada supplied the drugs.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation not stated. "Each subject received PGE2 or placebo orally in random order".
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Lactation	Unclear	Participants and study personnel were blinded to interventions. Uncertain whether outcome assessors were blinded.
Blinding? Adverse events	Unclear	The study did not address this outcome.
Incomplete outcome data addressed? Adverse events	Unclear	The study did not address this outcome.
Incomplete outcome data addressed? Lactation	Yes	Two participants dropped out from the placebo group because of severe breast engorgement and pain. Missing data were imputed using appropriate methods.
Free of selective reporting?	Yes	Comparison of outcome measures in the 'Methods' and 'Results' sections of the report indicated no evidence of selective outcome reporting.
Free of other bias?	Yes	The study appears free of other sources of bias.

Utian 1975

Methods	Method of randomisation not stated. Participants, clinicians and outcome assessors were blinded.
Participants	31 postpartum nonbreastfeeding women who were free from metabolic or surgical conditions which might interfere with the absorption, metabolism or excretion of the drugs, absence of concurrent medication. Setting: a university hospital in Cape Town, South Africa.
Interventions	Oral bromocriptine 2.5 mg twice daily for 14 days (n = 16) versus chlorotrianisene 24 mg twice daily for 14 days (n = 15).
Outcomes	Milk production, breast congestion and side effects (blood pressure changes, pulse rate, rebound lactation, 24 hour urinary output and thromboembolism.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation not stated.
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Adverse events	Unclear	Uncertain whether outcome assessors were blinded.
Blinding? Lactation	Unclear	Study participants and personnel were blinded to interventions. Uncertain whether outcome assessors were blinded.
Incomplete outcome data addressed? Lactation	Yes	7 (18.4%) of the 38 participants that entered the trial were lost to follow up. Drop-out rates were similar for both groups.
Incomplete outcome data addressed? Adverse events	Yes	Drop-out rates were similar for both groups.
Free of selective reporting?	Yes	Comparison of outcome measures in the 'Methods' and 'Results' sections of the report indicated no evidence of selective outcome reporting.
Free of other bias?	Yes	The study appears free of other sources of bias.

Varga 1972

Methods	Randomised trial.
Participants	60 consecutive nonbreastfeeding women. Setting: a university hospital in Switzerland.
Interventions	Oestrogen 20 mg twice daily for the first three days, 10 mg twice daily for the second three days, and 10 mg daily for the last three days, ergocryptine 5 mg twice daily for the first six days and 5 mg daily for the last three days, placebo was initiated within 24 hours after delivery, 12 hours on average.
Outcomes	Breast congestion, rebound lactation and thromboembolic disease.
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Method of sequence generation not stated. Women were "randomly assigned" to one of three groups.
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Adverse events	Unclear	Uncertain whether outcome assessor (same observer) was blinded.
Blinding? Lactation	Unclear	Participants and study personnel were blinded to interventions. Uncertain whether outcome assessor (same observer) was blinded. Three identical cachets were used containing either a placebo, stilbestrol or bromocriptine.
Incomplete outcome data addressed? Adverse events	Yes	No missing data.
Incomplete outcome data addressed? Lactation	Yes	No missing data.
Free of selective reporting?	Yes	Comparison of outcome measures in the 'Methods' and 'Results' sections of the report indicated no evidence of selective outcome reporting.
Free of other bias?	Yes	The study appears free of other sources of bias.

Venturini 1981

Methods	Randomised trial.
Participants	38 women with indications for suppression of lactation in the puerperium. All gave informed consent. All patient delivered vaginally. Exclusion criteria: Use of drugs that might interfere with results and nonco-operative women. Setting: a university hospital in Italy.
Interventions	Lisuride 0.2 mg three times daily for 15 days (n = 20) versus bromocriptine 2.5 mg three times daily for 15 days (n = 18).
Outcomes	Milk secretion, breast engorgement, breast pain, rebound lactation and side effects. Assessment of mammary activity was on a scale of 0 to 3.
Notes	Schering AG, Berlin-Bergkamen supplied the drugs used in the trial. One of the authors of the paper was a staff of Schering AG, Berlin-Bergkamen.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation not stated.
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Lactation	Yes	Participants, study personnel and outcome assessors were blinded to the interventions. The participants also doubled as outcome assessors.
Blinding? Adverse events	Yes	Participants, study personnel and outcome assessors were blinded to the interventions
Incomplete outcome data addressed? Lactation	Yes	4 (9.5%) out of the initial 42 women that entered the trial dropped out of the study because of side effects (1 from the lisuride group and 3 from bromocriptine group).
Incomplete outcome data addressed? Adverse events	Yes	4 (9.5%) out of the randomised participants dropped out of the study because of side effects (one from the lisuride group and three from bromocriptine group).
Free of selective reporting?	Yes	Comparison of outcome measures in the 'Methods' and 'Results' sections of the report indicated no evidence of selective outcome reporting.
Free of other bias?	Yes	The study appears free of other sources of bias.

Venturini 1988

Methods	Randomised trial.
Participants	45 women who for medical or personal reason did not want to breastfeed. Setting: a university hospital in Italy.
Interventions	Terguride 0.5 mg (n = 15), terguride 1 mg (n = 15), terguride 0.25 mg capsules were taken orally twice daily for 15 days (n = 15).
Outcomes	Milk secretion, congestion and breast pain, side effects during the first five days of treatment. Clinical assessments were scored according to a rating scale of 0 to 4 indicating increasing severity.
Notes	Schering AG, Berlin-Bergkamen supplied the drugs used in the trial. Three of the authors of the paper were staff of Schering AG, Berlin-Bergkamen.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation not stated.
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Lactation	Yes	Participants, study personnel and outcome assessors were blinded to the interventions. Capsules of identical appearance containing three different doses of terguride were given to the participants. The participants also doubled as outcome assessors.
Blinding? Adverse events	Yes	Participants, study personnel and outcome assessors were blinded to the interventions.
Incomplete outcome data addressed? Adverse events	Yes	No missing data.
Incomplete outcome data addressed? Lactation	Yes	No missing data.
Free of selective reporting?	Yes	Comparison of outcome measures in the 'Methods' and 'Results' sections of the report indicated no evidence of selective outcome reporting.
Free of other bias?	Yes	The authorship of the trial report was a potential threat to the validity of the results.

Vischi 1975

Methods	Randomised trial.
Participants	198 women unwilling to breastfeed or in whom lactation was not advised on medical grounds. Setting: obstetric departments of three hospitals in Northern Italy.
Interventions	Experiment groups: Oral quinestrol 2 mg single dose (n = 66), oral quinestrol 4 mg single dose (n = 66). Control group: oral placebo (n = 66)
Outcomes	Milk leakage, discomfort, and engorgement.
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Method of sequence generation not stated. Participants were allocated by a "random code" to one of the treatments.
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Adverse events	Unclear	Uncertain whether outcome assessor was blinded.
Blinding? Lactation	Unclear	Participants and personnel were blinded to the interventions. Uncertain whether outcome assessor was blinded.
Incomplete outcome data addressed? Adverse events	Yes	No missing data in the first week of assessment
Incomplete outcome data addressed? Lactation	Yes	No missing data in the first week of assessment. Loss to follow up was 59.6% after the first week assessment. Extracted data were restricted to that obtained in first week of assessment.
Free of selective reporting?	No	The study failed to include results for adverse events directly related to the interventions especially thromboembolism which was associated with oestrogen preparations in published studies before the trial.
Free of other bias?	Yes	The study appears free of other sources of bias.

Walker 1975

Methods	Randomised trial.
Participants	87 women who were delivered vaginally and who did not wish to breastfeed. Those who had general anaesthesia or were receiving concomitant therapy which might influence the results (e.g. diuretics, corticosteroids, phenothiazines) were excluded. Setting: Obstetrics and Gynaecology Department and General Practice Unit, Welsh National School of Medicine, Cardiff, UK.
Interventions	Bromocriptine 2.5 mg twice daily for 14 days (n = 32), quinestrol 4 mg immediately after delivery, followed by placebo twice daily (n = 28), placebo twice daily (n = 27).
Outcomes	Breast discomfort, congestion, milk leakage (scored on linear analogue scales by the woman), side effects, use of analgesic and rebound lactation.
Notes	Sandoz Ltd. provided financial support.

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Method of sequence generation not stated.
Allocation concealment?	Unclear	Participants were given the content of a "numbered envelope" which contained the intervention drug and placebo.
Blinding? Adverse events	Yes	Participants, study personnel and outcome assessors were blinded to the interventions.
Blinding? Lactation	Yes	Participants, study personnel and outcome assessors were blinded to the interventions. The participants also doubled as outcome assessors.
Incomplete outcome data addressed? Adverse events	Unclear	The study did not adequately report this outcome.
Incomplete outcome data addressed? Lactation	Yes	Three participants (1 from quinestrol arm and 2 from placebo arm) were withdrawn due to breast congestion and pain which was severe enough by the 4th or 5th day postpartum. Outcome data were presented for all participants.
Free of selective reporting?	No	The study failed to include results for adverse events directly related to the interventions especially thromboembolism which was associated with oestrogen preparations in published studies before the trial.
Free of other bias?	Yes	The study appears free of other sources of bias.

Watson 1969

Methods	Randomised trial.
Participants	99 women who had elected not to breastfeed as a statement of intent and those who could not breastfeed because of stillbirth. No cases of already established breastfeeding. Setting: Queen Elizabeth II Hospital, Welwyn Garden City, UK.
Interventions	50 women received 4 mg of quinestrol (plus 24 white tablets of placebo) while 50 other women received (Control group) 5 mg stilbestrol after delivery, then each tablets twice daily for two days, then 1 tablet thrice daily for two days, then 1 tablet twice daily for two days, then 1 tablet daily for two days.
Outcomes	Breast engorgement., number of women who required second line drug or method to achieve suppression, disturbance of menstrual pattern.
Notes	A personnel of William R. Warner & Co. Ltd. supplied the treatment packs and "arranged" the statistical compilation of the results.

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Method of sequence generation not stated.
Allocation concealment?	Yes	The tablets were made up of Identical packs identified by a code number the key to which was retained by the hospital pharmacist. Patients were allocated a sequential code number 1 to 100. The corresponding numbered treatment pack was opened by the labour ward Sister after entry into the trial.
Blinding? Lactation	Unclear	Study participants and personnel were blinded to the interventions. Uncertain whether outcome assessors were blinded.
Blinding? Adverse events	Unclear	The study did not report this outcome.
Incomplete outcome data addressed? Lactation	Yes	One participant (1%) among the 100 women who entered the trial was lost to follow-up. The participant was in stilbestrol arm.
Incomplete outcome data addressed? Adverse events	Unclear	The study did not report this outcome.
Free of selective reporting?	Yes	Comparison of outcome measures in the 'Methods' and 'Results' sections of the report indicated no evidence of selective outcome reporting.

Watson 1969 (*Continued*)

Free of other bias?	Unclear	Arrangement of statistical compilation of the results by the supplier of the treatment packs constituted a potential threat to validity of the results.

Weinstein 1976

Methods	Randomised trial.
Participants	75 women were randomly assigned to five groups including a placebo group. Setting: a university hospital in Israel.
Interventions	Interventions: stilbestrol 5 mg thrice daily for 14 days, clomiphene citrate 50 mg twice daily for 14 days, testosterone propionate as a single injection of 75 mg, bromocriptine 2.5 mg twice daily for 14 days. Control: placebo
Outcomes	Milk secretion, breast pain, engorgement, breast tenderness and rebound lactation. Clinical responses were graded as good, fair and poor
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation not stated. Participants were "randomly assigned to one of five treatment groups".
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Adverse events	Unclear	The study did not report this outcome.
Blinding? Lactation	No	There was no evidence of blinding.
Incomplete outcome data addressed? Lactation	Unclear	No missing data.
Incomplete outcome data addressed? Adverse events	Unclear	The study did not report this outcome.

Weinstein 1976 (*Continued*)

Free of selective reporting?	No	The study failed to include results for adverse events directly related to the interventions especially thromboembolism which was associated with oestrogen preparations in published studies before the trial.
Free of other bias?	Yes	The study appears free of other sources of bias.

Winter 1964

Methods	Randomised trial.
Participants	800 (first part of the study) and 98 (second part of the study) nonnursing postpartum women. Setting: a university hospital and a maternity hospital, Halifax, Nova Scotia, Canada.
Interventions	First part intervention group: stilbestrol 5 mg; control group: indistinguishable placebo. Second part of the study - intervention group: synthetic oxytocin 40 I.U as nasal spray; control group: indistinguishable placebo.
Outcomes	Breast engorgement, breast pain, milk leakage.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation not stated.
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Lactation	Unclear	Study participants, personnel and outcome assessors were blinded to the interventions.
Blinding? Adverse events	Unclear	The study did not report this outcome.
Incomplete outcome data addressed? Lactation	Yes	No missing data while in hospital.
Incomplete outcome data addressed? Adverse events	Unclear	The study did not report this outcome.

Winter 1964 (*Continued*)

Free of selective reporting?	Yes	Comparison of outcome measures in the 'Methods' and 'Results' sections of the report indicated no evidence of selective outcome reporting.
Free of other bias?	No	Study was conducted over a period of 2 years, and 7 residents and 18 interns participated over this period.

Yuen 1977

Methods	Randomised trial.
Participants	39 women who delivered at term after normal pregnancies and who had elected not to breastfeed their infants. Setting: a general hospital in Vancouver, British Columbia, Canada.
Interventions	18 women received bromocriptine 2.5 mg twice daily for 14 days while 21 received chlorotrianisene 24 mg twice daily for 7 days (made up to 14 days as chlorontrianisene placebo). Therapy started within two hours of delivery and continued for 14 days.
Outcomes	Breast leakage, breast swelling and breast pain. Nurses and participants assessed outcomes in hospital and at home respectively.
Notes	Personnel of Sandoz Pharmaceuticals provided medications, financial assistance and data analysis.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method of sequence generation not stated.
Allocation concealment?	Unclear	No information about allocation concealment to permit judgement.
Blinding? Adverse events	Unclear	The study did not adequately address this outcome.
Blinding? Lactation	Unclear	Participants and study personnel were blinded to the interventions. The capsules containing 2.5 mg bromocriptine were identical to those containing 24 mg chlorotrianisene or chlorotrianisene placebo. Uncertain whether outcome assessors were blinded.

Yuen 1977 (*Continued*)

Incomplete outcome data addressed? Lactation	Yes	One participant (2.5%) did not return for follow up on day 14.
Incomplete outcome data addressed? Adverse events	Unclear	The study did not adequately address this outcome.
Free of selective reporting?	No	The study failed to include results for adverse events directly related to the interventions especially thromboembolism, which was associated with oestrogen preparations in published studies before the trial.
Free of other bias?	Unclear	Data analysis by a personnel of the pharmaceutical company that supplied medications and medical assistance constituted a threat to the validity of the results.

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

Almeida 1986	This is a randomised double blind study evaluating the effect of bromocriptine mesylate on suppression of puerperal fever resulting from breast engorgement.
Bare 1960	This study was conducted to determine the efficacy and the optimum dosage of fluoxymesterone in the suppression of lactation. There was no evidence of randomisation. The patients were divided into four groups. Group I consisted of ward patients who received placebo and other groups were all private patients. The dosage of the intervention was administered on "a strict alternating basis".
Barns 1961	This study compares the effectiveness of a combination of testosterone enanthate and estradiol valerate in the suppression of postpartum lactation. There was no indication of randomisation.
Bhardwaj 1979	Bromocriptine and placebo were randomly allocated to 50 women who wished to suppress lactation. The study started with 20 women as a single-blind comparison between two parallel groups (with no evidence of randomisation) and later continued as a double-blind randomised trial involving 30 women. In the first 20 women, bromocriptine was compared with placebo plus breast binding while in the last 30 women, bromocriptine was compared with placebo alone. The results were not presented in a form suitable for differentiating between the two parts of the study. Data were presented mainly in means, and were not presented in a form suitable for extraction and inclusion in a meta-analysis.
Binn 1979	This double-blinded trial compared chlorotrianisene with placebo. Results were not presented in a usable form.
Booker 1970	This study compared combined and sequential type of oral contraceptive pills for suppressing lactation. Alternate allocation method was used.
Brooten 1983	This study compared three nonpharmacolgical measures (compression binder, standardised support bra and fluid restriction) with bromocriptine. The assignment of women to bromocriptine group was "by virtue of their physicians' treatment".
Caballero 1987	This is a double-blind study comparing metergoline with bromocriptine in the suppression of lactation. Although the study was described as randomised, allocation of interventions was by alternation.
Canales 1977	This study evaluated the effect of clomiphene in the suppression of puerperal milk secretion and serum prolactin. There was no indication of randomisation.
Cantis 1977	This was a single-blind study carried out in 42 women to assess the lactation suppressing activity of piribedil. There was no evidence of randomisation. Treatments were assigned to unbalanced groups of women (33 women received the active agent while 9 received placebo).
Cicinelli 1996	This study evaluated the effectiveness of nasal bromocriptine on serum prolactin.
David 1977	This study compared the effectiveness of stilbestrol to placebo on prolactin level.

(*Continued*)

De Aloysio 1988	This study compared the effect of dihydroergocristine to that of bromocriptine on prolactin secretion and postpartum lactation. All the puerperae enrolled in the study had a physiological delivery and wished to interrupt breastfeeding after at least three months of nursing.
De Cecco 1979	This study evaluated the effect of Lisuride on lactation and postpartum serum prolactin level. There was no indication of randomisation.
Del Pozo 1975	This study evaluated the action of Methergoline on plasma prolactin and milk secretion in the first seven postpartum days. There was no indication of randomisation and women were "divided" into two groups.
Duthie 1990	This randomised trial compared the efficacy, tolerance and effect on prolactin level of four different dosages of intramuscular bromocriptine retard. Patients were randomised into four equal groups. Loss to follow up was 10.8%. Variable numbers of women in the groups developed mild to moderate breast engorgement and milk flow prior to administration of bromocriptine. Results were not presented in a form that can be extracted and included in meta-analysis.
Fleming 1977	This double-blind trial compared the efficacy of pyridoxine, stilbestrol and a placebo in the inhibition of puerperal lactation. There was no indication of randomisation.
Foukas 1972	This double-blind trial compared diethylstilbestrol and pyridoxine with placebo in the suppression of lactation. There was no indication of any randomised comparison between the groups. Patients were divided into four unbalanced groups (86, 68, 75 and 25).
Garry 1956	This study was undertaken to evaluate the effectiveness of estrogen-androgen preparation in the suppression of lactation. There was no indication of randomisation. The patients were divided into two unequal groups (100 and 50).
Gillibrand 1968	Data to evaluate the validity of the methods used is not available in this published correspondence that described two clinical trials. It has been excluded because no full publication of the study could be located.
Gopalan 1997	This randomised double-blind study assessed the effectiveness of pyridoxine in inhibition of lactation and serum prolactin. The report is only available in abstract form. It will be considered when the full article is published.
Grant 1978	This randomised trial involving 136 women compared quinestrol and chlorotrianisene with placebo. Outcome measures included milk flow, breast engorgement, breast pain and lactation recorded over a period of 14 days. ITT was not used. The results were presented graphically in mean scores of a 4-point evaluation scale, which cannot be used for meta-analysis.
Kalir 1975	This study was conducted to evaluate the lactation suppression of clomiphene citrate. There was no indication of randomisation.
Kee 1989	This study evaluated the usefulness of serrapeptase (Dansen) in postpartum women with breast engorgement in a double blind randomised controlled trial.

(*Continued*)

King 1958	Study comparing chlorotrianisene with placebo. There was no indication of randomisation.
Kirkland 1960	This randomised study involving 160 women had the allocation concealment deciphered for the placebo group during the study resulting in unequal allocation of subjects to the placebo arm and consequent discontinuation of the arm. This questions adherence to the initially generated allocation sequence till the end of the trial. Data were presented in forms that cannot be extracted for meta-analysis (aggregates of scores).
Koshiishi 1971	This study evaluated the effect of a proteolytic enzyme (Bromelain) on breast engorgement.
Kulski 1978	The primary outcome of this randomised double-blind trial involving 26 women was the composition of mammary secretion due to ingestion of bromocriptine 2.5 mg twice daily for 14 days in women who elected not to breastfeed. Therefore, < 5ml of breast secretion was manually collected from each woman daily for 14 days. Although milk leakage and breast engorgement were part of the outcome measures, data are not presented in a form that can be extracted for the meta-analysis.
Lee 1971	This study compared chlormezanone (a non-hormonal tranquilizer) with Stilbesterol. There was no evidence of randomisation. Patients were allocated alternately into one of two groups.
Lee 1979	This study compares Ginsenocide triol with bromocriptine. The paper is only available in abstract form.
Llewellyn-Jones 1963	This double-blind trial compared the effectiveness of stilbestrol with placebo in the suppression of lactation. There was no indication of randomisation.
Louviere 1975	The primary purpose of this study was to evaluate the effectiveness of Deladumone OB in the suppression of postpartum breast engorgement and lactation. There was no indication of randomisation.
MacDonald 1965	This double-blind trial compared stilbesterol with placebo. Alternate allocation method was used.
MacLeod 1977	This study evaluated the dose response and timing of administration of bromocriptine. There was no evidence of randomisation. Patients were divided into three groups.
Markin 1960	This study compared the effectiveness of five preparations (diethylstibestrol, dienestrol plus mrthyltestosterone, conjugated equine estrogen plus methyltestosterone, testosterone propionate plus diethylstibestrol and testosterone enanthate plus estrdiol valerate) with placebo. Alternation method of allocation was used. "Drug E" or "Drug O" was administered by the nursing staff to the patients delivering on the even-numbered or the odd-numbered days of the month, respectively.
Masala 1978	This study was designed to assess the effect of tamoxifen on the inhibition of puerperal lactation. There was no indication of randomisation. Treatments were assigned to two unbalanced groups (60: experimental group and 20: placebo group).
McLachlan 1991	This randomised double-blind placebo controlled trial tested the efficacy of thermal ultrasound therapy as a treatment for severe postpartum breast engorgement.

(*Continued*)

Morris 1967	This study was designed to evaluate the effectiveness of quinestrol in suppressing puerperal lactation. There was no indication of randomisation.
Morris 1970	This double-blind study evaluated the effectiveness of three preparations; oral chlorotrianisene in three different dosage strengths; an intramuscular combination of two steroids, testosterone enanthate and estradiol valerate; and identical placebos in the inhibition of puerperal breast engorgement, discomfort and milk secretion. Allocation of patients does not suggest randomisation. For the Chlorotrianisene study, an unbalanced number of patients recieved the active agent and placebo (75 vs 25).
Nappi 1987	This study examined whether the side effects of bromoergocriptine could be prevented by combining bromoergocriptine treatment with the antiemetic domperidone, without affecting the prolactin lowering effect and subsequent inhibition of lactation.
Nappi 1990	This study assessed the effect of Ibopamine, a peripheral agonist on prolactin and milk production. Eighty participants were admitted into the study including 30 nursing mothers. Participants were randomly "divided" into 6 groups.
Ng 1972	This study compared Quinestrol with Ablacton. Alternate allocation method was used.
Osbourne 1978	This study compares the effect of bromocriptine and quinestrol on coagulation and fibrinolysis.
Primrose 1957	This study compares TACE, Premarin and Methyltestosterone, Stibesterol with placebo. There was no indication of randomisation.
Reisfield 1966	A double-blind study using hydrochlorthiazide and an identical placebo in 100 consecutive postpartum women. Data were presented in a form that is not usable (total days of symptoms: pain, discomfort, use of analgesics and ice packs).
Robuschi 1987	This study evaluated the effect of maternal administration of bromocriptine on fetal and maternal serum growth hormone concentrations.
Rolland 1978	This study describes two double-blind studies on the effect of bromocriptine compared with placebo and an estrogen/androgen compound. There was no indication of randomisation.
Roser 1966	This study compares the effect of testosterone enanthate and estradiol valerate (Deladumone 2X) on suppression of symptoms of postpartum lactation. There was no indication of randomisation. Women were "divided" into two groups.
Ryan 1962	This study evaluated the effectiveness of intranasal syntocinon compared to a placebo for relief of postpartum breast discomfort. Patients were instructed to begin assigned treatment when they first felt discomfort in their breasts. A total of 38.3% of women included in the study were excluded from the analysis as they did not experience enough discomfort to require the assignment of treatment.

(*Continued*)

Schneider 1964	Double-blind study comparing depot types of oestrogen and androgen together with a rapidly acting oestrogen against placebo. Treatments were allocated to alternative patients.
Seppala 1975	This double-blind study compared the effect of CB 154 (2-Br-alpha-ergocriptine methane sulphonate) with diethylstibestrol on established mammary secretion and congestion. There was no indication of randomisation. 39 patients were "divided into two groups".
Shapiro 1984	Compares bromocriptine with breast binders and analgesics for inhibiting lactation. Alternate allocation method was used.
Steele 1968	This study described the comparison of stibesterol with placebo in a double blind trial. Paper was presented as correspondence and full paper could not be located. There was no indication of randomisation in the published correspondence.
Stenchever 1962	There was no evidence of randomisation.
Tyson 1966	This study was designed to test the efficacy of a 3-day course of chlorotrianisene for prevention and treatment of postpartum breast engorgement. There was no evidence of randomisation.
Van der Heijden 1991	This study compared dopamine-agonist CV 205-502 with bromocriptine for lactation. There was no concealment of allocation. A two-to-one ratio was chosen to receive either CV 205-502 or Bromocriptine.
Willmott 1977	This double-blind placebo controlled study was undertaken to evaluate the clinical effectiveness of bromoergocrytine in suppressing lactation and observe any side effects over 28 days. There was no evidence of randomisation. Loss to follow up was 31.8%.
Zuckerman 1973	This study was designed to determine the effectiveness of clomiphene in inhibiting postpartum lactation. There was no indication of randomisation. Patients were divided into four uneven groups (110, 26, 31 and 10).

DATA AND ANALYSES

Comparison 1. Ergot derivatives versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤7 days postpartum	3	107	Risk Ratio (IV, Fixed, 95% CI)	0.36 [0.24, 0.54]
1.1 Bromocriptine versus placebo	3	107	Risk Ratio (IV, Fixed, 95% CI)	0.36 [0.24, 0.54]
2 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤14 days	2	76	Risk Ratio (IV, Random, 95% CI)	0.18 [0.03, 1.08]
2.1 Bromocriptine versus placebo	2	76	Risk Ratio (IV, Random, 95% CI)	0.18 [0.03, 1.08]
3 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤14 days	1	32	Risk Ratio (IV, Fixed, 95% CI)	0.19 [0.07, 0.48]
3.1 Cabergoline versus placebo	1	32	Risk Ratio (IV, Fixed, 95% CI)	0.19 [0.07, 0.48]
4 Rebound lactation	1	40	Risk Ratio (IV, Fixed, 95% CI)	15.26 [1.01, 231.20]

Comparison 2. Oestrogen preparations versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤ 7 days	6	883	Risk Ratio (IV, Random, 95% CI)	0.41 [0.29, 0.59]
1.1 Diethylstilbestrol versus placebo	3	288	Risk Ratio (IV, Random, 95% CI)	0.32 [0.07, 1.49]
1.2 Quinestrol versus placebo	3	342	Risk Ratio (IV, Random, 95% CI)	0.47 [0.30, 0.73]
1.3 Chlorotrianisene versus placebo	1	153	Risk Ratio (IV, Random, 95% CI)	0.51 [0.36, 0.73]
1.4 Hexestrol versus placebo	1	100	Risk Ratio (IV, Random, 95% CI)	0.41 [0.29, 0.57]
2 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤14 days	2	103	Risk Ratio (IV, Random, 95% CI)	0.19 [0.03, 1.34]

Comparison 3. Antioestrogen preparations versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤7 days	1	30	Risk Ratio (IV, Fixed, 95% CI)	1.0 [0.51, 1.95]
1.1 Clomiphene versus placebo	1	30	Risk Ratio (IV, Fixed, 95% CI)	1.0 [0.51, 1.95]
2 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤ 14 days	1	140	Risk Ratio (IV, Fixed, 95% CI)	0.71 [0.62, 0.82]
2.1 Tamoxifen versus placebo	1	140	Risk Ratio (IV, Fixed, 95% CI)	0.71 [0.62, 0.82]

Comparison 4. Pyridoxine versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤ 7 days	1	175	Risk Ratio (IV, Fixed, 95% CI)	0.95 [0.86, 1.06]
1.1 Pyridoxine versus placebo	1	175	Risk Ratio (IV, Fixed, 95% CI)	0.95 [0.86, 1.06]

Comparison 5. Combined oestrogen and androgen preparations versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤ 7 days	2	346	Risk Ratio (IV, Fixed, 95% CI)	0.10 [0.06, 0.17]
1.1 Testosterone oenanthate + oestradiol valereate	2	346	Risk Ratio (IV, Fixed, 95% CI)	0.10 [0.06, 0.17]

Comparison 6. Androgen preparations versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤ 7 days	1	30	Risk Ratio (IV, Fixed, 95% CI)	1.13 [0.60, 2.11]
1.1 Testosterone propionate versus placebo	1	30	Risk Ratio (IV, Fixed, 95% CI)	1.13 [0.60, 2.11]

Comparison 7. Pharmacologic treatment versus nonpharmacologic treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain	2		Risk Ratio (IV, Random, 95% CI)	Subtotals only
1.1 Bromocriptine versus any nonpharmacologic treatment	2	96	Risk Ratio (IV, Random, 95% CI)	0.31 [0.16, 0.61]
1.2 DIethylstibestrol versus any nonpharmacologic treatment	1	36	Risk Ratio (IV, Random, 95% CI)	0.19 [0.07, 0.49]
1.3 Oestradiol + testosterone esters versus any non pharmacologic treatment	1	36	Risk Ratio (IV, Random, 95% CI)	0.46 [0.28, 0.76]
1.4 Bendrofluazide versus any nonpharmacologic treatment	1	36	Risk Ratio (IV, Random, 95% CI)	0.68 [0.48, 0.94]
2 Rebound lactation	1	60	Risk Ratio (IV, Fixed, 95% CI)	5.0 [0.25, 99.95]

Comparison 8. Comparison of two pharmacologic treatments

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤7 days postpartum	11		Risk Ratio (IV, Random, 95% CI)	Subtotals only
1.1 Bromocriptine versus oestrogen preparations	4	340	Risk Ratio (IV, Random, 95% CI)	0.58 [0.25, 1.38]
1.2 Bromocriptine versus ergot derivative	3	228	Risk Ratio (IV, Random, 95% CI)	1.12 [0.37, 3.42]

1.3 Bromocriptine versus prostagladins	1	43	Risk Ratio (IV, Random, 95% CI)	0.55 [0.19, 1.60]
1.4 Bromocriptine versus pyridoxine	1	97	Risk Ratio (IV, Random, 95% CI)	0.93 [0.75, 1.15]
1.5 Quinestrol versus other oestrogen preparations	2	145	Risk Ratio (IV, Random, 95% CI)	0.91 [0.63, 1.32]
2 Rebound lactation	4	149	Risk Ratio (IV, Fixed, 95% CI)	0.65 [0.39, 1.10]
2.1 Bromocriptine versus oestrogen preparations	2	67	Risk Ratio (IV, Fixed, 95% CI)	0.61 [0.34, 1.07]
2.2 Bromocriptine versus ergot derivative	1	39	Risk Ratio (IV, Fixed, 95% CI)	2.11 [0.43, 10.19]
2.3 Bromocriptine versus prostagladins	1	43	Risk Ratio (IV, Fixed, 95% CI)	0.24 [0.03, 1.96]
3 Use of second line drug or method to achieve suppression of lactation	3		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
3.1 Bromocriptine versus oestrogen preparations	1	31	Risk Ratio (IV, Fixed, 95% CI)	0.31 [0.01, 7.15]
3.2 Bromocriptine versus ergot derivatives	1	40	Risk Ratio (IV, Fixed, 95% CI)	2.67 [0.82, 8.62]
3.3 Bromocriptine versus pyridoxine	1	97	Risk Ratio (IV, Fixed, 95% CI)	0.07 [0.01, 0.51]
4 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤14 days	6		Risk Ratio (IV, Random, 95% CI)	Subtotals only
4.1 Bromocriptine versus carbegoline	2	308	Risk Ratio (IV, Random, 95% CI)	1.38 [0.93, 2.05]
4.2 Bromocriptine versus diethylstilbestrol	1	38	Risk Ratio (IV, Random, 95% CI)	0.30 [0.07, 1.30]
4.3 Bromocriptine versus cyclophenil	1	24	Risk Ratio (IV, Random, 95% CI)	3.5 [0.16, 78.19]
4.4 Bromocriptine versus chlorotrianisene	1	39	Risk Ratio (IV, Random, 95% CI)	0.35 [0.19, 0.66]
4.5 Quinestrol versus other oestrogen preparations	1	99	Risk Ratio (IV, Random, 95% CI)	2.84 [1.56, 5.18]

Comparison 9. High versus low dose quinestrol

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Failure to suppress lactation as described by milk secretion, breast engorgement or breast pain at ≤ 7 days postpartum	1	132	Risk Ratio (IV, Fixed, 95% CI)	0.51 [0.33, 0.81]
1.1 Quinestrol 4 mg versus Quinestrol 2 mg	1	132	Risk Ratio (IV, Fixed, 95% CI)	0.51 [0.33, 0.81]

Comparison 10. Low versus high dose terguride

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Failure to suppress lactation as described by milk secretion, breast engorgement or breast pain at days 0 -15	1	45	Risk Ratio (IV, Fixed, 95% CI)	0.5 [0.29, 0.88]
1.1 Terguride 0.5-1.0 mg vs terguride 0.25 mg	1	45	Risk Ratio (IV, Fixed, 95% CI)	0.5 [0.29, 0.88]
2 Side effect: dizziness	1	45	Risk Ratio (IV, Fixed, 95% CI)	1.55 [0.07, 35.89]
2.1 Terguride 0.5-1.0 mg vs terguride 0.25 mg	1	45	Risk Ratio (IV, Fixed, 95% CI)	1.55 [0.07, 35.89]

Comparison 11. High versus low dose cabergoline

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Failure to suppress lactation as described by milk secretion, breast engorgement or breast pain	1	80	Risk Ratio (IV, Fixed, 95% CI)	0.14 [0.03, 0.59]

Comparison 12. Long course tamoxifen versus short course tamoxifen

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Failure to suppress lactation as described by milk secretion, breast engorgement or breast pain at D0-15	1	65	Risk Ratio (IV, Fixed, 95% CI)	0.75 [0.61, 0.92]
1.1 Tamoxifen (14 days course) vs tamoxifen (6 days course)	1	65	Risk Ratio (IV, Fixed, 95% CI)	0.75 [0.61, 0.92]

Analysis 1.1. Comparison 1 Ergot derivatives versus placebo, Outcome 1 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤7 days postpartum.

Review: Treatments for suppression of lactation

Comparison: 1 Ergot derivatives versus placebo

Outcome: 1 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤7 days postpartum

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
1 Bromocriptine versus placebo					
Dewhurst 1977	8/20	16/17		53.5 %	0.43 [0.25, 0.74]
Rolland 1973	6/30	9/10		29.1 %	0.22 [0.11, 0.47]
Weinstein 1976	4/15	8/15		17.4 %	0.50 [0.19, 1.31]
Total (95% CI)	**65**	**42**		**100.0 %**	**0.36 [0.24, 0.54]**
Total events: 18 (Treatment), 33 (Control)					
Heterogeneity: Chi^2 = 2.41, df = 2 (P = 0.30); I^2 =17%					
Test for overall effect: Z = 4.95 (P < 0.00001)					

Analysis 1.2. Comparison 1 Ergot derivatives versus placebo, Outcome 2 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤14 days.

Review: Treatments for suppression of lactation

Comparison: 1 Ergot derivatives versus placebo

Outcome: 2 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤14 days

Study or subgroup	Favours treatment n/N	Control n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
1 Bromocriptine versus placebo					
Dewhurst 1977	6/20	13/16		61.5 %	0.37 [0.18, 0.75]
Varga 1972	1/20	18/20		38.5 %	0.06 [0.01, 0.38]
Total (95% CI)	**40**	**36**		**100.0 %**	**0.18 [0.03, 1.08]**
Total events: 7 (Favours treatment), 31 (Control)					
Heterogeneity: Tau^2 = 1.25; Chi^2 = 3.30, df = 1 (P = 0.07); I^2 =70%					
Test for overall effect: Z = 1.87 (P = 0.061)					

Analysis 1.3. Comparison 1 Ergot derivatives versus placebo, Outcome 3 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤14 days.

Review: Treatments for suppression of lactation

Comparison: 1 Ergot derivatives versus placebo

Outcome: 3 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤14 days

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
1 Cabergoline versus placebo					
Melis 1988	4/24	7/8		100.0 %	0.19 [0.07, 0.48]
Total (95% CI)	**24**	**8**		**100.0 %**	**0.19 [0.07, 0.48]**
Total events: 4 (Treatment), 7 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 3.49 (P = 0.00049)					

Analysis 1.4. Comparison 1 Ergot derivatives versus placebo, Outcome 4 Rebound lactation.

Review: Treatments for suppression of lactation

Comparison: 1 Ergot derivatives versus placebo

Outcome: 4 Rebound lactation

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
Rolland 1973	21/30	0/10		100.0 %	15.26 [1.01, 231.20]
Total (95% CI)	**30**	**10**		**100.0 %**	**15.26 [1.01, 231.20]**
Total events: 21 (Treatment), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.96 (P = 0.049)					

Analysis 2.1. Comparison 2 Oestrogen preparations versus placebo, Outcome 1 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤ 7 days.

Review: Treatments for suppression of lactation

Comparison: 2 Oestrogen preparations versus placebo

Outcome: 1 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤ 7 days

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
1 Diethylstilbestrol versus placebo					
Schwartz 1973	6/80	51/78		9.4 %	0.11 [0.05, 0.25]
Stirrat 1968	8/50	42/50		11.0 %	0.19 [0.10, 0.36]
Weinstein 1976	11/15	8/15		12.0 %	1.38 [0.78, 2.41]
Subtotal (95% CI)	**145**	**143**		**32.3 %**	**0.32 [0.07, 1.49]**
Total events: 25 (Treatment), 101 (Control)					
Heterogeneity: Tau^2 = 1.76; Chi^2 = 33.21, df = 2 (P<0.00001); I^2 =94%					
Test for overall effect: Z = 1.46 (P = 0.15)					
2 Quinestrol versus placebo					
Firth 1969	33/50	50/50		16.0 %	0.66 [0.54, 0.81]
McGlone 1969	3/22	16/22		6.7 %	0.19 [0.06, 0.55]
Vischi 1975	53/132	62/66		15.9 %	0.43 [0.34, 0.53]
Subtotal (95% CI)	**204**	**138**		**38.6 %**	**0.47 [0.30, 0.73]**
Total events: 89 (Treatment), 128 (Control)					
Heterogeneity: Tau^2 = 0.11; Chi^2 = 12.14, df = 2 (P = 0.002); I^2 =84%					
Test for overall effect: Z = 3.32 (P = 0.00090)					
3 Chlorotrianisene versus placebo					
Schwartz 1973	25/75	51/78		14.4 %	0.51 [0.36, 0.73]
Subtotal (95% CI)	**75**	**78**		**14.4 %**	**0.51 [0.36, 0.73]**
Total events: 25 (Treatment), 51 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 3.68 (P = 0.00023)					
4 Hexestrol versus placebo					
Firth 1969	20/50	50/50		14.7 %	0.41 [0.29, 0.57]
Subtotal (95% CI)	**50**	**50**		**14.7 %**	**0.41 [0.29, 0.57]**
Total events: 20 (Treatment), 50 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 5.26 (P < 0.00001)					
Total (95% CI)	**474**	**409**		**100.0 %**	**0.41 [0.29, 0.59]**
Total events: 159 (Treatment), 330 (Control)					
Heterogeneity: Tau^2 = 0.20; Chi^2 = 48.72, df = 7 (P<0.00001); I^2 =86%					
Test for overall effect: Z = 4.81 (P < 0.00001)					

Analysis 2.2. Comparison 2 Oestrogen preparations versus placebo, Outcome 2 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤14 days.

Review: Treatments for suppression of lactation

Comparison: 2 Oestrogen preparations versus placebo

Outcome: 2 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤14 days

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
Cruttenden 1971	8/33	17/30		60.0 %	0.43 [0.22, 0.84]
Varga 1972	1/20	18/20		40.0 %	0.06 [0.01, 0.38]
Total (95% CI)	**53**	**50**		**100.0 %**	**0.19 [0.03, 1.34]**
Total events: 9 (Treatment), 35 (Control)					
Heterogeneity: Tau^2 = 1.55; Chi^2 = 3.87, df = 1 (P = 0.05); I^2 =74%					
Test for overall effect: Z = 1.67 (P = 0.096)					

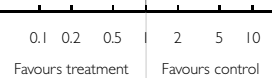
Analysis 3.1. Comparison 3 Antioestrogen preparations versus placebo, Outcome 1 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤7 days.

Review: Treatments for suppression of lactation

Comparison: 3 Antioestrogen preparations versus placebo

Outcome: 1 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤7 days

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
1 Clomiphene versus placebo					
Weinstein 1976	8/15	8/15		100.0 %	1.00 [0.51, 1.95]
Total (95% CI)	**15**	**15**		**100.0 %**	**1.00 [0.51, 1.95]**
Total events: 8 (Treatment), 8 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.0 (P = 1.0)					



Analysis 3.2. Comparison 3 Antioestrogen preparations versus placebo, Outcome 2 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤ 14 days.

Review: Treatments for suppression of lactation

Comparison: 3 Antioestrogen preparations versus placebo

Outcome: 2 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤ 14 days

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
1 Tamoxifen versus placebo					
Shaaban 1975	64/92	47/48		100.0 %	0.71 [0.62, 0.82]
Total (95% CI)	**92**	**48**		**100.0 %**	**0.71 [0.62, 0.82]**
Total events: 64 (Treatment), 47 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 4.74 (P < 0.00001)					

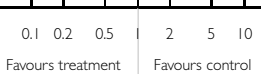
Analysis 4.1. Comparison 4 Pyridoxine versus placebo, Outcome 1 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤ 7 days.

Review: Treatments for suppression of lactation

Comparison: 4 Pyridoxine versus placebo

Outcome: 1 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤ 7 days

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
1 Pyridoxine versus placebo					
MacDonald 1976	80/93	74/82		100.0 %	0.95 [0.86, 1.06]
Total (95% CI)	**93**	**82**		**100.0 %**	**0.95 [0.86, 1.06]**
Total events: 80 (Treatment), 74 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.87 (P = 0.39)					



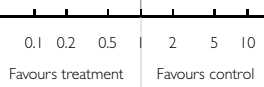
Analysis 5.1. Comparison 5 Combined oestrogen and androgen preparations versus placebo, Outcome 1 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤ 7 days.

Review: Treatments for suppression of lactation

Comparison: 5 Combined oestrogen and androgen preparations versus placebo

Outcome: 1 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤ 7 days

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
1 Testosterone oenanthate + oestradiol valereate					
Iliya 1966	6/102	79/90		50.9 %	0.07 [0.03, 0.15]
Schwartz 1973	6/76	42/78		49.1 %	0.15 [0.07, 0.32]
Total (95% CI)	**178**	**168**		**100.0 %**	**0.10 [0.06, 0.17]**
Total events: 12 (Treatment), 121 (Control)					
Heterogeneity: Chi^2 = 1.90, df = 1 (P = 0.17); I^2 =47%					
Test for overall effect: Z = 8.16 (P < 0.00001)					



Analysis 6.1. Comparison 6 Androgen preparations versus placebo, Outcome 1 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤ 7 days.

Review: Treatments for suppression of lactation

Comparison: 6 Androgen preparations versus placebo

Outcome: 1 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤ 7 days

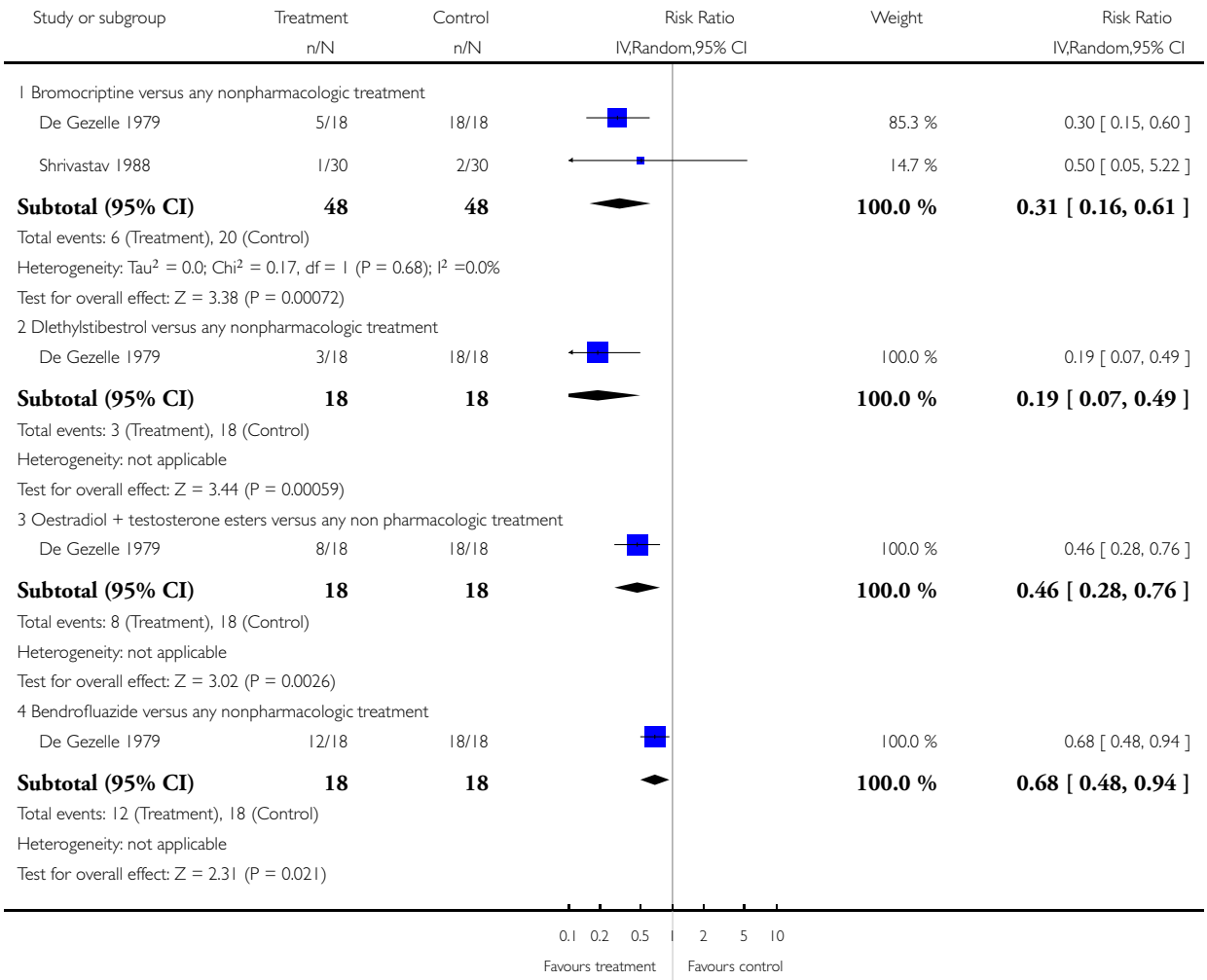
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
1 Testosterone propionate versus placebo					
Weinstein 1976	9/15	8/15		100.0 %	1.13 [0.60, 2.11]
Total (95% CI)	**15**	**15**		**100.0 %**	**1.13 [0.60, 2.11]**
Total events: 9 (Treatment), 8 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.37 (P = 0.71)					

Analysis 7.1. Comparison 7 Pharmacologic treatment versus nonpharmacologic treatment, Outcome 1 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain.

Review: Treatments for suppression of lactation

Comparison: 7 Pharmacologic treatment versus nonpharmacologic treatment

Outcome: 1 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain



Analysis 7.2. Comparison 7 Pharmacologic treatment versus nonpharmacologic treatment, Outcome 2 Rebound lactation.

Review: Treatments for suppression of lactation

Comparison: 7 Pharmacologic treatment versus nonpharmacologic treatment

Outcome: 2 Rebound lactation

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
Shrivastav 1988	2/30	0/30		100.0 %	5.00 [0.25, 99.95]
Total (95% CI)	**30**	**30**		**100.0 %**	**5.00 [0.25, 99.95]**
Total events: 2 (Treatment), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.05 (P = 0.29)					

Analysis 8.1. Comparison 8 Comparison of two pharmacologic treatments, Outcome 1 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤7 days postpartum.

Review: Treatments for suppression of lactation

Comparison: 8 Comparison of two pharmacologic treatments

Outcome: 1 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤7 days postpartum

Study or subgroup	Favours treatment n/N	Control n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
1 Bromocriptine versus oestrogen preparations					
Nilsen 1976	3/20	1/18		6.0 %	2.70 [0.31, 23.69]
Piya-Anant 2004	29/114	33/116		60.6 %	0.89 [0.58, 1.37]
Steenstrup 1977	2/20	8/21		13.0 %	0.26 [0.06, 1.09]
Utian 1975	3/16	10/15		20.4 %	0.28 [0.10, 0.83]
Subtotal (95% CI)	**170**	**170**		**100.0 %**	**0.58 [0.25, 1.38]**
Total events: 37 (Favours treatment), 52 (Control)					
Heterogeneity: Tau^2 = 0.42; Chi^2 = 7.23, df = 3 (P = 0.06); I^2 =59%					
Test for overall effect: Z = 1.23 (P = 0.22)					
2 Bromocriptine versus ergot derivative					
Fischer 1995	10/81	17/69		43.1 %	0.50 [0.25, 1.02]

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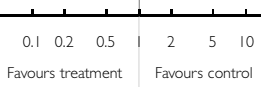
Study or subgroup	Favours treatment n/N	Control n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
Scapin 1982	13/20	4/20		29.9 %	3.25 [1.28, 8.27]
Venturini 1981	5/18	6/20		27.0 %	0.93 [0.34, 2.52]
Subtotal (95% CI)	**119**	**109**		**100.0 %**	**1.12 [0.37, 3.42]**
Total events: 28 (Favours treatment), 27 (Control)					
Heterogeneity: Tau^2 = 0.77; Chi^2 = 9.75, df = 2 (P = 0.01); I^2 =79%					
Test for overall effect: Z = 0.19 (P = 0.85)					
3 Bromocriptine versus prostagladins					
England 1988	4/22	7/21		100.0 %	0.55 [0.19, 1.60]
Subtotal (95% CI)	**22**	**21**		**100.0 %**	**0.55 [0.19, 1.60]**
Total events: 4 (Favours treatment), 7 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.11 (P = 0.27)					
4 Bromocriptine versus pyridoxine					
Boes 1980	37/49	39/48		100.0 %	0.93 [0.75, 1.15]
Subtotal (95% CI)	**49**	**48**		**100.0 %**	**0.93 [0.75, 1.15]**
Total events: 37 (Favours treatment), 39 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.69 (P = 0.49)					
5 Quinestrol versus other oestrogen preparations					
Bergsjo 1974	13/23	11/18		50.7 %	0.92 [0.55, 1.55]
Kuku 1968	17/52	19/52		49.3 %	0.89 [0.53, 1.52]
Subtotal (95% CI)	**75**	**70**		**100.0 %**	**0.91 [0.63, 1.32]**
Total events: 30 (Favours treatment), 30 (Control)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.01, df = 1 (P = 0.93); I^2 =0.0%					
Test for overall effect: Z = 0.50 (P = 0.62)					

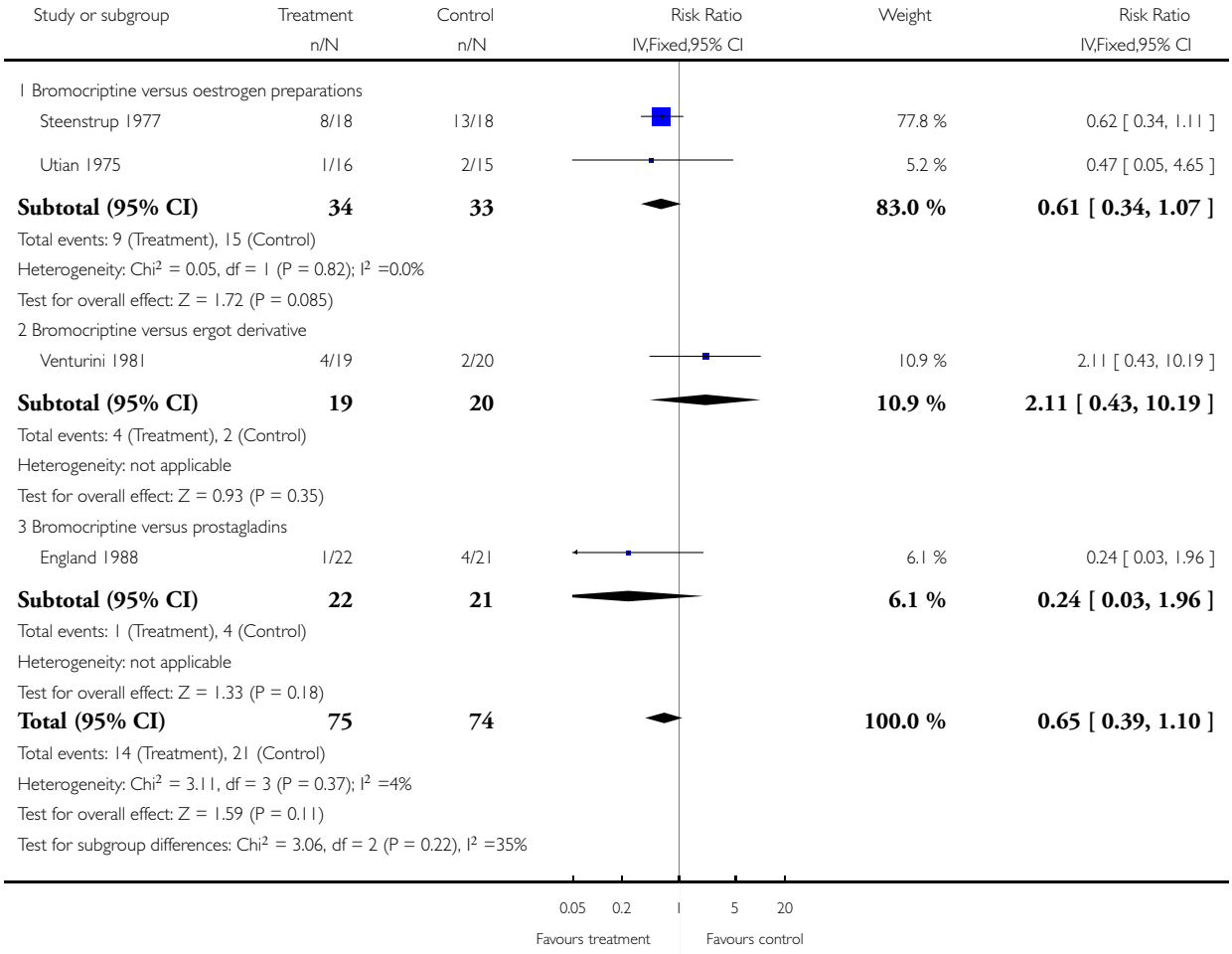


Analysis 8.2. Comparison 8 Comparison of two pharmacologic treatments, Outcome 2 Rebound lactation.

Review: Treatments for suppression of lactation

Comparison: 8 Comparison of two pharmacologic treatments

Outcome: 2 Rebound lactation

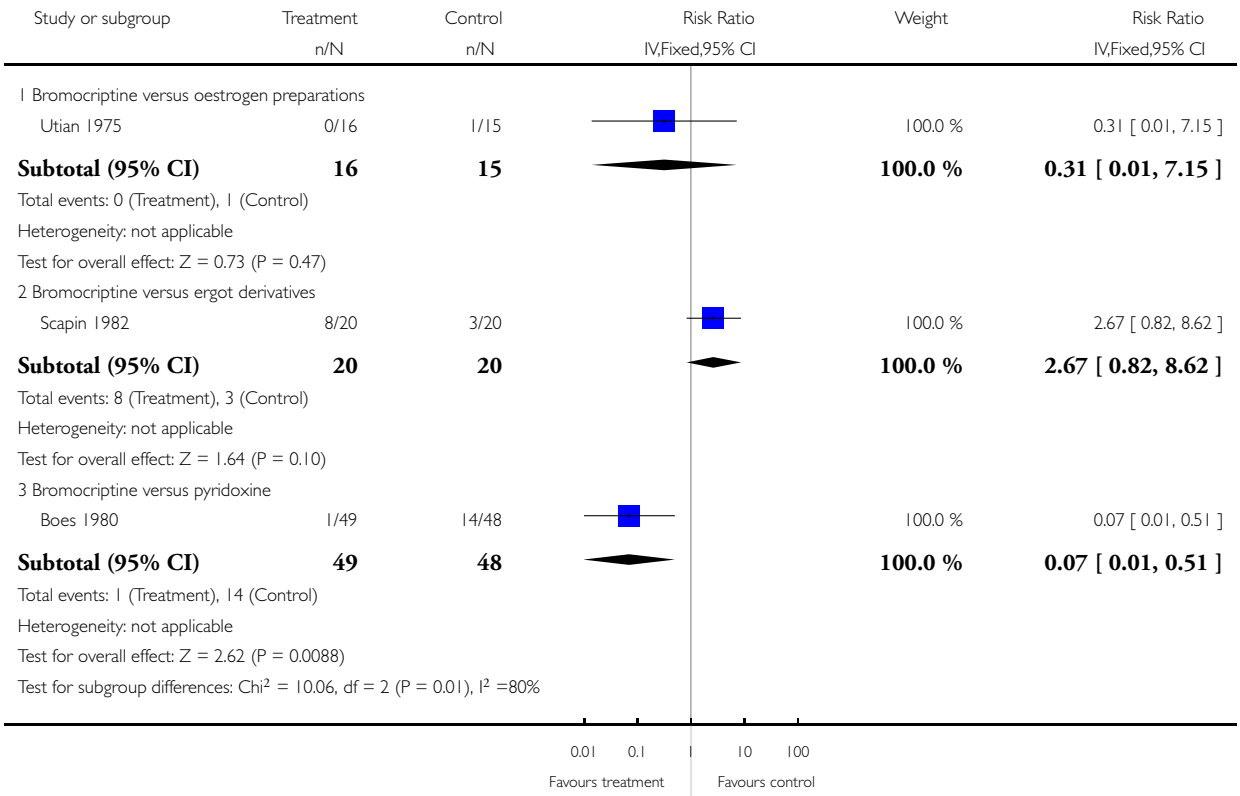


Analysis 8.3. Comparison 8 Comparison of two pharmacologic treatments, Outcome 3 Use of second line drug or method to achieve suppression of lactation.

Review: Treatments for suppression of lactation

Comparison: 8 Comparison of two pharmacologic treatments

Outcome: 3 Use of second line drug or method to achieve suppression of lactation

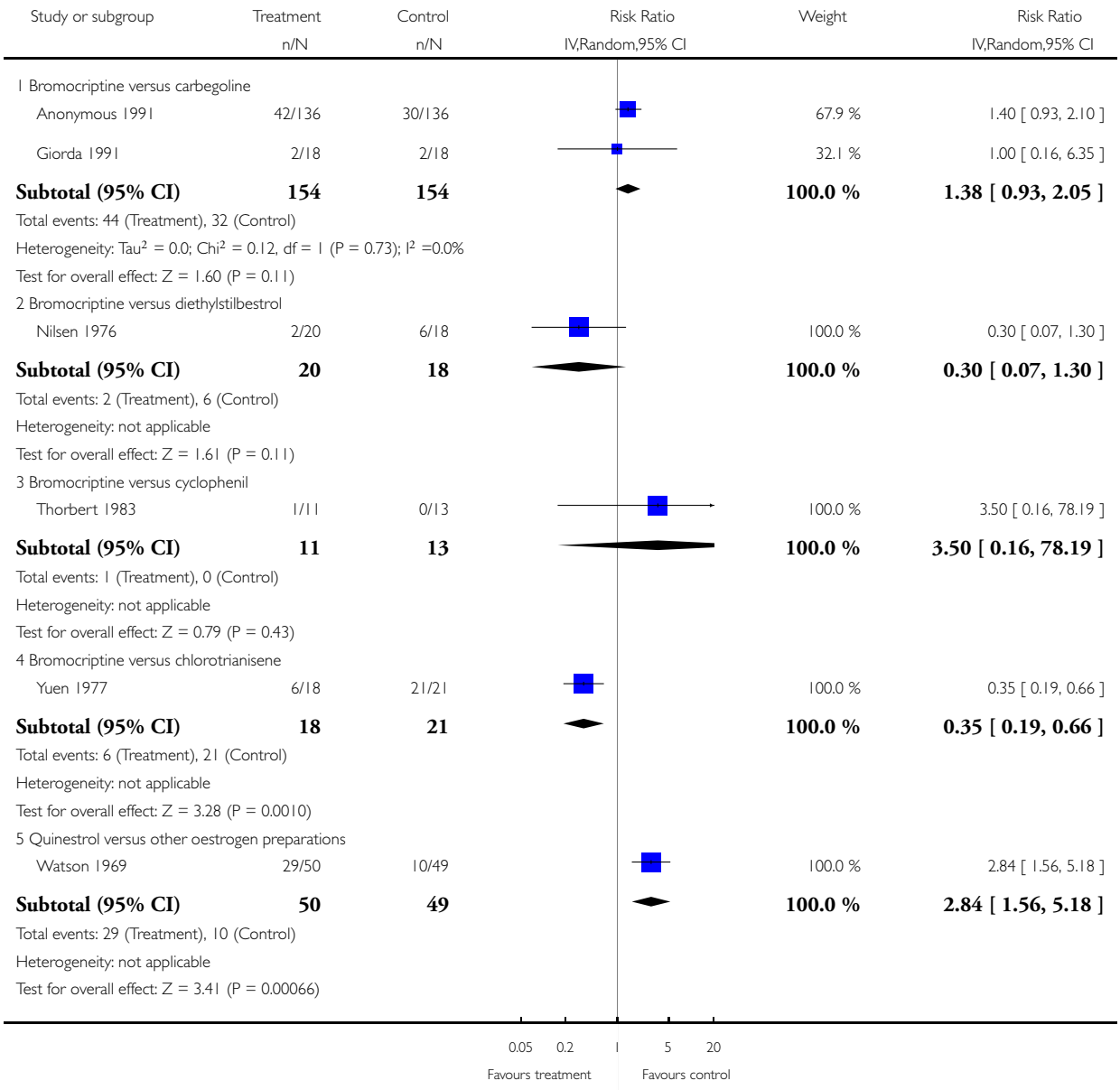


Analysis 8.4. Comparison 8 Comparison of two pharmacologic treatments, Outcome 4 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤14 days.

Review: Treatments for suppression of lactation

Comparison: 8 Comparison of two pharmacologic treatments

Outcome: 4 Failure to suppress lactation as indicated by milk secretion, breast engorgement or breast pain at ≤14 days



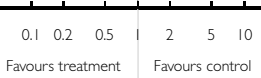
Analysis 9.1. Comparison 9 High versus low dose quinestrol, Outcome 1 Failure to suppress lactation as described by milk secretion, breast engorgement or breast pain at ≤ 7 days postpartum.

Review: Treatments for suppression of lactation

Comparison: 9 High versus low dose quinestrol

Outcome: 1 Failure to suppress lactation as described by milk secretion, breast engorgement or breast pain at ≤ 7 days postpartum

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
1 Quinestrol 4 mg versus Quinestrol 2 mg					
Vischi 1975	18/66	35/66		100.0 %	0.51 [0.33, 0.81]
Total (95% CI)	**66**	**66**		**100.0 %**	**0.51 [0.33, 0.81]**
Total events: 18 (Treatment), 35 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.87 (P = 0.0042)					



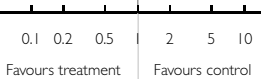
Analysis 10.1. Comparison 10 Low versus high dose terguride, Outcome 1 Failure to suppress lactation as described by milk secretion, breast engorgement or breast pain at days 0 -15.

Review: Treatments for suppression of lactation

Comparison: 10 Low versus high dose terguride

Outcome: 1 Failure to suppress lactation as described by milk secretion, breast engorgement or breast pain at days 0 -15

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
1 Terguride 0.5-1.0 mg vs terguride 0.25 mg					
Venturini 1988	11/30	11/15		100.0 %	0.50 [0.29, 0.88]
Total (95% CI)	**30**	**15**		**100.0 %**	**0.50 [0.29, 0.88]**
Total events: 11 (Treatment), 11 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.42 (P = 0.015)					

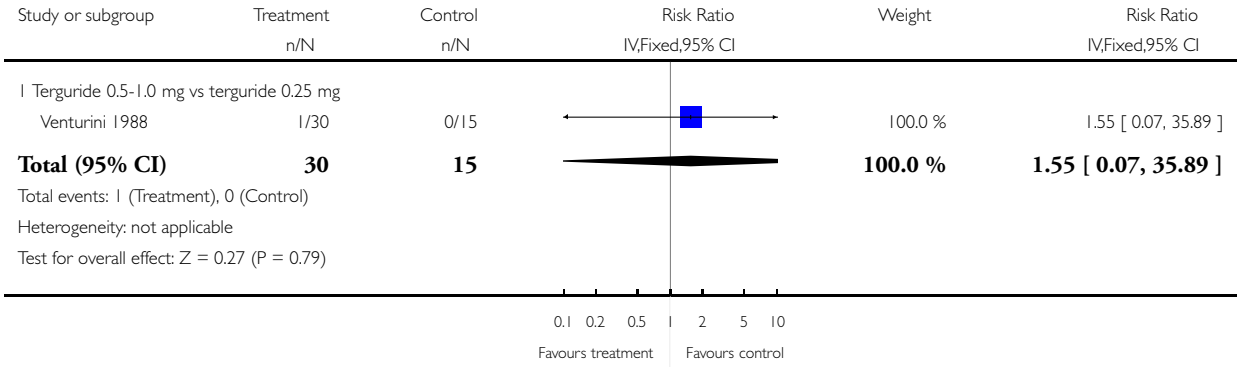


Analysis 10.2. Comparison 10 Low versus high dose terguride, Outcome 2 Side effect: dizziness.

Review: Treatments for suppression of lactation

Comparison: 10 Low versus high dose terguride

Outcome: 2 Side effect: dizziness

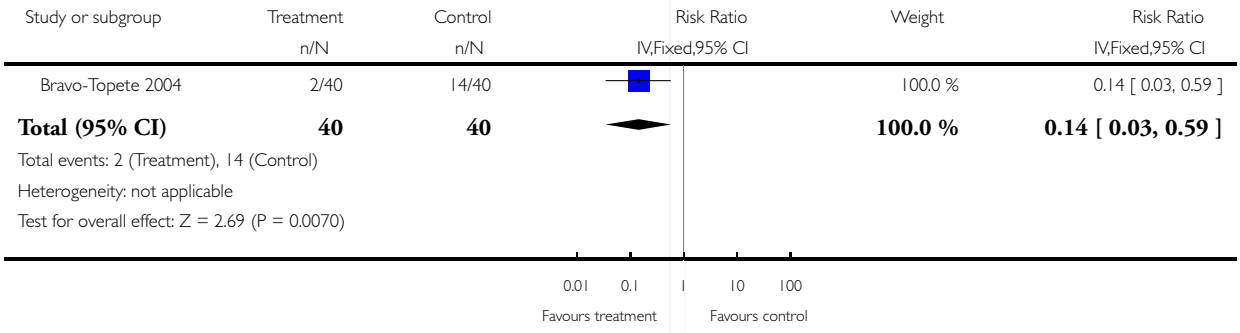


Analysis 11.1. Comparison 11 High versus low dose cabergoline, Outcome 1 Failure to suppress lactation as described by milk secretion, breast engorgement or breast pain.

Review: Treatments for suppression of lactation

Comparison: 11 High versus low dose cabergoline

Outcome: 1 Failure to suppress lactation as described by milk secretion, breast engorgement or breast pain



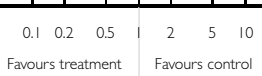
Analysis 12.1. Comparison 12 Long course tamoxifen versus short course tamoxifen, Outcome 1 Failure to suppress lactation as described by milk secretion, breast engorgement or breast pain at D0-15.

Review: Treatments for suppression of lactation

Comparison: 12 Long course tamoxifen versus short course tamoxifen

Outcome: 1 Failure to suppress lactation as described by milk secretion, breast engorgement or breast pain at D0-15

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
1 Tamoxifen (14 days course) vs tamoxifen (6 days course)					
Shaaban 1975	30/42	22/23		100.0 %	0.75 [0.61, 0.92]
Total (95% CI)	**42**	**23**		**100.0 %**	**0.75 [0.61, 0.92]**
Total events: 30 (Treatment), 22 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.72 (P = 0.0065)					



HISTORY

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CONTRIBUTIONS OF AUTHORS

Both review authors extracted, entered and double checked data. Both authors contributed to the writing of the review.

DECLARATIONS OF INTEREST

None known.

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Internal sources

- No sources of support supplied

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The definition of lactation suppression as pre-specified in the protocol for this review was revised in view of the definitions used by most trialists and the need to significantly reduce the clinical heterogeneity that would be introduced by the variable duration of outcome assessment when summarising effects of interventions. We evaluated the methodological quality of included trials by assessing the risk of bias for each study using the criteria outlined in the latest version of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2008).

INDEX TERMS

Medical Subject Headings (MeSH)

*Lactation [drug effects; physiology]; Bromocriptine [*therapeutic use]; Estrogens [*therapeutic use]; Hormone Antagonists [*therapeutic use]; Milk Ejection; Randomized Controlled Trials as Topic

MeSH check words

Female; Humans