National Institute for Health and Care Excellence

Draft for consultation

Intrapartum care for healthy women and babies

[C] Evidence review for sterile water injections

NICE guideline number CG190 (update)

Evidence review underpinning recommendations 1.6.12 to 1.6.14 in the NICE guideline

April 2023

Draft

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Sterile water injections

Review question

What is the effectiveness of injected water papules for pain relief during labour?

Introduction

Injections of sterile water have been suggested as an effective method to treat back pain for women in labour. They have the potential to provide a cheap and relatively easy method of pain relief and one that could be widely available in various birth settings, including home births and midwife led units.

There is currently little guidance available on the best approach for administering this intervention (including route of administration, site of administration, dose) and its effectiveness at relieving pain in labour. The aim of this review was to determine the effectiveness of injected water papules for pain relief during labour and to determine if they should be recommended as an intervention.

Summary of the protocol

See Table 1 for a summary of the Population, Intervention, Comparison and Outcome (PICO) characteristics of this review.

Table 1: Summary of the protocol (PICO table)

Population	• Women in labour who are pregnant with a single baby, who go into labour at term (37 to 42 weeks of pregnancy) and who do not have any pre-existing medical conditions or antenatal conditions that predispose to a higher risk birth • Women in labour whose baby has not been identified before labour to be at high risk of adverse outcomes • Singleton babies born at term (37 to 42 weeks of pregnancy) with no previously identified problems (for example, congenital malformations, genetic anomalies, intrauterine growth restriction, placental problems)
Intervention	• Intracutaneous or subcutaneous injection of sterile water (also known as sterile water papules or water blocks) injected on the lower back of women in labour
Comparison	• No treatment • Other non-pharmacological pain relieving strategies (such as acupuncture, TENS, labour in water pool) • Sham treatment/placebo (needle insertion with no fluid injection) • Saline injection • Different dose, injection technique (intracutaneous or subcutaneous) or site of injection within the lower back of sterile water
Outcome	**Critical** • General labour pain • Back pain during labour • Mode of birth (for example spontaneous vaginal, forceps, caesarean birth) **Important** • Women's experience of labour and birth • Use of any rescue pharmacological analgesia during labour, including epidural • Infection at the site of injection • Neonatal unit admission

TENS: transcutaneous electrical nerve stimulation

For further details see the review protocol in appendix A.

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in appendix A and the methods document (supplementary document 1).

Declarations of interest were recorded according to NICE's conflicts of interest policy.

Effectiveness

Included studies

Eleven studies were included for this review: 1 Cochrane systematic review (Derry 2012) included 7 randomised controlled trials (RCTs) (Ader 1990, Bahasadri 2006, Kushtagi 2009, Martensson 1999, Saxena 2009, Trolle 1991 and Wiruchpongsanon 2006), and 10 RCTs (Almassinokiani 2020, Farag 2015, Fouly 2018, Koyucu 2018, Labrecque 1999, Lee 2013, Lee 2020, Martensson 2008, Rai 2013 and Rezaie 2019).

Two RCTs compared sterile water injections to dry injections (Almassinokiani 2020, Koyucu 2018). One Cochrane systematic review (Derry 2012) and 5 RCTs compared sterile water injections to saline injections (Farag 2015, Fouly 2018, Lee 2020, Rai 2013 and Rezaie 2019). Two RCTs compared sterile water injections to non-pharmacological pain relieving strategies: transcutaneous electrical nerve stimulation (TENS) (Labrecque 1999) and acupuncture (Martensson 2008). One RCT compared a high dose of sterile water injections to a low dose of sterile water injections (Lee 2013). One RCT compared sterile water injections to standard care, which included massage, water bath and movement (Labrecque 1999). The studies were from Australia, Canada, Denmark, Egypt, India, Iran, Nepal, Sweden, Thailand, Turkey and the UK.

Routes and doses of administration varied between studies, with 9 studies using subcutaneous/subdermal administration (with individual injections of 0.1ml to 0.5ml) and 13 studies using intracutaneous/intradermal administration (with individual injections of 0.1ml to 0.5ml). Studies used a single injection or a pattern of 2-4 separate injections into the Michaelis' rhomboid.

The included studies are summarised in Table 2.

See the literature search strategy in appendix B and study selection flow chart in appendix C.

Excluded studies

Studies not included in this review are listed, and reasons for their exclusion are provided in appendix J.

Summary of included studies

Summaries of the studies that were included in this review are presented in Table 2.

Table 2: Summary of included studies

Study	Population	Intervention	Comparison	Outcomes
Almassinokiani 2020 Randomised controlled trial Iran	N=121 nulliparous women, with a singleton pregnancy at term. Second stage of labour (cervix 4cm or more). Risk status or if labour induced not reported.	Sterile water injections	Dry injection Sterile water injections – different technique	• General labour pain • Mode of birth – caesarean birth
Derry 2012 Cochrane systematic review Denmark, India, Iran, Sweden, Thailand	K= 7 (Ader 1990, Bahasadri 2009, Kushtagi 2009, Martensson 1999, Saxena 2009, Trolle 1991, Wiruchpongsanon 2006) N= 766 pregnant women at term.	Sterile water injections	Saline injections Sterile water injections – different technique	• Back pain during labour • Mode of birth – caesarean birth; instrumental vaginal birth; spontaneous vaginal birth • Women's experience of labour and birth

Study	Population	Intervention	Comparison	Outcomes
	Active stage of labour. Risk status or if labour induced not reported.			• Use of any rescue pharmacological analgesia during labour
Farag 2015 Randomised controlled trial Egypt	N=73 low risk pregnant women, with a singleton pregnancy at term. Labour not induced. Active phase of 1st stage of labour (cervix 3-5cm and >50% effacement).	Sterile water injections	Saline injections	• Back pain during labour • Mode of birth – caesarean birth; instrumental vaginal birth; spontaneous vaginal birth • Use of any rescue pharmacological analgesia during labour
Fouly 2018 Randomised controlled trial Egypt	N=330 pregnant women, with a singleton pregnancy at term. 1st stage of labour. Risk status not reported. Women who had labour induced were included, proportion of these women in the total sample was not reported.	Sterile water injections	Saline injections	• Back pain during labour • Mode of birth – caesarean birth; spontaneous vaginal birth
Koyucu 2018 Randomised controlled trial Turkey	N=168 low risk pregnant women, with a singleton pregnancy at term. Labour not induced. Active phase of 1st stage of labour (cervix 3-7cm).	Sterile water injections	Dry injections	• Back pain during labour • Mode of birth – caesarean birth; instrumental vaginal birth • Women's experience of labour and birth • Use of any rescue pharmacological analgesia during labour
Labrecque 1999 Randomised controlled trial	N=35 low risk pregnant women over 36 weeks gestation.	Sterile water injections	Standard care (back massage, whirlpool, walking,	• Back pain during labour • Mode of birth – caesarean birth

Study	Population	Intervention	Comparison	Outcomes
Canada	Active 1st stage of labour. If labour was induced not reported. Proportion of women between 36-37 weeks gestation not reported.		changing position) TENS	• Women's experience of labour and birth • Use of any rescue pharmacological analgesia during labour
Lee 2013 Randomised controlled trial Australia	N=306 low risk pregnant women, with a singleton pregnancy at term. 1st stage of labour. If labour was induced not reported.	Sterile water injections high dose (0.4ml)	Sterile water injections low dose (0.1ml)	• Back pain during labour • Mode of birth – caesarean birth; instrumental vaginal birth; spontaneous vaginal birth • Women's experience of labour and birth • Use of any rescue pharmacological analgesia during labour
Lee 2020 Randomised controlled trial Australia and UK	N=1166 low risk pregnant women, with a singleton pregnancy at term. Stage of labour not reported. Women whose labour was induced were included (<33%).	Sterile water injections	Saline injections	• Back pain during labour • Mode of birth – caesarean birth; instrumental vaginal birth; spontaneous vaginal birth • Women's experience of labour and birth • Use of any rescue pharmacological analgesia during labour • Neonatal admission
Martensson 2008 Randomised controlled trial Sweden	N=156 pregnancy women at term. Labour not induced. Stage of labour not reported. Risk status not reported.	Sterile water injections	Acupuncture	• General labour pain • Mode of birth – caesarean birth; instrumental vaginal birth; spontaneous vaginal birth • Use of any rescue pharmacological analgesia during labour
Rai 2013 Randomised controlled trial Nepal	N=240 pregnant women at term. Active phase of 1st stage (cervix more than 4cm).	Sterile water injections	Saline injections	• Back pain during labour • Mode of birth – caesarean birth; instrumental vaginal birth

Study	Population	Intervention	Comparison	Outcomes
	If labour was induced not reported.			• Women's experience of labour and birth • Neonatal admission
Rezaie 2019 Randomised controlled trial Iran	N=164 low risk pregnant women, with a singleton pregnancy at term. Cervix 4-6cm with >50% effacement. If labour was induced not reported.	Sterile water injections	Saline injections Sterile water injections – different technique	• Back pain during labour • Mode of birth – caesarean birth; instrumental vaginal birth; spontaneous vaginal birth

TENS: transcutaneous electrical nerve stimulation

See the full evidence tables in appendix D and the forest plots in appendix E.

Summary of the evidence

Across comparisons with dry injections, saline injections and standard care (massage, bath and movement), the majority of the evidence showed that sterile water injections had an important benefit in terms of general labour pain, back pain during labour and satisfaction. There was no evidence to suggest a difference in mode of birth, or use of other pharmacological analgesia. There was a possible harm in the comparison with saline injections, with an increase in neonatal admissions with the sterile water, but there were concerns around the quality of the evidence.

When compared to dry injections, sterile water injections at 0.4ml and 2ml doses showed an important benefit on general labour pains and back pains during labour. This was seen from 10 minutes up to 180 minutes, with the exception of 2ml dose at 10 minutes where there was no evidence of an important difference. The quality of the evidence ranged from low to high, with most of the evidence that showed a difference of high quality. Concerns were over imprecision for some outcomes, and indirectness where risk status or whether labour was induced was not reported. Overall there was no important benefit of sterile water injections over dry injections on caesarean birth, instrumental vaginal birth or the need for epidural analgesia, with the evidence of very low to moderate quality. High quality evidence showed an important benefit of sterile water injections over dry injections for satisfaction with treatment.

Overall sterile water injections showed an important benefit over saline injections in terms of back pain during labour. The quality of the evidence ranged from very low to moderate, with similar distribution between low and moderate and slightly more outcomes rated as very low. Most of the evidence was downgraded for indirectness due to not reporting on risk status or whether labour was induced. There were also concerns for risk of bias and imprecision for some of the evidence. The majority of the evidence showed a benefit of sterile water injections over saline injections on pain outcomes at the 0.4ml dose, from 10 minutes up to 120 minutes after injections. At doses of 0.6ml, the majority of the evidence showed no important benefits of sterile water injections over saline injections, with most of the evidence of moderate quality. At the 1ml dose low to moderate quality evidence showed an important benefit of sterile water injections over saline injections in terms of pain at 45 minutes and 90 minutes after injection, but not at other time points. The data was mixed at the 2ml dose, with some of the evidence showing an important benefit on pain, but some not. Overall, the majority of the evidence showed no evidence of an important difference on mode of birth, but

some evidence showed a possible increase in caesarean births with sterile water injections at 1ml, and a possible increase in instrumental vaginal births at 0.4ml. The findings were imprecise, and there were concerns around the indirectness of the population and also risk of bias. The evidence showed that women were satisfied with sterile water injections, but the quality of the evidence was very low, with the main concerns around risk of bias and indirectness of the population. When analysing by subgroup analysis, satisfaction was less apparent in high income settings. There was no evidence to suggest a difference between sterile water injections or saline in terms of the different types of rescue pharmacological analgesia, with the majority of the evidence being very low quality. The evidence showed a possible important harm of sterile water injections over saline injections on neonatal admissions, but the quality of the evidence was very low due to imprecision, risk of bias and indirectness.

Different doses of sterile water injections were compared. The evidence showed an important benefit of a high dose of sterile water injections (0.4ml) on pain outcomes, when compared to a low dose (0.1ml). The evidence was of very low quality, with imprecise findings, and concerns over the indirectness of the population, as whether the labour was induced was not reported. There were also some concerns over the risk of bias. There was no evidence of an important difference for caesarean births or instrumental vaginal births, but moderate quality evidence that showed there was no difference between the doses on spontaneous vaginal births. Very low quality evidence showed no important difference on whether women would use the same treatment again, and no evidence of an important difference for satisfaction or use of rescue pharmacological analgesia.

Subcutaneous injections of sterile water were compared to intracutaneous injections of sterile water, and overall the evidence showed no clear benefit of one technique over another on pain outcomes, mode of birth or satisfaction. Most of the evidence was rated low to very low quality, with only some of the evidence of moderate quality. Most of the concerns were around the directness of the evidence as risk status or whether labour was induced were not reported. There were some concerns over the risk of bias and also around the imprecision of some findings.

Sterile water injections were compared to other non-pharmacological pain relieving strategies. When compared to TENS, sterile water injections had an important benefit on reducing pain and reducing caesarean births, but there was no evidence of an important difference for satisfaction or use of epidural analgesia. The evidence was rated as very low quality with concerns over the risk of bias and imprecision. There were also concerns over the indirectness as some women were included between 36-37 weeks of gestation, and whether the labour was induced was not reported. When compared to acupuncture, sterile water injections had an important benefit in terms of general labour pain. The quality of the evidence was very low. There were some concerns over imprecision, but most of the concerns were around the indirectness as risk status was not reported, and risk of bias. There was no evidence of an important difference between sterile water injections and acupuncture on caesarean births or instrumental vaginal births, but moderate quality evidence showed no important difference on spontaneous vaginal births. Very low quality evidence suggested that there was no evidence of a difference between the comparators on use of other rescue analgesia.

There was no evidence reported for infection at the site of injection for any of the comparisons.

See appendix F for full GRADE tables.

Economic evidence

Included studies

A systematic review of the economic literature was conducted but no economic studies were identified which were applicable to this review question.

Excluded studies

Economic studies not included in this review are listed, and reasons for their exclusion are provided in appendix K.

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation.

The committee's discussion and interpretation of the evidence

The outcomes that matter most

As the aim of the review was to determine the effectiveness of water papules as a method of analgesia, the committee agreed that pain outcomes (general labour pain and back pain) and mode of birth were critical outcomes for this review. They agreed it was important to identify between general labour pain and back pain as sterile water injections could have an effect on one type of pain but not another. They agreed that mode of birth was a critical outcome as they wanted to find out whether sterile water injections have an impact on the number of women needing an assisted vaginal birth, or a caesarean birth.

The committee agreed that it was important to find out the impact of water papules on women's experiences of labour and birth, and so they chose this as an important outcome. The committee recognised the great importance of women's experience, but they were aware that data on this outcome was likely to be sparse and unlikely to inform decision-making in a meaningful way, so they prioritised other outcomes as critical. They also chose the use of rescue analgesia as an important outcome, as this would provide another indication of the effectiveness of water papules. As water papules involve the use of up to 4 different injection sites, the committee agreed it was important to find out whether there was increased risk of infection due to their use. Finally, the committee chose neonatal unit admission as an important outcome to determine if the use of sterile water injections had any adverse impact on the baby.

The quality of the evidence

The quality of the evidence for outcomes was assessed with GRADE and was rated as high to very low. The main issues were around the indirectness of the evidence. Most of the studies did not report the risk status of the women or whether the labour was induced. Some of the studies included women who had been induced, and some did not report the proportion of those out of the whole sample who had been induced. Some studies did not report on whether women received parenteral analgesia before the intervention. There were concerns for many outcomes around the imprecision of the estimate of effect. There were also concerns of risk of bias for many outcomes. The main issues were around the knowledge of the intervention and the potential for this to have an influence on subjective outcomes. Other concerns over bias were around not enough information provided on missing outcome data, or removing women from the study if they used rescue analgesia.

Benefits and harms

The committee discussed the evidence around sterile water injections and agreed to make recommendations supporting the use of sterile water injections for women experiencing back pain during labour. They agreed that the evidence on sterile water injections when compared with saline and dry injections were the most informative and supported these recommendations. They discussed concerns over the quality and paucity of evidence between comparisons with standard care and other non-pharmacological pain reliving strategies and agreed that this evidence was less useful in helping them make recommendations. The committee had concerns over the quality of the evidence, and therefore agreed they could not make a strong recommendation. They discussed that women should be given the option to choose sterile water injections as a method of analgesia for back pain, and in practice they would have the option to request different analgesia if sterile water injections were not an effective pain relieving strategy for them.

The committee discussed that there was some evidence showing a benefit on general labour pains, but agreed there was not enough evidence to support a recommendation and as most of the evidence of benefit was for back pain, they agreed to recommend sterile water injection for back pain during labour only.

The committee agreed that the most useful recommendations for practice would give clear guidance to practitioners on the dose of sterile water injections, and the route of injection. The committee discussed the injection route, and agreed that, although the majority of the evidence was for intracutaneous administration, as the evidence did not show a difference between outcomes when the two techniques were compared, they would make a recommendation for either intracutaneous or subcutaneous administration. They agreed that they would make it clear in the recommendation that both techniques could be used, and agreed this would help avoid confusion in practice. The committee also discussed that most midwives would be familiar with administering injections via the subcutaneous route and did not want to limit the intervention to midwives skilled in administration via intracutaneous injection only.

The committee agreed that it was important to make women aware that injections of sterile water could be painful. This was not an outcome of the review, but from their experience the committee were aware that women experience a short-lived feeling of pain or stinging at the site of injection. The committee discussed the variation across studies regarding the time of onset of pain relief, and some contradicting data which showed a benefit in terms of pain relief at various time points in some studies, but not the same benefit at the same time points in other studies. The committee discussed that the indirect population in some studies could explain this variation if some of the women had had their labour induced, and others not as this might affect the pain onset. They also discussed that it could be due to the fact that pain is a subjective outcome and felt differently among women. Nevertheless, they agreed that it was important to inform women about when they might expect to feel pain relief and how long it may last for and so they used the evidence to include in the recommendation that pain relief was likely to be felt from 10 minutes after the injections and could last up to 3 hours.

The committee discussed the evidence, which showed mixed results for pain relief with different doses. The committee noted that there could be a number of reasons for the conflicting findings such as different ways of measuring pain: some studies recorded the pain level on a pain scale, whereas others reported number of women reporting a certain percentage of pain reduction from baseline. They also discussed that stage of labour could be a factor. Sterile water injections can be administered during the latent and active phases of the first stage of labour, and even during the second stage. The studies did not consistently report which stage of labour women were in, with some studies using cervical dilation and others the stage of labour, therefore pre-specified subgroup analysis by stage of labour could not be carried out and the committee were unable to comment on how stage of labour could have an effect on pain. However, they agreed that the larger and more recent

trials using a 4 x 0.1ml dose with the intracutaneous route, showed a benefit for back pain relief. The committee also specified that a 4 x 0.5ml dose should be used with the subcutaneous route of administration, as most of the subcutaneous evidence corresponded with this dosage. The committee discussed that the majority of the evidence in terms of reduction in back pain with a 4 x 0.5ml dose showed a benefit, but that this was not universal and at some time points no difference was seen, and not of high quality, which was another reason that the committee did not make a strong recommendation. The committee recommended the site of injections to be in the Michaelis' Rhomboid region, which is in line with site of administration reported in the evidence.

The committee noted that some of the evidence suggested women would choose the same treatment again in the future, and they also discussed the potential harms of sterile water injections. The evidence showed sterile water injections may be associated with more neonatal admissions. Due to the very low quality of the evidence, and borderline statistical significance, the committee were not concerned. However, the committee also noted that this method of pain relief during labour did not lead to more instrumental or caesarean births, and the lack of evidence for harms further reinforced the committee's recommendation.

No evidence had been identified on infection at the site of injection, and although the committee noted that intracutaneous and subcutaneous injections are safe, they were aware they can rarely cause irritation at the injection site and lead to infections.

Cost effectiveness and resource use

As no economic evidence was identified and because this topic was not a high priority for economic evaluation, the committee made a qualitative assessment of the cost effectiveness. They noted that this was a low-cost intervention both in terms of consumables and staff time. The committee noted that there was evidence to suggest that water injections could be effective for back pain in labour and, although there were concerns with respect to the quality of the evidence, they reasoned that water injections could improve health-related quality of life at a cost that was acceptable to the NHS.

The committee discussed that recommending sterile water injections for back pain in labour could be a change in practice as they were not currently recommended in the guideline. However, they were aware that some midwives may already use them for women with back pain.

The committee agreed that the low cost of the intervention and the fact that midwives would already have the necessary skills to give subcutaneous injections meant that the recommendations would not have a great impact on NHS resources.

Recommendations supported by this evidence review

This evidence review supports recommendations 1.6.12 to 1.6.14.

References – included studies

Effectiveness

Ader 1991

Ader, L. (1991) Injections of sterile water for labour pain. Nursing times 87: 53

Almassinokiani 2020

Almassinokiani, F., Ahani, N., Akbari, P. et al. (2020) Comparative analgesic effects of intradermal and subdermal injection of sterile water on active labor pain. Anesthesiology and pain medicine 10(2)

Bahasadri 2006

Bahasadri, S., Ahmadi-Abhari, S., Dehghani-Nik, M. et al. (2006) Subcutaneous sterile water injection for labour pain: a randomised controlled trial. Australian & New Zealand journal of obstetrics & gynaecology 46(2): 102-106

Derry 2012

Derry, S., Straube, S., Moore, R. A. et al. (2012) Intracutaneous or subcutaneous sterile water injection compared with blinded controls for pain management in labour. Cochrane Database of Systematic Reviews

Farag 2015

Farag, A; Mohammed, K; Morsy, M (2015) Intracutaneous Sterile Water Injections for Relief of Back Pain during Labor. Medical Journal of Cairo University 83(1): 401-408

Fouly 2018

Fouly, Howieda, Herdan, Ragaa, Habib, Dina et al. (2018) Effectiveness of injecting lower dose subcutaneous sterile water versus saline to relief labor back pain: Randomized controlled trial. European journal of midwifery 2: 3

Koyucu 2018

Koyucu, R. G., Demirci, N., Yumru, A. E. et al. (2018) Effects of intradermal sterile water injections in women with low back pain in labor: a randomized, controlled, clinical trial. Balkan medical journal 35(2): 148-154

Kushtagi 2009

Kushtagi, P. and Bhanu, B. T. (2009) Effectiveness of subcutaneous injection of sterile water to the lower back for pain relief in labor. Acta obstetricia et gynecologica Scandinavica 88(2): 231-233

Labrecque 1999

Labrecque, M., Nouwen, A., Bergeron, M. et al. (1999) A randomized controlled trial of nonpharmacologic approaches for relief of low back pain during labor. Journal of family practice 48(4): 259-263

Lee 2013

Lee, N., Webster, J., Beckmann, M. et al. (2013) Comparison of a single vs. a four intradermal sterile water injection for relief of lower back pain for women in labour: a randomised controlled trial. Midwifery 29(6): 585-591

Lee 2020

Lee, N., Gao, Y., Collins, S. L. et al. (2020) Caesarean delivery rates and analgesia effectiveness following injections of sterile water for back pain in labour: a multicentre, randomised placebo controlled trial. Eclinicalmedicine 25

Martensson 1999

Martensson, L. and Wallin, G. (1999) Labour pain treated with cutaneous injections of sterile water: a randomised controlled trial. British journal of obstetrics and gynaecology 106(7): 633-7

Martensson 2008

Martensson, Lena; Stener-Victorin, Elisabet; Wallin, Gunnar (2008) Acupuncture versus subcutaneous injections of sterile water as treatment for labour pain. Acta Obstetricia et Gynecologica Scandinavica 87(2): 171-177

Rai 2014

Rai, R, Uprety, D, Pradhan, T et al. (2014) Subcutaneous Sterile Water Injection for Labor Pain: A Randomized Controlled Trial. Nepal Journal of Obstetrics and Gynaecology 8(2): 68-70

Rezaie 2019

Rezaie, Mehri, Shaabani, Sanaz, Jahromi, Farzin Sabouri et al. (2019) The Effect of Subcutaneous and Intracutaneous Injections of Sterile Water and Normal Saline on Pain Intensity in Nulliparous Women: A Randomized Controlled Trial. Iranian journal of nursing and midwifery research 24(5): 365-371

Saxena 2009

Saxena, K. N.; Nischal, H.; Batra, S. (2009) Intracutaneous injections of sterile water over the sacrum for labour analgesia. Indian journal of anaesthesia 53(2): 169-173

Trolle 1991

Trolle, B., Moller, M., Kronborg, H. et al. (1991) The effect of sterile water blocks on low back labor pain. American Journal of Obstetrics and Gynecology 164(5i): 1277-1281

Wiruchpongsanon 2006

Wiruchpongsanon, P. (2006) Relief of low back labor pain by using intracutaneous injections of sterile water: a randomized clinical trial. Chotmaihet thangphaet [Journal of the Medical Association of Thailand] 89(5): 571-576

Appendices

Appendix A Review protocols

Review protocol for review question: What is the effectiveness of injected water papules for pain relief during labour?

Table 3: Review protocol

Field	Content
PROSPERO registration number	CRD42021256259
Review title	What is the effectiveness of injected water papules for pain relief during labour?
Review question	What is the effectiveness of injected water papules for pain relief during labour?
Objective	To update the recommendations in CG190 (2014) for the effectiveness of pain-relieving strategies during the latent phase of labour. Surveillance has identified that injections of sterile water provide safe and effective pain management during labour.
Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE • International Health Technology Assessment database Searches will be restricted by: • No date limitations • English language only • Human studies only Other searches: • Inclusion lists of systematic reviews

Field	Content
	The full search strategies for MEDLINE database will be published in the final review. For each search, the principal database search strategy is quality assured by a second information scientist using an adaptation of the PRESS 2015 Guideline Evidence-Based Checklist.
Condition or domain being studied	Pain relieving strategies for women who are pregnant with a single baby, and in labour
Population	• Women in labour who are pregnant with a single baby, who go into labour at term (37 to 42 weeks of pregnancy) and who do not have any pre-existing medical conditions or antenatal conditions that predispose to a higher risk birth • Women in labour whose baby has not been identified before labour to be at high risk of adverse outcomes • Singleton babies born at term (37 to 42 weeks of pregnancy) with no previously identified problems (for example, congenital malformations, genetic anomalies, intrauterine growth restriction, placental problems)
Intervention	• Intracutaneous or subcutaneous injection of sterile water (also known as sterile water papules or water blocks) injected on the lower back of women in labour
Comparator	• No treatment • Other non-pharmacological pain relieving strategies (such as acupuncture, transcutaneous electrical nerve stimulation [TENS], labour in water pool) • Sham treatment/placebo (needle insertion with no fluid injection) • Saline injection • Different dose, injection technique or site of injection within the lower back of sterile water
Types of study to be included	Include published full-text papers: • Systematic reviews of RCTs • Parallel RCTs (individual or cluster) Conference abstracts will not be included because these do not typically have sufficient information to allow full critical appraisal.

Field	Content
Other exclusion criteria	Population: • Women in labour who are identified before labour to be at high risk, or whose baby is at high risk, of complications or adverse outcomes • Women with non-cephalic presentation • Women in preterm labour • Women with an intrauterine fetal death • Women with multi-fetal pregnancies • Women who are having their labour induced (until active labour is established) • Women who have had a previous caesarean birth or who are having a planned caesarean birth • Women who have had parenteral or regional analgesia since the onset of labour. If any study or systematic review includes <1/3 of women with the above characteristics, it will be considered for inclusion but, if included, the evidence will be downgraded for indirectness.
Context	This guideline will partly update the following: Intrapartum care for healthy women and babies (CG190)
Primary outcomes (critical outcomes)	• General labour pain • Back pain during labour • Mode of birth (for example spontaneous vaginal, forceps, vaginal breech, caesarean birth)
Secondary outcomes (important outcomes)	• Women's experience of labour and birth • Use of any rescue pharmacological analgesia during labour, including epidural • Infection at the site of injection • Neonatal admission (includes neonatal intensive care unit [NICU] and special care baby unit [SCBU])
Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI and de-duplicated. Titles and abstracts of the retrieved citations will be screened to identify studies that potentially meet the inclusion criteria outlined in the review protocol. Duplicate screening will not be undertaken for this question. Full versions of the selected studies will be obtained for assessment. Studies that fail to meet the inclusion criteria once the full version has been checked will be excluded at this stage. Each study excluded after checking the full version will be listed, along with the reason for its exclusion.

Field	Content
	A standardised form will be used to extract data from studies. The following data will be extracted: study details (reference, country where study was carried out, type and dates), participant characteristics, inclusion and exclusion criteria, details of the interventions if relevant, setting and follow-up, relevant outcome data and source of funding. One reviewer will extract relevant data into a standardised form, and this will be quality assessed by a senior reviewer.
Risk of bias (quality) assessment	Quality assessment of individual studies will be performed using the following checklists: • ROBIS tool for systematic reviews • Cochrane RoB tool v.2 for RCTs • Cochrane RoB tool v.2 for cluster-randomized trials The quality assessment will be performed by one reviewer and this will be quality assessed by a senior reviewer.
Strategy for data synthesis	Quantitative findings will be formally summarised in the review. Where multiple studies report on the same outcome for the same comparison, meta-analyses will be conducted using Cochrane Review Manager software. A fixed effect meta-analysis will be conducted and data will be presented as risk ratios if possible or odds ratios when required (for example, if only available in this form in included studies) for dichotomous outcomes, and mean differences or standardised mean differences for continuous outcomes. Heterogeneity in the effect estimates of the individual studies will be assessed using the I^2 statistic. Alongside visual inspection of the point estimates and confidence intervals, I^2 values of greater than 50% and 80% will be considered as significant and very significant heterogeneity, respectively. Heterogeneity will be explored as appropriate using sensitivity analyses and pre-specified subgroup analyses. If heterogeneity cannot be explained through subgroup analysis then a random effects model will be used for meta-analysis, or the data will not be pooled. The confidence in the findings across all available evidence will be evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group: http://www.gradeworkinggroup.org/ **Minimally important differences:** • Validated scales/continuous outcomes: published MIDs where available • All other outcomes & where published MIDs are not available: 0.8 and 1.25 for all relative dichotomous outcomes ; +/- 0.5x control group SD for continuous outcomes
Analysis of subgroups	Evidence will be stratified by: • Dose (volume) • Number of injections

Field	Content
	• Site of injection • BMI thresholds on booking: ○ Underweight range: <18.5 kg/m^2 ○ Healthy weight range: 18.5 to 24.9 kg/m^2 ○ Overweight range: 25 to 29.99 kg/m^2 ○ Obesity 1: 30 to 34.99 kg/m^2 ○ Obesity 2: 35 to 39.99 kg/m^2 • Setting: ○ alongside midwifery unit ○ freestanding midwifery unit ○ home (domiciliary) ○ obstetric unit/hospital-based maternity unit • Stage of labour: ○ Latent stage ○ First stage ○ Second stage Stratifications will be dealt with in a hierarchy (this is, where possible, stratify first by dose of sterile water injection, then number of injections, then site of injection, then BMI threshold, then within that by setting, and then stage of labour). Evidence will be subgrouped by the following only in the event that there is significant heterogeneity in outcomes: • Age of woman (<35 vs >/= 35) • Ethnicity: ○ White ○ Asian/Asian British ○ Black/African/Caribbean/Black British ○ Mixed/Multiple ethnic groups ○ Other ethnic group

Field	Content	
	• Women with disability vs not • Deprived socioeconomic group vs not • Country where the study was conducted: high income countries versus low and middle income countries (as defined by the OECD) Where evidence is stratified or subgrouped the committee will consider on a case by case basis if separate recommendations should be made for distinct groups. Separate recommendations may be made where there is evidence of a differential effect of interventions in distinct groups. If there is a lack of evidence in one group, the committee will consider, based on their experience, whether it is reasonable to extrapolate and assume the interventions will have similar effects in that group compared with others.	
Type and method of review	☒	Intervention
	☐	Diagnostic
	☐	Prognostic
	☐	Qualitative
	☐	Epidemiologic
	☐	Service Delivery
	☐	Other (please specify)
Language	English	
Country	England	
Anticipated or actual start date	01/06/2021	
Anticipated completion date	22/03/2023	
Named contact	5a. Named contact Guideline Development Team National Guideline Alliance (NGA) 5b. Named contact e-mail IPCupdate@nice.org.uk 5c. Organisational affiliation of the review	

Field	Content
	Guideline Development Team NGA, Centre for Guidelines, National Institute for Health and Care Excellence (NICE)
Review team members	From the Guideline Development Team NGA: • Senior Systematic Reviewer • Systematic Reviewer
Funding sources/sponsor	This systematic review is being completed by the Guideline Development Team NGA, Centre for Guidelines, which is part of the National Institute for Health and Care Excellence (NICE).
Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/cg190
Other registration details	None
URL for published protocol	https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=256259
Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.

Field	Content
Keywords	Back pain, Labour, Caesarean section, Sterile water injections, Obstetrics
Details of existing review of same topic by same authors	Not applicable
Additional information	None
Details of final publication	www.nice.org.uk

CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; DARE: Database of Abstracts of Reviews of Effects; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA: Health Technology Assessment; MID: minimally important difference; NGA: National Guideline Alliance; NHS: National health service; NICE: National Institute for Health and Care Excellence; OECD: Organisation for Economic Co-operation and Development; PRESS: Peer review of electronic search strategies; RCT: randomised controlled trial; RoB(IS): risk of bias (in systematic reviews); SD: standard deviation; TENS: transcutaneous electrical nerve stimulation

Appendix B Literature search strategies

Literature search strategies for review question: What is the effectiveness of injected water papules for pain relief during labour?

Review question search strategies

Database: Medline - OVID interface

Date of last search: 06/12/2022

#	Searches
1	PREGNANCY/
2	PARTURITION/
3	exp LABOR, OBSTETRIC/
4	exp DELIVERY, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	(pregnan$ or labo?r? or childbirth$ or partu$ or intra?part$ or peri?part$).ab,ti.
7	((during or giving or give) adj5 (birth$ or deliver$)).ti,ab.
8	or/1-7
9	exp INJECTIONS, SUBCUTANEOUS/
10	WATER/ad [Administration & Dosage]
11	8 and 9 and 10
12	((intracutaneous* or subcutaneous* or inject*) adj5 steril* adj3 water?).ti,ab.
13	(water adj3 papul*).ti,ab.
14	water block?.ti,ab.
15	or/12-14
16	8 and 15
17	11 or 16
18	limit 17 to english language
19	LETTER/
20	EDITORIAL/
21	NEWS/
22	exp HISTORICAL ARTICLE/
23	ANECDOTES AS TOPIC/
24	COMMENT/
25	CASE REPORT/
26	(letter or comment*).ti.
27	or/19-26
28	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
29	27 not 28
30	ANIMALS/ not HUMANS/
31	exp ANIMALS, LABORATORY/
32	exp ANIMAL EXPERIMENTATION/
33	exp MODELS, ANIMAL/
34	exp RODENTIA/
35	(rat or rats or mouse or mice).ti.
36	or/29-35
37	18 not 36
38	META-ANALYSIS/
39	META-ANALYSIS AS TOPIC/
40	(meta analy* or metanaly* or metaanaly*).ti,ab.
41	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
42	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
43	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
44	(search* adj4 literature).ab.
45	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
46	cochrane.jw.
47	or/38-46
48	randomized controlled trial.pt.
49	controlled clinical trial.pt.
50	pragmatic clinical trial.pt.
51	randomi#ed.ab.
52	placebo.ab.

#	Searches
53	randomly.ab.
54	CLINICAL TRIALS AS TOPIC/
55	trial.ti.
56	or/48-55
57	37 and 47
58	37 and 56
59	57 or 58

Database: Embase – OVID interface

Date of last search: 06/12/2022

#	Searches
1	*PREGNANCY/
2	*PERINATAL PERIOD/
3	exp *BIRTH/
4	exp *LABOR/
5	*PREMATURE LABOR/
6	*INTRAPARTUM CARE/
7	(pregnan$ or labo?r? or childbirth$ or partu$ or intra?part$ or peri?part$).ab,ti.
8	((during or giving or give) adj5 (birth$ or deliver$)).ti,ab.
9	or/1-8
10	SUBCUTANEOUS DRUG ADMINISTRATION/
11	WATER/ad [Drug Administration]
12	STERILE WATER/ad [Drug Administration]
13	11 or 12
14	9 and 10 and 13
15	WATER/sc [Subcutaneous Drug Administration]
16	STERILE WATER/sc [Subcutaneous Drug Administration]
17	15 or 16
18	9 and 17
19	((intracutaneous* or subcutaneous* or inject*) adj5 steril* adj3 water?).ti,ab.
20	(water adj3 papul*).ti,ab.
21	water block?.ti,ab.
22	or/19-21
23	9 and 22
24	14 or 18 or 23
25	limit 24 to english language
26	letter.pt. or LETTER/
27	note.pt.
28	editorial.pt.
29	CASE REPORT/ or CASE STUDY/
30	(letter or comment*).ti.
31	or/26-30
32	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
33	31 not 32
34	ANIMAL/ not HUMAN/
35	NONHUMAN/
36	exp ANIMAL EXPERIMENT/
37	exp EXPERIMENTAL ANIMAL/
38	ANIMAL MODEL/
39	exp RODENT/
40	(rat or rats or mouse or mice).ti.
41	or/33-40
42	25 not 41
43	SYSTEMATIC REVIEW/
44	META-ANALYSIS/
45	(meta analy* or metanaly* or metaanaly*).ti,ab.
46	((systematic or evidence) adj2 (review* or overview*)).ti,ab.
47	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
48	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
49	(search* adj4 literature).ab.
50	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
51	((pool* or combined) adj2 (data or trials or studies or results)).ab.
52	cochrane.jw.
53	or/43-52

#	Searches
54	random*.ti,ab.
55	factorial*.ti,ab.
56	(crossover* or cross over*).ti,ab.
57	((doubl* or singl*) adj blind*).ti,ab.
58	(assign* or allocat* or volunteer* or placebo*).ti,ab.
59	CROSSOVER PROCEDURE/
60	SINGLE BLIND PROCEDURE/
61	RANDOMIZED CONTROLLED TRIAL/
62	DOUBLE BLIND PROCEDURE/
63	or/54-62
64	42 and 53
65	42 and 63
66	64 or 65

Databases: Cochrane Central Register of Controlled Trials; and Cochrane Database of Systematic Reviews – Wiley interface

Date of last search: 06/12/2022

#	Searches
#1	MeSH descriptor: [Pregnancy] this term only
#2	MeSH descriptor: [Parturition] this term only
#3	MeSH descriptor: [Labor, Obstetric] explode all trees
#4	MeSH descriptor: [Delivery, Obstetric] explode all trees
#5	MeSH descriptor: [Obstetric Labor, Premature] this term only
#6	(pregnan* or labor* or labour* or childbirth* or partu* or intrapart* or intra-part* or peripart* or peri-part*):ti,ab
#7	((during or giving or give) near/5 (birth* or deliver*)):ti,ab
#8	#1 or #2 or #3 or #4 or #5 or #6 or #7
#9	MeSH descriptor: [Injections, Subcutaneous] explode all trees
#10	MeSH descriptor: [Water] this term only and with qualifier(s): [administration & dosage - AD]
#11	#8 and #9 and #10
#12	((intracutaneous* or subcutaneous* or inject*) near/5 steril* near/3 water*):ti,ab
#13	(water near/3 papul*):ti,ab
#14	("water block" or "water blocks"):ti,ab
#15	#12 or #13 or #14
#16	#8 and #15
#17	#11 or #16

Database: International Health Technology Assessment

Date of last search: 06/12/2022

#	Searches
	All: water
	AND All: sterilised OR sterilized OR papule OR papules OR block OR blocks

Health economics search strategies

Database: Medline – OVID interface

Date of last search: 06/12/2022

#	Searches
1	PREGNANCY/
2	PARTURITION/
3	exp LABOR, OBSTETRIC/
4	exp DELIVERY, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	(pregnan$ or labo?r? or childbirth$ or partu$ or intra?part$ or peri?part$).ab,ti.
7	((during or giving or give) adj5 (birth$ or deliver$)).ti,ab.

#	Searches
8	or/1-7
9	exp INJECTIONS, SUBCUTANEOUS/
10	WATER/ad [Administration & Dosage]
11	8 and 9 and 10
12	((intracutaneous* or subcutaneous* or inject*) adj5 steril* adj3 water?).ti,ab.
13	(water adj3 papul*).ti,ab.
14	water block?.ti,ab.
15	or/12-14
16	8 and 15
17	11 or 16
18	limit 17 to english language
19	LETTER/
20	EDITORIAL/
21	NEWS/
22	exp HISTORICAL ARTICLE/
23	ANECDOTES AS TOPIC/
24	COMMENT/
25	CASE REPORT/
26	(letter or comment*).ti.
27	or/19-26
28	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
29	27 not 28
30	ANIMALS/ not HUMANS/
31	exp ANIMALS, LABORATORY/
32	exp ANIMAL EXPERIMENTATION/
33	exp MODELS, ANIMAL/
34	exp RODENTIA/
35	(rat or rats or mouse or mice).ti.
36	or/29-35
37	18 not 36
38	ECONOMICS/
39	VALUE OF LIFE/
40	exp "COSTS AND COST ANALYSIS"/
41	exp ECONOMICS, HOSPITAL/
42	exp ECONOMICS, MEDICAL/
43	exp RESOURCE ALLOCATION/
44	ECONOMICS, NURSING/
45	ECONOMICS, PHARMACEUTICAL/
46	exp "FEES AND CHARGES"/
47	exp BUDGETS/
48	budget*.ti,ab.
49	cost*.ti,ab.
50	(economic* or pharmaco?economic*).ti,ab.
51	(price* or pricing*).ti,ab.
52	(financ* or fee or fees or expenditure* or saving*).ti,ab.
53	(value adj2 (money or monetary)).ti,ab.
54	resourc* allocat*.ti,ab.
55	(fund or funds or funding* or funded).ti,ab.
56	(ration or rations or rationing* or rationed).ti,ab.
57	ec.fs.
58	or/38-57
59	37 and 58

Database: Embase – OVID interface

Date of last search: 06/12/2022

#	Searches
1	*PREGNANCY/
2	*PERINATAL PERIOD/
3	exp *BIRTH/
4	exp *LABOR/
5	*PREMATURE LABOR/
6	*INTRAPARTUM CARE/
7	(pregnan$ or labo?r? or childbirth$ or partu$ or intra?part$ or peri?part$).ab,ti.
8	((during or giving or give) adj5 (birth$ or deliver$)).ti,ab.
9	or/1-8

#	Searches
10	SUBCUTANEOUS DRUG ADMINISTRATION/
11	WATER/ad [Drug Administration]
12	STERILE WATER/ad [Drug Administration]
13	11 or 12
14	9 and 10 and 13
15	WATER/sc [Subcutaneous Drug Administration]
16	STERILE WATER/sc [Subcutaneous Drug Administration]
17	15 or 16
18	9 and 17
19	((intracutaneous* or subcutaneous* or inject*) adj5 steril* adj3 water?).ti,ab.
20	(water adj3 papul*).ti,ab.
21	water block?.ti,ab.
22	or/19-21
23	9 and 22
24	14 or 18 or 23
25	limit 24 to english language
26	letter.pt. or LETTER/
27	note.pt.
28	editorial.pt.
29	CASE REPORT/ or CASE STUDY/
30	(letter or comment*).ti.
31	or/26-30
32	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
33	31 not 32
34	ANIMAL/ not HUMAN/
35	NONHUMAN/
36	exp ANIMAL EXPERIMENT/
37	exp EXPERIMENTAL ANIMAL/
38	ANIMAL MODEL/
39	exp RODENT/
40	(rat or rats or mouse or mice).ti.
41	or/33-40
42	25 not 41
43	HEALTH ECONOMICS/
44	exp ECONOMIC EVALUATION/
45	exp HEALTH CARE COST/
46	exp FEE/
47	BUDGET/
48	FUNDING/
49	RESOURCE ALLOCATION/
50	budget*.ti,ab.
51	cost*.ti,ab.
52	(economic* or pharmaco?economic*).ti,ab.
53	(price* or pricing*).ti,ab.
54	(financ* or fee or fees or expenditure* or saving*).ti,ab.
55	(value adj2 (money or monetary)).ti,ab.
56	resourc* allocat*.ti,ab.
57	(fund or funds or funding* or funded).ti,ab.
58	(ration or rations or rationing* or rationed).ti,ab.
59	or/43-58
60	42 and 59

Database: Cochrane Central Register of Controlled Trials – Wiley interface

Date of last search: 06/12/2022

#	Searches
#1	MeSH descriptor: [Pregnancy] this term only
#2	MeSH descriptor: [Parturition] this term only
#3	MeSH descriptor: [Labor, Obstetric] explode all trees
#4	MeSH descriptor: [Delivery, Obstetric] explode all trees
#5	MeSH descriptor: [Obstetric Labor, Premature] this term only
#6	(pregnan* or labor* or labour* or childbirth* or partu* or intrapart* or intra-part* or peripart* or peri-part*):ti,ab
#7	((during or giving or give) near/5 (birth* or deliver*)):ti,ab
#8	#1 or #2 or #3 or #4 or #5 or #6 or #7

#	Searches
#9	MeSH descriptor: [Injections, Subcutaneous] explode all trees
#10	MeSH descriptor: [Water] this term only and with qualifier(s): [administration & dosage - AD]
#11	#8 and #9 and #10
#12	((intracutaneous* or subcutaneous* or inject*) near/5 steril* near/3 water*):ti,ab
#13	(water near/3 papul*):ti,ab
#14	("water block" or "water blocks"):ti,ab
#15	#12 or #13 or #14
#16	#8 and #15
#17	#11 or #16
#18	MeSH descriptor: [Economics] this term only
#19	MeSH descriptor: [Value of Life] this term only
#20	MeSH descriptor: [Costs and Cost Analysis] explode all trees
#21	MeSH descriptor: [Economics, Hospital] explode all trees
#22	MeSH descriptor: [Economics, Medical] explode all trees
#23	MeSH descriptor: [Resource Allocation] explode all trees
#24	MeSH descriptor: [Economics, Nursing] this term only
#25	MeSH descriptor: [Economics, Pharmaceutical] this term only
#26	MeSH descriptor: [Fees and Charges] explode all trees
#27	MeSH descriptor: [Budgets] explode all trees
#28	budget*:ti,ab
#29	cost*:ti,ab
#30	(economic* or pharmaco?economic*):ti,ab
#31	(price* or pricing*):ti,ab
#32	(financ* or fee or fees or expenditure* or saving*):ti,ab
#33	(value near/2 (money or monetary)):ti,ab
#34	resourc* allocat*:ti,ab
#35	(fund or funds or funding* or funded):ti,ab
#36	(ration or rations or rationing* or rationed):ti,ab
#37	#18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36
#38	#17 and #37

Database: International Health Technology Assessment

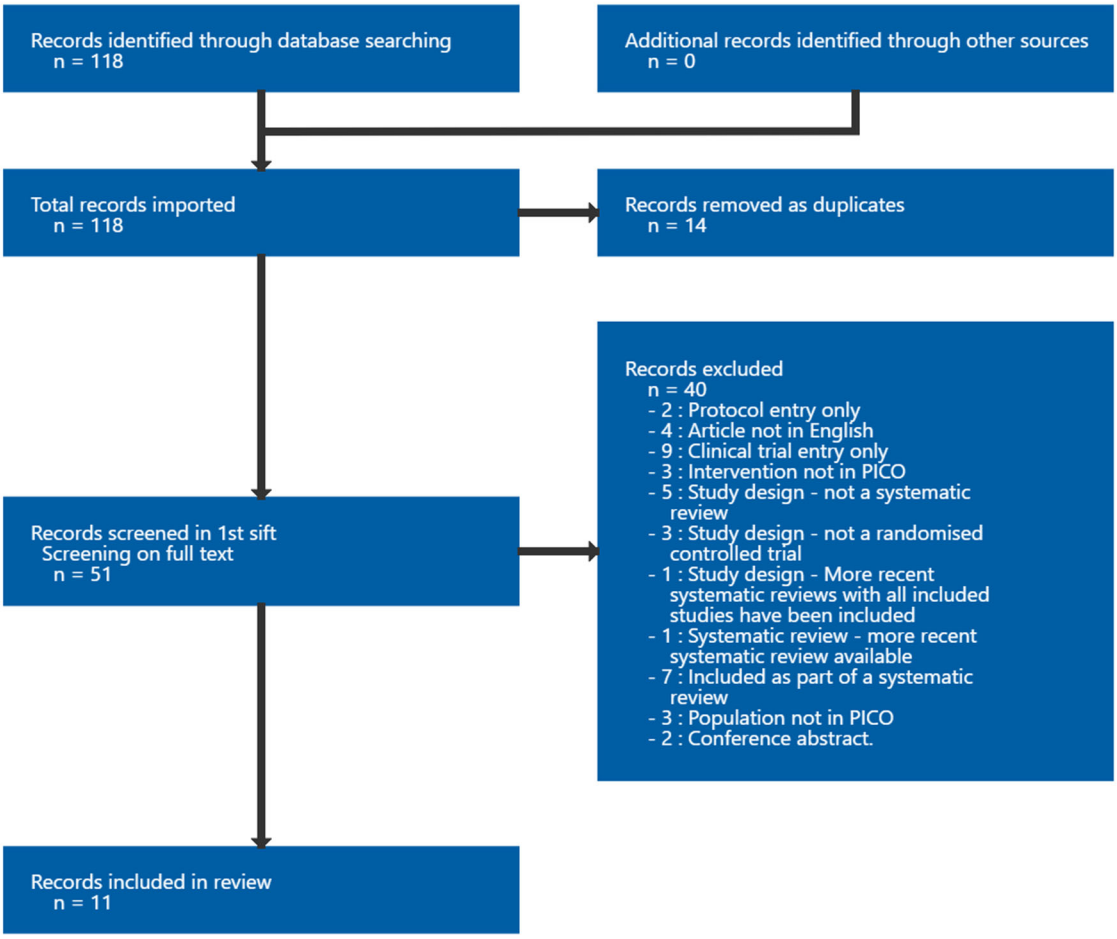
Date of last search: 06/12/2022

#	Searches
	All: water
	AND All: sterilised OR sterilized OR papule OR papules OR block OR blocks

Appendix C Effectiveness evidence study selection

Study selection for: What is the effectiveness of injected water papules for pain relief during labour?

Figure 1: Study selection flow chart



Note: for this review, de-duplication was done outside of EPPI in EndNote for practical reasons, therefore the study selection flowchart does not accurately reflect the records removed as duplicates.

Appendix D Evidence tables

Evidence tables for review question: What is the effectiveness of injected water papules for pain relief during labour?

Almassinokiani, 2020

Bibliographic Reference	Almassinokiani, F.; Ahani, N.; Akbari, P.; Rahimzadeh, P.; Akbari, H.; Sharifzadeh, F.; Comparative analgesic effects of intradermal and subdermal injection of sterile water on active labor pain; Anesthesiology and pain medicine; 2020; vol. 10 (no. 2)

Study details

Country/ies where study was carried out	Tehran, Iran
Study type	Randomised controlled trial (RCT)
Study dates	Not reported
Inclusion criteria	• Singleton pregnancy • Nulliparous women • Second stage of labour (defined at dilation of cervix at 4 cm or more) • Candidate for a vaginal delivery • Gestational age ≥37 weeks • Cephalic presentation • VAS pain score of ≥5
Exclusion criteria	• Women who request another method of analgesia
Patient characteristics	No significant differences between age, dilation of cervix before intervention or baseline pain scores.
Intervention(s)/control	Intradermal group • Intradermal injection with 0.5cc sterile water at 4 sacral points (total of 4 injections) • Injection with an insulin needle

	• Sites of injection are each posterior superior iliac spine, 3cm lower and 1cm inner each posterior superior iliac spines. <u>Subdermal group</u> • Subdermal injection with 0.5cc sterile water at 4 sacral points (total of 4 injections • Injection with an insulin need • Sites of injection the same as intradermal group <u>Control group</u> • Needle contact to the skin using an insulin needle, at the same sites of injection as the intradermal and subdermal groups
Sources of funding	Not reported
Sample size	N=121 randomised Control group: n=42 Intradermal group: n=40 Subdermal group: n=39
Other information	Setting: Maternity hospital. Risk status or if labour was induced not reported. If women used IM/IV analgesia prior to randomisation not reported 1 woman requested epidural analgesia in placebo group. This was after the intervention time points so not recorded as rescue analgesia used.

Outcomes

Outcome	Control group, N = 42	Intradermal group, N = 40	Subdermal group, N = 39
General labour pain 10 minutes after intervention (Visual analogue scale) Mean (SD)	6.83 (1.72)	7.72 (1.68)	6.85 (1.9)
General labour pain 30 minutes after intervention (Visual analogue scale) Mean (SD)	6.6 (1.91)	5.18 (1.94)	4.82 (1.93)
General labour pain 60 minutes after intervention (Visual analogue scale) Mean (SD)	7.17 (1.88)	4.95 (1.83)	4.25 (2.13)
General labour pain 90 minutes after intervention (Visual analogue scale) Mean (SD)	7.81 (1.68)	6.49 (1.99)	5.82 (2.74)
Caesarean birth 90 minutes after the intervention in all groups No of events	n = 1	n = 2	n = 1

Critical appraisal

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns *(Allocation was random. No information on allocation concealment, but not differences in baseline characteristics to suggest a concern.)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low *(Personnel administering injections were not involved in the labour after the intervention)*

Section	Question	Answer
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low *(1 woman was excluded due to use of other analgesia, and another women recruited in her place. This is unlikely to be of concern as the number is small (1))*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(Pain was participant reported but participants were not aware of their assigned intervention)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Some concerns *(A pre-specified protocol was not available to determine bias in selected reporting)*
Overall bias and Directness	Risk of bias judgement	Low
Overall bias and Directness	Overall Directness	Indirectly applicable
Overall bias and Directness	Risk of bias variation across outcomes	None

Derry, 2012

Bibliographic Reference	Derry, S.; Straube, S.; Moore, R. A.; Hancock, H.; Collins, S. L.; Intracutaneous or subcutaneous sterile water injection compared with blinded controls for pain management in labour; Cochrane Database of Systematic Reviews; 2012; (no. 1)

Study details

Country/ies where study was carried out	Denmark, India, Iran, Sweden, Thailand
Study type	Cochrane systematic review of randomised controlled trials (RCT)
Study dates	
Inclusion criteria	• Women at term, in the active stage of labour • Requiring pain relief for low back pain (not uterine contractions) • Women who had not had any analgesia since the start of labour or 3 hours into the study.
Exclusion criteria	None specified

Patient characteristics	Ader 1990 No significant differences between age, weight or gestational age. Pain at baseline not reported. Bahasadri 2006 No significant differences between age, weight, gestational age or parity. Pain at baseline was worse for the sterile water group than the saline group. Kushtagi 2009 No significant differences between age, parity, or BMI. No significant differences for pain at baseline. Martensson 1999 No significant differences between age, weight, gestational age or parity. No significant differences for pain at baseline. Saxena 2009; Trolle 1991; Wiruchpongsanon 2006 No significant differences between age, gestational age or parity. No significant differences for pain at baseline.
Intervention(s)/control	All studies compared sterile water injections with saline injections Ader 1990 • Intervention: 4 intracutaneous injections of sterile water at 0.1ml each • Control: 4 subcutaneous injections of saline water at 0.1 ml each • Administered in the Michaelis rhomboid region Bahasadri 2006

- Intervention: 1 subcutaneous injection of sterile water at 0.5ml
- Control: 1 subcutaneous injection of saline at 0.5ml
- Administered in the most painful region in lumbosacral area

Kushtagi 2009

- Intervention: 1 subcutaneous injection of sterile water at 0.5ml
- Control: 1 subcutaneous injection of saline at 0.5ml
- Administered in the Michaelis rhomboid region

Martensson 1999

- Intervention group 1: 4 intracutaneous injections of sterile water at 0.1ml each
- Intervention group 2: 4 subcutaneous injections of sterile water at 0.5ml each
- Control: 4 subcutaneous injections of saline water at 0.1 ml each
- Administered in the Michaelis rhomboid region

Saxena 2009

- Intervention: 4 intracutaneous injections of sterile water at 0.5ml each
- Control: 4 intracutaneous injections of saline water at 0.5ml each
- Administered in the Michaelis rhomboid region

Trolle 1991

- Intervention: 4 intracutaneous injections of sterile water at 0.1ml each
- Control: 4 intracutaneous injections of saline water at 0.1ml each
- Administered in the areas corresponding to the borders of the sacrum

Wiruchpongsanon 2006

- Intervention: 4 intracutaneous injections of sterile water at 0.1ml each
- Control: 4 intracutaneous injections of saline water at 0.1ml each
- Administered in the Michaelis rhomboid region

Sample size	Ader 1990 N=45 randomised Sterile water: n = 24 Isotonic saline: n = 21 Bahasadri 2006 N=100 randomised Sterile water: n = 50 Isotonic saline: n = 50 Kushtagi 2009 N=100 randomised Sterile water: n = 50 Isotonic saline: n = 50 Martensson 1999 N=99 randomised Sterile water, intracutaneous: n = 33 Sterile water, subcutaneous: n = 33 Isotonic saline: n = 33 Saxena 2009 N=100 randomised Sterile water: n = 50 Isotonic saline: n = 50 Trolle 1991

	N=272 randomised Sterile water: n = 141 Isotonic saline: n = 131 Wiruchpongsanon 2006 N=50 randomised Sterile water: n = 25 Isotonic saline: n = 25
Other information	Trolle 1991 included women who had pethidine (fewer than 10%). Setting: Ader 1990 Hospital labour ward Bahasadri 2006 Hospital Kushtagi 2009 Labour care facilities hospital Martensson 1999 Labour ward Saxena 2009 Hospital labour ward Trolle 1991 Not specified Wiruchpongsanon 2006 Hospital labour room

Outcomes

Ader 1990

Outcome	Sterile water injection (intracutaneous), , N = 24	Saline injection (subcutaneous), , N = 21
Caesarean birth No of events	n = 2	n = 1
Assisted vaginal birth No of events	n = 3	n = 3
Use of rescue epidural analgesia extracted from study No of events	n = 0	n = 0
Pethidine analgesia No of events	n = 1	n = 2
Paracervical block No of events	n = 0	n = 0

Bahasadri 2006

Outcome	Sterile water injection (subcutaneous), , N = 50	Saline injection (subcutaneous), , N = 50
Caesarean birth No of events	n = 2	n = 3
Instrumental vaginal birth No of events	n = 0	n = 0

Martensson 1999

Outcome	Sterile water injection (intracutaneous), , N = 33	Sterile water injection (subcutaneous), , N = 33	Saline injection (subcutaneous), , N = 33
Back pain score reduction ≥4cm at 10 minutes after injections extracted from individual study			
No of events	n = 20	n = 19	n = 8
Sample size	n = 32		n = 25
Back pain score reduction ≥4cm at 45 minutes after injections extracted from individual study			
No of events	n = 17	n = 15	n = 7
Sample size	n = 29	n = 29	n= 25
Back pain score reduction ≥4cm at 90 minutes after injections extracted from individual study			
No of events	n = 7	n = 7	n = 3
Sample size	n = 22	n = 24	n = 21
Caesarean birth			
No of events	n = 1	n = 1	n = 1
Instrumental vaginal birth			
No of events	n = 1	n = 1	n = 1
Would use treatment again extracted from individual study	n = 24	n = 25	n = 18
	n = 27	n = 31	n = 31

Outcome	Sterile water injection (intracutaneous), , N = 33	Sterile water injection (subcutaneous), , N = 33	Saline injection (subcutaneous), , N = 33
No of events Sample size			

Kushtagi 2009

Outcome	Sterile water injection (subcutaneous), , N = 50	Saline injection (subcutaneous), , N = 50
Caesarean birth No of events	n = 4	n = 6
Instrumental vaginal birth No of events	n = 2	n = 5
Spontaneous vaginal birth No of events	n = 44	n = 39
Other analgesia used (not specific) No of events	n = 1	n = 2

Saxena 2009

Outcome	Sterile water injection (intracutaneous), , N = 50	Saline injection (intracutaneous), , N = 50
Back pain score 10 minutes after intervention (Visual analogue scale) extracted from individual study Mean (SD)	34.2 (28.70)	73.4 (23.48)
Back pain score 45 minutes after intervention (Visual analogue scale) extracted from individual study Mean (SD)	33.2 (32.67)	77.4 (20.78)
Back pain score 90 minutes after intervention (Visual analogue scale) extracted from individual study Mean (SD)	49.3 (33.96)	83.7 (18.81)
Caesarean birth No of events	n = 2	n = 0

Trolle 1991

Outcome	Sterile water injection (intracutaneous), , N = 141	Saline injection (intracutaneous), , N = 131
Pain score after injection at 1 hour (Visual analogue scale) extracted from individual study Standardised Mean (p value) Sample size	 29.5 n = 132	 76 (<0.01) n = 121
Pain score after injection at 2 hours (Visual analogue scale) extracted from individual study	53.5 n = 100	82 (<0.01) n = 99

Outcome	Sterile water injection (intracutaneous), , N = 141	Saline injection (intracutaneous), , N = 131
Standardised Mean (p value) Sample size		
Caesarean birth No of events	n = 6	n = 15
Instrumental vaginal birth No of events	n = 22	n = 13
Would use same treatment again extracted from individual study No of events	n = 96	n = 66
Use of rescue pethidine analgesia No of events	n = 9	n = 11
Use of rescue Entonox analgesia No of events	n = 18	n = 21

Wiruchpongsanon 2006

Outcome	Sterile water injection (intracutaneous), , N = 25	Saline injection (intracutaneous), , N = 25
Back pain score reduction after injection at 30 minutes extracted from individual study Mean (SD)	55.1 (20.9)	18.6 (26.3)
Back pain score reduction after injection at 60 minutes extracted from individual study	69.2 (17.6)	16.1 (17.1)

Outcome	Sterile water injection (intracutaneous), , N = 25	Saline injection (intracutaneous), , N = 25
Mean (SD)		
Back pain score reduction after injection at 120 minutes extracted from individual study Mean (SD)	65.2 (13.5)	16.8 (16.5)
Caesarean section No of events	n = 0	n = 3
Assisted vaginal birth No of events	n = 3	n = 0

Critical appraisal

Quality of the Cochrane Systematic review assessed using AMSTAR checklist. Limitations for each of the included studies assessed with the Cochrane Risk of Bias Tool.	Answer
Derry 2012 systematic review	Total score:14/16
Ader 1990	Random sequence generation: Unclear risk Allocation concealment: Unclear risk Incomplete outcome data: Unclear risk Selective reporting: Low risk Other bias: High risk (treatment group size <50) Blinding of participants and personnel: Low risk Blinding of outcome assessment: Low risk
Bahasadri 2006	Random sequence generation: Low risk Allocation concealment: Low risk Incomplete outcome data: Low risk

Quality of the Cochrane Systematic review assessed using AMSTAR checklist. **Limitations for each of the included studies assessed with the Cochrane Risk of Bias Tool.**	**Answer**
	Selective reporting: Low risk Other bias: Unclear risk (treatment group size =50) Blinding of participants and personnel: Low risk Blinding of outcome assessment: Low risk
Kushtagi 2009	Random sequence generation: Low risk Allocation concealment: Low risk Incomplete outcome data: Low risk Selective reporting: Low risk Other bias: Unclear risk (treatment group size =50) Blinding of participants and personnel: Low risk Blinding of outcome assessment: Low risk
Martensson 1999	Random sequence generation: Low risk Allocation concealment: Low risk Incomplete outcome data: High risk Selective reporting: Unclear risk Other bias: High risk (treatment group size <50) Blinding of participants and personnel: Unclear risk Blinding of outcome assessment: Low risk
Saxena 2009	Random sequence generation: Low risk Allocation concealment: Unclear risk Incomplete outcome data: Unclear risk Selective reporting: Unclear risk Other bias: Unclear risk (treatment group size =50) Blinding of participants and personnel: High risk Blinding of outcome assessment: Low risk
Trolle 1991	Random sequence generation: Unclear risk Allocation concealment: Low risk Incomplete outcome data: Unclear risk

Quality of the Cochrane Systematic review assessed using AMSTAR checklist. Limitations for each of the included studies assessed with the Cochrane Risk of Bias Tool.	Answer
	Selective reporting: Low risk Other bias: Unclear risk (treatment group size 50-200) Blinding of participants and personnel: Low risk Blinding of outcome assessment: Low risk
Wiruchpongsanon 2006	Random sequence generation: Unclear risk Allocation concealment: Unclear risk Incomplete outcome data: Unclear risk Selective reporting: Unclear risk Other bias: High risk (treatment group size <50) Blinding of participants and personnel: Low risk Blinding of outcome assessment: Low risk

Farag, 2015

Bibliographic Reference	Farag, A; Mohammed, K; Morsy, M; Intracutaneous Sterile Water Injections for Relief of Back Pain during Labor; Medical Journal of Cairo University; 2015; vol. 83 (no. 1); 401-408

Study details

Country/ies where study was carried out	Cairo, Egypt
Study type	Randomised controlled trial (RCT)
Study dates	August 2008 to September 2009
Inclusion criteria	• Women with a singleton pregnancy aged between 20-35 • Gestational age of 37-42 weeks • Parity no more than 3 • Cephalic presentation

	• At the onset of active phase of 1st stage of labour (defined at 3-5 cm and >50% effacement) • Having back pain
Exclusion criteria	• High risk status defined as any of the following: 1. Antepartum haemorrhage 2. Placenta praevia 3. Cephalo-pelvic disproportion 4. Contraindications for vaginal delivery 5. Non-reassuring fetal status 6. Prior cervical surgery 7. Any observable spinal lesions 8. Neurological conditions 9. Suspicious or presence of dermatological pathology which could interfere with injections • Previous caesarean section (prior uterine scar) • Use of labour-inducing agents • Already received any form of analgesia before the study
Patient characteristics	No significant differences between age, gestation, parity, or BMI.
Intervention(s)/control	<u>Sterile water injections</u> • 4 intracutaneous injections of 0.1ml of sterile water were administered • Injections were with a 25-gauge needle • Injections were given into the Michaelis' rhomboid (two points over each posterior superior iliac spine two points 3cm below and 1cm medial to each posterior superior iliac spine) • The women lay on her side, or leant forwards over the bed, or sat sideways, or sat facing the back of a chair. <u>Placebo (saline injections)</u> • 4 intracutaneous injections of 0.1ml of normal saline (0.9% sodium chloride) • Needle type and injection site were the same as sterile water group

	Position of women during administration was the same as sterile water group
Duration of follow-up	Pain at 90 minutes post intervention
Sources of funding	Not reported
Sample size	N=73 randomised Sterile water injection group: n=43 (n=40 analysed*) Placebo (saline injection) group: n=30 (n=20 analysed*) *Women who requested further analgesia before 90 minutes were excluded and analysis was not performed for these women.
Other information	Setting: Labour and delivery unit of maternity hospital

Outcomes

Outcome	**Sterile water injections, , N = 40**	**Placebo (saline injections), , N = 20**
Back pain after injection at 10 minutes (Visual analogue scale) Mean (SD)	6.9 (1.4)	8.05 (0.75)
Back pain after injections at 45 minutes (Visual analogue scale) Mean (SD)	5 (1.7)	7.05 (1.1)
Reduction in back pain from baseline after injections at 90 minutes (Visual analogue scale) Mean (SD)	5.06 (1.32)	4.12 (0.91)
Vaginal delivery No of events	n = 32	n = 15

Outcome	Sterile water injections, , N = 40	Placebo (saline injections), , N = 20
Instrumental delivery No of events	n = 3	n = 3
Caesarean delivery No of events	n = 5	n = 2

Critical appraisal

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low *(Computer generated randomisation, sealed in opaque envelopes. No baseline differences to suggest problems with randomisation.)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low *(Participants and people administering injections were not aware of assignment)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	High *(Women who requested further analgesia before 90 minutes were excluded from the analysis. This was not specifically set out in the exclusion criteria. Excluding these women probably has an impact on the outcomes as the difference between the groups was large (approx 7% from the intervention group excluded, and 33% from the control group excluded).)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(Pain was participant reported but participants were not aware of their assigned intervention)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Some concerns *(Pre-specified protocol not available)*
Overall bias and Directness	Risk of bias judgement	High
Overall bias and Directness	Overall Directness	Directly applicable

Section	Question	Answer
Overall bias and Directness	Risk of bias variation across outcomes	None

Fouly, 2018

Bibliographic Reference	Fouly, Howieda; Herdan, Ragaa; Habib, Dina; Yeh, Chao; Effectiveness of injecting lower dose subcutaneous sterile water versus saline to relief labor back pain: Randomized controlled trial; European journal of midwifery; 2018; vol. 2; 3

Study details

Country/ies where study was carried out	Assiut, Egypt
Study type	Randomised controlled trial (RCT)
Study dates	June to October 2016
Inclusion criteria	• Women aged 18 or over with a singleton pregnancy • Gestational age 37-41 weeks • Primipara or multipara • Spontaneous or induced childbirth at 1st stage of labour • Low back pain of ≥6 on visual analogue scale • Cephalic presentation
Exclusion criteria	• Multiple pregnancies • Malpresentation • A previous caesarean section • Thrombocytopenia (as this may cause blood flow at injection site)
Patient characteristics	Age (mean ± standard deviation) Sterile water injection group: 24.6 ± 5.3 Control (saline injection) group: 22.4 ± 4.1 p<0.001

	Baseline pain measure by VAS (mean ± standard deviation) Sterile water injection group: 9.35 ± 0.79 Control (saline injection) group: 9.09 ± 0.93 P<0.005 No baseline difference for parity.
Intervention(s)/control	Sterile water injection • 2 injections of 0.5ml of sterile water were given simultaneously and subcutaneously. • Injection site was in the area of the Michaelis Rhomboid above the sacral area - the lateral two most painful points in the posterior superior iliac crests on each side. • Skin of injection site was cleaned with an alcohol wipe before injection. Control (saline) • 2 injections of saline solution were given simultaneously and subcutaneously. • Injection site was the same as for the sterile water group. Injections were administered by two investigators; an anaesthesiologist and a nursing lecturer with experience in subcutaneous injection.
Sources of funding	Not industry funded
Sample size	N=330 randomised Sterile water injection group: n=165 Control (saline injection) group: n=165
Other information	Setting: Labour unit in hospital. Women who had induced labour at first stage were included, but proportion of these women in the total sample was not reported. Risk status not reported. Whether women received IM/IV analgesia prior to randomisation not reported.

Outcomes

Outcome	Sterile water injection, , N = 165	Control (saline injection), , N = 165
Back pain score reduction after injections at 15 minutes (Visual analogue scale) Mean (SD)	2.15 (1.04)	1.97 (0.93)
Back pain score reduction after injections at 30 minutes (Visual analogue scale) Mean (SD)	2.92 (1.1)	2.5 (1.07)
Back pain score reduction after injections at 45 minutes (Visual analogue scale) Mean (SD)	3.48 (1.18)	2.88 (1.4)
Back pain score reduction after injections at 90 minutes (Visual analogue scale) Mean (SD)	3.7 (1.03)	2.85 (1.8)
Back pain score reduction after injections at 120 minutes (Visual analogue scale) Mean (SD)	3.73 (1.03)	3.72 (1.75)
Normal labour Definition not specified (assumed vaginal delivery) No of events	n = 159	n = 164
Caesarean section No of events	n = 6	n = 1

Critical appraisal

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low *(Randomisation using computer-generated table, allocation concealment using sealed opaque envelopes. Small imbalance between groups in age but unlikely to result in bias in the intervention effect estimate.)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low *(Participants were not aware of their allocation. The investigators administered injections, but the nurse caring for the woman was outside the room during this time. Intention to treat analysis.)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low *(Data was available for all participants)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(Pain was participant reported but participants were unaware of their intervention assignment.)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low *(Results were reported at different time points in 2 hours as stated in the pre-specified study protocol.)*
Overall bias and Directness	Risk of bias judgement	Low
Overall bias and Directness	Overall Directness	Indirectly applicable
Overall bias and Directness	Risk of bias variation across outcomes	None

Koyucu, 2018

Bibliographic Reference	Koyucu, R. G.; Demirci, N.; Yumru, A. E.; Salman, S.; Ayanoglu, Y. T.; Tosun, Y.; Tayfur, C.; Effects of intradermal sterile water injections in women with low back pain in labor: a randomized, controlled, clinical trial; Balkan medical journal; 2018; vol. 35 (no. 2); 148-154

Study details

Country/ies where study was carried out	Istanbul, Turkey
Study type	Randomised controlled trial (RCT)
Study dates	June 2013 - March 2014
Inclusion criteria	• Women aged 18-35 years with a singleton pregnancy • 37-42 weeks gestation • Not having a planned caesarean birth • Spontaneous onset of labour • Cephalic presenation • Healthy fetus • In the active phase of 1st stage of labour (3-7cm dilated cervix) • Severe low back pain (visual analogue scale >7) • Requiring pain relief
Exclusion criteria	• Second stage of labour • Any pharmacological analgesia before the intervention • Back pain of <7 on the visual analogue scale • Women whose labour is high risk
Patient characteristics	No significant differences between age, parity, BMI or pain scores at baseline.
Intervention(s)/control	<u>Sterile water group</u> • Four intradermal injection of 0.1 ml of sterile water were administered into the skin surround the rhombus of Michaelis over the sacral area. • The 1st injection were given on both sides of posterior superior iliac spines. • The 2nd injections were 1cm medial and 1-2cm inferior to the 1st injections. • Injections were given using an insulin needle. • Injections were given to both sides simultaneously by two midwives. • Injections were given at the peak point of contractions. <u>Dry injections (control)</u>

	• Participants received 4 dry injections, administered in the same way and in the same regions as the sterile water group.
Sources of funding	Not reported
Sample size	N=168 randomised Sterile water injection group n=84 Dry injection group n=84
Other information	Setting: Maternity clinic

Outcomes

Outcome	**Sterile water group, , N = 84**	**Dry injection group, , N = 84**
Back pain score reduction after injection at 10 minutes (Visual analogue scale) Back pain Mean (SD)	41.48 (6.97)	12.97 (11.06)
Back pain score reduction after injection at 30 minutes (Visual analogue scale) Back pain Mean (SD)	54.82 (7.81)	13.33 (12.05)
Back pain score reduction after injection at 60 minutes (Visual analogue scale) Back pain Mean (SD) Sample size	64.22 (8.15) n = 77	15.81 (10.98) n = 74
Back pain score reduction after injection at 120 minutes (Visual analogue scale) Back pain	62.16 (8.88) n = 67	13.28 (8.91) n = 64

Outcome	Sterile water group, , N = 84	Dry injection group, , N = 84
Mean (SD) Sample size		
Back pain score reduction after injection at 180 minutes (Visual analogue scale) Back pain Mean (SD) Sample size	 26.2 (13.56) n = 54	 10.96 (8.46) n = 52
Caesarean birth No of events	 n = 9	 n = 17
Instrumental vaginal birth No of events	 n = 0	 n = 0
Being satisfied No of events	 n = 71	 n = 30
Use of rescue epidural analgesia No of events	 n = 4	 n = 8

Critical appraisal

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low *(Randomisation sequence was computer generated. Allocation concealed using sealed envelopes.)*
Domain 2a: Risk of bias due to deviations from the intended	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low *(Participants were not aware of assignment. Midwives caring for women were aware but no deviations from intended intervention*

Section	Question	Answer
interventions (effect of assignment to intervention)		*that are not consistent with what could occur outside a trial context)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low *(Women were excluded if they requested epidural analgesia, but pain scores up to that point were recorded, and number of women requiring rescue epidural analgesia were recorded)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(Pain was participant reported but participants were not aware of their intervention assignment)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low *(Outcomes and time points were reported as specified in the protocol)*
Overall bias and Directness	Risk of bias judgement	Low
Overall bias and Directness	Overall Directness	Directly applicable
Overall bias and Directness	Risk of bias variation across outcomes	None

Labrecque, 1999

Bibliographic Reference	Labrecque, M.; Nouwen, A.; Bergeron, M.; Rancourt, J. F.; A randomized controlled trial of nonpharmacologic approaches for relief of low back pain during labor; Journal of family practice; 1999; vol. 48 (no. 4); 259-263

Study details

Country/ies where study was carried out	Quebec, Canada
Study type	Randomised controlled trial (RCT)
Study dates	September 1995 to January 1997
Inclusion criteria	• Pregnancy women 36 weeks' gestation • No medical or obstetric complications • Active first stage of labour

	• Complaining of low back pain during labour
Exclusion criteria	None specifically reported
Patient characteristics	No significant differences between age, parity, or pain at baseline.
Intervention(s)/control	<u>Sterile water injection</u> • 4 intradermal injections of 0.1cc of sterile water were administered in the lumbosacral area. • 25-gauge needle is used. • Injection sites are each posterior superior iliac spines, and two further sites 2 or 3cm below, and 1 to 2cm medial to the posterior superior iliac spines. • The woman can lay on her side in bed, lean forward over the bed, sit sideways on a chair, or sit facing the back of the chair. • Injections were given by either a nurse or physician during a contraction. • Injections were repeated on request. • Women could use any of the components of standard care once they received their assigned intervention. <u>TENS</u> • The nurse or physician attached 2 electrodes connected to a TENS unit to the skin on the lower back. • Units were set in normal mode. • Initial current intensities were adjusted according to tolerance, starting with a rate of 80 to 125 pulses per second and a pulse width of 60 to 100 per second. • Women could use any of the components of standard care once they received their assigned intervention. <u>Standard care</u> • 15 minute back massage with moisturising cream performed by partner or nurse. This was followed by continued massage, whirlpool baths, walking, or change or position
Sources of funding	Not industry funded

Sample size	N=35 randomised Standard care: n=12 Transcutaneous electrical nerve stimulation: (TENS): n=12 Sterile water group: n=11 (n=10 analysed, one women gave birth before injections administered)
Other information	Setting: Hospital No information on whether women who had labour induced were excluded from population. No information if they had IM/IV analgesia before randomisation. Proportion of women in the sample who were between 36 and 37 weeks not reported.

Outcomes

Outcome	**Sterile water injections, , N = 10**	**TENS, , N = 12**	**Standard care, , N = 12**
Mean pain intensity during intervention period (Visual analogue scale) Mean (SD)	32 (6)	66 (6)	79 (6)
Mean pain unpleasantness during intervention period (Visual analogue scale) Mean (SD)	30 (7)	78 (7)	73 (7)
Caesarean section No of events	% = 0	% = 33	% = 8
Mean Labour and Delivery Satisfaction Index score Mean (SD)	5.4 (0.4)	5.3 (0.4)	5.1 (0.7)

Outcome	Sterile water injections, , N = 10	TENS, , N = 12	Standard care, , N = 12
Use of rescue epidural analgesia No of events	% = 60	% = 75	% = 33

Critical appraisal

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns *(No information on whether participants were aware of their allocation before assignment, but not baseline imbalances to suggest any issues.)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Some concerns *(Participants were aware of their assignment as were people delivering the intervention. There were probably no deviations from the intended intervention as there is mention of 1 women not receiving the interventions due to birth, but no other mentions. However, concerns as there is no information regarding intention to treat or other appropriate analysis.)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low *(Outcome data available for nearly all participants)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	High *(Patient reported outcomes - pain and women's experience - could have been influenced by knowledge of the intervention and risk of bias is high. Knowledge of intervention could also have had an influence on epidural request, if participants already had an opinion of the effectiveness of the intervention. Risk of bias is low for mode of birth outcomes.)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Some concerns *(Not enough information as pre-specified protocol is not available)*
Overall bias and Directness	Risk of bias judgement	High
Overall bias and Directness	Overall Directness	Indirectly applicable

Section	Question	Answer
Overall bias and Directness	Risk of bias variation across outcomes	High risk of bias for pain, women's experience and epidural analgesia outcomes. Some concerns for mode of birth outcomes.

Lee, 2013

Bibliographic Reference	Lee, N.; Webster, J.; Beckmann, M.; Gibbons, K.; Smith, T.; Stapleton, H.; Kildea, S.; Comparison of a single vs. a four intradermal sterile water injection for relief of lower back pain for women in labour: a randomised controlled trial; Midwifery; 2013; vol. 29 (no. 6); 585-591

Study details

Country/ies where study was carried out	Brisbane, Australia
Study type	Randomised controlled trial (RCT)
Study dates	January 2010 to February 2011
Inclusion criteria	• Women ages 18 years or over with a singleton pregnancy • Gestational age 37-42 weeks • Cephalic presentation • In first stage of labour • Back pain ≥7cm on a visual analogue scale • No serious medical condition
Exclusion criteria	• Women who had used pharmacological analgesia prior to randomisation
Patient characteristics	No significant differences between age, parity, BMI, gestation or cervix dilation before intervention.
Intervention(s)/control	Single injection group • One intradermal injection of 0.1ml of sterile water was administered. • 23 gauge needle used.

	• Site of injection was the point on the back which was indicated by the woman to be most painful. • 2 midwives performed the procedure. Four injection group • Four intradermal injections of 0.1ml of sterile water were administered. • 23 gauge need used. • Site of injections were one each at the posterior superior iliac spine, and 2 at 2-3cm below and 1 cm medial to each posterior superior iliac spine. • 2 midwives performed the procedure.
Sources of funding	Pain up to 120 post intervention
Sample size	N=306 randomised Single injection group: n=147 Four injection group: n=158
Other information	Setting: Hospital No information on whether women who had labour induced were excluded from the population.

Outcomes

Outcome	**Single injection group, , N = 148**	**Four injection group, , N = 157**
Pain reduced greater than 30% at 10 minutes No of events	n = 96	n = 128
Pain reduced greater than 50% at 10 minutes No of events	n = 75	n = 107
Pain reduced greater than 30% at 30 minutes	n = 93	n = 117

Outcome	Single injection group, , N = 148	Four injection group, , N = 157
No of events		
Pain reduced greater than 50% at 30 minutes No of events	n = 68	n = 102
Pain reduced greater than 30% at 60 minutes No of events	n = 69	n = 95
Pain reduced greater than 50% at 60 minutes No of events	n = 48	n = 75
Pain reduced greater than 30% at 90 minutes No of events	n = 43	n = 64
Pain reduced greater than 50% at 90 minutes No of events	n = 31	n = 49
Pain reduced greater than 30% at 120 minutes No of events	n = 35	n = 45
Pain reduced greater than 50% at 120 minutes No of events	n = 27	n = 36
Caesarean section No of events	n = 23	n = 27
Instrumental vaginal birth No of events	n = 28	n = 33

Outcome	Single injection group, , N = 148	Four injection group, , N = 157
Normal vaginal birth not defined, assumed spontaneous vaginal No of events	n = 96	n = 98
Number of women who were 'very satisfied' or 'satisfied' with the treatment No of events	n = 88	n = 97
Number of women who would use the treatment again No of events	n = 91	n = 89
Use of rescue epidural analgesia No of events	n = 62	n = 70
Use of rescue nitrous oxide analgesia No of events	n = 47	n = 37
Use of rescue IM/IV analgesia No of events	n = 13	n = 17

Critical appraisal

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low *(Randomisation was computer generated and allocation concealed in opaque envelopes. No baseline differences that suggest a problem.)*

Section	Question	Answer
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Some concern *(Participants aware of assignment, midwives caring for participants were not aware of assignment. No sign of deviations from intended intervention and analysis appropriate.)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low *(Missing outcome data was mainly due to women not meeting protocol criteria. There were some women who were not included due to epidural analgesia, but those that were excluded received epidural before the start of pain assessment. For those that received epidural analgesia during intervention, pain was recorded up until epidural was received.)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	High *(High risk of bias for pain and women's experience as they were participant reported and participants were aware of assigned intervention. Knowledge of intervention could also have had an influence on epidural request, if participants already had an opinion of the effectiveness of the intervention. Risk of bias is low for mode of birth outcomes.)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low *(Data is in accordance with a pre-specified plan. All time points reported.)*
Overall bias and Directness	Risk of bias judgement	High
Overall bias and Directness	Overall Directness	Indirectly applicable
Overall bias and Directness	Risk of bias variation across outcomes	High risk of bias for pain, women's experience outcomes and epidural analgesia. Low risk of bias for mode of birth.

Lee, 2020

Bibliographic Reference	Lee, N.; Gao, Y.; Collins, S. L.; Martensson, L. B.; Randall, W.; Rowe, T. M.; Kildea, S.; Caesarean delivery rates and analgesia effectiveness following injections of sterile water for back pain in labour: a multicentre, randomised placebo controlled trial; Eclinicalmedicine; 2020; vol. 25

Study details

Country/ies where study was carried out	Australia and UK
Study type	Randomised controlled trial (RCT) Multi-centre, women were randomised 1:1
Study dates	December 9th 2012 to December 15th 2017
Inclusion criteria	• Women 18 years or older with a singleton pregnancy • Cephalic presentation • Gestational age between 37 - 41 weeks and 6 days • Spontaneous, induced or augmented labour • Women experiencing back pain in labour (self-assessed as ≥7 on a verbal pain scale (1-10)
Exclusion criteria	• Previous caesarean delivery • Significant co-morbidity • Contraindications to receiving injections (e.g. infection at the injection • site, bleeding disorders) • Used health insurance to access labour care from a private obstetrician
Patient characteristics	No significant differences between age, parity, BMI or cervix dilation at baseline.
Intervention(s)/control	<u>Sterile water injection:</u> • Women were administered 0.1-0.3 ml sterile water intracutaneously • Injection sites were the Michaelis Rhomboid. Two injections were given over the posterior superior iliac spines. The remaining 2 were given approximately 2cm below and 1 cm medial to the first 2 injections. <u>Saline water injections</u> • Women were administered 0.1-0.3 ml saline water intracutaneously • Injection sites were the same as in the sterile water group

Sources of funding	Not industry funded
Sample size	N=1166 women randomised Sterile water injections: n=587 (580 included in analysis) Saline placebo group: n=579 (567 included in analysis)
Other information	IM/IV use prior randomisation - number (%) Sterile water group: 75 (12.9) Saline placebo group: 62 (10.9) Induced labour - number (%) Sterile water group: 159 (27.4) Saline placebo group: 158 (27.9) Labour not recorded as spontaneous or induced - number (%) Sterile water group: 8 (1.4) Saline placebo group: 10 (1.8) Setting: Hospital maternity units

Outcomes

Outcome	**Sterile water group, , N = 580**	**Saline placebo group, , N = 567**
VAS pain score reduced at least 30% at 30 minutes (number of women reporting yes) No of events	n = 330	n = 163
VAS pain score reduced at least 30% at 60 minutes (number of women reporting yes)	n = 241	n = 128

Outcome	Sterile water group, , N = 580	Saline placebo group, , N = 567
No of events		
VAS pain score reduced at least 30% at 90 minutes (number of women reporting yes) No of events	n = 171	n = 88
VAS pain score reduced at least 50% at 30 minutes (number of women reporting yes) No of events	n = 235	n = 94
VAS pain score reduced at least 50% at 60 minutes (number of women reporting yes) No of events	n = 165	n = 85
VAS pain score reduced at least 50% at 90 minutes (number of women reporting yes) No of events	n = 125	n = 59
Caesarean section No of events	n = 97	n = 82
Spontaneous vaginal birth No of events	n = 339	n = 351
Instrumental vaginal birth No of events	n = 133	n = 123
How effective the injections were at relieving back pain (number of women reporting 'very effective' or 'rather effective') No of events	n = 266	n = 160
Satisfaction with the treatment (number of women reporting 'very satisfied' or 'satisfied') No of events	n = 277	n = 198

Outcome	Sterile water group, , N = 580	Saline placebo group, , N = 567
Would choose the same treatment again No of events	n = 237	n = 207
Use of rescue epidural analgesia No of events	n = 215	n = 221
Use of rescue Entonox analgesia No of events	n = 386	n = 383
Use of rescue IM/IV analgesia No of events	n = 102	n = 98
Neonatal admission admission to special care nursery, or intensive care nursery No of events	n = 70	n = 49

Critical appraisal

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low *(Randomisation prepared independently and allocation concealed in opaque bags. No baseline imbalances to suggest a problem with randomisation.)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low *(Participants and midwives were blinded, and analyses were performed using intention-to-treat.)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Some concerns *(Some of the data is missing due to not having clinical data*

Section	Question	Answer
		information. Unclear whether this would have an impact on outcomes. Balanced missing outcome between both groups.)
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(Outcome assessors were not aware of the assigned intervention)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low *(Time points specified in the protocol were pain at 10 and 45 minutes. The study reported pain at 30, 60 and 90 minutes. This difference is unlikely to have been due to selection of results.)*
Overall bias and Directness	Risk of bias judgement	Some concerns
Overall bias and Directness	Overall Directness	Directly applicable
Overall bias and Directness	Risk of bias variation across outcomes	None

Martensson, 2008

Bibliographic Reference	Martensson, Lena; Stener-Victorin, Elisabet; Wallin, Gunnar; Acupuncture versus subcutaneous injections of sterile water as treatment for labour pain; Acta Obstetricia et Gynecologica Scandinavica; 2008; vol. 87 (no. 2); 171-177

Study details

Country/ies where study was carried out	Sweden
Study type	Randomised controlled trial (RCT)
Study dates	Not reported
Inclusion criteria	• Gestational age 37-42 weeks • Spontaneous onset of labour • Requiring pain relief

Exclusion criteria	• Not had opioid analgesics, acupuncture, transcutaneous electrical nerve stimulation or sterile water injections within 10 h before inclusion • Not have been administered a paracervical nerve block, epidural or intrathecal analgesia • Labour not augmented
Patient characteristics	No significant differences for parity, gestational age, weight before gestational week 14, VAS pain score at baseline.
Intervention(s)/control	Sterile water injection • Women were given 4-8 subcutaneous injections of 0.5 ml of sterile water. • Injections were administered in the area where the woman felt pain, and repeated if necessary. • Needle used had a diameter of 0.4m and length 20mm. • Injections were administered during a contractions. • The first assessment took place 30 minutes after all the injections were given. • Treatment was administered by the delivered midwife. Acupuncture • Midwives performed acupuncture at 4-7 points depending on where the pain was perceived. • The needles were left in place for 40 minutes and stimulated manually every 10 minutes. • The first assessment took place 30 minutes after all the needles were in place.
Duration of follow-up	Pain 180 minutes after treatment
Sources of funding	Not reported
Sample size	N= 156 randomised Sterile water injections: 78 Acupuncture: n=78

Other information	Setting: Labour ward No information on risk status of population.

Outcomes

Outcome	**Sterile water injections, , N = 66**	**Acupuncture, , N = 62**
General labour pain 30 minutes after treatment (Visual analogue scale)		
Mean (SD)	52.3 (23.6)	69.7 (23.4)
General labour pain 60 minutes after treatment (Visual analogue scale)		
Mean (SD)	53.2 (26.2)	72.7 (22.5)
Sample size	n = 57	n = 56
General labour pain 90 minutes after treatment (Visual analogue scale)		
Mean (SD)	52.3 (24.7)	73.8 (20.5)
Sample size	n = 45	n = 41
General labour pain 120 minutes after treatment (Visual analogue scale)		
Mean (SD)	58.8 (25)	76.8 (22.4)
Sample size	n = 38	n = 34
General labour pain 150 minutes after treatment (Visual analogue scale)		
Mean (SD)	58.6 (25.9)	72 (21.9)
Sample size	n = 27	n = 22
General labour pain 180 minutes after treatment (Visual analogue scale)	62.7 (25.6)	79.5 (19.6)
	n = 24	n = 17

Outcome	Sterile water injections, , N = 66	Acupuncture, , N = 62
Mean (SD) Sample size		
Caesarean section No of events	n = 4	n = 5
Normal delivery not defined, assumed spontaneous vaginal No of events	n = 59	n = 51
Vacuum/forceps No of events	n = 3	n = 6
Use of rescue epidural analgesia No of events	n = 18	n = 17
Use of rescue paracervical nerve block No of events	n = 1	n = 2

Critical appraisal

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low *(Randomised was computer generated and allocation was concealed in envelopes. No baseline imbalances suggesting problems with randomisation)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	High *(Participants and people delivering the intervention were aware of the assignment. Some dropouts due to women regretting pain relief request could have been due to knowledge of the intervention but these are few and could occur outside the trial context.)*

Section	Question	Answer
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low *(Women who requested rescue epidural analgesia or rescue paracervical block were removed from analysis, but their pain scores were considered before removal, and number requesting rescue analgesia recorded)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	High *(High risk for pain as it is participant reported and participants were aware of their assignment. Knowledge of intervention could also have had an influence on other analgesia requested, if participants already had an opinion of the effectiveness of the intervention. Risk of bias is low for mode of birth outcomes.)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Some concerns *(Not pre-specified protocol available)*
Overall bias and Directness	Risk of bias judgement	High
Overall bias and Directness	Overall Directness	Indirectly applicable
Overall bias and Directness	Risk of bias variation across outcomes	High risk for pain outcomes and use of rescue analgesia. Low risk for other outcomes.

Rai, 2014

Bibliographic Reference	Rai, R; Uprety, D; Pradhan, T; Bhattarai, B; Acharya, S.; Subcutaneous Sterile Water Injection for Labor Pain: A Randomized Controlled Trial; Nepal Journal of Obstetrics and Gynaecology; 2014; vol. 8 (no. 2); 68-70

Study details

Country/ies where study was carried out	Nepal
Study type	Randomised controlled trial (RCT)
Study dates	Not reported
Inclusion criteria	• Women over 37 weeks gestation • Admitted to the labour room

	• In the active phase of the first stage of labour (cervical dilation of more than 4cm) • Severe low back pain, measured by visual analogue scale of ≥7, and requiring pain relief
Exclusion criteria	• If opioid analgesics were given prior to inclusion • If there was a language barrier • Previous caesarean birth (previous uterine scar) • Infection at the area of injection
Patient characteristics	No significant differences between age and weight. No information on parity.
Intervention(s)/control	<u>Sterile water injections</u> • Four subcutaneous injections of sterile water were given simultaneously at 4 different sites in the Michaelis' rhomboid lumbosacral region • 30 gauge needle used. • Volume of each injection was 0.1 ml. • Injections were given during uterine contractions. <u>Control group</u> • Four subcutaneous injections of isotonic saline were given in the same sites as the intervention group. • Needle and volume of injection was the same at intervention group. • Injections were given during uterine contractions.
Sources of funding	Not reported
Sample size	N=240 women randomised Sterile water group: n=120 Control group (saline): n=120

Other information	Setting: Labour room Risk status and if women were induced not reported.

Outcomes

Outcome	**Sterile water injections, , N = 120**	**Saline water injections, , N = 120**
Back pain after injections at 10 minutes (Visual analogue scale) Mean (SD)	3.64 (2.93)	7.63 (2.16)
Back pain after injections at 45 minutes (Visual analogue scale) Mean (SD)	3.27 (2.68)	7.69 (2.28)
Back pain after injections at 90 minutes (Visual analogue scale) Mean (SD)	3.32 (2.68)	4.63 (0.82)
Caesarean section No of events	% = 5	% = 3.3
Vacuum assisted vaginal delivery No of events	% = 0.8	% = 2.5
Would use the same technique in future pregnancy No of events	n = 100	n = 23
Neonatal admission No of events	n = 0	n = 0

Critical appraisal

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns *(Randomisation was computer generated but no information with regard to concealment of allocation. No baseline imbalances to suggest a problem with randomisation.)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low *(Single blind study, participants were unaware of intervention but likely people delivering the intervention were as study reported to be single blind). All participants received their assigned treatment so no indication there was deviation from assigned intervention.)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low *(Data was available for all women)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(Pain was participant reported but they were unaware of assignment)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Some concerns *(No pre-specified protocol available)*
Overall bias and Directness	Risk of bias judgement	Low
Overall bias and Directness	Overall Directness	Indirectly applicable
Overall bias and Directness	Risk of bias variation across outcomes	None

Rezaie, 2019

Bibliographic Reference	Rezaie, Mehri; Shaabani, Sanaz; Jahromi, Farzin Sabouri; Jahromi, Maryam Efafat; Dakhesh, Sheida; The Effect of Subcutaneous and Intracutaneous Injections of Sterile Water and Normal Saline on Pain Intensity in Nulliparous Women: A Randomized Controlled Trial; Iranian journal of nursing and midwifery research; 2019; vol. 24 (no. 5); 365-371

Study details

Country/ies where study was carried out	Iran

Study type	Randomised controlled trial (RCT)
Study dates	1 May 2012 to 1 October 2013
Inclusion criteria	• Nulliparous women with a singleton pregnancy • 37-42 weeks gestation • Cephalic presentation • Dilation 4-6cm, effacement >50%
Exclusion criteria	• High-risk pregnancy • Fetal distress in the first stage of labour • Drug abuse • Childbirth in less than 3 hours after the beginning of the study • Use of any other pharmacological or non-pharmacological analgesia
Patient characteristics	No significant differences between age and gestational age.
Intervention(s)/control	Intracutaneous sterile water injection • 0.15 cc sterile distilled water was injected intracutaneously into each Micheal rhomboid point • A total of 4 injections were given • Injections were conducted by an expert midwife Subcutaneous sterile water injection • 0.5 cc sterile distilled water was injection into each Micheal rhomboid point • A total of 4 injections were given • Injections were conducted by an expert midwife Intracutaneous saline injection • 0.15 cc saline water was injected intracutaneously • Location site and number of injections were the same as with the sterile water groups • Injections were conducted by an expert midwife

	Subcutaneous saline injection • 0.5 cc saline water was injected subcutaneously • Location site and number of injections were the same as with the sterile water groups • Injections were conducted by an expert midwife
Duration of follow-up	Pain at 180 minutes after intervention
Sources of funding	Not reported
Sample size	N=164 randomised Intracutaneous sterile water injections: n=41 Subcutaneous sterile water injections: n=41 Intracutaneous saline injections: n=41 Subcutaneous saline injections: n=41
Other information	Setting: Maternity hospital ward If women were induced not reported.

Outcomes

Outcome	Intracutaneous sterile water injection, , N = 41	Subcutaneous sterile water injection, , N = 41	Intracutaneous saline injection, , N = 41	Subcutaneous saline injection, , N = 41
Back pain after injection at 30 minutes (Visual analogue scale) Mean (SD)	6.71 (1.73)	6.64 (1.81)	6.92 (1.86)	7.43 (1.86)

Outcome	Intracutaneous sterile water injection, , N = 41	Subcutaneous sterile water injection, , N = 41	Intracutaneous saline injection, , N = 41	Subcutaneous saline injection, , N = 41
Back pain after injections at 60 minutes (Visual analogue scale) Mean (SD)	8.11 (1.69)	8.03 (1.67)	8.83 (1.51)	7.71 (1.5)
Back pain after injection at 90 minutes (Visual analogue scale) Mean (SD)	9.08 (1.19)	8.68 (1.42)	9.13 (1.12)	8.5 (1.06)
Back pain after injections at 120 minutes (Visual analogue scale) Mean (SD)	9.89 (0.45)	9.57 (0.83)	9.69 (0.64)	8.86 (1.14)
Back pain after injections at 150 minutes (Visual analogue scale) Mean (SD)	10 (0)	9.68 (1.13)	9.42 (0.73)	9.78 (0.71)
Back pain after injections at 180 minutes (Visual analogue scale) Mean (SD)	10 (0)	9.78 (0.88)	9.94 (0.31)	9.71 (0.71)
Caesarean section No of events	n = 2	n = 2	n = 4	n = 0
Normal vaginal birth No of events	n = 33	n = 36	n = 35	n = 30

Outcome	Intracutaneous sterile water injection, , N = 41	Subcutaneous sterile water injection, , N = 41	Intracutaneous saline injection, , N = 41	Subcutaneous saline injection, , N = 41
Vacuum assisted No of events	n = 6	n = 3	n = 4	n = 11

Critical appraisal

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low *(Allocation was random through the use of sealed cards. Allocation was concealed and no baseline imbalances to suggest problems with randomisation.)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low *(Participants and people delivering intervention were not aware of assignment. Same number of women analysed per group as were randomised so intention to treat analysis assumed.)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(Participants self-reporting outcomes were blinding, as were other assessors of outcomes)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low *(Outcomes were reported as pre-specified in the protocol.)*
Overall bias and Directness	Risk of bias judgement	Low
Overall bias and Directness	Overall Directness	Indirectly applicable
Overall bias and Directness	Risk of bias variation across outcomes	None

AMSTAR: A MeaSurement Tool to Assess systematic Reviews; BMI: body mass index; IM: intramuscular; IV: intravenous; RCT: randomised controlled trial; SD: standard deviation; TENS: transcutaneous electrical nerve stimulation; VAS: visual analogue scale

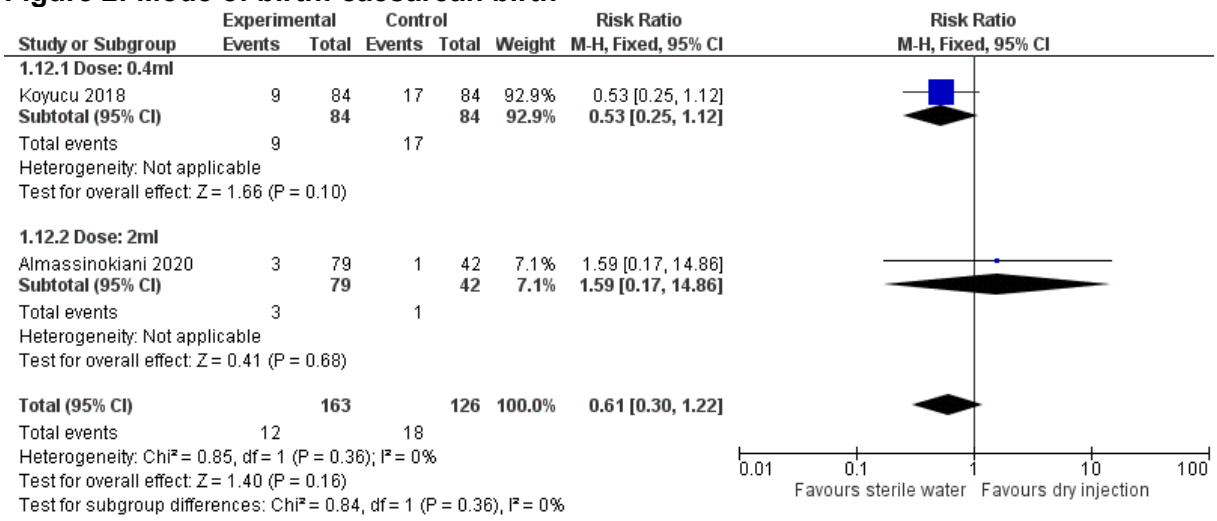
Appendix E Forest plots

Forest plots for review question: What is the effectiveness of injected water papules for pain relief during labour?

This section includes forest plots only for outcomes that are meta-analysed. Outcomes from single studies are not presented here; the quality assessment for such outcomes is provided in the GRADE profiles in appendix F.

Comparison 1: Sterile water injections versus dry injections

Figure 2: Mode of birth: caesarean birth



Comparison 2: Subcutaneous sterile water injections versus intracutaneous sterile water injections

Figure 3: Mode of birth: caesarean birth

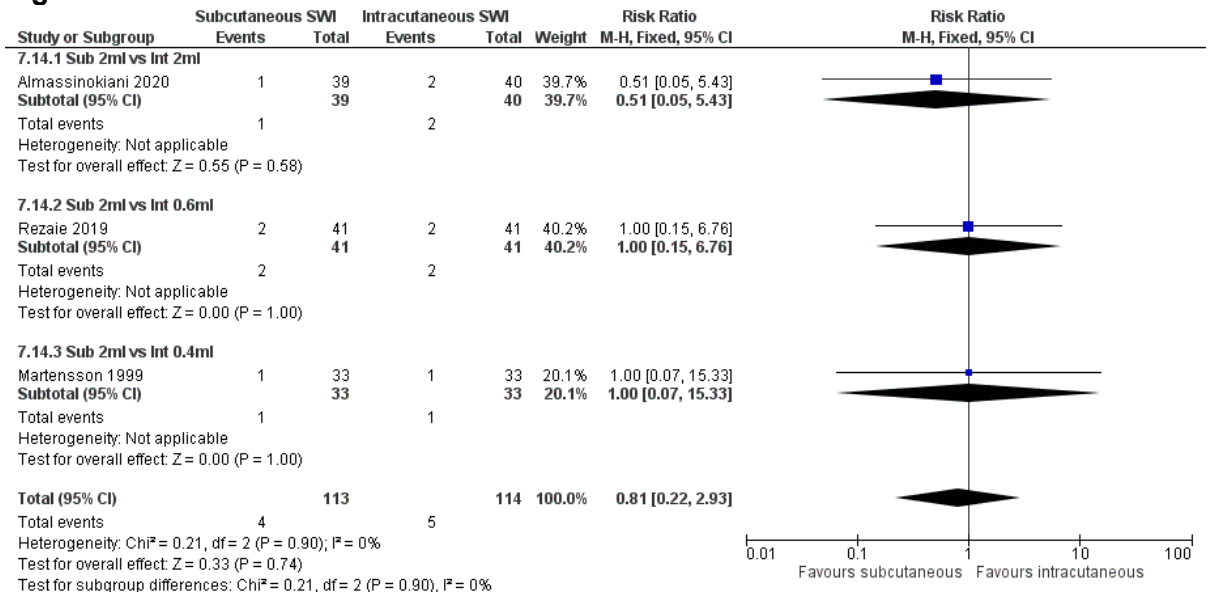
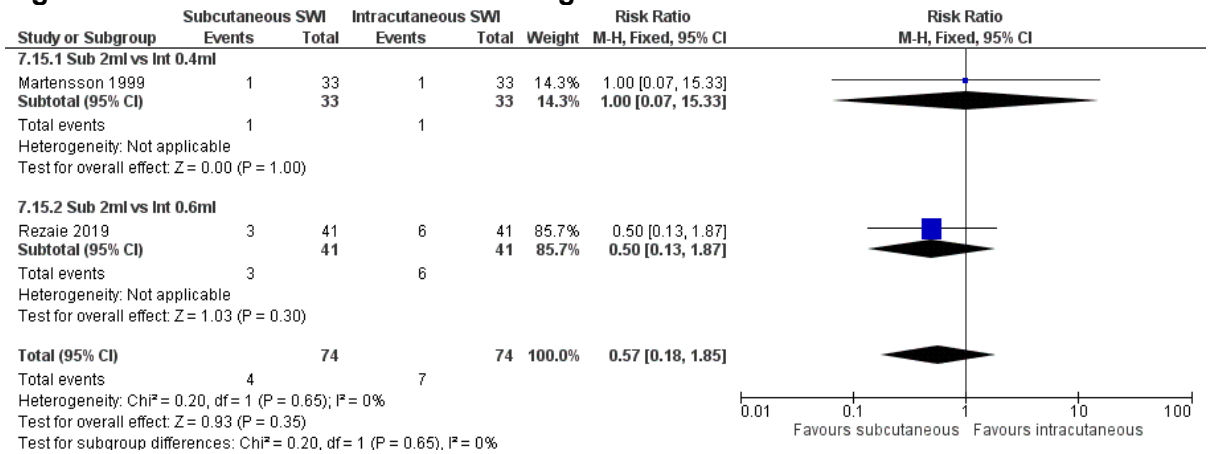


Figure 4: Mode of birth: instrumental vaginal birth



Comparison 3: Sterile water injections versus saline injections

Figure 5: Back pain: reduction in baseline in back pain after injections at 90 minutes

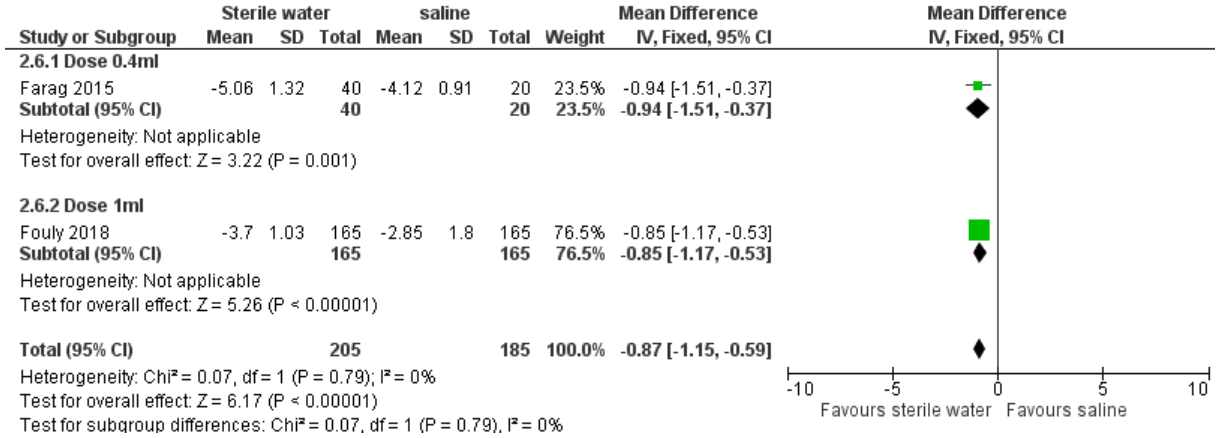


Figure 6: Back pain: pain score after 0.4ml injections at 10 minutes

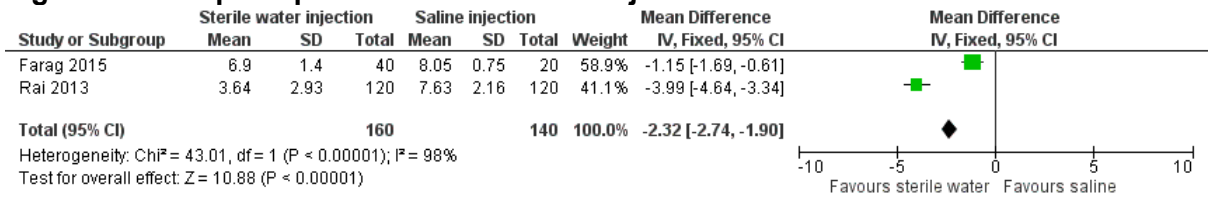


Figure 7: Back pain: pain score after 0.4ml injections at 45 minutes

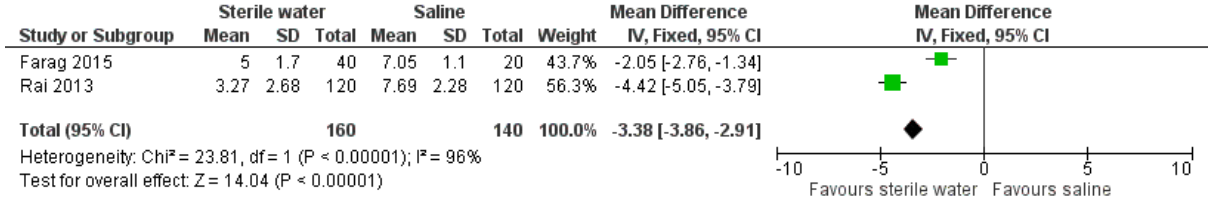


Figure 8: Back pain: score after injections at 90 minutes

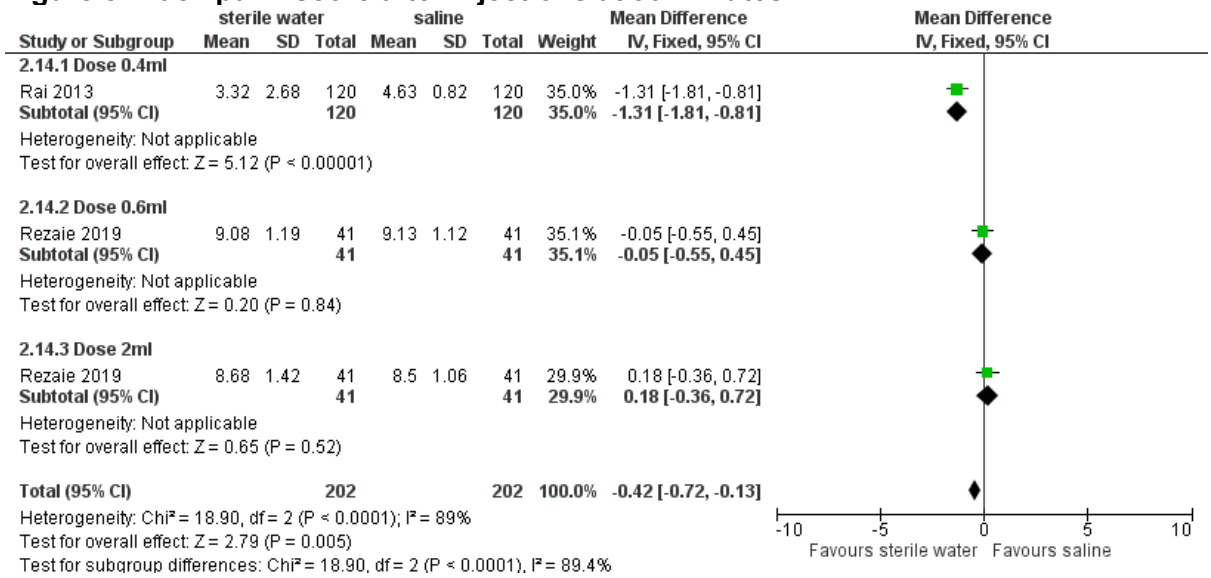


Figure 9: Mode of birth: caesarean birth

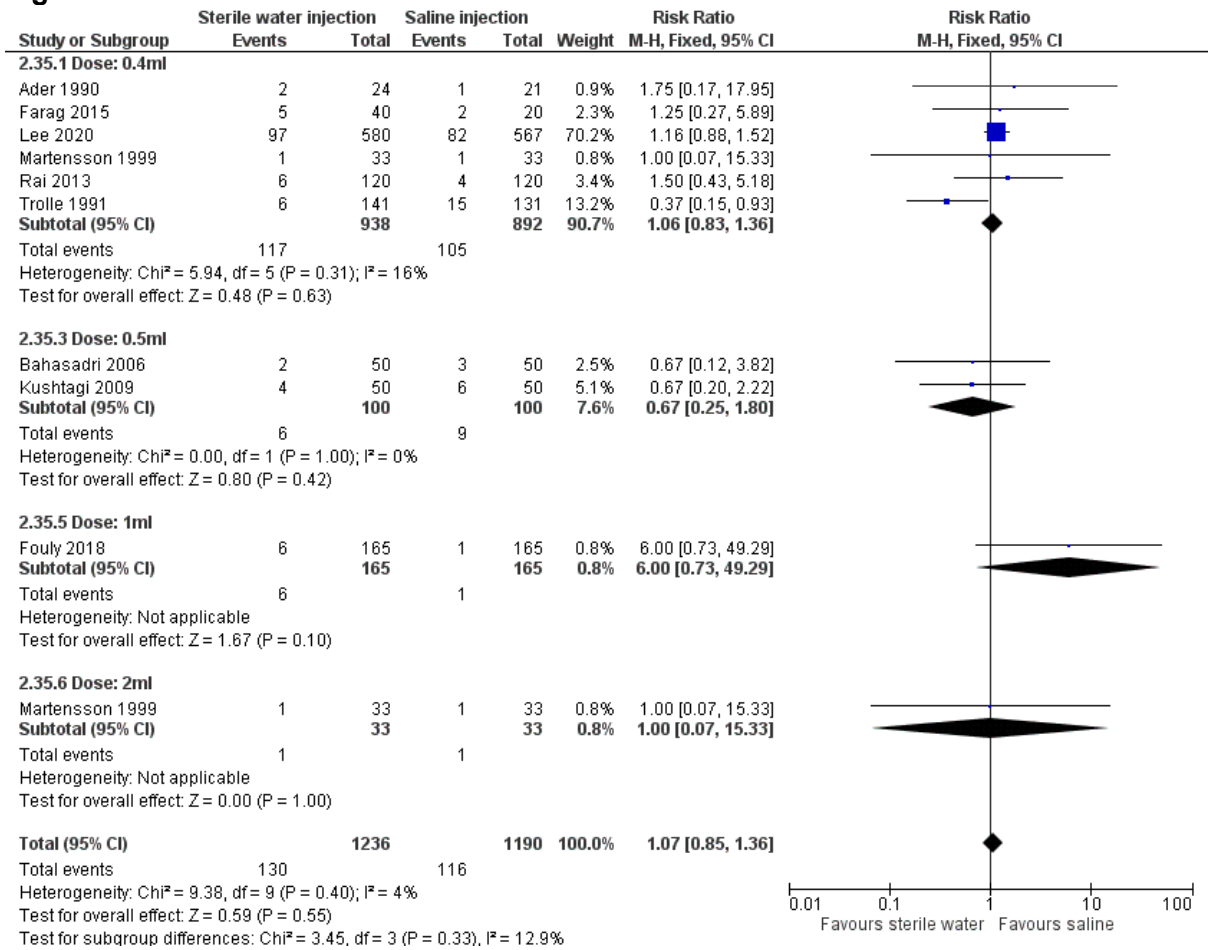


Figure 10: Mode of birth: caesarean birth

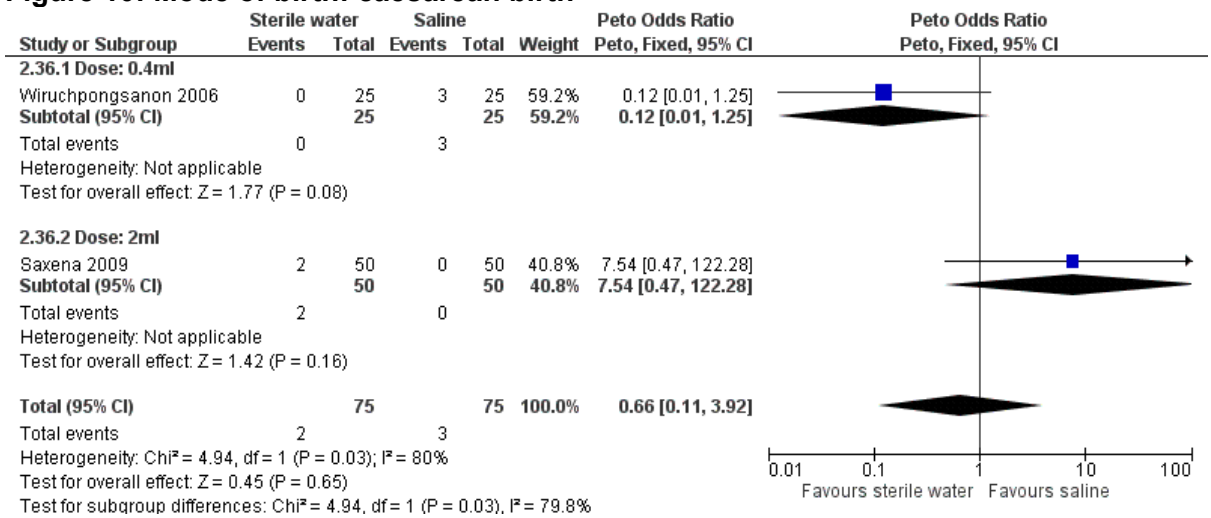


Figure 11: Mode of birth: instrumental vaginal birth

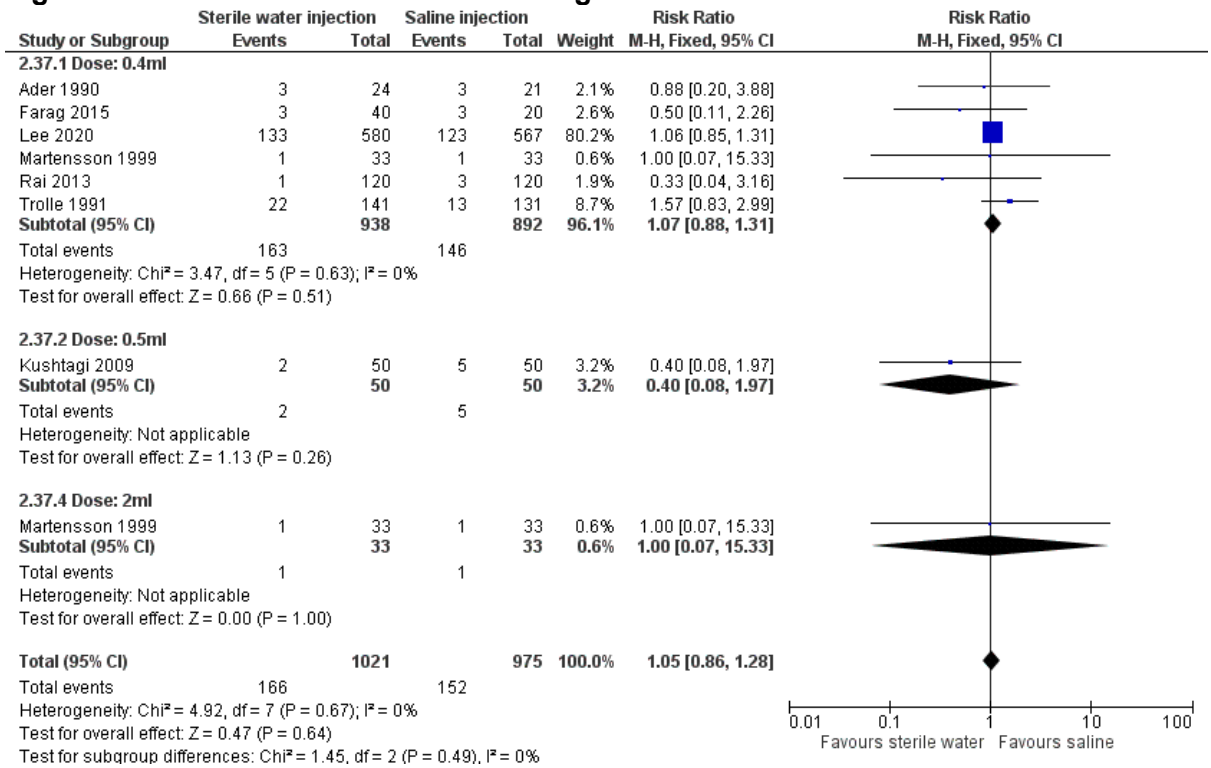


Figure 12: Mode of birth: spontaneous vaginal birth

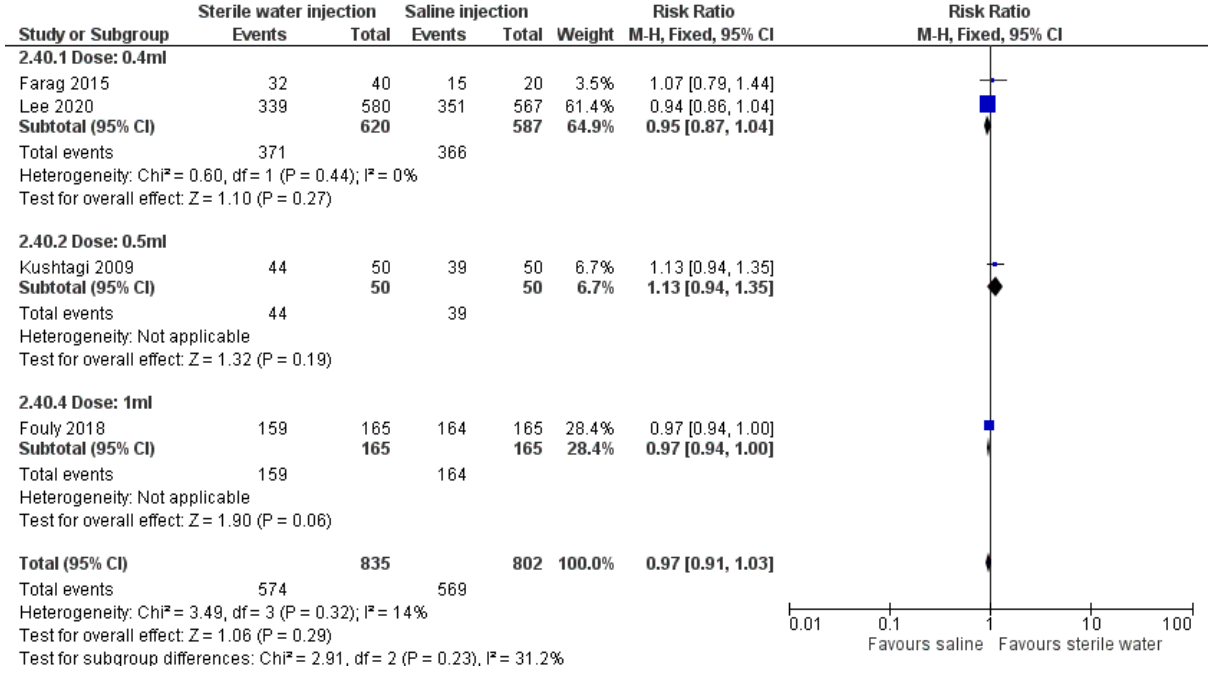


Figure 13: Women's experience of labour and birth: would use the same technique in future pregnancy

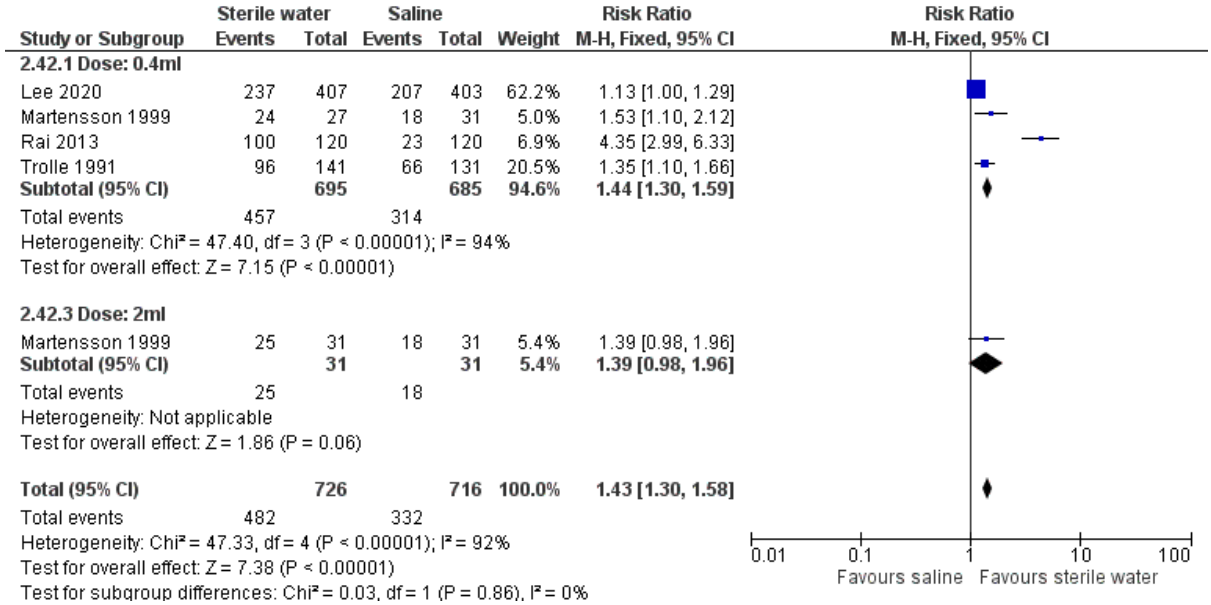


Figure 14: Women's experience of labour and birth: would use the same technique in future pregnancy – high income only

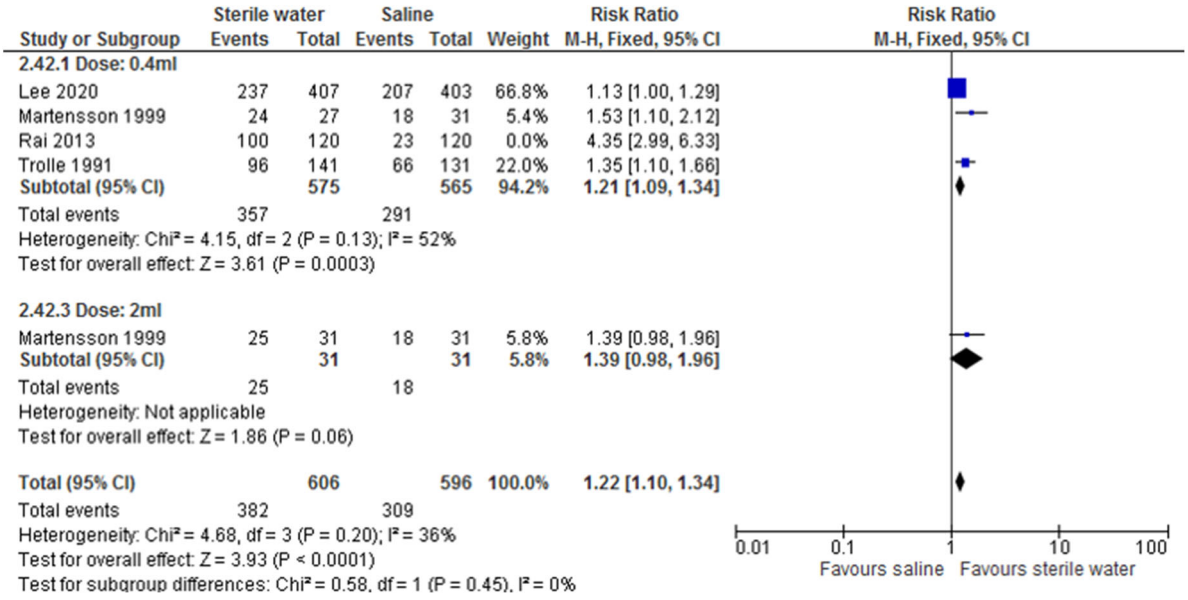


Figure 15: Use of rescue Entonox analgesia

Figure 16: Use of rescue pethidine analgesia

Appendix F GRADE tables

GRADE tables for review question: What is the effectiveness of injected water papules for pain relief during labour?

Table 4: Evidence profile for comparison 1: sterile water injections versus dry injections

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injections	Dry injections	Relative (95% CI)	Absolute		
General labour pain score after 2ml injections at 10 minutes (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Almassinokiani 2020)	randomised trials	no serious risk of bias	no serious inconsistency	serious[1]	serious[2]	none	79	42	-	MD 0.46 higher (0.19 lower to 1.11 higher)	LOW	CRITICAL
General labour pain score after 2ml injections at 30 minutes (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Almassinokiani 2020)	randomised trials	no serious risk of bias	no serious inconsistency	serious[1]	serious[2]	none	79	42	-	MD 1.6 lower (2.32 to 0.88 lower)	LOW	CRITICAL
General labour pain score after 2ml injections at 60 minutes (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Almassinokiani 2020)	randomised trials	no serious risk of bias	no serious inconsistency	serious[1]	no serious imprecision	none	79	42	-	MD 2.57 lower (3.29 to 1.85 lower)	MODERATE	CRITICAL
General labour pain score after 2ml injections at 90 minutes (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Almassinokiani 2020)	randomised trials	no serious risk of bias	no serious inconsistency	serious[1]	no serious imprecision	none	79	42	-	MD 1.65 lower (2.38 to 0.92 lower)	MODERATE	CRITICAL
Reduction from baseline in back pain after 0.4 ml injection at 10 minutes (measured with: visual analogue scale; range of scores: 0-100; Better indicated by lower values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injections	Dry injections	Relative (95% CI)	Absolute		
1 (Koyucu 2018)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	84	84	-	MD 28.51 lower (31.31 to 25.71 lower)	HIGH	CRITICAL
Reduction from baseline in back pain after 0.4 ml injection at 30 minutes (measured with: visual analogue scale; range of scores: 0-100; Better indicated by lower values)												
1 (Koyucu 2018)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	84	84	-	MD 41.49 lower (44.56 to 38.42 lower)	HIGH	CRITICAL
Reduction from baseline in back pain after 0.4 ml injection at 60 minutes (measured with: visual analogue scale; range of scores: 0-100; Better indicated by lower values)												
1 (Koyucu 2018)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	77	74	-	MD 48.41 lower (51.5 to 45.32 lower)	HIGH	CRITICAL
Reduction from baseline in back pain after 0.4 ml injection at 120 minutes (measured with: visual analogue scale; range of scores: 0-100; Better indicated by lower values)												
1 (Koyucu 2018)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	67	64	-	MD 48.88 lower (51.93 to 45.83 lower)	HIGH	CRITICAL
Reduction from baseline in back pain after 0.4 ml injection at 180 minutes (measured with: visual analogue scale; range of scores: 0-100; Better indicated by lower values)												
1 (Koyucu 2018)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	54	52	-	MD 15.24 lower (19.53 to 10.95 lower)	HIGH	CRITICAL
Caesarean birth												
2 (Almassinokiani 2020; Koyucu 2018)	randomised trials	no serious risk of bias	no serious inconsistency	serious[1]	serious[3]	none	12/163 (7.4%)	18/126 (14.3%)	RR 0.61 (0.3 to 1.22)	56 fewer per 1000 (from 100 fewer to 31 more)	LOW	CRITICAL
Caesarean birth – Dose: 0.4ml												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injections	Dry injections	Relative (95% CI)	Absolute		
1 (Koyucu 2018)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	9/84 (10.7%)	17/84 (20.2%)	RR 0.53 (0.25 to 1.12)	95 fewer per 1000 (from 152 fewer to 24 more)	MODERATE	CRITICAL
Caesarean birth – Dose: 2ml												
1 (Almassinokiani 2020)	randomised trials	no serious risk of bias	no serious inconsistency	serious[1]	very serious[4]	none	3/79 (3.8%)	1/42 (2.4%)	RR 1.59 (0.17 to 14.86)	14 more per 1000 (from 20 fewer to 330 more)	VERY LOW	CRITICAL
Instrumental vaginal birth												
1 (Koyucu 2018)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	0/84 (0%)	0/84 (0%)	RD 0.00 (-0.02 to 0.02)	0 fewer per 1000 (from 20 fewer to 20 more)	LOW	CRITICAL
Women satisfied with treatment												
1 (Koyucu 2018)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	71/84 (84.5%)	30/84 (35.7%)	RR 2.37 (1.75 to 3.2)	489 more per 1000 (from 268 more to 786 more)	HIGH	IMPORTANT
Use of rescue epidural analgesia												
1 (Koyucu 2018)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	4/84 (4.8%)	8/84 (9.5%)	RR 0.5 (0.16 to 1.6)	48 fewer per 1000 (from 80 fewer to 57 more)	LOW	IMPORTANT

CI: confidence interval; MD: mean difference; RR: risk ratio
1 Population is indirect due to risk status, if labour was induced, or if women used IM/IV analgesia prior to randomisation not reported
2 95% CI crosses 1 MID (0.5x control group SD, for general labour pain after 2ml injection at 10 minutes = 0.90)
3 95% CI crosses 1 MID
4 95% CI crosses 2 MIDs
5 Sample size <200

Table 5: Evidence profile for comparison 2: subcutaneous sterile water injections versus intracutaneous sterile water injections

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Subcutaneous sterile water injection	Intracutaneous sterile water injection	Relative (95% CI)	Absolute		
Reduction in baseline of 4cm or more in back pain after 2ml sub. Injections (vs 0.4ml int.) at 10 minutes (measured with: visual analogue scale)												
1 (Martensson 1999)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	19/33 (57.6%)	20/32 (62.5%)	RR 0.92 (0.62 to 1.37)	50 fewer per 1000 (from 237 fewer to 231 more)	VERY LOW	CRITICAL
Reduction in baseline of 4cm or more in back pain after 2ml sub. Injections (vs 0.4ml int.) at 45 minutes (measured with: visual analogue scale)												
1 (Martensson 1999)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	15/29 (51.7%)	17/29 (58.6%)	RR 0.88 (0.55 to 1.41)	70 fewer per 1000 (from 264 fewer to 240 more)	VERY LOW	CRITICAL
Reduction in baseline of 4cm or more in back pain after 2ml sub. Injections (vs 0.4ml int.) at 90 minutes (measured with: visual analogue scale)												
1 (Martensson 1999)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	7/24 (29.2%)	7/22 (31.8%)	RR 0.92 (0.38 to 2.2)	25 fewer per 1000 (from 197 fewer to 382 more)	VERY LOW	CRITICAL
General labour pain score after 2ml sub. Injections (vs 2ml int.) at 10 minutes (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Almassinokiani 2020)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	serious[4]	none	39	49	-	MD 0.87 lower (1.63 to 0.11 lower)	LOW	CRITICAL
General labour pain score after 2ml sub. Injections (vs 2ml int.) at 30 minutes (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Almassinokiani 2020)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	serious[4]	none	39	40	-	MD 0.36 lower (1.21 lower to 0.49 higher)	LOW	CRITICAL
General labour pain score after 2ml sub. Injections (vs 2ml int.) at 60 minutes (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Subcutaneous sterile water injection	Intracutaneous sterile water injection	Relative (95% CI)	Absolute		
1 (Almassinokiani 2020)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	serious[4]	none	39	40	-	MD 0.7 lower (1.58 lower to 0.18 higher)	LOW	CRITICAL
General labour pain score after 2ml sub. Injections (vs 2ml int.) at 90 minutes (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Almassinokiani 2020)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	serious[4]	none	39	40	-	MD 0.67 lower (1.73 lower to 0.39 higher)	LOW	CRITICAL
Back pain score after 2ml sub. Injections (vs 0.6ml int.) at 30 minutes (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none	41	41	-	MD 0.07 lower (0.84 lower to 0.7 higher)	MODERATE	CRITICAL
Back pain score after 2ml sub. Injections (vs 0.6ml int.) at 60 minutes (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none	41	41	-	MD 0.08 lower (0.81 lower to 0.65 higher)	MODERATE	CRITICAL
Back pain score after 2ml sub. Injections (vs 0.6ml int.) at 90 minutes (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	serious[4]	none	41	41	-	MD 0.4 lower (0.97 lower to 0.17 higher)	LOW	CRITICAL
Back pain score after 2ml sub. Injections (vs 0.6ml int.) at 120 minutes (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Subcutaneous sterile water injection	Intracutaneous sterile water injection	Relative (95% CI)	Absolute		
1 (Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none	41	41	-	MD 0.32 lower (0.61 to 0.03 lower)	MODERATE	CRITICAL
Back pain score after 2ml sub. Injections (vs 0.6ml int.) at 150 minutes (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none	41	41	-	MD 0 higher (0 to 0 higher)	MODERATE	CRITICAL
Back pain score after 2ml sub. Injections (vs 0.6ml int.) at 180 minutes (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none	41	41	-	MD 0 higher (0 to 0 higher)	MODERATE	CRITICAL
Caesarean birth												
3 (Almassinokiani 2020; Martensson 1999; Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	very serious[3]	none	4/113 (3.5%)	5/114 (4.3%)	RR 0.81 (0.22 to 2.93)	8 fewer per 1000 (from 34 fewer to 84 more)	VERY LOW	CRITICAL
Caesarean birth – Sub 2ml vs Int 2ml												
1 (Almassinokiani 2020)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	very serious[3]	none	1/39 (2.6%)	2/40 (5%)	RR 0.51 (0.05 to 5.43)	25 fewer per 1000 (from 47 fewer to 221 more)	VERY LOW	CRITICAL
Caesarean birth – Sub 2ml vs Int 0.6ml												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Subcutaneous sterile water injection	Intracutaneous sterile water injection	Relative (95% CI)	Absolute		
1 (Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	very serious[3]	none	2/41 (4.9%)	2/41 (4.9%)	RR 1 (0.15 to 6.76)	0 fewer per 1000 (from 41 fewer to 281 more)	VERY LOW	CRITICAL
Caesarean birth – Sub 2ml vs Int 0.4ml												
1 (Martensson 1999)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	very serious[3]	none	1/33 (3%)	1/33 (3%)	RR 1 (0.07 to 15.33)	0 fewer per 1000 (from 28 fewer to 434 more)	LOW	CRITICAL
Instrumental vaginal birth												
2 (Martensson 1999; Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	very serious[3]	none	4/74 (5.4%)	7/74 (9.5%)	RR 0.57 (0.18 to 1.85)	41 fewer per 1000 (from 78 fewer to 80 more)	VERY LOW	CRITICAL
Instrumental vaginal birth – Sub 2ml vs Int 0.4ml												
1 (Martensson 1999)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	very serious[3]	none	1/33 (3%)	1/33 (3%)	RR 1 (0.07 to 15.33)	0 fewer per 1000 (from 28 fewer to 434 more)	VERY LOW	CRITICAL
Instrumental vaginal birth – Sub 2ml vs Int 0.6ml												
1 (Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	very serious[3]	none	3/41 (7.3%)	6/41 (14.6%)	RR 0.5 (0.13 to 1.87)	73 fewer per 1000 (from 127 fewer to 127 more)	VERY LOW	CRITICAL
Spontaneous vaginal birth – Sub 2ml vs Int 0.6ml												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Subcutaneous sterile water injection	Intracutaneous sterile water injection	Relative (95% CI)	Absolute		
1 (Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	serious[5]	none	36/41 (87.8%)	33/41 (80.5%)	RR 1.09 (0.9 to 1.32)	72 more per 1000 (from 80 fewer to 258 more)	LOW	CRITICAL
Would use the same treatment in the future – Sub 2ml vs Int 0.4ml												
1 (Martensson 1999)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	serious[5]	none	25/31 (80.6%)	24/27 (88.9%)	RR 0.91 (0.73 to 1.13)	80 fewer per 1000 (from 240 fewer to 116 more)	LOW	IMPORTANT

CI: confidence interval; int: intracutaneous; MD: mean difference; RR: risk ratio; sub: subcutaneous
1 Very serious risk of bias in the evidence contributing to the outcomes as per RoB assessment in Derry 2012 (systematic review)
2 Population is indirect due to not reporting of risk status or if labour was induced
3 95% CI crosses 2 MIDs
4 95% CI crosses 1 MID (0.5x control group SD: for general labour pain score= 0.89 for back pain score =0.89)
5 95% CI crosses 1 MID

Table 6: Evidence profile for comparison 3: sterile water injections versus saline injections

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injections	Saline injections	Relative (95% CI)	Absolute		
Reduction in baseline of 4cm or more in back pain after 0.4ml injections at 10 minutes (measured with: visual analogue scale; range of scores: 0-10)												
1 (Martensson 1999)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	20/32 (62.5%)	8/32 (25%)	RR 2.5 (1.3 to 4.82)	375 more per 1000 (from 75	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injections	Saline injections	Relative (95% CI)	Absolute		
										more to 955 more)		
Reduction in baseline of 4cm or more in back pain after 0.4ml injections at 45 minutes (measured with: visual analogue scale; range of scores: 0-10)												
1 (Martensson 1999)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	17/29 (58.6%)	7/28 (25%)	RR 2.34 (1.15 to 4.77)	335 more per 1000 (from 37 more to 942 more)	VERY LOW	CRITICAL
Reduction in baseline of 4cm or more in back pain after 0.4ml injections at 90 minutes (measured with: visual analogue scale; range of scores: 0-10)												
1 (Martensson 1999)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	very serious[4]	none	7/22 (31.8%)	3/21 (14.3%)	RR 2.23 (0.66 to 7.49)	176 more per 1000 (from 49 fewer to 927 more)	VERY LOW	CRITICAL
Reduction in baseline of 4cm or more in back pain after 2ml injection at 10 minutes (measured with: visual analogue scale; range of scores: 0-10)												
1 (Martensson 1999)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	19/33 (57.6%)	8/32 (25%)	RR 2.3 (1.18 to 4.49)	325 more per 1000 (from 45 more to 872 more)	VERY LOW	CRITICAL
Reduction in baseline of 4cm or more in back pain after 2ml injection at 45 minutes (measured with: visual analogue scale; range of scores: 0-10)												
1 (Martensson 1999)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	15/29 (51.7%)	7/28 (25%)	RR 2.07 (1 to 4.3)	267 more per 1000 (from 0 more to 825 more)	VERY LOW	CRITICAL
Reduction in baseline of 4cm or more in back pain after 2ml injection at 90 minutes (measured with: visual analogue scale; range of scores: 0-10)												
1 (Martensson 1999)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	very serious[4]	none	7/24 (29.2%)	3/21 (14.3%)	RR 2.04 (0.6 to 6.91)	149 more per 1000 (from 57 fewer to 844 more)	VERY LOW	CRITICAL
Reduction in baseline in back pain after 0.4ml injection at 30 minutes (measured with: visual analogue scale; range of scores: 0-100; Better indicated by lower values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injections	Saline injections	Relative (95% CI)	Absolute		
1 (Wiruchpongsanon 2006)	randomised trials	very serious[5]	no serious inconsistency	serious[2]	no serious imprecision	none	25	25	-	MD 36.5 lower (49.67 to 23.33 lower)	VERY LOW	CRITICAL
Reduction in baseline in back pain after 0.4ml injection at 60 minutes (measured with: visual analogue scale; range of scores: 0-100; Better indicated by lower values)												
1 (Wiruchpongsanon 2006)	randomised trials	very serious[5]	no serious inconsistency	serious[2]	no serious imprecision	none	25	25	-	MD 53.1 lower (62.72 to 43.48 lower)	VERY LOW	CRITICAL
Reduction in baseline in back pain after 0.4ml injection at 120 minutes (measured with: visual analogue scale; range of scores: 0-100; Better indicated by lower values)												
1 (Wiruchpongsanon 2006)	randomised trials	very serious[5]	no serious inconsistency	serious[2]	no serious imprecision	none	25	25	-	MD 48.4 lower (56.76 to 40.04 lower)	VERY LOW	CRITICAL
Reduction in baseline in back pain after 1ml injection at 15 minutes (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Fouly 2018)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none	165	165	-	MD 0.18 lower (0.39 lower to 0.03 higher)	MODERATE	CRITICAL
Reduction in baseline in back pain after 1ml injection at 30 minutes (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Fouly 2018)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	serious[6]	none	165	165	-	MD 0.42 lower (0.65 to 0.19 lower)	LOW	CRITICAL
Reduction in baseline in back pain after 1ml injection at 45 minutes (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Fouly 2018)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	serious[6]	none	165	165	-	MD 0.6 lower (0.88 to 0.32 lower)	LOW	CRITICAL
Reduction in baseline in back pain after 1ml injection at 120 minutes (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injections	Saline injections	Relative (95% CI)	Absolute		
1 (Fouly 2018)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none	165	165	-	MD 0.01 lower (0.32 lower to 0.3 higher)	MODERATE	CRITICAL
Reduction in baseline in back pain after injections at 90 minutes (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
2 (Farag 2015; Fouly 2018)	randomised trials	serious[7]	no serious inconsistency	serious[2]	no serious imprecision	none	205	185	-	MD 0.87 lower (1.15 to 0.59 lower)	LOW	CRITICAL
Reduction in baseline in back pain after injections at 90 minutes - Dose 0.4ml (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Farag 2015)	randomised trials	very serious[8]	no serious inconsistency	no serious indirectness	no serious imprecision	none	40	20	-	MD 0.94 lower (1.51 to 0.37 lower)	LOW	CRITICAL
Reduction in baseline in back pain after injections at 90 minutes - Dose 1ml (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Fouly 2018)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none	165	165	-	MD 0.85 lower (1.17 to 0.53 lower)	MODERATE	CRITICAL
Reduction in baseline at least 30% in back pain after 0.4ml injections at 30 minutes- visual analogue scale 0-100 (assessed with: number of women)												
1 (Lee 2020)	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	no serious imprecision	none	330/580 (56.9%)	163/567 (28.7%)	RR 1.98 (1.71 to 2.29)	282 more per 1000 (from 204 more to 371 more)	MODERATE	CRITICAL
Reduction in baseline at least 30% in back pain after 0.4ml injections at 60 minutes- visual analogue scale 0-100 (assessed with: number of women)												
1 (Lee 2020)	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	no serious imprecision	none	241/580 (41.6%)	128/567 (22.6%)	RR 1.84 (1.54 to 2.2)	190 more per 1000 (from 122 more to 271 more)	MODERATE	CRITICAL
Reduction in baseline at least 30% in back pain after 0.4ml injections at 90 minutes- visual analogue scale 0-100 (assessed with: number of women)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injections	Saline injections	Relative (95% CI)	Absolute		
1 (Lee 2020)	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	no serious imprecision	none	171/580 (29.5%)	88/567 (15.5%)	RR 1.9 (1.51 to 2.39)	140 more per 1000 (from 79 more to 216 more)	MODERATE	CRITICAL
Reduction in baseline at least 50% in back pain after 0.4ml injections at 30 minutes- visual analogue scale 0-100 (assessed with: number of women)												
1 (Lee 2020)	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	no serious imprecision	none	235/580 (40.5%)	94/567 (16.6%)	RR 2.44 (1.98 to 3.01)	239 more per 1000 (from 162 more to 333 more)	MODERATE	CRITICAL
Reduction in baseline at least 50% in back pain after 0.4ml injections at 60 minutes- visual analogue scale 0-100 (assessed with: number of women)												
1 (Lee 2020)	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	no serious imprecision	none	165/580 (28.4%)	85/567 (15%)	RR 1.9 (1.5 to 2.4)	135 more per 1000 (from 75 more to 210 more)	MODERATE	CRITICAL
Reduction in baseline at least 50% in back pain after 0.4ml injections at 90 minutes- visual analogue scale 0-100 (assessed with: number of women)												
1 (Lee 2020)	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	no serious imprecision	none	125/580 (21.6%)	59/567 (10.4%)	RR 2.07 (1.55 to 2.76)	111 more per 1000 (from 57 more to 183 more)	MODERATE	CRITICAL
Back pain score after 0.4ml injections at 10 minutes (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
2 (Farag 2015; Rai 2013)	randomised trials	serious[7]	very serious[9]	serious[2]	no serious imprecision	none	160	140	-	MD 2.32 lower (2.74 to 1.9 lower)	VERY LOW	CRITICAL
Back pain score after 0.4ml injections at 45 minutes (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
2 (Farag 2015; Rai 2013)	randomised trials	serious[7]	very serious[9]	serious[2]	no serious imprecision	none	160	140	-	MD 3.38 lower (3.86 to 2.91 lower)	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injections	Saline injections	Relative (95% CI)	Absolute		
Back pain score after 0.4ml injections at 60 minutes (measured with: visual analogue scale; range of scores: 0-100; Better indicated by lower values)												
1 (Trolle 1991)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	132	121	-	MD 46.5 lower (63.12 to 29.88 lower)	VERY LOW	CRITICAL
Back pain score after 0.4ml injections at 120 minutes (measured with: visual analogue scale; range of scores: 0-100; Better indicated by lower values)												
1 (Trolle 1991)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	0	-	-	MD 28.5 lower (40.34 to 16.66 lower)	VERY LOW	CRITICAL
Back pain score after injections at 30 minutes (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)[10]												
1 (Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	serious[6]	none	82	82	-	MD 0.49 lower (1.05 lower to 0.06 higher)	LOW	CRITICAL
Back pain score after injections at 30 minutes - Dose 0.6ml (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none	41	41	-	MD 0.21 lower (0.99 lower to 0.57 higher)	MODERATE	CRITICAL
Back pain score after injections at 30 minutes - Dose 2ml (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	serious[6]	none	41	41	-	MD 0.79 lower (1.58 lower to 0 higher)	LOW	CRITICAL
Back pain score after injections at 60 minutes (measured with: visual analogue scale; Better indicated by lower values)[10]												
1 (Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none	82	82	-	MD 0.2 lower (0.68 lower to 0.29 higher)	MODERATE	CRITICAL
Back pain score after injections at 60 minutes - Dose 0.6ml (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injections	Saline injections	Relative (95% CI)	Absolute		
1 (Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	serious[6]	none	41	41	-	MD 0.72 lower (1.41 to 0.03 lower)	LOW .	CRITICAL
Back pain score after injections at 60 minutes - Dose 2ml (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	serious[6]	none	41	41	-	MD 0.32 higher (0.37 lower to 1.01 higher)	LOW	CRITICAL
Back pain score after injections at 90 minutes (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
2 (Rai 2013; Rezaie 2019)	randomised trials	serious[7]	no serious inconsistency	serious[2]	no serious imprecision	none	202	202	-	MD 0.42 lower (0.72 to 0.13 lower)	LOW	CRITICAL
Back pain score after injections at 90 minutes - Dose 0.4ml (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Rai 2013)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none	120	120	-	MD 1.31 lower (1.81 to 0.81 lower)	MODERATE	CRITICAL
Back pain score after injections at 90 minutes - Dose 0.6ml (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Rezaie 2019)	randomised trials	no serious risk of bias	serious[2]	no serious indirectness	no serious imprecision	none	41	41	-	MD 0.05 lower (0.55 lower to 0.45 higher)	MODERATE	CRITICAL
Back pain score after injections at 90 minutes - Dose 2ml (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Rezaie 2019)	randomised trials	no serious risk of bias	serious[2]	no serious indirectness	no serious imprecision	none	41	41	-	MD 0.18 higher (0.36 lower to 0.72 higher)	MODERATE	CRITICAL
Back pain score after injections at 120 minutes (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)[10]												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injections	Saline injections	Relative (95% CI)	Absolute		
1 (Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none	82	82	-	MD 0.32 higher (0.11 to 0.53 higher)	MODERATE	CRITICAL
Back pain score after injections at 120 minutes - Dose 0.6ml (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none	41	41	-	MD 0.2 higher (0.04 lower to 0.44 higher)	MODERATE	CRITICAL
Back pain score after injections at 120 minutes - Dose 2ml (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	serious[6]	none	41	41	-	MD 0.71 higher (0.28 to 1.14 higher)	LOW	CRITICAL
Back pain score after injections at 150 minutes (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)[10]												
1 (Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none	82	82	-	MD 0.1 lower (0.51 lower to 0.31 higher)	MODERATE	CRITICAL
Back pain score after injections at 150 minutes - Dose 0.6ml (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none	41	41	-	MD 0 higher (0 to 0 higher)	MODERATE	CRITICAL
Back pain score after injections at 150 minutes - Dose 2ml (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none	41	41	-	MD 0.1 lower (0.51 lower to 0.31 higher)	MODERATE	CRITICAL
Back pain score after injections at 180 minutes (measured with: visual analogue scale; Better indicated by lower values)[10]												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injections	Saline injections	Relative (95% CI)	Absolute		
1 (Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none	82	82	-	MD 0.07 higher (0.28 lower to 0.42 higher)	MODERATE	CRITICAL
Back pain score after injections at 180 minutes - Dose 0.6ml (measured with: visual analogue scale; Better indicated by lower values)												
1 (Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none	41	41	-	MD 0 higher (0 to 0 higher)	MODERATE	CRITICAL
Back pain score after injections at 180 minutes - Dose 2ml (measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1 (Rezaie 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none	41	41	-	MD 0.07 higher (0.28 lower to 0.42 higher)	MODERATE	CRITICAL
Back pain score after 2ml injections at 10 minutes (measured with: visual analogue scale; range of scores: 0-100; Better indicated by lower values)												
1 (Saxena 2009)	randomised trials	serious[5]	no serious inconsistency	serious[2]	no serious imprecision	none	50	50	-	MD 39.20 lower (49.48 to 28.92 lower)	LOW	CRITICAL
Back pain score after 2ml injections at 45 minutes (measured with: visual analogue scale; range of scores: 0-100; Better indicated by lower values)												
1 (Saxena 2009)	randomised trials	serious[5]	no serious inconsistency	serious[2]	no serious imprecision	none	50	50	-	MD 44.20 lower (54.93 to 33.47 lower)	LOW	CRITICAL
Back pain score after 2ml injections at 90 minutes (measured with: visual analogue scale; range of scores: 0-100; Better indicated by lower values)												
1 (Saxena 2009)	randomised trials	serious[5]	no serious inconsistency	serious[2]	no serious imprecision	none	50	50	-	MD 34.40 lower (45.16 to 23.64 lower)	LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injections	Saline injections	Relative (95% CI)	Absolute		
Treatment effective at relieving back pain (assessed with: women reporting 'very effective' or rather 'effective')												
1 (Lee 2020)	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	no serious imprecision	none	266/407 (65.4%)	160/403 (39.7%)	RR 1.65 (1.43 to 1.89)	258 more per 1000 (from 171 more to 353 more)	MODERATE	CRITICAL
Caesarean birth												
9 (Ader 1990; Bahasadri 2006; Farag 2015; Fouly 2018; Kushtagi 2009; Lee 2020; Martensson 1999; Rai 2013; Trolle 1991)	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	serious[3]	none	130/1236 (10.5%)	115/1157 (9.9%)	RR 1.07 (0.85 to 1.36)	7 more per 1000 (from 15 fewer to 36 more)	LOW	CRITICAL
Caesarean birth - Dose: 0.4ml												
6 (Ader 1990; Farag 2015; Lee 2020; Martensson 1999; Rai 2013; Trolle 1991)	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	serious[3]	none	117/938 (12.5%)	105/892 (11.8%)	RR 1.06 (0.83 to 1.36)	7 more per 1000 (from 20 fewer to 42 more)	LOW	CRITICAL
Caesarean birth – Dose: 0.5ml												
2 (Bahasadri 2006; Kushtagi 2009)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	very serious[4]	none	6/100 (6%)	9/100 (9%)	RR 0.67 (0.25 to 1.8)	30 fewer per 1000 (from 68 fewer to 72 more)	VERY LOW	CRITICAL
Caesarean birth – Dose: 1ml												
1 (Fouly 2018)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	very serious[4]	none	6/165 (3.6%)	1/165 (0.61%)	RR 6 (0.73 to 49.29)	30 more per 1000 (from 2 fewer to 293 more)	VERY LOW	CRITICAL
Caesarean birth – Dose: 2ml												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injections	Saline injections	Relative (95% CI)	Absolute		
1 (Martensson 1999)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	very serious[4]	none	1/33 (3%)	1/33 (3%)	RR 1 (0.07 to 15.33)	0 fewer per 1000 (from 28 fewer to 434 more)	VERY LOW	CRITICAL
Caesarean birth												
2 (Saxena 2009; Wiruchpongsanon 2006)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	very serious[4]	none	2/75 (2.7%)	3/75 (4%)	Peto OR 0.66 (0.11 to 3.92)	13 fewer per 1000 (from 35 fewer to 100 more)	VERY LOW	CRITICAL
Caesarean birth – Dose: 0.4ml												
1 (Wiruchpongsanon 2006)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	0/25 (0%)	3/25 (12%)	Peto OR 0.12 (0.01 to 1.25)	104 fewer per 1000 (from 119 fewer to 26 more)	VERY LOW	CRITICAL
Caesarean birth – Dose: 2ml												
1 (Saxena 2009)	randomised trials	serious[11]	no serious inconsistency	serious[2]	very serious[4]	none	2/50 (4%)	0/50 (0%)	Peto OR 7.54 (0.47 to 122.28)	40 more per 1000 (from 30 fewer to 110 more)	VERY LOW	CRITICAL
Instrumental vaginal birth												
7 (Ader 1990; Farag 2015; Kushtagi 2009; Lee 2020; Martensson 1999; Rai 2013; Trolle 1991)	randomised trials	serious[7]	no serious inconsistency	serious[2]	serious[3]	none	166/1021 (16.3%)	151/942 (16%)	RR 1.05 (0.86 to 1.28)	8 more per 1000 (from 22 fewer to 45 more)	VERY LOW	CRITICAL
Instrumental vaginal birth – Dose: 0.4ml												
6 (Ader 1990; Farag 2015; Lee 2020; Martensson 1999; Rai 2013; Trolle 1991)	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	serious[3]	none	163/938 (17.4%)	146/892 (16.4%)	RR 1.07 (0.88 to 1.31)	11 more per 1000 (from 20	LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injections	Saline injections	Relative (95% CI)	Absolute		
										fewer to 51 more)		
Instrumental vaginal birth – Dose: 0.5ml												
1 (Kushtagi 2009)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	very serious[4]	none	2/50 (4%)	5/50 (10%)	RR 0.4 (0.08 to 1.97)	60 fewer per 1000 (from 92 fewer to 97 more)	VERY LOW	CRITICAL
Instrumental vaginal birth – Dose: 2ml												
1 (Martensson 1999)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	very serious[4]	none	1/33 (3%)	1/33 (3%)	RR 1 (0.07 to 15.33)	0 fewer per 1000 (from 28 fewer to 434 more)	VERY LOW	CRITICAL
Instrumental vaginal birth – Dose: 0.4ml												
1 (Wiruchpongsanon 2006)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	3/25 (12%)	0/25 (0%)	Peto OR 8.05 (0.8 to 81.12)	120 more per 1000 (from 20 fewer to 260 more)	VERY LOW	CRITICAL
Instrumental vaginal birth – Dose: 0.5ml												
1 (Bahasadri 2006)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	very serious[12]	none	0/50 (0%)	0/50 (0%)	RD 0.00 (-0.04 to 0.04)	0 fewer per 1000 (from 40 fewer to 40 more)	VERY LOW	CRITICAL
Spontaneous vaginal birth												
4 (Farag 2015; Fouly 2018; Kushtagi 2009; Lee 2020)	randomised trials	serious[7]	no serious inconsistency	serious[2]	no serious imprecision	none	574/835 (68.7%)	569/802 (70.9%)	RR 0.97 (0.91 to 1.03)	21 fewer per 1000 (from 64 fewer to 21 more)	LOW	CRITICAL
Spontaneous vaginal birth – Dose: 0.4ml												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injections	Saline injections	Relative (95% CI)	Absolute		
2 (Farag 2015; Lee 2020)	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	no serious imprecision	none	371/620 (59.8%)	366/587 (62.4%)	RR 0.95 (0.87 to 1.04)	31 fewer per 1000 (from 81 fewer to 25 more)	MODERATE	CRITICAL
Spontaneous vaginal birth – Dose: 0.5ml												
1 (Kushtagi 2009)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	serious[3]	none	44/50 (88%)	39/50 (78%)	RR 1.13 (0.94 to 1.35)	101 more per 1000 (from 47 fewer to 273 more)	LOW	CRITICAL
Spontaneous vaginal birth – Dose: 1ml												
1 (Fouly 2018)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none	159/165 (96.4%)	164/165 (99.4%)	RR 0.97 (0.94 to 1)	30 fewer per 1000 (from 60 fewer to 0 more)	MODERATE	CRITICAL
Women satisfied with treatment												
1 (Lee 2020)	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	serious[3]	none	277/407 (68.1%)	198/403 (49.1%)	RR 1.39 (1.23 to 1.56)	192 more per 1000 (from 113 more to 275 more)	LOW	IMPORTANT
Would use the same technique in future pregnancy												
4 (Lee 2020; Martensson 1999; Rai 2013; Trolle 1991)	randomised trials	serious[7]	very serious[9]	no serious indirectness	no serious imprecision	none	482/726 (66.4%)	314/685 (45.8%)	RR 1.43 (1.3 to 1.58)	197 more per 1000 (from 138 more to 266 more)	VERY LOW	IMPORTANT
Would use the same technique in future pregnancy (high income only)												
3 (Lee 2020; Martensson 1999; Trolle 1991)	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	no serious imprecision	none	382/606 (63%)	309/596 (51.8%)	RR 1.22 (1.10 to 1.34)	114 more per 1000 (from 52	MODERATE	IMPORTANT

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injections	Saline injections	Relative (95% CI)	Absolute		
										more to 176 more)		
Would use the same technique in future pregnancy – Dose: 0.4ml												
4 (Lee 2020; Martensson 1999; Rai 2013; Trolle 1991)	randomised trials	serious[7]	very serious[9]	no serious indirectness	no serious imprecision	none	457/695 (65.8%)	314/685 (45.8%)	RR 1.44 (1.3 to 1.59)	202 more per 1000 (from 138 more to 270 more)	VERY LOW	IMPORTANT
Would use the same technique in future pregnancy – Dose 0.4ml (high income only)												
3 (Lee 2020; Martensson 1999; Trolle 1991)	randomised trials	serious[7]	serious inconsistency[13]	no serious indirectness	no serious imprecision	none	357/575 (62.1%)	291/565 (51.5%)	RR 1.21 (1.09 to 1.34)	108 more per 1000 (from 46 more to 175 more)	LOW	IMPORTANT
Would use the same technique in future pregnancy - Dose: 2ml (high income)												
1 (Martensson 1999)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	serious[3]	none	25/31 (80.6%)	18/31 (58.1%)	RR 1.39 (0.98 to 1.96)	226 more per 1000 (from 12 fewer to 557 more)	LOW	IMPORTANT
Use of rescue epidural analgesia - Dose: 0.4ml												
1 (Ader 1990)	randomised trials	very serious[11]	no serious inconsistency	serious[2]	no serious imprecision	none	0/24 (0%)	0/21 (0%)	RD 0.00 (-0.08 to 0.08)	0 more per 1000 (from 80 fewer to 80 more)	VERY LOW	IMPORTANT
Use of rescue epidural analgesia - Dose: 0.4ml												
1 (Lee 2020)	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	no serious imprecision	none	215/580 (37.1%)	221/567 (39%)	RR 0.95 (0.82 to 1.1)	19 fewer per 1000 (from 70 fewer to 39 more)	MODERATE	IMPORTANT
Use of rescue IM/IV analgesia												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injections	Saline injections	Relative (95% CI)	Absolute		
1 (Lee 2020)	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	serious[3]	none	102/580 (17.6%)	98/567 (17.3%)	RR 1.02 (0.79 to 1.31)	3 more per 1000 (from 36 fewer to 54 more)	LOW	IMPORTANT
Use of rescue Entonox analgesia												
2 (Lee 2020; Trolle 1991)	randomised trials	serious[7]	no serious inconsistency	serious[2]	no serious imprecision	none	404/721 (56%)	404/698 (57.9%)	RR 0.98 (0.90 to 1.06)	12 fewer per 1000 (from 58 fewer to 35 more)	LOW	IMPORTANT
Use of rescue pethidine analgesia												
2 (Ader 1990; Trolle 1991)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	very serious[4]	none	10/165 (6.1%)	13/152 (8.6%)	RR 0.71 (0.32 to 1.57)	25 fewer per 1000 (from 58 fewer to 49 more)	VERY LOW	IMPORTANT
Use of rescue paracervical block analgesia												
1 (Ader 1990)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	0/24 (0%)	0/21 (0%)	RD 0.00 (-0.08 to 0.08)	0 more per 1000 (from 80 fewer to 80 more)	VERY LOW	IMPORTANT
Use of rescue non-specific analgesia												
1 (Kushtagi 2009)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	very serious[4]	none	1/50 (2%)	2/50 (4%)	RR 0.5 (0.05 to 5.34)	20 fewer per 1000 (from 38 fewer to 174 more)	VERY LOW	IMPORTANT
Neonatal admissions - Dose: 0.4ml												
1 (Rai 2013)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	very serious[14]	none	0/120 (0%)	0/120 (0%)	RD 0.00 (-0.02 to 0.02)	0 fewer per 1000 (from 20	VERY LOW	IMPORTANT

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injections	Saline injections	Relative (95% CI)	Absolute		
										fewer to 20 more)		
Neonatal admissions - Dose: 0.4ml												
1 (Lee 2020)	randomised trials	serious[7]	no serious inconsistency	serious[2]	serious[3]	none	70/580 (12.1%)	49/567 (8.6%)	RR 1.4 (0.99 to 1.97)	35 more per 1000 (from 1 fewer to 84 more)	VERY LOW	IMPORTANT

CI: confidence interval; MD: mean difference; RD: risk difference; RR: risk ratio
1 Very serious risk of bias in the evidence contributing to the outcomes as per RoB assessment in Derry 2012 (systematic review)
2 Population is indirect due to not reporting of risk status or if labour was induced
3 95% CI crosses 1 MID
4 95% CI crosses 2 MIDs
5 Very serious risk of bias in the evidence contributing to the outcomes as per RoB assessment in Derry 2012 (systematic review)
6 95% CI crosses 1 MID (0.5x control group SD: for reduction in back pain 1ml = 0.47 for back pain score pooled 0.6ml and 2ml = 0.93; for back pain score 2ml = 0.81; for back pain score 0.6ml = 1.10)
7 Serious risk of bias in the evidence contributing to the outcomes as per RoB 2
8 Very serious risk of bias in the evidence contributing to the outcomes as per RoB 2
9 Very serious heterogeneity unexplained by subgroup analysis
10 Combined doses from single study with multiple arms
11 Serious risk of bias in the evidence contributing to the outcomes as per RoB assessment in Derry 2012 (systematic review)
12 Sample size <200
13 Serious heterogeneity unexplained by subgroup analysis
14 Sample size between 200 and 400

Table 7: Evidence profile for comparison 4: sterile water injections versus standard care (massage, bath, movement)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injection	Standard care (massage, bath, movement)	Relative (95% CI)	Absolute		
Back pain score after 0.4ml injections during the intervention (measured with: visual analogue scale; range of scores: 0-100; Better indicated by lower values)												
1 (Labrecque 1999)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	10	12	-	MD 47 lower (52.04 to 41.96 lower)	VERY LOW	CRITICAL
Back pain unpleasantness score after 0.4ml injections during the intervention (measured with: visual analogue scale; range of scores: 0-100; Better indicated by lower values)												
1 (Labrecque 1999)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	10	12	-	MD 43 lower (48.87 to 37.13 lower)	VERY LOW	CRITICAL
Caesarean birth												
1 (Labrecque 1999)	randomised trials	serious[3]	no serious inconsistency	serious[2]	very serious[4]	none	0/10 (0%)	1/12 (8.3%)	Peto OR 0.16 (0 to 8.19)	69 fewer per 1000 (from 83 fewer to 343 more)	VERY LOW	CRITICAL
Satisfaction with birth (measured with: Labour and delivery satisfaction index; range of scores: 1-6; Better indicated by lower values)												
1 (Labrecque 1999)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[5]	none	10	12	-	MD 0.3 higher (0.17 lower to 0.77 higher)	VERY LOW	IMPORTANT
Use of rescue epidural analgesia												
1 (Labrecque 1999)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	very serious[4]	none	6/10 (60%)	4/12 (33.3%)	RR 1.8 (0.7 to 4.64)	267 more per 1000 (from 100 fewer to 1000 more)	VERY LOW	IMPORTANT

CI: confidence interval; MD: mean difference; OR: odds ratio; RR: risk ratio
1 Very serious risk of bias in the evidence contributing to the outcomes as per RoB 2
2 Population is indirect due to not reporting if labour was induced, and not reporting proportion of women between 36-37 weeks gestation, or whether women received IM/IV analgesia before randomisation)
3 Serious risk of bias in the evidence contributing to the outcomes as per RoB 2
4 95% CI crosses 2 MIDs
5 95% CI crosses 1 MID (0.5x control group SD: for satisfaction with birth = 0.35)

Table 8: Evidence profile for comparison 5: sterile water injections versus TENS

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injection	TENS	Relative (95% CI)	Absolute		
Back pain score after 0.4 ml injections during the intervention (measured with: visual analogue scale; range of scores: 0-100; Better indicated by lower values)												
1 (Labrecque 1999)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	10	12	-	MD 34 lower (39.04 to 28.96 lower)	VERY LOW	CRITICAL
Back pain unpleasantness score after 0.4ml injections during the intervention (measured with: visual analogue scale; range of scores: 0-100; Better indicated by lower values)												
1 (Labrecque 1999)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	10	12	-	MD 48 lower (53.87 to 42.13 lower)	VERY LOW	CRITICAL
Caesarean birth												
1 (Labrecque 1999)	randomised trials	serious[3]	no serious inconsistency	serious[2]	serious[4]	none	0/10 (0%)	4/12 (33.3%)	Peto OR 0.12 (0.01 to 0.99)	277 fewer per 1000 (from 2 fewer to 328 fewer)	VERY LOW	CRITICAL
Satisfaction with birth (measured with: Labour and delivery satisfaction index; range of scores: 1-6; Better indicated by lower values)												
1 (Labrecque 1999)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	very serious[5]	none	10	12	-	MD 0.1 higher (0.24 lower to 0.44 higher)	VERY LOW	IMPORTANT
Use of rescue epidural analgesia												
1 (Labrecque 1999)	randomised trials	very serious[1]	no serious inconsistency	serious[3]	very serious[6]	none	6/10 (60%)	9/12 (75%)	RR 0.8 (0.44 to 1.46)	150 fewer per 1000 (from 420 fewer to 345 more)	VERY LOW	IMPORTANT

CI: confidence interval; MD: mean difference; OR: odds ratio; RR: risk ratio; TENS: transcutaneous electrical nerve stimulation
1 Very serious risk of bias in the evidence contributing to the outcomes as per RoB 2
2 Population is indirect due to not reporting if labour was induced, and not reporting proportion of women between 36-37 weeks gestation, or whether women received IM/IV analgesia before randomisation)
3 Serious risk of bias in the evidence contributing to the outcomes as per RoB 2
4 95% CI crosses 1 MID
5 95% CI crosses 2 MIDs (0.5x control group SD: for satisfaction with birth= 0.20)
6 95% CI crosses 2 MIDs

Table 9: Evidence profile for comparison 6: sterile water injections high dose (0.4ml) versus sterile water injections low dose (0.1ml)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injection high dose (0.4ml)	Sterile water injections low dose (0.1ml)	Relative (95% CI)	Absolute		
Reduction in baseline greater than 30% in back pain after injections at 10 minutes (measured with: visual analogue scale)												
1 (Lee 2013)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	128/147 (87.1%)	96/138 (69.6%)	RR 1.25 (1.1 to 1.42)	174 more per 1000 (from 70 more to 292 more)	VERY LOW	CRITICAL
Reduction in baseline greater than 50% in back pain after injections at 10 minutes (measured with: visual analogue scale)												
1 (Lee 2013)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	107/147 (72.8%)	75/138 (54.3%)	RR 1.34 (1.12 to 1.61)	185 more per 1000 (from 65 more to 332 more)	VERY LOW	CRITICAL
Reduction in baseline greater than 30% in back pain after injections at 30 minutes (measured with: visual analogue scale)												
1 (Lee 2013)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	117/139 (84.2%)	93/136 (68.4%)	RR 1.23 (1.08 to 1.41)	157 more per 1000 (from 55 more to 280 more)	VERY LOW	CRITICAL
Reduction in baseline greater than 50% in back pain after injections at 30 minutes (measured with: visual analogue scale)												
1 (Lee 2013)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	102/139 (73.4%)	68/136 (50%)	RR 1.47 (1.21 to 1.78)	235 more per 1000 (from 105 more to 390 more)	VERY LOW	CRITICAL
Reduction in baseline greater than 30% in back pain after injections at 60 minutes (measured with: visual analogue scale)												
1 (Lee 2013)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	95/125 (76%)	69/108 (63.9%)	RR 1.19 (1 to 1.41)	121 more per 1000 (from 0 more to 262 more)	VERY LOW	CRITICAL
Reduction in baseline greater than 50% in back pain after injections at 60 minutes (measured with: visual analogue scale)												
1 (Lee 2013)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	75/125 (60%)	48/108 (44.4%)	RR 1.35 (1.05 to 1.74)	156 more per 1000 (from 22 more to 329 more)	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injection high dose (0.4ml)	Sterile water injections low dose (0.1ml)	Relative (95% CI)	Absolute		
Reduction in baseline greater than 30% in back pain after injections at 90 minutes (measured with: visual analogue scale)												
1 (Lee 2013)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	64/100 (64%)	43/82 (52.4%)	RR 1.22 (0.95 to 1.57)	115 more per 1000 (from 26 fewer to 299 more)	VERY LOW	CRITICAL
Reduction in baseline greater than 50% in back pain after injections at 90 minutes (measured with: visual analogue scale)												
1 (Lee 2013)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	49/100 (49%)	31/82 (37.8%)	RR 1.3 (0.92 to 1.82)	113 more per 1000 (from 30 fewer to 310 more)	VERY LOW	CRITICAL
Reduction in baseline greater than 30% in back pain after injections at 120 minutes (measured with: visual analogue scale)												
1 (Lee 2013)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	45/83 (54.2%)	35/70 (50%)	RR 1.08 (0.8 to 1.47)	40 more per 1000 (from 100 fewer to 235 more)	VERY LOW	CRITICAL
Reduction in baseline greater than 50% in back pain after injections at 120 minutes (measured with: visual analogue scale)												
1 (Lee 2013)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	very serious[4]	none	36/83 (43.4%)	27/70 (38.6%)	RR 1.12 (0.77 to 1.65)	46 more per 1000 (from 89 fewer to 251 more)	VERY LOW	CRITICAL
Caesarean birth												
1 (Lee 2013)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	very serious[4]	none	27/158 (17.1%)	23/147 (15.6%)	RR 1.09 (0.66 to 1.82)	14 more per 1000 (from 53 fewer to 128 more)	VERY LOW	CRITICAL
Instrumental vaginal birth												
1 (Lee 2013)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	very serious[4]	none	33/158 (20.9%)	28/147 (19%)	RR 1.1 (0.7 to 1.72)	19 more per 1000 (from 57 fewer to 137 more)	VERY LOW	CRITICAL
Spontaneous vaginal birth												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injection high dose (0.4ml)	Sterile water injections low dose (0.1ml)	Relative (95% CI)	Absolute		
1 (Lee 2013)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none	98/158 (62%)	96/147 (65.3%)	RR 0.95 (0.8 to 1.13)	33 fewer per 1000 (from 131 fewer to 85 more)	MODERATE	CRITICAL
Women who were 'very satisfied' or 'satisfied' with the treatment												
1 (Lee 2013)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	97/129 (75.2%)	88/133 (66.2%)	RR 1.14 (0.97 to 1.33)	93 more per 1000 (from 20 fewer to 218 more)	VERY LOW	IMPORTANT
Women would use the same treatment again												
1 (Lee 2013)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	89/126 (70.6%)	91/136 (66.9%)	RR 1.06 (0.9 to 1.24)	40 more per 1000 (from 67 fewer to 161 more)	VERY LOW	IMPORTANT
Use of rescue epidural analgesia												
1 (Lee 2013)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	70/157 (44.6%)	62/148 (41.9%)	RR 1.06 (0.82 to 1.38)	25 more per 1000 (from 75 fewer to 159 more)	VERY LOW	IMPORTANT
Use of rescue IM/IV analgesia												
1 (Lee 2013)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	very serious[4]	none	17/157 (10.8%)	13/148 (8.8%)	RR 1.23 (0.62 to 2.45)	20 more per 1000 (from 33 fewer to 127 more)	VERY LOW	IMPORTANT

CI: confidence interval; IM: intramuscular; IV:intravenous; RR: risk ratio
1 Very serious risk of bias in the evidence contributing to the outcomes as per RoB 2
2 Population is indirect due to not reporting if labour was induced
3 95% CI crosses 1 MID
4 95% CI crosses 2 MIDs

Table 10: Evidence profile for comparison 7: sterile water injections versus acupuncture

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injection	Acupuncture	Relative (95% CI)	Absolute		
General labour pain score after 2ml injections at 30 minutes (measured with: visual analogue scale; range of scores: 0-100; Better indicated by lower values)												
1 (Martensson 2008)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	66	62	-	MD 17.4 lower (25.55 to 9.25 lower)	VERY LOW	CRITICAL
General labour pain score after 2ml injections at 60 minutes (measured with: visual analogue scale; range of scores: 0-100; Better indicated by lower values)												
1 (Martensson 2008)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	57	56	-	MD 19.5 lower (28.5 to 10.5 lower)	VERY LOW	CRITICAL
General labour pain score after 2ml injections at 90 minutes (measured with: visual analogue scale; range of scores: 0-100; Better indicated by lower values)												
1 (Martensson 2008)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	45	41	-	MD 21.5 lower (31.06 to 11.94 lower)	VERY LOW	CRITICAL
General labour pain score after 2ml injections at 120 minutes (measured with: visual analogue scale; range of scores: 0-100; Better indicated by lower values)												
1 (Martensson 2008)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	38	34	-	MD 18 lower (28.95 to 7.05 lower)	VERY LOW	CRITICAL
General labour pain score after 2ml injections at 150 minutes (measured with: visual analogue scale; range of scores: 0-100; Better indicated by lower values)												
1 (Martensson 2008)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	27	22	-	MD 13.4 lower (26.79 to 0.01 lower)	VERY LOW	CRITICAL
General labour pain score after 2ml injections at 180 minutes (measured with: visual analogue scale; range of scores: 0-100; Better indicated by lower values)												
1 (Martensson 2008)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	24	17	-	MD 16.8 lower (30.65 to 2.95 lower)	VERY LOW	CRITICAL
Caesarean birth												
1 (Martensson 2008)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	very serious[4]	none	4/66 (6.1%)	5/62 (8.1%)	RR 0.75 (0.21 to 2.67)	20 fewer per 1000 (from 64 fewer to 135 more)	VERY LOW	CRITICAL
Spontaneous vaginal birth												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sterile water injection	Acupuncture	Relative (95% CI)	Absolute		
1 (Martensson 2008)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none	59/66 (89.4%)	51/62 (82.3%)	RR 1.09 (0.94 to 1.25)	74 more per 1000 (from 49 fewer to 206 more)	MODERATE	CRITICAL
Instrumental vaginal birth												
1 (Martensson 2008)	randomised trials	no serious risk of bias	no serious inconsistency	serious[2]	very serious[4]	none	3/66 (4.5%)	6/62 (9.7%)	RR 0.47 (0.12 to 1.8)	51 fewer per 1000 (from 85 fewer to 77 more)	VERY LOW	CRITICAL
Use of rescue epidural analgesia												
1 (Martensson 2008)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	very serious[4]	none	18/66 (27.3%)	17/62 (27.4%)	RR 0.99 (0.57 to 1.75)	17 fewer per 1000 (from 31 fewer to 131 more)	VERY LOW	IMPORTANT
Use of rescue paracervical nerve block analgesia												
1 (Martensson 2008)	randomised trials	very serious[1]	no serious inconsistency	serious[2]	very serious[4]	none	1/66 (1.5%)	2/62 (3.2%)	RR 0.47 (0.04 to 5.05)	59 more per 1000 (from 13 fewer to 401 more)	VERY LOW	IMPORTANT

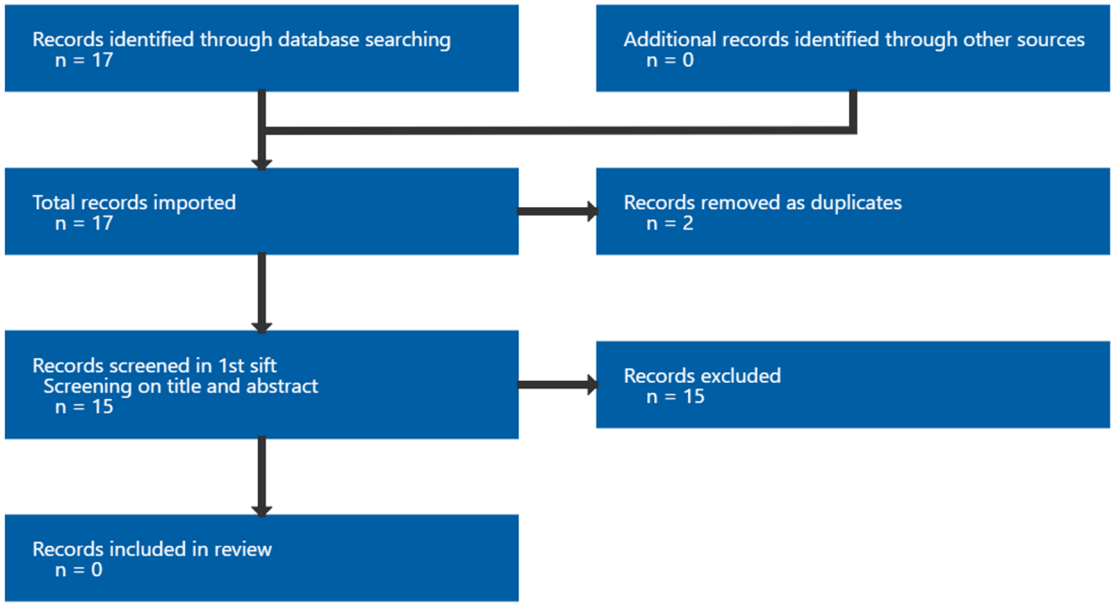
CI: confidence interval; MD: mean difference; RR: risk ratio
1 Very serious risk of bias in the evidence contributing to the outcomes as per RoB 2
2 Population is indirect due to not reporting of risk status
3 95% CI crosses 1 MID (0.5x control group SD: for general labour pain score= 9.10)
4 95% CI crosses 2 MIDs

Appendix G Economic evidence study selection

Economic evidence for review question: What is the effectiveness of injected water papules for pain relief during labour?

No economic evidence was identified which was applicable to this review question.

Figure 17: Study selection flow chart



Appendix H Economic evidence tables

Economic evidence tables for review question: What is the effectiveness of injected water papules for pain relief during labour?

No evidence was identified which was applicable to this review question.

Appendix I Economic model

Economic model for review question: What is the effectiveness of injected water papules for pain relief during labour?

No economic analysis was conducted for this review question.

Appendix J Excluded studies

Excluded studies for review question: What is the effectiveness of injected water papules for pain relief during labour?

Excluded effectiveness studies

Table 11: Excluded studies and reasons for their exclusion

Study	Reason
Ader, L. (1991) Injections of sterile water for labour pain. Nursing times 87: 53	- Study design - not a randomised controlled trial Commentary on the systematic review by Ader 1990
Ader, L.; Hansson, B.; Wallin, G. (1990) Parturition pain treated by intracutaneous injections of sterile water. Pain 41(2): 133-138	- Included as part of a systematic review See Derry 2012
Anderson, F. W. J. and Johnson, C. T. (2005) Complementary and alternative medicine in obstetrics. International Journal of Gynecology and Obstetrics 91(2): 116-124	- Study design - not a systematic review A narrative description of the literature. No new additional studies matching our PICO identified
Bahasadri, S., Ahmadi-Abhari, S., Dehghani-Nik, M. et al. (2006) Subcutaneous sterile water injection for labour pain: a randomised controlled trial. Australian & New Zealand journal of obstetrics & gynaecology 46(2): 102-106	- Included as part of a systematic review See Derry 2012
Balsbaugh, T. A. (1999) Cutaneous injections of sterile water for the relief of labor pain. Journal of family practice 48(10): 746-747	- Study design - not a randomised controlled trial Commentary and summary of randomised controlled trial by Martensson 1999
Bergmann, R. (1997) Pain management: an alternative to sterile water injections?. Jordmorbladet: 11-13	- Article not in English
Ctri (2019) To study labour analgesia with drotavarin and water block. http://www.who.int/trialsearch/Trial2.aspx?TrialID=CTRI/2019/09/021125	- Clinical trial entry only Protocol checked and comparator does not meet PICO as it is pharmacological, therefore full results not retrieved
Cui, J. Z., Geng, Z. S., Zhang, Y. H. et al. (2016) Effects of intracutaneous injections of sterile water in patients with acute low back pain: a randomized, controlled, clinical trial. Brazilian journal of medical and biological research = revista brasileira de pesquisas medicas e biologicas 49(3)	- Population not in PICO Population not pregnant women in labour
Dahl, V. and Aarnes, T. (1991) Sterile water papulae for analgesia during labor. Tidsskrift for den Norske laegeforening 111(12): 1484-1487	- Article not in English
Euctr, G. B. (2015) Impact on Caesarean Section Rates Following Injections of Sterile Water. http://www.who.int/trialsearch/Trial2.aspx?TrialID=EUCTR2014-004343-12-GB	- Clinical trial entry only Full published results under Lee 2020 (ID 7401856)

Study	Reason
Fogarty, V. (2008) Intradermal sterile water injections for the relief of low back pain in labour-A systematic review of the literature. Women and birth 21(4): 157-163	- Study design - More recent systematic reviews with all included studies have been included
Hosseini, L. (2010) The effects of subcutaneous injection of sterile water on labor pain. Journal of maternal-fetal & neonatal medicine 23(s1): 614	- Conference abstract
Hosseini, L.; Najar, S.; Haghighizadeh, M. H. (2010) Effect of Subcutaneous Injection of Sterile Water on Labor Pain, Type of Labor, and Satisfaction with Pain Management in Nulliparous Women. HAYAT 16(1): 41-48	- Article not in English
Huntley, Alyson L.; Coon, Joanna Thompson; Ernst, Edzard (2004) Complementary and alternative medicine for labor pain: a systematic review. American journal of obstetrics and gynecology 191(1): 36-44	- Intervention not in PICO Systematic review, most of the included studies do not meet the intervention in our PICO. The studies that do meet the PICO have already been included
Hutton, E. K., Kasperink, M., Rutten, M. et al. (2009) Sterile water injection for labour pain: a systematic review and meta-analysis of randomised controlled trials. BJOG : an international journal of obstetrics and gynaecology 116(9): 1158-66	- Systematic review - more recent systematic review available Derry 2012 is a more recent Cochrane review than Hutton 2009 with almost all the same included studies. Derry 2012 has been included, and further additional references included from Hutton 2009
Irct20170924036365N (2019) effect of intra dermal and sub dermal injection of sterile water on active labor pain. http://www.who.int/trialsearch/Trial2.aspx?TrialID=IRCT20170924036365N2	- Clinical trial entry only Full published results assessed under Almassinokiani 2020 (ID 7401815)
Irct20180128038535N (2018) The effect of subcutaneous and intracutaneous injection of distilled sterilized water and normal saline on the severity of childbirth pain. http://www.who.int/trialsearch/Trial2.aspx?TrialID=IRCT20180128038535N1	- Clinical trial entry only For published results decision see Rezaie 2019 (ID 7401882)
Irct20181023041427N (2018) Effect of subcutaneous sterile water injection on back pain of Women with Active Phase of Labor. http://www.who.int/trialsearch/Trial2.aspx?TrialID=IRCT20181023041427N1	- Clinical trial entry only Unable to locate full published results
Jones, L., Othman, M., Dowswell, T. et al. (2012) Pain management for women in labour: an overview of systematic reviews. Cochrane Database of Systematic Reviews	- Intervention not in PICO Systematic review with most of the included studies not meeting the intervention criteria as specified in our PICO. Included studies meeting the criteria have been checked and no additional randomised controlled studies were identified

Study	Reason
Kushtagi, P. and Bhanu, B. T. (2009) Effectiveness of subcutaneous injection of sterile water to the lower back for pain relief in labor. Acta obstetricia et gynecologica Scandinavica 88(2): 231-233	- Included as part of a systematic review See Derry 2012
Lee, N., Coxeter, P., Beckmann, M. et al. (2011) A randomised non-inferiority controlled trial of a single versus a four intradermal sterile water injection technique for relief of continuous lower back pain during labour. BMC pregnancy and childbirth 11: 21	- Protocol entry only Full published results assessed under Lee 2013 (ID 7401861)
Lee, N., Leiser, M.B., Halter-Wehrli, M.Y. et al. (2022) Two versus four sterile water injections for managing back pain in labour. Women and Birth 35(supplement1): 8	- Conference abstract
Lee, N., Martensson, L. B., Homer, C. et al. (2013) Impact on Caesarean section rates following injections of sterile water (ICARIS): a multicentre randomised controlled trial. BMC pregnancy and childbirth 13	- Protocol entry only Full published results assessed under Lee 2020 (ID 7401856)
Martensson, L.; Nyberg, K.; Wallin, G. (2000) Subcutaneous versus intracutaneous injections of sterile water for labour analgesia: A comparison of perceived pain during administration. British Journal of Obstetrics and Gynaecology 107(10): 1248-1251	- Population not in PICO Women were not pregnant
Martensson, L. and Wallin, G. (1999) Labour pain treated with cutaneous injections of sterile water: a randomised controlled trial. British journal of obstetrics and gynaecology 106(7): 633-7	- Included as part of a systematic review See Derry 2012
Martensson, Lena B., Hutton, Eileen K., Lee, Nigel et al. (2018) Sterile water injections for childbirth pain: An evidenced based guide to practice. Women and birth : journal of the Australian College of Midwives 31(5): 380-385	- Study design - not a systematic review A narrative description of current literature. 2 additional studies identified and have been included (Rai 2013, Farag 2015)
Martensson, Lena B, Gunnarsson, Britt-Marie, Karlsson, Sandra et al. (2022) Effect of topical local anaesthesia on injection pain associated with administration of sterile water injections - a randomized controlled trial. BMC anesthesiology 22(1): 35	- Population not in PICO Not pregnant women
Martensson, Lena and Wallin, Gunnar (2008) Sterile water injections as treatment for low-back pain during labour: A review. Australian and New Zealand Journal of Obstetrics and Gynaecology 48(4): 369-374	- Study design - not a systematic review Not a systematic review but a narrative description of literature. No additional new studies matching our PICO were identified
Nct (2012) Intracutaneous Sterile Water Injections. https://clinicaltrials.gov/show/NCT01513447	- Clinical trial entry only Full results not available as study stopped early due to not recruiting enough eligible participants
Nct (2014) EMLA and Sterile Water Injections - Pain From Injections. https://clinicaltrials.gov/show/NCT02213185	- Clinical trial entry only Protocol checked and intervention does not meet the PICO so full published results not looked for
Nct (2016) Sterile Water Injections For Pain Relief İn Labor. https://clinicaltrials.gov/show/NCT02697994	- Clinical trial entry only Full published results assessed under Koyucu 2018 (ID 7401808)

Study	Reason
Nct (2016) Subcutaneous Sterile Water Injection for Relief of Low Back Pain. https://clinicaltrials.gov/show/NCT02813330	- Clinical trial entry only Full published results assessed under Fouly 2018 (ID 7401840)
Saxena, K. N.; Nischal, H.; Batra, S. (2009) Intracutaneous injections of sterile water over the sacrum for labour analgesia. Indian journal of anaesthesia 53(2): 169-173	- Included as part of a systematic review See Derry 2012
Simkin, Penny P. and O'Hara, MaryAnn (2002) Nonpharmacologic relief of pain during labor: Systematic reviews of five methods. American Journal of Obstetrics and Gynecology 186(5suppl): S131-S159	- Intervention not in PICO Most of the included studies do not match the intervention in our PICO. The studies that do have already been included
Simkin, Penny and Bolding, April (2004) Update on nonpharmacologic approaches to relieve labor pain and prevent suffering. Journal of Midwifery and Women's Health 49(6): 489-504	- Study design - not a systematic review Narrative review of the literature. No new additional studies meeting our PICO were identified
Tournaire, M. and Theau-Yonneau, A. (2007) Complementary and alternative approaches to pain relief during labor. Evidence-based complementary and alternative medicine 4(4): 409-417	- Study design - not a systematic review Not a systematic review but a narrative description of literature. Most of the studies described do not match our intervention. Those that do have already been included
Trolle, B., Moller, M., Kronborg, H. et al. (1991) The effect of sterile water blocks on low back labor pain. American Journal of Obstetrics and Gynecology 164(5i): 1277-1281	- Included as part of a systematic review See Derry 2012
Trolle, G. B.; Hvidman, L. E.; Guldholt, I. S. (1986) Lumbar pain in parturient women treated with sterile water injections. Ugeskrift for laeger 148(20): 1200-1202	- Article not in English
Wallin, G.; Martensson, L.; Nikodem, C. (2000) Cutaneous lumbosacral injections of sterile water were more effective than 'placebo' injections for relieving first stage labour pain. Evidence-Based Medicine 5(2): 56	- Study design - not a randomised controlled trial Commentary on Martensson 1999, which has been assessed separately (ID 7401866)
Wiruchpongsanon, P. (2006) Relief of low back labor pain by using intracutaneous injections of sterile water: a randomized clinical trial. Chotmaihet thangphaet [Journal of the Medical Association of Thailand] 89(5): 571-576	- Included as part of a systematic review See Derry 2012

Excluded economic studies

No economic evidence was identified for this review.

Appendix K Research recommendations – full details

Research recommendations for review question: What is the effectiveness of injected water papules for pain relief during labour?

No research recommendations were made for this review question.