

Review Article

Conventional landmark palpation vs. preprocedural ultrasound for neuraxial analgesia and anaesthesia in obstetrics – a systematic review and meta-analysis with trial sequential analyses

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Summary

The aim of this systematic review and meta-analysis was to examine the efficacy, time taken and the safety of neuraxial blockade performed for obstetric patients with the assistance of preprocedural ultrasound, in comparison with the landmark palpation method. The bibliographic databases Central, CINAHL, EMBASE, Global Health, MEDLINE, Scopus and Web of Science were searched from inception to 13 February 2020 for randomised controlled trials that included pregnant women having neuraxial procedures with preprocedural ultrasound as the intervention and conventional landmark palpation as the comparator. For continuous and dichotomous outcomes, respectively, we calculated the mean difference using the inverse-variance method and the risk ratio with the Mantel–Haenszel method. In all, 22 trials with 2462 patients were included. Confirmed by trial sequential analysis, preprocedural ultrasound increased the first-pass success rate by a risk ratio (95%CI) of 1.46 (1.16–1.82), $p = 0.001$ in 13 trials with 1253 patients. No evidence of a difference was found in the total time taken between preprocedural ultrasound and landmark palpation, with a mean difference (95%CI) of 50.1 (–13.7 to 113.94) s, $p = 0.12$ in eight trials with 709 patients. The quality of evidence was graded as low and very low, respectively, for these co-primary outcomes. Sub-group analysis underlined the increased benefit of preprocedural ultrasound for those in whom the neuraxial procedure was predicted to be difficult. Complications, including postpartum back pain and headache, were decreased with preprocedural ultrasound. The adoption of preprocedural ultrasound for neuraxial procedures in obstetrics is recommended and, in the opinion of the authors, should be considered as a standard of care, in view of its potential to increase efficacy and reduce complications without significant prolongation of the total time required.

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Introduction

Neuraxial blockade has become a mainstay of obstetric analgesia and anaesthesia. Conventionally, the appropriate site of needle insertion is located by the palpation of anatomical landmarks. It is recognised that such landmark

palpation methods can be challenging in obstetrics due to a more pronounced lumbar lordosis, soft tissue oedema and the increasing rate of obesity [1]. Further, the physiological changes of pregnancy can predispose to an increased incidence of complications, including dural and vascular

puncture owing, respectively, to rises in cerebrospinal fluid pressure with uterine contraction and venous distension [1,2].

Given the challenges and complications associated with the conduct of neuraxial blockade in obstetrics, the introduction of preprocedural ultrasound could provide additional information to facilitate the procedure. Indeed, in 2008, the National Institute for Health and Care Excellence recommended its use for the placement of epidural catheters [3], but the widespread adoption of preprocedural ultrasound has not followed. In a national survey of obstetric units in the UK, only one in five reported its use for neuraxial analgesia and anaesthesia [4]. It has been suggested that preprocedural ultrasound may result in limited benefit, if any, for those patients without indicators of predicted difficulty [5] and might take longer to perform than landmark palpation [6].

In recent years, a number of meta-analyses and systematic reviews have evaluated the efficacy and safety of preprocedural ultrasound compared with landmark palpation methods in obstetric and non-obstetric patients [7, 8]. It is possible, however, in view of the heterogeneity in their inclusion criteria that the utility of preprocedural ultrasound could be different when examined solely in obstetrics. To date, only a single obstetric meta-analysis, limited by a small number of trials, has been conducted [9] and hence the possibility of a type 2 statistical error cannot be excluded. Moreover, since these systematic reviews have been performed, many trials have been published, potentially adding weight to the available evidence base. None of the previous meta-analyses have investigated the total time taken with preprocedural ultrasound relative to landmark palpation methods. Further, there is a need to examine the influence of the experience of the sonographer and operator as well as the predicted difficulty of the neuraxial procedure.

Our aim was to conduct a systematic review and meta-analysis to examine the efficacy, time taken and the safety of neuraxial blockade performed for obstetric patients with the assistance of preprocedural ultrasound in comparison to the anatomical landmark palpation method. In order to control for the risk of false negative and false positive findings, we used trial sequential analysis with the objective of increasing the reliability and validity of our systematic review.

Methods

We adhered to the recommendations from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses

(PRISMA) [10] and registered the meta-analysis and systematic review in the PROSPERO database.

To find relevant trials for this meta-analysis, a systematic search of the electronic databases, Central, CINAHL, Embase, Global Health, MEDLINE, Scopus and Web of Science, was conducted from inception to 13 February 2020. Controlled text words and vocabulary terms, associated with the main constituents of the review were chosen, including *neuraxial analgesia* or *anaesthesia* and *ultrasound*. Further details of the search strategy can be found in the online Supporting Information, Appendix S1.

After retrieved records were entered into a reference management software program, Rayyan (Qatar Computing Research Institute, 2016, Doha, Qatar), we removed the duplicates and screened the remainder for eligibility. Only randomised controlled trials that: first, included pregnant women having neuraxial procedures, to include combined-spinal epidural, epidural or spinal, with non-automated preprocedural ultrasound as the intervention and conventional landmark palpation as the comparator; and second, had been published in the English language, were considered for inclusion. Two authors (BY and DO) independently screened titles and abstracts of the retrieved records, and the full texts of potentially eligible articles were reviewed. Discrepancies were settled by further deliberation until consensus was achieved or, if needed, involvement of the third author (ND). Moreover, we manually reviewed the references of all included records for hitherto unidentified trials.

Once we had selected all trials to be included, assessment of risk of bias and extraction of data were independently performed by two authors (BY and ND). Discrepancies were settled by further deliberation until consensus was achieved or, if needed, involvement of the second author (DO). The Cochrane Collaboration's tool can be implemented to evaluate for different types of bias, to include selection (random sequence generation and allocation concealment), performance and detection (blinding), attrition (incomplete outcome data) and reporting (selective reporting) bias, and hence evaluates the methodological quality of trials [11]. Continuous outcomes were extracted as means and standard deviations. In cases where the mean and the standard deviation had not been reported, we followed recommendations from the Cochrane Collaboration. The mean was approximated to be equivalent to the median, and the standard deviation to the interquartile range/1.35 or the range/4 [12]. Dichotomous outcomes were extracted as numbers or incidence. Data presented in graphical rather than numerical format were

extracted with a plot digitising software program, Plot Digitizer (Version 2.1; Free Software Foundation, Boston, USA). In the event that we required further information on trial methodology or data, the respective authors were contacted up to three times in order to request this.

Characteristics extracted from the trials included the following: the sample size and number of patients in each study arm; the indication for the neuraxial procedure; the nature of the neuraxial technique; the experience of the sonographer and operator; and the predicted difficulty of the neuraxial procedure. Our co-primary outcomes were the first-pass success rate and the total time taken for the identification of the needle insertion point and the performance of the neuraxial procedure. For the purposes of this systematic review, a 'needle redirection' was defined as the backward followed by the forward movement of the needle without removing it from the skin; 'skin puncture' referred to the complete withdrawal of the needle from the skin and subsequent re-insertion; and 'first-pass' was a single skin puncture with no needle redirections. Secondary outcomes included: first intervertebral space success rate; first skin puncture success rate; number of attempted intervertebral spaces; need to attempt more than one intervertebral space; number of skin punctures; need for three or more skin punctures; number of needle redirections; need for three or more needle redirections; total number of skin punctures and needle redirections; need for three or more skin punctures and needle redirections; preprocedural predicted ultrasound distance compared with real needle to target distance; number of attempts required to pass the epidural catheter; need to call for help; time taken for identification of exact point of needle insertion; time taken for performance of neuraxial procedure; technical inability to site neuraxial block; incidence of asymmetrical or patchy neuraxial blockade; failure rate of analgesia or anaesthesia after neuraxial injection; rate of inadequate dermatomal level of blockade; need for epidural top up before skin incision, supplemental analgesia or conversion to general anaesthesia; incidence of paraesthesia, 'bloody tap' or vascular cannulation, dural puncture, post-dural puncture headache, postpartum headache, postpartum back pain and neurological sequelae; need for epidural blood patch; patient-reported pain during performance of neuraxial procedure and in labour or caesarean section; and patient satisfaction.

After transferring the data from a standardised data collection form in Microsoft® Excel (Microsoft Corp, Redmond, WA, USA) to Review Manager (Version 5.3; The Nordic Cochrane Centre, Copenhagen, Denmark), we only conducted meta-analysis for an outcome if it was reported

by two or more randomised controlled trials. Statistical heterogeneity, I^2 , due to clinical or methodological diversity, was calculated for each outcome with predefined thresholds for low (25–49%), moderate (50–74%) and high (more than or equal to 75%) levels [13]. If the heterogeneity was low, we assumed that the interventional true effect did not differ between trials and the fixed effect model represented the best estimate of the effect of the intervention. Should the heterogeneity be moderate or high, we assumed that the interventional true effect did differ between trials, and selected the DerSimonian and Laird random effects model. For continuous outcomes, the inverse-variance method was used, where the weight specified to each trial is the inverse of the effect estimate variance, leading to the calculation of a weighted mean difference (95%CI). For dichotomous outcomes, the Mantel–Haenszel method was used, resulting in the calculation of a risk ratio (95%CI). All statistical tests were two-tailed and the level of statistical significance was set at 5%. To investigate statistical heterogeneity in regard to our co-primary outcomes, we undertook prespecified subgroup analyses for: the experience of the sonographer; experience of the operator; and the predicted difficulty of the neuraxial procedure.

For each outcome, the quality of evidence was rated for risk of bias, inconsistency, indirectness, imprecision and publication bias, resulting in a summary grading of the quality of evidence for all outcomes with reference to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system [14]. We evaluated the likelihood risk of publication bias by performing Duval and Tweedie's trim and fill test, and Egger's linear regression test, using Comprehensive Meta-Analysis (Version 3.3; Biostat, New Jersey, USA).

Last, we performed trial sequential analysis with TSA Viewer (Version 0.9.5.10 Beta; Copenhagen Trial Unit, Copenhagen, Denmark). In cumulative meta-analysis, adjusted significance testing accounts for the strength of the available evidence and controls for the risk of type 1 and type 2 statistical errors during repeated significance testing as the amount of data increase [15]. The strength of the available evidence can be considered by determining the optimal information size for a reliable meta-analysis. We can derive the optimal information size from first, the risk of type-1 and type-2 statistical errors that we set respectively at 5% and 20%; and second, the difference we intended to detect, which we set at 50% for the first-pass success rate and 120 s for the total time taken for preparation and performance of the intervention. To control for the risk of type-1 statistical error, the Lan and DeMets alpha-spending

function was used to adjust the threshold for statistical significance, or trial sequential boundary, to compensate for the higher risk of random error before the data in the meta-analysis has reached the optimal information size. To control for the risk of type-2 statistical error, an extension of the Lan and DeMets alpha-spending function was used to adjust the threshold for no difference, or the futility boundary, prior to the data in the meta-analysis passing its optimal information size.

Results

Of the original 4978 unique records identified by our search strategy, 22 randomised controlled trials met the inclusion criteria [16–37]. Details of the screening process are shown in Fig. 1 and the results of the risk of bias assessment are found in Fig. 2. Most of the trials did not describe measures to blind participants, personnel or outcome assessors, and hence were at risk of performance and detection bias. In the 18 instances where details of trial methodology or missing data were needed, 10 authors responded with the required information [16, 18, 20, 21, 27–30, 32, 33].

Overall, the number of patients included in each trial ranged from 20 to 370. The included trials comprised a total of 2462 patients, in whom only conventional landmark

palpation was conducted in 1232 and preprocedural ultrasound was performed in 1230. Characteristics of the trials are presented in Table 1. In eight trials, the indication for the neuraxial procedure was labour analgesia [17, 18, 23, 28, 29, 32, 35, 37], in 13 trials, it was for elective caesarean section [16, 19–22, 24, 26, 27, 30, 31, 33, 34, 36], and in one trial, it was labour analgesia or elective caesarean section [25]. The neuraxial technique was combined spinal-epidural [19, 24, 26, 28, 36], epidural [17, 18, 23, 25, 29, 31, 32, 35, 37] or spinal [16, 20–22, 27, 30, 33, 34] in five, nine and eight trials, respectively. In two trials, the neuraxial technique was predicted to be easy [16, 17], whereas it was predicted to be difficult in seven trials [20, 22, 23, 27, 32, 34, 36] and heterogeneous in 10 trials [18, 19, 21, 28–31, 33, 35, 37]. Further, in one trial, preprocedural ultrasound was conducted before epidural catheterisation followed by the performance of spinal anaesthesia [31]. In six trials, the sonographer and the operator were not the same anaesthetist [19, 27, 29, 30, 33, 35, 37].

Our first co-primary outcome, the first-pass success rate, was reported in 1253 patients by 13 trials [16, 17, 19, 21, 22, 24, 26–29, 31, 33, 36]. It was increased by a risk ratio (95%CI) of 1.46 (1.16–1.82), $p = 0.001$, $I^2 = 72%$ with ultrasound compared with landmark methods (Fig. 3). The

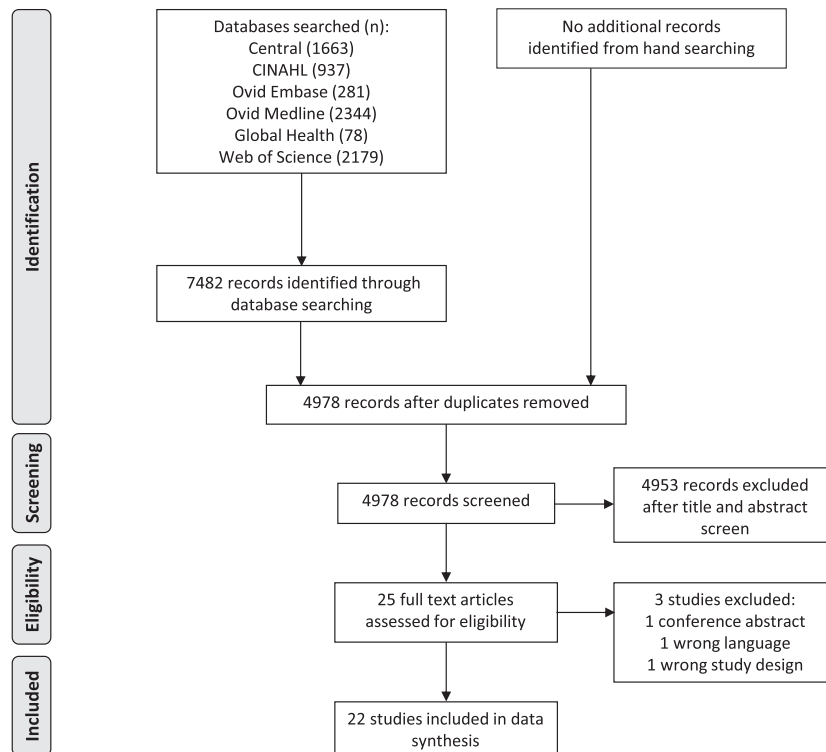


Figure 1 PRISMA flow diagram summarising the retrieved, included and the excluded randomised controlled trials. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Ansari et al [16]	+	?	-	+	+	+	?
Arzola et al [17]	+	+	-	+	+	+	?
Balaban et al [28]	+	+	-	-	+	+	?
Chin et al [31]	+	+	-	-	+	+	?
Creaney et al [32]	+	+	-	-	+	+	?
Dhanger et al [33]	+	+	-	-	+	+	?
Ekinci et al [34]	?	+	-	-	+	+	?
Grau et al [18]	?	+	-	-	+	+	?
Grau et al [35]	?	+	-	-	+	+	?
Grau et al [36]	?	?	-	-	+	+	?
Grau et al [37]	?	+	-	-	+	+	?
Li et al [19]	+	?	+	+	+	+	?
Nassar et al [20]	+	+	-	-	+	+	?
Perna et al [21]	?	+	-	-	+	+	?
Sahin et al [22]	+	+	?	-	+	+	?
Tawfik et al [23]	+	+	-	+	+	+	?
Tubinis et al [24]	?	+	-	-	+	+	?
Turkstra et al [25]	+	+	+	+	+	+	?
Urfalioglu et al [26]	?	?	-	+	+	+	?
Vallejo et al [27]	+	?	-	-	+	+	?
Wang et al [29]	+	?	-	-	+	+	?
Wilkes et al [30]	?	+	-	-	-	+	?

Figure 2 Risk of bias assessment of included trials using the Cochrane’s Collaboration’s tool. ?, unclear risk; -, high risk; +, low risk.

quality of evidence was graded as low consequent to downgrading for serious limitations and inconsistency. Sub-group analyses showed the influence of the predicted difficulty of the neuraxial procedure on this outcome ($p = 0.03$), but not the experience of the sonographers; (risk ratios (95%CI) for junior, senior and unspecified sonographers were, respectively, 1.20 (0.88–1.64), 1.50 (1.14–1.96) and 1.46 (0.89–2.39), $p = 0.56$) or the operators, (risk ratios (95%CI) for junior, senior and junior and senior operators were respectively, 0.64 (0.27–1.47), 1.56 (1.17–2.08) and 1.43 (1.03–1.98), $p = 0.14$). Neither the Duval and Tweedie’s trim and fill test nor did the Egger’s test suggest the presence of publication bias. In the trial sequential analysis, the optimal information size of 1225 patients was reached and the Z-curve had crossed the trial sequential monitoring boundary, revealing firm evidence for the superiority of ultrasound compared with landmark techniques (Fig. 4).

Our second co-primary outcome, the time taken for the identification of the needle insertion point and the performance of the neuraxial procedure, was reported in 709 patients by eight trials [17, 20, 22, 27, 28, 32, 34, 36]. No difference was demonstrated between ultrasound and landmark methods ($p < 0.00001$, $I^2 = 93\%$) (Fig. 5). The quality of evidence was graded as very low consequent to downgrading for serious limitations, inconsistency and imprecision. Sub-group analyses showed the influence of the predicted difficulty of the neuraxial procedure on this outcome ($p = 0.0002$), but not the experience of the sonographers (mean differences (95%CI) for junior, senior and unspecified sonographers were respectively, -32.77 (-264.77 to 199.36), 39.43 (-102.34 to 181.20) and 97.98 (11.43–184.52) s, $p = 0.51$) or the operators (mean differences (95%CI) for junior, senior, and junior and senior operators were, respectively, -73.36 (-225.76 to 79.03), 89.14 (19.79–158.48) and 81.00 (30.05–131.95) s, $p = 0.05$). Neither the Duval and Tweedie’s trim and fill test nor Egger’s test suggested the presence of publication bias. In the trial sequential analysis, the optimal information size of 754 patients was not reached, yet the Z-curve had crossed the futility boundary, suggesting the equivalence of ultrasound and landmark techniques (Fig. 6).

The results of the meta-analyses for our secondary outcomes are listed in Table 2. The quality of evidence for each primary and secondary outcome is presented in the online Supporting Information, Table S1. There were insufficient data to facilitate meta-analysis of the other outcomes. In individual trials, no differences were shown between preprocedural ultrasound and conventional landmark palpation in: the need for additional epidural

Table 1 Characteristics of the included trials.

Reference	Group (n)	Indication	Nature of neuraxial technique	Position	Method of ultrasound localisation	Experience of sonographer	Experience of operator	Predicted difficulty	Primary outcome
Ansari et al. [16]	Ultrasound (75) Landmark (75)	Elective LSCS	Spinal	Sitting	Longitudinal and transverse	Experienced Three anaesthetists who had previously performed 200–300 USG neuraxial blocks	Experienced	Easy Exclusion: BMI ≥ 35 kg.m ⁻² or difficulty in palpation of bony landmarks	Time to perform intervention
Arzola et al. [17]	Ultrasound (60) Landmark (68)	Labour analgesia	Epidural	Sitting	Longitudinal and transverse	Junior second year resident anaesthetists, and senior fellows on 1-year obstetric anaesthesia fellowship programme	Junior second year resident anaesthetists, and senior fellows on 1-year obstetric anaesthesia fellowship programme	Easy Inclusion: Ease in palpation of bony landmarks	Number of intervertebral spaces at which neuraxial insertion was attempted, number of needle redirections and time to perform intervention
Balaban et al. [18]	Ultrasound (20) Landmark (20)	Labour analgesia	Epidural	Lateral	Longitudinal and transverse	Experienced Single anaesthetist	Experienced Single anaesthetist	Heterogeneous	Number of intervertebral spaces at which neuraxial insertion was attempted and number of skin punctures
Chin et al. [19]	Ultrasound (105) Landmark (110)	Elective LSCS	CSE	Sitting	Longitudinal and transverse	Experienced Five anaesthetists	Experience varied from trainee to consultant anaesthetist	Heterogeneous	First-pass success rate and difficulty of insertion
Creaney et al. [20]	Ultrasound (10) Landmark (10)	Elective LSCS	Spinal	Sitting	Longitudinal and transverse	Junior anaesthetic trainees in first 2 years of training and on initial 6 months of obstetric anaesthesia training, with experience of 10 previous lumbar punctures	Junior anaesthetic trainees in first 2 years of training and on initial 6 months of obstetric anaesthesia training, with experience of 10 previous lumbar punctures	Difficult Inclusion: Impalpable spinous processes	Number of patients who needed an attempt at neuraxial insertion at more than one intervertebral space and number of needle redirections
Dhanger et al. [21]	Ultrasound (50) Landmark (50)	Elective LSCS	Spinal	Lateral	Longitudinal and transverse	Experienced Anaesthetists who had previously performed more than 50 USG neuraxial blocks	Experienced	Heterogeneous	Number of skin punctures
Ekinci et al. [22]	Ultrasound (32) Landmark (32)	Elective LSCS	Spinal	Sitting	Longitudinal and transverse	Experienced Two anaesthetists	Experienced Two anaesthetists	Difficult Inclusion: Difficulty in palpation of spinous processes and intervertebral spaces	Number of skin punctures and time to perform intervention as well as total procedural time
Grau et al. [23]	Ultrasound (36) Landmark (36)	Labour analgesia	Epidural	Sitting	Longitudinal and transverse	Experienced Single anaesthetist	Experienced Single anaesthetist	Difficult Inclusion: BMI > 33 kg.m ⁻² , marked deformity of spine and history of previously difficult epidural anaesthesia	Not specified
Grau et al. [24]	Ultrasound (40) Landmark (40)	Elective LSCS	CSE	Sitting	Longitudinal and transverse	Experienced Single anaesthetist	Experienced Single anaesthetist	Not specified	Not specified
Grau et al. [25]	Ultrasound (150) Landmark (150)	Labour analgesia or elective LSCS	Epidural	Not specified	Longitudinal and transverse	Experienced Single anaesthetist	Experienced Single anaesthetist	Not specified	Not specified
Grau et al. [26]	Ultrasound (20) Landmark (10)	Elective LSCS	CSE	Sitting	Longitudinal and transverse	Experienced Single anaesthetist	Experienced Single anaesthetist	Not specified	Not specified
Li et al. [27]	Ultrasound (40) Landmark (40)	Elective LSCS	Spinal	Lateral	Longitudinal and transverse	Experienced Single anaesthetist who had previously performed more than 150 USG neuraxial blocks	Experienced Three anaesthetists with 3 years of experience in spinal anaesthesia	Difficult Inclusion: BMI > 30 kg.m ⁻²	Success rate on first skin puncture
Nassar et al. [28]	Ultrasound (55) Landmark (55)	Labour analgesia	CSE	Sitting	Longitudinal and transverse	Experienced Anaesthetist with more than 10 years of experience in anaesthesia	Experienced Anaesthetist with more than 10 years of experience in anaesthesia	Heterogeneous	First-pass success rate

(continued)

Table 1 (continued)

Reference	Group (n)	Indication	Nature of neuraxial technique	Position	Method of ultrasound localisation	Experience of sonographer	Experience of operator	Predicted difficulty	Primary outcome
Perna et al. [29]	Ultrasound (30) Landmark (28)	Labour analgesia	Epidural	Sitting	Longitudinal and transverse	Experienced Single anaesthetist who normally performs more than 150 epidural procedures per year	Experienced Single anaesthetist who normally performs more than 150 epidural procedures per year	Heterogeneous	Number of skin punctures and needle redirections
Sahin et al. [30]	Ultrasound (50) Landmark (50)	Elective LSCS	Spinal	Sitting	Longitudinal and transverse	Experienced Single anaesthetist who had previously performed 150 USG neuraxial blocks	Experienced Resident anaesthetists with 4 years of experience in performing neuraxial blocks	Heterogeneous	Success rate on first skin puncture
Tawfik et al. [31]	Ultrasound (53) Landmark (55)	Elective LSCS	Epidural	Sitting	Longitudinal and transverse	Experienced Single anaesthetist who had 4 years of experience in USG neuraxial blocks	Experienced Single anaesthetist with 10 years of experience in anaesthesia	Heterogeneous	First-pass success rate
Tubinis et al. [32]	Ultrasound (75) Landmark (75)	Labour analgesia	Epidural	Sitting	Transverse	Junior first to third year resident anaesthetists with experience of at least 10 epidural blocks	Junior first to third year resident anaesthetists with experience of at least 10 epidural blocks	Difficult Inclusion: BMI $\geq 35 \text{ kg.m}^{-2}$	Time to perform intervention
Turkstra et al. [33]	Ultrasound (40) Landmark (40)	Elective LSCS	Spinal	Sitting	Longitudinal and transverse	Experienced Five anaesthetists	Junior first or second year resident anaesthetists with experience of at least three and no more than 25 obstetric spinal blocks	Heterogeneous	Number of skin punctures and needle redirections
Urfalioglu et al. [34]	Ultrasound (48) Landmark (49)	Elective LSCS	Spinal	Sitting	Longitudinal and transverse	Experienced Single anaesthetist who had previously performed more than 100 USG neuraxial blocks	Experienced Single anaesthetist with more than 5 years of experience	Difficult Inclusion: BMI $> 30 \text{ kg.m}^{-2}$	Number of skin punctures and needle redirections
Vallejo et al. [35]	Ultrasound (189) Landmark (181)	Labour analgesia	Epidural	Sitting	Longitudinal and transverse	Experienced Single anaesthetist who had 6 months of experience in USG neuraxial blocks	Junior first year resident anaesthetists with experience of no more than five epidural blocks	Heterogeneous	Epidural failure rate
Wang et al. [36]	Ultrasound (30) Landmark (30)	Elective LSCS	CSE	Lateral	Longitudinal and transverse	Not specified	Experienced Single anaesthetist with more than 10 years of experience	Difficult Inclusion: BMI $\geq 30 \text{ kg.m}^{-2}$	Success rate at first intervertebral space
Wilkes et al. [37]	Ultrasound (22) Landmark (28)	Labour analgesia	Epidural	Sitting	Longitudinal	Not specified	Junior resident anaesthetists	Heterogeneous	Pressure pain threshold at neuraxial insertion site

CSE, combined spinal-epidural; LSCS, lower segment caesarean section; USG, ultrasound guided.

injection prior to skin incision [19]; the incidence of post-dural puncture headache; the need for epidural blood patch [35]; and the patient-reported pain during the performance of the neuraxial procedure [19].

Discussion

Our meta-analysis and systematic review has indicated that preprocedural ultrasound improved indices of efficacy, including the first-pass success rate, with no increase in the

overall time taken to identify the insertion point of the needle and perform the neuraxial procedure. The quality of evidence for these two co-primary outcomes, however, was rated as low and very low respectively. Relative to palpation of anatomical landmarks, preprocedural ultrasound further decreased the incidence of complications, including: technical inability to site the neuraxial block; failure of analgesia or anaesthesia; 'bloody tap' or vascular cannulation; and postpartum back pain and headache.

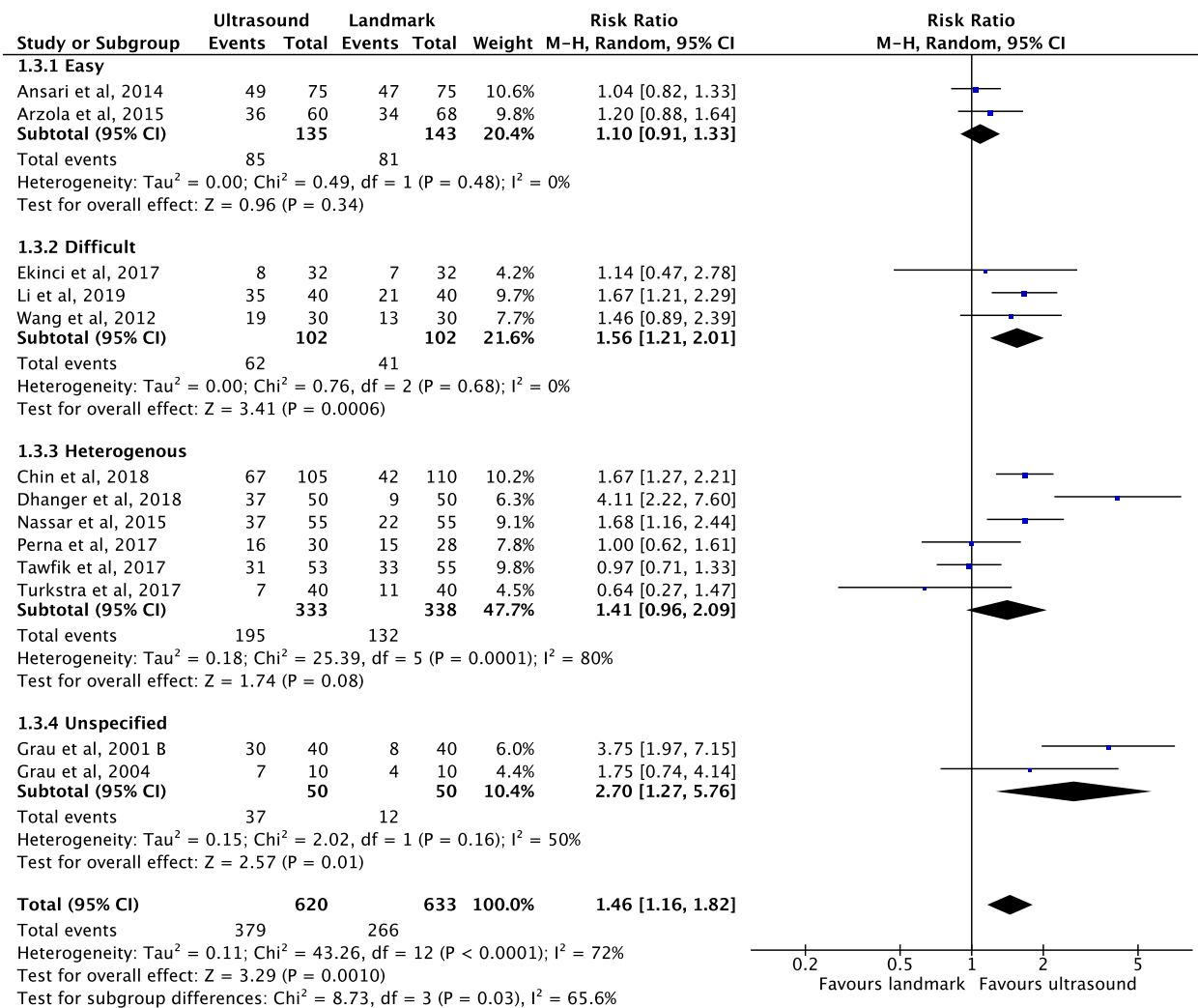


Figure 3 Forest plot of the first-pass success rate according to the predicted difficulty of the neuraxial procedure. M-H, Mantel-Haenszel.

In addition to the challenges presented by lumbar lordosis, soft tissue oedema and obesity in parturients [1], the area of the ideal skin puncture site is smaller, the soft tissue channel between the spinous processes is narrower and the needle to epidural space distance is greater [38]. It can hence be expected that preprocedural ultrasound should be found to increase measures of efficacy, given its capacity to delineate the underlying anatomy, including the midline of the spine, insertion point of the needle, optimal angle of the needle trajectory and the depth of the epidural space. Further, it is possible that the perceived delay in the completion of a neuraxial procedure when preprocedural ultrasound is used, something we did not find overall, could have previously dissuaded clinicians from incorporating it into their routine practice, particularly in obstetric anaesthesia where timely performance may be of vital importance [39].

For those patients in whom the neuraxial procedure was predicted to be easy, preprocedural ultrasound offered limited benefit in regard to the first-pass success rate. Given that the increase of approximately 1 min in the overall time taken to perform the procedure with ultrasound is not likely to be clinically significant, the adoption of preprocedural ultrasound in such patients could still be considered to allow anaesthetists to attain adequate competence and experience. In those patients for whom the neuraxial procedure was predicted to be difficult, the increase in first-pass success rate with preprocedural ultrasound was not associated with an increase in the total time taken to perform the procedure.

Interestingly, the first-pass success rate and the overall time taken to perform the procedure were not affected by the experience of the sonographer or the operator.

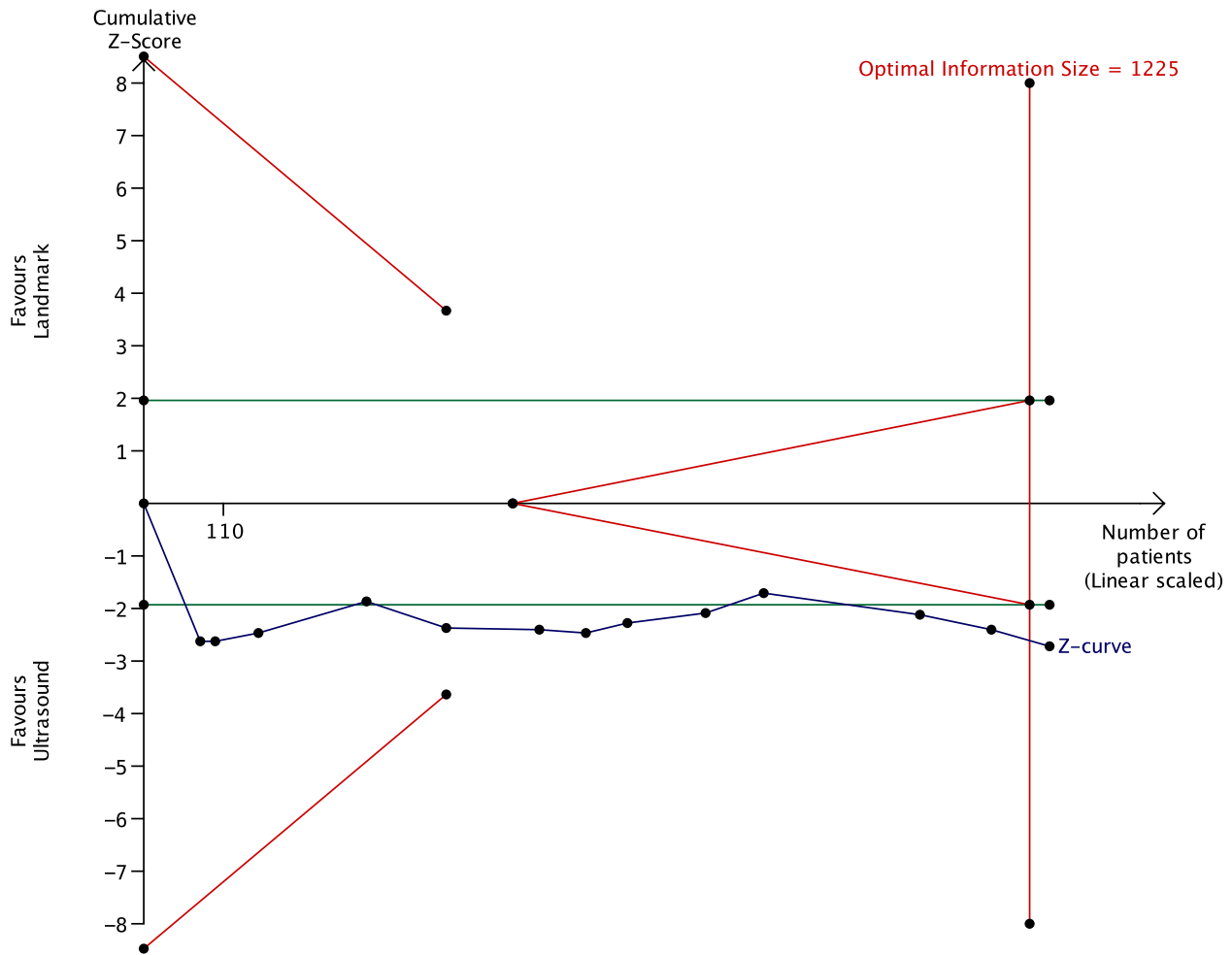


Figure 4 Trial sequential analysis for the first-pass success rate. The green line depicts the conventional threshold for statistical significance at $p = 0.05$ and the outer and the inner angled red lines, respectively, represent the adjusted threshold for statistical significance and the futility boundaries. The blue line depicts the Z-curve and the vertical red line is the optimal information size.

Preprocedural ultrasound may therefore not in fact be a technique whose value is only evident when performed by experts. This is in contrast to the results of previous studies that explored the ‘learning curves’ of anaesthetists in ultrasonography of the neuraxis. Halpern et al revealed that between 22 and 36 scans were needed to achieve reliability criteria in the determination of the correct level of the lumbar spinous process [40], while Margarido et al showed that 20 supervised attempts and teaching sessions were not sufficient to attain competence in the identification of the ideal insertion point of the needle and the depth of the epidural space [41].

The potential for preprocedural ultrasound to increase the operator’s technical ability to site the neuraxial block, decrease the incidence of failure of analgesia or anaesthesia, and reduce the intra-operative pain score, is

attractive. Further, it could support the desire to meet the standards set by the Royal College of Anaesthetists in the UK in relation to epidural analgesia during labour, and caesarean section technique and failure rate [39]. It has been hypothesised that a decrease in the number of skin punctures and needle redirections might decrease the development of microhaematomas and thus the rate of postpartum back pain [37]. Moreover, many reported cases of spinal haematomas have been associated with ‘bloody tap’ and difficult or traumatic neuraxial placements [42].

Our results, including the number of skin punctures and needle redirections, are similar to those published in three previous meta-analyses [7–9]. Some differences, however, are notable. Shaikh et al. did not demonstrate any influence of the predicted difficulty of the neuraxial procedure on their outcomes of number of skin punctures, needle

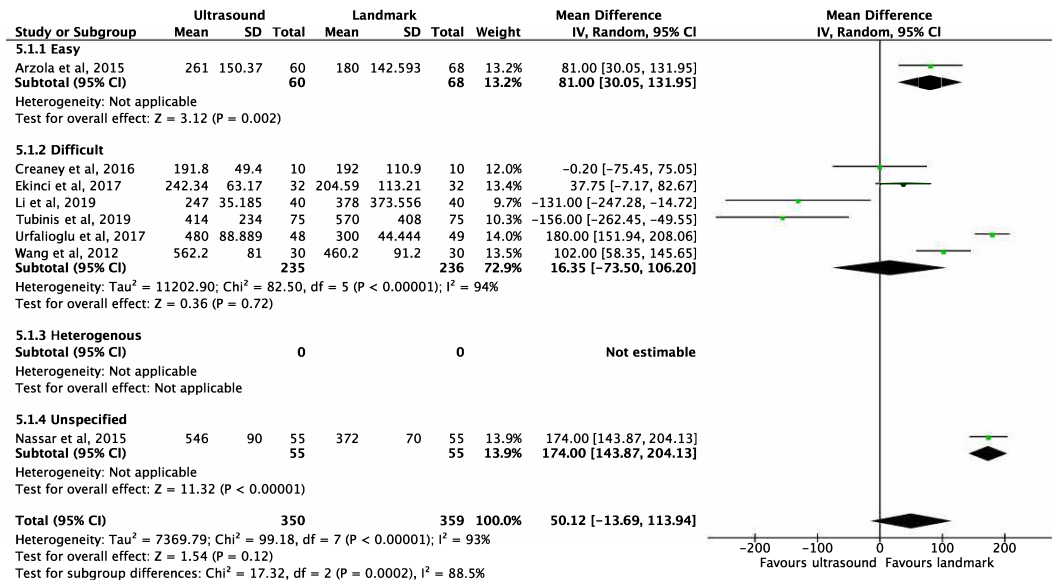


Figure 5 Forest plot of the time taken for identification of the needle insertion point and performance of the intervention according to the predicted difficulty of the neuraxial procedure. IV, inverse variance.

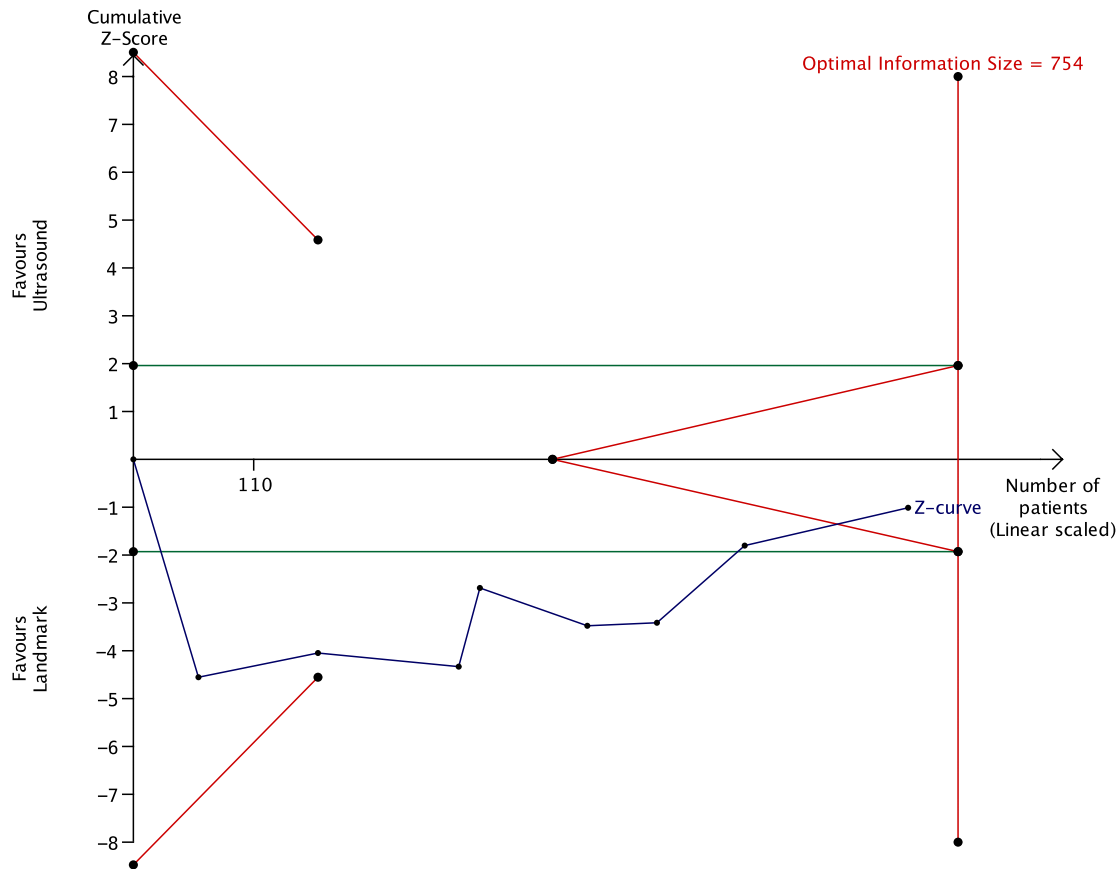


Figure 6 Trial sequential analysis for the time taken for identification of the needle insertion point and performance of the intervention. The green line depicts the conventional threshold for statistical significance at p = 0.05 and the outer and the inner angled red lines, respectively, represent the adjusted threshold for statistical significance and the futility boundaries. The blue line depicts the Z-curve and the vertical red line is the optimal information size.

Table 2 Meta-analysis of the secondary outcomes. Values are mean difference, standardised mean difference or risk ratio.

Outcomes	Number of trials	Number of patients		Effect size (95%CI)	I ² (%)	p value
		Ultrasound	Landmark			
Efficacy						
First intervertebral space success rate [17, 18, 20, 24, 26, 27, 30, 36]	8	260	268	1.26 (1.09–1.47)	81	0.002
First skin puncture success rate [16, 18, 19, 21, 22, 30, 31]	7	385	392	1.41 (1.12–1.78)	87	0.003
Number of attempted intervertebral spaces [18, 22, 23, 25]	4	238	238	−0.16 (−0.24 to −0.08)	0	< 0.0001
Need to attempt more than one intervertebral space [17, 18, 20, 24, 26, 27, 30, 36]	8	260	268	0.12 (0.05–0.25)	0	< 0.00001
Number of skin punctures [16, 18, 21, 22, 27, 28, 31, 34]	8	373	376	−0.66 (−1.04 to −0.28)	94	0.0007
Need for three or more skin punctures [16, 18, 21, 30]	4	195	195	0.17 (0.07–0.42)	45	0.0002
Number of needle redirections [16, 20–22, 28, 29, 31, 32, 34, 37]	10	450	457	−1.02 (−1.42 to −0.62)	82	< 0.00001
Need for three or more needle redirections [21, 30]	2	100	100	0.09 (0.02–0.36)	0	0.0007
Total number of skin punctures and needle redirections [23, 25, 27, 29, 33, 35]	6	485	475	−1.08 (−1.56 to −0.60)	78	< 0.0001
Need for three or more skin punctures and needle redirections [24, 26, 36]	3	80	80	0.17 (0.06–0.51)	0	0.001
Ultrasound distance compared with real needle to target distance (cm) [21, 24, 25, 29, 30, 35]	6	509	499	−0.28 (−0.67–0.11)	93	0.170
Number of attempts required to pass the epidural catheter [23, 25]	2	186	186	−0.51 (−1.10–0.08)	92	0.090
Need to call for help [17, 33, 35]	3	289	289	0.85 (0.64–1.14)	0	0.280
Time						
Time taken for identification of needle insertion point(s) [20, 21, 24–28, 32, 36]	9	460	460	52.90 (14.10–91.70)	99	0.008
Time taken for performance of neuraxial procedure(s) [16–18, 20, 21, 27, 28, 30–33]	11	528	538	−13.79 (−29.03–1.45)	70	0.080
Complications and adverse effects						
Technical inability to site neuraxial block [17, 27, 29, 31]	4	183	191	0.12 (0.02–0.63)	0	0.010
Incidence of asymmetrical neuraxial blockade [23, 25, 26, 29]	4	226	224	0.37 (0.11–1.21)	0	0.100
Incidence of patchy neuraxial blockade [23, 26]	2	46	46	0.33 (0.06–2.02)	0	0.230
Failure rate of analgesia or anaesthesia after neuraxial injection [16, 23, 25, 29, 30, 32, 35]	7	605	595	0.43 (0.22–0.84)	0	0.010
Rate of inadequate dermatomal level of blockade [16, 32]	2	150	150	0.60 (0.19–1.88)	19	0.380
Need for supplemental analgesia [19, 25, 27, 33]	4	335	340	0.66 (0.42–1.04)	19	0.080

(continued)

Table 2 (continued)

Outcomes	Number of trials	Number of patients		Effect size (95%CI)	I ² (%)	p value
		Ultrasound	Landmark			
Need for conversion to general anaesthesia [19, 20, 30]	3	165	170	0.73 (0.24–2.25)	0	0.580
Incidence of paraesthesia [18, 21, 30, 33, 36]	5	190	190	0.52 (0.13–2.03)	62	0.350
Incidence of bloody tap or vascular cannulation [18, 21, 25, 27–31, 33]	9	488	488	0.54 (0.35–0.85)	0	0.008
Incidence of dural puncture [17–19, 25, 28, 29, 31, 35, 36]	9	692	697	0.81 (0.32–2.09)	0	0.670
Incidence of postpartum headache [23, 25–27, 30, 34, 36]	7	364	365	0.49 (0.29–0.82)	44	0.006
Incidence of postpartum back pain [23, 25–27, 30, 31, 34, 36]	8	417	420	0.62 (0.45–0.87)	22	0.005
Incidence of neurological sequelae [16, 25, 27, 36]	4	295	295	0.67 (0.11–3.93)	0	0.650
Patient reported outcomes						
Pain in labour and/or caesarean section [23, 25, 26, 29]	4	226	224	−0.96 (−1.70 to −0.21)	77	0.010
Satisfaction [16, 23, 25, 26, 31]	5	324	326	−0.37 (−0.75–0.01)	79	0.060

redirections and failed procedures [8]. They evaluated trials with differing characteristics, however, examining interventions as diverse as real-time ultrasound for procedures such as diagnostic lumbar punctures in the emergency room in paediatric, non-obstetric and obstetric patients. In contrast to the present systematic review, that has a maximum of 13 trials in which the neuraxial procedure was predicted to be easy, difficult, heterogeneous or unspecified, their sub-group analyses included up to eight trials in which it was predicted to be difficult or heterogeneous. Unlike our meta-analysis, Perlas et al did not find that preprocedural ultrasound decreased the incidence of back pain or headache compared with landmark palpation methods [7]. It is likely that this may be related to the limited number of trials that reported on these particular outcomes in their systematic review.

This meta-analysis has several limitations. First, most of the included trials were at risk of performance and detection biases, leading to the downgrading of the quality of evidence. Second, nomenclature describing needle manipulation and movement was not consistent, resulting in multiple secondary outcomes unsuitable for pooling. Third, the inclusion criteria of the trials that selected patients in whom the neuraxial procedure was predicted to be difficult were heterogeneous. Of these seven trials, four included patients if their BMI was > 30 or 35 kg.m^{−2}, one used a BMI > 33 kg.m^{−2}, marked deformity of the spine or previously difficult neuraxial anaesthesia, and two included

patients if the neuraxial landmarks were difficult to palpate. Difficulty in the palpation of neuraxial landmarks has been demonstrated to correlate with predicted difficulty of the neuraxial procedure [43–46], and increased BMI has been inconsistently found to relate to predicted difficulty of the neuraxial procedure [44, 46, 47]. Obesity does, however, increase the likelihood of limited back flexion and difficulty in the palpation of neuraxial landmarks [44]. Other reported risk factors predicting difficulty with the neuraxial procedure, for which preprocedural ultrasound is unlikely to be helpful, are the ability of the patient to flex her back, and patient positioning [44, 45]. Fourth, the definition of 'junior' and 'experienced' operators varied. Junior operators ranged from anaesthetic trainees in their initial 6 months of obstetric anaesthesia training, with experience of 10 previous lumbar punctures [20], to junior first or second year resident anaesthetists with experience of as many as 25 obstetric spinal blocks [33]. Such differences in baseline experience prior to the start of the trial might result in variability in procedural proficiency. Fifth, meta-analysis of some outcomes, such as the need for three or more skin punctures and needle redirections, included fewer than four trials and/or less than 200 patients, leading to possible imprecision and unreliability [48]. Last, only one of the included trials was sufficiently powered to examine outcomes related to complications [37].

In conclusion, the use of preprocedural ultrasound increased the first-pass success rate and decreased the

incidence of complications without an increase in overall procedural time when compared with the traditional method of landmark palpation. In view of this, the authors recommend the use of preprocedural ultrasound for neuraxial procedures in obstetrics. Future trials should standardise the definition of nomenclature associated with the outcomes. Moreover, although the trial sequential analyses surpassed the optimal information size for our co-primary outcomes, this may not apply to the sub-group analyses. Therefore, future trials should explore the influence of preprocedural ultrasound in obstetric patients with specified indices potentially predictive of difficulty with the neuraxial procedure, and with sonographers and operators of varied experience.

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Supporting Information

Additional supporting information may be found online via the journal website.

Table S1. GRADE quality of evidence assessment for each outcome.

Appendix S1. Search strategy.