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Femoral Nerve Block Improves Analgesia Outcomes after Total Knee Arthroplasty

A Meta-analysis of Randomized Controlled Trials

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ABSTRACT

Background: Femoral nerve blockade (FNB) is a common method of analgesia for postoperative pain control after total knee arthroplasty. We conducted a systematic review to compare the analgesia outcomes in randomized controlled trials that compared FNB (with and without sciatic nerve block) with epidural and patient-controlled analgesia (PCA).

Methods: We identified 23 randomized controlled trials that compared FNB with PCA or epidural analgesia. These studies included 1,016 patients, 665 with FNB, 161 with epidural, and 190 with PCA alone.

Results: All 10 studies of single-shot FNB (SSFNB) used concurrent PCA opioids. SSFNB was found to reduce PCA morphine consumption at 24 h (−19.9 mg, 95% credible interval [CrI]: −35.2 to −4.6) and 48 h (−38.0 mg, 95% CrI: −56.0 to −19.7), pain scores with activity (but not at rest) at 24 and 48 h (−1.8 visual analog pain scale, 95% CrI: −3.3 to −0.02 at 24 h; −1.5 visual analog pain scale, 95% CrI: −2.9 to −0.02 at 48 h) and reduce the incidence of nausea (0.37 odds ratio, 95% CrI: 0.1 to 0.9) compared with PCA alone. SSFNB had similar morphine consumption and pain scores compared with SSFNB plus sciatic nerve block, and SSFNB plus continuous FNB.

Conclusions: SSFNB or continuous FNB (plus PCA) was found to be superior to PCA alone for postoperative analgesia for patients having total knee arthroplasty. The impact of adding a sciatic block or continuous FNB to a SSFNB needs to be studied further.

What We Already Know about This Topic

- Femoral nerve block, either as a single shot or continuously with a catheter, is now commonly used for analgesia after total knee arthroplasty

What This Article Tells Us That Is New

- In a meta-analysis of 23 studies, single-shot femoral nerve block improved analgesia and reduced morphine dose compared with intravenous patient-controlled analgesia
- These studies did not demonstrate further improvement with continuous compared with single-shot femoral nerve block alone

TOTAL knee arthroplasty (TKA) is a common surgery to help improve mobility and quality of life. More than 13,000 procedures were performed in Ontario in patients aged 65 and older in 1998–1999.[1] The pain after TKA is severe and does not fade noticeably for 48–72 h after the surgery.[2] Effective pain control allows for earlier ambulation and initiation of physiotherapy, which hastens recovery, reduces the length of stay in the hospital, and lowers the risk of postoperative complications, such as thromboembolic disease or nosocomial infections.[3,4]

Patient-controlled analgesia (PCA) opioids and epidural and femoral nerve block (FNB) are commonly used analgesic options for TKA. PCA morphine or other opioids are frequently used as the primary analgesic for TKA. The use of opioids is associated with side effects such as nausea, vomiting, pruritus, and sedation.[5] These side effects can have negative effects on patient comfort and safety as well as delaying the start of phys-

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iotherapy, which will negatively impact functional rehabilitation.[6] Lumbar epidural analgesia is another common method of analgesia for TKA, and some physicians state that it provides better pain relief than other postoperative analgesic options.[3] There are, however, many adverse effects associated with epidural analgesia, including significant perioperative hypotension, urinary retention, pruritus, and respiratory depression.[3,7,8] In addition, sensation and ambulation are affected in the nonoperative leg. These adverse effects may limit the early initiation of physiotherapy after TKA. The use of epidural analgesia may interfere with the commencement of anticoagulation therapy to prevent thromboembolic events due to the risk of epidural hematoma. Without the use of anticoagulant prophylaxis, knee replacements are associated with a 40–70% risk of deep vein thrombosis and 1–2% risk of fatal pulmonary embolism.[3] Both epidural analgesia and FNB reduce opiate consumption and the associated side effects.[7]

FNB is a common method of analgesia for postoperative pain control after TKA. It is an easy technique to master and has a low risk of complications.†† One method of ensuring excellent femoral anesthesia is the 3-in-1 technique, which blocks the femoral, lateral femoral cutaneous, and obturator nerves.[9] Anesthesiologists can also perform sciatic nerve block when complete anesthesia of the knee is necessary. The femoral nerve alone only provides sensation to the anteromedial aspect of the knee, whereas the sciatic nerve innervates the posterior aspect of the knee. FNBs can be performed as a single shot or as a continuous block using a catheter and an infusion. Continuous nerve blocks have the advantage of permitting the delivery of analgesia for a longer postoperative duration than single-shot nerve blocks.[9] FNB does not provide a motor blockade to the nonoperative leg, which may encourage earlier ambulation. It also avoids the risk of epidural hematoma that is associated with the use of anticoagulants simultaneously with epidural analgesia.[5,7] Nerve blocks have also been shown to result in a reduced need for parenteral or oral analgesia to control pain and in reported pain levels.[10]

To determine the relative effectiveness of FNB analgesia for TKA, in the first 3 days postoperatively, we conducted a meta-analysis of all randomized trials that compared the PCA opioids alone or epidural analgesia *versus* FNB for the following outcomes: opioid consumption, pain scores, opioid side effects, knee range of motion, length of stay, and patient satisfaction. In addition to comparing FNB with PCA opioids and epidural analgesia, this review also addresses this question: are analgesia outcomes improved with a FNB improved by the addition of (1) a sciatic nerve block and (2) a continuous FNB?

Materials and Methods

Study Identification

Trials were identified by several methods. Randomized trials of epidural or PCA opioids *versus* FNB for pain control of primary unilateral TKA were identified by MEDLINE from 1950 to October 2009, EMBASE from 1980 to October 2009, CINAHL, CCTR, and Google Scholar. The following search terms were used in MEDLINE: Arthroplasty, Replacement, Knee; Analgesia, Epidural; Anesthesia, Epidural; Epidural; Analgesia, Patient-controlled; Analgesics, Opioid; Morphine; Nerve Block. The reference lists of selected studies were reviewed for additional studies. English language restrictions were applied due to resource constraints. Unpublished studies were not identified.

Study Selection

Suitable studies were identified by reading each abstract that was found by the search. J.E. P. and A. A. read all abstracts, and agreement on inclusion into the review was reached by consensus. The inclusion criteria were determined before the search and were as follows:

Population. Men and women over the age of 18 who had undergone primary TKA were included. Studies in which the patient population was undergoing revision or bilateral TKA were excluded.

Intervention. Included studies compared the analgesic effects of epidural or PCA opioid analgesia *versus* FNB (single shot or continuous) on analgesia outcomes after TKA.

Outcomes. Included studies assessed at least pain scores and opioid consumption. Additional outcomes that were extracted if available included knee range of motion, opioid side effects (nausea, pruritus, and sedation), block side effects, length of stay, patient satisfaction, and mobility of the nonoperative leg (early ambulation). These outcomes were analyzed for up to 72 h postoperatively.

Methodology. The studies that were included were prospective, randomized, controlled trials. Cohort studies, case reports, observational studies, and experimental models were excluded. Randomized controlled trials were included despite results or quality assessment ratings.

Study Evaluation

Each study that was included in the analysis was assessed independently by each author (J. E. P., A. A., and L. H.). The assessment was performed using a modified version of the five-

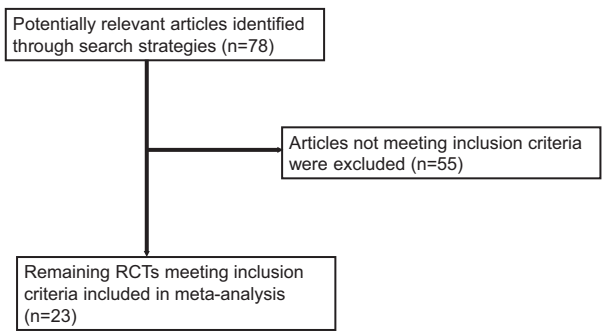

Fig. 1. Study selection process. RCTs = randomized control trials.

†† www.nysora.com/techniques/femoral_nerve_block. Last date accessed January 6, 2010.

Table 1. Summary of Included Studies

Reference	Interventions	Nerve Block Details	Placebo Block in PCA Group	PCA Opioid in FNB Group	Analgesia Adjuncts	Outcomes	Quality Score(/5)
Allen *et al.*, 1998[19]	SSFNB (12) SSFNB + Sciatic (12) PCA (12)	Technique: nerve stimulator Type: 3-in-1 block Drugs: 30 ml 0.25% B per block	Yes	Yes Morphine 1 mg q10 min	Ketorolac IV Ibuprofen PO	Pain scores: rest and activity Opioid consumption and adverse effects Patient satisfaction	4
Barrington *et al.*, 2005[20]	CFNB (53) Epidural (55)	Technique: nerve stimulator Type: FNB Drugs: 25 ml 0.25% B followed by 0.2% B at 0.1 ml per kg per h	No PCA group	No	Rofecoxib PO Oxycodone PO If these were not effective IV morphine commenced	Pain scores: rest and activity Opioid consumption and adverse effects Knee range of motion Length of stay	3
Dang *et al.*, 2005[37]	CFNB (14) CFNB + Sciatic (13)	Technique: nerve stimulator Type: FNB + SNB Drugs: 15 ml 0.75% R	No PCA group	Yes Morphine 0.15 mg/kg q6 h	Paracetamol IV Ketoprofen IV		4
Davies *et al.*, 2004[21]	SSFNB + Sciatic (30) Epidural (29)	Technique: nerve stimulator Type: 3-in-1 block Drugs: 0.375% B (30 ml FNB, 25 ml SNB)	No PCA group	Yes Morphine 1 mg q5 min	Diclofenac PO	Pain scores: activity Opioid consumption and adverse effects Patient satisfaction Knee range of motion Length of stay	3
Ganapathy *et al.*, 1999[22]	CFNB 0.2% B (22) CFNB 0.1% B (20) PCA (20)	Technique: nerve stimulator Type: 3-in-1 block Drugs: 30-ml bolus followed by 10 ml/h (0.1% B or 0.2% B)	Yes	Yes Morphine 1.5 mg q6 min	Indomethacin rectal	Pain scores: activity Opioid consumption and adverse effects Knee range of motion	5
Good *et al.*, 2007[32]	SSFNB (22) PCA (20)	Technique: nerve stimulator Type: FNB Drugs: 40 ml 0.5% B	Yes	Yes Morphine 1 mg/h		Pain scores: activity Opioid consumption and adverse effects Patient satisfaction Knee range of motion Length of stay	4
Hirst *et al.*, 1996[23]	SSFNB (11) CFNB (11) PCA (11)	Technique: nerve stimulator Type: 3-in-1 block Drugs: 20 ml 0.5% B (SSFNB) or 20 ml 0.5% B followed by 0.125% B at 6 ml/h (CFNB)	Yes	Yes Morphine 1.5 mg q7 min		Pain scores: rest and activity Opioid consumption and adverse effects Patient satisfaction	4

(*continued*)

Table 1. Continued

Reference	Interventions	Nerve Block Details	Placebo Block in PCA Group	PCA Opioid in FNB Group	Analgesia Adjuncts	Outcomes	Quality Score(/5)
Hunt *et al.*, 2009[33]	SSFNB + Sciatic (33) PCA (24)	Technique: nerve stimulator Type: FNB Drugs: 10–15 ml 0.5% B	Yes	Yes Morphine 1–2 mg q10 min		Pain scores: rest and activity Opioid consumption	3
Kadic *et al.*, 2009[34]	CFNB (27) PCA (26)	Technique: nerve stimulator Type: FNB Drugs: 20–25 ml 0.75% R	Yes	Yes Morphine 1 mg q6 min	Paracetamol PO Diclofenac PO	Pain scores: activity Opioid consumption and adverse effects Knee range of motion	3
Kaloul *et al.*, 2004[24]	CFNB (20) PCA (20)	Technique: nerve stimulator Type: 3-in-1 block Drugs: 30 ml 0.5% R followed by 0.2% R at 12 ml/h	No	Yes Morphine 1 mg q5 min	Indomethacin rectal Oxycodone or acetaminophen/ codeine PO	Pain scores: rest and activity Opioid consumption Patient satisfaction	3
Macalou *et al.*, 2004[25]	SSFNB (29) PCA (28)	Technique: nerve stimulator Type: 3-in-1 block Drugs: 25 ml 0.5% B and 2% lidocaine	Yes	Yes Morphine 1 mg q7 min	Propacetamol ketoprofen IV	Pain scores: rest Opioid consumption and adverse effects	4
McNamee *et al.*, 2001[26]	SSFNB + Sciatic B (25) SSFNB + Sciatic R (25) PCA (24)	Technique: nerve stimulator Type: FNB + SNB Drugs: 2 mg/kg B 7.5 mg/ml divided equally between FNB and SNB or 2 mg/kg R 7.5 mg/ml divided equally between FNB and SNB	Yes	Yes Morphine 1 mg q5 min		Pain scores activity Opioid consumption and adverse effects	5
Mistraletti *et al.*, 2006[12]	CFNB + Sciatic (8) Epidural (8) PCA (8)	Technique: nerve stimulator Type: FNB + SNB Drugs: lidocaine 2% 0.25 ml/kg injected into each catheter (FNB and SNB) followed by 0.2% R at 8 ml/h in FNB and 0.2% R at 4 ml/h in SNB	No	No	Naproxen PO Acetaminophen PO	Pain scores: rest and activity Opioid consumption Knee range of motion Length of stay	3
Morin *et al.*, 2005[35]	CFNB (30) CFNB + Sciatic (30) PSOAS[regis] (30)	Technique: nerve stimulator Type: FNB + SNB + PSOAS Drugs: 0.2% ropivacaine infusion 14 ml/h	No	No	Diclofenal PO Piritramide IV	Pain scores: rest and activity	2

(*continued*)

Table 1. Continued

Reference	Interventions	Nerve Block Details	Placebo Block in PCA Group	PCA Opioid in FNB Group	Analgesia Adjuncts	Outcomes	Quality Score(/5)
Ng *et al.*, 2001[27]	SSFNB 0.25% R (12) SSFNB 0.5% R (12) SSFNB 0.25% B (12) PCA (12)	Technique: nerve stimulator Type: 3-in-1 block Drugs: 30 ml 0.25% R or 0.5% R or 0.25% B	Yes	Yes Morphine 1 mg q5 min	Acetaminophen PO	Pain scores: rest and activity Opioid consumption and adverse effects Length of stay	5
Ozen *et al.*, 2006[36]	SSFNB 0.375% R (15) PCA (15)	Technique: nerve stimulator Type: 3-in-1 block Drugs: 40 ml 0.375% R	No	Yes Morphine 1 mg q15 min		Pain scores: rest and activity Opioid consumption	5
Salinas *et al.*, 2006[38]	SSFNB 0.375% R (18) CFNB 0.375% R + 0.2% R (18)	Technique: nerve stimulator Type: 3-in-1 block Drugs: 30 ml 0.375% R + 0.25 μg/ml epinephrine, As above + 0.2% R 10 ml/h	No	Yes Morphine 1 mg q5 min	Oxycodone PO Ibuprofen PO	Pain scores: rest and activity Opioid consumption	4
Seet *et al.*, 2006[5]	CFNB 0.15% R (17) CFNB 0.2% R (18) PCA (20)	Technique: nerve stimulator Type: 3-in-1 block Drugs: 10 ml/h for first 24 h followed by 5 ml/h. (0.15% R or 0.2% R)	No	Yes Morphine 1 mg q5 min	Rofecoxib PO Paracetamol PO	Pain scores: rest and activity Opioid consumption and adverse effects Patient satisfaction Knee range of motion Length of stay	2
Shum *et al.*, 2009[39]	PCA morphine (20) CFNB 0.15% R (20) CFNB 0.20% R (20)	Technique: nerve stimulator Type: 3-in-1 block Drugs: morphine 1 mg bolus lockout 5 min/max 8 mg/h, 0.15% R 10 ml/h, 0.20% R 10 ml/h		Yes Morphine 1 mg q5 min, max dose 8 mg/h		Pain scores: rest and activity Opioid consumption and adverse effects Functional outcomes in 2 yr	3
Singelyn *et al.*, 1998[28]	CFNB (15) Epidural (15) PCA (15)	Technique: nerve stimulator Type: 3-in-1 block Drugs: 37 ml 0.25% B followed by 0.125% B with sufentanil 0.1 μg/ml and clonidine 1 μg/ml at 10 ml/h	No	No	Propacetamol IV Piritramide IM	Pain scores: rest and activity Opioid consumption and adverse effects Knee range of motion Length of stay	3

(*continued*)

Table 1. Continued

Reference	Interventions	Nerve Block Details	Placebo Block in PCA Group	PCA Opioid in FNB Group	Analgesia Adjuncts	Outcomes	Quality Score(/5)
Sundarathiti *et al.*, 2009[31]	CFNB (30) Epidural (31)	Technique: nerve stimulator Type: 3-in-1 block + lumbar epidural Drugs: 0.25% L-bupivacaine 20 ml + 0.125% L-Bupivacaine 8 ml/h As above + 0.125% mg/ml morphine 4 ml/h	No PCA group	No	Tramadol IV Ultracet PO Acetaminophen PO	Pain scores: rest and activity (ordinal data) Opioid consumption and adverse effects Motor blockade	2
Wang *et al.*, 2002[29]	SSFNB (15) PCA (15)	Technique: nerve stimulator Type: FNB Drugs: 40 ml 0.25% B	Yes	Yes Morphine 1 mg q5 min		Pain scores: rest and activity Opioid consumption and adverse effects Knee range of motion Length of stay	5
Zaric *et al.*, 2006[30]	CFNB + Sciatic (26) Epidural (23)	Technique: nerve stimulator Type: FNB + SNB Drugs: 30 ml R 7.5 mg/mL in each catheter (FNB and SNB) followed by R 2 mg/ml and sufentanil 1 μg/ml at 5 ml/h in FNB, and R 0.5 mg/ml at 5 ml/h in SNB	No PCA group	Yes Morphine 2 mg q6 min	Paracetamol PO	Pain scores: rest and activity Opioid consumption and adverse effects Knee range of motion Length of stay	3

B = bupivacaine; CFNB = continuous femoral nerve block (n = 176); CFNB + Sciatic (n = 34); Epidural (n = 130); FNB = femoral nerve block; IM = intramuscular; IV = intravenous; PCA = patient-controlled analgesia (n = 185); PO = orally; PSOAS = continuous posterior lumbar plexus; R = ropivacaine; SNB = sciatic nerve block; SSFNB = single-shot femoral nerve block (n = 103), SSFNB + Sciatic (n = 92).

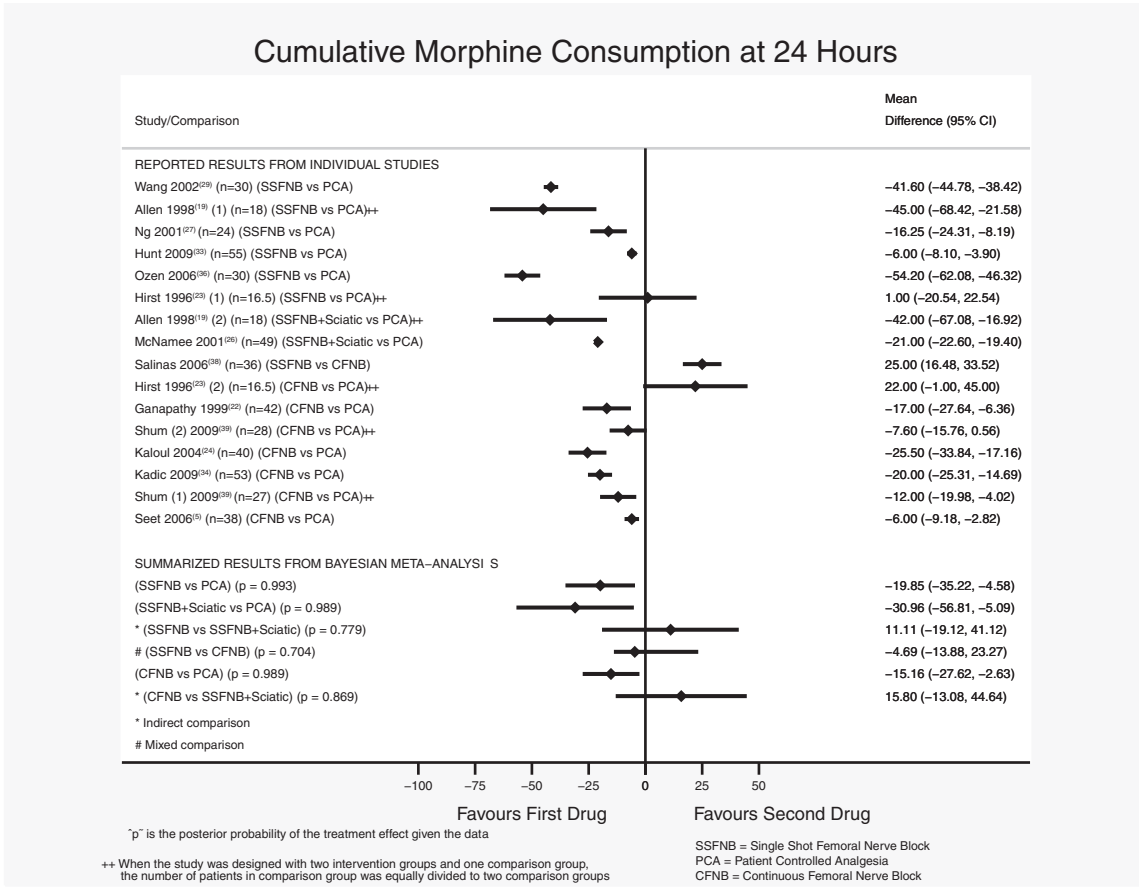

Fig. 2. Cumulative morphine consumption at 24 h. * = indirect comparison; # = mixed comparison; p = posterior probability of the treatment effect given the data; ++ = when the study number was designed with two intervention groups and one comparison group, the number of patients in the comparison group was equally divided into two comparison groups. CFNB = continuous femoral nerve block; PCA = patient-controlled analgesia; Sciatic = sciatic nerve block; SSFNB = single-shot femoral nerve block.

point methodological quality scale designed by Jadad *et al.*[11] To receive full points, a study had to be randomized, be double-blind, show completeness of follow-up, use suitable techniques to create the randomization sequence, and describe an acceptable blinding method. The modification of the five-point methodological scale was in relation to completeness of follow-up. In the original scale completeness of follow-up had to be clearly stated, whereas in the modified version completeness of follow-up was accepted when a description of withdrawals or dropouts was given or if all the patients enrolled in the study were accounted for in the results.

Data Extraction

The data from each study were extracted by two authors (A. A. and L. H.), and verified by an author (J. E. P., A. A. or L. H.) other than the one who extracted the data. Any discrepancies were resolved by consensus. Data extracted included study design, surgical details, type, anesthetic details, number of subjects in each treatment group, baseline characteristics of subjects, analgesia type and details, time for administering intervention, visual analog pain scale scores at rest and with activity, opioid consumption, knee range of motion, length of stay, patient satisfaction, mobility of the nonoperative leg, and analgesic adjuncts used.

A Priori Hypothesis for Sources of Heterogeneity

Before analyzing the results, potential sources of heterogeneity among studies were identified, and hypotheses were formulated to explain this heterogeneity. First, the use of analgesic adjuncts (nonsteroidal antiinflammatory drugs, acetaminophen, and gabapentin) may not be consistent across studies. Any benefit seen for FNB may therefore be a combination of the benefit of the FNB and adjunct used. Second, the dose, type of analgesic, and regimen may not be the same in each study for each respective analgesic option (PCA opioids, epidural, or FNB). Any discrepancy across studies with regard to the benefits of FNB may be a result of different dosing, analgesic agents, and regimens. Third, FNBs may be used in conjunction with sciatic nerve blocks. Once again, this may complicate the interpretation of the results, and is it is not possible to determine what proportion of pain relief is due to the FNB. Fourth, FNBs may be given as continuous or single shot. Continuous FNB (CFNB) may

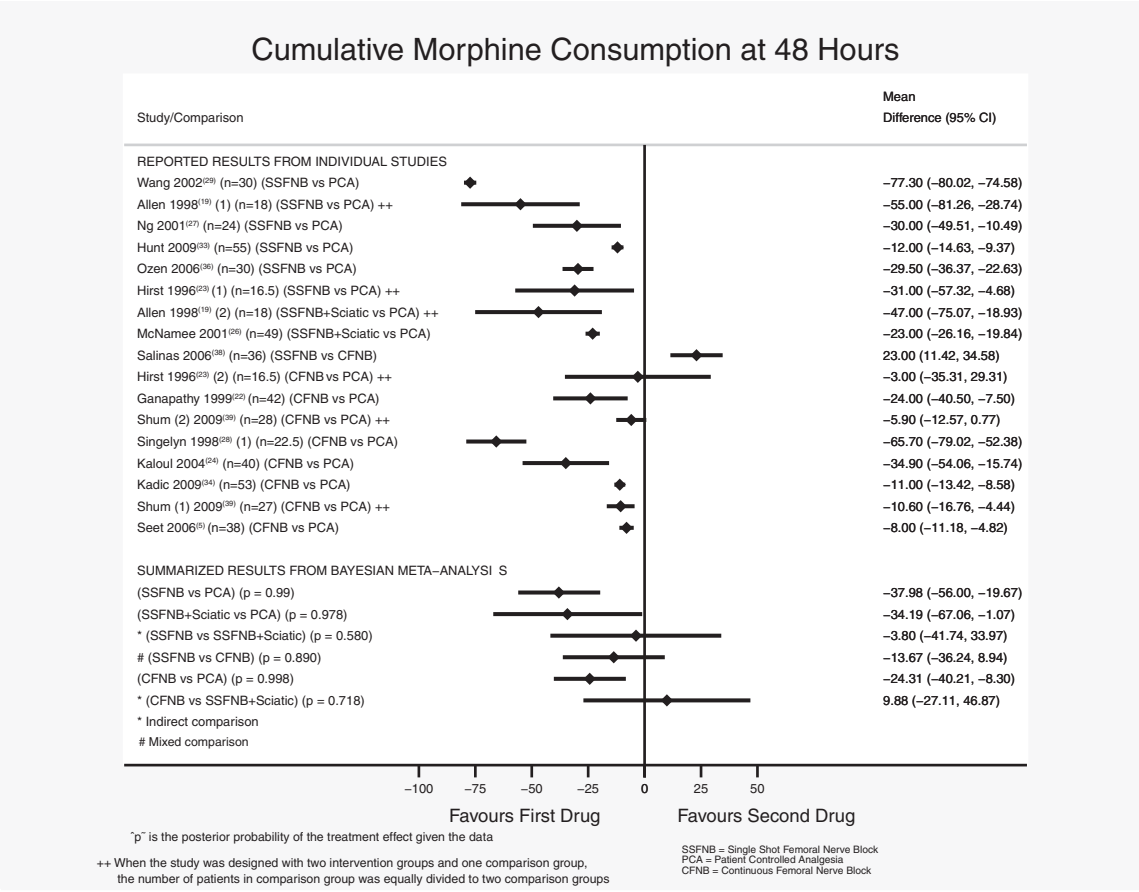

Fig. 3. Cumulative morphine consumption at 48 h. * = indirect comparison; # = mixed comparison; p = posterior probability of the treatment effect given the data; ++ = when the study number was designed with two intervention groups and one comparison group, the number of patients in the comparison group was equally divided into two comparison groups. CFNB = continuous femoral nerve block; PCA = patient-controlled analgesia; Sciatic = sciatic nerve block; SSFNB = single-shot femoral nerve block.

have a more positive profile for pain management than single-shot FNB (SSFNB).

Statistical Analysis

Standard deviations not stated or graphically represented were estimated as range/4 or interquartile range/1.35 where range = maximum value − minimum value and interquartile range = Q3–Q1, with Q1 and Q3 as the first and third quartiles. When SE was given, SD was calculated using the following formula: SE = SD/(square root of n). For the article by Mistraletti *et al.*[12] where no estimate of SD could be made for opioid consumption in the epidural group, the SD for the FNB group was used for both groups. The 95% CI was used to estimate the range when required, and the median was used to estimate the mean if mean values were not given. When necessary, the range was estimated as the most extreme values of a variable, for example range = 10 for a pain scale of 0–10. For side effects, which were expressed as incidence during time intervals, the single highest incidence was used to capture anybody who experienced that side effect at least once.

To synthesize all possible treatment effects around using femoral nerve block, we applied the Bayesian random-effects model with mixed-treatment comparison methods that allowed both direct and indirect comparisons. Key to the Bayesian method is the incorporation of prior beliefs, in the form of a prior probability distribution combined with observed data, in the form of a likelihood function, to yield a posterior distribution.[13] Unlike the direct comparison method which simply compares treatment A with treatment B, indirect comparison assesses the treatment effect between treatment A and treatment B using treatment C as a common comparator. In our model, we expressed the comparison as $\theta AB = \theta AC - \theta BC$. When no common comparator was needed as a transit link, the indirect comparison reduced to direct comparison[14,15]; and when both direct and indirect links existed, two types of comparisons were naturally combined to report the designed treatment comparison.

We adopted the ROBUST criteria in reporting the results of our Bayesian analyses.[16] Our dataset contained both continuous outcomes and binary outcomes. For the continuous outcome, the treatment effect was measured as mean differ-

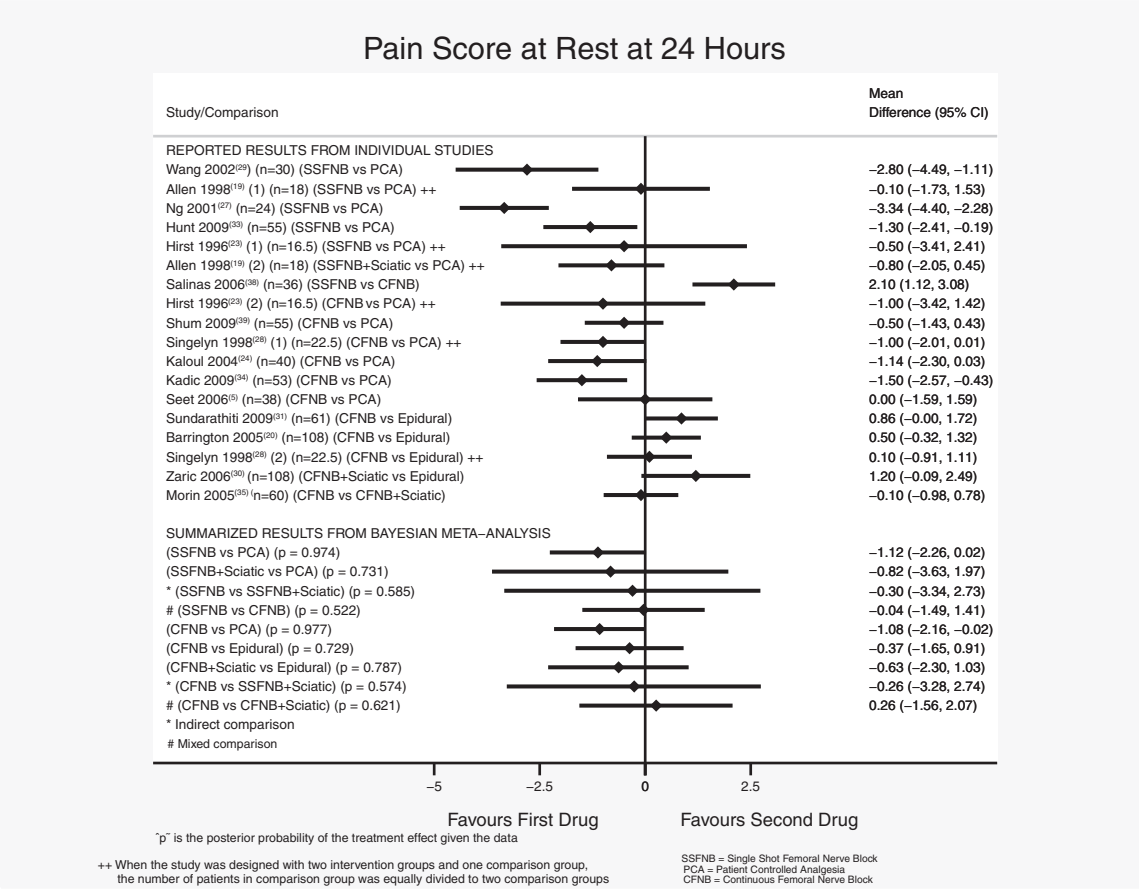

Fig. 4. Pain scores at rest at 24 h. * = indirect comparison; # = mixed comparison; p = posterior probability of the treatment effect given the data; ++ = when the study number was designed with two intervention groups and one comparison group, the number of patients in the comparison group was equally divided into two comparison groups. CFNB = continuous femoral nerve block; Epidural = epidural nerve block; PCA = patient-controlled analgesia; Sciatic = sciatic nerve block; SSFNB = single-shot femoral nerve block.

ence, and for the binary outcome, the treatment effect was measured as log odds ratio. We assumed that in each comparison, treatment effect was normally distributed as $\theta \sim$ Normal (μ, σ 2). The first parameter μ is the mean, which represents the treatment effect across all trials. The second parameter σ 2 is the variance, which represents the between-study variability. Furthermore, we assumed *a priori* that μ itself follows another Normal distribution, and σ follows a Uniform distribution. For the choice of priors, we used non-informative priors as $\mu \sim$ Normal (0, 1.0E5) and $\sigma \sim$ Uniform (0,50). In this setting, because the variance of the prior was large, *i.e.*, the information was little, the pooled trial data dominated the results of posterior distribution, which led the result similar to that obtained from a traditional non-Bayesian meta-analysis.

We report the treatment effects as point estimates (mean difference or odds ratio, the exponential form of log odds ratio) with associated 95% credible interval which were obtained from the posterior distributions. The posterior probability of treatment effects greater or less than 0 for continuous outcomes, and greater or less than 1 for binary outcomes were also reported. The analysis was performed using the software WinBUGS 1.4,‡‡ which generates inferences using the Gibbs sampler; and the forest plots that graphically summarized the results from the Bayesian analysis were produced using STATA10.1 (StataCorp, College Station, TX). The stability of the Bayesian model and convergence of the Bayesian simulations were assessed graphically using the time series plots of the density function of the posterior distribution and the autocorrelation plot.[17] The details about the Bayesian code, number of iterations, and initial values can be found in appendix 1.

For the reader, when interpreting results from Bayesian methods it is important to recognize two unique differences from the traditional frequentist approach: (1) the use of a prior probability in combination with the observed data to generate the results and (2) the resulting posterior probability *p* is interpreted differently from the

‡‡ www.mrc-bsu.cam.ac.uk/bugs/winbugs. Last date accessed January 6, 2010.

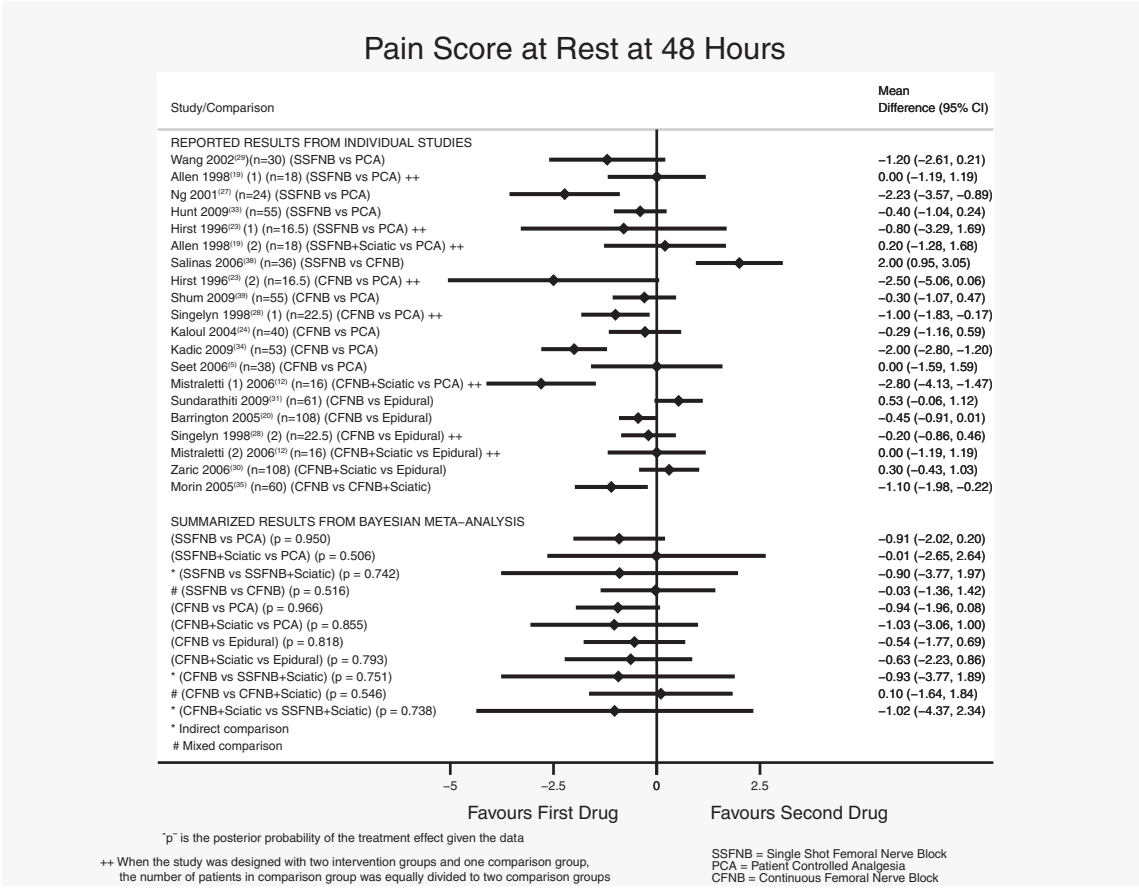

Fig. 5. Pain scores at rest at 48 h. * = indirect comparison; # = mixed comparison; p = posterior probability of the treatment effect given the data; ++ = when the study number was designed with two intervention groups and one comparison group, the number of patients in the comparison group was equally divided into two comparison groups. CFNB = continuous femoral nerve block; Epidural = epidural nerve block; PCA = patient-controlled analgesia; Sciatic = sciatic nerve block; SSFNB = single-shot femoral nerve block.

classic *P* value[18] as the posterior probability of treatment 1 is better than treatment 2. In the results quoted in this study, a noninformative prior distribution was used, which means that the observed results were not influenced by the prior distribution. Further, the 95% credible interval is intuitively interpreted as the interval within which the effect lives with a 0.95 probability. This is different from the frequentist approach, which generates a point estimate with a 95% CI, and this cannot be interpreted in terms of probabilities like the Bayesian results.

Results

Included Studies

Seventy-seven studies were initially identified as potentially relevant. Fifty-four studies (appendix 2) were then excluded for not meeting the inclusion criteria. The reasons for exclusion were as follows: 17 studies were not randomized control trials, 29 studies did not have either FNB or control group, 5 studies did not include measured outcomes, 1 included surgeries other than knee arthroplasty, and 2 studies included the same study population as an earlier study. Figure 1 summarizes the study selection process. The remaining 23 studies were included in the analysis.[5,12,19–39] Study characteristics and the data extracted from these studies are presented in table 1.

Of the 23 studies included, 14 compared FNB with PCA, and 4 compared FNB with epidural, 3 compared different types of FNB, and 2 compared FNB with both epidural and PCA. A total of 1,016 patients were included in the studies, 665 received FNB, 161 epidural and 190 PCA. There were three types of FNBs in the treatment groups: SSFNB (7 studies/136 patients), SSFNB plus sciatic nerve block (SSFNB + Sciatic, 3 studies/62 patients), and CFNB (13 studies/352 patients) and CFNB + Sciatic, 2 studies/43 patients). Only two studies addressed the comparison of SSFNB *versus* SSFNB + Sciatic or CFNB: one study[19] compared SSFNB with SSFNB + Sciatic, and two studies[23,38] compared SSFNB with CFNB.

All 23 studies used a nerve stimulator for the nerve blocks, none used ultrasound guidance, 13 of the 23 FNBs were 3-in-1 blocks, 13 used bupivacaine, 13 used ropivacaine, and

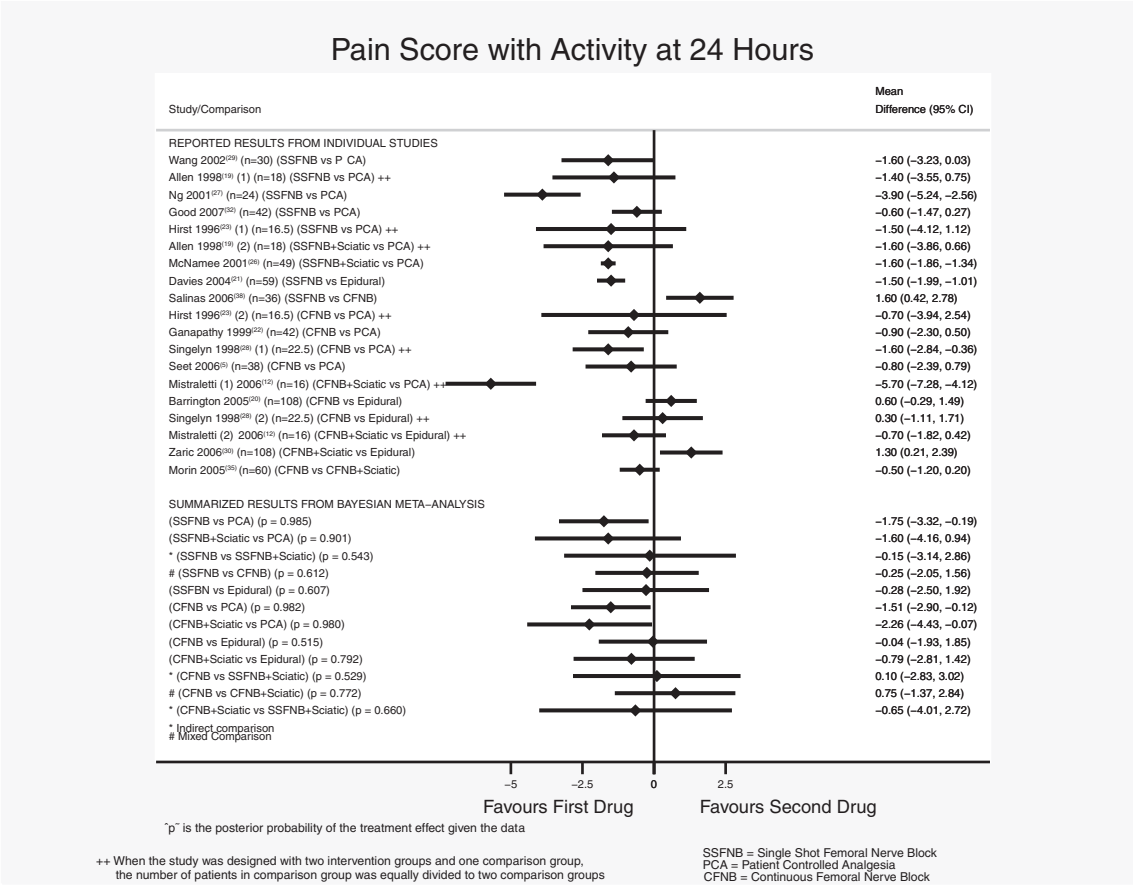

Fig. 6. Pain scores with activity at 24 h. * = indirect comparison; # = mixed comparison; p = posterior probability of the treatment effect given the data; ++ = when the study number was designed with two intervention groups and one comparison group, the number of patients in the comparison group was equally divided into two comparison groups. CFNB = continuous femoral nerve block; Epidural = epidural nerve block; PCA = patient-controlled analgesia; Sciatic = sciatic nerve block; SSFNB = single-shot femoral nerve block.

2 used lidocaine. Of the 15 studies with a PCA group, 10 used a placebo/sham block in the PCA control group. Eighteen studies utilized concurrent PCA opioids in the FNB treatment groups: all 10 studies with SSFNB and/or SSFNB + Sciatic and 8 of the 13 studies with CFNB. Several of the studies used concurrent analgesia adjuncts. Eleven studies used acetaminophen and nonsteroidal antiinflammatory drugs, and 5 studies used oral opioids.

All 23 studies reported opioid consumption and pain scores; however, only 14 studies included pain scores for both rest and activity (5 studies reported pain only at rest and 4 studies reported pain only with activity). Sixteen studies reported analgesia side effects, 14 reported knee range of motion and length of stay, and 9 reported patient satisfaction.

All 23 studies were randomized and had complete follow-up of patients, 15 were double-blinded, 14 described a suitable technique for randomization, and 10 (of the 15 blinded studies) described an adequate method of blinding. The quality scores ranged from 2 to 5, with a mean of 3.7. Five of the 23 studies had a quality score of 5 of 5, meaning that they were randomized, double-blinded, had complete follow up, and had suitable randomization and blinding methods.[12,22,25,28,35]

Opioid Consumption

SSFNB, SSFNB + Sciatic, and CFNB had significantly less morphine consumption (compared with PCA alone) at 24 h with differences of −20, −31, and −15 mg, respectively (see fig. 2). Similarly, the SSFNB, SSFNB + Sciatic, and CFNB groups had significantly less morphine consumption at 48 h compared with PCA with differences of −38, −34, and −24 mg, respectively (see fig. 3). SSFNB was equivalent to SSFNB + Sciatic and CFNB in terms of morphine consumption at both 24 and 48 h. The epidural groups were not included in these comparisons because there was no concurrent intravenous PCA in these groups. A sensitivity analysis was done to compare morphine consumption between studies both with and without analge-

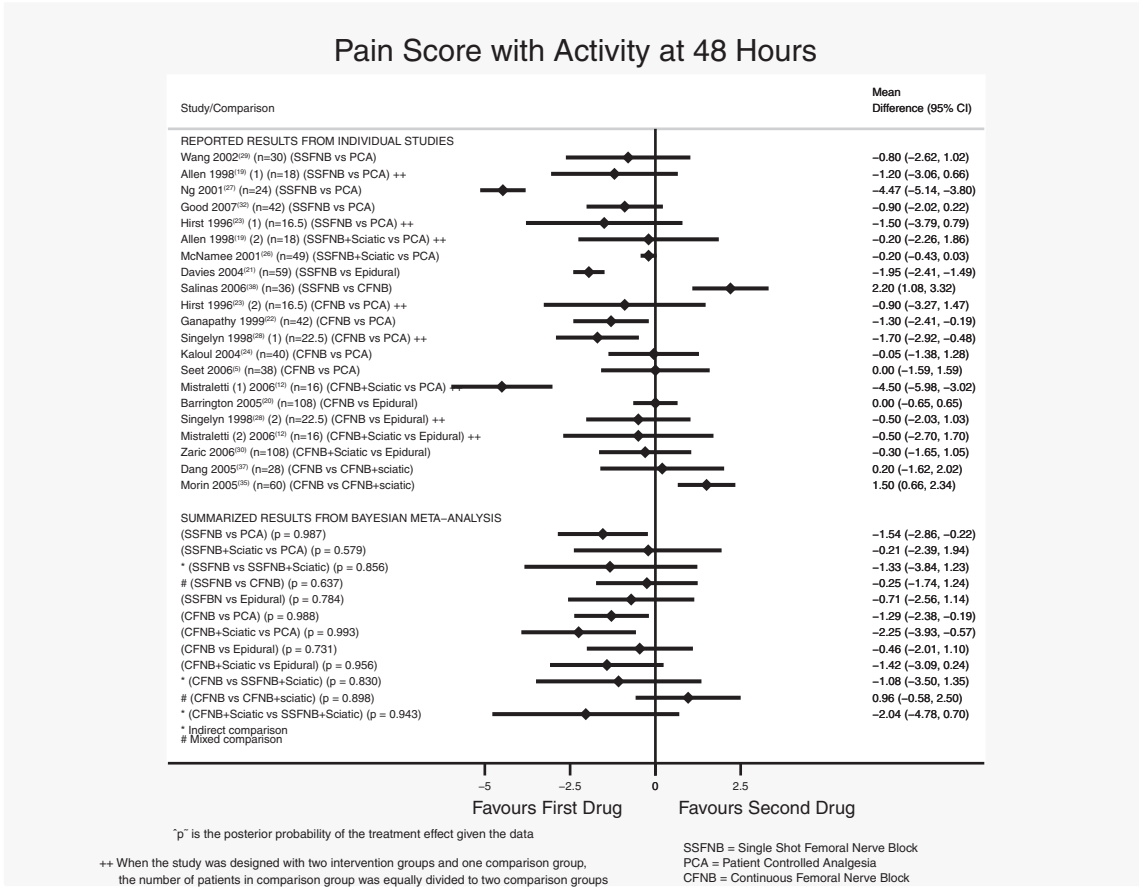

Fig. 7. Pain scores with activity at 48 h. * = indirect comparison; # = mixed comparison; p = posterior probability of the treatment effect given the data; ++ = when the study number was designed with two intervention groups and one comparison group, the number of patients in the comparison group was equally divided into two comparison groups. CFNB = continuous femoral nerve block; Epidural = epidural nerve block; PCA = patient-controlled analgesia; Sciatic = sciatic nerve block; SSFNB = single-shot femoral nerve block.

sia adjuncts. Three studies[23,26,29] did not use analgesia adjuncts, and when morphine consumption was compared between these studies the groups with significant differences did not change from the original analysis. Similarly, when all studies with analgesia adjuncts were compared, the groups with significant differences were also the same as with the original analysis.

Pain Scores with Rest

At 24 h, CFNB had less pain at rest (−1.1) than PCA (see fig. 4). At 48 h there were no significant differences between the groups (see fig. 5). SSFNB was equivalent to SSFNB + Sciatic and CFNB in terms of pain at rest at 24 and 48 h.

Pain Scores with Activity

SSFNB, CFNB, and CFNB + Sciatic had less pain with activity (−1.8, −1.5, and −2.3, respectively) at 24 h compared with PCA (see fig. 6). SSFNB, CFNB, and CFNB + Sciatic has less pain with activity (−1.5, −1.3, and −2.3, respectively) at 48 h compared with PCA, otherwise there were no significant differences between groups (see fig. 7). SSFNB was equivalent to SSFNB + Sciatic and CFNB in terms of pain with activity at 24 and 48 h.

Opioid Side Effects

Because of the small number of studies that reported side effects all FNBs (SSFNB, SSFNB + Sciatic, CFNB, and CFNB + Sciatic) were grouped together for the purpose of comparing with PCA. FNB groups had significantly less nausea (0.31 Odds) compared with PCA, but there were no differences in terms of pruritus or sedation (see figs. 8–10).

Knee Range of Motion, Patient Satisfaction, and Hospital Length of Stay

There were no between treatment groups in knee range of motion (at 48 h), patient satisfaction, and hospital length of stay, see figures 11–13.

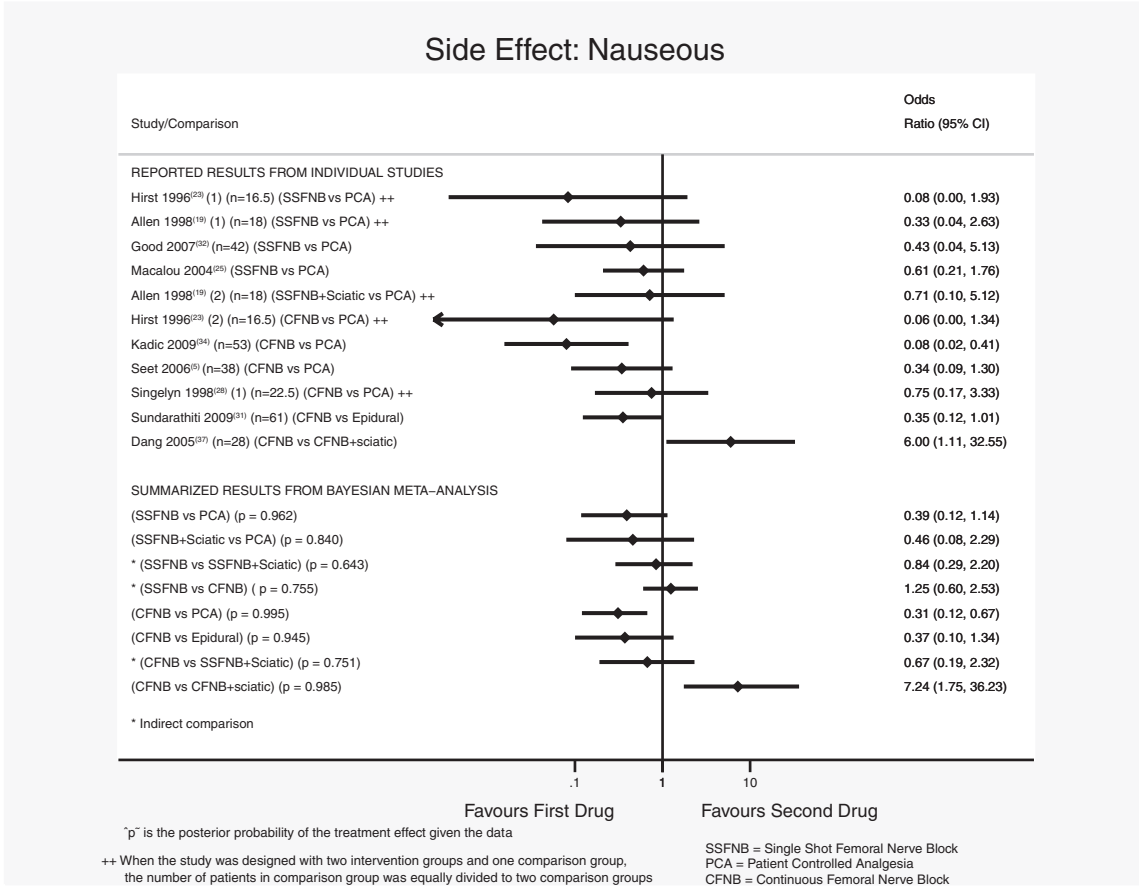

Fig. 8. Incidence of nausea, femoral nerve block versus PCA. * = indirect comparison; p = posterior probability of the treatment effect given the data; ++ = when the study number was designed with two intervention groups and one comparison group, the number of patients in the comparison group was equally divided into two comparison groups. CFNB = continuous femoral nerve block; Epidural = epidural nerve block; PCA = patient-controlled analgesia; Sciatic = sciatic nerve block; SSFNB = single-shot femoral nerve block.

Motor Block

There were no differences in the degree of motor block between the PCA and FNB groups or between the operative and nonoperative leg in the FNB groups (see fig. 14).

Discussion

Our results showed that SSFNB (plus concurrent PCA) compared with PCA alone demonstrated reduced morphine consumption at 24 and 48 h, lower pain scores with activity at 24 and 48 h, and a reduced incidence of nausea. These results were robust to a sensitivity analysis that examined the impact of analgesia adjuncts. FNB showed no advantage compared with PCA for pruritus, sedation, knee range of motion, motor block, patient satisfaction, or hospital length of stay. The addition of a sciatic nerve block or a CFNB to a SSFNB did not reduce morphine consumption or pain scores.

Our systematic review has a number of strengths. The study focuses on an explicit clinical problem: how does SSFNB compare with PCA and epidural analgesia and is it advantageous to do a concurrent sciatic nerve block or CFNB? Adhering to clearly defined *a priori* inclusion and exclusion criteria, a comprehensive literature search was performed using multiple sources. Eligibility decisions and data extraction were conducted in duplicate; the level of agreement was high among reviewers. In addition, the trial flow summarizing the review profile was clearly described, and the individual study characteristics are described in detail in table 1.

There are some limitations to this review. As mentioned at the beginning of the discussion, some of the quantitative analyses were based on indirect comparison; that is, Bayesian inference methods were used to compare treatments that were not compared head to head in the same randomized control trial.[18] This approach was necessary to address the question of the utility of both the sciatic and CFNB because of the small amount of information available from direct pairwise comparisons available in the original randomized control trials. For these indirect comparisons it is important to remember that they are not randomized and therefore subject to the same biases as observational studies.[40] The direct comparisons were limited by the small number of trials that addressed the issue, only one trial[19] with 36 patients addressed SSFNB *versus* SSFNB + Sciatic, and only two trials[23,38] with a total of 69 patients addressed the compari-

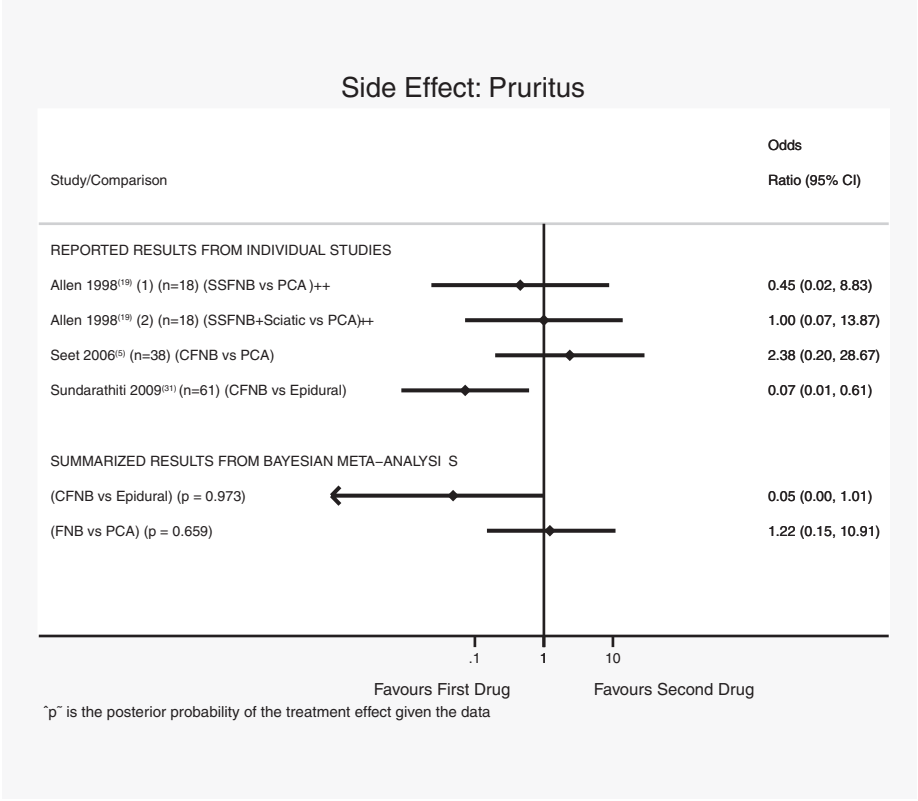

Fig. 9. Incidence of pruritus, femoral nerve block versus PCA. ++ = when the study number was designed with two intervention groups and one comparison group, the number of patients in the comparison group was equally divided into two comparison groups. CFNB = continuous femoral nerve block; Epidural = epidural nerve block; FNB = femoral nerve block; p = posterior probability of the treatment effect given the data; PCA = patient-controlled analgesia; Sciatic = sciatic nerve block; SSFNB = single-shot femoral nerve block.

son of SSFNB *versus* CFNB. Interestingly, of the two trials that addressed SSFNB *versus* CFNB, the one that used ropivacaine[38] showed an advantage (in terms of reduced pain scores and opioid consumption) to using CFNB, whereas the one that used bupivacaine[23] did not. This difference may have been due to the faster resolution of motor and sensory function with ropivacaine blocks *versus* bupivacaine blocks.[41] The longer duration of action of a SSFNB with

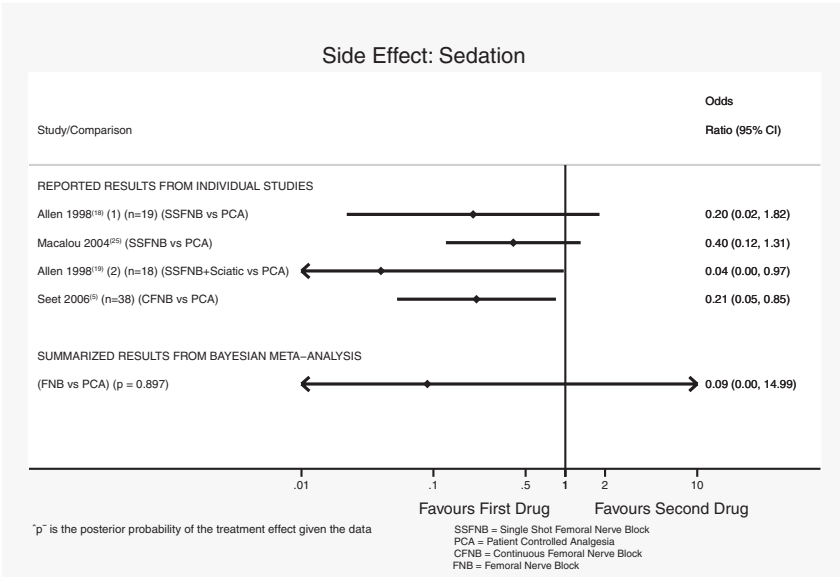

Fig. 10. Incidence of sedation, femoral nerve block versus PCA. CFNB = continuous femoral nerve block; FNB = femoral nerve block; p = posterior probability of the treatment effect given the data; PCA = patient-controlled analgesia; Sciatic = sciatic nerve block; SSFNB = single-shot femoral nerve block.

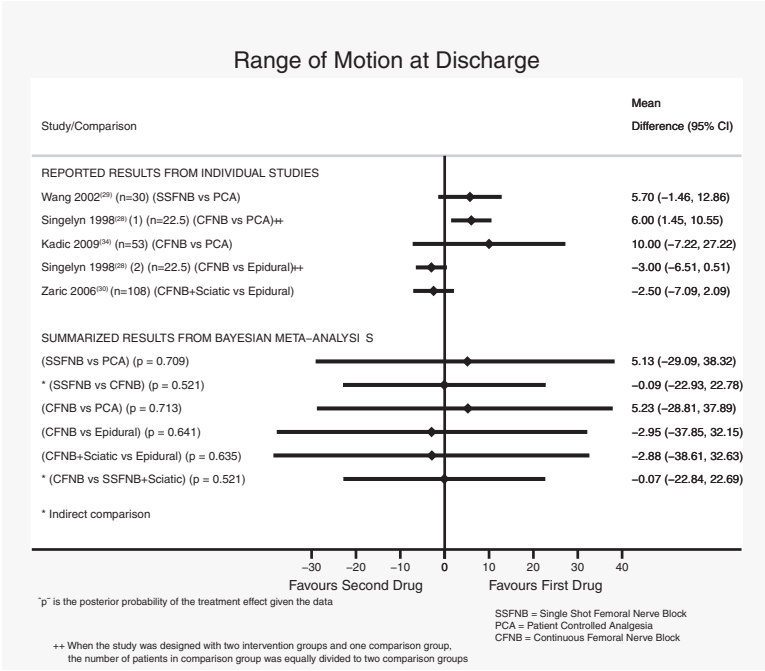

Fig. 11. Knee range of motion at discharge. * = indirect comparison; p = posterior probability of the treatment effect given the data; ++ = when the study number was designed with two intervention groups and one comparison group, the number of patients in the comparison group was equally divided into two comparison groups. CFNB = continuous femoral nerve block; Epidural = epidural nerve block; PCA = patient-controlled analgesia; Sciatic = sciatic nerve block; SSFNB = single-shot femoral nerve block.

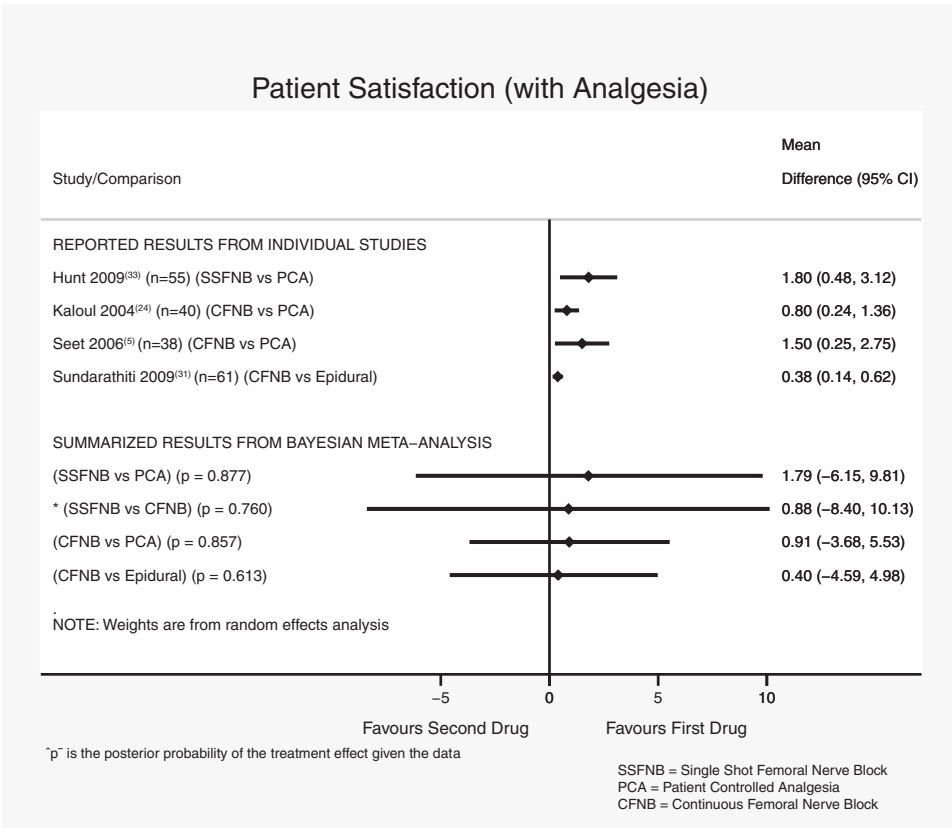

Fig. 12. Patient satisfaction with analgesia. * = indirect comparison; p = posterior probability of the treatment effect given the data. CFNB = continuous femoral nerve block; Epidural = epidural nerve block; PCA = patient-controlled analgesia; Sciatic = sciatic nerve block; SSFNB = single-shot femoral nerve block.

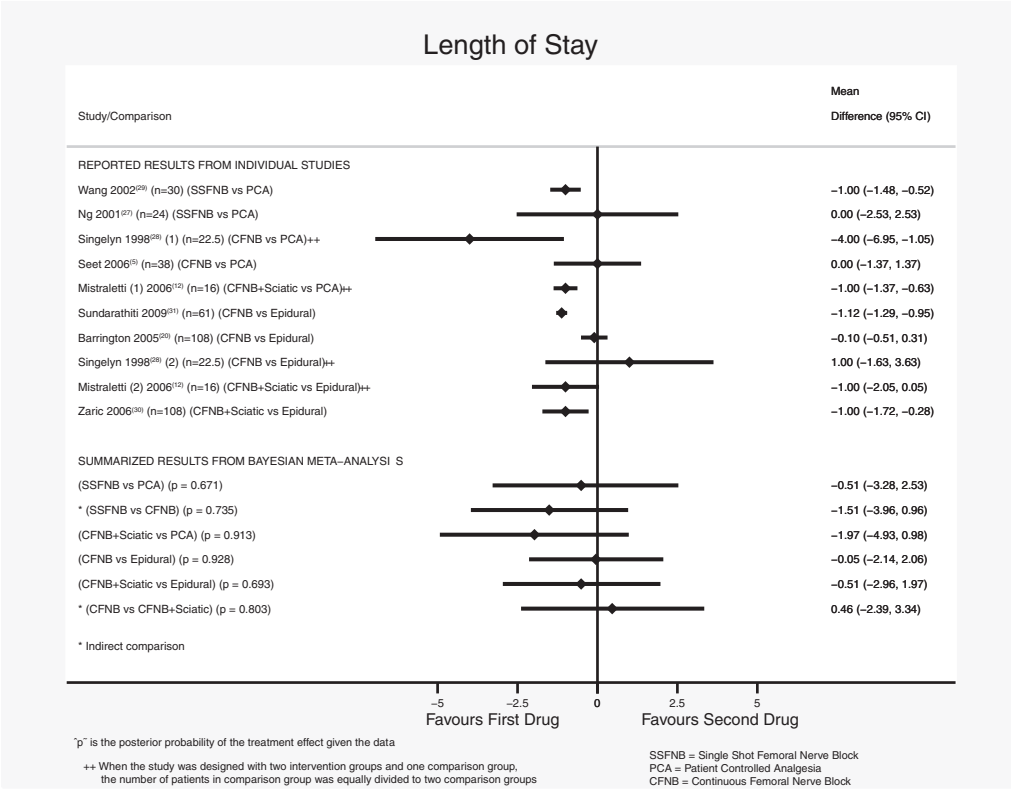

Fig. 13. Hospital length of stay (in days). * = indirect comparison; p = posterior probability of the treatment effect given the data; ++ = when the study number was designed with two intervention groups and one comparison group, the number of patients in the comparison group was equally divided into two comparison groups. CFNB = continuous femoral nerve block; Epidural = epidural nerve block; PCA = patient-controlled analgesia; Sciatic = sciatic nerve block; SSFNB = single-shot femoral nerve block.

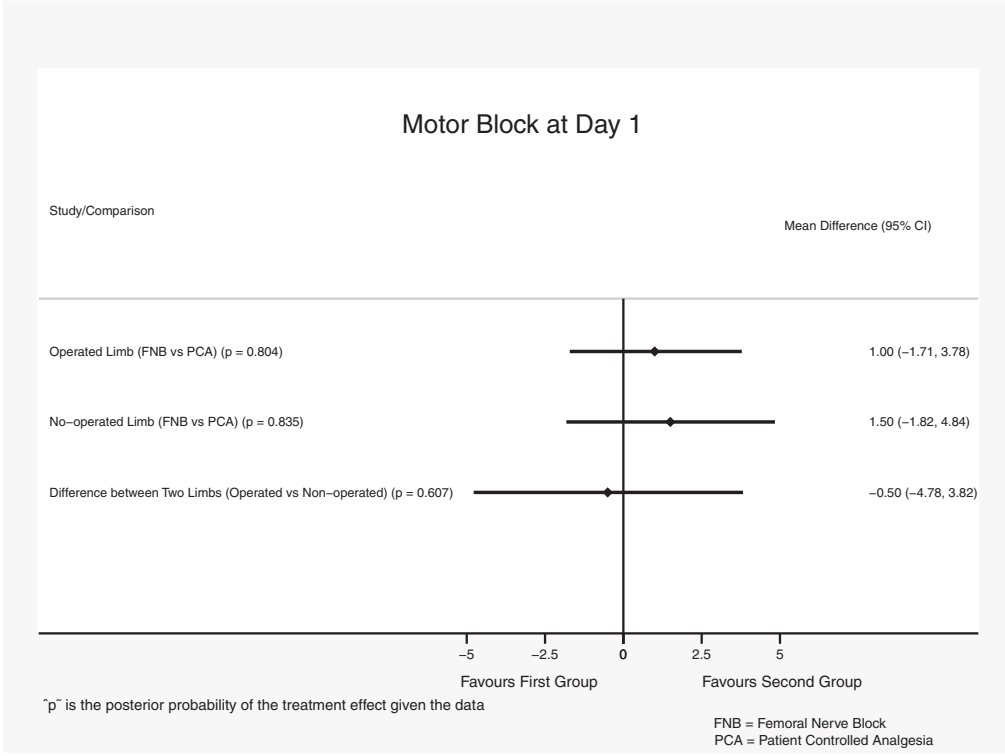

Fig. 14. Motor block of operative and nonoperative leg. CI = confidence interval; p = posterior probability of the treatment effect given the data; FNB = femoral nerve block; PCA = patient-controlled analgesia.

bupivacaine could have masked any benefit seen with CFNB.

Given that adding a sciatic nerve block or a CFNB over a SSFNB alone does not offer any advantages in terms of reduced morphine consumption, pain scores, or side effects, the current evidence does not support doing these additional blocks. This finding reflects the current state of evidence, and because of the paucity of randomized controlled trials that made direct comparisons it could be viewed as hypothesis-generating. This issue will likely spark some lively debate among clinicians that promote regional anesthesia. It is worth noting that CFNB was shown to be clearly superior to PCA alone in terms of reduced morphine consumption (at 24 and 48 h), reduced pain scores (at rest at 24 h and with activity at 24 and 48 h), reduced nausea, and a trend toward decreased pruritus.

Although FNB has consistently been shown to offer advantages in terms of analgesia outcomes, many clinicians (especially surgeons) are concerned about the issue of prolonged quadriceps weakness.[42] Motor block results from this review showed that there were no significant differences between FNB and PCA groups and the operative and nonoperative leg at 24 h after surgery. Unfortunately, these results were only based on three studies because the rest did not report motor block outcomes quantitatively, and it was not possible to estimate the incidence of this complication among the 665 patients treated with FNB in this review. It has been estimated that this complication occurs in about 2% of patients.[41] This complication is important because it can lead to falls, fractures, and delays in ambulation. It is worth noting that the FNB group did not have a longer length of stay than the PCA control group. A prospective study of 3,996 patients who had upper or lower limb blockade showed that the incidence of neurologic dysfunction was 1.7%, and complete recovery had occurred for most by 12 weeks and all by 25 weeks.

In conclusion, FNB and CFNB (plus PCA) are superior to PCA alone or epidural for postoperative analgesia for patients having TKA. Under the conditions of our statistical model and inclusion criteria, however, there is a lack of evidence that sciatic nerve block or CFNB in addition to a single injection FNB provides additional analgesic or recovery benefits. In the future, high quality randomized controlled trials are needed that offer more head-to-head comparisons of SSFNB *versus* SSFNB plus CFNB for TKA. Also, studies are needed that better prospectively evaluate the complications of FNB, especially the issue of prolonged quadriceps weakness and falls, and more head-to-head comparisons of SSFNB *versus* SSFNB + Sciatic and CFNB would help settle the question of whether these additional blocks are of benefit.

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Appendix 1. Bayesian Code for Primary Outcomes

model {# trial specific comparison
for (*i* in 1:N) {#N: number of total groups
y[*i*]~dnorm(*ψ*[*i*],tau0) # normal likelihood
ψ[*i*]~*μ*[*s*[*i*]]−*δ*[*i*] * (1-equals(*t*[*i*],*b*[*i*])) # model
δ[*i*] ~ dnorm(*md*[*i*],tau) # random effects of trial-specific difference
md[*i*] −*d*[*t*[*i*]] − *d*[*b*[*i*]] # mean difference
}
for(*j* in 1:NS) {#NS: number of studies
μ[*j*]~dnorm(0, 0.00001) #noninformative prior for mean difference
}
# direct comparison
d[1]<0
for (*k* in 2:NT) {#NT: number of treatment
d[*k*]~dnorm(0, 0.0001) # noninformative priors for mean difference
p[*k*]<step(0-day[*k*]) # calculating posterior probability
}
#all mean differences of all possible comparisons
for (*c* in 1:(NT-1)) {
for (*k* in (*c* + 1):NT) {
pw.diff[*c*,*k*] <(*d*[*k*] − *d*[*c*]) # difference
.prob.diff[*c*,*k*]<step(0-pw.diff[*c*,*k*]) # posterior probability
}
}
tau0<1/(SD*SD) # precision (1/variance)
tau</(SD*SD) # between-study precision
SD~dunif (0,50) # noninformative prior for standard deviance
b.var<1/tau # between-study variance
}
Number of iteration: 300,000
Number of burn-in (discarded): 5,000
Number chain: 2
Partial initial value
Chain-1 list (SD = 2, *d* = *c*(0,0,0))
Chain-2 list (SD = 4, *d* = c(−5,−5,−5))

Appendix 2. Excluded Studies

	First Author	Year	Reference	Reason
43	Adam F	2005	Anesth Analg 100: 475–80	Intervention
44	Allen JG	1998	Reg Anesth Pain Med 23:142–6	Intervention
45	Barrington MJ	2008	Anesth Analg 106:1316–21	Intervention
46	Beaulieu P	2006	Anesth Analg 103:768–74	Intervention
47	Ben-David B	2003	Anesth Analg 96:1537	Methodology
48	Ben-David B	2004	Anesth Analg 98:747–9	Methodology
49	Bergeron SG	2009	Clin Orthop 467:1458–62	Intervention
50	Bogoch ER	2002	J Arthroplasty 17:398–401	Intervention
51	Bunburaphong P	2006	J Med Assoc Thai 89:462–7	Intervention
52	Buvanendran A	2006	J Knee Surg 19:133–6	Methodology
53	Capdevila X	1999	Anesthesiology 91:8–15	Population
54	Casati A	2005	Anesth Analg 100:866–72	Intervention
55	Chelly JE	2001	J Arthroplasty 16:436–45	Outcomes
56	Cook P	2003	J Arthroplasty 18:583–6	Methodology
57	De Ruyter ML	2006	J Arthroplasty 21:1111–7	Methodology
58	Duarte VM	2006	JOPAN 21:311–6	Methodology
59	Edwards JL	2006	Br J Nursing. 15:S20–5	Outcomes
60	Edwards ND	1992	Anesth Analg 75:265–7	Intervention
61	Eledjam JJ	2002	Reg Anesth Pain Med 27:604–11	Intervention
62	Enneking FK	2002	Baillieres Best Practice & Research in Clinical Anaesthesiology 16:285–94	Methodology
63	Faust AM	2006	Reg Anesth Pain Med 31:591	Intervention
64	Guay J	2005	Anesth Analg 100:1547	Methodology
65	Guay J	2006	Pain Med 7:476–82	Population (same study population as Kaloul *et al.* 2004 included study)
66	Hayek SM	2006	Anesth Analg 103:1565–70	Outcomes
67	Heid F	2008	Anesth Analg 106:1559–61	Intervention
68	Huang Y-S	2007	Anesth Analg 104:1230–5	Intervention
69	Ilfeld BM	2006	Anesth Analg 102:87–90	Methodology
70	Ilfeld BM	2007	Reg Anesth Pain Med 32:46–54	Methodology
71	Ilfeld BM	2008	Anesthesiology 108:703–13	Intervention
72	Ilfeld BM	2009	Anesth Analg 108:1320–5	Population
73	Jack NTM	2005	Br J Anaesth 95:250–4	Methodology
74	Juelsgaard P	2001	Reg Anesth Pain Med 26:105–10	Intervention
75	Kardash K	2007	Anesth Analg 105:853–8	Intervention
76	Mannion S	2005	Br J Anaesth 94:352–6	Intervention
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