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Clinical effectiveness of transversus abdominis plane (TAP) block for pain relief after Caesarean Section: a meta-analysis

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Abstract

Background

The effectiveness of Transversus Abdominis Plane (TAP) block in the provision of acute pain relief after Caesarean Section, in comparison to normal practice, remains uncertain.

This systematic review examines the published randomised evidence.

Methods Electronic literature databases were searched from inception to November 2015 for randomised controlled trials that assessed the effectiveness of TAP block following caesarean section. Trials were eligible if comparisons were made against no block or placebo, and/ or intrathecal morphine. Risk of bias was assessed using the Cochrane tool.

Data for consistent outcomes were meta-analysed where possible and presented as either mean differences with 95% confidence intervals or incidence of a particular event.

Results

Nineteen published studies fulfilled our inclusion criteria, of which nine compared TAP block with placebo TAP and all but one were blinded. TAP block significantly reduced pain at rest 6 hours after caesarean section when compared with placebo or no TAP block (-3.58; 95% CI -6.27 to -0.90 p=0.009) however, this effect diminished at 24 hours (-1.05; 95% CI -2.08 to -0.01p=0.05). Morphine consumption is significantly reduced with TAP block usage. Co-administration of intrathecal morphine and TAP block significantly improved pain at rest and on movement in the short term (-0.54; 95% CI -1.00 to -0.08 p=0.02) and (-1.02; 95% CI -1.66 to -0.39 p=0.002) respectively, compared to placebo TAP block and intrathecal morphine.

Conclusions

TAP block provides effective analgesia after Caesarean Section, however additional benefits of TAP block are more difficult to demonstrate when long acting intrathecal opioids are administered.

51 Keywords

52 Transversus Abdominis Plane block, TAP block, Caesarean Section, Caesarean delivery

Introduction

Acute pain from the site of abdominal incision can complicate birth by Caesarean Section (CS). Failure to achieve adequate pain control is one of the most common reasons for poor satisfaction among women who give birth by CS.[1] CS is a very common surgical procedure, with an increasing prevalence. An approximate 166, 000 CS deliveries are performed annually in England alone (data for 2014/2015). [2] Adequate postoperative analgesia following CS hastens post-operative mobilisation, decreases maternal morbidity and facilitates bonding with the newborn.[3] Neuraxial opioids can provide effective post-operative pain relief for many hours after surgery, although their administration has a well-defined risk of side effects including nausea, pruritis, urinary retention and the potential for delayed respiratory depression.[4] Alternative modalities of pain relief offer the prospect of a beneficial reduction in side effect profile with no loss in analgesic effectiveness. [1]

The last two decades has seen peripheral nerve blockade gain prominence in the prevention and treatment of acute post-operative pain. The success of ultrasound guided peripheral nerve localisation with nerve stimulation has fuelled new innovation in block technique and indication. These novel blocks can be performed with minimal risk of complications to the patient.[5, 6] Tranversus Abdominis Plane (TAP) block's mechanism of action requires anaesthesia to the sensory nerve supply of the anterior abdominal wall. [6-8] Blockade of sensory nerves is achieved in the neurofascial plane between the internal oblique and transversus abdominis muscles through a well-defined entrance at the triangle of Petit. [7, 8] The use of TAP block to alleviate pain after non-obstetric abdominal surgery has become established. [9] However, evidence from recently published clinical trials have shown encouraging results that suggest that TAP block is effective for treating postoperative pain following CS. This systematic review and meta-analysis collated data from all published randomised controlled trials of TAP block to assess its effectiveness in reducing patient-reported postoperative pain scores and reducing opioid usage following CS.

Methods

The systematic review was based on a prospective protocol designed using widely recommended methods and reported to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. [10-12] No institutional review board approval was needed for this review.

Identification of studies

A comprehensive literature search strategy was used to search the following bibliographic databases, Embase, Medline and the Cochrane Library (CENTRAL), from database inception to November 2015. We adapted the search strategy used in a previous Cochrane review [9] by replacing search terms pertaining to abdominal surgery with variations for CS as MeSH terms or text. The Clinical Trials registers found at www.clinicaltrials.gov, www.isrctn.com and the World Health Organisation (WHO) International Clinical Trials Research Platform (ICTRP) were searched to identify ongoing trials. The authors of these trials were contacted via email to ask if they would be willing to contribute unpublished data. Bibliographies of all relevant primary articles and reviews were hand searched to identify articles missed by the electronic searches. A comprehensive database was constructed using Reference Manager 12.0 (Thomson Reuters) to store all identified references. No language restrictions were applied.

Study selection and data extraction procedures

Studies eligible for inclusion in the review were selected in a two-step process. First, citations identified by the electronic database searches were screened. Full manuscripts were obtained for those citations that met or potentially met the predetermined inclusion criteria. Two reviewers then independently inspected the manuscripts to confirm that they fulfilled the following criteria:

1. Population: Women undergoing elective Caesarean section
2. Interventions: TAP block using any local anaesthetic agent, alone or in addition to intra-thecal morphine (ITM).
3. Comparator: No or placebo TAP block, alone or in addition to ITM. Studies comparing different doses of local anaesthetic in TAP block were excluded unless there was a control group.

4. Outcomes: Pain scores (at rest and on movement), opioid consumption, complications (nausea, vomiting, pruritis) and maternal satisfaction.
5. Study design: Randomized controlled trial (RCT) where the action of TAP block could be assessed independently of any ITM administered.

We extracted data on study characteristics, methods and results on to a pre-designed pro-forma in duplicate.

Methodological quality assessment

All manuscripts selected for inclusion were assessed using the risk of bias tool developed by the Cochrane Collaboration. [9] A study was considered to be of high quality if it provided evidence of adequate randomisation sequence generation and allocation concealment, if blinding was used, if there was minimal missing outcome data or it was adequately addressed, and if the published paper was free of selective reporting and free of other biases.

Data synthesis

If a trial comparing various doses of TAP block was amongst those trials thought to be eligible for inclusion, every attempt was made to include this data. However, in these circumstances, a form of data manipulation was necessary before the data were used. A validated and recognized formula used by the Cochrane Collaboration enabled us to combine data from the various dosage arms and compare this against the placebo/ control arm.

Trials were grouped according to the question they addressed a) the effectiveness of TAP block in the absence of ITM b) the addition of TAP block to ITM and c) comparison of ITM against TAP block. Where trials addressed more than two questions, the appropriate groups' data were included in each comparison. No further subdivision of questions by technique, local anaesthetic used or dose was undertaken.

Outcome data were extracted from all included studies, as number of women, means and standard deviations for continuous variables and as proportions for dichotomous outcomes. If data was provided in another format, the author of the trial was contacted to ask if they could

provide raw data. Failing this, every attempt was made to convert these values to allow the greatest amount of data to be combined. This outcome data was used to generate forest plots. Pain scores presented as a visual analogue scale (VAS) score were standardized to a 0-10 point continuous scale. Where a VAS score was presented as median and interquartile range (IQR) and the group size was more than 20, these were assumed to follow a normal distribution, with the median assumed to be the mean and standard deviation=IQR/1.35. Data transformed in this way was added to meta-analyses in a secondary sensitivity analyses. Cumulative opioid consumption was considered, with opioid drugs other than morphine converted to morphine equivalent doses, using a published equivalence formula.[13] Incidence of postoperative nausea and vomiting (PONV) was variously reported as one entity, or as separate conditions. In the latter case, we used the nausea data to avoid double counting. Pruritis was also measured in a variety of ways. Where possible, data were collapsed into a dichotomous measure of present or absent. All statistical analyses were performed in Review Manager 5.1 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration 2011). Heterogeneity was described by the I^2 statistic and where significant, a random effects model was used to produce the summary estimate.

Results

A total of 186 citations were identified through the electronic literature database searches. Of these, 146 were excluded after screening of the titles and abstracts. A further 21 citations were discarded upon closer inspection, being either duplicate publications, not using a study design of interest (letters, reviews etc.), or not using a relevant intervention. The remaining 19 articles were included in the systematic review, [14-28] [29-32] (Figure 1). Three abstracts were included in the systematic review, from one of which we were able to obtain unpublished data from the author.[32] A search of the Clinical Trials register identified thirteen relevant ongoing trials. However, none of these trials were at a suitable stage to contribute unpublished data.

Table 1 provides a summary of the characteristics of both the included published trials and of the ongoing studies in addition to a breakdown of the quality criteria per trial; this is also depicted visually in figure 2.

Nine trials evaluated the efficacy of TAP block versus a placebo TAP block [14-17, 19-22, 30, 31] and three against no TAP block (only standard care) [18, 23, 29], all of these in the absence of

ITM. Kagwa et al randomised patients to TAP block or 'sham' TAP block. Sham blocks involved pressing a transducer with a needleless syringe over each flank. We consider this to be equivalent to 'No TAP block'. [31]. Three trials compared ITM and placebo TAP block against an intrathecal placebo and TAP block [22, 24, 25], and five compared ITM together with TAP block against ITM and placebo TAP block.[22, 26-28, 32] The trial by McMorrow et al undertook all three comparisons. Trials, such as Puddy et al, reporting comparisons with intrathecal diamorphine were excluded from the meta-analysis since the analgesic profile of intrathecal diamorphine is substantially different to ITM, particularly in duration of action and side effects. These trials were retained in the systematic review. Fifteen of the nineteen included trials involved women undergoing an elective CS, [17-29, 31, 32] with the remainder not specifying the nature of the CS. Trials involving emergency CS only were excluded since they form a distinct group. Women undergoing emergency CS may have "laboured" prior to CS, are more likely to have the performed under epidural anaesthesia and may have a substantially different post-operative pain experience.. Tan et al stated that they included patients scheduled to undergo elective or ("Category 3") CS delivery in which no maternal or foetal compromise existed. We felt it was appropriate to include this trial, as CS is often performed in the context of an unsuccessful induction of labour without maternal or foetal compromise. There was an intention to perform bilateral TAP block in all trials, although this was not explicitly stated by Kagwa et al.[31] Ultrasound guided technique was used in fourteen studies. [14-17, 21, 23-28, 30-32] and four trials used the anatomical landmark technique [18, 20, 22, 29] whilst in the final study, the approach was unclear.[19]

Bupivacaine was the local anaesthetic of choice in eight trials [14, 16, 18, 22, 24, 32, 29, 31] whilst eight trials used Ropivacaine [15, 20, 21, 25-28, 30], three others used Levobupivacaine.[17, 19, 23] Seventeen trials performed CS under spinal anaesthesia [14-17, 19-22, 24-32] , while general anaesthesia was used in two trials.[18, 23]

A variety of supplementary postoperative analgesia regimens were used. The majority of trials provided a combination of paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs) and opioids, the latter administered either orally or via patient controlled analgesia (PCA). [15, 20, 22, 24-28, 32] Three studies solely used morphine PCA [14, 17, 23], one used a combination of NSAIDs and intravenous opioids [18]. Paracetamol and ketoroloc were administered by Hoydonckx et al.[19] McKeen et al prescribed women paracetamol, naproxen and oxycodone [21] . Standard analgesia in the Srivastava et al trial consisted of diclofenac and intravenous tramadol[29]. Postoperative analgesia in the trial by Sriramka et al comprised oral

paracetamol and IV morphine [30], patients in the Kagwa et al trial received postoperative analgesia in the form of paracetamol and diclofenac [31], while the study by Bollag et al used paracetamol, diclofenac, intravenous morphine and for breakthrough pain, oral tramadol.[16]

Pain scores were reported in all included trials, however, it was not possible to use data from every trial due to inconsistencies in the way the data was presented or the pain symptoms described. Where the primary outcome was explicitly stated by the included trials, the most frequently employed was morphine consumption (or equivalent), being specified by eight trials.[14, 15, 17, 20, 23, 25, 29, 30] Other commonly measured outcomes included, pain scores at rest [18, 31], pain on movement [22, 26-28, 31], wound hyperalgesia [16] and time to first analgesic request [24, 32]. McKeen et al chose to have four primary outcomes, pain at rest, pain on movement, quality of recovery and cumulative opioid consumption.[21] The abstract by Hoydonckx et al did not provide details of what they considered their primary outcome to be. [19]

Figure 2 depicts the quality of the trials included in this review (a more detailed breakdown is given in table 1). The majority of trial reports provided adequate information to assess quality criteria. Two studies were only available in abstract format and attempts to contact the corresponding authors for further information were unsuccessful.[19, 31] Strict, random group allocation concealment was a feature of 12 studies, whilst 18 were blinded. Only nine trials provided a satisfactory level of detail to show that their trial was free of attrition and other biases. We would have expected all women to have been followed up for the primary outcome, irrespective of protocol compliance, but whether this was done was unclear in seven studies. There were inherent blinding complications in the four trials that compared TAP block to no TAP block, but these trials have indicated that investigators and patients were blinded to treatment allocation.[18, 23, 29, 31] Patients in the 'no treatment' groups in the Eslamian et al, Kagwa et al and Tan et al trials received no injections therefore the skin was not punctured. Tan et al, was able to blind patients, by placing a pressure dressing over the site where the TAP block would have been injected. This is similar to treatment of patients in the control arm of the Srivastava et al trial, who did not receive a block, but they still had their skin punctured on both sides by palpating the triangle of Petit. Patients in this trial, had pressure dressings applied to their abdominal wounds that covered the skin puncture sites.[29]

Pain at rest

TAP block versus Control (or no treatment)

Nine out of the thirteen trials that compared TAP block with a control, provided disaggregated data on pain at rest. [14, 16-18, 20-23, 29] whereas pain scores could not be disaggregated in one trial,[15] and the abstracts by Hoydonckx et al and Kagwa et al did not give any actual useable data [19, 31]. Sriramka et al reported overall VAS scores rather than pain scores specific to pain at rest and/ or pain on movement. Their reported findings were that patients randomised to TAP block reported lower pain scores on the VAS (median 26 v 47mm, p=0.008). Attempts to contact the author for unpublished data were unsuccessful.[30] Pooled results for pain at rest, at 6 hours postoperatively favoured of TAP block (mean difference -3.58; 95% CI -6.27 to -0.90 p=0.009). However, this significance had disappeared by 24 hours (mean difference -1.05; 95% CI -2.08 to -0.01 p=0.05) (Figure 3). Overall results, combining both time points indicate that TAP block, when compared to control, is effective for pain at rest (mean difference -2.06; 95% CI -3.21 to -0.90 p=0.0005).

(ITM and Placebo TAP block) versus (Placebo ITM and TAP block)

Results from the two trials with clearly reported data [22, 25] showed no difference between TAP block and ITM at 6 hours (mean difference 7.21; 95% CI -6.99 to 21.41 p=0.32) or 24 hours postoperatively (mean difference 8.37; 95% CI -8.82 to 25.57 p=0.34) (Figure 4). Overall results support these findings (mean difference 2.46; 95% CI -0.20 to 5.11 p=0.07). Data from the trial by Kanazi et al could not be included in the forest plot, as it was non-normally distributed and it considered both somatic and visceral pain at 2 and 4 hours post-operatively.[24] Pain scores at rest were not significantly different at 6 and 24 hours after CS.

(ITM and TAP block) versus (ITM and Placebo TAP block)

All five trials included in this comparison provided data which were used to produce the forest plot as seen in figure 5.[22, 26-28, 32] Although Puddy et al provided data, we were unable to include this in the meta-analysis, as their comparison involved diamorphine. Therefore, based on data from the remaining four trials, short term results suggest that a combination of ITM and TAP block are more effective than ITM alone in the immediate post-operative

period (6 hours) (mean difference -0.54; 95% CI -1.00 to -0.08 p=0.02), however, this effect is not sustained at 24 hours (mean difference 0.03 95% CI -0.54 to 0.59 p=0.92). Combining data over both time points suggest no effect (mean difference -0.27; 95% CI -0.68 to 0.13 p=0.19)

Pain on movement

TAP block versus Control (or no treatment)

Nine trials provided data for these meta-analyses.[14, 16-18, 20-23, 29] TAP block was shown to be no more effective than control for treating pain on movement at 6 hours postoperatively (mean difference -1.96; 95% CI -4.08 to 0.16 p=0.07) (see figure 6) (data for the 6 hour time point was provided by 5 trials). At 24 hours, a statistically significant effect was seen (in favour of TAP block) (mean difference -4.02; 95% CI -6.48 to -1.57 p=0.001). Combining data from both time points for an overall effect, followed this significant trend (mean difference -3.09; 95% CI -4.76 to -1.42 p=0.0003). As previously stated, abstracts by Hoydonckx et al and Kagwa et al did not contain useable data. [19, 31] Other trials unable to contribute data were Bealvy et al and Sriramka et al, who reported overall pain scores, rather than differentiation, pain at rest and pain on movement scores. [15, 30]

(ITM and Placebo TAP block) versus (Placebo ITM and TAP block)

As with pain at rest, data for this outcome was only available in two trials.[22, 25] Data in an unsuitable format, prevented Kanazi et al from contributing data. [24] Pooled results from these trials found no difference between TAP block and ITM for alleviating pain on movement, at both 6 hours (mean difference 7.62; 95% CI -7.53 to 22.77 p=0.32), and 24 hours (mean difference 8.87; 95% CI -9.11 to 26.84 p=0.33), after CS (see figure 7). Overall pooled results (using both time points) corroborates this finding (mean difference 2.03; 95% CI -0.31 to 4.37 p=0.09).

(ITM and TAP block) versus (ITM and Placebo TAP block)

All five trials included in this comparison provided data for this outcome. However, it was only possible to use data from four trials, after the exclusion of data from the Puddy et al trial. [22, 26-28] As illustrated in figure 8, a statistically significant effect was seen at 6 hours, which showed that a combination of both ITM and TAP block was more effective than ITM alone (mean difference -1.02; 95% CI -1.66 to -0.39 p=0.002). This effect however, could not be detected at 24 hours (mean difference 0.23; 95% CI -0.35 to 0.82 p=0.43). The overall pooled effect was not statistically significant (mean difference -0.31; 95% CI -0.95 to 0.34 p=0.35).

Morphine consumption

TAP block versus Control (or no treatment)

Three trials each provided morphine consumption data at 2, 6 and 12 hours postoperatively and six at 24 hours.[14, 15, 17, 20, 21, 23] Pooled data at all four time points found a statistically significant lower consumption of morphine in the group using TAP block, as seen in figure 9 (2 hours: Mean difference 3.23mg; 95% CI -5.37 to -1.09 p=0.003), (6 hours: mean difference 12.27mg; 95% CI -13.76 to -10.77 p< 0.00001), (12 hours: mean difference 19.86mg; 95% CI -27.33 to -12.39 p< 0.00001), 24 hours (mean difference 23.48mg; 95% CI -32.41 to --14.55 p<0.00001). Overall pooled results across all time points, follow a similar trend (mean difference 16.25mg; 95% CI -22.94 to -9.56 p<0.00001). Seven trials were unable to contribute any data. Bollag et al, McMorrow et al, Sriramka et al and Srivastava et al presented the time points as ranges rather than at single time-points.[16, 22, 29, 30] Therefore, we were unable to combine this with the cumulative data. Eslamian et al provided data in a format that did not allow for merging with other data. [18] The abstracts by Hoydonckx et al and Kagwa et al did not give any data.[19] [31]

(ITM and Placebo TAP block) versus (Placebo ITM and TAP block)

Of the three trials reporting morphine or morphine equivalent dosage, only data from Loane et al was 'useable', therefore a forest plot is not provided. Loane et al reported no difference in morphine consumption between the groups at 0-2hours (mean difference 0.70mg; 95% CI -1.59 to 0.20 p=0.13), 2-6hours (mean difference 0.62mg; 95% CI -0.87 to 2.11p=0.42) and 6-10 hours (mean difference 0.85mg; 95% CI -0.33 to 2.03 p=0.16) postoperatively.[25] However, this difference became statistically significant between 10-24 hours, with lower use

in the ITM group, (mean difference 4.80mg; 95% CI 1.76 to 7.84 p=0.002). Both Kanazai and McMorrow et al noted a statistically significant difference in morphine or equivalent opioid consumption between 6-12 hours but no other time point.[22, 24] These two trials provided cumulative data, so were not combined with data from Loane et al.

(ITM and TAP block) versus (ITM and Placebo TAP block)

It was thought unsuitable to create a forest plot for this comparison and outcome as only Costello et al were able to contribute data. Their results showed that morphine consumption remained unaffected at both 24 and 48 hours postoperative (mean difference 0.00mg; 95% CI -0.30 to 0.30 p=1.00) and (mean difference 0.00mg; 95% CI -0.10 to 0.10 p=1.00) respectively.[26] McMorrow et al also did not observe a difference in morphine consumption at any time point, for example reporting a median consumption of 5mg and 6mg in the ITM and TAP block, and ITM and placebo TAP, respectively, at 24 hours.[22] Data from the Lee et al and Singh et al trials were not in a compatible format and therefore were not included.[27, 28] Data provided by Puddy et al again could not contribute to the meta-analysis.[32]

Postoperative nausea and vomiting

TAP block versus Control (no treatment)

Seven trials were in a format which allowed us to combine data on post-operative nausea and vomiting at 24 hours post-delivery (see figure 10).[14-17, 21-23] Pooled results found a 49% reduction in nausea and vomiting with TAP block compared to control (OR 0.51; 95% CI 0.24to 1.12 p=0.10). McDonnell et al noted 5 women in the control group developed nausea at some point, compared to none in the TAP block group, but there were no statistical differences at any particular time point.[20] Sriramka et al, narratively reported that significant differences in incidence and severity of PONV were seen in the first hour post-surgery, but this effect was not present post 24 hours.[30] Whilst providing data, Srivastava et al, were not explicit regarding the time point PONV outcomes was measured at (no corresponding author email address was provided), therefore we were unable to amalgamate their data with other trials.[29] PONV was not an outcome measured by Eslamian et al.[18] No useable data were found in the abstracts by Hoydonckx et al and Kagwa et al.[19, 31]

(ITM and Placebo TAP block) versus (Placebo ITM and TAP block)

Pooled results from the two trials reporting rates found a statistically significant reduction in nausea and vomiting at 24 hours, in favour of TAP block (OR 0.26; 95% CI 0.08 to 0.88 p=0.03), see figure 11.[22, 25] Kanazi et al noted a trend towards greater levels of nausea in the ITM group before 12 hours that disappeared thereafter.[24]

(ITM and TAP block) versus (ITM and Placebo TAP block)

Merging of data from three of the trials in this comparison found no evidence of a difference between the ITM and TAP block group and ITM alone group in the incidence of postoperative nausea and vomiting (OR 0.86; 95% CI 0.28 to 2.59p=0.79).[22, 26, 27] (see figure 12) Singh et al reported 45% of the ITM and placebo TAP group required anti-emetic administration within the first 24 hours, compared to 30% and 26% in the ITM with high and low dose TAP blocks, respectively. After 24 hours, the requirement for antiemetic use was

negligible.[28] Data from Puddy et al was again unable to contribute to this meta-analysis, as Diamorphine was used as part of their intervention.[32]

Pruritis

TAP block versus Control (or no treatment)

Pooled data from six trials found no statistically significant difference between TAP block and control in terms of pruritis (OR 1.58; 95% CI 0.85 to 2.95p=0.15) seen in figure 13.[15-17, 21-23] The remaining seven trials either provided data for this outcome in a format not appropriate for meta-analysis, or simply do not measure this outcome.

(ITM and Placebo TAP block) versus (Placebo ITM and TAP block)

Two trials reported substantial rates of pruritis at 24 hours, up to 75% of patients in the placebo ITM and TAP group and up to 85% in the ITM and placebo TAP group, however, the directionality of the differences were contradictory and hence showed no overall difference in incidence of pruritis when combined (OR 0.96; 95% CI 0.05 to 19.03 p=0.98) (see figure 14).[22, 25] In contrast, Kanazi et al, whilst observing a significant excess of pruritis in the ITM and placebo TAP group before 12 hours, saw rates of less than 15% at all time points.[24]

(ITM and TAP block) versus (ITM and Placebo TAP block)

There was a consistent trend towards higher pooled pruritis rates in the group receiving ITM and TAP block, compared with the ITM alone group, (OR 2.63; 95% CI 1.16 to 5.96 p=0.02) (see figure 15).[22, 26, 27] Whilst no data was presented by Singh et al, they did state that there was no difference between groups in the occurrence or severity of pruritis.[28] Data from the Puddy et al was not included in this analysis.[32]

393

Maternal Satisfaction

Due to the variation in how satisfaction with analgesia was captured and reported, no meta-analyses were attempted and results are explained narratively.

TAP block versus Control (or no treatment)

Seven trials measured satisfaction and provided data.[14, 15, 17, 21-23, 29] Satisfaction was extremely high in the Baaj et al trial, with 19/20 women in the control arm finding the treatment acceptable or good, compared to all women in the intervention arm.[14] Raw data provided by Belavy et al demonstrated a statistically significant effect in favour of TAP block, (mean difference 13.60 points (on a scale of 0-100); 95% CI 0.79 to 26.41 p=0.04).[15] This is in stark contrast to results reported by McKeen et al. Unpublished data sent to us showed no difference in satisfaction between the two arms (mean difference 0.00 points; 95% CI -0.91 to 0.91 p=1.00) (figure not presented).[21] McMorrow et al also measured satisfaction on a 100mm anchored visual analogue scale, observing a median score of 76 in both groups at 24 hours, and no difference either at other time points.[22] Equally high levels of satisfaction were found amongst women in the Tan et al trial, with 16/20 in the TAP block arm very satisfied with the procedure, compared to 5/20 in the control arm.[23] Canovas et al recorded response to satisfaction with treatment using a three point scale, very satisfied, moderately satisfied and little satisfaction. However, data was only provided for the women whose response was either ‘very satisfied’ or ‘moderately satisfied’. Women reporting lower satisfaction after treatment, were assumed to be the remainder of the sample in that arm More patients were either ‘very satisfied’ or ‘moderately satisfied’ with TAP block than control (28/30 v 26/30).[17] Srivastava et al described satisfaction with pain relief was significantly higher in the TAP block arm, reporting median satisfaction scores of 7 (IQR: 5-10) for the TAP block arm compared to 4 (IQR: 1-7) for the control arm. This result was statistically significant at $p < 0.005$.[29] The remaining six studies either did not measure or report satisfaction with analgesia.

(ITM and Placebo TAP block) versus (Placebo ITM and TAP block)

Kanazi et al presented satisfaction data on a three point scale: highly satisfied, satisfied and dissatisfied. 26/28 women in the ITM and placebo TAP group were either satisfied or highly satisfied, compared to 22/29 women in the intrathecal placebo and TAP block group.[24] McMorrow et al reported a non-significantly higher median satisfaction score in the ITM and placebo TAP group at all time points.[22] Satisfaction was not measured by Loane et al.[25]

(ITM and TAP block) versus (ITM + Placebo TAP block)

Satisfaction data as means and standard deviations were available from two trials. Firstly, from Costello et al who sent us unpublished data and secondly, Singh et al who presented this data in the text of their paper.[26, 28] Plotting of data from both these trials at 6, 12, 24 and 48 hours found no overall statistically significant difference between the two groups, (Weighted mean difference 0.11; 95% CI -0.16 to 0.38 p=0.43). (No forest plot has been generated for this particular outcome in this comparison, as it was thought to be superfluous for two trials). Similarly, to the other comparisons, within the McMorrow et al trial, there was no statistically significant difference between groups in terms of median satisfaction score, but with a wider range of satisfaction scores (for example, at 24 hours a median score of 73, IQR 30-94) in the ITM and TAP block group.[22] Lee et al reported satisfaction rates at 24 hours post-operatively, with more patients satisfied with TAP block given in conjunction with ITM rather than placebo TAP block and ITM (92% v 83%). This trend continued at 48 hours, with 96% of patients who underwent TAP block in addition to ITM being satisfied with their treatment, compared to 83% who had had ITM alone with placebo TAP block. These values at 24 and 48 hours postoperative, were not statistically significant, p=0.417 at 24 hours and p=0.190 at 48 hours.[27] Puddy et al did not report satisfaction as an outcome.[32]

Discussion

Main findings

The evidence generated by this meta-analysis demonstrates that TAP block is an effective intervention in providing acute pain relief after CS. Whilst TAP block may not confer much additional analgesia when intrathecal opioids are used; it is at least as effective. Our findings support the premise that TAP block could offer particular advantages in the context of General Anaesthesia for Caesarean section, when the only alternative is systemic opioid analgesia.

The greatest analgesic effect was seen in women who had been given TAP block in the absence of ITM. Pooled results found that TAP block was more effective than control at alleviating pain at rest, reducing pain by a clinically meaningful 3.5 point out of 10 [33], although this effect was greater in the short term and diminished by 24 hours. ITM was no more beneficial than TAP block for pain at rest. When TAP block and ITM were combined, the effect was superior in the short term to ITM alone, but again this effect was not sustained at 24 hours. TAP block was more effective in alleviating pain on movement compared to control. However, when TAP block was compared to ITM, this effect was lost. This was also the case when TAP block and ITM were compared to ITM alone.

TAP block alone (when compared against control (placebo or no TAP block)) was again the most effective modality, in reducing post-operative opioid consumption, in this case, reducing post-operative morphine consumption by more than half. However, when compared to ITM, this short term benefit was lost. There was no difference between TAP block and ITM at 2, 6 and 10 hours postoperatively. However, ITM was superior to TAP block at 24 hours. When the two were combined, and compared against ITM, no difference was found. These findings support the premise that TAP offers particular advantages when central opioids are not administered.

TAP block was superior in reducing the incidence of PONV when compared to ITM but not when compared to control. This effect must be taken in the context of any differences in opioid consumption. A combination of TAP block and ITM, was no more effective than ITM

alone, suggesting that the administration of neuraxial morphine is the most potent arbiter of the prevalence of PONV after CS.

No evidence of differential rates of pruritis were observed between women receiving TAP block, ITM or control, whilst the addition of TAP block to ITM increased the rate of reported pruritis. There was considerable variation in the pooled rates of pruritis in the TAP block group, from 30-62%, and those only receiving ITM, in the three comparisons, making it imprudent to rank the groups for this adverse event.

More women were satisfied with TAP block than control. However, when TAP block was compared with ITM, a greater number of women preferred ITM. When these two treatment options were combined, no difference in satisfaction was found. Whilst maternal satisfaction with their childbirth experience is increasingly recognised as a vital aspect of care, maternal satisfaction with planned Caesarean Section is very high and any effect of the addition of TAP may be difficult to detect.

Strengths and limitations

The strength of our review lies in the systematic methodology with which trials were identified and their quality appraised. Risk of bias was assessed using widely accepted Cochrane collaboration tools. The quality of included trials in general was good. The inclusion of the Hoydonckx et al trial, which was only available as an abstract, will have almost certainly contributed to worsening the overall impression of quality of the included trials.

A further strength is that we have tried to reflect clinical practice as much as possible. Although intrathecal diamorphine is widely used in UK practice, the single trial using diamorphine in their intervention arm were excluded from analysis. This was justifiable since intrathecal morphine and diamorphine are quite distinct in their pharmacology, effectiveness and duration of action. The side effect profiles of the two agents also differ substantially. Diamorphine is not available for analgesia in USA or mainland Europe. In this sense, UK practice is unusual. It is hoped that by retaining this study in the systematic

review, our findings are relevant to as wide an audience as possible.

Several sources of heterogeneity were identified. Despite a certain degree of standardisation amongst the population (most patients were undergoing an elective CS), the intervention was a source of heterogeneity. All trials fell into two broad groups, those that used ultrasound guided techniques and those that used anatomical landmark techniques. The choice and dose of the local anaesthetic was much more varied. The local anaesthetic agent used to perform TAP block was not standard amongst the trials. Once trials had been separated into their comparisons, further separation according to type of local anaesthetic agent used would not have been possible with the limited number of trials available. Further heterogeneity was avoided, by keeping our methods of analysis consistent, for example our conversion of tramadol consumption data to morphine consumption. We tried to compensate for this heterogeneity by using a random effects model throughout the analysis. This provided more conservative confidence intervals.

Due to variations in how postoperative nausea and vomiting outcomes was measured, we made the following assumption, in order to be able to combine as much data as possible. Some trials provided 'PONV' data, which was a combined score of nausea and vomiting, others described separate scores for nausea and vomiting. For these trials, we used nausea data alone, since using data for both nausea and vomiting would risk some patients being double-counted.

Interpretation

As our review and previous others have highlighted, TAP block is an effective analgesic intervention for acute pain following CS. Our meta-analysis generates further compelling evidence for the effectiveness of intrathecal opioids in providing pain relief after CS. TAP block, may be able to reduce or even replace the need for intrathecal opioid analgesia, thereby, reducing the incidence of central opioid related side effects, but the evidence at present would not favour a widespread change in practice. Nonetheless, TAP offers particular advantages in the context of CS where neuraxial opioids are not utilised.

The results of our review are supported by those found by other systematic reviews.[34, 35] Abdallah et al found that TAP block was more effective than placebo for providing analgesic relief. It also was superior at reducing the need for morphine in the first 24 hours after surgery, based on an analgesic regimen that excluded spinal morphine. Mishriky et al corroborated these findings. This review included a third comparator, ITM. They reported that postoperative analgesia was significantly improved by TAP block in women who had not received ITM. However, this benefit was lost in women who had received ITM. Improved analgesia was seen with ITM, compared to TAP block alone. A further narrative review, by Sharkey et al reinforced this sentiment which was convergent in opinion with the Mishriky et al review.[36] Our results are broadly convergent with the other evidence synthesis in the field. Fusco et al, found that TAP block reduced both opioid consumption and opioid related side effects. There were also improvements in postoperative pain and patient satisfaction with TAP block.[37] Reviews by Ripolles et al and Baeriswyl et al are broader systematic reviews, focussing on all types of abdominal surgery, including CS. These reviews confirmed the analgesic efficacy provided by TAP block.[38, 39]

Implications for research

This review has highlighted gaps in the evidence, which could be subjected to future study. CS is a common intervention, which is becoming more prevalent. Therefore, research in this area is pertinent to a large, productive population. The potential benefit of TAP block over a control for post-CS analgesia, in the absence of ITM, is supported by several trials. Future research should focus on assessing the effectiveness of ITM compared to and in addition to TAP block. Larger, well designed, adequately powered trials are needed to achieve this. Three local anaesthetic agents were used in the trials included in this review, with Bupivacaine being the most common. As our results have shown, combining TAP block and ITM has beneficial outcomes particularly for pain at rest. Assessing whether lower doses of this treatment option has implications for improved analgesia and reduction of opioid-induced side effects is also another area worth pursuing.

Implications for practice

The findings of our review have shown that TAP block is most effective in relieving postoperative pain following a CS delivery, in patients who have not received ITM. There is much more uncertainty surrounding the use of TAP block instead of ITM or in addition to it. Future trials should consider this an area for exploration.

Disclosure of interests

MJW holds a position on the editorial board of the International Journal of Obstetric Anaesthesia

No other disclosure of interests were declared

Contribution to authorship

JPD conceived the idea for the review. RC performed literature searches for published evidence, while LS searched for ongoing trials. RC and LS screened results of their respective searches. JPD screened citations thought to be eligible for inclusion. RC and JPD undertook double data extraction. Statistical analysis of the results was performed by RC. Initial and all subsequent drafts of the manuscript were prepared by RC. LS produced tables for inclusion in the manuscript. MJW provided clinical guidance when needed and assisted in writing the manuscript. All authors read the final manuscript and provided comments and feedback.

Details of ethics approval

No ethics approval was required

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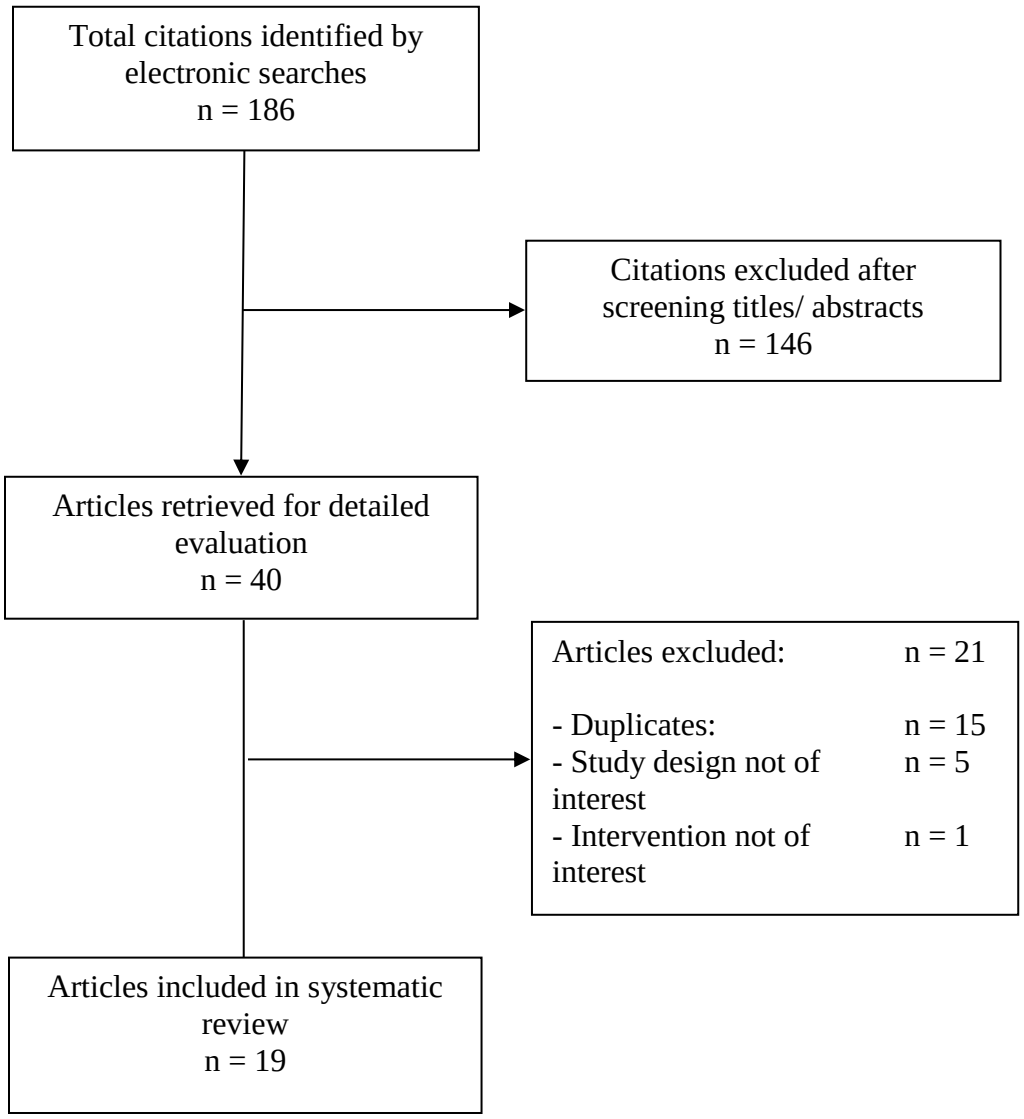

Figure 1: Study selection of trials included in the systematic review of the clinical effectiveness of TAP block for analgesia after Caesarean section

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Author	***Randomised sample size (Intervention/ Comparator)***	***Procedure***	***TAP (TAP) block Intervention***	***Comparator 1***	***Comparator 2***	***Comparator 3***	***Intra-operative anaesthetic***	***Post-operative analgesia***	***Primary/ Secondary Outcomes***	***Quality****

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Published										
TAP block versus Control (or no treatment)										
Baaj	20/20	Caesarean delivery	Bilateral Ultrasound guided TAP block with Bupivacaine 0.25%	Saline TAP block	-	-	Spinal anaesthetic with fentanyl and bupivacaine	PCA- IV morphine	Primary: -Total Morphine consumption over 24 hours post-op Secondary*:* -Accumulative morphine doses at 6,10,12,18 and 24 hours post-op -Pain measured using VAS during 24 hours post-op and during mobilization 24 hours after surgery. -Severity of nausea/ vomiting and sedation -Satisfaction with pain relief -Pain relief during mobilization 24 hours after surgery	-Adequate sequence generation: Unclear - Allocation concealment: Unclear -Blinding: Yes -Incomplete outcome data addressed: Unclear -Free of selective reporting: Unclear -Free of other bias: Unclear
Belavy	25/25	Caesarean delivery	Bilateral ultrasound landmark guided	Saline TAP block	-	-	Spinal anaesthetic with fentanyl and	Paracetamol 1g every 6 hour, ibuprofen	Primary: -Total morphine	-Adequate sequence

			TAP block with Ropivacaine 0.5%				bupivacaine	400mg x3 and PCA- IV morphine	requirement 24 hours post-op Secondary: -Time to first morphine demand and cumulative morphine doses measured at 612,18 and 24 hours -Average pain score measured using VAS over 24 hours post-op (at rest and during mobilisation). -Nausea, vomiting, pruritus and drowsiness assessed using 4 point scale -Satisfaction with pain relief, measured using VAS -Local complications with TAP block -Doses of antiemetics administered	generation: Yes - Allocation concealment: Yes -Blinding: Yes -Incomplete outcome data addressed: Yes -Free of selective reporting: Yes -Free of other bias: Unclear
Bollag	90	Caesarean delivery	Bilateral TAP block with bupivacaine	Bilateral TAP block with bupivacaine	Saline (placebo) TAP block	-	Spinal anaesthetic with bupivacaine, fentanyl and	Intravenous morphine as needed,	Primary: -Wound hyperalgesia index at 48 hours	-Adequate sequence generation: Yes

			0.375%	0.375% and clonidine 150µg			morphine	paracetamol 1g every 6 hours and diclofenac 75mg every 8 hours.	Secondary: -Pain scores at rest 6, 12, 18, 24, 36 & 48hrs post-op -Pain scores during movement 6, 12, 18, 24, 36 & 48hrs post-op -Patient first request for analgesic medication 48hrs post-op -Morphine consumption 48hrs post-op -Correlation between preoperative mechanical summation (mTS) & amount of hyperalgesia & post-op pain assessed 48hrs post-op -Side-effects e.g. nausea, vomiting (PONV), constipation, urinary retention, de-ambulation & motility 48hrs post-op -Chronic pain at 3, 6 & 12 months post-op by phone with the Short-Form McGill Pain	- Allocation concealment: Yes: -Blinding: Yes -Incomplete outcome data addressed: Yes -Free of selective reporting: Yes -Free of other bias: Unclear

									Questionnaire 2 (SF-MPQ-2)	
Canovas	30/30/30	Elective caesarean section	Bilateral TAP block with levobupivacaine 0.5% plus 10µg fentanyl	Saline TAP blockplus10µg fentanyl	Saline TAP block plus 0.1mg morphine	-	Spinal anaesthesia with hyperbaric bupivacaine	Morphine bolus through a system of patient-controlled analgesia	Primary: -Pain relief at 12 and 24 hours postoperative Secondary: -Side effects at 12 and 24 hours postoperative - Satisfaction at 12 and 24 hours postoperative	-Adequate sequence generation: Yes - Allocation concealment: Unclear -Blinding: : Yes -Incomplete outcome data addressed: Yes -Free of selective reporting: Yes -Free of other bias: Yes
Eslamian	25/25	Elective caesarean delivery	Bilateral TAP block (double pop at the end of the procedure) using anatomical technique with Bupivacaine 0.25%	No TAP block, but standard analgesia	-	-	General anaesthesia with sufentanil and thiopental	Diclofenac 100mg and tramadol 50mg every 4 hours as rescue medication	Primary: -Pain intensity scores measured using VAS 1yr post-op Secondary: -Analgesic requirements 1yr post-op	-Adequate sequence generation: Yes - Allocation concealment: Unclear -Blinding: Yes -Incomplete outcome data addressed: Yes -Free of selective

										reporting: Yes -Free of other bias: Unclear
Hoydonckx	25/25	Elective caesarean delivery	Bilateral TAP block with levobupivacaine 0.375% and saline PCEA	Bilateral TAP block with saline and PCEA with levobupivacaine 0.03%	-	-	Spinal epidural anaesthesia	Paracetamol and ketorolac for 48 hours.	-Pain measured using VAS at regular intervals over 6 days after surgery -Side effects measured using VAS at regular intervals over 6 days after surgery -Duration of hospital stay -Patient satisfaction	-Adequate sequence generation: Unclear - Allocation concealment: Unclear -Blinding: Unclear -Incomplete outcome data addressed: Unclear -Free of selective reporting: Unclear -Free of other bias: Unclear
Kagwa	84/86	Elective, urgent or emergency Caesarean section	Ultrasound guided TAP block with bupivacaine	Sham TAP block			Spinal anaesthesia (no other information given)	Paracetamol 1000mg and diclofenac 50mg, every 8 hours for 3 days	Primary: -Numerical rating scale scores (pain at rest and on movement) measured at 8, 16 and 24 hours	-Adequate sequence generation: Unclear - Allocation concealment: Unclear -Blinding: Yes

										-Incomplete outcome data addressed: No -Free of selective reporting: Unclear -Free of other bias: Yes
McDonnell	25/25	Elective caesarean delivery	Bilateral loss of resistance TAP block using anatomical technique with 0.75% ropivacaine	Saline TAP block	-	-	Spinal anaesthetic with fentanyl and bupivacaine	Paracetamol 1g every 6 hour, diclofenac 100mg every 18 hours and PCA-morphine	Primary: - Morphine consumption 48 hours post-op Secondary: -Time to first request for morphine -Side effects associated with morphine consumption -Incidence/ severity of pain, nausea and sedation assessed on arrival at PACU, then 2,4,6,12,24,36 and 48 hours post-op -Pain at rest and on movement measured using VAS -Prolonged and superior	-Adequate sequence generation: Yes - Allocation concealment: Yes -Blinding: Yes -Incomplete outcome data addressed: Unclear -Free of selective reporting: Yes -Free of other bias: Unclear

									analgesia up to 36 post-op	
McKeen	41/42	Elective caesarean delivery	Bilateral ultrasound guided TAP block with 0.25% ropivacaine	Bilateral ultrasound guided TAP block with 0.9% saline placebo			Spinal anaesthesia with hyperbaric bupivacaine, fentanyl and preservative-free morphine	Naprosyn 250mg (every 8 hours, paracetamol 1000mg every 6 hours, and oxycodone 2.5-5mg every 6 hours, as needed.	Primary: -Pain on rest -Pain on movement -Quality of recovery -Cumulative opioid consumption Secondary: -Health-related quality of life Other: -Postoperative nausea and vomiting -Pruritis -Urine retention	-Adequate sequence generation: Yes - Allocation concealment: Yes -Blinding: Yes -Incomplete outcome data addressed: Unclear -Free of selective reporting: Yes -Free of other bias: Yes
McMorrow	20/20/20/20	Elective caesarean delivery	Bilateral TAP block using anatomical landmark with bupivacaine 0.375% and spinal saline	Saline TAP block and spinal saline (control)			Spinal anaesthetic with fentanyl and bupivacaine	Paracetamol 1g and diclofenac 100mg (and PCA morphine 1mg/ 5 minutes)	Primary: -Pain on movement Secondary: -Pain at rest -Morphine consumption -Proportion of patients with adequate analgesia	-Adequate sequence generation: Unclear - Allocation concealment: Yes -Blinding: Yes -Incomplete outcome data

									-Satisfaction -Sedation -Nausea -Pruritus All assessed at 6,12,24,36 and 48 hours post-op.	addressed: Yes -Free of selective reporting: Yes -Free of other bias: Yes
Sriramka	25/25	Caesarean section	Bilateral ultrasound-guided TAP block with ropivacaine 0.5%	Saline TAP block (placebo)			Spinal anaesthesia with hyperbaric bupivacaine and fentanyl	Oral paracetamol 600mg, 6 hourly with IV morphine, 3mg	Primary: -Morphine consumption at 24 hours Secondary: -VAS scores -Side effects associated with morphine consumption	-Adequate sequence generation: Unclear - Allocation concealment: Unclear -Blinding: Yes -Incomplete outcome data addressed: Unclear -Free of selective reporting: Yes -Free of other bias: Yes
Srivastava	31/31	Elective or non-urgent caesarean (where no foetal	Bilateral TAP block using landmark technique, with	Standard care with no TAP block	-	-	Spinal anaesthesia with bupivacaine and fentanyl	Diclofenac 75mg 8 hourly and IV PCA tramadol.	Primary: -Tramadol consumption at 48 hours	-Adequate sequence generation: Yes - Allocation

		or maternal compromise existed).	bupivacaine 0.25%						Secondary: -Pain scores at rest and on movement -Time of first analgesia -Side effects -Satisfaction with pain management	concealment: Yes -Blinding: Yes -Incomplete outcome data addressed: No -Free of selective reporting: Yes -Free of other bias: Yes
Tan	20/20	Elective or grade 3 emergency caesarean delivery	Bilateral ultrasound guided TAP block (double pop) with Levobupivacaine 0.25%	Standard care with no TAP block	-	-	General anaesthesia with Thiopentone, suxamethonium and atracurium	PCA morphine (max dose 40mg in 4 hours)	Primary: - Morphine consumption 24 hours post-op Secondary: -Pain scores at rest and activity - Sedation - Nausea and vomiting - Use of antiemetic medication - Overall maternal satisfaction	-Adequate sequence generation: Yes - Allocation concealment: Yes -Blinding: Yes -Incomplete outcome data addressed: Yes -Free of selective reporting: Yes -Free of other bias: Yes
(ITM and Placebo TAP block) versus (Placebo ITM and TAP block)										
Kanazi	30/30	Elective caesarean	Bilateral ultrasound	Bilateral ultrasound	-	-	Spinal anaesthetic with bupivacaine	Diclofenac 100mg every 12	Primary:	-Adequate sequence

		delivery	guided saline TAP with subarachnoid morphine	guided TAP block with 0.375% bupivacaine with epinephrine and saline.			combined with morphine for the subarachnoid morphine group. The TAP group received saline spinal anaesthesia	hours and IV paracetamol 1g every 6 hours.	-Time to first analgesic request Secondary: -Number of supplemental analgesic requirements -Pain (at rest and on movement) measured using VAS -Sedation -Nausea/ vomiting -Pruritus scores -Respiratory depression All assessed on arrival to PACU, then 2,4,6,12,24,36, and 48 hours post-op -Patient satisfaction assessed 48 hours post-op	generation: Yes - Allocation concealment: Yes -Blinding: Yes -Incomplete outcome data addressed: Unclear -Free of selective reporting: Yes -Free of other bias: Unclear
Loane	34/35	Elective caesarean delivery	Bilateral ultrasound guided TAP block with ropivacaine 0.5%	Sham TAP block with ITM 100 µg	-	-	Spinal anaesthesia with bupivacaine and fentanyl	Rectal naproxen 500mg and acetaminophen 975mg at the end of surgery	Primary: -Morphine equivalent consumption at 24 hours post-op	-Adequate sequence generation: Yes - Allocation concealment: Yes

			(no ITM given)						Secondary : -Pain scores at rest & on movement as assessed by VAS on arrival to recovery & at 2, 6, 10 &24hrs post-spinal drug administration -Post-operative nausea & vomiting scores 3months post-op -Sedation score 3months post-op -Presence or absence of itch 3months post-op -Abdominal scar pain 3mnths post-op	-Blinding: Yes -Incomplete outcome data addressed: Yes -Free of selective reporting: Yes -Free of other bias: Unclear
McMorrow	20/20/20/20	Elective caesarean delivery	Bilateral TAP block using anatomical landmark with bupivacaine 0.375% and spinal saline	Saline TAP block and spinal morphine (100µg)			Spinal anaesthetic with fentanyl and bupivacaine	Paracetamol 1g and diclofenac 100mg (and PCA morphine 1mg/ 5 minutes)	Primary: -Pain on movement Secondary: -Pain at rest -Morphine consumption -Proportion of patients with adequate analgesia -Satisfaction -Sedation	-Adequate sequence generation: Unclear - Allocation concealment: Yes -Blinding: Yes -Incomplete outcome data addressed: Yes -Free of selective

									-Nausea -Pruritus All assessed at 6,12,24,36 and 48 hours post-op.	reporting: Yes -Free of other bias: Yes
(ITM and TAP block) versus (ITM and Placebo TAP block)										
Costello	50/50	Elective caesarean delivery	Bilateral ultrasound guided TAP block with Ropivacaine 0.375% and spinal morphine	Saline TAP block and spinal morphine	-	-	Spinal anaesthetic with fentanyl, bupivacaine and morphine	Paracetamol 1g every 6 hour, diclofenac 50mg every 8 hours and morphine on request	Primary: -Pain score on movement 24 hours post-op Secondary: -Pain score at rest and on movement, measured using VAS at 6,12, 24 and 48 hours post-op -Total supplemental narcotic consumption in first 48 hours post-op -Patient satisfaction with pain management -Presence of abdominal pain 6 weeks post-op	-Adequate sequence generation: Yes - Allocation concealment: Unclear -Blinding: Yes -Incomplete outcome data addressed: Yes -Free of selective reporting: Unclear -Free of other bias: Unclear
Lee	26/25	Elective	Bilateral	Saline TAP	-	-	Combined spinal	Analgesics	Primary:	-Adequate

		caesarean delivery	ultrasound guided TAP block with Ropivacaine 0.5% and ITM	block and ITM			epidural with bupivacaine, fentanyl and morphine	administered according to severity of pain using a verbal rating scale (0-no pain, 10-worst pain). Mild pain (rated 1-3) paracetamol given (2x500mg every 6 hours), For moderately severe pain (rated 4-5), IV ketorolac 30mg or oral ibuprofen 800mg given every 6 hours as needed. For severe breakthrough pan (rated 6-10), either IV morphine 2mg every 10 minutes as needed up to 6mg or two paracetamol 300mg or codeine 30mg tablets or two	-Difference in pain on movement scores, as measured by verbal rating scale. Secondary: -Pain at rest scores -Analgesic consumption -Opioid side effects -Satisfaction with procedure and analgesia	sequence generation:: Yes - Allocation concealment: Yes -Blinding: Yes -Incomplete outcome data addressed: Unclear -Free of selective reporting: Yes -Free of other bias: Yes

								oxycodone 5mg or paracetamol 325mg tablets every 6 hours as needed.		
McMorrow	20/20/20/20	Elective caesarean delivery	Bilateral TAP block with bupivacaine 0.375% and spinal morphine (100µg)	Saline TAP block and spinal morphine (100µg)			Spinal anaesthetic with fentanyl and bupivacaine	Paracetamol 1g and diclofenac 100mg (and PCA morphine 1mg/ 5 minutes)	Primary: -Pain on movement Secondary: -Pain at rest -Morphine consumption -Proportion of patients with adequate analgesia -Satisfaction -Sedation -Nausea -Pruritus All assessed at 6,12,24,36 and 48 hours post-op.	-Adequate sequence generation: Unclear - Allocation concealment: Yes -Blinding: Yes -Incomplete outcome data addressed: Yes -Free of selective reporting: Yes -Free of other bias: Yes
Puddy	23/25	Elective caesarean delivery	Bilateral ultrasound guided TAP block with bupivacaine 0.25 – 0.5%. All patients received	Saline TAP block. All patients received subarachnoid anaesthesia with 0.5% bupivacaine and	-	-	Spinal anaesthetic with heavy bupivacaine and diamorphine	Paracetamol and diclofenac and morphine on request.	Primary: -Time to first postoperative dose of morphine Secondary:	-Adequate sequence generation: Yes - Allocation concealment: Yes -Blinding: Yes -Incomplete

			subarachnoid anaesthesia with 0.5% bupivacaine and 300mcg diamorphine	300mcg diamorphine.					-Pain scores -Morphine consumption All assessed at 2,6,24 and 48 hours post-op	outcome data addressed: Yes -Free of selective reporting: Yes -Free of other bias: Unclear
Singh	20/20/20	Elective caesarean delivery	Spinal morphine and 'high dose – max 300mg' TAP block with Ropivacaine 0.5%	Spinal morphine and 'low dose – max 150mg' TAP block with Ropivacaine 0.5%	Spinal morphine and saline TAP block	-	Spinal anaesthetic with bupivacaine, fentanyl and morphine	Paracetamol and for rescue analgesia codeline or oxycodone were given	Primary: -Pain on movement Secondary: -Pain scores at rest and with movement -Maternal satisfaction with pain management -Anaesthesiologists satisfaction with local anaesthetic deposition -Nausea -Pruritis -Sedation -Total opioid consumption -Total antiemetic consumption -Time to first request	-Adequate sequence generation: Yes - Allocation concealment: Yes -Blinding: Yes -Incomplete outcome data addressed: Yes -Free of selective reporting: Yes -Free of other bias: Yes

									additional analgesia All assessed at 6,12,24,36,48 and 72 hours post-op	
Ongoing										
										Status
Cambic	200	Caesarean delivery	15ml 0.25% ropivacaine per side	15ml 0.5% ropivacaine per side	15ml 0.75% ropivacaine per side	Saline TAP block	Spinal anaesthesia with 0.75% bupivacaine and fentanyl		Primary: -Hydromorphone consumption 24hrs post-operativeSecondary: -Opioid consumption 48 & 72hrs post-operative	Recruiting
Carvalho	100	Caesarean section	TAP block injected bilaterally with 20ml 0.375% ropivacaine	Bilateral injection of 20ml saline solution	-	-	No details provided	No details provided	Primary: -Pain score by VAS on movement at 24 hours postoperatively Secondary: -Pain at rest and on movement by VAS o at 6, 12, 24 & 48hours postoperatively -Opioid consumption at 6, 12, 24 & 48 hours	Completed

									postoperatively -Time to first maternal request for supplemental analgesia -Maternal satisfaction with pain management on a scale of 0-10, at 6, 12, 24 & 48 hours postoperatively -Presence of pain 6 weeks postoperatively	
Cowlishaw	50	Caesarean section	Ultrasound guided Tap block with 20ml of 0.5% ropivacaine on each side (total 200mg)	20ml saline on each side			Not stated	Not stated	Primary: -Morphine dose from patient controlled analgesia (PCA) Secondary : -Highest sedation score recorded -Number of doses of antiemetics -Self-reported nausea and vomiting -Self-reported pruritus -Visual analogue pain score	Completed

Eslamian	60	Elective caesarean delivery	TAP block injected bilaterally with 15cc bupivacaine 0.25%	No TAP, but standard analgesia	-	-	General anaesthesia		Primary: -Pain intensity scores measured using VAS 1yr post-operativeSecondary: -Analgesic requirements 1yr post-op	Recruitment status unknown because information has not been verified recently
Frenk	80	Caesarean section	Ultrasound guided TAP block with Ropivavcaine	No TAP block, just ITM as part of spinal anaesthesia	-	-	Spinal anaesthesia with 1.4ml of 0.75% hyperbaric bupivacaine	SQ morphine every 4 hours as requested and 30mg IV ketorolac every 6 hours until subjects start eating	Primary: -Quality of recovery after Caesarean section Secondary: -Incidence of nausea/ vomiting -Incidence and severity of pruritis -Overall oral narcotic use during 48 hours postoperatively	Recruitment status unknown because information has not been verified recently
Guirguis	60	Elective caesarean delivery	TAP with 0.5% bupivacaine	TAP with 0.25% bupivacaine	Normal saline		*No details provided*	*No details provided*	Primary: -Post-caesarean pain e.g. Number of PCA boluses used by patients Secondary: -Pain score measured	Recruitment status unknown because information has not been verified recently

									by VAS	
Hart	50	Elective caesarean delivery	Ultrasound guided TAP block of 20ml per side of 0.5% ropivacaine	Saline Tap of 0.9% sodium chloride	-	-		IV hydromorphine administered after patient pressing button when in pain. IV ketorolac every 8hrs for 24 hours after surgery	Primary: -Hydromorphine consumed by PCA in first 24hrs after surgery Secondary: -Categorical pain scores & VAS pain scores at rest & with movement 24hrs post-op -Narcotic side-effects e.g. nausea & sedation	Withdrawn prior to enrolment
McKeen	86	Caesarean delivery	Ultrasound guided TAP block of 0.25% ropivicaine (maximum 1.5mg/kg) in addition to ITM	20ml saline placebo	-	-	*No details provided*	No details provided	Primary: -Postoperative pain, measured by an NRS -Quality of recovery score (QoR) -Self Assessment Diary in the first 24 hours postoperative period Secondary: -NRS/QoR – 48 hour opioid consumption side effects – nausea,	Completed

									sedation -TAP block success rates and duration of block effect assessed using a patient diary completed every 2 hours while the patient is awake -Persistent pain outcomes assessed at 30 days and 6 months using 5-minute SF-36 health survey	
Modest	240	Uncomplicated caesarean delivery	Ultrasound guided TAP block of 0.25% bupivacaine	Sham TAP block	-	-	Local spinal anaesthesia	Non-opioid oral analgesic regimen (paracetamol and diclofenac)	Primary: -Pain at rest: measured using the visual numerical rating score, at 0,8,16 and 24 hours after the caesarean section -Pain on movement: measured using the visual numerical rating score, at 0,8,16 and 24 hours after the caesarean section Secondary: -Patient satisfaction with	Recruitment status unknown because information has not been verified recently

									their pain control: measured in a personal interview, with a yes/ no answer. Other: -Reduction in need for nurse-administered rescue pain medication over the first 24 hours post-surgery as compared to controls. Measured during a personal interview	
Preston	70	Elective caesarean delivery	Ultrasound guided TAP block of 1.5mg/kg of 0.5% ropivacaine (to maximum dose of 20mls = 100mg on each side)	Placebo Tap block of 100micrograms of spinal morphine	-	-	Spinal anaesthesia for surgery provided with 9-12mg heavy bupivacaine & 10mcg fentanyl	Standard post-caesarean analgesia & PONV orders resumed	Primary: -Morphine equivalents used in the first 24hrs post-delivery Secondary : -Pain scores at rest & with movement as assessed by VAS on arrival to recovery & at 2, 6, 10 & 24hrs post-spinal drug administration -Post-operative nausea	Completed

									& vomiting scores 3months post-op -Sedation score 3months post-op -Presence or absence of itch 3months post-op -Abdominal scar pain 3months post-op	
Starr	16	Elective caesarean section	Trans-abdominis TAP block injection on one side with 30ml ropivacaine, containing 300mg ropivacaine in addition of 1:300,000 epinepherene	Placebo injection on the other side	-	-	No details provided	No details provided	Primary -Difference in pain perception based upon VAS scores at rest between blocked and unblocked side in each patient (Time frame: 4, 6, 8, 12, 16, 20 & 24 hours post-TAP placement) Secondary: -Difference in pain perception between sides is equal (Time frame: 4, 6, 8, 12, 16, 20, & 24 hours post TP	Recruitment status unknown because information has not been verified recently
Tosetti	180	Caesarean section	TAP block with ropivacaine and clonidine	Spinal anaesthesia with ITM in addition	-	-	No details provided	No details provided	Primary: -Cumulative incidence of nausea and/or vomiting	Recruiting

				to the standard spinal anaesthesia drugs e.g. bupivacaine and fentanyl, morphine is added					at 24 hours (Time frame: 6 & 24 hours postoperatively from nurses' records in the recovery room (at 6 hours) and on the ward (at 24 hours) and counterchecked by asking the patient) Secondary: -Cumulative incidence of pruritus at 24 hours, inquired directly from the patient at 6 & 24 hours -Cumulative incidence of treated nausea and vomiting at 24 hours (inquired indirectly from the patient at 6 & 24 hours) -Cumulative incidence of sedation at 6 & 24 hours (sedation defined as an observer's assessment of alertness and sedation (OAAS) score lower than 4 -Cumulative incidence of arterial hypotension	

									(defined as a systolic blood pressure of less than 100mmHg for longer than 5 minutes from nurse records at 6 & 24 hours) -Cumulative incidence of bradycardia defined as a heart rate of less than 50/min for longer than 5 minutes (from nurses records at 6 & 24 hours) -Cumulative incidence of respiratory depression defined as a respiratory frequency of less than 8/min for longer than 5 minutes (from nurses records at 6 & 24 hours) -Cumulative morphine consumption at 24 hours (recorded in the memory of the patient controlled analgesia PCA pump) -Time until first PCA request (recorded in the memory of the PCA pump) -Pain score at rest at 24 & 48 hours	

									postoperatively using the NRS scale 0-10 -Pain score on movement at 24 & 48 hours postoperatively using the numerical rating scale NRS 0-10 -Maternal satisfaction at 24 & 48 hours postoperatively measured on a numeric rating scale and with the questionnaire “quality of recovery” QoR40	
EUCTR2006-004053-20-IE	Not stated	Lower segment Caesarean section	Tap block injection with 0.75% ropivacaine	Placebo injection			Not stated	Not stated	Primary: -Time to request for supplemental analgesia (morphine) -Total morphine usage at 4, 12, 24 & 48 hours - Visual analog scores (VAS, 0=no pain, 10=worst imaginable) at rest and at movement at 30 minutes & at 2, 4, 6,	Recruitment may be ongoing or finished

									12 & 24 hours -Categorical pain scores (none=0, mild=1, moderate=2, severe=3) -Sedation scores -Patient satisfaction Secondary: -Sedation -Postoperative nausea and vomiting - Patients satisfaction -Tertiary measures: systemic absorption of ropivacaine -Effect on the stress response to injury	

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761 Table 1: Table of characteristics of (ongoing and) published trials included in the systematic review of the clinical effectiveness of TAP block

762 for analgesia after Caesarean section

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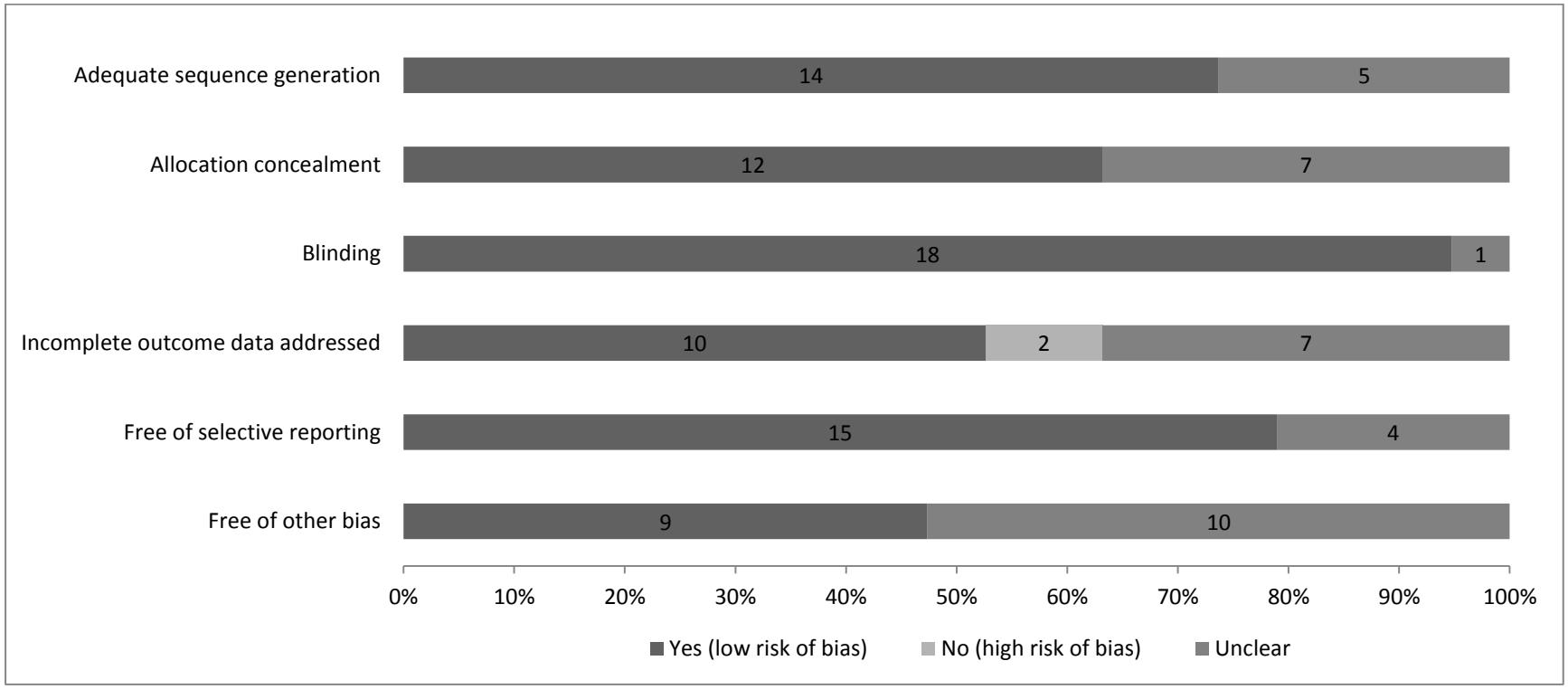

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768 Figure 2: Quality of trials included in the systematic review of the clinical effectiveness of TAP block for analgesia after Caesarean section

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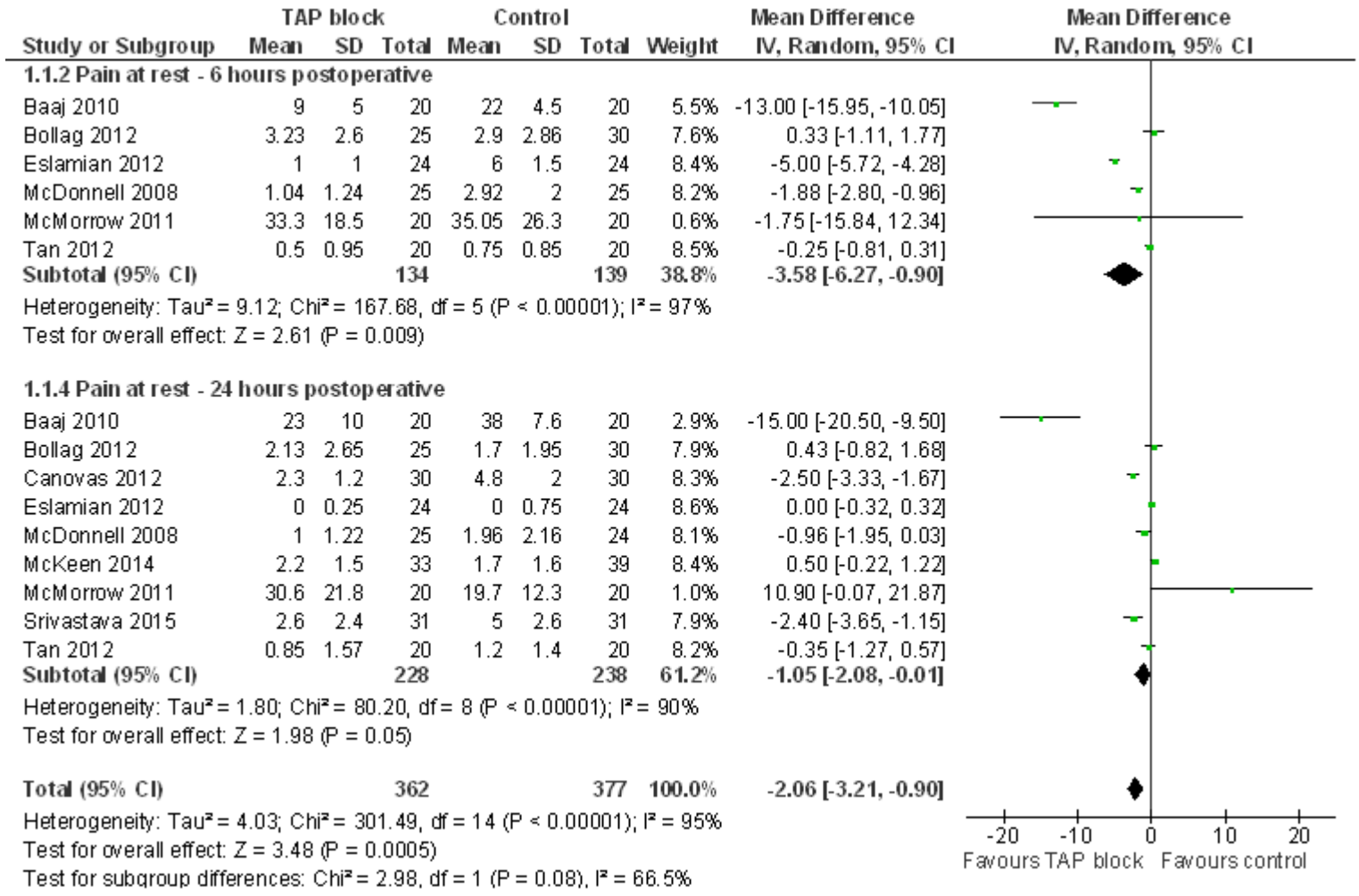

Figure 3: Pain at rest measured in the TAP v Control trials

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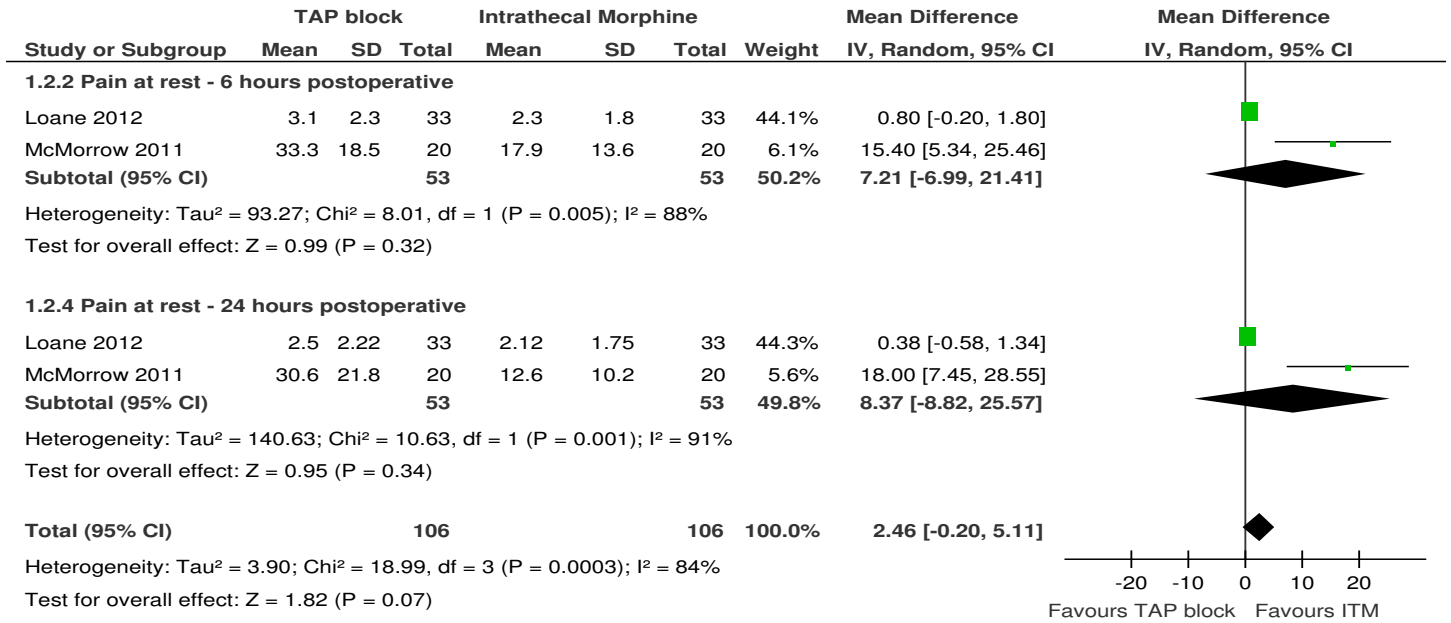

Figure 4: Pain at rest measured in the (ITM + Placebo TAP) v (Placebo ITM + TAP) trials

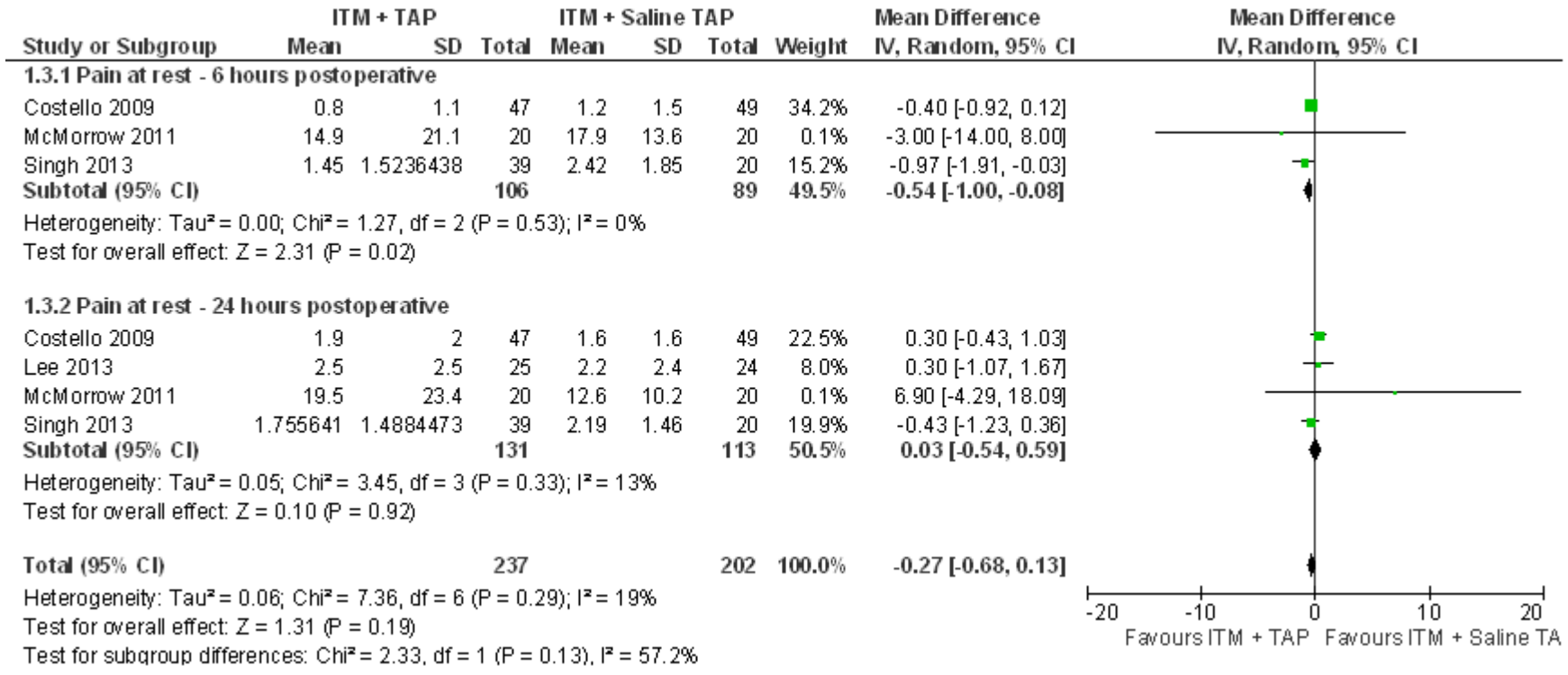

Figure 5: Pain at rest measured in the (ITM + TAP) v (ITM + Placebo TAP) trials

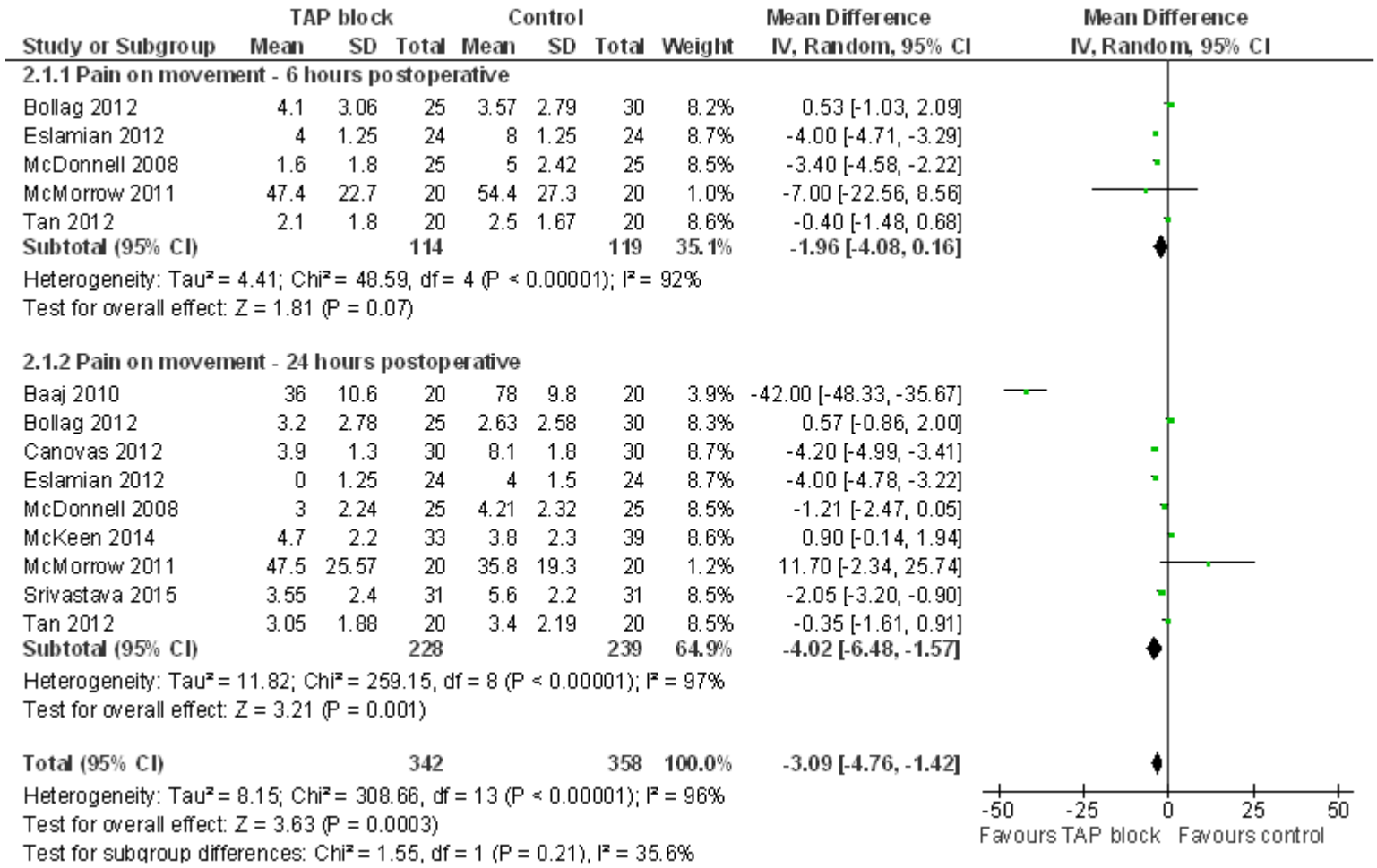

Figure 6: Pain on movement measured in the TAP v Control trials

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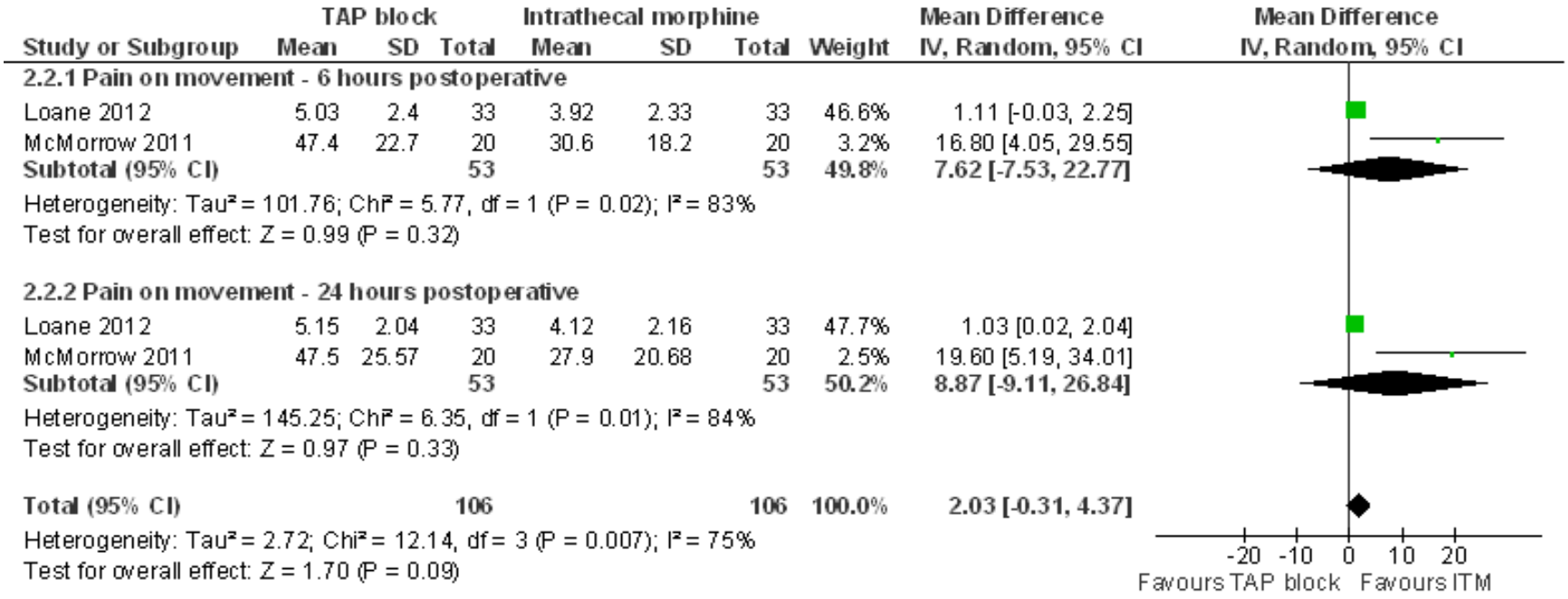

Figure 7: Pain on movement measured in the (ITM + Placebo TAP) v (Placebo ITM + TAP) trials

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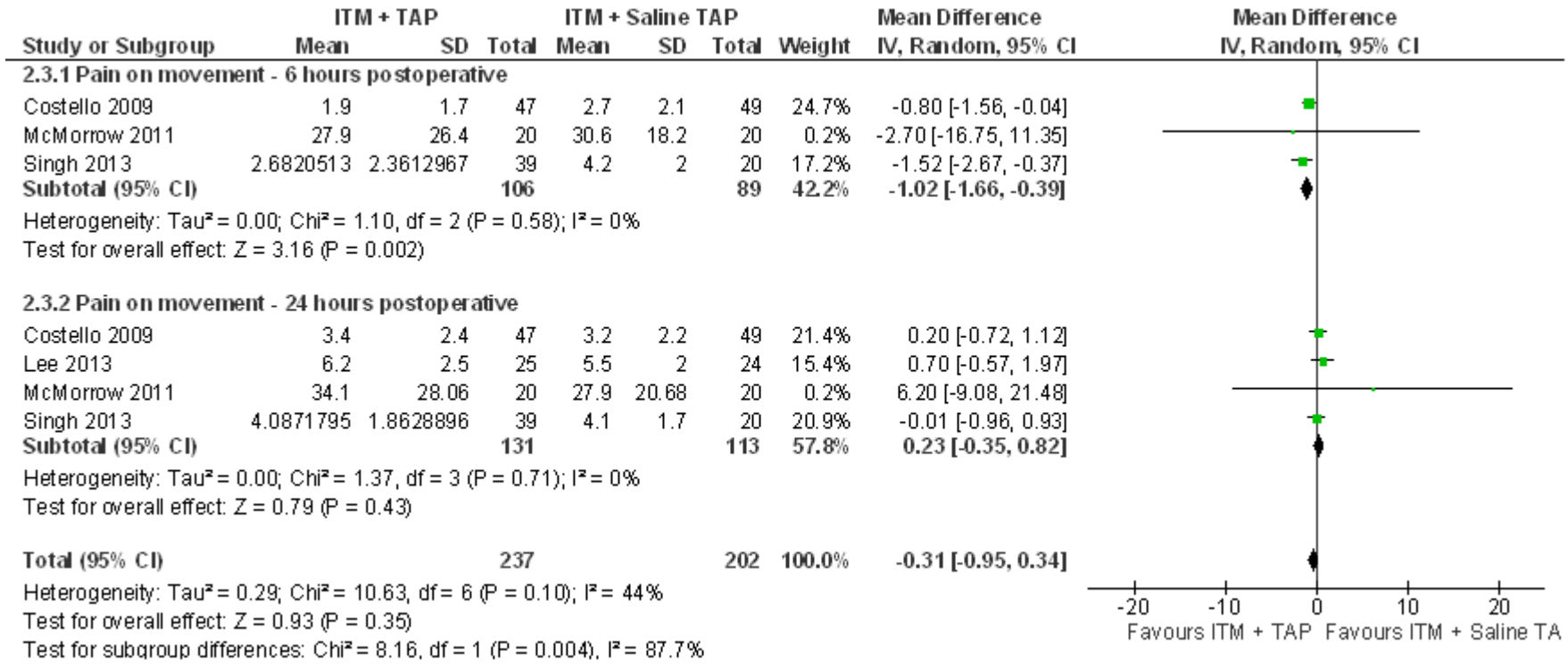

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804 Figure 8: Pain on movement measured in the (ITM + TAP) v (ITM + Placebo TAP) trials

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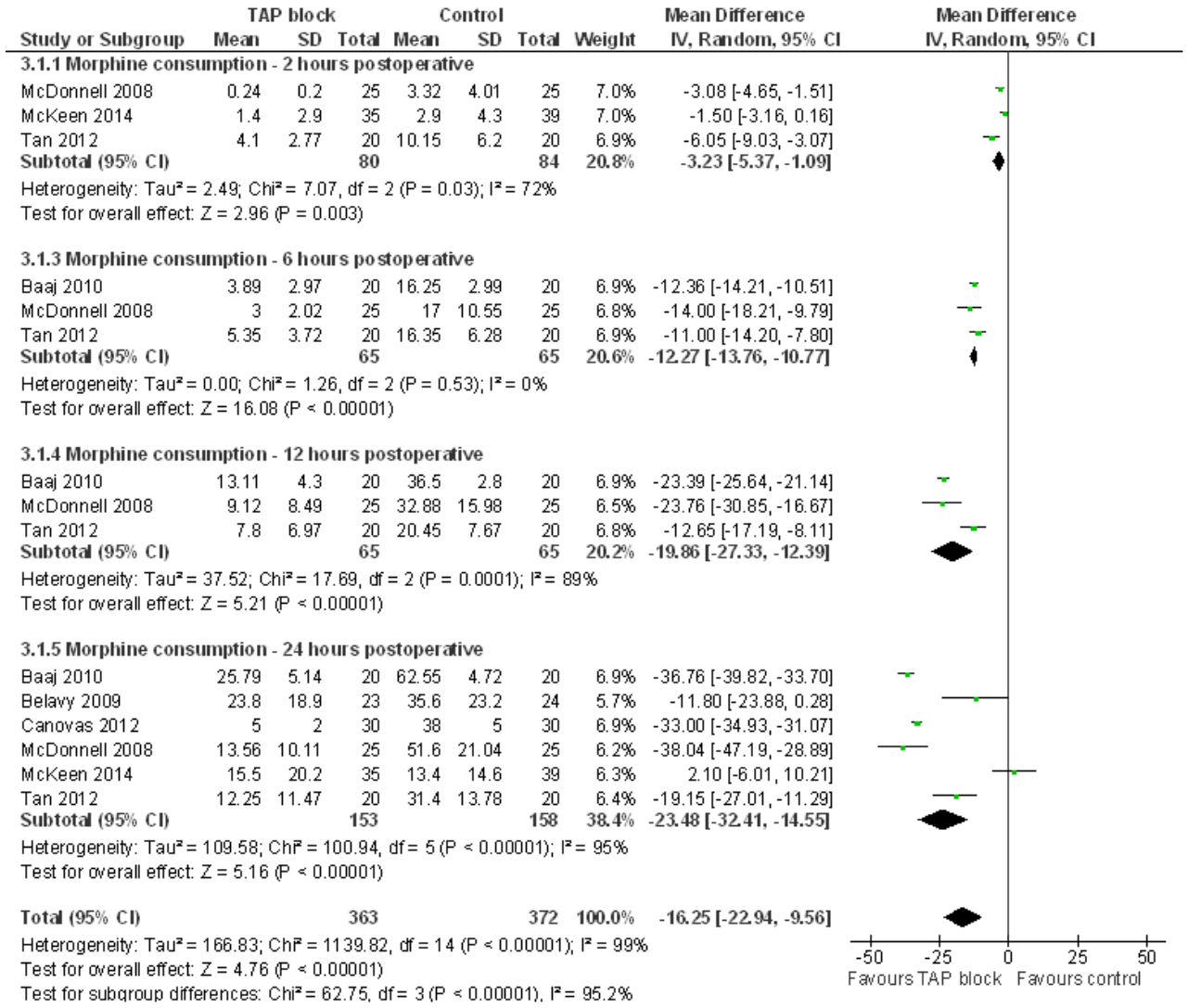

Figure 9: Morphine consumption measured in the TAP v Control trials

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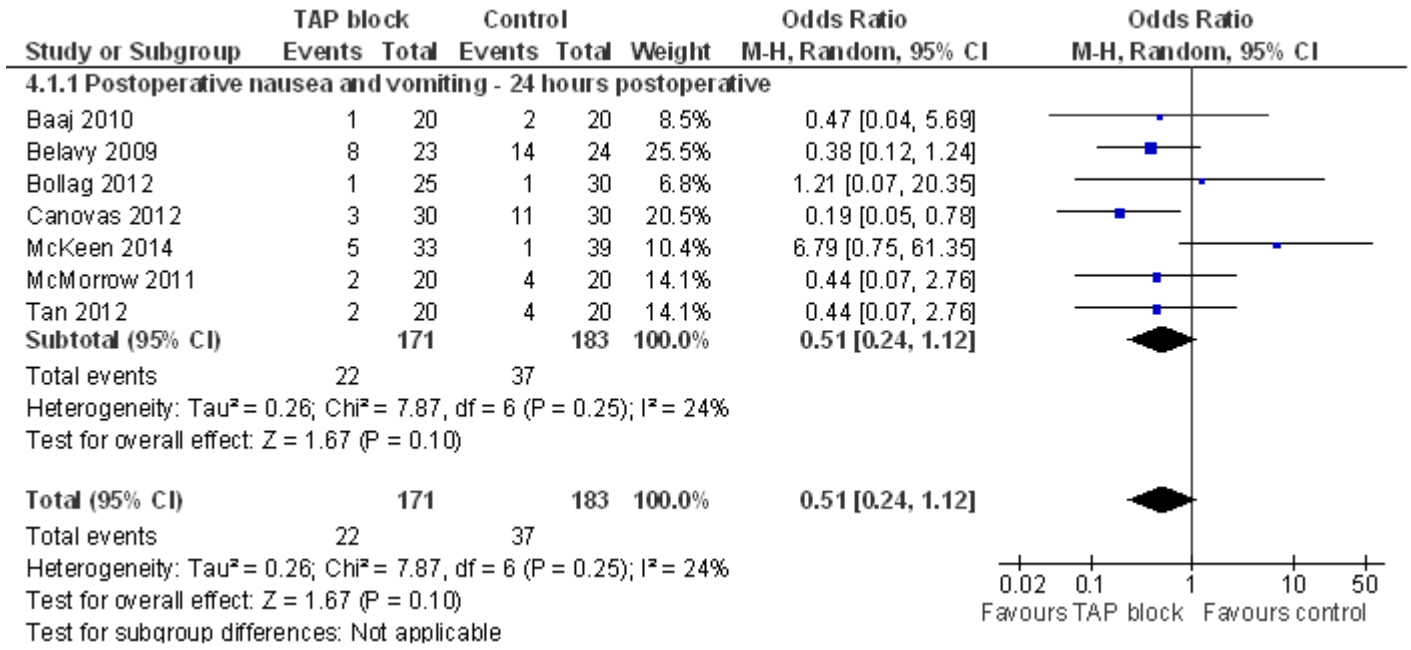

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821 Figure 10: Postoperative nausea and vomiting measured in the TAP v Control trials

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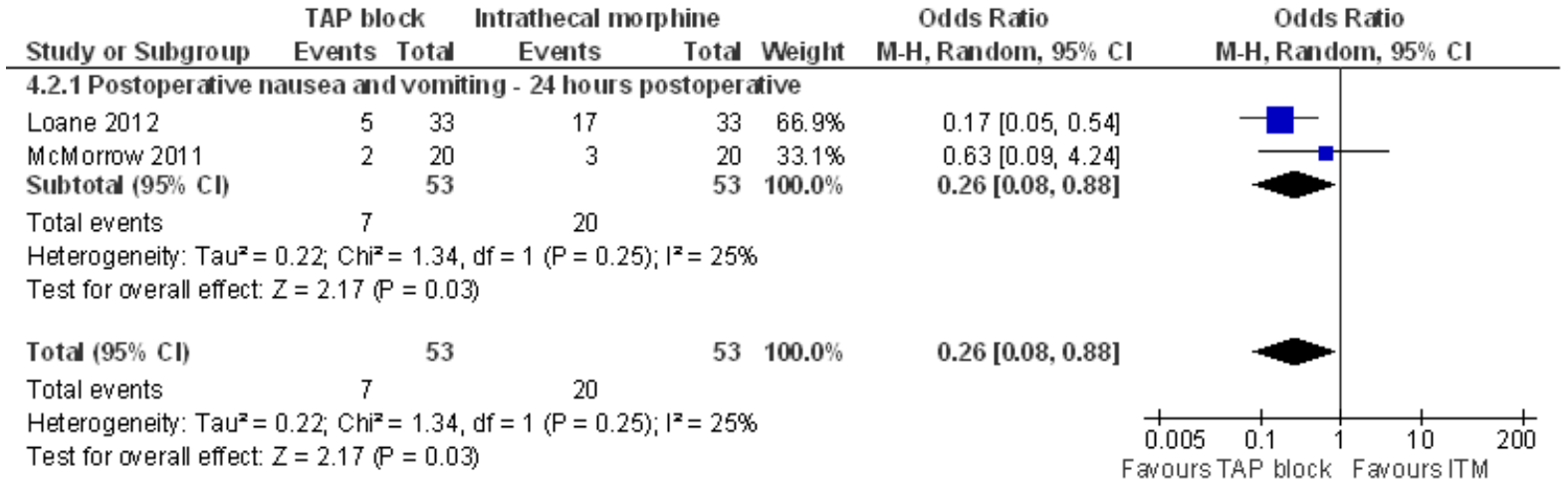

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827 Figure 11: Postoperative nausea and vomiting measured in the (ITM + Placebo TAP) v (Placebo ITM + TAP) trials

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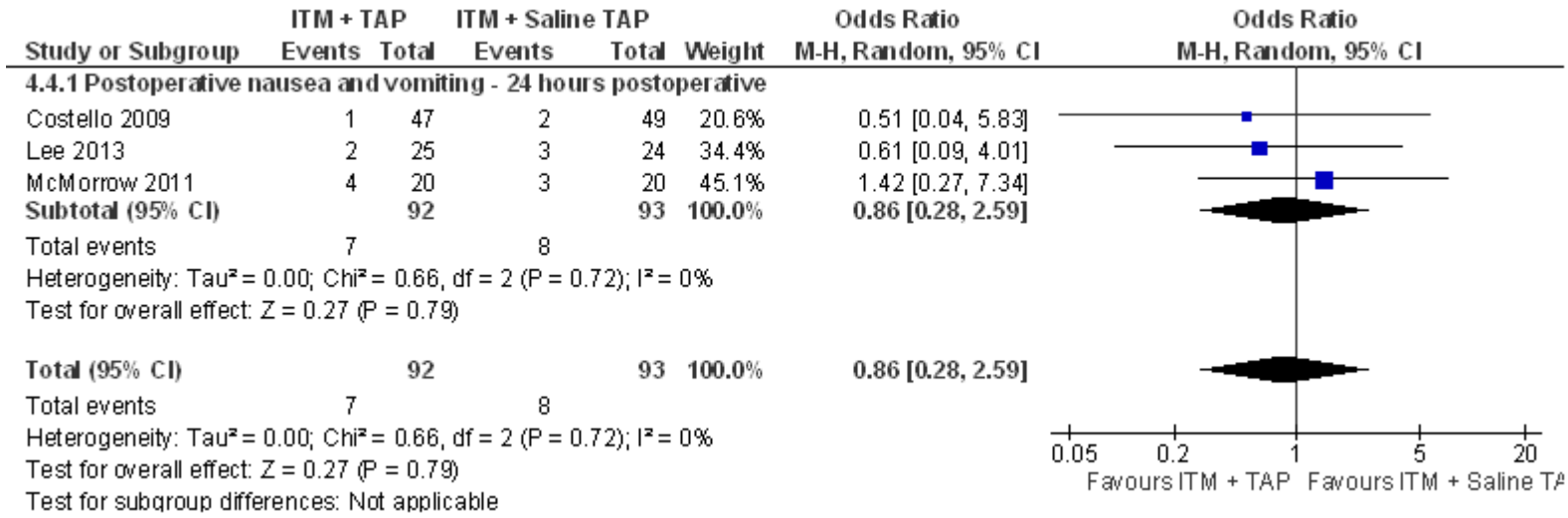


Figure 12: Postoperative nausea and vomiting measured in the (ITM + TAP) v (ITM + Placebo TAP) trials

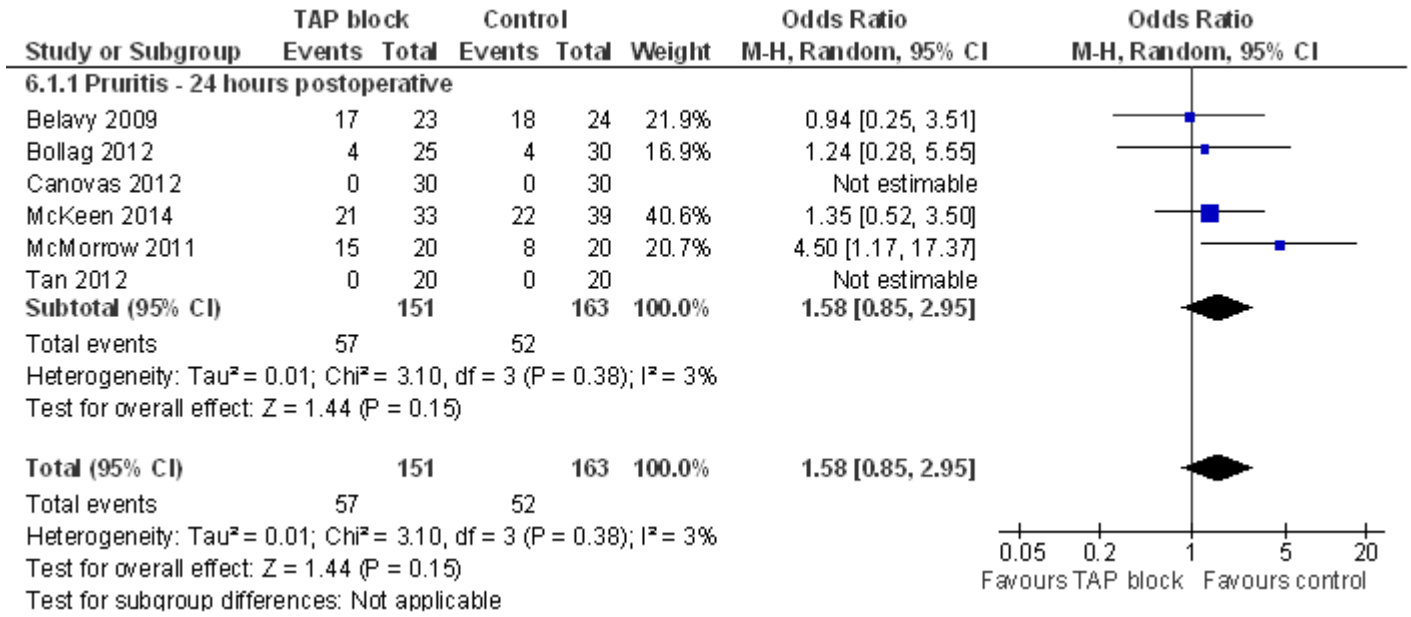
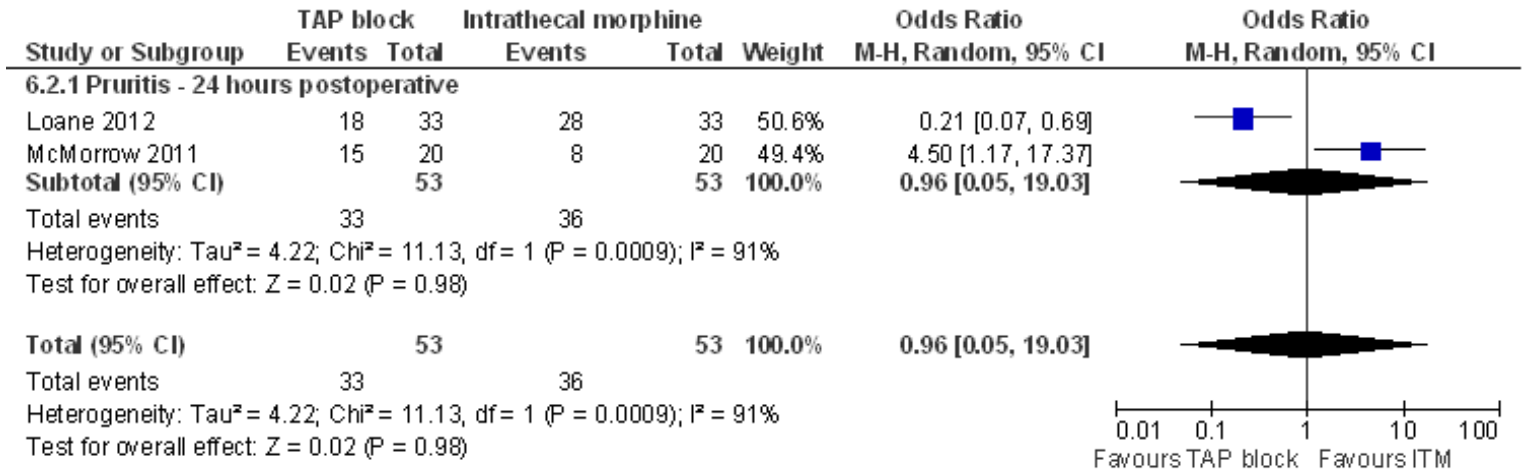


Figure 13: Pruritis measured in the TAP v Control trials



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841 Figure 14: Pruritis measured in the (ITM + Placebo TAP) v (Placebo ITM + TAP) trials

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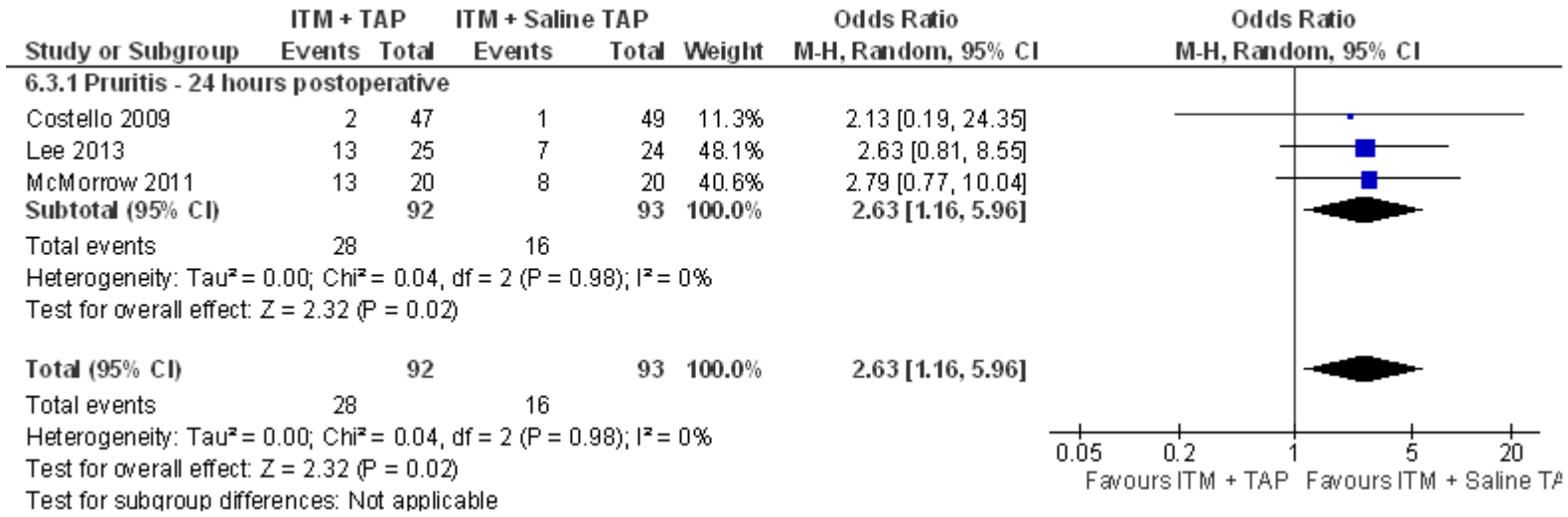

Figure 15: Pruritis measured in the (ITM + TAP) v (ITM + Placebo TAP) trials

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