Posthysterectomy pain is caused by abdominal incision and traumatic manipulation of the intra-abdominal structures. Optimal pain management consists of a multimodal pain regimen combined with transversus abdominis plane (TAP) block. We searched PubMed, EMBASE, and Cochrane Database for randomized controlled trials evaluating the opioid-sparing effects of TAP block in patients undergoing hysterectomy. The primary outcome was morphine consumption in the perioperative phase extending to 48 hours after surgery. The secondary outcomes were pain scores at rest and during coughing, time of first postoperative analgesia, and incidence of postoperative nausea and vomiting (PONV) and sedation.

Twenty-three trials were selected consisting of 1,554 patients. Morphine consumption showed a reduction of 3.6 mg intraoperatively (mean difference [MD], −3.57; 95% CI, −6.88 to −0.25); 2.9 mg in the recovery room (MD, −2.86; 95% CI, −5.55 to −0.15); 3.4 mg at 24 hours (MD, −3.43; 95% CI, −6.77 to −0.09), and 29 mg at 48 hours (MD, −28.68; 95% CI, −44.35 to −13.01) after surgery in favor of TAP block. Pain scores were lower at rest, and the incidence of PONV and sedation were reduced. Although opioid-sparing effects of TAP block were significant perioperatively, its clinical application is debatable because of substantial heterogeneity across studies.

Keywords: Hysterectomy, morphine consumption, opioid-sparing effect, pain scores, transversus abdominis plane block.

Opioid-Sparing Effects of Transversus Abdominis Plane Block in Elective Hysterectomy: A Systematic Review and Meta-Analysis

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Terri D. Kane, DNAP, CRNA

Considerable pain and discomfort are common in patients after hysterectomy. Posthysterectomy pain is largely parietal pain inflicted by abdominal incision and visceral pain caused by organ manipulation and trauma during surgery.1 Multimodal analgesia with different classes of agents such as nonsteroidal anti-inflammatory drugs and other regional anesthesia techniques such as incisional site infiltration with local anesthetic (LA) optimize pain control by covering the ilioinguinal and iliohypogastric nerves innervating the skin and sympathetic (L2-L4) and parasympathetic (S2-S5) nerves innervating the uterus, fallopian tubes, and vagina.1 In addition, multimodal strategies may mitigate opioid side effects, including postoperative nausea and vomiting (PONV) and sedation.

The use of a transversus abdominis plane (TAP) block in multimodal therapy for hysterectomy has been examined in the past decade. The block involves the injection of the LA in the neurovascular bundle between the internal oblique muscle and transversus abdominis muscle containing the thoracolumbar nerve fibers of T6-L1.2 Several meta-analyses have investigated the analgesic efficacy of TAP block for both adult and pediatric patients.3-5 One meta-analysis in patients undergoing hysterectomy, published in 2013, reported the short-term efficacy of TAP block as evidenced by reduction in pain scores at rest and in 24-hour morphine consumption.6 Since then, a number of trials have been published with varying results in terms of morphine consumption and opioid-related side effects. To our knowledge, no recent systematic reviews have been conducted for hysterectomy and the opioid requirements in the perioperative period extending up to 48 hours after surgery.

This article examines the reported opioid-sparing effects of TAP block when used as part of multimodal drug therapy in patients undergoing total abdominal, laparoscopic, or vaginal hysterectomy, performed under general or spinal anesthesia or both.

Methods

The PICO (population or patient, intervention, control or comparison, outcome) format was used to locate the evidence addressing the clinical inquiry: Does the use of TAP block reduce opioid consumption in patients undergoing total hysterectomy? The study was designed following the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.7

• Search Strategy. The electronic databases in our literature search included MEDLINE (PubMed), EMBASE,
Google Scholar, and The Cochrane Review Database. Specific MeSH (medical subject headings) terms or keywords used singularly and in combination included transversus abdominis plane block, total abdominal hysterectomy, total laparoscopic hysterectomy, hysterectomy, and TAP block. The reference lists from retrieved sources and the “similar articles” tool in PubMed were examined for relevance to the clinical inquiry. Evidence was limited to full-text, English-language, peer-reviewed journal articles examining the effects of TAP block on perioperative opioid requirements during hysterectomy. The latest search was conducted on December 27, 2016.

• **Study Inclusion Criteria and Data Extraction.** The review authors screened the title and abstract of each article. Randomized controlled trials (RCTs) were included in the review if they compared TAP block with saline placebo and other regional techniques such as local skin infiltration, epidural analgesia, and pain management techniques such as patient-controlled analgesia (PCA) and ketorolac for total abdominal, laparoscopic, and vaginal hysterectomy. Retrospective studies, case reports, abstract-only articles, editorials, expert opinions, studies using another TAP block as comparison, and poster presentations were excluded.

Review authors (T.D.T., J.L.H.) extracted data separately. Differences of opinion were settled by discussion with the third author (J.M.-N.). The following data were obtained from each trial: number and age range of participants; physical status classification; location of surgical incision; TAP block methods and techniques; types, concentration, and dosages of LA; timing of the block; opioid use in the perioperative period; pain scores during rest and on movement; time of first postoperative analgesia; and the incidence of PONV and sedation.

• **Risk of Bias.** The review authors (T.D.T., T.D.K.) assessed the methodological quality according to the guidelines recommended by the Cochrane Handbook for Systematic Reviews of Interventions. Consensus resolved any discrepancies or disagreements. The risks of bias of the included studies are presented in Figure 1.

• **Summary of Measures and Statistical Analysis.** The primary outcome was morphine consumption in the perioperative phase up to 48 hours after hysterectomy. Perioperative opioids were converted to intravenous (IV) morphine equivalents using previously published equianalgesic conversion factors (10 mg of IV morphine = 100 mg of IV tramadol = 1.5 mg of IV hydromorphone = 100 µg of IV fentanyl = 75 mg of IV pethidine). When there were more than 2 intervention groups, data were processed individually for analysis. The secondary outcomes examined were morphine consumption in the perioperative phase up to 48 hours after hysterectomy, opioid use in the perioperative period, pain scores during rest and on movement, time of first postoperative analgesia, the incidence of sedation and PONV. Visual analog and numeric intensity scores were converted to a 0- to 10-point scale (0 = no pain and 10 = worst possible pain) for analysis. When outcome measures were presented in graphical form, the study authors were contacted for raw and additional data. If correspondence with authors was unsuccessful, the mean and standard deviation were extracted using WebPlotDigitizer.

We used Review Manager (RevMan 5.3) for meta-
analysis. For dichotomous outcomes, combined data were calculated using the risk ratio (RR) with 95% CI. For continuous variables, results were reported as the mean difference (MD). In studies only reporting the median and range (or interquartile range), the mean and standard deviation (SD) were calculated using the statistical algorithms proposed by Wan and colleagues. In addition, when standard error of the mean (SEM) was presented, the data were summarized using the formula \( SD = SEM \times \text{Square root of } n \), where \( n \) represents the number of participants.

The random-effects model for analysis was used anticipating methodological and clinical heterogeneity. The benchmark for statistical significance was \( P < .05 \). Using the I² statistic to assess variation between studies, we considered I² greater than 50% as evidence of heterogeneity. When I² was less than 50%, the data were pooled with a fixed effect model. In extracted data containing significant heterogeneity, subgroup and sensitivity analyses were performed. Subgroup analyses were performed for timing and techniques of TAP block and surgical approaches of hysterectomy. Sensitivity analysis used the leave-one-out method to assess the effect of each trial on the overall effect size. Publication bias was assessed using the funnel plot and confirmed by funnel plot regression test. We considered asymmetric configuration of the funnel plot as suggestive of publication bias. Table 1 presents the glossary of statistical terms used in this systematic review and meta-analysis.

### Results

The authors screened 181 titles and abstracts. After reviewing full-text articles, 23 studies were subsequently included for review and meta-analysis totaling 1,554 patients. The search and evidence selection process are described in Figure 2. Fourteen studies enrolled ASA class 1 and 2 patients, and 9 included ASA class 3 patients. Only 3 studies randomized women with malignant pathology results. Patients were scheduled for an elective total abdominal hysterectomy (TAH), total laparoscopic hysterectomy, robotic-assisted hysterectomy, or laparoscopically assisted vaginal hysterectomy. Patients in the TAP group underwent general endotracheal anesthesia whereas spinal anesthesia was used in 2 studies. Sixteen trials used lower abdominal transverse incision ( Pfannenstiel, supra pubic, and longitudinal), 1 trial, midline incision, 1 trial, vertical incision, and 6 trials, single and multiple laparoscopic port incision. Thirteen studies compared TAP block with normal saline for sham block, and 3 with LA incision infiltration. Two trials each compared TAP block with PCA morphine or epidural analgesia. One trial each compared TAP block with PCA fentanyl or IV ketorolac. Thirteen initiated the TAP block before incision and 10 at the end of surgery. The characteristics of the eligible studies are summarized in Table 2.

The types, concentration, and dose of LA for TAP block varied by study. Ten trials used bupivacaine, 10 used ropivacaine, and 3 used levobupivacaine. The amount of LA ranged between 30 and 40 mL injected bilaterally. Only one study determined loss of sensation via cold temperature after TAP block. The TAP block techniques used were anatomical, ultrasound (US)-guided, and direct visualization done by the surgeon in the surgical field.

Visual analog and numeric scores were used to assess pain both at rest and during movement. The types of movement varied and included coughing, repositioning, knee and hip flexion, and awakening. Seven trials did not specify the types of activities during movement and the time points assessed, 4 studies did not report time points assessed at rest, and 4 studies failed to specify whether pain scores recorded were at rest or during movement. Two studies reported on the quality of recovery using a validated (with high internal consistency) 40-item quality of recovery questionnaire. Of these 2 studies, only one reported better quality of recovery scores in patients treated with TAP block compared with saline placebo. Only a single study reported failure rate of the TAP block and no other complications were reported in the remaining studies.

**Primary Outcomes.** Figure 3 summarizes the results of the primary outcomes, described in detail here.

**24-Hour Morphine Consumption.** The 24-hour morphine consumption was reported in 14 trials comprising 699 patients. Pooled analysis showed a significant reduction of morphine requirement with TAP block (MD, −3.43; 95% CI, −6.77 to −0.09; \( P = .04 \); see Figure 3). A much larger IV morphine equivalent reduction was seen when a subset of the studies that compared TAP block with no TAP block saline placebo were analyzed (MD, −5.00, 95% CI, −7.25 to −2.75, \( P < .0001 \)). There was substantial heterogeneity in the overall analysis of 24-hour morphine consumption (I² = 99%). To determine sources of statistical heterogeneity, subgroup analyses were conducted for the techniques and timing of TAP block, and the surgical methods of hysterectomy.

When the techniques of TAP block were analyzed, combined data from 12 RCTs demonstrated no difference with the US-guided technique in morphine use compared with surgical site infiltration with LA, PCA morphine, epidural analgesia, and placebo (MD, −2.29; 95% CI, −5.92 to 1.33; \( P = .22 \)). However, when an US-guided approach was compared with saline
<table>
<thead>
<tr>
<th>Statistical parameter</th>
<th>Definition/interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment</td>
<td>Describes concealment of allocation of treatment and control. Examples on how to conceal allocation assignment of study intervention and control include the use of sequentially numbered, opaque, sealed envelopes and sequentially number drug containers/syringes prepared by investigators blinded to the study.(^8)</td>
</tr>
<tr>
<td><strong>Cochrane Handbook for Systematic Reviews of Interventions</strong></td>
<td>This is a guide for authors interested in writing intervention systematic review using The Cochrane Collaboration group protocols.(^8) The handbook is readily available online at <a href="http://handbook.cochrane.org/">http://handbook.cochrane.org/</a></td>
</tr>
<tr>
<td>Continuous outcome</td>
<td>An outcome that exists on a numerical scale for each participant and is summarized as the mean or median</td>
</tr>
<tr>
<td>Dichotomous outcome</td>
<td>A measure with only 2 outcomes, such as nausea, no nausea; admitted, discharged</td>
</tr>
<tr>
<td>Fixed-effects model</td>
<td>We assume that effect size varies only because of sampling error. Information from a small study can be ignored because larger studies have presumably better information</td>
</tr>
<tr>
<td>Funnel plot</td>
<td>Describes a “simple scatter plot” that is used to detect publication bias by visual inspection. Asymmetric configuration of the funnel plot may indicate a possible publication bias.(^8)</td>
</tr>
</tbody>
</table>
| **\(I^2\) statistic** | Evaluates the null hypothesis that the included studies in a systematic review and meta-analysis are assessing the same effect. \(I^2\) statistic is one of the methods that determines the heterogeneity of the results between studies. The test reports a range between 0% and 100%. An \(I^2\) of 0% means no heterogeneity in-between studies. Grading of \(I^2\) is as follows\(^6\,\,14\):  
  - < 25% = low heterogeneity  
  - 25% to 50% = moderate heterogeneity  
  - 51% to 100% = high or substantial heterogeneity |
| Mean difference | A summary of studies that all assess the same outcome but measure it in a variety of ways |
| PICO format | A method by which the study question is formulated. It is an acronym that stands for population (patient), intervention, control (comparison), and outcome |
| **PRISMA statement** | Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) is a set of requirements for inclusion in a systematic review with or without meta-analysis such as search sources, risk of bias, synthesis of results, study characteristics, summary of evidence, limitations, and conclusions\(^7\) |
| Random sequence generation | Describes how the participants were allocated to study groups. Examples of random sequence generation methods are random tables and computer-generated sequence.\(^9\) |
| Random-effects model | When the variables are treated as if they arise from random causes and a mean distribution of effect is estimated |
| Risk of bias | The Cochrane Handbook for Systematic Reviews of Interventions outlined the methodological quality assessment of studies in systematic review and meta-analysis. The 6 domains of risk of bias assessment include random sequence generation, allocation concealment, blinding of participants, personnel and outcomes assessors, incomplete outcomes data, selective reporting and other sources of bias. Each category is appraised to “high risk”, “low risk”, and “unclear risk”.\(^8\) |

**Table 1.** Statistical Parameters Used in the Systematic Review and Meta-Analysis Examining Opioid-Sparing Effects of Transversus Abdominis Plane Block in Patients Undergoing Elective Hysterectomy
placebo and no TAP block, morphine consumption was reduced by an average of 4.93 mg ($P < .00001$). Furthermore, TAP block performed using the landmark anatomical approach showed a reduction of 18.50 mg of IV morphine equivalent compared with saline placebo. When TAP block performed using a surgeon-assisted direct laparoscopic view approach was compared with placebo, IV morphine equivalent was reduced by 4 mg.

Patients with TAP blocks placed before surgical incision showed a significant difference in morphine consumption compared with placebo, ketorolac, PCA morphine, and surgical site LA infiltration (MD, $-4.39; 95\% \text{ CI}, -8.12 \text{ to } -0.66; P = .02$). Conversely, when the block was performed at the end of surgery, patients treated with TAP block demonstrated no difference in morphine consumption compared with placebo (MD, $-3.84; 95\% \text{ CI}, -8.46 \text{ to } 0.77; P = .10$).

There was no difference in 24-hour morphine consumption for patients who underwent TAH and were treated with TAP block compared with placebo, surgical site infiltration, epidural analgesia, and PCA fentanyl (MD, $-4.33; 95\% \text{ CI}, -8.71 \text{ to } 0.05; P = .05$).

Similarly, no significant morphine reduction was observed in TAP block recipients undergoing laparoscopic hysterectomy compared with placebo, PCA morphine, and LA incisional site infiltration (MD, $-1.47; 95\% \text{ CI}, -7.61 \text{ to } 4.67; P = .64$).

Using the leave-one-out method, we carried out sensitivity analysis by initially excluding studies with high risk of bias for random sequence generation, allocation concealment, and blinding. After the analysis, pooled estimates of 24-hour morphine consumption did not affect substantial heterogeneity.

- **Intraoperative Morphine Consumption.** Six studies, totaling 280 patients, showed a significant reduction in intraoperative total morphine consumption by TAP block recipients compared with control group patients (MD, $-3.57; 95\% \text{ CI}, -6.88 \text{ to } -0.25; P = .03$). This analysis suggested a very substantial heterogeneity ($I^2 = 99\%$; see Figure 3). When TAP block was compared with saline placebo, the average reduction was 4.7 mg (MD, $-4.76; 95\% \text{ CI}, -8.67 \text{ to } -0.85; P = .02, I^2 = 99\%$).

- **Postanesthesia Care Unit (PACU) Morphine Consumption.** Six articles representing 287 patients reported total morphine use in the PACU. Figure 3 shows a significant difference between TAP block
<table>
<thead>
<tr>
<th>Source country</th>
<th>N</th>
<th>Comparison groups</th>
<th>Type, concentration, and dose LA</th>
<th>Technique</th>
<th>Timing</th>
<th>Multimodal analgesia</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amr &amp; Amin, 2011</td>
<td>68</td>
<td>TAP after induction and before incision TAP after surgery and before emergence Sham block</td>
<td>Levobupivacaine 0.375%, 20 mL</td>
<td>Anatomical landmark-based</td>
<td>Preincisional</td>
<td>IV fentanyl IV morphine</td>
<td>Sensory block was assessed using cold sensation at the level of T7-L1 6% TAP failure rate Chronic pain reduced in 3 and 6 months after surgery in preincisional TAP vs sham block</td>
</tr>
<tr>
<td>Atim et al, 2011</td>
<td>55</td>
<td>TAP block Skin infiltration with 0.25% bupivacaine, 20 mL Sham block</td>
<td>Bupivacaine 0.25%, 20 mL</td>
<td>Ultrasound-guided</td>
<td>Preincisional</td>
<td>IV diclofenac PCA tramadol IM pethidine</td>
<td>Pfannenstiel incision TAP block performed preincisional and skin infiltration at the end of surgery</td>
</tr>
<tr>
<td>Bhattacharjee et al, 2014</td>
<td>90</td>
<td>TAP block Sham block with NS</td>
<td>Bupivacaine 0.25% (0.5 mL/kg bodyweight)</td>
<td>Anatomical landmark-based</td>
<td>Preincisional</td>
<td>IV fentanyl IV infusion paracetamol IV tramadol</td>
<td>Lower abdominal transverse incision No opioid-related side effects</td>
</tr>
<tr>
<td>Calle et al, 2014</td>
<td>197</td>
<td>TAP block Sham block with NS</td>
<td>Bupivacaine, 1.5 mg/kg, 20 mL</td>
<td>Surgeon-assisted direct view</td>
<td>At end of surgery</td>
<td>IV morphine IV tramadol Oral acetaminophen</td>
<td>No clinical signs of TAP complications Multiple laparoscopic ports</td>
</tr>
<tr>
<td>Carney et al, 2008</td>
<td>50</td>
<td>TAP block Sham block with NS</td>
<td>Ropivacaine, 0.75% 1.5 mg/kg</td>
<td>Anatomical landmark-based</td>
<td>Preincisional</td>
<td>Rectal acetaminophen Rectal diclofenac Oral paracetamol</td>
<td>Transverse lower abdominal incision More than 1 person performing block</td>
</tr>
<tr>
<td>De Oliveira et al, 2011</td>
<td>66</td>
<td>TAP 0.5% ropivacaine TAP 0.25% ropivacaine Sham block</td>
<td>Ropivacaine 0.5%, 20 mL Ropivacaine 0.25%, 20 mL</td>
<td>Ultrasound-guided</td>
<td>Preincisional</td>
<td>IV ketorolac IV hydromorphone Oral hydrocodone Oral paracetamol Oral ibuprofen</td>
<td>QoR-40 questionnaire used to assess patient satisfaction</td>
</tr>
<tr>
<td>El-Kabariety 2013</td>
<td>66</td>
<td>TAP block with 0.5% levobupivacaine + 2 mL of NS TAP block with 0.5% levobupivacaine + 2 mL 0.1% tramadol Sham block</td>
<td>Levobupivacaine 0.5%, 20 mL</td>
<td>Ultrasound-guided</td>
<td>Preincisional</td>
<td>IV paracetamol IM diclofenac IM morphine</td>
<td>Patient satisfaction score from pain relief recorded at 48 hours after surgery Pfannenstiel incision</td>
</tr>
<tr>
<td>Gasanova et al, 2013</td>
<td>74</td>
<td>TAP with ketorolac 30 mg IV TAP block IV ketorolac</td>
<td>Bupivacaine 0.5%, 20 mL</td>
<td>Ultrasound-guided</td>
<td>At end of surgery</td>
<td>Oral acetaminophen IV fentanyl IV morphine PCA morphine</td>
<td>Included patients with Pfannenstiel incision or below-the-umbilicus vertical incision</td>
</tr>
<tr>
<td>Study</td>
<td>N</td>
<td>Type of Pain Management</td>
<td>Route of Administration</td>
<td>Timing</td>
<td>Sedation</td>
<td>Adjuvants</td>
<td>Incision Site</td>
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<tr>
<td>Gasanova et al, 2015&lt;sup&gt;24&lt;/sup&gt; USA</td>
<td>58</td>
<td>TAP Surgical site infiltration&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Bupivacaine 0.5%, 20 mL</td>
<td>Ultrasound-guided</td>
<td>At end of surgery&lt;sup&gt;3&lt;/sup&gt;</td>
<td>IV hydromorphone PCA Morphine Oral acetaminophen IV ketorolac Oral hydrocodone Oral ibuprofen IV dexamethasone</td>
<td>Use different bupivacaine Pfannenstiel incision</td>
</tr>
<tr>
<td>Gawad et al, 2015&lt;sup&gt;25&lt;/sup&gt; Egypt</td>
<td>80</td>
<td>TAP block Sham block&lt;sup&gt;d&lt;/sup&gt; with NS</td>
<td>Bupivacaine 0.25%, 20 mL</td>
<td>Ultrasound-guided</td>
<td>Preincisona&lt;sup&gt;2&lt;/sup&gt;</td>
<td>IV fentanyl Suprapubic abdominal transverse incision No complications with TAP block</td>
<td></td>
</tr>
<tr>
<td>Gharaei et al, 2013&lt;sup&gt;26&lt;/sup&gt; Iran</td>
<td>42</td>
<td>TAP block PCA fentanyl</td>
<td>Ropivacaine 0.2%, 0.5 mg/kg</td>
<td>Ultrasound-guided</td>
<td>At end of surgery&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Fentanyl infusion No attrition rate mentioned Ramsay sedation scale used</td>
<td></td>
</tr>
<tr>
<td>Ghisi et al, 2016&lt;sup&gt;27&lt;/sup&gt; Italy</td>
<td>44</td>
<td>TAP block PCA morphine</td>
<td>Levobupivacaine 0.375%, 20 mL</td>
<td>Ultrasound-guided</td>
<td>Preincisiona&lt;sup&gt;2&lt;/sup&gt;</td>
<td>PCA morphine Laparoscopic port incision</td>
<td></td>
</tr>
<tr>
<td>Huang et al, 2016&lt;sup&gt;28&lt;/sup&gt; China</td>
<td>71</td>
<td>TAP with PCA morphine LA infiltration to ports (for 8-mm port incision or greater, 0.375% ropivacaine, 7 mL; for 5-mm port incision or lesser, 0.375% ropivacaine, 3 mL)</td>
<td>Ropivacaine 0.375%, 15 mL</td>
<td>Ultrasound-guided</td>
<td>Preincisiona&lt;sup&gt;2&lt;/sup&gt;</td>
<td>IV parecoxib Unable to assess sensory blockade after TAP Included patients undergoing TLH and LAVH Four-port laparoscopic incision Patient satisfaction score evaluated 24 hours after surgery</td>
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<tr>
<td>Kane et al, 2014&lt;sup&gt;29&lt;/sup&gt; USA</td>
<td>56</td>
<td>TAP No TAP No sham or placebo</td>
<td>Ropivacaine 0.5%, 20 mL with 1:200,000 epinephrine</td>
<td>Ultrasound-guided</td>
<td>At end of surgery&lt;sup&gt;3&lt;/sup&gt;</td>
<td>IV ketorolac Single- and multiple-port laparoscopic incisions; single port, at umbilicus; multiple ports, at umbilicus; suprapubic midline; and right to left quadrant incision QoR-40&lt;sup&gt;k&lt;/sup&gt; questionnaire used starting POD 1 Patient’s mean weight was BMI of 31 mg/kg&lt;sup&gt;2&lt;/sup&gt;, may indicate block placement difficulty Delayed OR time</td>
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<td>Kishore et al, 2014&lt;sup&gt;30&lt;/sup&gt; India</td>
<td>40</td>
<td>TAP block No TAP block</td>
<td>Bupivacaine 0.25%, 20 mL</td>
<td>Ultrasound-guided</td>
<td>At end of surgery&lt;sup&gt;3&lt;/sup&gt;</td>
<td>PCA morphine Oral paracetamol Rectal indomethacin</td>
<td>All patients were under SAB using hyperbaric 0.5% bupivacaine Pfannenstiel incision</td>
</tr>
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<td>Marais et al, 2014&lt;sup&gt;31&lt;/sup&gt; South Africa</td>
<td>30</td>
<td>TAP block Sham block&lt;sup&gt;d&lt;/sup&gt; with NS</td>
<td>Bupivacaine 0.25%, 20 mL</td>
<td>Ultrasound-guided</td>
<td>Preincisiona&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Oral paracetamol Rectal indomethacin PCA morphine Pfannenstiel or midline abdominal incision</td>
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</tr>
<tr>
<td>Source Country</td>
<td>N</td>
<td>Comparison Groups</td>
<td>TAP Block Description</td>
<td>Multimodal Analgesia</td>
<td>Comments</td>
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<tr>
<td>Zimbabwe</td>
<td>32</td>
<td>TAP block</td>
<td>Bupivacaine 0.25%, 20 mL + 4 mg of dexamethasone</td>
<td>IM pethidine</td>
<td>No standardization of postoperative analgesia</td>
<td></td>
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<tr>
<td>India</td>
<td>100</td>
<td>TAP block vs Sham</td>
<td>Ropivacaine 0.25%, 1 mg/kg (maximum of 20 mL)</td>
<td>IV tramadol</td>
<td>All patients under SAB with hyperbaric 0.5% bupivacaine, 3.5 mL Pfannenstiel incision</td>
<td></td>
<td></td>
</tr>
<tr>
<td>India</td>
<td>60</td>
<td>TAP block vs No TAP</td>
<td>Ropivacaine 0.75%, 1.5 mg/kg</td>
<td>PCA tramadol</td>
<td>All blocks were performed by a single investigator. No blinding with epidural and TAP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>India</td>
<td>113</td>
<td>TAP block</td>
<td>Ropivacaine 0.25%, 20 mL</td>
<td>IM lornoxicam</td>
<td>All participants have BMI ≥ 40 kg/m². Epidural and PCA morphine sulfate were initiated after surgery in PACU. Sedation assessed using Ramsay Sedation Scale.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Denmark</td>
<td>46</td>
<td>TAP block</td>
<td>Ropivacaine 0.75%, 20 mL</td>
<td>PCA morphine sulfate</td>
<td>Preoperative celecoxib, 200 mg, and acetaminophen, 2 g. At end of surgery, sufentanil administered based on ideal body weight. No complications with TAP block. Mean time to first mobilization was shorter in TAP compared with placebo (275 mins vs 346 min).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Denmark</td>
<td>65</td>
<td>TAP block</td>
<td>Ropivacaine 0.5%, 20 mL</td>
<td>Oral paracetamol</td>
<td>Robotic-assisted laparoscopic hysterectomy. Five patients received morphine and dexamethasone before induction, which was in violation of study protocol. No LA infiltration at laparoscopic port sites.</td>
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<tr>
<td>Sri Lanka</td>
<td>40</td>
<td>TAP block</td>
<td>Bupivacaine 0.25%, 20 mL</td>
<td>Rectal diclofenac</td>
<td>TAH for benign conditions. All patients received pethidine, 50-75 mg, and rectal diclofenac, 50-100 mg, before incision. TAP block done after abdominal incision. Suprapubic transverse incision.</td>
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Table 2. Randomized Controlled Trials Examining the Opioid-Sparing Effects of Transversus Abdominis Plane Block in Patients Undergoing Elective Hysterectomy
Abbreviations: BMI, body mass index; IM, intramuscular; IV, intravenous; LA, local anesthetic; LAVH, laparoscopic-assisted vaginal hysterectomy; NS, normal saline; OR, operating room; PCA, patient-controlled analgesia; POD, postoperative day; PONV, postoperative nausea and vomiting; SAB, subarachnoid block; TAP, transversus abdominis plane; TLH, total laparoscopic hysterectomy; LAVH, laparoscopically assisted vaginal hysterectomy.

Elective hysterectomy.

Local anesthetic dose at each side.

Postoperative multimodal analgesia regimen.

Invasive placebo TAP block categorized as grade 3 and 4 on Serious Harm and Morbidity (SHAM) scale. Grade 0 = no placebo intervention, grade 1 = noninvasive placebo with minimal risk of harm, grade 2 = minimally invasive placebo with risk of minor complications, grade 3a = invasive placebo with moderate risk of complications but no placebo drug administered, grade 4 = invasive placebo procedure with major risk of complication and placebo drug administered.

NS amount is similar to LA amount in milliliters.

Used of anatomical landmarks to determine injection site of LA in the lumbar triangle of Petit. A "pop" indicates appropriate needle depth.

Before or after induction.

Bupivacaine 0.25% injected into the skin and subcutaneous tissues.

A 42-item quality of recovery questionnaire measuring 5 domains: physical comfort, emotional state, physical independence, psychological support, and pain.

Liposomal bupivacaine, 266 mg in 60 mL, injected into preperitoneal, subfacial, and subcutaneous planes.

Six- and 48-Hour Postsurgery Morphine Consumption.

Six- and 48-Hour Postsurgery Morphine Consumption.

Pooled analysis of 2 studies composed of 66 patients showed reduction of IV morphine equivalent by an average of 4.9 mg (MD, −4.87; 95% CI, −5.49 to −4.25; P < .00001) 6 hours after surgery (see Figure 3). Four studies that included 239 patients showed a large reduction in morphine consumption 48 hours after hysterectomy (MD, −28.68; 95% CI, −44.35 to −13.01; P = .0003; see Figure 3).

Secondary Outcomes.

Second- and 48-Hour Postsurgery Morphine Consumption.

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Figure 3. Forest Plot of Intravenous (IV) Morphine Equivalent Consumption (mg) Intraoperatively, in
Postanesthesia Care Unit (PACU), and 6, 24, and 48 Hours After Surgery
Abbreviations: random, random-effects model; TAP, transversus abdominis plane.

Eight RCTs recorded the first request of postoperative analgesia. Pooled analysis showed patients treated with TAP block delayed asking for rescue analgesia by an average of 3 hours (MD, 189.4; 95% CI, 148.17 to 230.71; $P < .00001$). The $I^2$ statistics showed substantial heterogeneity ($I^2 = 100\%$).

- **Postoperative Nausea and Vomiting.** Combined data from 10 RCTs (N = 591) showed the risk of PONV was reduced by 44% in patients treated with TAP block (RR, 0.56; 95% CI, 0.41 to 0.76; $P = .0002$). Patients treated with TAP block experienced less PONV (15%) compared with control (26%). The $I^2$ statistics showed moderate heterogeneity ($I^2 = 48\%$; Figure 6).

- **Sedation.** Four studies comprising 230 patients reported the incidence of postoperative sedation. Fewer patients experienced sedation in TAP group (10%) compared with control (31%). The risk of sedation after hysterectomy was reduced by 68% in patients treated with TAP block (RR, 0.32; 95% CI, 0.18 to 0.57; $P = .0001$). The pooled results showed no significant heterogeneity ($I^2 = 0\%$; Figure 7).

- **Risk of Bias.** Twenty-two studies had a low risk of random sequence generation, and 19 studies had a low risk of allocation concealment. Seventy percent of the studies blinded the participants and the investigators, and 80% blinded outcomes assessors. The overall quality of the included studies was moderate based on substantial heterogeneity and possible publication bias.

- **Funnel Plot.** By visual inspection, the funnel plot was asymmetric, suggesting potential publication bias. The possibility of publication bias was supported by a
funnel plot regression test \((t = −3.895; P = .002)\).

**Discussion**

This systematic review and meta-analysis suggested that a single-shot TAP block in patients undergoing hysterectomy reduced morphine requirements intraoperatively and up to 48 hours after surgery. In addition, women treated with TAP block reported low pain intensity scores at rest in the early postoperative period but not during coughing. The timing of first postoperative analgesia was delayed with TAP block. Similarly, the opioid adverse side effects such as PONV and sedation were significantly lower in patients treated with TAP block.

The reduction in 24-hour IV morphine equivalent requirement that we found was similar to that in previous meta-analyses examining TAP block in abdominal surgery and laparoscopic cases.39,40 In our review, the included trials favored TAP block for a modest reduction of 3.4 mg of morphine equivalent compared with a 23.71-mg reduction in a systematic review of 9 RCTs using TAP block in lower abdominal surgery.39 However, the overall perioperative IV morphine equivalent reduction of 6.52 mg was comparable to meta-analyses conducted in 2 other reviews showing a reduction of an average 5.7 mg40 and 9.0 mg.41 It is possible that the relatively moderate reduction we report here may be attributed to the type of surgery, because our review investigated hysterectomy cases, whereas previous studies investigated a variety of surgical procedures. Another possibility is variability in clinical practice in terms of multimodal pain management protocols, which may lead to variation in overall morphine consumption.

Our review also showed a lower 24-hour morphine use during TAH than during total laparoscopic hyster-

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**Figure 4. Forest Plot of Pain Intensity Scores at Rest at 4 Different Time Points (2, 4, 24, and 48 hours) After Hysterectomy**

Abbreviations: IV, intravenous; random, random-effects model; TAP, transversus abdominis plane.
A possible explanation for this difference is that pain in open hysterectomy is more profound compared with laparoscopic surgery; hence, TAP block has better pain coverage in open hysterectomies. In a meta-analysis of 7 studies of laparoscopic cholecystectomy, US-guided TAP block reduced morphine use by 9.1 mg. In our meta-analysis, only 4 studies reported morphine use during laparoscopic surgery. Of these, only one trial favored TAP block over the control. Three of the studies identified that TAP block did not adequately block the multiple laparoscopic port, larger midline, and umbilical incisions.

The reduction of morphine consumption averaged 2.8 mg in the recovery room and 28.6 mg 48 hours after surgery. The previous meta-analysis in hysterectomy patients found a short-term effect of TAP block for up to 24 hours. Our current meta-analysis suggested a long-term effect of the block. The reduction of morphine use late in the perioperative phase is not completely understood. However, the prolonged duration of TAP block may be attributed to the larger dose of LA (15-20 mL on each side) and the poorly vascularized TAP area resulting in decreased drug clearance.

The timing of the block affected morphine consumption after hysterectomy. Preincisional block showed a reduction in morphine use compared with preemergence block. These findings are consistent with the previous review reporting that preincisional block placement was effective in pain control. Furthermore, our finding is similar to the RCT results reported by Shin and colleagues when they examined the preemptive analgesic effects of TAP block in gynecologic surgeries with lower transverse incision. Their study demonstrated significant reduction of opioid requirement in the PACU.

In our systematic review, US-guided technique had similar opioid-sparing effects compared with local skin infiltration, PCA with morphine, epidural analgesia, and placebo. These results can be explained by the inclusion of 2 studies comparing TAP block with epidural analgesia and skin infiltration. In previous RCTs, epidural analgesia and skin infiltration have been shown to provide superior pain coverage. Niraj and colleagues reported higher rescue analgesia requirements with TAP block compared with epidural anesthesia. Additionally, a subfascial and preperitoneal infiltration provided more superior pain control by targeting the visceral component of hysterectomy pain, which is often not covered by TAP block.

Postoperative pain scores at rest at 2 different time points (2 and 4 hours after surgery) favored the TAP block, which is consistent with other reviews. Although the pooled estimates of pain scores at rest was statistically significant, the effect size was small to moderate, raising...
the question of its clinical importance. In our review, we used coughing for pain scores on movement. Our meta-analysis showed that patients treated with TAP block had similar pain scores compared with placebo during coughing. Although our results failed to demonstrate the beneficial effects of TAP block on pain scores during coughing, it must be noted that morphine consumption was reduced, perhaps indicating better pain control.

Reports of opioid side effects differ between reviews. In our meta-analysis, TAP block reduced the incidence of PONV and sedation. Although these reductions were statistically significant, the data available were limited with small sample sizes.

Methodological and clinical heterogeneity were present across studies regarding the primary outcome of morphine consumption. The between-study heterogeneity can be attributed to the different types, concentrations, and doses of LA used; the timing and techniques of the block; varied postoperative analgesic strategies; and the types of hysterectomy approaches. To determine other sources of heterogeneity, we performed subgroup analyses, and the results still indicated high heterogeneity. In our sensitivity analysis, we excluded one study at a time as proposed by The Cochrane Collaboration. However, the findings were virtually unchanged, with substantial heterogeneity.

Our review had some limitations. First, most of the RCTs showed small to medium effect size given their sample sizes. Studies with small samples sizes at times report larger effect sizes, which may lead to reporting bias. Second, we included trials that used sham block as the control. This type of invasive placebo exposes patients to risks of serious complications such as accidental liver laceration and bowel perforation. Although no major complications were reported in all RCTs, the sham blocks used in a number of studies are categorized as grade 3 or 4 on a 0 to 4 Serious Harm and Morbidity (SHAM) scale, which determines the extent of invasiveness and ultimate harm in research. A recent Cochrane editorial recommended exclusion of sham blocks in systematic reviews, but a Google search showed that sham blocks were still reported in numerous systematic reviews and meta-analysis studies published in 2016. Third, evaluation of the sensory level of TAP block was performed in only one study. The assessment of sensory block is crucial because this can introduce bias in the block’s efficacy and in patient assessment of pain. Finally, types of opioids varied between studies, and conversion to IV morphine equivalent using published conversion factors may have introduced bias to final analyses.

The funnel plot showed some possibility of publication-
tion bias because of an asymmetric dispersion of effects. The inclusion of only English-language studies may introduce biased conclusions; however, a systematic review examining inclusion of studies with a language limitation found no evidence of systematic bias.30

We identified areas for future studies. Compared with previous meta-analyses, the reported reduction in morphine equivalents associated with TAP blocks in the research reviewed here was moderate. There were insufficient data on whether the opioid-sparing effects persisted up to 48 hours after surgery. Further RCTs are required to examine the opioid-sparing effect of single-shot TAP block and continuous infusion of the LA. Because TAP blocks do not cover visceral pain, more studies on the systematic effects of the LA absorption and comparison with epidural and skin infiltration are needed. Additional studies on optimal dose of the LA are needed to assess the efficacy of TAP block.

Conclusion

As part of multimodal pain management, TAP block has moderate opioid-sparing effects up to 48 hours after hysterectomy. Likewise, patients who underwent TAP blocks had fewer opioid-related side effects. Although the data analyzed for this article demonstrated statistical significance in morphine consumption, pain scores at rest at 2 and 4 hours after surgery, and the incidence of PONV and sedation, we caution readers on the degree to which postoperative opioid dosing, whether for morphine or other narcotics, can be reduced in patients who have received TAP blocks because there is considerable heterogeneity between studies, small sample sizes, and moderate methodological quality of the included studies.

REFERENCES
