**PROSPECT METHODOLOGY PRIMER**

1. Once the Working Group identifies the surgical procedure (new or update) to be reviewed, a subgroup will be selected. The subgroup consists of at least two members of the Working group and co-opted external members as required (e.g., surgeons and/or anesthesiologists) with specific expertise in the surgical procedure to be reviewed. In addition, specialists in literature searches and/or data analysis may also be included in the subgroup. The subgroup may also include research fellows assisting with the project.
2. The Working group will select a leader of the subgroup (must be a member of Prospect Working Group) who will be ultimately responsible for the timely completion of the project including manuscript submission for publication, if applicable, and presentation on the Prospect website.
3. For new procedures, the subgroup, with the assistance of the Working group, will determine the time period for literature search. For updates, the literature search will be from the end date of the previous review.
4. The subgroup will determine the search terms for the literature search. The search terms will be as broad as possible, to maximize the search and reduce the risk of missing relevant publications. Search terms will include words or phrases related to pain and possible interventions, as well as procedure-specific terms. For example, pain-related terms will include, but not limited to: pain OR analgesi* OR anaesthe* OR anesthe* OR vas OR "visual analog*" OR vrs OR mcgill OR epidural OR neuraxial OR intrathecal OR spinal OR caudal OR interpleural OR “peripheral nerve” OR “peripheral block” OR intercostal OR “nerve block” OR NSAID OR COX-2 OR paracetamol OR acetaminophen OR gabapentin OR pregabalin OR clonidine OR opioid OR ketamine OR corticosteroid). These terms will be applied in various combinations, together with the use of the “related articles” function to maximize the search.
5. Inclusion criteria for studies include randomized controlled clinical trials (RCTs) and systematic reviews of analgesic, anesthetic and operative interventions, published in the English language, addressing pain management relating to the surgical procedure being reviewed. In addition, included RCT’s should report pain scores using a linear pain scale, e.g. visual analogue scale (VAS) or verbal or numerical rating scale (VRS or NRS).
6. One of the members of the subgroup will be given the responsibility of performing the literature search with the help of a librarian who is familiar with the process described by the Cochrane Collaboration. Several electronic databases (e.g., Ovid Medline, Medline InProcess, other non-indexed citations, and Medline EPub ahead of print, Embase, and Cochrane controlled trials register published by the Cochrane Library) will be utilized to identify studies.
7. Once the literature search is performed, a step-wise approach will be used to identify RCTs for inclusion. Two members of the subgroup will select the studies independently by screening the titles and/or abstracts according to a priori defined inclusion criteria (see above). The results between the two reviewers will be noted and discussed aiming for consensus. Abstracts (if only titles were screened) and/or full-text of the papers included from the first step will be reviewed and irrelevant papers will be excluded. At any stage, in the case of insoluable discrepancies between the two reviewers, a third reviewer will be involved in the discussion. In addition, reference lists of all relevant studies from the electronic search will be manually searched to identify additional eligible

studies.

8. Once the studies for inclusion are finalized, the excluded studies will be tabulated with reasons for exclusion.
9. All included studies will be assessed for quality of reporting of methodology and results using the Cochrane Collaboration's tool.
    - *Numerical scores (total 1–5) for study quality:* assigned using the method proposed by Jadad 1996, to indicate whether a study reports appropriate randomisation, double-blinding and statements of possible withdrawals.
    - *Allocation concealment assessment:* indicates whether there was adequate prevention of foreknowledge of treatment assignment by those involved in recruitment (A adequate, B unclear, C inadequate, D not used).
    - *Statistical analyses and patient follow-up assessment:* indicates whether statistical analyses were reported, and whether patient follow-up was greater or less than 80%.
    - *Additional study quality assessment:* including an assessment of how closely the study report meets the requirements of the CONSORT statement.
10. The included studies will be grouped into three subgroups of preoperative, intraoperative, and postoperative interventions. Within each of these subgroups, the studies will be further placed into groups based upon the analgesic technique (e.g., epidural analgesia, peripheral nerve blocks, field blocks, surgical site infiltration, paracetamol, non-steroidal anti-inflammatory drugs, cyclooxygenase-2 specific inhibitors, etc.). The studies assessing the effects of surgical techniques on analgesic outcomes will be grouped separately.
11. Information from the included studies will be tabulated. The information recorded will include, but not be limited to, intervention evaluated, characteristics of study design, treatment in the control group (e.g., placebo, active comparator), patient numbers in each group, population (age, gender, opioid tolerance and psychiatric ailments, etc.), details about surgical procedure, duration of follow-up, pain scores at rest/on movement, supplementary analgesic use, time to first request for rescue analgesia, opioid-related adverse events such as postoperative nausea and vomiting, any other additional outcomes assessed, Jadad score, patient follow-up >80% and stats reported, allocation concealment, and Met CONSORT reporting guidelines or not. In addition, a separate column will include the conclusions of the study in details.
12. The table will also include a column on critical evaluation for relevance of the study design with respect to the analgesic/analgesic technique in current perioperative care practice. For example, did the study groups include a "basic" analgesic technique (i.e., acetaminophen and non-steroidal anti-inflammatory drugs/COX-2 specific inhibitors)? Also, determine if the analgesic intervention would further improve postoperative pain relief and/or outcome when added to the "basic" analgesic regimen. For example, adding intravenous lidocaine infusion or TAP blocks to patients undergoing laparoscopic cholecystectomy is not beneficial over the "basic" analgesic regimen of paracetamol + NSAIDs or COX-2 specific inhibitors + port site infiltration). Furthermore, the comment column will include analysis of the balance between the invasiveness of the analgesic technique and the consequences of postoperative pain as well as a balance between the analgesic efficacy and adverse event profile of the analgesic technique.

13. Quantitative analyses will be performed if the studies determined suitable according to the Prospect criteria (see the previous bullet), are homogenous, and data are reported in a suitable manner. In addition, for the studies to be grouped together they should have uniformity in the analgesic technique(s) utilized. Studies that do not report mean and standard deviation data (for continuous variables), or proportion of patients affected (for dichotomous variables), will not be included in the meta-analyses.
14. The subgroup will prepare a draft table/flow diagram of the recommendations of analgesic, anaesthetic or surgical interventions. In addition, a list of interventions not recommended with reasons for non-recommendation will be prepared. Recommendations will be presented with a brief explanation of the evidence on which they are based upon. To be recommended the intervention must be proven to be beneficial in at least two RCT's. Other factors that may be considered include the quality of the study (e.g., the sample size, Jadad scores, and other quality measures described above). In addition, the analgesic intervention should usually be considered to further improve postoperative pain relief and/or outcome when added to the "basic" analgesic regimen. Alternatively, the intervention would be beneficial if the "basic" analgesic technique with the intervention is not possible or is contraindicated. Furthermore, a balance between the invasiveness of the intervention and the risks (based on the current evidence of risks) of the intervention will be considered.
15. The documents with the tables and other detailed information will be sent to the members of the Working group at least 6 weeks prior to the face-to-face meeting of the Working group.
16. Working Group members will critically examine the recommendations and those not recommended by the subgroup prior to the face-to-face meeting. Each Working group member will email their comments to the subgroup leader. These comments will be collated for presentation during the face-to-face meeting.
17. During the face-to-face meeting one of the members of the subgroup, as determined by the subgroup leader, will briefly present (using PowerPoint) the reasons for recommendations and non-recommendations. Thereafter, the strength of recommendations will be graded based upon the agreement between the members of the Working group. The group will also develop clinical questions that need to be answered in the future.
18. After the face-to-face meeting the subgroup will prepare a final document, which will include comments discussed during the meeting.
19. The final document with the consensus agreements will be circulated (*via* email) to the Working group for a review and approval. ***No major changes will be entertained during this final review***.
20. Finally, the subgroup will prepare a manuscript for publication in a peer-reviewed journal, if appropriate. Subsequently, a web copy will be prepared with the help of a medical writer.

**Relationship between quality and source of evidence of the study and levels of evidence (LoE) and grades of recommendation (GoR). Allocation concealment assessment: A–adequate; B–Unclear; C–inadequate; D–not used. GoR are based on overall LoE, considering balance of clinical practice information and evidence. NA: not applicable.**

<table>
<tr><th></th><th colspan="5">Study quality assessments</th><th>Level of Evidence (LoE)</th><th>Grade of recommendation (based on overall LoE, considering balance of clinical practice information and evidence)</th></tr>
<tr><th>Study type</th><th>Statistical analyses and patient follow-up assessment</th><th></th><th>Allocation concealment</th><th>Jadad scores</th><th>Additional assessment of overall study quality required to judge LoE</th><th></th><th>Procedure-specific</th></tr>
<tr><td>Systematic review with homogeneous results</td><td>N/A</td><td></td><td>N/A</td><td>N/A</td><td>N/A</td><td>1</td><td>A</td></tr>
<tr><td rowspan="5">Randomised controlled trial (RCT)</td><td rowspan="5">Statistics reported and >80% follow-up</td><td rowspan="5">AND</td><td>A</td><td>(1–5)</td><td>N/A</td><td rowspan="5">1</td><td rowspan="5">A<br>(based on two or more studies or a single large, well-designed study)</td></tr>
<tr><td colspan="3">OR</td></tr>
<tr><td>B</td><td>(3–5)</td><td>N/A</td></tr>
<tr><td colspan="3">OR</td></tr>
<tr><td>B</td><td>(1–2)</td><td>Yes</td></tr>
<tr><td rowspan="5">RCT</td><td rowspan="5">Statistics not reported or questionable or <80% follow-up</td><td rowspan="5">AND /OR</td><td>B</td><td>(1–2)</td><td>Yes</td><td rowspan="5">2</td><td rowspan="5">B<br>(or extrapolation from one procedure-specific LoE 1 study)</td></tr>
<tr><td colspan="3">OR</td></tr>
<tr><td>C</td><td>(1–5)</td><td>N/A</td></tr>
<tr><td colspan="3">OR</td></tr>
<tr><td>D</td><td>(1–5)</td><td>N/A</td></tr>
<tr><td>Non-systematic review, cohort study, case study; (e.g. some adverse effects evidence)</td><td>N/A</td><td></td><td colspan="3">N/A</td><td>3</td><td>C</td></tr>
<tr><td>Clinical practice information (expert opinion); inconsistent evidence</td><td>N/A</td><td></td><td colspan="3">N/A</td><td>4</td><td>D</td></tr>
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