Practice Guidelines for the Prevention, Detection and Management of Respiratory Depression Associated with Neuraxial Opioid Administration

An Updated Report by the American Society of Anesthesiologists Task Force on Neuraxial Opioids and the American Society of Regional Anesthesia and Pain Medicine [*]

PRACTICE guidelines are systematically developed recommendations that assist the practitioner and patient in making decisions about health care. These recommendations may be adopted, modified, or rejected according to clinical needs and constraints, and are not intended to replace local institutional policies. In addition, practice guidelines developed by the American Society of Anesthesiologists (ASA) are not intended as standards or absolute requirements, and their use cannot guarantee any specific outcome. Practice guidelines are subject to revision as warranted by the evolution of medical knowledge, technology, and practice. They provide basic recommendations that are supported by a synthesis and analysis of the current literature, expert and practitioner opinion, open forum commentary, and clinical feasibility data.

This document updates the "Guidelines for the Prevention, Detection and Management of Respiratory Depression Associated with Neuraxial Opioid Administration: An Updated Report by the ASA Task Force on Neuraxial Opioids," adopted by ASA in 2008 and published in 2009.[†]

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[*] Supplemental Digital Content is available for this article. Direct URL citations appear in the printed text and are available in both the HTML and PDF versions of this article. Links to the digital files are provided in the HTML text of this article on the Journal's Web site (www.anesthesiology.org). A complete bibliography used to develop these updated Guidelines, arranged alphabetically by author, is available as Supplemental Digital Content, http://links.lww.com/ALN/___

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[†] Practice Guidelines for the Prevention, Detection and Management of Respiratory Depression Associated with Neuraxial Opioid Administration: an Updated Report by the American Society of Anesthesiologists Task Force on Neuraxial Opioids. Anesthesiology 2009; 110:218-230

Methodology

A. Definitions of Neuraxial Opioid Analgesia and Respiratory Depression

Neuraxial opioid analgesia refers to the epidural or spinal administration of opioids, including single injection, continuous or intermittent infusion, and patient-controlled analgesia. For these Guidelines, respiratory depression may be indicated by: (1) reduced respiratory rate (*e.g.*, to < 10 breaths per minute), (2) reduced oxygen saturation (*e.g.*, arterial oxygen saturation < 90%), or (3) hypercapnia/hypercarbia (*e.g.*, arterial carbon dioxide tension > 50 mmHg). Other measures of respiratory function (*e.g.*, tidal volume) or clinical signs (*e.g.*, drowsiness, sedation, periodic apnea, cyanosis) may also provide indications of respiratory depression.

B. Purposes of the Guidelines

The purposes of these updated Guidelines are to improve patient safety and enhance the quality of anesthetic care by reducing the incidence and severity of neuraxial opioid-related respiratory depression or hypoxemia. In addition, these Guidelines are intended to reduce the incidence and severity of adverse outcomes related to reduced respiratory rate or oxygen levels (*e.g.*, cardiac arrest, brain damage, death).

C. Focus

These updated Guidelines focus on the management of all patients receiving epidural or spinal opioids in inpatient (*e.g.*, operating rooms, intensive care units, labor and delivery suites, postoperative surgical floors, hospital wards) or ambulatory (*e.g.*, stand-alone outpatient facilities) settings. The Guidelines do not apply to patients with chronic or cancer pain (except those with acute postoperative pain), patients with preexisting implantable drug delivery systems, or patients with contraindications to spinal or epidural opioids (*e.g.*, coagulopathy, sepsis).

D. Application

These updated Guidelines are intended for use by anesthesiologists. They also may serve as a resource for other physicians administering neuraxial opioids and other health care providers involved in the management of patients receiving neuraxial opioids.

E. Task Force Members and Consultants

In 2014, the ASA Committee on Standards and Practice Parameters requested that the updated Guidelines published in 2009 be re-evaluated. This current update consists of a literature evaluation, new surveys and an update of the evidence-based guideline nomenclature. A summary of recommendations is found in appendix 1.

This update was developed by an ASA appointed task force of 10 members, including anesthesiologists in both private and academic practice from various geographic areas of the United States and consulting methodologists from the ASA Committee on Standards and Practice Parameters.

The Task Force developed these updated Guidelines by means of a seven-step process. First, they reached consensus on the criteria for evidence. Second, original published research studies from peer-reviewed journals relevant to neuraxial opioid administration were reviewed and evaluated. Third, expert consultants were asked to: (1) participate in opinion surveys on the effectiveness of various neuraxial opioid management strategies and (2) review and comment on a draft of the Guidelines developed by the Task Force. Fourth, opinions about the Guideline recommendations were solicited from a random sample of active members of the ASA. Fifth, the Task Force held an open forums at a major national meetings[‡] to solicit input on its draft recommendations. Sixth, the consultants were surveyed to assess their opinions on the feasibility of

[‡] American Society of Regional Anesthesia and Pain Medicine, 40th Annual Meeting, Las Vegas, Nevada, May 15, 2015.

implementing the updated Guidelines. Seventh, all available information was used to build consensus within the Task Force to finalize the updated Guidelines *(appendix 1)*.

F. Availability and Strength of Evidence

Preparation of these Guidelines followed a rigorous methodological process. Evidence was obtained from two principal sources: scientific evidence and opinion-based evidence (appendix 2).

Scientific Evidence:

Scientific evidence used in the development of these updated Guidelines is based on cumulative findings from literature published in peer-reviewed journals. Literature citations are obtained from PubMed and other healthcare databases, direct internet searches, Task Force members, liaisons with other organizations and from manual searches of references located in reviewed articles.

Findings from the aggregated literature are reported in the text of the Guidelines by evidence category, level, and direction. Evidence categories refer specifically to the strength and quality of the *research design* of the studies. Category A evidence represents results obtained from randomized-controlled trials (RCTs), and Category B evidence represents observational results obtained from non-randomized study designs or RCTs without pertinent comparison groups. When available, Category A evidence is given precedence over Category B evidence for any particular outcome. These evidence categories are further divided into evidence levels. Evidence levels refer specifically to the strength and quality of the summarized study *findings* (*i.e.*, statistical findings, type of data, and the number of studies reporting/replicating the findings within the two evidence categories. In this document, only the highest level of evidence is included in the summary report for each intervention-outcome pair, including a directional designation of benefit, harm, or equivocality for each outcome.

Category A: RCTs report comparative findings between clinical interventions for specified outcomes. Statistically significant ($p < 0.01$) outcomes are designated as either beneficial (B) or

harmful (H) for the patient; statistically nonsignificant findings are designated as equivocal (E).

Level 1: The literature contains a sufficient number of RCTs to conduct meta-analysis,[§] and meta-analytic findings from these aggregated studies are reported as evidence.

Level 2: The literature contains multiple RCTs, but the number of RCTs is not sufficient to conduct a viable meta-analysis for the purpose of these updated Guidelines. Findings from these RCTs are reported separately as evidence.

Level 3: The literature contains a single RCT and findings are reported as evidence.

Category B: Observational studies or RCTs without pertinent comparison groups may permit *inference* of beneficial or harmful relationships among clinical interventions and clinical outcomes. Inferred findings are given a directional designation of beneficial (B), harmful (H), or equivocal (E). For studies that report statistical findings, the threshold for significance is $p < 0.01$.

Level 1: The literature contains observational comparisons (*e.g.*, cohort, case-control research designs) with comparative statistics between clinical interventions for a specified clinical outcome.

Level 2: The literature contains non-comparative observational studies with associative statistics (*e.g.*, relative risk, correlation, sensitivity/specificity).

Level 3: The literature contains noncomparative observational studies with descriptive statistics (*e.g.*, frequencies, percentages).

Level 4: The literature contains case reports.

Insufficient Literature: The *lack* of sufficient scientific evidence in the literature may occur when the evidence is either unavailable (*i.e.*, no pertinent studies found) or inadequate. Inadequate literature cannot be used to assess relationships among clinical interventions and outcomes because a clear interpretation of findings is not obtained due to methodological concerns (*e.g.*, confounding

[§] All meta-analyses are conducted by the ASA methodology group. Meta-analyses from other sources are reviewed but not included as evidence in this document.

of study design or implementation), or the study does not meet the criteria for content as defined in the "Focus" of the Guidelines.

Opinion-Based Evidence:

All opinion-based evidence (*e.g.*, survey data, open-forum testimony, internet-based comments, letters, and editorials) relevant to each topic was considered in the development of these updated Guidelines. However, only the findings obtained from formal surveys are reported in the current update.

Opinion surveys were developed by the Task Force to address each clinical intervention identified in the document. Identical surveys were distributed to expert consultants and a random sample of ASA members.

Category A: Expert Opinion. Survey responses from Task Force-appointed expert consultants are reported in summary form in the text, with a complete listing of consultant survey responses reported in Appendix 2.

Category B: Membership Opinion. Survey responses from active ASA members are reported in summary form in the text, with a complete listing of ASA member survey responses reported in Appendix 2.

Survey responses from expert and membership sources are recorded using a 5-point scale and summarized based on median values.[**]

Strongly Agree:	Median score of 5 (At least 50% of the responses are 5)
Agree:	Median score of 4 (At least 50% of the responses are 4 or 4 and 5)
Equivocal:	Median score of 3 (At least 50% of the responses are 3, or no other response category or combination of similar categories contain at least 50% of the responses)
Disagree:	Median score of 2 (At least 50% of responses are 2 or 1 and 2)
Strongly Disagree:	Median score of 1 (At least 50% of responses are 1)

[**] *When an equal number of categorically distinct responses are obtained, the median value is determined by calculating the arithmetic mean of the two middle values. Ties are calculated by a predetermined formula.*

Category C: Informal Opinion. Open-forum testimony obtained during development of these Guidelines, Internet-based comments, letters and editorials are all informally evaluated and discussed during the formulation of Guideline recommendations. When warranted, the Task Force may add educational information or cautionary notes based on this information.

Guidelines

Identification of Patients at Increased Risk of Respiratory Depression

Identification of patients with risk factors for respiratory depression includes conducting a focused history (*e.g.*, reviewing medical records) and physical examination.

Literature findings: Although it is well accepted clinical practice to review medical records and conduct a physical examination, comparative studies are insufficient to directly evaluate the impact of these practices. Studies with observational findings and case reports suggest that certain patient or clinical characteristics (*e.g.*, obesity, obstructive sleep apnea, coexisting disease) may be associated with respiratory depression when neuraxial opioids are used *(Category B1/B4-H evidence).*[1-5]

Survey findings: Both the consultants and ASA members strongly agree that (1) a focused history and physical examination should be conducted before administering neuraxial opioids, (2) particular attention should be directed toward signs, symptoms, or a history of sleep apnea, co-existing diseases or conditions, current medications, and adverse effects following opioid administration, and (3) a physical examination should include, but is not limited to, baseline vital signs, airway, heart, lung, and cognitive function.

Recommendations for identification of patients at increased risk of respiratory depression.

- Conduct a focused history and physical examination before administering neuraxial opioids.
    - Direct particular attention toward signs, symptoms, or a history of sleep apnea, co-existing diseases or conditions (*e.g.*, diabetes, obesity), current medications (including preoperative opioids), and adverse effects following opioid administration.
    - A physical examination should include, but is not limited to, baseline vital signs, airway, heart, lung, and cognitive function.

Prevention of Respiratory Depression after Neuraxial Opioid Administration

Prevention of respiratory depression includes consideration of noninvasive positive pressure ventilation and drug selection. Drug selection includes (1) route of administration, (2) type of drug, (*i.e.*, hydrophilic or lipophilic opioids), (3) dose selection, and (4) drug combinations.

Noninvasive Positive Pressure Ventilation.

Literature findings: The literature is insufficient to assess the efficacy of noninvasive positive pressure ventilation when used for the prevention of respiratory depression in patients who have been administered neuraxial opioids.

Survey findings: Both the consultants and ASA members strongly agree that patients with a history of sleep apnea treated with noninvasive positive airway pressure should be encouraged to bring their own equipment to the hospital.

Route of Administration.

Routes of administration considered by these Guidelines include: (1) single-injection neuraxial opioids compared with parenteral opioids, (2) continuous infusion epidural opioids compared with parenteral opioids, and (3) extended-release epidural morphine.

Literature findings for single-injection neuraxial opioids compared with parenteral opioids: Meta-analysis of RCTs indicates no significant difference in the frequency of respiratory depression (*Category A1-E evidence)*, and less somnolence or sedation *(Category A1-B evidence)* for single-injection epidural opioids compared with intramuscular opioids.[6-13] Additional RCTs comparing single-injection epidural opioids compared with intravenous opioids report inconsistent findings regarding respiratory depression, respiratory failure, somnolence or sedation *(Category A2-E evidence).*[14-19] RCTs comparing patient-controlled epidural opioids (PCEA) with intravenous PCA opioids are equivocal regarding respiratory depression and hypoxemia (*Category A2-E evidence*).[20-23] An RCT comparing intrathecal sufentanil with intravenous sufentanil reports equivocal findings for respiratory depression and hypoxemia *(Category A1-E evidence).*[24]

Insufficient literature was found comparing single-injection neuraxial opioids with other systemic routes of administration (*e.g.*, oral, transdermal, rectal, nasal).

Literature findings for continuous infusion epidural opioids compared with parenteral opioids: Meta-analysis of RCTs indicate less respiratory depression when continuous infusion of epidural opioids are compared with intravenous infusion of opioids *(Category A1-B evidence).*[25-29] RCTs evaluating differences in hypercarbia are equivocal *(Category A2-E evidence).*[28-31] Meta-analysis findings from RCTs evaluating differences in somnolence or sedation are equivocal (*Category A1-E evidence).*[25,32-35]

Literature findings for extended-release epidural morphine: A single RCT reports no significant difference in the frequency of respiratory depression when extended-release epidural morphine is compared with intravenous PCA morphine (*Category C2-E evidence).*[36] In addition, RCTs report no significant differences in respiratory depression, hypoxia, and sedation or somnolence when extended-release epidural morphine is compared with conventional (*i.e.*, immediate-release) epidural morphine (*Category C2-E evidence).*[37-39]

<u>*Survey findings for route of administration:*</u> The consultants agree and ASA members neither agree nor disagree that single-injection neuraxial opioids may be safely used in place of parenteral opioids without altering the risk of respiratory depression. The consultants and ASA members both neither agree nor disagree that single-injection neuraxial fentanyl or sufentanil may be safe alternatives to single-injection neuraxial morphine. The consultants and ASA members both agree that, when clinically suitable, extended-release epidural morphine may be used in place of intravenous or conventional (*i.e.,* immediate-release) epidural morphine, although extended monitoring may be required. Both the consultants and ASA members neither agree nor disagree that continuous epidural opioids are preferred to parenteral opioids for anesthesia and analgesia for reducing the risk of respiratory depression.

Type of Drug (i.e., Hydrophilic or Lipophilic Opioids).

Hydrophilic or lipophilic opioids considered by these Guidelines include: (1) single-injection epidural hydrophilic *versus* lipophilic opioids, (2) single-injection intrathecal hydrophilic *versus* lipophilic opioids, and (3) continuous infusion epidural hydrophilic *versus* lipophilic opioids.

<u>*Literature findings:*</u> RCTs report no differences in the frequency of respiratory depression, ventilatory response to carbon dioxide, somnolence or sedation when single-injection morphine is compared with single-injection fentanyl or sufentanil, administered by either an epidural or intrathecal route. (*Category A2-E evidence).*[40-44] RCT findings for respiratory depression are inconsistent when comparing continuous epidural administration of morphine to fentanyl or sufentanil (*Category A2-E evidence)*[45-48]; RCT findings for hypoxemia and hypercarbia are equivocal (Category A2-E evidence).[47,49] In addition, RCTs findings for sedation or somnolence are equivocal *(Category A2-E evidence).*[45-47,50,51]

<u>*Survey findings for type of drug:*</u> The consultants and ASA members both agree that, when clinically suitable, appropriate doses of continuous epidural infusion of fentanyl or sufentanil may

be used in place of continuous infusion of morphine or hydromorphone without increasing the risk of respiratory depression. The ASA members agree and the consultants strongly agree that, given the unique pharmacokinetic effect of the various neuraxially administered opioids, appropriate duration of monitoring should be matched with the drug. Both the consultants and ASA members strongly agree that, based on the duration of action of hydrophilic opioids, neuraxial morphine or hydromorphone should not be administered to outpatient surgical patients.

Dose Selection: (i.e., Low-Dose Compared with High-Dose Neuraxial Opioids)

Literature findings: Meta-analysis of RCTs indicates that the frequency of respiratory depression is reduced when lower doses of single-injection epidural morphine or sufentanil are compared with higher doses *(Category A1-B evidence)*.[37,52-55] RCTs are equivocal regarding respiratory depression, frequency of hypoxemia, hypercarbia, and sedation or somnolence when lower doses of single-injection intrathecal opioids are administered compared with higher doses (*Category A1-E evidence)*.[56-62] An RCT reports equivocal findings for respiratory depression, and another RCT reports equivocal findings for sedation when higher doses of *continuous infusion* of epidural fentanyl are compared with lower doses *(Category A3-E evidence)*.[63,64]

Survey findings for dose selection: The consultants and ASA members both strongly agree that the lowest efficacious dose of neuraxial opioids should be administered to minimize the risk of respiratory depression.

Neuraxial Opioids Combined with Parenteral Opioids or Hypnotics.

Literature findings: The literature is insufficient to assess whether the addition of parenteral opioids, hypnotics, or dissociative anesthetics (*e.g.*, ketamine) to neuraxial opioids is associated with increased occurrence of respiratory depression or hypoxemia.

Survey findings for drug combinations: Both the consultants and ASA members strongly agree that (1) parenteral opioids or hypnotics should be administered cautiously in the presence of

neuraxial opioids and (2) the concomitant administration of neuraxial opioids and parenteral opioids, sedatives, hypnotics, or magnesium requires increased monitoring (*e.g.*, intensity, duration, or additional methods of monitoring).

Recommendations for prevention of respiratory depression.

Noninvasive positive pressure ventilation:

- Encourage patients with a history of sleep apnea treated with noninvasive positive airway pressure to bring their own equipment to the hospital.

Route of administration:

- Single-injection neuraxial opioids may be safely used in place of parenteral opioids without altering the risk of respiratory depression or hypoxemia.
    - Single-injection neuraxial fentanyl or sufentanil may be safe alternatives to single-injection neuraxial morphine.
- When clinically suitable, extended-release epidural morphine may be used in place of intravenous or conventional (*i.e.*, immediate-release) epidural morphine, although extended monitoring may be required.
- Continuous epidural opioids are preferred to parenteral opioids for anesthesia and analgesia for reducing the risk of respiratory depression.

Type of drug:

- When clinically suitable, appropriate doses of continuous epidural infusion of fentanyl or sufentanil may be used in place of continuous infusion of morphine or hydromorphone without increasing the risk of respiratory depression.
- Given the unique pharmacokinetic effect of the various neuraxially administered opioids, match the appropriate duration of monitoring with the drug.

- Based on the duration of action of hydrophilic opioids, do not administer neuraxial morphine or hydromorphone to outpatient surgical patients.

Dose selection:

- Administer the lowest efficacious dose of neuraxial opioids to minimize the risk of respiratory depression.

Drug combinations:

- Administer parenteral opioids or hypnotics cautiously in the presence of neuraxial opioids.
- The concomitant administration of neuraxial opioids and parenteral opioids, sedatives, hypnotics, or magnesium requires increased monitoring (*e.g.*, intensity, duration, or additional methods of monitoring).

Monitoring for Respiratory Depression

Respiratory depression monitoring includes: (1) consideration of techniques to detect respiratory depression and (2) perioperative monitoring for respiratory depression.

Techniques to Detect Respiratory Depression.

Detection of respiratory depression includes measurement of: (1) oxygen saturation levels, (2) carbon dioxide levels, and (3) level of sedation.

Literature findings: RCTs have shown pulse oximetry to be effective in detecting hypoxemia in patients receiving a variety of anesthetics, including neuraxial techniques.[65-69] However, these studies do not provide separate data for neuraxial opioid anesthesia. Although the literature is insufficient to evaluate carbon dioxide monitoring for neuraxial opioids, literature reporting end-tidal carbon dioxide monitoring for *parenteral* opioids suggest that such monitoring is effective in

detecting hypercapnia or hypercarbia.[††] The literature is insufficient regarding whether monitoring patients' level of sedation reduces the risk of respiratory depression. The literature is insufficient regarding whether continuous monitoring with either pulse oximetry, electrocardiogram, or ventilation is associated with improved detection of respiratory depression or hypoxemia for patients administered neuraxial opioids.

Survey findings for detection of respiratory depression: Both the consultants and ASA members strongly agree that (1) all patients receiving neuraxial opioids should be monitored for adequacy of ventilation, oxygenation, and level of consciousness and (2) increased monitoring may be warranted in patients at increased risk of respiratory depression.

Perioperative monitoring for respiratory depression.

Perioperative monitoring for respiratory depression includes: (1) monitoring after administration of single-injection neuraxial lipophilic opioids, (2) monitoring during or after continuous infusion or PCEA with neuraxial lipophilic opioids, (3) monitoring after administration of single-injection neuraxial hydrophilic opioids, and (4) monitoring during or after continuous infusion or PCEA with neuraxial hydrophilic opioids.

Monitoring after administration of single-injection neuraxial lipophilic opioids:

Literature findings: The literature is insufficient to assess whether any time interval is optimal for detecting respiratory depression or reducing risks associated with respiratory depression.

Survey findings: Both the consultants and ASA members agree that (1) monitoring should be performed for a minimum of 2 hours after administration, (2) *continual* (*i.e.*, repeated regularly and frequently in steady rapid succession) monitoring should be performed for the first 20 min after administration, followed by monitoring at least once per hour until 2 hours have passed, and (3)

[††] American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists: Practice guidelines for sedation and analgesia by non-anesthesiologists: An Updated Report. ANESTHESIOLOGY 2002; 96:1004-17.

after 2 hours, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.

Monitoring during or after continuous infusion or PCEA with neuraxial lipophilic opioids:

Literature findings: The literature is insufficient to assess whether any time interval is optimal for detecting respiratory depression or reducing risks associated with respiratory depression.

Survey findings: The consultants and ASA members both strongly agree that monitoring should be performed during the entire time the infusion is in use. The consultants and ASA members both agree that (1) monitoring should be continual for the first 20 minutes after initiation, followed by monitoring at least once per hour until 12 hours have passed, (2) from 12-24 hours, monitor at least once every 2 hours and after 24 hours, monitor at least once every 4 hours, and (3) after discontinuation of (CIE) or PCEA with neuraxial lipophilic opioids, the frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.

Monitoring after administration of single-injection neuraxial hydrophilic opioids (not including sustained or extended release epidural morphine):

Literature findings: The literature is insufficient to assess whether any time interval is optimal for detecting respiratory depression or reducing risks associated with respiratory depression.

Survey findings: Both the consultants and ASA members agree that (1) monitoring should be performed for a minimum of 24 hours after administration and (2) monitoring should be performed at least once per hour for the first 12 hours after administration, followed by monitoring at least once every 2 hours for the next 12 hours (*i.e.*, from 12 to 24 hours). The ASA members agree and the consultants strongly agree that after 24 hours, the frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.

Monitoring during or after continuous infusion or PCEA with neuraxial hydrophilic opioids:

Literature findings: The literature is insufficient to assess whether any time interval is optimal for detecting respiratory depression or reducing risks associated with respiratory depression.

Survey findings: The consultants and ASA members both strongly agree that monitoring should be performed during the entire time the infusion is in use. Further, the consultants and ASA members both agree that (1) monitoring at least once every hour should be performed for the first 12 hours after initiation, followed by monitoring at least once every 2 hours for the next 12 hours and (2) after 24 hours, monitoring should be performed at least once every 4 hours. The ASA members agree and the consultants strongly agree that after discontinuation of continuous infusion or PCEA, the frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.

Monitoring after administration of sustained or extended-release epidural morphine:

Literature findings: The literature is insufficient to assess whether any time interval is optimal for detecting respiratory depression or reducing risks associated with respiratory depression.

Survey findings: Both the consultants and ASA members agree that (1) monitoring at least once every hour should be performed during the first 12 hours after administration, and at least once every 2 hours for the next 12 hours (*i.e.*, 12-24 hours) and (2) after 24 hours, monitoring should be performed at least once every 4 hours for a minimum of 48 hours.

Recommendations for detection and monitoring for respiratory depression.

- Monitor all patients receiving neuraxial opioids for adequacy of ventilation (*e.g.*, respiratory rate, depth of respiration [assessed without disturbing a sleeping patient]), oxygenation (*e.g.*, pulse oximetry when appropriate), and level of consciousness.[⌗⌗]
- Increased monitoring (*e.g.*, intensity, duration, or additional methods of monitoring) may be warranted for patients at increased risk of respiratory depression (*e.g.*, unstable

[⌗⌗] In cases with other concerning signs, it is acceptable to awaken a sleeping patient to assess level of consciousness.

medical condition, obesity, obstructive sleep apnea,[§§] concomitant administration of opioid analgesics or hypnotics by other routes, extremes of age).

Single-injection neuraxial lipophilic opioids (e.g., fentanyl):

- Monitor for *a minimum* of 2 hours after administration.
- Monitor continually (*i.e.,* repeated regularly and frequently in steady rapid succession[***]) *for the first 20 min* after administration, followed by monitoring *at least* once per hour until 2 hours have passed.[†††]
- After 2 hours, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.

Continuous infusion or PCEA with neuraxial lipophilic opioids:

- Monitor during the entire time the infusion is in use.
- Monitor continually for the first 20 min after initiation, followed by monitoring *at least* once per hour until 12 hours have passed.
- From 12-24 hours, monitor *at least* once every 2 hours, and after 24 hours, monitor *at least* once every 4 hours.
- After discontinuation of continuous infusion or PCEA with neuraxial lipophilic opioids, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.

[§§] "Hospitalized patients who are at increased risk of respiratory compromise from OSA should have continuous pulse oximetry monitoring after discharge from the recovery room. Continuous monitoring may be provided in a critical care or stepdown unit, by telemetry on a hospital ward, or by a dedicated, appropriately trained professional observer in the patient's room. Continuous monitoring should be maintained as long as patients remain at increased risk. Intermittent pulse oximetry or continuous bedside oximetry without continuous observation does not provide the same level of safety." From: American Society of Anesthesiologists Task Force on Perioperative Management of Obstructive Sleep Apnea: Practice guidelines for the perioperative management of obstructive sleep apnea. ANESTHESIOLOGY 2006; 104:1081-93

[***] "American Society of Anesthesiologists: Standards for Basic Anesthetic Monitoring. In: Standards, Guidelines and Statements 2006: http://www.asahq.org/publicationsAndServices/standards/02.pdf

[†††] Including during transport to the PACU.

*Single-injection neuraxial hydrophilic opioids (e.g., morphine, **not including** sustained or extended release epidural morphine):*

- Monitor for a *minimum* of 24 hours after administration.
- Monitor *at least* once per hour for the first 12 hours after administration, followed by monitoring *at least* once every 2 hours for the next 12 hours (*i.e.*, from 12 to 24 hours).
- After 24 hours, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.

Continuous infusion or PCEA with neuraxial hydrophilic opioids:

- Monitor during the entire time the infusion is in use.
- Monitor *at least* once every hour for the first 12 hours after initiation, followed by monitoring *at least* once every 2 hours for the *next* 12 hours.
- After 24 hours, monitor *at least* once every 4 hours.
- After discontinuation of continuous infusion or PCEA, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.

Sustained or extended-release epidural morphine:

- Monitor *at least* once every hours during the first 12 hours after administration, and *at least* once every 2 hours for the next 12 hours (*i.e.*, 12-24 hours).
- After 24 hours, monitor *at least* once every 4 hours for a minimum of 48 hours.

Management and Treatment of Respiratory Depression

Interventions for management and treatment for respiratory depression considered by these Guidelines include: (1) supplemental oxygen, (2) reversal agents, and (3) noninvasive positive pressure ventilation.

Supplemental Oxygen.

Literature findings: The literature is insufficient to assess whether supplemental oxygen will reduce the frequency or severity of hypoxia or hypoxemia when neuraxial opioids are administered. Other literature supports the use of supplemental oxygen when non-neuraxial anesthetic techniques (*e.g.*, general anesthesia, sedation and analgesia) are administered.[‡‡‡]

Survey findings: The consultants agree and ASA members strongly agree that, for patients receiving neuraxial opioids, supplemental oxygen should be available. The consultants and ASA members both strongly agree that supplemental oxygen should be administered to patients with altered level of consciousness, respiratory depression, or hypoxemia and continued until the patient is alert and no respiratory depression or hypoxemia is present.

Reversal Agents.

Literature findings: Although there are insufficient comparative studies to assess the efficacy of naloxone or naltrexone *to treat* respiratory depression in patients administered neuraxial opioids, case reports suggest an association between the administration of naloxone and reversal of opioid-induced respiratory depression (*Category B3-B evidence).*[70-79] RCTs comparing naloxone[80,81] or naltrexone [82-84] with placebo are equivocal regarding *preprocedure prophylaxis* for respiratory depression, hypoxemia, sedation or somnolence (*Category A2-E evidence*). Other literature supports the use of naloxone for respiratory depression when systemic opioids are administered.[§§§]

Survey findings for reversal agents: The consultants and ASA members both strongly agree that (1) intravenous access should be maintained if recurring respiratory depression occurs and (2)

[‡‡‡] American Society of Anesthesiologists Task Force on Management of the Difficult Airway: Practice guidelines for management of the difficult airway: An Updated Report. ANESTHESIOLOGY 2003; 98:1269-77; and American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists: Practice guidelines for sedation and analgesia by non-anesthesiologists: An Updated Report. ANESTHESIOLOGY 2002; 96:1004-17

[§§§] American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists: Practice guidelines for sedation and analgesia by non-anesthesiologists: An Updated Report. ANESTHESIOLOGY 2002; 96:1004-17

reversal agents should be available for administration to all patients experiencing significant respiratory depression following neuraxial opioid administration.

Noninvasive Positive Pressure Ventilation.

Literature findings: The literature is insufficient to assess the efficacy of noninvasive positive pressure ventilation *to manage* patients who have been administered neuraxial opioids. Other literature supports the use of noninvasive positive pressure ventilation for patients with respiratory compromise.[****]

Survey findings for noninvasive positive pressure ventilation: Both the consultants and ASA members strongly agree that (1) non-invasive positive pressure ventilation may be considered for improving ventilatory status and (2) if frequent or severe airway obstruction or hypoxemia occurs during postoperative monitoring, initiate non-invasive positive pressure ventilation.

Recommendations for management and treatment of respiratory depression.

- For patients receiving neuraxial opioids, supplemental oxygen should be available.
- Administer supplemental oxygen to patients with altered level of consciousness, respiratory depression or hypoxemia and continue until the patient is alert and no respiratory depression or hypoxemia is present.[††††]
- Maintain intravenous access if recurring respiratory depression occurs.
- Reversal agents should be available for administration to all patients experiencing significant respiratory depression following neuraxial opioid administration.
    - In the presence of severe respiratory depression, initiate appropriate resuscitation.

[****] American Society of Anesthesiologists Task Force on Perioperative Management of Obstructive Sleep Apnea: Practice guidelines for the perioperative management of obstructive sleep apnea. ANESTHESIOLOGY 2006; 104:1081-93

[††††] The Task Force cautions that routine use of supplemental oxygen may increase the duration of apneic episodes and may hinder detection of atelectasis, transient apnea, and hypoventilation.

- Noninvasive positive pressure ventilation may be considered for improving ventilatory status.
- If frequent or severe airway obstruction or hypoxemia occurs during postoperative monitoring, initiate non-invasive positive pressure ventilation.

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Appendix 1: Summary of Recommendations

Identification of Patients at Increased Risk of Respiratory Depression

- Conduct a focused history and physical examination before administering neuraxial opioids.
    - Direct particular attention toward signs, symptoms, or a history of sleep apnea, co-existing diseases or conditions (*e.g.*, diabetes, obesity), current medications (including preoperative opioids), and adverse effects following opioid administration.
    - A physical examination should include, but is not limited to, baseline vital signs, airway, heart, lung, and cognitive function.

Prevention of Respiratory Depression after Neuraxial Opioid Administration

Noninvasive positive pressure ventilation:

- Encourage patients with a history of sleep apnea treated with noninvasive positive airway pressure to bring their own equipment to the hospital.

Route of administration:

- Single-injection neuraxial opioids may be safely used in place of parenteral opioids without altering the risk of respiratory depression or hypoxemia.
    - Single-injection neuraxial fentanyl or sufentanil may be safe alternatives to single-injection neuraxial morphine.
- When clinically suitable, extended-release epidural morphine may be used in place of intravenous or conventional (*i.e.*, immediate-release) epidural morphine, although extended monitoring may be required.
- Continuous epidural opioids are preferred to parenteral opioids for anesthesia and analgesia for reducing the risk of respiratory depression.

Type of drug:

- When clinically suitable, appropriate doses of continuous epidural infusion of fentanyl or sufentanil may be used in place of continuous infusion of morphine or hydromorphone without increasing the risk of respiratory depression.
- Given the unique pharmacokinetic effect of the various neuraxially administered opioids, match the appropriate duration of monitoring with the drug.
- Based on the duration of action of hydrophilic opioids, do not administer neuraxial morphine or hydromorphone to outpatient surgical patients.

Dose selection:

- Administer the lowest efficacious dose of neuraxial opioids to minimize the risk of respiratory depression.

Drug combinations:

- Administer parenteral opioids or hypnotics cautiously in the presence of neuraxial opioids.
- The concomitant administration of neuraxial opioids and parenteral opioids, sedatives, hypnotics, or magnesium requires increased monitoring (*e.g.*, intensity, duration, or additional methods of monitoring).

Monitoring for Respiratory Depression

- Monitor all patients receiving neuraxial opioids for adequacy of ventilation (*e.g.*, respiratory rate, depth of respiration [assessed without disturbing a sleeping patient]), oxygenation (*e.g.*, pulse oximetry when appropriate), and level of consciousness.[‡‡‡‡]
- Increased monitoring (*e.g.*, intensity, duration, or additional methods of monitoring) may be warranted for patients at increased risk of respiratory depression (*e.g.*, unstable medical condition, obesity, obstructive sleep apnea,[§§§§] concomitant administration of opioid analgesics or hypnotics by other routes, extremes of age).

Single-injection neuraxial lipophilic opioids (e.g., fentanyl):

- Monitor for *a minimum* of 2 hours after administration.
- Monitor continually (*i.e.*, repeated regularly and frequently in steady rapid succession[*****]) *for the first 20 min* after administration, followed by monitoring *at least* once per hour until 2 hours have passed.
- After 2 hours, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.

Continuous infusion or patient-controlled epidural analgesia (PCEA) with neuraxial lipophilic opioids:

- Monitor during the entire time the infusion is in use.
- Monitor continually for the first 20 min after initiation, followed by monitoring *at least* once per hour until 12 hours have passed.
- From 12-24 hours, monitor *at least* once every 2 hours, and after 24 hours, monitor *at least* once every 4 hours.
- After discontinuation of continuous infusion or PCEA with neuraxial lipophilic opioids, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.

Single-injection neuraxial hydrophilic opioids (e.g., morphine, ***not including*** *sustained or extended release epidural morphine):*

- Monitor for a *minimum* of 24 hours after administration.
- Monitor *at least* once per hour for the first 12 hours after administration, followed by monitoring *at least* once every 2 hours for the next 12 hours (*i.e.*, from 12 to 24 hours).
- After 24 hours, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.

Continuous infusion or PCEA with neuraxial hydrophilic opioids:

- Monitor during the entire time the infusion is in use.

[‡‡‡‡] In cases with other concerning signs, it is acceptable to awaken a sleeping patient to assess level of consciousness.

[§§§§] "Hospitalized patients who are at increased risk of respiratory compromise from OSA should have continuous pulse oximetry monitoring after discharge from the recovery room. Continuous monitoring may be provided in a critical care or stepdown unit, by telemetry on a hospital ward, or by a dedicated, appropriately trained professional observer in the patient's room. Continuous monitoring should be maintained as long as patients remain at increased risk. Intermittent pulse oximetry or continuous bedside oximetry without continuous observation does not provide the same level of safety." From: American Society of Anesthesiologists Task Force on Perioperative Management of Obstructive Sleep Apnea: Practice guidelines for the perioperative management of obstructive sleep apnea. ANESTHESIOLOGY 2006; 104:1081-93

[*****] "American Society of Anesthesiologists: Standards for Basic Anesthetic Monitoring. In: Standards, Guidelines and Statements 2006: http://www.asahq.org/publicationsAndServices/standards/02.pdf

- Monitor *at least* once every hour for the first 12 hours after initiation, followed by monitoring *at least* once every 2 hours for the *next* 12 hours.
- After 24 hours, monitor *at least* once every 4 hours.
- After discontinuation of continuous infusion or PCEA, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.

Sustained or extended-release epidural morphine:

- Monitor *at least* once every hours during the first 12 hours after administration, and *at least* once every 2 hours for the next 12 hours (*i.e.*, 12-24 hours).
- After 24 hours, monitor *at least* once every 4 hours for a minimum of 48 hours.

Management and Treatment of Respiratory Depression

- For patients receiving neuraxial opioids, supplemental oxygen should be available.
- Administer supplemental oxygen to patients with altered level of consciousness, respiratory depression or hypoxemia and continue until the patient is alert and no respiratory depression or hypoxemia is present.[††††]
- Maintain intravenous access if recurring respiratory depression occurs.
- Reversal agents should be available for administration to all patients experiencing significant respiratory depression following neuraxial opioid administration.
    - In the presence of severe respiratory depression, initiate appropriate resuscitation.
- Noninvasive positive pressure ventilation may be considered for improving ventilatory status.
- If frequent or severe airway obstruction or hypoxemia occurs during postoperative monitoring, initiate non-invasive positive pressure ventilation.

[††††] The Task Force cautions that routine use of supplemental oxygen may increase the duration of apneic episodes and may hinder detection of atelectasis, transient apnea, and hypoventilation.

Appendix 2: Methods and Analyses

A. State of the Literature.

For these updated Guidelines, a review of studies used in the development of the previous update was combined with studies published subsequent to approval of the update in 2008.[‡‡‡‡‡] The scientific assessment of these Guidelines was based on evidence linkages or statements regarding potential relationships between clinical interventions and outcomes. The interventions listed below were examined to assess their impact on a variety of outcomes related to respiratory depression related to neuraxial opioid anesthesia and analgesia.[§§§§§]

Identification of patients at increased risk of respiratory depression

- Medical records review (focused history)
- Physical examination

Prevention of respiratory depression

- Positive pressure ventilation
- Drug selection
  - Route of administration
    - Single-injection neuraxial opioids vs parenteral opioids
    - Extended-release epidural morphine vs parenteral morphine
    - Extended-release epidural morphine vs immediate release epidural morphine
    - Continuous infusion epidural opioids vs parenteral opioids
  - Type of drug
    - Single-injection epidural hydrophilic opioids (e.g., morphine, hydromorphone) vs lipophilic opioids (e.g., fentanyl/sufentanil).
    - Single-injection intrathecal hydrophilic opioids vs lipophilic opioids
    - Continuous infusion epidural hydrophilic opioids vs lipophilic opioids
  - Dose selection
    - High vs low doses of single-injection/single-dose epidural opioids (i.e., morphine, hydromorphone, fentanyl, or sufentanil)
    - High vs low doses of single-injection/single-dose intrathecal opioids
    - High vs low doses of continuous infusion epidural (CIE) opioids
    - Single-injection/single-dose epidural morphine vs extended-release epidural morphine
    - Dose reduction vs cessation of opioids
  - Drug combinations

[‡‡‡‡‡] American Society of Anesthesiologists: Practice Guidelines for the Prevention, Detection and Management of Respiratory Depression Associated with Neuraxial Opioid Administration: an Updated Report by the American Society of Anesthesiologists Task Force on Neuraxial Opioids. Anesthesiology 2009; 110:218-30

[§§§§§] Unless otherwise specified, outcomes for the listed interventions refer to the reduction or detection of respiratory depression or hypoxemia

- Neuraxial opioids with vs without parenteral opioids or hypnotics

Monitoring for respiratory depression

- Detection of respiratory depression
  - Pulse oximetry monitoring
  - End-tidal CO_2 monitoring
  - Monitoring level of sedation
- Timing and duration of monitoring
  - Continuous vs intermittent monitoring

Management of respiratory depression

- Supplemental oxygen
- Reversal drugs
  - Naloxone vs no naloxone
  - Naltrexone vs no naltrexone
- Positive pressure ventilation

For the literature review, potentially relevant clinical studies were identified *via* electronic and manual searches of the literature. The updated searches covered an 8-year period from 2008 through 2015. Over 2000 new citations that addressed topics related to the evidence linkages were identified. These articles were reviewed and those meeting the appropriate criteria as outlined in the "Focus" section above were combined with pre-2008 articles used in the previous update, resulting in a total of 167 articles that contained direct linkage-related evidence. A complete bibliography used to develop these Guidelines, organized by section, is available as Supplemental Digital Content 2, http://links.lww.com/ALN/___.

Initially, each pertinent study finding was classified and summarized to determine meta-analysis potential. Literature pertaining to 4 evidence linkages contained enough studies with well-defined experimental designs and statistical information sufficient for meta-analyses. These linkages were: (1) single-injection epidural opioids vs intramuscular opioids, (2) continuous infusion epidural opioids vs intravenous opioid infusion, (3) high vs low doses of single-injection epidural opioids, and (4) high vs low doses of single-injection intrathecal opioids.

General variance-based effect-size estimates or combined probability tests were obtained for continuous outcome measures, and Mantel-Haenszel odds-ratios were obtained for dichotomous outcome measures. Two combined probability tests were employed as follows: (1) the Fisher combined test, producing chi-square values based on logarithmic transformations of the reported P values from the independent studies, and (2) the Stouffer combined test, providing weighted representation of the studies by weighting each of the standard normal deviates by the size of the sample. An odds-ratio procedure based on the Mantel-Haenszel method for combining study results using 2 x 2 tables was used with outcome frequency information. An acceptable significance level was set at $P < 0.01$ (one-tailed). Tests for heterogeneity of the independent studies were conducted to assure consistency among the study results. DerSimonian-Laird random-effects odds ratios were obtained when significant heterogeneity was found ($P < 0.01$). To control for potential publishing bias, a "fail-safe n" value was calculated. No search for unpublished studies was conducted, and no reliability tests for locating research results were done. To be accepted as significant findings, Mantel-Haenszel odds-ratios must agree with combined test results whenever both types of data are assessed. In the absence of Mantel-Haenszel odds-ratios, findings from both the Fisher and weighted Stouffer combined tests must agree with each other to be acceptable as significant.

For the previous update, interobserver agreement among Task Force members and two methodologists was established by interrater reliability testing. Agreement levels using a kappa (κ) statistic for two-rater agreement pairs were as follows: (1) type of study design, $\kappa = 0.78$-0.90; (2) type of analysis, $\kappa = 0.74$-1.00; (3) evidence linkage assignment, $\kappa = 0.79$-1.00; and (4) literature inclusion for database, $\kappa = 0.70$-1.00. Three-rater chance-corrected agreement values were: (1) study design, Sav = 0.86, Var (Sav) = 0.009; (2) type of analysis, Sav = 0.82, Var (Sav) = 0.017; (3)

linkage assignment, Sav = 0.85, Var (Sav) = 0.004; (4) literature database inclusion, Sav = 0.79, Var (Sav) = 0.310. These values represent moderate to high levels of agreement.

B. Consensus-Based Evidence.

Consensus was obtained from multiple sources, including: (1) survey opinion from consultants who were selected based on their knowledge or expertise in neuraxial opioid administration, (2) survey opinions solicited from active members of the ASA, (3) testimony from attendees of publicly-held open forums at a national anesthesia meeting, (4) Internet commentary, and (5) Task Force opinion and interpretation. A survey was sent to consultants and ASA members in May of 2015 covering all evidence linkages. The rate of return among consultants was 35% (n = 48 of 138), and 135 surveys were received from active ASA members. Survey results are reported in Tables 2 and 3, and summarized in the text of the Guidelines.

For the previous update, the consultants were asked to indicate which, if any, of the evidence linkages would change their clinical practices if the Guidelines were instituted. The rate of return was 14% (n = 17 of 123). The percent of responding Consultants expecting *no change* associated with each linkage were as follows: (1) history and physical examination = 94%, (2) single-injection neuraxial opioid administration = 88%, (3) continuous epidural opioid administration = 88%, (4) extended-release epidural opioid administration = 71%, (5) monitoring for adequacy of ventilation, oxygenation, and level of consciousness = 59%, (6) supplemental oxygen administration = 88%, and (7) use of noninvasive positive pressure ventilation = 100%. Fifty-nine percent of the respondents indicated that the Guidelines would have *no effect* on the amount of time spent on a typical case, and 41% indicated that there would be an increase of the amount of time spent on a typical case with the implementation of these Guidelines.

Table 1. Meta-Analysis Summary

Linkages	N	Fisher Chi-square	p	Weighted Stouffer Zc	p	Effect Size	Mantel Haenszel OR	Confidence Interval	Heterogeneity Significance	Heterogeneity Effect Size
Single-injection epidural opioids versus intramuscular opioids										
Respiratory Depression	5						1.12	0.42-3.03		0.165
Somnolence/Sedation	7						0.46	0.25-0.84		0.296
Continuous infusion epidural opioids versus intravenous opioid infusion										
Respiratory Depression	5						0.31	0.11-0.90		0.159
Somnolence/Sedation	5	13.70	0.187	1.45	0.074	0.07			0.803	0.818
High versus *low doses of epidural opioids*										
Respiratory Depression	5						5.79	1.62-20.74		0.847
High versus *low doses of intrathecal opioids*										
Hypoxemia	5						1.75	0.52-5.92		0.688

OR = odds ratio

Table 2: Consultant Survey Responses****

	N	Percent Responding to Each Item: Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
Identification of Patients at Increased Risk of Respiratory Depression:						
1. Conduct a focused history and physical examination before administering neuraxial opioids	48	72.9*	22.9	2.1	0.0	2.1
2. Direct particular attention toward signs, symptoms, or a history of sleep apnea, co-existing diseases or conditions (*e.g.*, diabetes, obesity), current medications (including pre-operative opioids), and adverse effects following opioid administration	48	87.5*	6.2	2.1	2.1	2.1
3. A physical examination should include, but is not limited to, baseline vital signs, airway, heart, lung, and cognitive function	48	60.4*	29.2	8.3	0.0	2.1
Prevention of Respiratory Depression after Neuraxial Opioid Administration:						
Noninvasive positive pressure ventilation:						
4. Encourage patients with a history of sleep apnea treated with noninvasive positive airway pressure to bring their own equipment to the hospital	48	77.1*	14.6	4.2	2.1	2.1
Route of administration:						
5. Single-injection neuraxial opioids may be safely used in place of parenteral opioids without altering the risk of respiratory depression or hypoxemia	46	26.1	23.9*	15.2	26.1	8.7
6. Single-injection neuraxial fentanyl or sufentanil may be safe alternatives to single-injection neuraxial morphine	46	17.4	26.1	32.6*	17.4	6.5
7. When clinically suitable, extended-release epidural morphine may be used in place of intravenous or conventional (*i.e.*, immediate-release) epidural morphine, although extended monitoring may be required	46	34.8	32.6*	15.2	10.9	6.5
8. Continuous epidural opioids are preferred to parenteral opioids for anesthesia and analgesia for reducing the risk of respiratory depression	46	17.4	23.9	26.1*	21.7	10.9
Type of drug:						
9. When clinically suitable, appropriate doses of continuous epidural infusion of fentanyl or						

******* N = the number of consultants who responded to each item. An asterisk beside a percentage score indicates the median.

sufentanil may be used in place of continuous infusion of morphine or hydromorphone without increasing the risk of respiratory depression	44	20.4	34.1*	27.3	11.4	6.8
10. Given the unique pharmacokinetic effect of the various neuraxially administered opioids, match the appropriate duration of monitoring with the drug	44	50.0*	38.6	9.1	0.0	2.3
11. Based on the duration of action of hydrophilic opioids, do not administer neuraxial morphine or hydromorphine to outpatient surgical patients	44	52.3*	29.5	15.9	0.0	2.3
Dose Selection:						
12. Administer the lowest efficacious dose of neuraxial opioids to minimize the risk of respiratory depression	44	70.4*	18.2	9.1	0.0	2.3
Drug combinations:						
13. Administer parenteral opioids or hypnotics cautiously in the presence of neuraxial opioids	44	65.9*	25.0	2.3	4.5	2.3
14. The concomitant administration of neuraxial opioids and parenteral opioids, sedatives, hypnotics, or magnesium requires increased monitoring (*e.g.*, intensity, duration, or additional methods of monitoring)	44	56.8*	34.1	2.3	4.5	2.3
Monitoring for Respiratory Depression:						
15. Monitor all patients receiving neuraxial opioids for adequacy of ventilation, oxygenation, and level of consciousness	44	61.4*	31.8	2.3	2.3	2.3
16. Increased monitoring may be warranted in patients at increased risk of respiratory depression	44	79.5*	15.9	0.0	2.3	2.3
Monitoring for single-injection neuraxial lipophilic opioids (e.g., fentanyl):						
17. Monitor for a *minimum* of 2 hours after administration	44	34.1	54.5*	9.1	0.0	2.3
18. Monitor *continually* (*i.e.*, repeated regularly and frequently in steady rapid succession) *for the first 20 min* after administration, followed by monitoring *at least* once per hour until two hours have passed	44	31.8	40.9*	22.7	2.3	2.3
19. After 2 hours, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications	44	47.7	40.9*	4.5	4.5	2.3
Monitoring for continuous infusion or patient-controlled epidural analgesia (PCEA) with neuraxial lipophilic opioids:						
20. Monitor during the entire time the infusion is in use	43	60.5*	27.9	7.0	2.3	2.3
21. Monitor continually for the first 20 min after initiation, followed by monitoring *at least*						

once per hour until 12 hours have passed	43	20.9	41.9*	25.6	9.3	2.3
22. From 12-24 hours, monitor *at least* every 2 hours, and after 24 hours, monitor *at least* once every 4 hours	43	20.9	46.5*	18.6	9.3	4.6
23. After discontinuation of CIE or PCEA with neuraxial lipophilic opioids, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent concurrent medications	43	48.8	39.5*	7.0	0.0	4.6
Monitoring for single-injection neuraxial hydrophilic opioids (e.g., morphine, <u>not including</u> sustained or extended release epidural morphine):						
24. Monitor for a *minimum* of 24 hours after administration	43	44.2	34.9*	11.6	2.3	7.0
25. Monitor *at least* once per hour for the first 12 hours after administration, followed by monitoring *at least* once every 2 hours for the next 12 hours *(i.e.*, from 12 to 24 hours)	43	39.5	27.9*	20.9	9.3	2.3
26. After 24 hours, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications	43	51.2*	41.9	4.6	0.0	2.3
Monitoring for continuous infusion or PCEA neuraxial hydrophilic opioids:						
27. Monitor during the entire time the infusion is in use	42	57.1*	30.9	9.5	0.0	2.4
28. Monitor *at least* once every hour for the first 12 hours after initiation, followed by monitoring *at least* once every 2 hours for the next 12 hours	42	30.9	40.5*	19.0	7.1	2.4
29. After 24 hours, monitor *at least* once every 4 hours	42	30.9	42.9*	14.3	7.1	4.8
30. After discontinuation of continuous infusion or PCEA, frequency of monitoring should be dictated by the patient's overall clinical and concurrent medications	42	52.4*	33.3	4.8	4.8	4.8
Monitoring for sustained or extended-release epidural morphine:						
31. Monitor *at least* once every hour during the first 12 hours after administration, and *at least* once every 2 hours for the next 12 hours (*i.e.*, 12-24 hours)	42	45.2	30.9*	14.3	7.1	2.4
32. After 24 hours, monitor *at least* once every 4 hours for a minimum of 48 hours	42	35.7	28.6*	21.4	9.5	4.8
Management and Treatment of Respiratory Depression:						
33. For patients receiving neuraxial opioids, supplemental oxygen should be available	41	41.7	36.6*	12.2	7.3	2.4
34. Administer supplemental oxygen to patients with altered level of consciousness, respiratory depression or hypoxemia and continue until the patient is alert and no respiratory depression or hypoxemia is present	41	58.5*	29.3	7.3	2.4	2.4

35. Maintain intravenous access if recurring respiratory depression occurs	41	82.9*	14.6	0.0	0.0	2.4
36. Reversal agents should be available for administration to all patients experiencing significant respiratory depression following neuraxial opioid administration	41	80.5*	14.6	2.4	0.0	2.4
37. In the presence of severe respiratory depression, initiate appropriate resuscitation	41	87.8*	9.8	0.0	0.0	2.4
38. Noninvasive positive pressure ventilation may be considered for improving ventilatory status	41	53.7*	31.7	7.3	4.9	2.4
39. If frequent or severe airway obstruction or hypoxemia occurs during postoperative monitoring, initiate non-invasive positive pressure ventilation	41	53.7*	26.8	9.8	7.3	2.4

Table 3: ASA Membership Survey Responses [††††††]

	N	Percent Responding to Each Item: Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
Identification of Patients at Increased Risk of Respiratory Depression:						
1. Conduct a focused history and physical examination before administering neuraxial opioids	135	75.6*	20.0	4.4	0.0	0.0
2. Direct particular attention toward signs, symptoms, or a history of sleep apnea, co-existing diseases or conditions (*e.g.*, diabetes, obesity), current medications (including pre-operative opioids), and adverse effects following opioid administration	135	77.8*	20.7	1.5	0.0	0.0
3. A physical examination should include, but is not limited to, baseline vital signs, airway, heart, lung, and cognitive function	135	69.6*	27.4	2.2	0.0	0.7
Prevention of Respiratory Depression after Neuraxial Opioid Administration:						
Noninvasive positive pressure ventilation:						
4. Encourage patients with a history of sleep apnea treated with noninvasive positive airway pressure to bring their own equipment to the hospital	132	69.7*	22.0	7.6	0.8	0.0
Route of administration:						
5. Single-injection neuraxial opioids may be safely used in place of parenteral opioids without altering the risk of respiratory depression or hypoxemia	127	10.2	28.3	22.0*	32.3	7.1
6. Single-injection neuraxial fentanyl or sufentanil may be safe alternatives to single-injection neuraxial morphine	127	10.2	37.8	24.4*	21.3	6.3
7. When clinically suitable, extended-release epidural morphine may be used in place of intravenous or conventional (*i.e.*, immediate-release) epidural morphine, although extended monitoring may be required	127	12.6	45.7*	29.1	10.2	2.4
8. Continuous epidural opioids are preferred to parenteral opioids for anesthesia and analgesia for reducing the risk of respiratory depression	127	5.5	31.5	37.8*	20.5	4.7

[††††††] N = the number of members who responded to each item. An asterisk beside a percentage score indicates the median.

Type of drug:						
9. When clinically suitable, appropriate doses of continuous epidural infusion of fentanyl or sufentanil may be used in place of continuous infusion of morphine or hydromorphone without increasing the risk of respiratory depression	124	11.3	45.2*	22.6	19.3	1.6
10. Given the unique pharmacokinetic effect of the various neuraxially administered opioids, match the appropriate duration of monitoring with the drug	124	46.0	41.9*	8.9	3.2	0.0
11. Based on the duration of action of hydrophilic opioids, do not administer neuraxial morphine or hydromorphine to outpatient surgical patients	124	63.7*	27.4	7.3	0.0	1.6
Dose Selection:						
12. Administer the lowest efficacious dose of neuraxial opioids to minimize the risk of respiratory depression	123	58.5*	35.0	5.7	0.8	0.0
Drug combinations:						
13. Administer parenteral opioids or hypnotics cautiously in the presence of neuraxial opioids	121	71.9*	23.1	4.1	0.8	0.0
14. The concomitant administration of neuraxial opioids and parenteral opioids, sedatives, hypnotics, or magnesium requires increased monitoring (*e.g.*, intensity, duration, or additional methods of monitoring)	121	62.8*	33.1	3.3	0.8	0.0
Monitoring for Respiratory Depression:						
15. Monitor all patients receiving neuraxial opioids for adequacy of ventilation, oxygenation, and level of consciousness	121	66.9*	28.1	4.1	0.8	0.0
16. Increased monitoring may be warranted in patients at increased risk of respiratory depression	121	80.2*	18.2	1.6	0.0	0.0
Monitoring for single-injection neuraxial lipophilic opioids (e.g., fentanyl):						
17. Monitor for a *minimum* of 2 hours after administration	120	35.0	52.5*	5.8	6.7	0.0
18. Monitor *continually* (*i.e.*, repeated regularly and frequently in steady rapid succession) *for the first 20 min* after administration, followed by monitoring *at least* once per hour until two hours have passed	120	29.2	43.3*	19.2	8.3	0.0
19. After 2 hours, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications	120	33.3	55.8*	9.2	1.7	0.0
Monitoring for continuous infusion or patient-controlled epidural analgesia (PCEA) with neuraxial lipophilic opioids:						

20. Monitor during the entire time the infusion is in use	116	50.9*	37.9	6.9	4.3	0.0
21. Monitor continually for the first 20 min after initiation, followed by monitoring *at least* once per hour until 12 hours have passed	116	23.3	40.5*	25.9	10.3	0.0
22. From 12-24 hours, monitor *at least* every 2 hours, and after 24 hours, monitor *at least* once every 4 hours	116	19.0	45.7*	23.3	12.1	0.0
23. After discontinuation of CIE or PCEA with neuraxial lipophilic opioids, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent concurrent medications	116	40.5	53.4*	4.3	1.7	0.0
Monitoring for single-injection neuraxial hydrophilic opioids (e.g., morphine, <u>not including</u> sustained or extended release epidural morphine):						
24. Monitor for a *minimum* of 24 hours after administration	112	40.2	48.2*	7.1	4.5	0.0
25. Monitor *at least* once per hour for the first 12 hours after administration, followed by monitoring *at least* once every 2 hours for the next 12 hours (i.e., from 12 to 24 hours)	112	28.6	53.6*	13.4	4.5	0.0
26. After 24 hours, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications	112	41.1	52.7*	5.4	0.9	0.0
Monitoring for continuous infusion or PCEA neuraxial hydrophilic opioids:						
27. Monitor during the entire time the infusion is in use	108	59.3*	32.4	3.7	4.6	0.0
28. Monitor *at least* once every hour for the first 12 hours after initiation, followed by monitoring *at least* once every 2 hours for the next 12 hours	108	28.7	43.5*	19.4	8.3	0.0
29. After 24 hours, monitor *at least* once every 4 hours	108	25.9	36.1*	25.9	12.1	0.0
30. After discontinuation of continuous infusion or PCEA, frequency of monitoring should be dictated by the patient's overall clinical and concurrent medications	108	43.5	48.1*	4.6	3.7	0.0
Monitoring for sustained or extended-release epidural morphine:						
31. Monitor *at least* once every hour during the first 12 hours after administration, and *at least* once every 2 hours for the next 12 hours (*i.e.*, 12-24 hours)	108	32.4	36.1*	25.9	5.6	0.0
32. After 24 hours, monitor *at least* once every 4 hours for a minimum of 48 hours	108	22.2	35.2*	33.3	8.3	0.9
Management and Treatment of Respiratory Depression:						
33. For patients receiving neuraxial opioids, supplemental oxygen should be available	105	63.8*	29.5	5.7	0.0	0.9
34. Administer supplemental oxygen to patients						

with altered level of consciousness, respiratory depression or hypoxemia and continue until the patient is alert and no respiratory depression or hypoxemia is present	105	62.9*	33.3	0.9	1.9	0.0
35. Maintain intravenous access if recurring respiratory depression occurs	105	86.7*	12.4	0.0	0.9	0.0
36. Reversal agents should be available for administration to all patients experiencing significant respiratory depression following neuraxial opioid administration	105	87.6*	11.4	0.0	0.9	0.0
37. In the presence of severe respiratory depression, initiate appropriate resuscitation	105	93.3*	5.7	0.9	0.0	0.0
38. Noninvasive positive pressure ventilation may be considered for improving ventilatory status	105	62.9*	23.8	8.6	3.8	0.0
39. If frequent or severe airway obstruction or hypoxemia occurs during postoperative monitoring, initiate non-invasive positive pressure ventilation	105	52.4*	28.6	11.4	7.6	0.0