Docket Number 2005P-0267
Attachment 2 to Comments of
American Society of Anesthesiologists

# ATTACHMENT 2

## PRACTICE GUIDELINES FOR SEDATION AND ANALGESIA BY NON-ANESTHESIOLOGISTS

(Approved by the House of Delegates on October 25, 1995, and last amended on October 17, 2001)

***An Updated Report by the American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists***

*Anesthesiology*
96: 1004-1017, 2002
© 2002 American Society of Anesthesiologists
Lippincott Williams & Wilkins, Inc.

Developed by the American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists:

Jeffrey B. Gross, M.D. (Chair)
Farmington, CT

Peter L. Bailey, M.D.
Rochester, NY

Richard T. Connis, Ph.D.
Woodinville, WA

Charles J. Coté, M.D.
Chicago, IL

Fred G. Davis, M.D.
Burlington, MA

Burton S. Epstein, M.D.
Washington, DC

Lesley Gilbertson, M.D.
Boston, MA

David G. Nickinovich, Ph.D.
Bellevue, WA

John M. Zerwas, M.D.
Houston, TX

Gregory Zuccaro, Jr., M.D.
Cleveland, OH

Correspondence to:

Jeffrey B. Gross, M.D.
Department of Anesthesiology (M/C 2015)
University of Connecticut School of Medicine
Farmington, CT 06030-2015

Supported by the American Society of Anesthesiologists under the direction of James F. Arens, M.D., Chairman, Committee on Practice Parameters. Approved by the House of Delegates, October 17, 2001. A list of the references used to develop these guidelines is available by writing to the American Society of Anesthesiologists.

Reprint Requests to: American Society of Anesthesiologists, 520 N. Northwest Highway, Park Ridge, IL 60068-2573

Key Words: Conscious sedation; deep sedation; analgesia; practice guidelines; propofol; ketamine

Abbreviated Title: Practice Guidelines for Sedation and Analgesia

## Introduction

Anesthesiologists possess specific expertise in the pharmacology, physiology, and clinical management of patients receiving sedation and analgesia. For this reason, they are frequently called upon to participate in the development of institutional policies and procedures for sedation and analgesia for diagnostic and therapeutic procedures. To assist in this process, the American Society of Anesthesiologists has developed these **Guidelines for Sedation and Analgesia by Non-Anesthesiologists**.

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. Practice guidelines are not intended as standards or absolute requirements. The use of practice guidelines cannot guarantee any specific outcome. Practice guidelines are subject to revision as warranted by the evolution of medical knowledge, technology, and practice. The guidelines provide basic recommendations that are supported by analysis of the current literature and by a synthesis of expert opinion, open forum commentary, and clinical feasibility data.

This revision includes data published since the Guidelines for Sedation and Analgesia by Non-Anesthesiologists were adopted by the American Society of Anesthesiologists in 1995; it also includes data and recommendations for a wider range of sedation levels than was previously addressed.

### A. Definitions

"Sedation and analgesia" comprise a continuum of states ranging from **Minimal Sedation (Anxiolysis)** through **General Anesthesia**. Definitions of levels of sedation / analgesia, as developed and adopted by the American Society of Anesthesiologists, are given in Table 1. These guidelines specifically apply to levels of sedation corresponding to **Moderate Sedation (frequently called "Conscious Sedation")** and **Deep Sedation**, as defined in Table 1.

### B. Focus

These guidelines are designed to be applicable to procedures performed in a variety of settings (*e.g.*, hospitals, freestanding clinics, physician, dentist, and other offices) by practitioners who are not specialists in anesthesiology. Because **Minimal Sedation ("Anxiolysis")** entails minimal risk, the guidelines specifically exclude it. Examples of **Minimal Sedation** include peripheral nerve blocks, local or topical anesthesia and either (1) less than 50% $N_2O$ in $O_2$ with no other sedative or analgesic medications by any route, or (2) a single, oral sedative or analgesic medication administered in doses appropriate for the unsupervised treatment of insomnia, anxiety or pain. The guidelines also exclude

patients who are not undergoing a diagnostic or therapeutic procedure (e.g., postoperative analgesia, sedation for treatment of insomnia). Finally, the guidelines do not apply to patients receiving general or major conduction anesthesia (e.g., spinal or epidural/caudal block), whose care should be provided, medically directed, or supervised by an anesthesiologist, the operating practitioner, or another licensed physician with specific training in sedation, anesthesia, and rescue techniques appropriate to the type of sedation or anesthesia being provided.

## C. Purpose

The purpose of these guidelines is to allow clinicians to provide their patients with the benefits of sedation/analgesia while minimizing the associated risks. Sedation/analgesia provides two general types of benefit: First, sedation/analgesia allows patients to tolerate unpleasant procedures by relieving anxiety, discomfort, or pain. Second, in children and uncooperative adults, sedation/analgesia may expedite the conduct of procedures which are not particularly uncomfortable but which require that the patient not move. At times these sedation practices may result in cardiac or respiratory depression which must be rapidly recognized and appropriately managed to avoid the risk of hypoxic brain damage, cardiac arrest, or death. Conversely, inadequate sedation/analgesia may result in undue patient discomfort or patient injury because of lack of cooperation or adverse physiological or psychological response to stress.

## D. Application

These guidelines are intended to be general in their application and broad in scope. The appropriate choice of agents and techniques for sedation/analgesia is dependent upon the experience and preference of the individual practitioner, requirements or constraints imposed by the patient or procedure, and the likelihood of producing a deeper level of sedation than anticipated. Because it is not always possible to predict how a specific patient will respond to sedative and analgesic medications, practitioners intending to produce a given level of sedation should be able to rescue patients whose level of sedation becomes deeper than initially intended. For moderate sedation, this implies the ability to manage a compromised airway or hypoventilation in a patient who <u>responds purposefully</u> following repeated or painful stimulation, while for deep sedation, this implies the ability to manage respiratory or cardiovascular instability in a patient who <u>does not respond purposefully</u> to painful or repeated stimulation. Levels of sedation referred to in the recommendations relate to the level of sedation intended by the practitioner. Examples are provided to illustrate airway assessment, preoperative fasting, emergency equipment, and recovery procedures. However, clinicians and their institutions have ultimate responsibility for selecting patients, procedures, medications, and equipment.

## E. Task Force Members and Consultants

The ASA appointed a Task Force of 10 members to (a) review the published evidence; (b) obtain the opinion of a panel of consultants including non-anesthesiologist physicians and dentists who routinely administer sedation / analgesia as well as of anesthesiologists with a special interest in sedation / analgesia (see appendix I); and (c) build consensus within the community of practitioners likely to be affected by the guidelines. The Task Force included anesthesiologists in both private and academic practices from various geographic areas of the United States, a gastroenterologist, and methodologists from the ASA Committee on Practice Parameters.

This Practice Guideline is an update and revision of the ASA *Guidelines for Sedation and Analgesia by Non-Anesthesiologists.*[1] The Task Force revised and updated the Guidelines by means of a five-step process. First, original published research studies relevant to the revision and update were reviewed and analyzed; only articles relevant to the administration of sedation by non-anesthesiologists were evaluated. Second, the panel of expert consultants was asked to (a) participate in a survey related to the effectiveness and safety of various methods and interventions which might be used during sedation/analgesia, and (b) review and comment upon the initial draft report of the Task Force. Third, the Task Force held Open Forums at two major national meetings to solicit input on its draft recommendations. National organizations representing most of the specialties whose members typically administer sedation/analgesia were invited to send representatives. Fourth, the consultants were surveyed to assess their opinions on the feasibility and financial implications of implementing the revised and updated Guidelines. Finally, all of the available information was used by the Task Force to finalize the guidelines.

## F. Availability and Strength of Evidence

Evidence-based guidelines are developed by a rigorous analytic process. To assist the reader, the Guidelines make use of several descriptive terms that are easier to understand than the technical terms and data that are used in the actual analyses. These descriptive terms are defined below.

The following terms describe the strength of scientific data obtained from the scientific literature:

Supportive: There is sufficient quantitative information from adequately designed studies to describe a statistically significant relationship ($P<0.01$) between a clinical

---

[1] Anesthesiology 1996; 84:459-471

intervention and a clinical outcome, using the technique of meta-analysis.

Suggestive: There is enough information from case reports and descriptive studies to provide a directional assessment of the relationship between a clinical intervention and a clinical outcome. This type of qualitative information does not permit a statistical assessment of significance.

Equivocal: Qualitative data have not provided a clear direction for clinical outcomes related to a clinical intervention and (1) there is insufficient quantitative information or (2) aggregated comparative studies have found no quantitatively significant differences among groups or conditions.

The following terms describe the lack of available scientific evidence in the literature:

Inconclusive: Published studies are available, but they cannot be used to assess the relationship between a clinical intervention and a clinical outcome because the studies either do not meet predefined criteria for content as defined in the "Focus of the Guidelines," or do not provide a clear causal interpretation of findings due to research design or analytic concerns.

Insufficient: There are too few published studies to investigate a relationship between a clinical intervention and clinical outcome.

Silent: No studies that address a relationship of interest were found in the available published literature.

The following terms describe survey responses from the consultants for any specified issue. Responses were solicited on a 5-point scale; ranging from '1'(strongly disagree) to '5' (strongly agree) with a score of '3' being neutral.

Strongly Agree: Median score of '5' (At least 50% of the responses were '5')

Agree: Median score of '4' (At least 50% of the responses were '4' or '5')

Equivocal: Median score of '3' (At least 50% of the scores were 3 or less)

Disagree: Median score of '2' (At least 50% of responses were '1' or '2')

Strongly Disagree: Median score of '1' (At least 50% of responses were '1')

## Guidelines

1. **Patient Evaluation**:

There is insufficient published evidence to evaluate the relationship between sedation / analgesia outcomes and the performance of a preoperative patient evaluation. There is suggestive evidence that some pre-existing medical conditions may be related to adverse outcomes in patients receiving either moderate or deep sedation / analgesia. The consultants strongly agree that appropriate pre-procedure evaluation (history, physical examination) increases the likelihood of satisfactory sedation and decreases the likelihood of adverse outcomes for both moderate and deep sedation.

*Recommendations:* Clinicians administering sedation/analgesia should be familiar with sedation-oriented aspects of the patient's medical history and how these might alter the patient's response to sedation / analgesia. These include: (1) abnormalities of the major organ systems; (2) previous adverse experience with sedation/analgesia as well as regional and general anesthesia; (3) drug allergies, current medications and potential drug interactions; (4) time and nature of last oral intake; and (5) history of tobacco, alcohol or substance use or abuse. Patients presenting for sedation/analgesia should undergo a focused physical examination including vital signs, auscultation of the heart and lungs, and evaluation of the airway. (Refer to Example I.) Pre-procedure laboratory testing should be guided by the patient's underlying medical condition and the likelihood that the results will affect the management of sedation/analgesia. These evaluations should be confirmed immediately before sedation is initiated.

**2. <u>Pre-procedure preparation</u>:**

The literature is insufficient regarding the benefits of providing the patient (or her/his guardian, in the case of a child or impaired adult) with pre-procedure information about sedation and analgesia. For moderate sedation the consultants agree and for deep sedation the consultants strongly agree that appropriate pre-procedure counseling of patients regarding risks, benefits, and alternatives to sedation and analgesia increases patient satisfaction.

Sedatives and analgesics tend to impair airway reflexes in proportion to the degree of sedation/analgesia achieved. This dependence on level of sedation is reflected in the consultants opinion: They agree that pre-procedure fasting decreases risks during moderate sedation, while strongly agreeing that it decreases the risk of deep sedation. In emergency situations, when pre-procedure fasting is not practical, the consultants agree that the target level of sedation should be modified (i.e., less sedation should be administered) for moderate sedation, while strongly agreeing that it should be modified for deep sedation. The literature does not provide sufficient evidence to test the hypothesis that pre-procedure fasting results in a decreased incidence of adverse outcomes in patients undergoing either moderate or deep sedation

*Recommendations:* Patients (or their legal guardians in the case of minors or legally incompetent adults) should be informed of and agree to the administration of sedation / analgesia including the benefits, risks, and limitations associated with this therapy, as well as possible alternatives. Patients undergoing sedation/analgesia for elective procedures should not drink fluids or eat solid foods for a sufficient period of time to allow for gastric emptying prior to their procedure, as recommended by the American Society of Anesthesiologists "Guidelines for Preoperative Fasting" [2] (Example II). In urgent, emergent, or other situations where gastric emptying is impaired, the potential for pulmonary aspiration of gastric contents must be considered in determining (1) the target level of sedation, (2) whether the procedure should be delayed or (3) whether the trachea should be protected by intubation.

## 3. Monitoring

**Level of consciousness:** The response of patients to commands during procedures performed with sedation/analgesia serves as a guide to their level of consciousness. Spoken responses also provide an indication that the patients are breathing. Patients whose only response is reflex withdrawal from painful stimuli are deeply sedated, approaching a state of general anesthesia, and should be treated accordingly. The literature is silent regarding whether monitoring patients' level of consciousness improves patient outcomes or decreases risks. The consultants strongly agree that monitoring level of consciousness reduces risks for both moderate and deep sedation. The members of the Task Force believe that many of the complications associated with sedation and analgesia can be avoided if adverse drug responses are detected and treated in a timely manner (*i.e.*, prior to the development of cardiovascular decompensation, or cerebral hypoxia). Patients given sedatives and/or analgesics in unmonitored settings in anticipation of a subsequent procedure may be at increased risk of these complications.

**Pulmonary ventilation**: It is the opinion of the Task Force that the primary causes of morbidity associated with sedation/analgesia are drug-induced respiratory depression and airway obstruction. For both moderate and deep sedation, the literature is insufficient to evaluate the benefit of monitoring ventilatory function by observation or auscultation. However, the consultants strongly agree that monitoring of ventilatory function by observation or auscultation reduces the risk of adverse outcomes associated with sedation/analgesia. The consultants were equivocal regarding the ability of capnography to decrease risks during moderate sedation, while agreeing that it may decrease risks during deep sedation. In circumstances where patients are physically separated from the care giver, the Task Force

[2] Anesthesiology 1999; 90:896-905

believes that automated apnea monitoring (by detection of exhaled $CO_2$ or other means) may decrease risks during both moderate and deep sedation, while cautioning practitioners that impedance plethysmography may fail to detect airway obstruction. The Task Force emphasizes that because ventilation and oxygenation are separate though related physiological processes, monitoring oxygenation by pulse oximetry is not a substitute for monitoring ventilatory function.

**Oxygenation**: Published data suggests that oximetry effectively detects oxygen desaturation and hypoxemia in patients who are administered sedatives / analgesics. The consultants strongly agree that early detection of hypoxemia through the use of oximetry during sedation/analgesia decreases the likelihood of adverse outcomes such as cardiac arrest and death. The Task Force agrees that hypoxemia during sedation and analgesia is more likely to be detected by oximetry than by clinical assessment alone.

**Hemodynamics:** Although there is insufficient published data to reach a conclusion, it is the opinion of the Task Force that sedative and analgesic agents may blunt the appropriate autonomic compensation for hypovolemia and procedure-related stresses. On the other hand, if sedation and analgesia are inadequate, patients may develop potentially harmful autonomic stress responses (e.g., hypertension, tachycardia). Early detection of changes in patients' heart rate and blood pressure may enable practitioners to detect problems and intervene in a timely fashion, reducing the risk of these complications. The consultants strongly agree that regular monitoring of vital signs reduces the likelihood of adverse outcomes during both moderate and deep sedation. For both moderate and deep sedation, a majority of the consultants indicated that vital signs should be monitored at 5-minute intervals once a stable level of sedation is established. The consultants strongly agree that continuous electrocardiography reduces risks during deep sedation, while they were equivocal regarding its effect during moderate sedation. However, the Task Force believes that electrocardiographic monitoring of selected individuals (e.g., patients with significant cardiovascular disease or dysrhythmias) may decrease risks during moderate sedation.

*Recommendations*: Monitoring of patient response to verbal commands should be routine during moderate sedation, except in patients who are unable to respond appropriately (*e.g.*, young children, mentally impaired or uncooperative patients), or during procedures where movement could be detrimental. During deep sedation, patient responsiveness to a more profound stimulus should be sought, unless contraindicated, to ensure that the patient has not drifted into a state of general anesthesia.. During procedures where a verbal response is not possible (*e.g.*, oral surgery, upper endoscopy), the ability to give a "thumbs up" or other indication of consciousness in response to verbal or tactile (light tap) stimulation suggests that the patient will be able to control his airway and take deep breaths if

necessary, corresponding to a state of moderate sedation. Note that a response limited to reflex withdrawal from a painful stimulus is **not** considered a purposeful response and thus represents a state of general anesthesia.

All patients undergoing sedation/analgesia should be monitored by pulse oximetry with appropriate alarms. If available, the variable pitch "beep", which gives a continuous audible indication of the oxygen saturation reading, may be helpful. In addition, ventilatory function should be continually monitored by observation and/or auscultation. Monitoring of exhaled $CO_2$ should be considered for all patients receiving deep sedation and for patients whose ventilation cannot be directly observed during moderate sedation. When possible, blood pressure should be determined before sedation/analgesia is initiated. Once sedation/analgesia is established, blood pressure should be measured at 5-minute intervals during the procedure, unless such monitoring interferes with the procedure (e.g., pediatric MRI where stimulation from the BP cuff could arouse an appropriately-sedated patient). Electrocardiographic monitoring should be used in all patients undergoing deep sedation; it should also be used during moderate sedation in patients with significant cardiovascular disease or those who are undergoing procedures where dysrhythmias are anticipated.

**4. <u>Recording of monitored parameters:</u>** The literature is silent regarding the benefits of contemporaneous recording of patients' level of consciousness, respiratory function or hemodynamics. Consultant opinion agrees with the use of contemporaneous recording for moderate sedation, and strongly agrees with its use for patients undergoing deep sedation. It is the consensus of the Task Force that unless technically precluded (e.g., uncooperative or combative patient) vital signs and respiratory variables should be recorded before initiating sedation/analgesia, after administration of sedative/analgesic medications, at regular intervals during the procedure, upon initiation of recovery, and immediately before discharge. It is the opinion of the Task Force that contemporaneous recording (either automatic or manual) of patient data may disclose trends which could prove critical in determining the development or cause of adverse events. Additionally, manual recording ensures that an individual caring for the patient is aware of changes in patient status in a timely fashion.

*Recommendations:* For both moderate and deep sedation, patients' level of consciousness, ventilatory and oxygenation status, and hemodynamic variables should be assessed and recorded at a frequency which depends upon the type and amount of medication administered, the length of the procedure, and the general condition of the patient. At a minimum, this should be: (1) before the beginning of the procedure; (2) following administration of sedative/analgesic agents; (3) at regular intervals during the

procedure, (4) during initial recovery; and (5) just before discharge. If recording is performed automatically, device alarms should be set to alert the care team to critical changes in patient status.

**5. Availability of an individual responsible for patient monitoring:** Although the literature is silent on this issue, the Task Force recognizes that it may not be possible for the individual performing a procedure to be fully cognizant of the patient's condition during sedation/analgesia. For moderate sedation, the consultants agree that the availability of an individual other than the person performing the procedure to monitor the patient's status improves patient comfort and satisfaction and that risks are reduced. For deep sedation, the consultants strongly agree with these contentions. During moderate sedation, the consultants strongly agree that the individual monitoring the patient may assist the practitioner with interruptible ancillary tasks of short duration; during deep sedation, the consultants agree that this individual should have no other responsibilities.

*Recommendation:* A designated individual, other than the practitioner performing the procedure, should be present to monitor the patient throughout procedures performed with sedation/analgesia. During deep sedation, this individual should have no other responsibilities. However, during moderate sedation, this individual may assist with minor, interruptible tasks once the patient's level of sedation/analgesia and vital signs have stabilized, provided that adequate monitoring for the patient's level of sedation is maintained.

**6. Training of personnel:** Although the literature is silent regarding the effectiveness of training on patient outcomes, the consultants strongly agree that education and training in the pharmacology of agents commonly used during sedation / analgesia improves the likelihood of satisfactory sedation and reduces the risk of adverse outcomes from either moderate or deep sedation. Specific concerns may include: (1) potentiation of sedative-induced respiratory depression by concomitantly administered opioids; (2) inadequate time intervals between doses of sedative or analgesic agents resulting in a cumulative overdose; and (3) inadequate familiarity with the role of pharmacological antagonists for sedative and analgesic agents.

Because the primary complications of sedation/analgesia are related to respiratory or cardiovascular depression, it is the consensus of the Task Force that the individual responsible for monitoring the patient should be trained in the recognition of complications associated with sedation/analgesia. Because sedation/analgesia constitute a continuum, practitioners administering moderate sedation should be able to rescue patients who enter a state of deep sedation, while those intending to administer deep sedation should be able to rescue patients who enter a state of general anesthesia. Therefore, the consultants strongly agree that at least one qualified individual trained in

basic life support skills (CPR, bag-valve-mask ventilation) should be present in the procedure room during both moderate and deep sedation. In addition, the consultants strongly agree with the immediate availability (1-5 minutes away) of an individual with advanced life support skills (e.g., tracheal intubation, defibrillation, use of resuscitation medications) for moderate sedation and in the procedure room itself for deep sedation.

*Recommendations*: Individuals responsible for patients receiving sedation/analgesia should understand the pharmacology of the agents that are administered, as well as the role of pharmacologic antagonists for opioids and benzodiazepines. Individuals monitoring patients receiving sedation/analgesia should be able to recognize the associated complications. At least one individual capable of establishing a patent airway and positive pressure ventilation, as well as a means for summoning additional assistance should be present whenever sedation/analgesia are administered. It is recommended that an individual with advanced life support skills be immediately available (within 5 minutes) for moderate sedation and within the procedure room for deep sedation.

**7. Availability of emergency equipment**: Although the literature is silent, the consultants strongly agree that the ready availability of appropriately-sized emergency equipment reduces the risk of both moderate and deep sedation. The literature is also silent regarding the need for cardiac defibrillators during sedation/analgesia. During moderate sedation, the consultants agree that a defibrillator should be immediately available for patients with both mild (e.g., hypertension) and severe (e.g., ischemia, congestive failure) cardiovascular disease. During deep sedation, the consultants agree that a defibrillator should be immediately available for all patients.

*Recommendations:* Pharmacologic antagonists as well as appropriately-sized equipment for establishing a patent airway and providing positive pressure ventilation with supplemental oxygen should be present whenever sedation/analgesia is administered. Suction, advanced airway equipment, and resuscitation medications should be immediately available and in good working order (*e.g.*, Example III). A functional defibrillator should be immediately available whenever deep sedation is administered, and when moderate sedation is administered to patients with mild or severe cardiovascular disease.

**8. Use of supplemental oxygen:** The literature supports the use of supplemental oxygen during moderate sedation, and suggests the use of supplemental oxygen during deep sedation to reduce the frequency of hypoxemia. The consultants agree that supplemental oxygen decreases patient risk during moderate sedation, while strongly agreeing with this view for deep sedation.

*Recommendations:* Equipment to administer supplemental oxygen should be present when sedation/analgesia is administered. Supplemental oxygen should be considered for moderate sedation

and should be administered during deep sedation unless specifically contraindicated for a particular patient or procedure. If hypoxemia is anticipated or develops during sedation/analgesia, supplemental oxygen should be administered.

**9. Combinations of Sedative/Analgesic Agents:** The literature suggests that combining a sedative with an opioid provides effective moderate sedation; it is equivocal regarding whether the combination of a sedative and an opioid may be more effective than a sedative or an opioid alone in providing adequate moderate sedation. For deep sedation, the literature is insufficient to compare the efficacy of sedative-opioid combinations with that of a sedative, alone. The consultants agree that combinations of sedatives and opioids provide satisfactory moderate and deep sedation. However, the published data also suggest that combinations of sedatives and opioids may increase the likelihood of adverse outcomes including ventilatory depression and hypoxemia; the consultants were equivocal on this issue for both moderate and deep sedation. It is the consensus of the Task Force that fixed combinations of sedative and analgesic agents may not allow the individual components of sedation/analgesia to be appropriately titrated to meet the individual requirements of the patient and procedure while reducing the associated risks.

*Recommendations*: Combinations of sedative and analgesic agents may be administered as appropriate for the procedure being performed and the condition of the patient. Ideally, each component should be administered individually to achieve the desired effect (*e.g.*, additional analgesic medication to relieve pain; additional sedative medication to decrease awareness or anxiety). The propensity for combinations of sedative and analgesic agents to cause respiratory depression and airway obstruction emphasizes the need to appropriately reduce the dose of each component as well as the need to continually monitor respiratory function.

**10. Titration of intravenous sedative/analgesic medications:** The literature is insufficient to determine whether administration of small, incremental doses of intravenous sedative/analgesic drugs until the desired level of sedation and/or analgesia is achieved is preferable to a single dose based on patient size, weight, or age. The consultants strongly agree that incremental drug administration improves patient comfort and decreases risks for both moderate and deep sedation.

*Recommendations:* Intravenous sedative/analgesic drugs should be given in small, incremental doses which are titrated to the desired endpoints of analgesia, and sedation. Sufficient time must elapse between doses to allow the effect of each dose to be assessed before subsequent drug administration. When drugs are administered by non-intravenous routes (*e.g.*, oral, rectal, intramuscular, transmucosal), allowance should be made for the time required for drug absorption before supplementation is

considered. Because absorption may be unpredictable, administration of repeat doses of oral medications to supplement sedation / analgesia is not recommended.

**11. Anesthetic induction agents used for sedation / analgesia (propofol, methohexital, ketamine)**

The literature suggests that when administered by non-anesthesiologists, propofol and ketamine can provide satisfactory moderate sedation, and suggests that methohexital can provide satisfactory deep sedation. The literature is insufficient to evaluate the efficacy of propofol or ketamine administered by non-anesthesiologists for deep sedation. There is insufficient literature to determine whether moderate or deep sedation with propofol is associated with a different incidence of adverse outcomes than similar levels of sedation with midazolam. The consultants are equivocal regarding whether use of these medications affects the likelihood of producing satisfactory moderate sedation, while agreeing that using them increases the likelihood of satisfactory deep sedation. However, the consultants agree that *avoiding* these medications decreases the likelihood of adverse outcomes during moderate sedation, and are equivocal regarding their effect on adverse outcomes during deep sedation.

The Task Force cautions practitioners that methohexital and propofol can produce rapid, profound decreases in level of consciousness and cardiorespiratory function, potentially culminating in a state of general anesthesia. The Task Force notes that ketamine also produces dose-related decreases in level of consciousness culminating in general anesthesia. Although it may be associated with less cardiorespiratory depression than other sedatives, airway obstruction, laryngospasm, and pulmonary aspiration may still occur with ketamine. Furthermore, because of its dissociative properties, some of the usual signs of depth of sedation may not apply (e.g., the patient's eyes may be open while in a state of deep sedation or general anesthesia). The Task Force also notes that there are no specific pharmacological antagonists for any of these medications.

*Recommendations*: Even if moderate sedation is intended, patients receiving propofol or methohexital by any route should receive care consistent with that required for deep sedation. Accordingly, practitioners administering these drugs should be qualified to rescue patients from any level of sedation including general anesthesia. Patients receiving ketamine should be cared for in a manner consistent with the level of sedation which is achieved.

**12. <u>Intravenous Access</u>**: Published literature is equivocal regarding the relative efficacy of sedative /analgesic agents administered intravenously as compared to agents administered by non-intravenous routes to achieve moderate sedation; the literature is insufficient on this issue for deep sedation. The literature is equivocal regarding the comparative safety of these routes of administration for moderate sedation, and insufficient for deep sedation. The consultants strongly agree that intravenous

administration of sedative and analgesic medications increases the likelihood of satisfactory sedation for both moderate and deep sedation. They also agree that it decreases the likelihood of adverse outcomes. For both moderate and deep sedation, when sedative/analgesic medications are administered intravenously, the consultants strongly agree with maintaining intravenous access until patients are no longer at risk for cardiovascular or respiratory depression, because it increases the likelihood of satisfactory sedation and decreases the likelihood of adverse outcomes. In those situations where sedation is begun by non-intravenous routes (*e.g.*, oral, rectal, intramuscular) the need for intravenous access is not sufficiently addressed in the literature. However, initiation of intravenous access after the initial sedation takes effect allows additional sedative/analgesic and resuscitation drugs to be administered if necessary.

*Recommendations:* In patients receiving intravenous medications for sedation/analgesia, vascular access should be maintained throughout the procedure and until the patient is no longer at risk for cardiorespiratory depression. In patients who have received sedation/analgesia by non-intravenous routes, or whose intravenous line has become dislodged or blocked, practitioners should determine the advisability of establishing or reestablishing intravenous access on a case-by-case basis. In all instances, an individual with the skills to establish intravenous access should be immediately available.

**13. <u>Reversal Agents</u>:** Specific antagonist agents are available for the opioids (*e.g.*, naloxone) and benzodiazepines (*e.g.*, flumazenil). The literature supports the ability of naloxone to reverse opioid-induced sedation and respiratory depression. Practitioners are cautioned that acute reversal of opioid-induced analgesia may result in pain, hypertension, tachycardia, or pulmonary edema. The literature supports the ability of flumazenil to antagonize benzodiazepine-induced sedation and ventilatory depression in patients who have received benzodiazepines alone or in combination with an opioid. The consultants strongly agree that the immediate availability of reversal agents during both moderate and deep sedation is associated with decreased risk of adverse outcomes. It is the consensus of the Task Force that respiratory depression should be initially treated with supplemental oxygen and, if necessary, positive pressure ventilation by mask. The consultants disagree that the use of sedation regimens which are likely to require *routine* reversal with flumazenil or naloxone improves the quality of sedation or reduces the risk of adverse outcomes.

*Recommendations:* Specific antagonists should be available whenever opioid analgesics or benzodiazepines are administered for sedation/analgesia. Naloxone and/or flumazenil may be administered to improve spontaneous ventilatory efforts in patients who have received opioids or benzodiazepines, respectively. This may be especially helpful in cases where airway control and

positive pressure ventilation are difficult. Prior to or concomitantly with pharmacological reversal, patients who become hypoxemic or apneic during sedation/analgesia should: (1) be encouraged or stimulated to breathe deeply; (2) receive supplemental oxygen; and (3) receive positive pressure ventilation if spontaneous ventilation is inadequate. Following pharmacological reversal, patients should be observed long enough to ensure that sedation and cardiorespiratory depression does not recur once the effect of the antagonist dissipates. The use of sedation regimens which include routine reversal of sedative or analgesic agents is discouraged.

**14. Recovery care:** Patients may continue to be at significant risk for developing complications after their procedure is completed. Decreased procedural stimulation, delayed drug absorption following non-intravenous administration, and slow drug elimination, may contribute to residual sedation and cardiorespiratory depression during the recovery period. Examples include intramuscular meperidine-promethazine-chlorpromazine mixtures and oral or rectal chloral hydrate. When sedation/analgesia is administered to outpatients, one must assume that there will be no medical supervision once the patient leaves the medical facility. Although there is not sufficient literature to examine the effects of post-procedure monitoring on patient outcomes, the consultants strongly agree that continued observation, monitoring, and predetermined discharge criteria decrease the likelihood of adverse outcomes for both moderate and deep sedation. It is the consensus of the Task Force that discharge criteria should be designed to minimize the risk for cardiorespiratory depression after patients are released from observation by trained personnel.

*Recommendations:* Following sedation/analgesia, patients should be observed in an appropriately staffed and equipped area until they are near their baseline level of consciousness and are no longer at increased risk for cardiorespiratory depression. Oxygenation should be monitored periodically until patients are no longer at risk for hypoxemia. Ventilation, and circulation should be monitored at regular intervals until patients are suitable for discharge. Discharge criteria should be designed to minimize the risk of central nervous system or cardiorespiratory depression following discharge from observation by trained personnel (*e.g.*, Example IV.)

**15. Special Situations:** The literature suggests and the Task Force members concur that certain types of patients are at increased risk for developing complications related to sedation/analgesia unless special precautions are taken. In patients with significant underlying medical conditions (e.g. extremes of age; severe cardiac, pulmonary, hepatic or renal disease; pregnancy; drug or alcohol abuse) the consultants agree that pre-procedure consultation with an appropriate medical specialist (e.g., cardiologist, pulmonologist) decreases the risk associated with moderate sedation and strongly agree that it decreases

the risks associated with deep sedation. In patients with significant sedation-related risk factors (e.g., uncooperative patients, morbid obesity, potentially difficult airway, sleep apnea) the consultants are equivocal regarding whether preprocedure consultation with an anesthesiologist increases the likelihood of satisfactory moderate sedation while agreeing that it decreases adverse outcomes; the consultants strongly agree that preprocedure consultation increases the likelihood of satisfactory outcomes while decreasing the risk associated with deep sedation. The Task Force notes that in emergency situations, the benefits of awaiting pre-procedure consultations must be weighed against the risk of delaying the procedure.

For moderate sedation, the consultants are equivocal regarding whether the immediate availability of an individual with postgraduate training in anesthesiology increases the likelihood of a satisfactory outcome or decreases the associated risks. For deep sedation the consultants agree that the immediate availability of such an individual improves the likelihood of satisfactory sedation and that it will decrease the likelihood of adverse outcomes.

*Recommendations:* Whenever possible, appropriate medical specialists should be consulted prior to administration of sedation to patients with significant underlying conditions. The choice of specialists depends on the nature of the underlying condition and the urgency of the situation. For severely compromised or medically unstable patients (*e.g.*, anticipated difficult airway, severe obstructive pulmonary disease, coronary artery disease, or congestive heart failure), or if it is likely that sedation to the point of unresponsiveness will be necessary to obtain adequate conditions, practitioners who are not trained in the administration of general anesthesia should consult an anesthesiologist.

## Example I: Airway Assessment Procedures for Sedation and Analgesia

Positive pressure ventilation, with or without tracheal intubation, may be necessary if respiratory compromise develops during sedation/analgesia. This may be more difficult in patients with atypical airway anatomy. Also, some airway abnormalities may increase the likelihood of airway obstruction during spontaneous ventilation. Some factors which may be associated with difficulty in airway management are:

History:

Previous problems with anesthesia or sedation

Stridor, snoring, or sleep apnea

Advanced rheumatoid arthritis

Chromosomal abnormality (e.g. trisomy 21)

Physical Examination:

| | |
|---|---|
| Habitus: | Significant obesity (especially involving the neck and facial structures) |
| Head and Neck: | Short neck, limited neck extension, decreased hyoid-mental distance (<3 cm in an adult), neck mass, cervical spine disease or trauma, tracheal deviation, dysmorphic facial features (*e.g.*, Pierre-Robin syndrome) |
| Mouth: | Small opening (< 3 cm in an adult); edentulous; protruding incisors; loose or capped teeth; dental appliances; high, arched palate; macroglossia; tonsillar hypertrophy; non-visible uvula |
| Jaw: | Micrognathia, retrognathia, trismus, significant malocclusion |

Example II: Summary of American Society of Anesthesiologists Pre-Procedure Fasting Guidelines[1]

| Ingested Material | Minimum Fasting Period [2] |
|---|---|
| Clear liquids [3] | 2 h |
| Breast milk | 4 h |
| Infant formula | 6 h |
| Non-human milk [4] | 6h |
| Light meal [5] | 6h |

[1] These recommendations apply to healthy patients who are undergoing elective procedures. They are not intended for women in labor. Following the guidelines does not guarantee a complete gastric emptying has occurred.

[2] The fasting periods noted above apply to all ages.

[3] Examples of clear liquids include water, fruit juices without pulp, carbonated beverages, clear tea, and black coffee.

[4] Since non-human milk is similar to solids in gastric emptying time, the amount ingested must be considered when determining an appropriate fasting period.

[5] A light meal typically consists of toast and clear liquids. Meals that include fried or fatty foods or meat may prolong gastric emptying time. Both the amount and type of foods ingested must be considered when determining an appropriate fasting period.

## Example III: Emergency Equipment for Sedation and Analgesia

Appropriate emergency equipment should be available whenever sedative or analgesic drugs capable of causing cardiorespiratory depression are administered. The table below should be used as a guide, which should be modified depending upon the individual practice circumstances. Items in brackets are recommended when infants or children are sedated.

**Intravenous Equipment:**

Gloves
Tourniquets
Alcohol wipes
Sterile gauze pads
Intravenous catheters [24, 22 gauge]
Intravenous tubing [pediatric 'microdrip'--60 drops/ml]
Intravenous fluid
Assorted needles for drug aspiration, i.m. injection [intraosseous bone marrow needle]
Appropriately sized syringes [1 ml syringes]
Tape

**Basic Airway Management Equipment:**

Source of compressed $O_2$ (tank with regulator or pipeline supply with flowmeter)
Source of suction
Suction catheters [pediatric suction catheters]
Yankauer-type suction
Face masks [infant/child face masks]
Self-inflating breathing bag-valve set [pediatric bag-valve set]
Oral and nasal airways [infant/child sized airways]
Lubricant

**Advanced Airway Management Equipment** (for practitioners with intubation skills)

Laryngeal mask airways [pediatric laryngeal mask airways]

Laryngoscope handles (tested)

Laryngoscope blades [pediatric laryngoscope blades]

Endotracheal tubes:

Cuffed 6.0, 7.0, 8.0 mm i.d.

[Uncuffed 2.5, 3.0, 3.5, 4.0, 4.5, 5.0, 5.5, 6.0 mm i.d.]

Stylet [appropriately sized for endotracheal tubes]

**Pharmacologic Antagonists**

Naloxone

Flumazenil

**Emergency Medications:**

Epinephrine

Ephedrine

Vasopressin

Atropine

Nitroglycerin (tablets or spray)

Amiodarone

Lidocaine

Glucose (50%) [10% or 25% glucose]

Diphenhydramine

Hydrocortisone, methylprednisolone, or dexamethasone

Diazepam or Midazolam

## Example IV: Recovery and Discharge Criteria Following Sedation and Analgesia

Each patient-care facility in which sedation/analgesia is administered should develop recovery and discharge criteria which are suitable for its specific patients and procedures. Some of the basic principles which might be incorporated in these criteria are enumerated below.

### A. General Principles

1. Medical supervision of recovery and discharge following moderate or deep sedation is the responsibility of the operating practitioner or a licensed physician
2. The recovery area should be equipped with or have direct access to appropriate monitoring and resuscitation equipment
3. Patients receiving moderate or deep sedation should be monitored until appropriate discharge criteria are satisfied. The duration and frequency of monitoring should be individualized depending upon the level of sedation achieved, the overall condition of the patient, and the nature of the intervention for which sedation/analgesia was administered. Oxygenation should be monitored until patients are no longer at risk for respiratory depression.
4. Level of consciousness, vital signs and oxygenation (when indicated) should be recorded at regular intervals
5. A nurse or other individual trained to monitor patients and recognize complications should be in attendance until discharge criteria are fulfilled.
6. An individual capable of managing complications (e.g., establishing a patent airway and providing positive pressure ventilation) should be immediately available until discharge criteria are fulfilled.

### B. Guidelines for Discharge

1. Patients should be alert and oriented; infants and patients whose mental status was initially abnormal should have returned to their baseline. Practitioners and parents must be aware that pediatric patients are at risk for airway obstruction should the head fall forward while the child is secured in a car seat.
2. Vital signs should be stable and within acceptable limits.

3. Use of scoring systems may assist in documentation of fitness for discharge.
4. Sufficient time (up to 2 hours) should have elapsed following the last administration of reversal agents (naloxone, flumazenil) to ensure that patients do not become resedated after reversal effects have worn off.
5. Outpatients should be discharged in the presence of a responsible adult who will accompany them home and be able to report any post-procedure complications.
6. Outpatients and their escorts should be provided with written instructions regarding post-procedure diet, medications, activities, and a phone number to be called in case of emergency.

Table 1: **Continuum of Depth of Sedation**
**Definition of General Anesthesia and Levels of Sedation / Analgesia**
(Developed by the American Society of Anesthesiologists)
(Approved by ASA House of Delegates on October 13, 1999)

| | Minimal Sedation ("Anxiolysis") | Moderate Sedation / Analgesia ("Conscious Sedation") | Deep Sedation / Analgesia | General Anesthesia |
|---|---|---|---|---|
| Responsiveness | Normal response to verbal stimulation | Purposeful* response to verbal or tactile stimulation | Purposeful* response following repeated or painful stimulation | Unarousable, even with painful stimulus |
| Airway | Unaffected | No intervention required | Intervention may be required | Intervention often required |
| Spontaneous Ventilation | Unaffected | Adequate | May be inadequate | Frequently inadequate |
| Cardiovascular Function | Unaffected | Usually maintained | Usually maintained | May be impaired |

**Minimal Sedation (Anxiolysis)** is a drug-induced state during which patients respond normally to verbal commands. Although cognitive function and coordination may be impaired, ventilatory and cardiovascular functions are unaffected.

**Moderate Sedation/Analgesia ("Conscious Sedation")** is a drug-induced depression of consciousness during which patients respond purposefully* to verbal commands, either alone or accompanied by light tactile stimulation. No interventions are required to maintain a patent airway, and spontaneous ventilation is adequate. Cardiovascular function is usually maintained.

**Deep Sedation/Analgesia** is a drug-induced depression of consciousness during which patients cannot be easily aroused but respond purposefully* following repeated or painful stimulation. The ability to independently maintain ventilatory function may be impaired. Patients may require assistance in maintaining a patent airway, and spontaneous ventilation may be inadequate. Cardiovascular function is usually maintained.

**General Anesthesia** is a drug-induced loss of consciousness during which patients are not arousable, even by painful stimulation. The ability to independently maintain ventilatory function is often impaired. Patients often require assistance in maintaining a patent airway, and positive pressure ventilation may be required because of depressed spontaneous ventilation or drug-induced depression of neuromuscular function. Cardiovascular function may be impaired.

Because sedation is a continuum, it is not always possible to predict how an individual patient will respond. Hence, practitioners intending to produce a given level of sedation should be able to rescue patients whose level of sedation becomes deeper than initially intended. Individuals administering **Moderate Sedation/Analgesia ("Conscious Sedation")** should be able to rescue patients who enter a state of **Deep Sedation/Analgesia**, while those administering **Deep Sedation/Analgesia** should be able to rescue patients who enter a state of general anesthesia.

*Reflex withdrawal from a painful stimulus is NOT considered a purposeful response.

**Appendix: Methods and Analyses.**

The scientific assessment of these Guidelines was based on the following statements, or evidence linkages. These linkages represent directional statements about relationships between obstetrical anesthetic interventions and clinical outcomes.

1. A pre-procedure patient evaluation, (i.e., history, physical examination, laboratory evaluation, consultation):
   a. Improves clinical efficacy (i.e., satisfactory sedation and analgesia).
   b. Reduces adverse outcomes.

2. Pre-procedure preparation of the patient (e.g., counseling, fasting):
   a. Improves clinical efficacy (i.e., satisfactory sedation and analgesia).
   b. Reduces adverse outcomes.

3. Patient monitoring (i.e., level of consciousness, pulmonary ventilation (observation, auscultation), oxygenation (pulse oximetry), automated apnea monitoring (capnography), hemodynamics (ECG, BP, HR):
   a. Improves clinical efficacy (i.e., satisfactory sedation and analgesia).
   b. Reduces adverse outcomes.

4. Contemporaneous recording of monitored parameters (e.g., level of consciousness, respiratory function, hemodynamics) at regular intervals in patients receiving sedation and/or analgesia:
   a. Improves clinical efficacy (i.e., satisfactory sedation and analgesia).
   b. Reduces adverse outcomes.

5. Availability of an individual who is dedicated solely to patient monitoring and safety:
   a. Improves clinical efficacy (i.e., satisfactory sedation and analgesia).
   b. Reduces adverse outcomes.

6a. Education and training of sedation and analgesia providers in the pharmacology of sedation/analgesia agents:
   a. Improves clinical efficacy (i.e., satisfactory sedation and analgesia).
   b. Reduces adverse outcomes.

6b. The presence of an individual(s) capable of establishing a patent airway, positive pressure ventilation and resuscitation (i.e. advanced life-support skills) during a procedure:
   a. Improves clinical efficacy (i.e., satisfactory sedation and analgesia).
   b. Reduces adverse outcomes.

7. Availability of appropriately sized emergency and airway equipment (e.g., LMA, defibrillators):
   a. Improves clinical efficacy (i.e., satisfactory sedation and analgesia).
   b. Reduces adverse outcomes.

8. The use of supplemental oxygen during procedures performed with sedation and/or analgesia:
   a. Improves clinical efficacy (i.e., satisfactory sedation and analgesia).
   b. Reduces adverse outcomes.

9. Use of sedative agents combined with analgesic agents (e.g., sedative/analgesic cocktails, fixed combinations of sedatives and analgesics, titrated combinations of sedatives and analgesics):
   a. Improves clinical efficacy (i.e., satisfactory sedation and analgesia).
   b. Reduces adverse outcomes.

10. Titration of intravenous sedative/analgesic medications to achieve the desired effect:
   a. Improves clinical efficacy (i.e., satisfactory sedation and analgesia).
   b. Reduces adverse outcomes.

11. Intravenous sedation/analgesic medications specifically designed to be used for general anesthesia (i.e., methohexital, propofol and ketamine):
   a. Improves clinical efficacy (i.e., satisfactory sedation and analgesia).
   b. Reduces adverse outcomes.

12a. Administration of sedative/analgesic agents by the intravenous route:
   a. Improves clinical efficacy (i.e., satisfactory sedation and analgesia).
   b. Reduces adverse outcomes.

12b. Maintaining or establishing intravenous access during sedation and/or analgesia until the patient is no longer at risk for cardiorespiratory depression:
   a. Improves clinical efficacy (i.e., satisfactory sedation and analgesia).
   b. Reduces adverse outcomes.

13. Availability of reversal agents *(naloxone and flumazenil only)* for the sedative and/or analgesic agents being administered:
   a. Improves clinical efficacy (i.e., satisfactory sedation and analgesia).
   b. Reduces adverse outcomes.

14. Post-procedural recovery observation, monitoring, and predetermined discharge criteria reduce adverse outcomes.

15. Special regimens (e.g., pre-procedure consultation, specialized monitoring, *special sedatives/techniques*) for patients with special problems (e.g., uncooperative patients; extremes of age; severe cardiac, pulmonary, hepatic, renal, or central nervous system disease; morbid obesity; sleep apnea; pregnancy; drug or alcohol abuse; emergency/unprepared patients; metabolic and airway difficulties):
   a. Improves clinical efficacy (i.e., satisfactory sedation and analgesia).
   b. Reduces adverse outcomes.

Scientific evidence was derived from aggregated research literature, and from surveys, open presentations and other consensus-oriented activities. For purposes of literature aggregation, potentially relevant clinical studies were identified via electronic and manual searches of the literature. The

electronic search covered a 36-year period from 1966 through 2001. The manual search covered a 44-year period of time from 1958 through 2001. Over 3000 citations were initially identified, yielding a total of 1876 non-overlapping articles that addressed topics related to the 15 evidence linkages. Following review of the articles, 1519 studies did not provide direct evidence, and were subsequently eliminated. A total of 357 articles contained direct linkage-related evidence.

A directional result for each study was initially determined by a literature count, classifying each outcome as either supporting a linkage, refuting a linkage, or neutral. The results were then summarized to obtain a directional assessment of support for each linkage. Literature pertaining to three evidence linkages contained enough studies with well-defined experimental designs and statistical information to conduct formal meta-analyses. These three linkages were: linkage 8 [supplemental oxygen], linkage 9 [benzodiazepines combined with opioids versus benzodiazepines alone], linkage 13 [naloxone for antagonism of opioids, flumazenil for antagonism of benzodiazepines, and flumazenil for antagonism of benzodiazepine-opioid combinations].

Combined probability tests were applied to continuous data, and an odds-ratio procedure was applied to dichotomous study results. 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) and effect size estimates were calculated. Interobserver agreement was established through assessment of interrater reliability testing. Tests for heterogeneity of the independent samples were conducted to assure consistency among the study results. To assess potential publishing bias, a "fail-safe N" value was calculated for each combined probability test. No search for unpublished studies was conducted, and no reliability tests for locating research results were done.

Meta-analytic results are reported in Table 2. The following outcomes were found to be significant for combined probability tests: (1) <u>oxygen saturation</u> - linkage 8 [supplemental oxygen]; (2) <u>sedation recovery</u> - linkage 13 [naloxone for antagonism of opioids and flumazenil for antagonism of benzodiazepine-opioid combinations]; (3) <u>psychomotor recovery</u> - linkage 13 [flumazenil for antagonism of benzodiazepines], and (4) <u>respiratory/ventilatory recovery</u> - linkage 13 [naloxone for antagonism of opioids, flumazenil for antagonism of benzodiazepines, and flumazenil for antagonism of benzodiazepine-opioid combinations]. To be considered acceptable findings of significance, both the

Fisher and weighted Stouffer combined test results must agree. Weighted effect size values for these linkages ranged from r = 0.19 to r = 0.80, representing moderate to high effect size estimates.

Mantel-Haenszel odds ratios were significant for the following outcomes: (1) hypoxemia - linkage 8 [supplemental oxygen] and linkage 9 [benzodiazepine-opioid combinations versus benzodiazepines alone]; (2) sedation recovery - linkage 13 [flumazenil for antagonism of benzodiazepines], and (3) recall of procedure - linkage 9 [benzodiazepine-opioid combinations]. To be considered acceptable findings of significance, Mantel-Haenszel odds-ratios must agree with combined test results when both types of data are assessed.

Agreement among Task Force members and two methodologists was established by interrater reliability testing. Agreement levels using a Kappa statistic for two-rater agreement pairs were as follows: (1) type of study design, k = 0.25 to 0.64; (2) type of analysis, k = 0.36 to 0.83; (3) evidence linkage assignment, k = 0.78 to 0.89; and (4) literature inclusion for database, k = 0.71 to 1.00. Three-rater chance-corrected agreement values were: (1) study design, Sav = 0.45, Var (Sav) = 0.012; (2) type of analysis, Sav = 0.51, Var (Sav) = 0.015; (3) linkage assignment, Sav = 0.81 Var (Sav) = 0.006; (4) literature database inclusion, Sav = 0.84 Var (Sav) = 0.046. These values represent moderate to high levels of agreement.

The findings of the literature analyses were supplemented by the opinions of Task Force members as well as by surveys of the opinions of a panel of Consultants, as described in the text of the Guidelines. The rate of return for this Consultant survey was 78% (N = 51/65). Median agreement scores from the Consultants regarding each linkage are reported in Table 3.

For moderate sedation, Consultants were supportive of all of the linkages with the following exceptions: linkage 3 (electrocardiogram monitoring and capnography), linkage 9 (sedatives combined with analgesics for reducing adverse outcomes), linkage 11 (avoiding general anesthesia sedatives for improving satisfactory sedation), linkage 13b (routine administration of naloxone), linkage 13c (routine administration of flumazenil), and linkage 15b (anesthesiologist consultation for patients with medical conditions to provide satisfactory moderate sedation). In addition, Consultants were equivocal regarding whether postgraduate training in anesthesiology improves moderate sedation or reduces adverse outcomes.

For deep sedation, Consultants were supportive of all of the linkages with the following exceptions: linkage 9 (sedatives combined with analgesics for reducing adverse outcomes), linkage 11 (avoiding general anesthesia sedatives), linkage 13b (routine administration of naloxone), and linkage 13c (routine administration of flumazenil).

The Consultants were asked to indicate which, if any, of the evidence linkages would change their clinical practices if the updated Guidelines were instituted. The rate of return was 57% (N = 37/65). The percent of responding Consultants expecting *no change* associated with each linkage were as follows: pre-procedure patient evaluation - 94%; pre-procedure patient preparation- 91%; patient monitoring - 80%; contemporaneous recording of monitored parameters - 91%; availability of individual dedicated solely to patient monitoring and safety - 91%; education and training of sedation/analgesia providers in pharmacology - 89%; presence of an individual(s) capable of establishing a patent airway - 91%; availability of appropriately sized emergency and airway equipment - 94%, use of supplemental oxygen during procedures - 100%, use of sedative agents combined with analgesic agents - 91%, titration of sedatives/analgesics - 97%, intravenous sedation/analgesia with agents designed for general anesthesia - 77%, administration of sedative/analgesic agents by the intravenous route - 94%, maintaining or establishing intravenous access - 97%, availability/use of flumazenil - 94%, availability/use of naloxone - 94%, observation and monitoring during recovery - 89%, special care for patients with underlying medical problems - 91%, and special care for uncooperative patients - 94%. Seventy-four percent of the respondents indicated that the Guidelines would have *no effect* on the amount of time spent on a typical case. Nine respondents (26%) indicated that there would be an increase in the amount of time they would spend on a typical case with the implementation of these Guidelines. The amount of increased time anticipated by these respondents ranged from 1-60 minutes.

* Readers with special interest in the statistical analyses used in establishing these Guidelines can receive further information by writing to the American Society of Anesthesiologists: 520 North Northwest Highway, Park Ridge, Illinois 60068-2573.

**Table 2. Meta-Analysis Summary**

| Linkages | No. Studies | Fisher χ2 | p | Weighted Stouffer Zc | p | Effect Size | Mantel-Haenszel χ2 | p | Odds Ratio | Heterogeneity Significance | Heterogeneity Effect Size |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 8. Supplemental Oxygen | | | | | | | | | | | |
| Oxygen Saturation [1] | 5 | 71.40 | < 0.001 | 5.44 | < 0.001 | 0.40 | * | * | * | > 0.90 (NS) | > 0.50 (NS) |
| Hypoxemia [1] | 7 | * | * | * | * | * | 44.15 | < 0.001 | 0.20 | * | > 0.50 (NS) |
| 9a. Sedatives/Opioids Combined: Benzodiazepines + Opioids | | | | | | | | | | | |
| Sedation Efficacy | 7 | * | * | * | * | * | 3.79 | > 0.05 (NS) | 1.47 | * | < 0.01 |
| Recall of Procedure | 6 | * | * | * | * | * | 18.47 | < 0.001 | 2.57 | * | < 0.01 |
| Hypoxemia | 5 | * | * | * | * | * | 11.78 | < 0.001 | 2.37 | * | > 0.05 (NS) |
| 13a. Reversal Agents: Naloxone for opioids | | | | | | | | | | | |
| Sedation Recovery *At 5 minutes* [1,2,3] | 5 | 38.36 | < 0.001 | 3.13 | < 0.001 | 0.23 | * | * | * | > 0.30 (NS) | > 0.02 (NS) |
| Respiration/Ventilation [1,2,3] | 5 | 38.72 | < 0.001 | 3.97 | < 0.001 | 0.33 | * | * | * | > 0.10 (NS) | < 0.001 |
| 13b. Reversal Agents: Flumazenil for benzodiazepines | | | | | | | | | | | |
| Sedation Recovery *At 5 minutes* | 6 | * | * | * | * | * | 104.76 | < 0.001 | 8.15 | * | > 0.10 (NS) |
| Psychomotor Recovery *At 15 minutes* | 5 | 41.80 | < 0.001 | 1.69 | .0455 (NS) | 0.20 | * | * | * | > 0.70 (NS) | > 0.50 (NS) |
| *At 30 minutes* | 5 | 43.02 | < 0.001 | 3.36 | < 0.001 | 0.19 | * | * | * | > 0.90 (NS) | > 0.50 (NS) |
| Respiration/Ventilation [2,3] | 6 | 53.25 | < 0.001 | 5.03 | < 0.001 | 0.80 | * | * | * | < 0.01 | < 0.001 |
| 13c. Reversal Agents: Flumazenil for benzodiazepine-opioid combinations | | | | | | | | | | | |
| Sedation Recovery *At 5 minutes* | 5 | 72.12 | < 0.001 | 6.76 | < 0.001 | 0.37 | * | * | * | < 0.001 | < 0.001 |
| Respiration/Ventilation [2,3] | 6 | 55.06 | < 0.001 | 5.11 | < 0.001 | 0.25 | * | * | * | > 0.10 (NS) | < 0.001 |
| Nausea/Vomiting | 5 | * | * | * | * | * | 0.28 | > 0.80 (NS) | 1.22 | * | > 0.70 (NS) |

[1] Non-randomized comparative studies are included
[2] Studies in which anesthesiologist administered benzodiazepines, opioids or reversal agents are included
[3] Studies in which subjects consist of ICU, postoperative patients or volunteers with no procedures are included

## Table 3. Consultant Survey Summary

| Linkage/Intervention | Outcome | Moderate Sedation N | Moderate Sedation Median* or Percent | Deep Sedation N | Deep Sedation Median* or Percent |
|---|---|---|---|---|---|
| 1. Pre-procedure patient evaluation | *Satisfactory sedation* | 51 | 5 | 51 | 5 |
| | *Adverse outcomes* | 51 | 5 | 51 | 5 |
| 2. Pre-procedure fasting | *Satisfactory sedation* | 51 | 4 | 51 | 5 |
| | *Adverse outcomes* | 51 | 4 | 51 | 5 |
| 3. Monitoring | | | | | |
| a. Level of consciousness | *Satisfactory sedation* | 51 | 5 | 49 | 5 |
| | *Adverse outcomes* | 51 | 5 | 50 | 5 |
| b. Breathing (observation/auscultation) | *Satisfactory sedation* | 51 | 5 | 49 | 5 |
| | *Adverse outcomes* | 51 | 5 | 50 | 5 |
| c. Pulse oximetry | *Satisfactory sedation* | 51 | 5 | 50 | 5 |
| | *Adverse outcomes* | 51 | 5 | 50 | 5 |
| d. Blood pressure/heart rate | *Satisfactory sedation* | 50 | 4 | 49 | 5 |
| | *Adverse outcomes* | 50 | 5 | 49 | 5 |
| e. Electrocardiogram | *Satisfactory sedation* | 51 | 3 | 50 | 4 |
| | *Adverse outcomes* | 51 | 3 | 49 | 5 |
| f. Capnography | *Satisfactory sedation* | 50 | 3 | 48 | 4 |
| | *Adverse outcomes* | 50 | 3 | 49 | 4 |
| 4. Contemporaneous recording | *Satisfactory sedation* | 51 | 4 | 50 | 5 |
| | *Adverse outcomes* | 51 | 4 | 50 | 5 |
| 5. Individual for patient monitoring | *Satisfactory sedation* | 49 | 4 | 48 | 5 |
| | *Adverse outcomes* | 49 | 4 | 48 | 5 |
| 6a. Education and training | *Satisfactory sedation* | 50 | 5 | 49 | 5 |
| | *Adverse outcomes* | 50 | 5 | 49 | 5 |
| 6b. Individual with basic life support skills present in room | | 50 | 5 | 49 | 5 |
| 6c. Availability of ALS skills | | | | | |
| In the procedure room | | 2 | 4.2% | 39 | 79.6% |
| Immediate vicinity (1-5 minutes) | | 27 | 56.2% | 8 | 16.3% |
| Same building (5-10 minutes) | | 14 | 29.2% | 2 | 4.1% |
| Outside provider | | 5 | 10.4% | 0 | 0.0% |
| 7. Emergency IV and airway equipment | *Adverse outcomes* | 51 | 5 | 49 | 5 |
| 8. Supplemental oxygen | *Adverse outcomes* | 50 | 4 | 49 | 5 |
| 9. Sedatives combined with analgesics | *Satisfactory sedation* | 50 | 4 | 49 | 4 |
| | *Adverse outcomes* | 50 | 3 | 49 | 3 |
| 10. Titration | *Satisfactory sedation* | 51 | 5 | 50 | 5 |
| | *Adverse outcomes* | 51 | 5 | 50 | 5 |
| 11. Avoiding GA sedatives | *Satisfactory sedation* | 50 | 3 | 49 | 2 |
| | *Adverse outcomes* | 50 | 4 | 49 | 3 |
| 12a. IV sedatives | *Satisfactory sedation* | 51 | 5 | 50 | 5 |
| | *Adverse outcomes* | 51 | 4 | 50 | 4 |
| 12b. IV access | *Satisfactory sedation* | 50 | 4 | 49 | 5 |
| | *Adverse outcomes* | 50 | 5 | 49 | 5 |
| 13a. Immediate availability of naloxone | | | | | |

| | | | | | |
|---|---|---|---|---|---|
| or flumazenil | *Adverse outcomes* | 51 | 5 | 51 | 5 |
| 13b. Routine administration of naloxone | *Satisfactory sedation* | 37 | 2 | 37 | 2 |
| | *Adverse outcomes* | 37 | 2 | 37 | 2 |
| 13c. Routine administration of flumazenil | *Satisfactory sedation* | 37 | 1 | 37 | 2 |
| | *Adverse outcomes* | 37 | 2 | 37 | 2 |
| 14. Observation, monitoring & D/C criteria | *Adverse outcomes* | 50 | 5 | 49 | 5 |
| 15a.Med specialist consult, med conditions | *Satisfactory sedation* | 50 | 4 | 49 | 5 |
| | *Adverse outcomes* | 50 | 4 | 49 | 5 |
| 15b.Anesthesiologist consultation, patients with underlying medical conditions | *Satisfactory sedation* | 51 | 3 | 50 | 4 |
| | *Adverse outcomes* | 51 | 4 | 50 | 5 |
| 15c.Anesthesiologist consultation, patients with significant sedation risk factors | *Satisfactory sedation* | 51 | 4 | 50 | 5 |
| | *Adverse outcomes* | 51 | 4 | 50 | 5 |
| 16. Postgraduate training in anesthesiology | *Satisfactory sedation* | 51 | 3 | 50 | 4 |
| | *Adverse outcomes* | 51 | 3 | 50 | 4 |
| 17. In emergency situations, sedate patients less deeply | | 51 | 4 | 51 | 5 |

* Strongly Agree: Median score of '5' (At least 50% of the responses were '5')
Agree: Median score of '4' (At least 50% of the responses were '4' or '5')
Equivocal: Median score of '3' (At least 50% of the scores were 3 or less)
Disagree: Median score of '2' (At least 50% of responses were '1' or '2')
Strongly Disagree: Median score of '1' (At least 50% of responses were '1')

## PROPOFOL BY NON-ANESTHESIOLOGISTS

| | Author | Date | Title, Journal | Let/ Abs | Med Spc | Res Design | ST | N | ASA/ Health Status | Patient Age (yrs) | Mod/ Deep | Procedure | Anesth Agent | Route | Dosage |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Propofol administered by anesthesiologists vs non-anesthesiologists** | | | | | | | | | | | | | | | |
| 1 | Vargo JJ, | 2004 | Anesthes | Abs | Anesth/non | RS | C | 14572 | ASA 1-4 | * | M | Colonoscopy | Propofol | IV | * |
| **Propofol single-agents - observational studies, case reports, or non-pertinent comparison groups** | | | | | | | | | | | | | | | |
| 1 | Baptista / | 2005 | Propofol | Abs | Gastroent | RS | D | 7000 | ASA 1-2 (70% | * | * | Endoscopy | Propofol | * | median = 10-2 |
| 2 | Gangi S, | 2004 | Cardiova | * | Gastroent | RS | C | 165 | * | * | * | Colonoscopy | Propofol | IV | * |
| 3 | Heuss LT | 2003 | Safety of | * | Gastroent | NR | D | 1284 | ASA 1-4 | μ = 64 | * | Gastroscopy | Propofol | IV | 20 mg initial b |
| 4 | Heuss LT | 2003 | Consciou | * | Gastroent | NR | D | 4473 | ASA 1-4 | <70, 70-85 | * | EGD, colonc | Propofol | IV | 146.5 mg vs 1 |
| 5 | Heuss LT | 2003 | Risk stra | * | Gastroent | NR | D | 2574 | ASA 1-4 | * | * | Colonoscopy | Propofol | IV | 20 mg (initial |
| 6 | Heuss LT | 2003 | Nurse-ad | Abs | Gastroent | NR | D | 10351 | * | * | * | Various GI | Propofol | * | * |
| 7 | Rex DK, | 2004 | Nurse ad | Abs | Gastroent | RS | D | 28697 | * | * | * | Colonoscopy | Propofol | IV | * |
| 8 | Rex DK, | 2002 | Safety of | * | Gastroent | NR | D | 2000 | * | * | * | Mixed endos | Propofol | IV | 20-40 mg initi |
| 9 | Tohda G, | 2005 | Propofol | Abs | Gastroent | RS | D | 25200 | ASA 1-3 | * | M | Upper endos | Propofol | IV | 0.8-1.0 mg/kg |
| 10 | Walker J, | 2003 | Nurse-ad | * | Gastroent | NR | D | 9152 | ASA 1-4 | 8-96 | * | Endoscopy | Propofol | IV | 30-50 mg (init |
| 11 | Yusoff I, | 2004 | Endoscop | * | Gastroent | NR | D | 500 | ASA 1-2 | * | M | Endoscopy | Propofol | IV | 10 mg/ml (20- |
| **Propofol combined with other agents - observational studies, case reports, non-pertinent comparison groups or no single-agent control groups** | | | | | | | | | | | | | | | |
| 1 | Cohen LE | 2003 | Propofol | * | Gastroent | NR | D | 819 | ASA 1-4 | μ = 59 | * | Endoscopy | Propofol+ | IV | Propofol (52 c |
| 2 | Kulling D | 2003 | Safety of | * | Gastroent | NR | D | 300 | ASA 1-3 | μ = 53 | M | Colonoscopy | Propofol+ | IV | 0.25 or 0.5 mg |
| **Propofol vs benzodiazepines** | | | | | | | | | | | | | | | |
| 1 | Carlsson | 1995 | Sedation | * | Gastroent | RA | Y | 90 | Healthy | μ = 44 | * | Endoscopy | Propofol | IV | Propofol (0.6 |
| 2 | Vargo JJ, | 2002 | Gastroen | Abs | Gastroent | RS | C | 537892 | ASA 1-4 | * | M | Colonoscopy | Propofol | IV | * |
| **Propofol vs benzodiazepines+opioids** | | | | | | | | | | | | | | | |
| 1 | Kongkam | 2004 | Non-anes | Abs | Gastroent | RA | Y | 75 | * | μ = 58 | * | ERCP (endo | Propofol | IV (contin | Propofol (μ = |
| 2 | Sipe BW, | 2002 | Propofol | * | Gastroent | RA | Y | 80 | ASA 1-2 | μ = 53 | * | Endoscopy | Propofol | IV | Propofol (μ = |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 3 | Ulmer BJ | 2003 | Propofol | * | Gastroent | RA | Y | 100 | * | * | * | Colonoscopy | Propofol | IV | Propofol (μ = |
| 4 | Vargo JJ. | 2002 | Gastroen | * | Gastroent | RA | Y | 75 | ASA 1-3 | μ = 55 | * | ERCP (endo | Propofol | IV | Propofol (loac |

**Propofol+opioids vs benzodiazepines+opioids**

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Koshy G. | 2000 | Propofol | * | Gastroent | NR | Y | 274 | ASA 1-4 | μ = 59 | M | Colonoscopy | Propofol+ | IV | 20-120 mg pr |

| Intvn #1 | Intvn #2 | Sedation Outcomes | Analgesia Outcomes | Physiologic Outcomes | Complications/ Side Effects |
|---|---|---|---|---|---|
| Propofol admi | Propofol admi | * | * | * | Cardiolpulmonary complications (adjust |
| Propofol (adm | * | Time to recovery of normal neuro | * | $PO_2$ desaturation < 85% | Pain at injection site (28% of pts) |
| Propofol | Non-Propofol | * | * | * | Cardiovascular complications (odds rati |
| Propofol | * | * | * | $SaO_2$ < 90% (3.6% of A | Emergency interventions/jaw thrust man |
| Propofol (adm | * | * | * | SaO2 < 90% (2.0% of pa | Emergency interventions/jaw thrust man |
| Propofol (adm | * | * | * | $SaO_2$ (< 90% = 1.7% of | * |
| Propofol | * | * | * | $SaO_2$ (< 90% = 0.83%; < | * |
| Propofol | * | * | * | * | Assisted ventilation required (0.14% of |
| Propofol | * | * | * | O2 saturation of < 90%; | Restlessness (0.1% of patients; 2/2000) |
| Propofol | * | * | * | $SpO_2$ (< 90% = 6.5% of | Required oxygen via nasal cannula (7.2 |
| Propofol (adm | * | * | * | Prolonged apnea, hypoxe | Laryngospasm (0.02% of pts) |
| Propofol | * | * | * | $O_2$ saturation < 90% (3% | Recall of procedure (0.6%) |
| Propofol+mid | * | * | * | $O_2$ saturation (< 90% 9% | * |
| Propofol+peth | * | * | * | $O_2$ saturation (mean low | * |
| Propofol | Midazolam | Level of sedation (deeper, p < 0.0 | * | $O_2$ saturation (< 90%; 92 | Nausea (13% vs 9%), discomfort (VAS; |
| Propofol | Standard seda | * | * | * | Cardiopulmonary complications (adjust |
| Propofol (adm | Midazolam+n | * | * | $O_2$ saturation (< 90%; 14 | * |
| Propofol (adm | Midazolam+n | Time to sedation ($\mu$ = 2.1 vs 7.0 m | Pain (at discharge, 10% | * | * |

| | | | | |
|---|---|---|---|---|
| Propofol (adm | Midazolam+fe | Time to sedation ($\mu$ = 2.1 vs 6.1 m | * | $O_2$ desaturation (requirin * |
| Propofol (adm | Midazolam+m | * | * | $O_2$ saturation (< 90%; 36 Discomfort (VAS; 6.3 vd 8.7), gagging ( |
| Propofol+fent | Midazolam+m | Deeper level of sedation (1.84 tim | * | $O_2$ saturation <90% (7.3 * |