Title of Systematic Review Protocol
A systematic review contrasting the administration of propofol for sedation of non-mechanically ventilated patients in non-critical care areas by anesthesia providers to that of non-anesthesia trained healthcare providers

Center conducting review
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March 2011

Expected Completion date
November 2011

Review Questions/Objectives
This systematic review seeks to synthesize the best available evidence on the administration of propofol for sedation by anesthesia providers and non-anesthesia trained providers of non-mechanically ventilated patients in non-critical care settings.
**Background**

Administration of propofol for sedation by non-anesthesia trained providers is clouded in controversy. Customarily, sedation for outpatient procedures has been performed using a benzodiazepine and opioid combination. While the benzodiazepine and opioid combination remains the most frequent choice, the use of propofol for sedation is increasing. The use of sedation has been especially useful for gastrointestinal endoscopic procedures. In 2008, Benson et al. looked at the sedation practices for endoscopic procedures in both developed and developing countries, and found that a benzodiazepine/opioid combination is the preferred method, but that propofol use was on the increase. There was no significant difference in sedation practices across developed and developing countries. Heuss et al. noted that in Switzerland, 43% of the endoscopists had used propofol, with 81% of those giving the drug without an anesthesia provider present. In 2006, the European Society of Gastrointestinal Endoscopy, conducted a survey of its members around Europe, the Mediterranean area, and the Middle East, reporting that in the majority of the countries the endoscopist or nurse was administering the sedation. While many different drugs were being used, they reported that propofol use was increasing. In the United States, a 2006 survey of members in the American College of Gastroenterologists, indicated that almost three quarters of physicians used a benzodiazepine/opioid combination for sedation, with the rest using propofol as the primary agent. The survey further denoted that an anesthesia provider was present in 27.8% of all endoscopic procedures. Due to the fact that the percentage of cases in which propofol was used closely resembled the percentage of cases in which an anesthesia provider was involved, may indicate that when propofol was used, an anesthesia provider was administering the propofol. In the United States laws regarding who may administer propofol for sedation varies, with some states allowing any registered nurse to administer propofol, while others restrict its use to only certified registered nurse anesthetists (CRNA) who are specifically trained in anesthesia, and the use of anesthetic agents. This limitation by some states, coupled with the increased cost of an anesthesia provider administering propofol, the longer recovery times, and slower turnover times using other agents, in the competitive United States healthcare system, has brought fuel to the debate regarding who should be allowed to use propofol for sedation, along with a search for alternatives.

Propofol, originally developed and marketed as an agent for induction and maintenance of general anesthesia, has become one of the drugs of choice in gastrointestinal endoscopy units, cardiac catheterization units, emergency rooms, and radiology for conscious sedation in outpatient procedures due to its properties as an ultra-short acting agent. The rapid response to sedation is similar to the intravenous barbiturates, and benzodiazepines, however, recovery is quicker, with patients able to ambulate earlier. Patients also report a subjective feeling of wellbeing and a decreased incidence of postoperative nausea and vomiting. According to the package insert propofol can also be used in monitored anesthesia care (MAC) for sedation during diagnostic procedures, as well as sedation in intubated, mechanically ventilated adult patients in intensive care units.
In many of these environments individuals not formally trained in the use of general anesthesia are administering propofol. Often the individual dispensing the propofol is a registered nurse without training in anesthesia techniques or agents, and supervised by non-anesthesia trained physicians, such as gastroenterologists, cardiologists, radiologists, or emergency room physicians.

Much of the questions regarding propofol administration resides around the off-label use of propofol for various procedures in non-mechanically ventilated patients in a variety of settings outside of critical care units. The United States Federal Drug Administration (FDA) considers propofol to be an anesthetic agent. Current package labeling in the “Dosing and Administration” guidelines approved by the FDA for propofol indicates that only individuals trained in administering general anesthesia, and not directly involved with the procedure should administer propofol. Administering propofol to a non-mechanically ventilated patient by an individual not trained in anesthesia breaches the guidelines set forth by the FDA. Due to its pharmacokinetic properties, propofol is a short acting hypnotic agent. Using a two-compartment kinetic model, it has a distribution half-life of 2 – 8 minutes and a 1 – 3 hour elimination half-life. Propofol has both a hepatic and extrahepatic clearance profile, and is rapidly metabolized through conjugation with glucuronide and sulphate, then eliminated by the kidneys. Propofol acts upon gamma aminobutyric acid (GABA) receptors that activate cellular membrane chloride channels resulting in hyperpolarization of the neuron with resulting sedation, amnesia, and hypnosis. Onset is rapid, occurring within seconds of intravenous administration. There are dose dependent depressive effects upon the respiratory and cardiovascular systems, which can produce respiratory depression, apnea, and hypotension. The use of propofol in non-critical care settings such as gastrointestinal endoscopy units, emergency rooms, cardiac catheterization units, and radiology has become increasingly popular. Patients undergoing procedures in these settings prefer and usually require sedation. The use of opioids and benzodiazepines have traditionally been used to provide the necessary decreased anxiety and comfort for various procedures in which general anesthesia is unnecessary; however, the use of these combinations of drugs tends to result in complications and adverse side effects such as nausea, vomiting, respiratory depression, delayed onset, and extended recovery profiles. Propofol, with its short acting properties and increased patient satisfaction, allows for quicker turnover and more procedures to be performed versus traditional procedural sedation using opioids and benzodiazepines.

Within the United States, the American Society of Anesthesiologists (ASA), and the American Association of Nurse Anesthetists (AANA) jointly issued a position statement endorsing the FDA approved guideline for propofol administration contending that not doing so could place patient safety in jeopardy. The assertion is that sedation lies along a continuum that may change rapidly, with a patient quickly moving from moderate sedation to deep sedation and even general anesthesia with subsequent loss of airway control and reflexes along with profound changes in hemodynamic stability often seen with general anesthesia. The anesthesia professional is trained in all aspects of airway management and administration of general anesthesia, and can therefore, recognize and intervene appropriately for the patient’s safety.
These organizations maintain that non-anesthesia trained healthcare providers have not received the requisite training and use of general anesthetic agents such as propofol; training they feel is vital to patient safety.

The American College of Gastroenterology (ACG), American Gastroenterological Association (AGA) and American Society for Gastrointestinal Endoscopy (ASGE), in turn, jointly issued a position statement indicating that propofol can be safely administered by non-anesthesia trained physicians and registered nurses who have received adequate training in the administration of propofol. The statement further states that personnel should be capable of rescuing the patient from general anesthesia and severe respiratory depression. These organizations maintain that propofol has been successfully administered by non-anesthesia trained personnel with few adverse reactions to patients. Furthermore, they assert patient satisfaction is increased, and costs are lowered when anesthesia services are not required. In 2005, ACG petitioned the FDA to amend the propofol label warning regarding propofol administration and allowing non-anesthesia trained professionals to administer propofol. In August 2010, the FDA denied the ACG petition to change the labeling of propofol.

The World Organization of Digestive Endoscopy (OMED), Hellenic Society of Gastroenterology (HSG), United European Gastroenterology Federation and the European Society of Gastrointestinal Endoscopy (ESGE), funded a conference of experts in anesthesiology, gastroenterology, and medical jurisprudence from 12 countries and four continents to look at the agreements and divergence on various positions regarding sedation in endoscopy procedures. The consensus of the conference was that gastroenterologists and nurses who had received appropriate training in the use of propofol for sedation could safely administer propofol for sedation in low-risk patients. The experts also agreed that these non-anesthesia trained providers would require didactic teaching in the pharmacology, adverse effects, monitoring, and management of complications of sedation, supervised patient care, and simulation training in critical incidents related to endoscopy and sedation.

Prior to the commencement of the review, a search of Cochrane Library of Systematic Reviews, JBI Library of Systematic Reviews, DARE database, and MEDLINE was performed. The Cochrane Library of Systematic Reviews revealed that in 2008, a systematic review had as a secondary objective, the synthesis of studies contrasting the administration of propofol by anesthesiologists to that of non-anesthesiologists. A MEDLINE search found that in 2006 Harrington did a narrative review looking at the current evidence regarding the safety of nurse administered propofol for sedation. No systematic review of the proposed topic was located.
For the purpose of this review we’ll use the following definitions:

Safety is defined as the ability to prevent an untoward or adverse physiologic events, or should an adverse event happen, to expeditiously correct the event.

Non-anesthesia trained healthcare providers are defined as nurses and physicians without formal anesthesia training in an accredited or certified anesthesia training program.

Anesthesia providers are defined as nurses, physicians, and anesthesiologist assistants who have received formal anesthesia training in an accredited or certified anesthesia training program.

Non-critical care situations are defined as those situations outside of a designated intensive care or critical care unit. (i.e., an endoscopy unit or cardiac catheterization laboratory)

Propofol administration for sedation refers to the use of propofol as the primary pharmacological agent for inducing a state of calm and restfulness.

Inclusion Criteria

Types of participants
This systematic review will consider non-anesthesia trained health care providers, and anesthesia providers administering propofol for sedation in non-critical care situations on (all adult and paediatric) patients who are not mechanically ventilated while undergoing gastrointestinal endoscopy, cardiac catheterization, and procedural sedation for emergency room and radiology procedures.

Types of interventions
The intervention of interest is the use of propofol sedation administered by non-anesthesia trained health care providers, and formally trained anesthesia providers for patients in non-critical care environments who were not mechanically ventilated while undergoing gastrointestinal endoscopies, cardiac catheterization, and procedural sedation for emergency room and radiology procedures.
Types of outcome measures
This systematic review will consider as outcomes: procedure time, return to baseline functioning, postoperative recovery time, mean amount of propofol administered, patient satisfaction, incidence of adverse hemodynamic and respiratory events, unplanned admission to hospital, and death of patients undergoing gastrointestinal endoscopy, cardiac catheterization, or procedural sedation for emergency room and radiology procedures while administering propofol for sedation. Adverse hemodynamic and respiratory events that will be considered are respiratory arrest, airway obstruction, hypoxia requiring intervention, hypotension, bradycardia, and arrhythmias.

Types of studies
The review will consider any randomized controlled trial, cohort studies, comparative case-control studies and other comparative studies and case series/report studies involving the administration of propofol for sedation of non-mechanically ventilated patients. The setting for these studies will be limited to non-critical care environments, such as endoscopy, cardiac catheterization, or procedural sedation for emergency room and radiology procedures.

Search strategy
The search strategy aims to find both published and unpublished studies and papers. The search will be limited to English language reports beginning with the commercial use of propofol in 1989 through 2011. An initial limited search of MEDLINE, OVID, and CINAHL will be undertaken followed by an analysis of the text words contained in the title and abstract and the index terms used to describe the article. A second search using all identified keywords and index terms will then be undertaken across all included databases. Thirdly, the reference list of all identified reports and articles will be searched for additional studies.

The databases to be searched include:
CINAHL
MEDLINE
Nursing@Ovid
PubMed
Elsevier Science Direct
EMBASE

The search for unpublished studies will include:
Mednar
Proquest

Initial keywords to be used will include:
Nurse administered propofol sedation (NAPS)
Registered nurse sedation
Conscious sedation
Assessment of methodological quality
Papers selected for retrieval will be assessed independently by two reviewers, using standardized appraisal instruments from the Joanna Briggs Institute (JBI) System for the Unified Management, Assessment and Review of Information (SUMARI) package (see Appendix I). Any disagreements that arise between reviews will be resolved through discussion, or if necessary with a third reviewer.

Data extraction
Data will be extracted from papers included in the review using standardized data extraction tools from the Joanna Briggs Institute System for the Unified Management, Assessment and Review of Information package (see Appendix II).

Data synthesis
If appropriate, a meta-analysis of quantitative results will be performed (using Mastari module of JBI SUMARI software). If meta-analysis is not appropriate, a narrative summary of the results will be reported.

Potential conflict of interest
The primary reviewer is a certified registered nurse anesthetist (CRNA) and member of the American Association of Nurse Anesthetists.

The secondary reviewer is a certified gastroenterology registered nurse and member of the Society of Gastroenterology Nurses & Associates, Inc., and the Society of International Gastroenterological Nurses and Endoscopy Associates.
References


### JBI Critical Appraisal Checklist for Experimental Studies

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<th>Question</th>
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<th>No</th>
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<tr>
<td>1. Was the assignment to treatment groups truly random?</td>
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<td>2. Were participants blinded to treatment allocation?</td>
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<td>3. Was allocation to treatment groups concealed from the allocator?</td>
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<td>4. Were the outcomes of people who withdrew described and included in the analysis?</td>
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<tr>
<td>5. Were those assessing outcomes blind to the treatment allocation?</td>
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<td>6. Were the control and treatment groups comparable at entry?</td>
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<td>7. Were groups treated identically other than for the named interventions?</td>
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<td>8. Were outcomes measured in the same way for all groups?</td>
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<td>9. Were outcomes measured in a reliable way?</td>
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<td>10. Was appropriate statistical analysis used?</td>
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**Overall appraisal:**
- Include [ ]
- Exclude [ ]
- Seek further info. [ ]

**Comments (Including reasons for exclusion):**

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# JBI Critical Appraisal Checklist for Comparable Cohort/Case Control

**Reviewer** ______________________  **Date** ____________  **Author** ______________________  **Year** ____________  **Record Number** ______

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<td>1. Is sample representative of patients in the population as a whole?</td>
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<td>2. Are the patients at a similar point in the course of their condition/illness?</td>
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<td>3. Has bias been minimised in relation to selection of cases and of controls?</td>
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<td>4. Are confounding factors identified and strategies to deal with them stated?</td>
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<td>5. Are outcomes assessed using objective criteria?</td>
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<td>6. Was follow up carried out over a sufficient time period?</td>
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<td>9. Was appropriate statistical analysis used?</td>
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**Overall appraisal:**  Include [ ]  Exclude [ ]  Seek further info [ ]

**Comments (Including reason for exclusion):**

________________________________________________________________________
JBI Critical Appraisal Checklist for Descriptive/Case Series

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<td>2. Were the criteria for inclusion in the sample clearly defined?</td>
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<td>3. Were confounding factors identified and strategies to deal with them stated?</td>
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<td>4. Were outcomes assessed using objective criteria?</td>
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<td>5. If comparisons are being made, was there sufficient descriptions of the groups?</td>
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Overall appraisal:  Include [ ] Exclude [ ] Seek further info [ ]

Comments (Including reason for exclusion)

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Appendix II: JBI Data extraction tool

JBI Data Extraction Form for Experimental/Observational Studies

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<td>Journal</td>
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**Study Method**

- RCT
- Quasi-RCT
- Longitudinal
- Retrospective
- Observational
- Other

**Participants**

- Setting
- Population
- Sample size

**Interventions**

- Intervention 1
- Intervention 2
- Intervention 3

**Clinical outcome measures**

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**Study results**

**Dichotomous data**

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**Continuous data**

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**Authors Conclusions**

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**Comments**

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