For laboring mothers (P), does the use of nitrous oxide (I) for pain management during labor provide a higher level of safety (O) for mother and fetus compared to the use of an epidural (C)?

The purpose of this translational research study is to examine the overall safety of nitrous oxide as an analgesic in comparison to the use of an epidural in laboring mothers and fetuses.

According to Anim-Somah (2011) 58% of mothers in the United States use an epidural as their main method of pain control; however, there is a less invasive method of pain control that could be used in the U.S. “Entonox”, a premixed solution of 50% nitrous oxide and 50% oxygen is used in many countries, including Canada, Australia, New Zealand, Brazil, Iran, and China (Rossen, 2002). The American College of Nurse Midwives (ACNM) recommends that women have access to nitrous oxide in the U.S. and that research should be continued to facilitate the use of nitrous oxide as a labor analgesic. A scavenging system is required for excess gas in the environment to meet the recommended standard set forth by the National Institute for Occupational Safety and Health (1994) and to reduce occupational reproductive health risks for female healthcare workers exposed to leftover gas.

Nitrous oxide:
- Self-administered via a face mask
- Dissipates in five minutes of the woman ceasing to breathe the drug (ACNM, 2009)
- Passes across the placental barrier and is rapidly sequestered through the mother's lungs; maternal hypoxic episodes can occur by hyperventilation during contractions, though the increased oxygen in the inhaled drug appears to offset the hypoxia (Reynolds, 2009)
- Most common side effects from nitrous oxide used in labor are nausea, vomiting, dizziness, dry mouth, drowsiness (Rossen, 2002)

Epidural:
- Administered into fatty tissue surrounding nerve roots in the spine (Henry, Hockenberry, Lowdermilk, Wilson, 2014)
- Typical drugs used are fentanyl and either bupivacaine, levobupivacaine, or ropivacaine (Reynolds, 2009)
- Increased risk of instrumental delivery is statistically significant side effect (Anim-Somah, Smyth, & James, 2011)
- Potential to 1) impair breastfeeding (Reynolds, 2009, Tamagawa, 2012), 2) cause loss of short-term variability in fetal heart tones, fetal decelerations, fetal bradycardia (Reynolds, 2006), 3) cause loss of bear down ability which could increase instrumentation use (Tamagawa, 2012, Anim-Somah, et al., 2011), 4) reduce in blood pressure (of 20%, or more) that could result in a “clinically significant” decrease in placental perfusion and fetal oxygen delivery (Anim-Somah, et al., 2011)
- Short-term episodes of fetal bradycardia irrelevant to fetal outcome, if unattained to decreased placental perfusion due to hypotonic uterus, vasovagal constriction, or maternal hypotension (Reynolds, 2009).

Compared to an epidural, nitrous oxide has inherent safety characteristics due to the nature of its administration (face mask vs. puncture in the epidural space). An epidural places a patient at risk for many side effects and adverse effects: infection, wronful puncture, catheter-acquired urinary tract infection (due to urinary catheter placement), and falls (due to change in lower limb motor sensation).

This is a translational research study utilizing a literature review design. All authors have completed the National Institute of Health (NIH) Office of Extramural Research’s online training, “Protecting Human Research Participants”, this semester and hold current certification. Databases searched were PubMed, CINHAL, Cochrane, and Medline using key words including “nitrous oxide”, “Entonox”, “safety”, “labor and delivery”. Over 300 articles were found and approximately 50 articles were appraised.

Strengths & Limitations
Nitrous oxide may be a clinically significant and potentially safer alternative to labor analgesia than an epidural. Nitrous oxide (it is a less invasive method of labor analgesia than an epidural). An epidural is administered via bolus injection; continuous infusion, or with a patient-controlled pump into the epidural canal at the lower region of the spine where the nerves lie that transmit pain signals from the uterus and birth canal. There are specific side effects of the epidural due to its invasive nature and concentration of medication. The side effects are: sudden onset of hypotension (could decrease perfusion and oxygen to fetus), uterine retention (requires insertion of a urinary catheter), decreased sensations, and uterine contractility (mother at increased risk for fetal, accidental puncture, pain, increase on course of labor, and possible effects to fetus (Anim-Somah, et al., 2011).

Rossen (2011) notes that safe practice of nitrous oxide requires that it be self-administered by a mask or mouthpiece and that the patient be given the device without assistance; the concentration of nitrous oxide should not exceed 50%, and that the volume of nitrous oxide given to the patient should not exceed 1.5 L/min. The equipment to capture the exhaling gas, the majority of studies on nitrous oxide efficacy were done outside the U.S., thus, the literature review relies heavily on those sources.

The review of literature supports the safety and efficacy of nitrous oxide as an analgesic for laboring mothers, though more research is needed to determine if it is safer compared to epidural analgesia.

Strengths of Findings:
- Five individual research studies (three randomized controlled trials, a randomized clinical trial, and a prospective survey) aimed to determine the efficacy and safety of nitrous oxide. They each published findings in which there were no significant statistical differences or outcomes. Variables evaluated in the study include: maternal pain levels, blood pressure, oxygen saturation, duration of labor, and Apgar scores (one minute and five minutes), as well as maternal side effects. Three of the randomized controlled trials had a significant reduction in pain and labor duration in comparison to the oxygen control group. It was noted that the common side effects of nitrous oxide involved dizziness, nausea, drowsiness, and dry mouth. The prospective survey by Onody (2008), evaluated 25,828 subjects over a four-year period and confirmed the pharmacological safety of nitrous oxide in 191 hospitals. In addition, two systematic reviews (Rossen and Roesen) also determined the efficacy and safety of nitrous oxide. Of these, Rossen could be considered a landmark study.

A comprehensive review by Anim-Somah (2011), determined from 38 studies that epidural analgesia is a more invasive method of pain control and requires more interventions for proper use. In Khadem (2013), there was no significant statistical difference between the two interventions in terms of safety.

Limitations of Findings:
- Most studies gathered for our literature review were conducted by foreign health services and institutions, which may be a result of epidural analgesia during the randomized method of pain relief to laboring mothers in the United States. Additionally, there is a limited number of clinical comparisons between epidural analgesia and nitrous oxide, especially with regard to safety. More current research is needed to determine the position of efficacy and safety of nitrous oxide in relation to epidural analgesia.

Conclusion & Recommendations
This translational research study analyzed the safety of nitrous oxide when compared to the use of an epidural for analgesia in the laboring mother and fetus. The literature suggests that nitrous oxide does provide pain relief during labor and delivery. However, the side effects of an epidural are potentially more severe to both mother and fetus. The literature also examined side effects in the laboring mother that included hypotension, loss of maternal blood flow, loss of feeling in the lower extremities preventing ambulation. Although nitrous oxide may not be as effective as pain relief as an epidural, the literature suggests that the side effects for the laboring mother are minor and include nausea, vomiting, agitation, diziness, drowsiness, and euphoria. More extensive research needs to be conducted to further evaluate the safety of nitrous oxide in labor for mothers and fetuses when compared to the epidural.

After reviewing the research, it is proposed that further research is necessary to better understand the benefits and risks for nitrous oxide. Research would benefit the patient’s understanding of the differences nitrous oxide and epidural analgesia offer. Education regarding pain management options for laboring mothers and families could be implemented during the prenatal period. Providing information regarding different types of pain management for laboring mothers would allow mothers to feel more as part of their laboring experience. Throughout the literature, several studies indicated the use of nitrous oxide outside of the United States. Further research is recommended focusing on nitrous oxide use in the United States.