

## Paramedic CAT (Critically Appraised Topic) Worksheet

**Title:** Safety and effectiveness of the use of Nitrous Oxide as analgesia for Primary Care Paramedics in the prehospital setting.

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**2<sup>nd</sup> Party Appraiser:**

**Clinical Scenario:** A BLS crew in a rural community of Newfoundland and Labrador without the support of ALS respond for a patient who has fallen from a ladder and is suspected by the witness to have broken the tibia and fibula bones of his left leg. The patient is clearly suffering an excruciating level of pain and the anticipated transport time to the local emergency department is one hour. As it stands there exists no form of analgesia in the BLS protocols in NL, if Nitrous Oxide were an available and sanctioned medication for the BLS provider could this treatment benefit their patient and ease his comfort in a safe and effective manner?

**PICO (Population – Intervention – Comparison – Outcome) Question:**

A prognostic review (no comparison): Is it safe or effective for the BLS responders to use Nitrous Oxide as a treatment of analgesia in patient care?

**Search Strategy:**

(emergency medical services[TIAB] OR prehospital OR paramedic OR ambulance OR "emergency medical technician") AND (Nitrogen oxide OR Nitrous oxide OR N2O OR entonox[tiab])

**Search Outcome:**

137 results

### Relevant Papers:

Author, Date	Population: Sample Characteristics	Design (LOE)	Outcomes	Results	Strengths/ Weaknesses
Louis Ducassé, MD, 2013	During a one-year period 648 patients were screened for inclusion criteria of which 60 patients were randomly assigned to treatment. There were no statistical differences in age. The median age was 34 years, 66% male, and an initial median pain score of 6/10 prior to treatment.	Prospective, randomized, multicenter, double-blind trial.  LOE 1	This research was an evaluation of the efficacy of nitrous oxide and oxygen used as a treatment in the prehospital setting.  -Provider satisfaction -Patient Satisfaction -Efficacy of	At T15 (15 minutes), 67% of the patients in the N2O group had an NRS (numeric rating scale 1-10) score of 3 or lower versus 27% of those in the MA group (delta = 40%, 95% confidence interval [CI] = 17% to 63%; p < 0.001). The median pain scores	This study has a lot of strengths in that it was a randomized, multicenter, double blind trial and a great degree of consideration in patient ethics. The researchers concluded great success in the efficacy of N2O mixed with O2 to reducing patient pain and suffering with little to no adverse affects. Some patients reported experiencing nausea but this

			analgesia -Adverse Effects	were lower in the N2O group at T15, 2 (IQR = 1 to 4) versus 5 (IQR = 3 to 6). There was a difference at 5 minutes that persisted at all subsequent time points. Four patients (one in the N2O group) experienced adverse events (nausea) during the protocol.	could not be directly attributed to the N2O and the effects of N2O were fully reversible within 5 minutes of removing the gas.  The only weakness I noted was that all 60 patients evaluated were trauma patients and such this study did not evaluate its use in other patient emergency settings such as abdominal pain, back pain or a migraine headache. The study also did not evaluate the safety of its use as a treatment for analgesia which is part of my PICO question however it did state that the study reinforces the ongoing use of N2O with clear protocols, training, supervision and revision of a medical director. Lastly this trial was performed by 'fire service nurses', which indicates to me they would have a university degree in nursing whereas I would like to know it's efficacy and safety being delivered by primary care paramedics with one to two years of training and education.
S C Faddy, 2005	Following a literature search of 1585 citations matching search criteria 33 studies described relevance potential to their systematic review. Of the 33, 12 studies satisfied all the reviewers' subject and methodology criteria. These 12 studies included a wide variety of patient populations	Systematic review with use of Meta View (Review Manager version 4.1 for Windows, Oxford, England; the Cochrane Collaboration, 2000). In the end 12	Purpose of the study was to determine if a 'lay responder', a person with training below that of an Emergency Medical Technician could safely treat a patient with N2O for pain management. Outcomes	<b>Adverse Events:</b> Nausea: Test for overall effect: $z = 0.92$ ( $p = 0.36$ )  Vomiting: Test for overall effect: $z = 0.74$ ( $p = 0.46$ )  Dizziness: Test for overall effect: $z = 0.67$ ( $p = 0.50$ )	There are several weaknesses to this systematic review, all of the studies reviewed have low sample sizes and there also exists population bias in that there is a wide range of ages and lack of concern regarding medical conditions or comorbidities, which may affect the results in the studies. The Authors also did not exclude studies of poor

	<p>representing children, adolescents and adult patients experiencing a broad spectrum of pain sources, which mimicked injuries and conditions similar to that of the prehospital setting.</p>	<p>randomised controlled studies comparing 50% N2O with either a placebo or another form of analgesia were analyzed.</p> <p>LOE 2</p>	<p>analyzed were:</p> <ul style="list-style-type: none"> <li>-Adverse events of N2O compared with placebo or conventional analgesia</li> <li>-Recovery time</li> <li>-Need for additional analgesia medication</li> </ul>	<p>Drowsiness: Test for overall effect: <math>z = 0.23</math> (<math>p = 0.82</math>)</p> <p>Headache: Test for overall effect: <math>z = 0.28</math> (<math>p = 0.78</math>)</p> <p><b>Recovery Time:</b> See table 3 below (copied from S C Faddy, 2005)</p> <p><b>Need for additional analgesia medication:</b> See table 4 below (copied from S C Faddy, 2005)</p>	<p>methodological quality (non-randomized control). It should also be noted that this review is also over a decade old and many of the studies included in it range from 1975-2001 which seems not ideal.</p> <p>The authors themselves included a statement regarding some of the weaknesses: " A potential weakness of this review is the methodological quality of the primary studies. As shown in table 2, only seven of the 12 randomised studies included in this review gave adequate information on the method of randomisation. Five of these studies gave information on allocation concealment. Eight studies gave adequate information on the methods of blinding. However, collection of outcome data was complete in nearly all studies."</p>
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**Table 3** Comparison of recovery time of patients receiving 50% nitrous oxide (N<sub>2</sub>O) and patients given placebo or conventional analgesia

Study	No of patients	Study population	Pain source	Recovery time (min)		p value
				50% N <sub>2</sub> O	Control	
50% nitrous oxide v placebo Saunders <i>et al</i> , 1994 <sup>20</sup>	60	Adult	Colonoscopy	32*	36*	Not stated
50% nitrous oxide v conventional medication Forbes and Collins, 2000 <sup>32</sup>	102	Adult	Colonoscopy	30 (30-45)	60 (30-110)	<0.0001
Natini-Gudmarsson <i>et al</i> , 1996 <sup>10</sup>	38	Adult	Colonoscopy	49 (28-148)	83 (29-300)	<0.05
Evans <i>et al</i> , 1995 <sup>1</sup>	30	Children	Fracture reduction	30 (15-60)†	83 (60-150)†	<0.01
Saunders <i>et al</i> , 1994 <sup>20</sup>	59	Adult	Colonoscopy	32*	60*	<0.001
Lindblom <i>et al</i> , 1994 <sup>21</sup>	50	Adult	Colonoscopy	0 (0-5)‡	37.5 (10-75)‡	0.0001

Recovery time stated as median (range) unless stated otherwise: \*median; †mean (range); ‡median (interquartile range).

**Table 4** Need for additional medication in patients receiving 50% nitrous oxide (N<sub>2</sub>O) compared with placebo or conventional analgesia

Study	No of patients	Study population	Pain source	Additional medication (n (%))		p value
				50% N <sub>2</sub> O	Control	
<b>50% nitrous oxide v placebo</b>						
Triner <i>et al</i> , 1999 <sup>19</sup>	22	Adult	Migraine headache	2 (20)	10 (83)	0.008
Saunders <i>et al</i> , 1994 <sup>20</sup>	60	Adult	Colonoscopy	3 (10)	13 (43)	0.007
<b>50% nitrous oxide v conventional medication</b>						
Natini-Gudmarsson <i>et al</i> , 1996 <sup>15</sup>	38	Adult	Colonoscopy	0 (0)	1 (5)	0.31
Saunders <i>et al</i> , 1994 <sup>20</sup>	59	Adult	Colonoscopy	3 (10)	5 (17)	0.47
Lindblom <i>et al</i> , 1994 <sup>21</sup>	50	Adult	Colonoscopy	1 (4)	5 (20)	0.19
Harrison <i>et al</i> , 1987 <sup>22</sup>	70	Adult	Labour	1 (5)	40 (80)	<0.0001

**Comments:** Presented are only two studies of several which at a quick glance support the use of nitrous oxide for analgesia in the prehospital setting. But outside of medical research papers there are also several EMS jurisdictions where nitrous oxide is currently in use and I think there stands a lot to learn about it's efficacy, safety, success and patient outcomes from talking to the medical oversight personnel in those regions. I think it's safe to say that the results are still inconclusive to this question and that more research needs to be done to adequately answer this question.

**Consider:** Undoubtedly there are several factors one must consider when creating, changing or updating local protocols and practitioner practice. In this day and age liabilities are ever more prevalent so one must be vigilant when it comes to making changes in local practitioner protocols and ensuring that the appropriate educational training and practice exist to safely see through a change in protocols. Regardless if the evidence exists to support a change in practice these types of considerations come into play and effect decision-making. Any small change has province wide consequences and as such concerns such as financial feasibility become issues of concern, as one must ensure that all practitioners have the necessary tools, resources and education to keep up to date with changes in practice. There's also the financial cost of purchasing and maintaining the required equipment of such an offered service. It may be deemed too expensive of a product to implement versus another option of analgesia such as IV or IM analgesia considering that all ambulances are already equipped with the necessary administration equipment such as syringes, needles and IV supplies.

**Clinical Bottom Line:** I'm no expert in this field and I would never dare state that the adequate level of clinical research existed to support nitrous oxide, as a safe option of analgesia for the BLS practitioner to provide in patient care however perhaps there's enough evidence to support a conversation with one's local medical director to further evaluate it's potential in patient management.

**References:**

Ducassé, Louis, MD (2013). Nitrous Oxide for Early Analgesia in the Emergency Setting: A Randomized, Double-blind Multicenter Prehospital Trial. *ACADEMIC EMERGENCY MEDICINE* 2013; 20:178–184 © 2013 by the Society for Academic Emergency Medicine

Faddy, S C (2005). A systematic review of the safety of analgesia with 50% nitrous oxide: can lay responders use analgesic gases in the prehospital setting? *Emerg Med J* 2005;22:901–906. doi: 10.1136/emj.2004.020891