



Formation of a National Perinatal Nitrous Oxide Data Registry: The Intrapartum Nitrous Oxide Workgroup I-NOW

RESEARCH

BARBARA ORLANDO 

CRISTINA WOOD 

DEBORAH STEIN 

JESSICA ANDERSON

**Author affiliations can be found in the back matter of this article*



Levy
Library
Press

ABSTRACT

Background: There are a variety of labor analgesic options for parturients, such as intravenous opioids, neuraxial interventions, hydrotherapy, hypnosis, as well as inhaled nitrous oxide (N₂O). Inhaled N₂O has been utilized outside of the United States (U.S.) for decades but has only recently gained popularity in the U.S. as a labor analgesic. There are no current multi-center data registries evaluating N₂O use as a labor analgesic regarding conversion rates, side effects, and delivery outcomes.

Methods: We created the first multi-center N₂O data registry to gather maternal and newborn outcome data from several institutions across the U.S. All centers were required to sign a Memorandum of Understanding (MOU) which stated that at least 80% of all parturients utilizing N₂O for labor would be included in the database. We hypothesized that the data would assist in counseling and consenting parturients regarding incidence of side effects, conversion rates and etiologies, as well as neonatal outcomes. This manuscript demonstrates the steps taken to create the data registry, including institutional enrollment, development of a data collection tool, selection of the data management system and administrator, organization of multiple institutional review boards, delineation of responsibilities and challenges encountered with implementation.

Conclusion: The development of a multi-center data registry was successfully created as we saw a need for a safe data-sharing system to answer mutually determined research questions, and to collect strong data information in order to provide evidenced based data to patients and providers.

CORRESPONDING AUTHOR:

Barbara Orlando

Mount Sinai West and
Morningside Hospitals, US

barbara.orlando@mountsinai.org

KEYWORDS:

Multi-center; nitrous oxide;
labor analgesia; REDCap®;
data registry

TO CITE THIS ARTICLE:

Orlando B, Wood C, Stein D, Anderson J. Formation of a National Perinatal Nitrous Oxide Data Registry: The Intrapartum Nitrous Oxide Workgroup I-NOW. *Journal of Scientific Innovation in Medicine*. 2021; 4(2): 38, pp. 1–4. DOI: <https://doi.org/10.29024/jsim.129>

INTRODUCTION

Close to four million women in the US give birth each year and for most of them pain control during labor is a major concern [1]. Easy access to effective and safe pain management options is essential to provide care for the parturient. Inhaled nitrous oxide (N₂O) has a long history of use in European countries and Australia and is becoming more mainstream in the U.S. [2].

The limited use of N₂O for labor analgesia in the U.S. is likely due to both an increase in popularity of neuraxial analgesia [3] and concerns for the safe delivery of N₂O to the parturient and the staff caring for her. In 2007 utilization of N₂O in the U.S., for labor analgesia, was as low as 1% [4], however, a supporting position statement from the American College of Nurse-Midwives was published in 2010 and the FDA approved a safe delivery system in 2012 that both increased use in the U.S. [5]. While there is anecdotal evidence regarding the safety of N₂O for both mother and baby, as well as its efficacy in reducing pain during labor, there is a paucity of scientific data and no large multi-center N₂O database to further evaluate the evidence. The available data suggests that although N₂O provides minimal analgesia to laboring women, it does help them cope with labor pain [6] and they are just as satisfied with N₂O as they are with neuraxial analgesia [7].

Following this observation, the health care providers at the University of Colorado introduced N₂O into clinical practice as a labor analgesic and this led to the development of the Intrapartum Nitrous Oxide Workgroup (I-NOW) and ultimately the creation of a novel multi-center perinatal N₂O data registry. The focus of this manuscript involves the development of a novel multi-center workgroups and data registry.

METHODS

In November 2014, the University of Colorado Hospital implemented N₂O as a labor analgesic and initiated discussions with other institutions also offering N₂O in labor, which resulted in the creation of the Intrapartum Nitrous Oxide Workgroup (I-NOW). I-NOW included nurse-midwives, anesthesiologists, obstetricians, obstetric nurses, and family medicine physicians from the University of Colorado (CU), University of New Mexico (UNM), Vanderbilt University, Mount Sinai West (Icahn School of Medicine), University of North Carolina (UNC), and Brigham and Women's Hospital. Monthly virtual meetings were conducted to establish workgroup structure, research interests and development of a data collection tool, IRB protocol and memorandums of understanding (MOU), see **Table 1**. MOU required each institution to include at least 80% of all laboring parturients utilizing N₂O for labor analgesia.

Table 1 Steps for the formation of a Multi-Institutional Data Registry.

STEPS FOR THE FORMATION OF A MULTI-INSTITUTIONAL DATA REGISTRY
Find group of -interested collaborators
Budget plan
Identify the data relevant to the study
Find safe, secure data repository
Develop a data collection tool
Sign Memorandums of Understanding between institutions
Complete Institutional Review Board approval (each institution goes through own IRB including informed consent approval)
Collect and enter data
Monthly meeting with one representative of each group to assess issues encountered and progress made
Continue collaborations for scholarship/ dissemination of research questions

The data collection tool was developed and housed at CU following input from all participating institutions and included 147 data points per patient (See questionnaire attached: addendum). There were many reiterations of this tool over a 10-month period. A statistician reviewed the data collection tool and it was pre-tested at CU. Data collection was audited every 6 months for data completeness and each institution only had access to their own data. A data administrator,

housed at CU, was responsible for all data management and available to assist all institutions with data entry and access issues. The goal was to obtain data on 8000 mother/neonate dyads to evaluate after 3 years.

After completion of all institutional MOUs and approval of each institutional IRB, each institution obtained access and training for the REDCap® database. I-NOW chose the REDCap® Data Management System as the data repository for the project due to programming expertise, data management, branching logic and extensive formatting options. A system within REDCap® allows for practice data entry prior to full implementation; this helps with discovering missed items or missed data point. REDCap® provides automated export procedures for unified data downloads to Excel and common statistical packages (SPSS; SAS; Stata, R). The I-NOW reviewed and approved all research requests and released only de-identified data to the requesting institution. This novel database was titled the National Perinatal Nitrous Oxide Data Registry.

Industry support was identified and secured from Porter Instruments, a division of Parker Industries and U.S. supplier of the Nitronox® machine used to administer perinatal N₂O at CU. A Sponsorship Agreement was vetted through CU's legal team and \$5000 was secured as support for the data administrator. Porter Instruments has no rights to involvement in the dissemination of any research related to the data registry. Originally, participating institutions had no funding for research assistants, however, four institutions have secured funding for data collection and entry.

RESULTS

The database collected almost 2000 parturients over 3 years. Unfortunately, two institutions (New Mexico and Brigham) withdrew due to inability to meet MOU requirements regarding data entry. Several publications have already resulted from this novel data registry and include a data analysis of the Satisfaction, Adverse Effects, and Predictors of Conversion to Neuraxial Analgesia [8] and nitrous oxide use for labor analgesia at high and low-altitude institutions [9]. This I-Now group creation was presented at a few national meetings [10–12].

These publications and presentations have contributed uniquely to field of N₂O use in labor with this large database, especially in areas that had not been well studied in the past such as maternal side effects and satisfaction, baby safety, and impact of high altitude on N₂O usage.

CONCLUSION

Clinicians from six academic institutions throughout the U.S. formed the National Perinatal Nitrous Oxide Data Registry to gather clinical data to better understand the best-use, benefits, risks, and side effects of perinatal N₂O use for labor analgesia.

Today's technical advancements, including conference calls, emails, meeting schedulers and electronic data management systems, have made it possible for clinicians to create a large data sharing system while being located throughout the country.

The process of development of a multicenter data registry is feasible for clinical experts who see the use of a systematic, safe data-sharing system to answer research questions not otherwise answerable without a large, more diverse data set, but who have minimal research funding. These projects take a great deal of time, dedication and commitment on the part of the participants to initiate and maintain, but allow for a tremendous amount of data collection and information that might be used to better counsel and care for our patients.

ADDITIONAL FILE

The additional file for this article can be found as follows:

- **Nitrous Oxide Data Collection Instrument.** RedCap questionnaire. DOI: <https://doi.org/10.29024/jsim.129.s1>

FUNDING INFORMATION

Porter Instrument Division (Parker Hannafin, Hatfield, PA).

COMPETING INTERESTS

The authors have no competing interests to declare.

AUTHOR AFFILIATIONS

Barbara Orlando  orcid.org/0000-0002-0260-7696
Mount Sinai West and Morningside Hospitals, US

Cristina Wood  orcid.org/0000-0002-1031-7840
University of Colorado School of Medicine, US

Deborah Stein  orcid.org/0000-0001-6484-2459
Mount Sinai West and Morningside Hospitals, US

Jessica Anderson
University of Colorado Anschutz Medical Campus, US

REFERENCES

1. **WHO Reproductive Health Library.** *WHO recommendation on relaxation techniques for pain management during labour (February 2018)*. The WHO Reproductive Health Library; Geneva: World Health Organization.
2. **Collins MR, Starr SA, Bishop JT, Baysinger C.** Nitrous oxide for labor analgesia: expanding analgesic options for women in the United States. *Rev Obstet Gynecol.* 2012; 5(3–4): e126–131.
3. **Rooks JP.** Nitrous oxide for pain in labor—why not in the United States? *Birth.* 2007; 34(1): 3–5. DOI: <https://doi.org/10.1111/j.1523-536X.2006.00150.x>
4. **Sutton CD, Butwick AJ, Riley ET, Carvalho B.** Nitrous oxide for labor analgesia: Utilization and predictors of conversion to neuraxial analgesia. *J Clin Anesth.* 2017 Aug; 40: 40–45. Epub 2017 Apr 19. DOI: <https://doi.org/10.1016/j.jclinane.2017.04.005>
5. **Rollins M, Arendt K, Carvalho B, Vallejo M, Zakowski M.** Nitrous Oxide: ASA Committee on Obstetric Anesthesia Working Group. 2020. *Nitrous Oxide | American Society of Anesthesiologists (ASA) (asahq.org)*.
6. **Likis FE, Andrews JC, Collins MR,** et al. Nitrous oxide for the management of labor pain: a systematic review. *Anesth Analg.* 2014; 118(1): 153–167. DOI: <https://doi.org/10.1213/ANE.0b013e3182a7f73c>
7. **Richardson MG, Lopez BM, Baysinger CL, Shotwell MS, Chestnut DH.** Nitrous Oxide During Labor: Maternal Satisfaction Does Not Depend Exclusively on Analgesic Effectiveness. *Anesth Analg.* 2017 Feb; 124(2): 548–553. DOI: <https://doi.org/10.1213/ANE.0000000000001680>
8. **Nodine, PM, Collins MR, Wood CL, Anderson JL, Orlando BS, McNair BK, Mayer DC, Stein DJ.** Nitrous Oxide Use During Labor: Satisfaction, Adverse Effects, and Predictors of Conversion to Neuraxial Analgesia. *Journal of Midwifery & Women's Health.* 2020; 65: 335–341. DOI: <https://doi.org/10.1111/jmwh.13124>
9. **Wood C, Arbet J, Amura C, Nodine P, Collins M, Orlando B, Mayer D, Stein D, Anderson J.** Multi-center study evaluating nitrous oxide use for labor analgesia at high and low-altitude institutions. *Anesthesia and Analgesia* 2021. In press.
10. **Collins M, and the Intrapartum Nitrous Oxide Workgroup (I-NOW).** “Nitrous Oxide: Best Kept Secret in Europe that the United States is Now Discovering”. *13th Annual International Labor and Birth Research Conference*, Ann Arbor, MI. June 25–27, 2018.
11. **Anderson J, Collins M.** Representing the Perinatal Nitrous Oxide Work Group (PNOWG) “Development of Multisite National Data Repository on the Use of Nitrous Oxide in Labor and Birth: Process, Pitfalls and Path for the Future”. *Presented at American College of Nurse-Midwives (ACNM) Annual Meeting*, Chicago, IL. May 24, 2017.
12. **Nodine P, Harker E, Anderson JA, Collins MR, Orlando B, Leeman L, Gopman S, Stein D, Wood C.** Formation of a multi-institutional data registry: Process and pitfalls. *Poster presentation 30th Annual Rocky Mountain Interprofessional Research and Evidence-Based Practice Symposium*. Denver, CO. 2018.

TO CITE THIS ARTICLE:
Orlando B, Wood C, Stein D,
Anderson J. Formation of a
National Perinatal Nitrous
Oxide Data Registry: The
Intrapartum Nitrous Oxide
Workgroup I-NOW. *Journal
of Scientific Innovation in
Medicine.* 2021; 4(2): 38,
pp. 1–4. DOI: <https://doi.org/10.29024/jsim.129>

Submitted: 16 May 2021
Accepted: 27 July 2021
Published: 03 August 2021

COPYRIGHT:
© 2021 The Author(s). This is an
open-access article distributed
under the terms of the Creative
Commons Attribution 4.0
International License (CC-BY
4.0), which permits unrestricted
use, distribution, and
reproduction in any medium,
provided the original author
and source are credited. See
<http://creativecommons.org/licenses/by/4.0/>.

*Journal of Scientific Innovation
in Medicine* is a peer-reviewed
open access journal published
by Levy Library Press.