Characteristics, Motivations, And Experiences Of Women Using Nitrous Oxide During Childbirth

Gwendolyn Towers

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Characteristics, Motivations, and Experiences of Women Using Nitrous Oxide During Childbirth

A Thesis Submitted to the
Yale University School of Medicine,
In Partial Fulfillment of the Requirements for the
Degree of Doctor of Medicine

Gwendolyn Towers
2021
Abstract

CHARACTERISTICS, MOTIVATIONS, AND EXPERIENCES OF WOMEN USING NITROUS OXIDE IN CHILDBIRTH

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Nitrous oxide labor analgesia is growing in popularity in the United States, with little known regarding the factors driving this trend or about women’s experiences with the method. This study, which includes both a quantitative and a qualitative component, contributes to our understanding of the use of nitrous oxide labor analgesia in the US by exploring the following: (1) who uses the method and how these women differ from women who labor with no pharmacologic analgesia or with only neuraxial analgesia; (2) why women choose to use nitrous oxide; and (3) what their experiences are like. Using medical record and survey data, we compared demographic and clinical characteristics of women who used nitrous oxide, with or without epidural, to women who used no pharmacologic pain management and women who used only epidural. A subset of women using nitrous oxide was interviewed, and emergent themes were identified. In our sample of 107 parturients, 34% used nitrous oxide, with or without epidural, 36% received epidural only, and 30% received no pharmacologic analgesia. Women using nitrous oxide had lower parity (median=1, interquartile range [IQR]=1) and longer labor duration (median=10 hours, IQR=19.1) compared to women receiving no pharmacologic analgesia (median=2, IQR=1; median=2.7 hours, IQR=3.5, respectively). Their proportions of women undergoing labor augmentation (19.4%) and cesarean birth
(13.9%) were lower than those receiving epidural alone (35.9%; 28.2%, respectively) and higher than those using no pharmacologic pain management (6.3%; 6.3%, respectively). Most women using nitrous oxide expressed being motivated by interest in low-intervention birth. Half of women using nitrous oxide progressed to neuraxial analgesia, with inadequate pain control and exhaustion the most commonly cited reasons for the transition. Though many women using nitrous oxide reported inadequate pain relief, most reported that it nonetheless improved their experiences and enhanced their feelings of control over their births. In our study, women interested in low-intervention birth perceived nitrous oxide as an attractive complement to their labors. Despite providing incomplete analgesia, nitrous oxide may enhance women’s feelings of control and facilitate empowering birth experiences.
Acknowledgements

My sincerest gratitude to my mentor, Dr. Jessica Illuzzi, who has taught me so much, not only about research, but also about how to be a mentor and an advocate for women in labor. I have been so inspired by your commitment to making physiologic birth accessible to all women, and I hope to enact these values as I develop in my own practice. Thank you also to Michelle Telfer for your insightful contributions and to all the midwives who provided my first introduction to childbirth. Most of all, thank you to all the women who, for the chance to improve birthing experiences for women to come, took time to speak with me while exhausted, nursing, or caring for your children. Learning from each of you has been the highlight of my time during medical school.

To my family—my mother, my sister, Christine, and all the extraordinary women who have raised me—I am more grateful than I could ever express. It is your unflagging strength and infinite capacity for care and selflessness that have inspired this work. It is for you and because of you that I have chosen this path. To David, to all my dear friends, especially to Anna, June, and Noam, thank you for making medical school a time of joy and laughter.

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Introduction

Mechanism of Nitrous Oxide

Nitrous oxide is an inhaled anesthetic, analgesic, and anxiolytic known for inducing dissociation and a state of euphoria. While the precise mechanisms of nitrous oxide’s effects remain an area of investigation, it has been hypothesized to act upon opioid receptors in the periaqueductal grey matter of the midbrain.\(^1,2\) Endogenous opioid release in the midbrain then stimulates descending noradrenergic neuronal pathways, ultimately inducing analgesia as norepinephrine acts on \(\alpha_2\) adrenoreceptors in the dorsal horn of the spinal cord. Because nitrous oxide-induced anxiolysis and sedation is reversible by flumazenil, modulation of \(\gamma\)-aminobutyric acid receptors has been posited as a mechanism for its anxiolytic effects. Additionally, in a mechanism similar to the actions of ketamine, nitrous oxide may inhibit N-methyl-D-aspartate receptors to induce a euphoric state.\(^3\)

History of Nitrous Oxide Labor Analgesia

Nitrous oxide was first synthesized in England in 1772 and first employed for labor pain management in Poland in 1881.\(^4,5\) In 1933, self-administration of nitrous oxide for laboring women became more widely available, with the invention of the Minnitt Apparatus, which was designed to administer 45% nitrous oxide in air.\(^6,7\) In 1961, the British Oxygen Company introduced Entonox, a single-tank delivery system that dispenses a blend of 50% nitrous oxide in oxygen, addressing the concern for hypoxia presented by the Minnitt Apparatus.\(^8\) Though Entonox remains in widespread use in the
United Kingdom, it has never been approved for use by the United States Food and Drug Administration (FDA).

While nitrous oxide is a common method of labor pain management worldwide, used by 50-75% of women delivering in the UK, it has historically been far less commonly employed in the US. From 1975 to 1985, nitrous oxide was a component of 6% of American labors, with a further decline into near-obsolescence as rates of epidural use more than doubled during this period.\textsuperscript{9-14} From the 1980s to the mid-2010s, nitrous oxide labor analgesia was available at only a single US institution, the University of California, San Francisco. In 2012, the FDA approved the reissued Nitronox apparatus, a portable nitrous oxide delivery system that issues a blend of 50% nitrous oxide in oxygen, which was subsequently adopted by hospitals and birth centers throughout the US.\textsuperscript{15} Currently, two delivery systems—Nitronox and Pro-Nox—are approved for use by the FDA. Though still of limited popularity, offered by approximately 500 American birth centers and hospitals, the availability of nitrous oxide labor analgesia is increasing.

\textit{Typical Use of Nitrous Oxide During Labor}

Nitrous oxide may be used at any point during labor, most commonly during the first, second, and third stages, and during cervical exams, laceration repairs, and the placement of neuraxial analgesia. It is customarily used intermittently, with contractions, and is self-administered via facemask as a sweet-smelling gas blended with 50% oxygen. Because nitrous oxide has the lowest blood solubility of any inhaled anesthetic, it acts rapidly on the tissues of the nervous system and is rapidly cleared, reaching maximal effects 50 seconds following initial inhalation and cleared by exhalation in unchanged
form within minutes.\textsuperscript{10,16} To compensate for the brief time lag between inhalation and full analgesic effect, it is recommended that parturients begin inhalation of nitrous oxide 30-50 seconds prior to the onset of a contraction. Parturients are typically counseled and coached by a maternity care provider or labor support person regarding the use of nitrous oxide. Importantly, the gas is self-administered in order to avoid overuse if the parturient experiences increasing levels of sedation. Additional labor monitoring, including the use of pulse oximetry, is not routinely indicated. Because continuous monitoring is not required and because the effects of nitrous oxide rapidly dissipate following cessation of use, laboring women are able to ambulate when not actively using the method.

\textit{Safety and Adverse Effects of Nitrous Oxide Labor Analgesia}

In the laboring woman, nitrous oxide, like other inhaled anesthetics, increases respiratory rate and decreases tidal volume. Because the effect on respiratory rate is stronger, nitrous oxide ultimately induces an increase in minute ventilation. However, when combined with the ventilatory depression induced by opioids, nitrous oxide may cause a more pronounced depression. Additionally, nitrous oxide blunts physiologic responses to low oxygen tension, and rapid cessation of nitrous oxide may cause a diffusion hypoxia, whereby nitrous oxide floods the alveoli and displaces oxygen. Therefore, while the partial pressure of oxygen in a 50\% nitrous oxide blend is greater than that in ambient air, should a parturient become hypoxemic during the course of her labor, nitrous oxide may blunt her ability to respond appropriately. Despite these theoretical concerns, several studies evaluating maternal oxygen saturation across a variety of labor pain management methodologies have found that nitrous oxide when
self-administered causes either no, or only a very slight, increase in risk for desaturation.\textsuperscript{10,17}

From a cardiovascular perspective, nitrous oxide does impair myocardial contractility, yet at the subanesthetic concentrations used during labor, nitrous oxide has little influence on cardiac output, stroke volume, and heart rate.\textsuperscript{16} However, when combined with the effects of opioids, the depressive effects of nitrous oxide on the myocardium may be unmasked. Therefore, use of nitrous oxide is contraindicated in patients who have received opioids in the last two hours or who are hemodynamically unstable.\textsuperscript{16}

A common concern regarding the use nitrous oxide in labor is the risk of excessive sedation. For this reason, it is critical that a mask delivering nitrous oxide not be secured to the face, but be held to the mouth and nose only by the parturient herself. This ensures that, should a parturient approach excessive sedation, she will release the mask and temporary seal to inhale ambient air, with the effects of nitrous oxide dissipating rapidly. Because nitrous oxide does not impair maternal laryngeal reflexes of coughing and airway protection, its use presents no increased risk of aspiration.\textsuperscript{18}

Contraindications to the use of nitrous oxide in labor include: maternal hypoxia or desaturation; lung disease, including pulmonary hypertension and emphysema; recent administration of opioids; and current drug- or alcohol- induced intoxication or otherwise impaired consciousness.\textsuperscript{16} Because nitrous oxide oxidizes cobalamin into its inactive form, it is not an appropriate choice in those with un-repleted vitamin B12 deficiency. As nitrous oxide is able to diffuse from the bloodstream into air spaces, its use is contraindicated in the cases of recent inner ear or vitreoretinal surgery and current bowel
obstruction. Because nitrous oxide induces cerebral vasodilation, increased intracranial blood volume follows. For this reason, use of nitrous oxide is contraindicated in those with elevated intracranial pressure.

Nitrous oxide has no known negative effects on fetal or neonatal outcomes. While nitrous oxide readily crosses the placenta, once a neonate begins spontaneous respirations, nitrous oxide is rapidly eliminated, preventing respiratory or central nervous system depression. Furthermore, the intensity and frequency of uterine contractions are unaffected by the method. In the neonate, nitrous oxide causes no detrimental effects on Apgar scores, neonatal neurobehavioral scores, or suckling behavior.

Adverse effects from nitrous oxide use are mild and include dizziness, drowsiness, and nausea, though it is difficult to distinguish nausea as an adverse effect of medication from the nausea that frequently accompanies labor.

Because nitrous oxide is excreted primarily by exhalation in unchanged form, occupational exposure presents a concern. Long-term occupational exposure to nitrous oxide has been linked to symptoms of headache, fatigue, and irritability; reproductive risks, including spontaneous abortion, congenital abnormalities, and reduced fertility; megaloblastic anemia due to oxidation of active cobalamin; and neurologic disease, including paresthesia and muscle weakness. The National Institute for Occupational Safety and Health recommends an exposure limit of 25ppm as a time-weighted average. Compliance with these recommendations is achieved by the use of a demand-valve mask and a scavenging system. The most commonly used nitrous oxide delivery system in the US is equipped with a scavenging system, such that a patient’s exhalations are collected within the face mask and routed to a remotely located central vacuum system. It is
generally accepted that these measures are sufficient to eliminate significant occupational risk.27–29

History of Labor Pain Management in the US

Following Queen Victoria’s use of chloroform during labor in 1853, in the early 1900s, first-wave feminists began asserting their “right to a pain-free birth.”30,31 “Twilight sleep” deliveries became a common means of giving birth in the United States throughout the first half of the 20th century. In this method, women were dosed with a disinhibiting and amnesic, but neither pain-reducing nor anesthetizing, blend of scopolamine and morphine, then delivered by forceps, After a leading advocate for “twilight sleep” birth died during childbirth, and Ladies’ Home Journal published a damning exposé on the method in 1958, the popularity of the method declined considerably.32 Second-wave feminists in the 1960s and 1970s criticized this disengaged approach to childbirth, instead asserting that birth can be an empowering experience. These women encouraged a return to unmedicated childbirth, aided by the use of psychoprophylactic techniques, including the Lamaze and Bradley methods, which reached their heights of popularity in the 1970s. Psychoprophylactic approaches to labor pain management became less common with the advent of neuraxial analgesia. Neuraxial analgesia became widely available in the US in the late 1970s and has since steadily risen in prominence, used by 22% of women in 1981, 51% in 1992, and 73% in 2018.33–35 However, for unclear reasons, over the course of the last decade, interest in lower-intervention birth has increased: in 2016, 8.8% of births were midwife-attended, an increase from 3% in 1989.36–38 Additionally, rates of home birth have increased every
year since 2004, with 1.4% of births in 2012 taking place in the home, a rate equivalent to that seen in 1975, at the peak of the natural childbirth movement.\textsuperscript{36–41} Furthermore, while 44% of women in a 2006 Listening to Mothers survey believed that labor should not be interfered with unless medically necessary, 74% of women endorsed this sentiment in 2018.\textsuperscript{40,42,43}

Coinciding with the rise in interest in lower-intervention birth, nitrous oxide, too, has grown in popularity over the course of the last decade, a trend so noteworthy as to be covered by magazines and newspapers oriented towards the general public.\textsuperscript{44,45} Offered by a single US institution prior to FDA approval of Nitronox in 2012, it was offered by 5 institutions in 2014 and by over 500 hospitals and birth centers in 2019.

Despite growing interest in this form of labor pain management, very few studies have assessed the demographics, labor characteristics, and labor outcomes of women in the US who choose to use nitrous oxide.\textsuperscript{46} Additionally, women’s motivations for electing to labor with the method have not been explored. Furthermore, very few studies have examined how women use nitrous oxide. Whether nitrous oxide delays initiation of epidural or even eliminates the need for it altogether also remains unclear.

\textit{Efficacy of Nitrous Oxide Labor Analgesia}

Despite its growing popularity and well-established safety record, the literature provides few clear conclusions regarding nitrous oxide’s efficacy as a pain management tool. Furthermore, few studies have been completed in the US, presenting significant challenges to generalizability, in consideration of the exceptionally culturally-dependent attitudes toward pain in childbirth.\textsuperscript{47,48}
Evaluating the efficacy of labor pain management is difficult: the influence of psychosocial factors on perception of labor pain, the ethical concerns preventing true randomization, the lack of a consistently-used standardized scale for assessing pain, and the effects of recall bias render interpretation of the literature complex. Further complicating efforts at interpreting these data, in most studies, parturients are advised to begin inhaling nitrous oxide at the onset of contractions, rather than in anticipation of them, as is necessary for optimal analgesic effect.

While multiple studies have attempted, few have succeeded in demonstrating clinically significant analgesia with the use of nitrous oxide. Though there are few high quality studies and most are subject to the limitations previously described, it is nonetheless generally agreed that nitrous oxide is inferior to neuraxial analgesia and approximately equivalent to placebo for the purposes of analgesia. Despite incomplete pain relief, however, many women using nitrous oxide have reported that the method enhances their satisfaction with childbirth, that it contributes to a more positive birth experience, or that they would choose to use the method again in future births.

While international data do suggest that women are largely satisfied with nitrous oxide, norms and expectations surrounding childbirth differ greatly between cultures, as demonstrated by the widely varying rates of epidural and nitrous oxide utilization between countries and even between states within the US. Further complicating matters, work that has been completed internationally frequently assigns control groups to methods of labor pain management, such as pethidine, that are not routinely used in the US. Therefore, it remains unclear what needs or desires nitrous oxide fulfills for the laboring woman in the US, if it augments her satisfaction with labor without lessening the
physical pain she experiences. For women who choose to employ adjuncts to nitrous oxide in their labor or who transition to other forms of labor pain management, the motivations driving this decision have yet to be rigorously examined or described by laboring women themselves.\textsuperscript{56} Thus far, only a single, recently published, qualitative domestic study begins to address these concerns by examining women’s self-characterized experiences with the method.\textsuperscript{39}

\textit{Current Guidelines Regarding the Use of Nitrous Oxide in Labor}

Despite these limitations in our understanding about the use of nitrous oxide in labor, both the American College of Obstetricians and Gynecologists and the American College of Nurse-Midwives recognize the potential benefits of the method and recommend that it be made widely available to all eligible women.\textsuperscript{57,58}

\textit{Statement of Purpose}

While nitrous oxide has long been employed for labor pain management in much of the world and has been found to be safe and contributory to a satisfying birth experience, widely varying medical practices and culturally-dependent expectations of and attitudes towards pain in childbirth prevent ready generalization of this international data to the American laboring population, which is only recently beginning to adopt nitrous oxide as a labor tool. This dearth of literature has long been recognized, with repeated calls for additional research assessing how nitrous oxide affects women’s experiences of childbirth in the US, adverse effects of nitrous oxide, and how to facilitate optimal use of the method.\textsuperscript{11,49,51}
This study contributes to our understanding of the use of nitrous oxide labor analgesia in the US by exploring: (1) who uses the method and how these women differ from women who labor with no pharmacologic analgesia or with only neuraxial analgesia; (2) why women choose to use nitrous oxide; and (3) what their experiences are like. Through demographic survey data and medical record review, we characterize—demographically and clinically—the women who choose to use nitrous oxide. These characteristics are presented in Part A of the Results. Additionally, through semi-structured interviews, we explore women’s motivations for choosing nitrous oxide labor pain management and their experiences with the method. These qualitative data regarding women’s experiences with nitrous oxide are reported in Part B of the Results.

Rigorous characterization of the use of nitrous oxide labor analgesia in the US will facilitate improved counseling for pregnant women, will provide valuable information to hospitals and birth centers considering offering nitrous oxide, and will better elucidate women’s needs and desires during labor, all contributing to improved and empowering birthing experiences.
Methods

i. Research Team Contributions

After review of the literature regarding nitrous oxide labor analgesia, this author, Gwendolyn Towers, developed the guiding research questions and designed this study with Dr. Jessica Illuzzi. This entailed determining what information would be obtained by medical record review and demographics questionnaires and developing an interview guide for semi-structured interviews. I authored a research proposal and applied to the Yale University Institutional Review Board to acquire approval for this research.

Over the course of several months, I obtained verbal consent from women in the postpartum unit at the St. Raphael campus of Yale-New Haven Hospital, administered demographic questionnaires to all participating women, and interviewed a subset of women who labored with nitrous oxide regarding their experiences. Additionally, I performed medical record review to obtain information regarding the labor characteristics and outcomes of women in the study. With guidance from Dr. Illuzzi, I performed statistical analysis to examine the quantitative data.

Regarding the qualitative portion of this work, I transcribed each of the interviews. In order to facilitate coding of the resulting transcripts, I established a collaboration with Michelle Telfer, CNM. Each member of the research team independently coded these transcripts. I compiled and streamlined these codes, leading an iterative coding process. Final themes and subthemes were arrived at collectively and approved by all collaborators.
 Portions of this work have been submitted as a manuscript for publication in *Birth*. I drafted this submitted manuscript and led revisions, with contributions from Dr. Illuzzi and Michelle Telfer, both of whom approved the final submission.

*ii. Ethics Statement*

The research reported here was conducted in accordance with the ethical principles of human subjects research, as outlined in the Belmont Report. Informed consent was obtained from all research subjects prior to their participation in this study, in recognition of participants’ autonomy. The principle of beneficence was upheld by minimizing time spent with research participants in order to avoid excessive disruptions. To facilitate the just conduct of human subjects research, adult women of every race and ethnicity, socioeconomic status, age, sexual orientation, and religion were eligible for participation, ensuring that as many women as possible may benefit from this work.

*iii. Human Subjects Research*

This study was approved by the Institutional Review Board (IRB) of Yale University. A waiver of written consent was obtained; instead, participating women provided informed verbal consent. Because this work examined laboring with nitrous oxide, an experience applicable only to biological females, only women were included in this study. As previously mentioned, adult women of every race and ethnicity, socioeconomic status, age, sexual orientation, and religion were eligible for participation. Due to limitations in resources, women speaking a primary language other than English were unable to participate.
iv. Data Collection Methods

IRB approval from Yale University was obtained. Informed verbal consent for all portions of this study was provided by each participant. Between June and December 2018, eligible participants were approached and data were collected during their immediate post-partum hospital stays.

Inclusion criteria for participation in this study were the following:

- Delivery at the St. Raphael Campus of Yale-New Haven Hospital
- Delivery by vaginal birth or unplanned cesarean birth
- ≥18 years of age
- Labor with any of the following: no pharmacologic pain management, nitrous oxide with or without epidural, or epidural only

Exclusion criteria for participation in this study were the following:

- Primary language other than English
- Planned cesarean birth

Only women who delivered at Vidone Birthing Center at the St. Raphael Campus of Yale-New Haven Hospital were eligible for participation, as during the initial period of recruitment and data collection, this midwife-run labor and delivery service was the only Yale-New Haven Hospital facility offering nitrous oxide labor analgesia.

Demographic Data

Demographic data were obtained from two sources: a demographics questionnaire and medical record review. The demographics questionnaire ascertained information
regarding highest level of educational attainment—high school/General Educational Development (GED) or less, some college or college degree, and some graduate/professional training or graduate/professional degree. Additionally, the questionnaire inquired as to women’s initial plans for managing their labor pain. Medical record review provided additional demographic information, including age, variety of health insurance coverage, and race and ethnicity. Health insurance coverage was categorized as private insurance or Medicaid; no study participants were uninsured or covered by alternate forms of health insurance. Racial and ethnic categorizations were white, Hispanic, black, and Asian. These demographic covariates were examined, as cultural influences have been demonstrated to influence perspectives on pain in childbirth.

**Clinical Characteristics**

Information pertaining to the following clinical covariates was obtained by medical record review: maternal body mass index (BMI), gestational age, neonatal birthweight, oxytocin induction of labor, and parity. Maternal BMI was included in the analysis as it is known that rates of epidural utilization and cesarean birth are higher in women with elevated BMIs. Gestational age, neonatal birthweight, and oxytocin induction of labor were included as they may influence the duration of labor or intensity of labor pain felt, which may be reflected in choice of analgesia. Finally, the effects of parity on choice of labor analgesia were examined, as women who are more parous generally experience shorter labors, which may influence choices regarding pain management.
Variety of Analgesia Used

Participants in this study were divided into three groups: women who used nitrous oxide, with or without epidural, and the comparison groups of women who used no pharmacologic analgesia and women who used only an epidural. The comparison groups of no pharmacologic analgesia and only neuraxial analgesia were chosen because these are the most common means of managing labor pain in the US.61,62 Use of opioid analgesia was infrequent in our study population and hence could not constitute a fourth comparison group.

Type(s) of analgesia used was determined by medical record review: thorough review of progress notes and procedure notes written by obstetricians, midwives, anesthesiologists, and nurses provided information regarding labor pain management methods. This information was further verified by review of delivery notes, in which mode of labor analgesia is reported. If nitrous oxide was used at any point during labor, progress notes were reviewed to determine when the method was initiated and ceased. Participants were considered to have trialed nitrous oxide adequately only if usage of at least 30 minutes was documented. This decision was made because use of nitrous oxide for less than 30 minutes suggests a brief trial and rejection of the method, which does not constitute true labor with nitrous oxide. While medical records did include approximate start and end times for use of nitrous oxide, granular detail, such as the proportion of contractions over which it was used and the total time of active inhalation, was not available.
Labor and Neonatal Outcomes of Interest

For the portion of the study evaluating labor outcomes and neonatal outcomes, participants were again stratified by method(s) of analgesia used—no pharmacologic analgesia, nitrous oxide with or without epidural, and epidural only. Labor outcomes of interest include rates of labor augmentation with oxytocin, rates of cesarean birth, and duration of labor, both second stage and overall. These variables were examined due to the continuing debate regarding whether use of neuraxial analgesia prolongs labor or increases risk for cesarean birth. In contrast to neuraxial analgesia, nitrous oxide is postulated to decrease labor duration by increasing mobility during labor. Medical record extraction provided information regarding these variables. Duration of labor was calculated as time of hospital admission to time of birth, or in the case of induction of labor, as time of oxytocin administration to time of birth. Duration of second stage is reported only for vaginal deliveries. Neonatal outcomes of interest include neonatal disposition (a stay in the neonatal intensive care unit [NICU] or immediately rooming-in) and 1- and 5-minute Apgar scores, obtained from medical record review. Neonatal outcomes were examined due to repeated calls for additional assessment of the safety of nitrous oxide. Dilation at time of epidural initiation and duration of epidural use were assessed when applicable in order to determine whether use of nitrous oxide delays time to initiation of epidural. Dilation at time of epidural initiation was determined by first identifying time of epidural placement from flowsheets in participants’ medical records, then by taking note of the cervical dilation reported in the progress note penned most closely to the time of epidural initiation. Duration of epidural use was calculated as time from epidural placement to time of birth. Finally, dilation at time of nitrous oxide
initiation and duration of nitrous oxide use were reported as these variables may be of interest to hospitals and birth centers considering offering the method. Because exact timing of initiation of nitrous oxide is not explicitly reported in our electronic medical records, this was determined by nursing notes or provider progress notes in which the patient was reported as using nitrous oxide. Dilation at time of nitrous oxide initiation and duration of nitrous oxide use were calculated similarly to dilation at time of epidural initiation.

**Semi-Structured Interviews**

Women who consented to the previously described portions of the study and who used nitrous oxide, with or without additional neuraxial analgesia, were invited to participate in the qualitative component of the study. All women who used nitrous oxide were invited to be interviewed, with recruitment for interviews ceasing when thematic saturation was reached. If consent for the qualitative portion of the study was provided, an interview took place immediately. A pre-determined interview guide comprised of the following questions framed the discussions:

- Why did you choose to use nitrous oxide during your labor?
- What, if anything, about nitrous oxide was positive for your birth experience?
- What did you expect nitrous oxide to feel like?
- Did nitrous oxide meet your expectations?
- What needs, if any, did you have that nitrous oxide did not fulfill?
- (If participant converted to neuraxial analgesia or otherwise ceased to use nitrous oxide prior to delivery) Why did you cease to use nitrous oxide?
Interviews generally included each of these questions, as applicable, but also incorporated follow-up questions specifically addressing participants’ responses.

v. Data Analysis

Quantitative Data Analysis

In order to determine how, if at all, women who use nitrous oxide differ, demographically and clinically, from women who use other methods of labor pain management and to assess for differences in labor and neonatal outcomes, we compared women who used nitrous oxide, with or without epidural, to women who used no pharmacologic pain management and women who used only epidural.

Distributions for each continuous variable were plotted and visually assessed for normality. For normally distributed data, analysis of variance was used to compare the three groups, with summary statistics recorded as mean ± standard deviation (SD). For non-normally distributed data, the Kruskal-Wallis test was performed; for these, summary statistics are reported as median (interquartile range [IQR]). Chi-square test was used to compare differences across the three groups. All statistical analysis was performed using SAS version 9.4 (SAS Institute, Cary, NC).

Interview Analysis

Recorded and transcribed interviews were manually and independently coded with involvement from this author, Dr. Illuzzi, and Michelle Telfer. Each coder assigned a summarizing code to pertinent portions of each transcript. Research team members then convened and together reviewed each other’s coded transcripts, ensuring consistency of
interpretation. Here, and at several additional points throughout the process, disagreements in interpretation were resolved by consensus. Based on a resulting shared, revised coding manual, coding was independently repeated by all authors. Once again, inconsistencies in coding were discussed and disagreements were resolved. At this point, we noted the number of unique transcripts to which each code was assigned. From this, emergent themes and subthemes were collaboratively identified.
Results

A. Demographic and Clinical Characteristics of Women Using Nitrous Oxide During Childbirth

Between June and December 2018, 603 women delivered vaginally or by unplanned cesarean birth at the St. Raphael’s Campus of Yale-New Haven Hospital. From this population, women under the age of 18 and non-English speakers were excluded, due to ineligibility for participation in our study. Of the remaining women, a random convenience sample of 116 was invited to participate, with 107 (92%) consenting. On each day during which data collection occurred, all eligible women were approached, ensuring that the population sampled reflects the population of women birthing at this facility. Among the 107 study participants, 36 (34%) used nitrous oxide, alone or with an epidural; 39 (36%) used an epidural alone; and 32 (30%) used no pharmacologic intervention (Figure 1). Of patients using nitrous oxide, half went on to receive an epidural.
Table 1 describes demographic characteristics of the study sample, stratified by analgesic use. There were no significant differences in maternal age, educational attainment, insurance coverage, or race/ethnicity across the three analgesia groups.
Table 1: Demographic Characteristics of Study Sample

<table>
<thead>
<tr>
<th></th>
<th>No Pharmacologic Analgesia</th>
<th>Nitrous Oxide(^a) ± Epidural</th>
<th>Epidural Only</th>
<th>(p) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD</td>
<td>28.1 ± 5.5</td>
<td>28.7 ± 5.7</td>
<td>28.1 ± 5.3</td>
<td>0.86</td>
</tr>
<tr>
<td>Education(^b), n (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.51</td>
</tr>
<tr>
<td>HS/GED or Less</td>
<td>13 (40.6)</td>
<td>10 (29.4)</td>
<td>15 (38.5)</td>
<td></td>
</tr>
<tr>
<td>Some College or College Degree</td>
<td>15 (46.9)</td>
<td>14 (41.2)</td>
<td>17 (43.6)</td>
<td></td>
</tr>
<tr>
<td>Some Graduate Training or</td>
<td>4 (12.5)</td>
<td>10 (29.4)</td>
<td>7 (18.0)</td>
<td></td>
</tr>
<tr>
<td>Graduate Degree</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insurance, n (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.73</td>
</tr>
<tr>
<td>Private</td>
<td>12 (37.5)</td>
<td>14 (38.9)</td>
<td>12 (30.8)</td>
<td></td>
</tr>
<tr>
<td>Medicaid</td>
<td>20 (62.5)</td>
<td>22 (61.1)</td>
<td>27 (69.2)</td>
<td></td>
</tr>
<tr>
<td>Race/Ethnicity, n (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.64</td>
</tr>
<tr>
<td>White</td>
<td>12 (38.7)</td>
<td>15 (41.7)</td>
<td>19 (48.7)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>7 (22.6)</td>
<td>11 (30.6)</td>
<td>11 (28.2)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>10 (32.3)</td>
<td>10 (27.8)</td>
<td>8 (20.5)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>2 (6.5)</td>
<td>0 (0)</td>
<td>1 (2.6)</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\)Only women who used nitrous oxide for ≥30 minutes are included for analysis in the nitrous oxide group.

\(^b\)Education data was unavailable for two subjects.

Table 2 provides the clinical characteristics of the study sample. There were no significant differences in maternal BMI, gestational age, neonatal birthweight, and proportion undergoing oxytocin induction across the three analgesia groups. However, on pairwise comparison, women using nitrous oxide had lower parity (median=1, IQR=1) compared to women receiving no pharmacologic analgesia (median=2, IQR=1).
Table 2: Clinical Characteristics of Study Sample

<table>
<thead>
<tr>
<th></th>
<th>No Pharmacologic Analgesia n=32 (30.0%)</th>
<th>Nitrous Oxide$^A$ ± Epidural n=36 (33.6%)</th>
<th>Epidural Only n=39 (36.4%)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal BMI (kg/m$^2$), mean ± SD</td>
<td>32.7 ± 5.0</td>
<td>32.54 ± 5.1</td>
<td>32.7 ± 5.6</td>
<td>0.99</td>
</tr>
<tr>
<td>Gestational Age (Week), mean ± SD</td>
<td>39.6 ± 0.9</td>
<td>40.1 ± 1.2</td>
<td>40.0 ± 1.2</td>
<td>0.13</td>
</tr>
<tr>
<td>Neonate Birthweight (g), mean ± SD</td>
<td>3441.1 ± 461.7</td>
<td>3542.3 ± 448.9</td>
<td>3499.9 ± 571.7</td>
<td>0.56</td>
</tr>
<tr>
<td>Oxytocin Induction of Labor, n (%)</td>
<td>3 (9.4)</td>
<td>11 (30.6)</td>
<td>11 (28.2)</td>
<td>0.08</td>
</tr>
<tr>
<td>Parity$^B$, median (IQR)</td>
<td>2 (1)</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

$^A$Only women who used nitrous oxide for ≥30 minutes are included for analysis in the nitrous oxide group.

$^B$Parity is inclusive of the delivery assessed in this study. Parity is reported as median (IQR).

Summary statistics for outcomes of interest, including labor characteristics, duration of analgesic use and dilation at time of initiation, and neonatal outcomes are provided in Table 3. Women using nitrous oxide had rates of labor augmentation (19.4%) and cesarean birth (13.9%) lower than those receiving epidural alone (35.9%; 28.2%, respectively) but higher than those using no pharmacologic pain management (6.3%; 6.3%, respectively). Their overall labor duration (median=10 hours, IQR=19.1) and duration of second stage (median=0.8 hours, IQR=1.7) were longer than those of women receiving no pharmacologic analgesia (median=2.6 hours, IQR=3.5; median=0.2 hours, IQR=0.5, respectively). Aside from rates of labor augmentation and cesarean birth and duration of second stage and labor overall, women using nitrous oxide do not differ from women using no pharmacologic pain management or women using only neuraxial analgesia in other countries.
Table 3: Labor and Neonatal Outcomes

<table>
<thead>
<tr>
<th></th>
<th>No Pharmacologic Analgesia</th>
<th>Nitrous Oxide(^a) ± Epidural</th>
<th>Epidural Only (n=39) (36.4%)</th>
<th>(p) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxytocin Augmentation of Labor, n (%)</td>
<td>2 (6.3)</td>
<td>7 (19.4)</td>
<td>14 (35.9)</td>
<td>0.01</td>
</tr>
<tr>
<td>Cesarean Birth, n (%)</td>
<td>2 (6.3)</td>
<td>5 (13.9)</td>
<td>11 (28.2)</td>
<td>0.04</td>
</tr>
<tr>
<td>Duration of Labor(^b) (hrs)</td>
<td>2.7 (3.5)</td>
<td>10 (19.1)</td>
<td>12.4 (15.3)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Duration of Second Stage(^c) (hrs)</td>
<td>0.2 (0.5)</td>
<td>0.8 (1.7)</td>
<td>1.0 (2.2)</td>
<td>0.01</td>
</tr>
<tr>
<td>NICU Stay, n (%)</td>
<td>0 (0)</td>
<td>1 (2.8)</td>
<td>0 (0)</td>
<td>0.37</td>
</tr>
<tr>
<td>1-Minute Apgar</td>
<td>9 (1)</td>
<td>9 (1)</td>
<td>9 (1)</td>
<td>0.10</td>
</tr>
<tr>
<td>5-Minute Apgar</td>
<td>9 (1)</td>
<td>9 (1)</td>
<td>9 (1)</td>
<td>0.45</td>
</tr>
<tr>
<td>Epidural Dilation (cm)</td>
<td></td>
<td>5 (2)</td>
<td>5 (3)</td>
<td>0.41</td>
</tr>
<tr>
<td>Epidural Duration (hrs)</td>
<td></td>
<td>9.1 (8.1)</td>
<td>7.3 (6.1)</td>
<td>0.12</td>
</tr>
<tr>
<td>Nitrous Oxide Dilation (cm)</td>
<td></td>
<td>5 (1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nitrous Oxide Duration (hrs)</td>
<td></td>
<td>2.5 (4.0)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Unless otherwise indicated, all data are reported as median (IQR).

\(^a\)Only women who used nitrous for \(\geq\)30 minutes are included for analysis in the nitrous oxide group.

\(^b\)Duration of labor is defined as either time of admission to time of birth or time of oxytocin induction to time of birth.

\(^c\)Duration of second stage is reported only for vaginal births.

B. Self-Characterized Experiences of Nitrous Oxide-Assisted Childbirth

To elicit women’s motivations for laboring with nitrous oxide and to identify salient features of their experiences, a subset of women was interviewed, with interviews ceasing when thematic saturation was reached at 8 participants. For each participant interviewed, a summary of her labor plans and outcomes is provided in Table 4. From the qualitative data elicited through interviews, five themes and many subthemes emerged, with a high degree of interrelation across and within themes. They are summarized in Table 5 and
reported below, with the number of women contributing to each theme or subtheme denoted in parentheses and study identifiers denoted in italics. Narrative segments have been edited for clarity and brevity.

**Table 4: Labor Plans and Labor Outcomes for Interview Participants**

<table>
<thead>
<tr>
<th>Study Code</th>
<th>Prenatal Counseling on N₂O</th>
<th>Planned to Use N₂O</th>
<th>Planned to Use Only N₂O</th>
<th>Epidural</th>
<th>Labor Duration (Hrs)</th>
<th>Birth Method</th>
<th>Parity(^A)</th>
<th>Induction</th>
</tr>
</thead>
<tbody>
<tr>
<td>033</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>16.75</td>
<td>V</td>
<td>1</td>
<td>N</td>
</tr>
<tr>
<td>055</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>31.95</td>
<td>C</td>
<td>1</td>
<td>N</td>
</tr>
<tr>
<td>062</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>1.38</td>
<td>V</td>
<td>2</td>
<td>N</td>
</tr>
<tr>
<td>091</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>23.97</td>
<td>C</td>
<td>2</td>
<td>N</td>
</tr>
<tr>
<td>106</td>
<td>Y</td>
<td>N</td>
<td>—</td>
<td>Y</td>
<td>36.35</td>
<td>V</td>
<td>1</td>
<td>N</td>
</tr>
<tr>
<td>107</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>24.53</td>
<td>V</td>
<td>1</td>
<td>N</td>
</tr>
<tr>
<td>108</td>
<td>Y</td>
<td>N</td>
<td>—</td>
<td>Y</td>
<td>31.27</td>
<td>C</td>
<td>1</td>
<td>N</td>
</tr>
<tr>
<td>109</td>
<td>Y</td>
<td>N</td>
<td>—</td>
<td>Y</td>
<td>40.5</td>
<td>V</td>
<td>1</td>
<td>Y</td>
</tr>
</tbody>
</table>

\(^A\)Parity is inclusive of the delivery assessed in this study.

**I. Desire for a Low-Intervention Birth Experience**

Nearly every woman (n=7) cited interest in low-intervention birth as a motivation for using nitrous oxide.

I wanted the full experience. I wanted to feel what it felt like to give birth naturally, without drugs. I was looking to have the most natural birth I possibly could. I didn’t want to get an epidural, I didn’t want morphine, and nitrous oxide seemed like a good way to take the edge off a little bit without something more heavy-duty. 107

A subset (n=4) of the women expressing interest in low-intervention birth also declared a belief in physiologic birth, a trust in their bodies’ capabilities.
I knew that my body was going to do what it would do naturally, and I knew that nitrous wouldn’t affect that. For a long time, I really trusted my body, and I see birth as one of the few things that can be not impacted a lot by science and medicine. It’s just something women’s bodies have been doing since the beginning of time. 033

I wanted to allow nature to work its magic, the way it’s supposed to. 062

Many women (n=4) appreciated that, because of its transient effects, nitrous oxide induces only a brief departure from their baseline states.

I thought it sounded really good because it only goes into my system, [it] doesn’t affect her. Also I really like that it’s only in there as long as you’re breathing it and that it leaves quickly. So it seemed like a really safe thing to try. 033

It’s a nice, pleasant dissociative that’s short-lasting and not immobilizing completely, for long periods of time. 055

II. Prioritizing Safety and Minimization of Side Effects

Several women (n=4) explained their interest in nitrous oxide by expressing an aversion to epidural, citing concerns regarding its perceived safety and side effect profile as well as the additional interventions it necessitates.
[I don’t like] how [epidurals] make you feel after labor. You need the urinary catheter and it makes babies a little bit sleepier. I didn’t really want that. With my [first child] … I ended up having two urinary catheters. And it was a little traumatic for me. I know it’s a simple thing, but I just didn’t like it. 062

It still took me three hours to make the decision to actually get the epidural, because I was very scared of the pain of the procedure itself. 108

Similarly, three women expressed an interest in nitrous oxide as an alternative to narcotics, to which they had previously experienced adverse reactions.

No narcotics because I can’t stand them, really they’re terrible and make me throw up everywhere. 055

In contrast to epidural and narcotics, many (n=3) women perceived nitrous oxide to be a safe option for mother and baby.

Why did I start using nitrous oxide. Well, first of all because it doesn’t have any impact on me or the baby and there isn’t any risk, as far as I’m concerned. 108

III. Shortcomings of Nitrous Oxide Labor Analgesia
A majority (n=5) of women reported that nitrous oxide provided inadequate pain relief. Each of these women proceeded to epidural, with several (n=3) explicitly citing inadequate pain control as a reason for seeking neuraxial analgesia.

I didn’t want an epidural, to be immobilized. But obviously that went right out the window because you just want to be numb at a certain point if you’re in that much pain and you can’t push. 055

[Nitrous did not meet my need for] pain relief. [Mobility] would have been [important], but I think in my particular situation, I was just in too much physical pain to be up and eating and walking around, so that was not something that was going to be important to me at that time. 091

Three women reported feeling exhausted during their labors, citing inadequate pain control as a barrier to rest. Exhaustion was the second most commonly cited reason for transitioning to an epidural.

The tipping point that made me decide to get the epidural was that I hadn’t slept in over 24 hours, and I had another day and a half ahead of me. There’s no way that I would have been able to get through that because it was way too bad to be able to sleep through. 107
At some point, I was just too exhausted to deal with the contractions, and that’s when I started thinking about the epidural. 108

Side effects of nitrous oxide were rarely discussed. Of potential side effects, only dizziness was reported, by two women. For one of these women, dizziness sufficiently compromised her experience that she felt she was losing some control.

In my longer contractions, I wanted to keep breathing it in because it was helping, but it also made me feel a little dizzy, which went away immediately after I stopped breathing in. 033

What I really didn’t like was that it made me feel dizzy and I felt like I was losing a bit of control while I was using it. Then, at the same time, [it wasn’t] giving me the relief that I needed because [the contractions] were so intense. In my mind, I’d hoped either to be dizzy enough to not feel it as much or to not be as dizzy. 108

Two women were dissatisfied with the delivery of nitrous oxide, with one woman reporting initial difficulty timing inhalation to her contractions and with the other reporting that inhalation of nitrous oxide was in itself exhausting and commanded excessive attention.
To have to pull on that kind of nitrous mask is so exhausting, it takes your focus. You can’t even focus on the actual effect of the nitrous because you’re trying so hard to breathe it in. 055

It was something I had to get the hang of over a couple of contractions, because it takes a minute to kick in. At first, I would already be in the middle of a contraction when it started working, but then I started starting it a little bit earlier, before the contractions. 107

IV. Improved Coping

Though the majority of women reported that nitrous oxide provided inadequate pain relief, nearly all women reported beneficial effects beyond pain control, with many women (n=5) referencing an improved emotional state.

I felt better emotionally. At first, I didn’t even realize it was affecting me because it was so subtle, but it was just enough to get me to a different state of mind, where I could push through. 033

It was kind of like having a glass of wine. I could still feel the pain, but I was much better able to handle and process it. I was in a calmer, more relaxed state to just deal with it. 062
[Nitrous] makes you slightly less stressed about it so you can get yourself back together, but it is not pain relief, that’s the only thing, so it really just depends on the person. 091

I was scared to get the cervical exam, so they said it might help me calm down, take some of the pain away. [I liked] the calming effect it had. 109

The majority of women (n=6) reported that nitrous oxide enhanced their capacity to cope with their labors, either by increasing their tolerance, or by decreasing the intensity of their experiences.

I knew nitrous would give me a little mental edge for the pain. It really helped me get through that tough period without the feeling of “I’m gonna give up.” 033

It just took the edge off of everything, my anxiety, the pressure of getting the exam. It’s like laughing gas at the dentist, though not as potent. It took the edge off, it wasn’t as bad, it made it a more tolerable experience. 109

Though some women reported difficulties with inhalation of nitrous oxide, other women (n=3) found that the act of inhaling nitrous oxide improved their experiences by providing an object for focus.
I had something to focus on, because when you’re taking it, you’re just focusing on breathing in and out really deeply, so the fact that I could focus on that during the contractions really helped me feel in control. 033

It was nice to be able to have a tool, physically in your hands, that helps you get to that goal. 091

I found that it gave me something to focus on, whereas when I was laboring at home, I was all over the place. When you’re in that much pain, it’s hard to focus on something, and it forced me to focus on my breathing. The little bit of pain management did take away the overwhelming “Oh my god, I feel like I’m going to die from this contraction.” It was like “Okay, I can probably do this.” 107

Several women (n=3) endorsed feeling the expected dissociative effects of nitrous oxide, reporting feeling disconnected from their physical experiences.

[Nitrous] alter[ed] my mind state a little bit, or ma[d]e me care less about the pain. 033

It’s like out-of-body. 055
It took my mind off the pain. After a little while, I started to laugh with my cousins. [It takes your] mind off the pain, especially when you have a family member around and they’re there to support you. 106

For some women (n=2), nitrous oxide provided a means for avoiding or ameliorating trauma, allowing them to experience pain without suffering.

I knew there was going to be pain no matter what. I didn’t want to feel traumatized by the pain, like I was suffering from it, and I think nitrous helped with that. [My midwives] said that there’s pain, and that’s something people mostly expect from childbirth, that’s something that’s supposed to happen, whereas suffering, when you cross over to that zone of feeling kind of traumatized by the birth… It was really helpful during that time, where it was really hard, to have something else to use to help. 033

V. Enhanced Agency

The majority of women (n=5) reported either enhanced feelings of control over their labors and bodies as a consequence of nitrous oxide use, or appreciation for the control they were able to exert over nitrous oxide and their labors more broadly.

I had no control with what happened to my [first child]. It was an emergency and everything turned out fine, but when it’s an experience that you have no say in, it does come back, and it was a traumatic experience. So this time, everything was
okay and healthy, so there was an element of “Okay, I can control stuff now. I can control things with her birth.” It was important to me that I could do that. 062

[I liked that] you’re able to control the usage yourself and that nobody else is in control of it for you. 091

For many women, preserving mobility was cited as a priority. Four women expressed either disappointment over the immobilizing nature of neuraxial analgesia, or appreciation for preserved mobility with nitrous oxide use. In some cases, interest in preserving mobility was explicitly explained by a desire to maintain control.

I really wanted to not have an epidural, which was based on me wanting to feel able to move around during the birth. 033

[The epidural] takes the power of your labor away from you a little bit. I wanted to get up and change positions… and all of those options were taken away from me as soon as I got the epidural. 107

I [could] still walk around, not while I use[d] it, but in between. 108

Many women (n=4) reported feeling empowered during or following their nitrous oxide-assisted labor experiences.
I do feel really good about [not using an epidural]. I feel really good that I didn’t need one. 033

It was very painful, a very intense labor, but very fast. But ultimately, I feel so empowered from it, from being able to make the decisions that I made. Birth doesn’t have to be a negative experience, it can be a really positive one, and it was. I was empowered. 062

If [surgery] had been necessary, I would have automatically consented to it if he were at risk. But if it wasn’t, then I really wanted to go through that and experience that, and it was incredible. It was the hardest thing I’ve ever done, but it was *weeps*… The experience of having that kind of birth made it all worth it. These are happy tears, I’m sorry. There’s just nothing that could ever compare to seeing my son being born the way that I did. 107

The majority (n=6) of women interviewed used nitrous oxide as adjunctive analgesia, and the majority of women (5) reported valuing a wide range of options for labor pain management.

I think it was a really positive experience for me. I really thought it was a good option to have. 033
I’m not somebody who’s very strict in their vision of how things are going to go, so I like to leave as many options as possible, so if I could have made it through on just the nitrous, that would have been fantastic for me. 091

I think I would recommend it to everyone to try out, but that’s what I would say about all the pain management options. 108
Table 5: Themes and Subthemes Regarding Experiences with Nitrous Oxide Labor Analgesia

<table>
<thead>
<tr>
<th>Theme</th>
<th>Subtheme</th>
<th>Count (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Desire for a Low-Intervention Birth Experience</strong></td>
<td>Stated desire for a low-intervention birth experience (n=7)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Belief in physiologic birth (n=4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Transient effects (n=4)</td>
<td></td>
</tr>
<tr>
<td><strong>Prioritizing Safety and Minimization of Side Effects</strong></td>
<td>Concerns regarding perceived safety and side effects of neuraxial analgesia (n=4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Concerns regarding perceived safety and side effects of narcotics (n=3)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Safety of nitrous oxide (n=3)</td>
<td></td>
</tr>
<tr>
<td><strong>Shortcomings of Nitrous Oxide Labor Analgesia</strong></td>
<td>Inadequate pain control (n=5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Failure to meet expectations (n=2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Exhaustion (n=3)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Side effects (n=3)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dissatisfaction with delivery of nitrous oxide (n=2)</td>
<td></td>
</tr>
<tr>
<td><strong>Improved Coping</strong></td>
<td>Improved emotional state (n=5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Increased tolerance or decreased intensity of experience (n=6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Object for focus (n=3)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dissociative effects (n=3)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Avoiding trauma (n=2)</td>
<td></td>
</tr>
<tr>
<td><strong>Enhanced Agency</strong></td>
<td>Increased control (n=5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Preservation of mobility (n=4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Empowerment (n=4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Valuing options (n=5)</td>
<td></td>
</tr>
</tbody>
</table>

Eight women who used nitrous oxide labor analgesia were interviewed. The number of unique women contributing to each subtheme is reported in parentheses.
Discussion

In response to growing interest in nitrous oxide labor analgesia, in recent years, there have been repeated calls for investigation of women’s experiences with nitrous oxide, its safety for both mother and fetus, and women’s satisfaction with the method.\textsuperscript{10,11,16} Though many of these data are available internationally, from regions in which nitrous oxide has long been a mainstay of obstetric practice, their generalizability to the laboring population in the US remains questionable, in consideration of the highly culturally dependent perspectives towards childbirth and labor pain. Using data from a contemporary sample of women delivering at the St. Raphael Campus of Yale-New Haven Hospital in the US, this study characterizes women who employ nitrous oxide for labor pain management, as well as their labor courses and outcomes; and elucidates women’s motivations for using nitrous oxide and their experiences with the method. In contrast to the only other existing qualitative research on nitrous oxide labor analgesia, this study provides verbatim explications of trends revealed in the accompanying descriptive quantitative data, and each woman’s comments may be contextualized by her plans for labor and the outcomes of her labor.\textsuperscript{63}

Effects of Nitrous Oxide on Labor Outcomes

In our sample, women who used nitrous oxide, with or without epidural, had rates of labor augmentation and cesarean birth intermediate to those who received no pharmacologic pain management and those who used epidural alone. These findings may in part be explained by the well-documented slowed progression of labor following epidural placement, with slowly progressing labors more likely to require augmentation.
or result in cesarean birth. However, these findings may also reflect that slowly progressing labors are more likely to lead women to choose epidural analgesia. These patterns may also be explained in part by the mobility that is facilitated by use of nitrous oxide: as a consequence of how nitrous oxide is used, with the parturient seated or recumbent while actively using the method and otherwise free to ambulate, mobility with nitrous oxide should be intermediate to that seen in women using no pharmacologic analgesia and those using neuraxial analgesia. Because the uterus contracts most effectively when a laboring woman maintains an upright position, how conducive each form of analgesia is to ambulation may explain increasing rates of augmentation and cesarean birth with increasingly immobilizing forms of analgesia. While increased mobility was endorsed by some interviewed women as a positive feature of nitrous oxide labor analgesia, our study was not able to evaluate levels of mobility with nitrous oxide, as compared to other pain management methods, and we are not aware that any other study has done so. Because the benefits of ambulation and upright positioning in labor are well-established, further research in which labors are closely observed, with duration of nitrous oxide use and time out of bed documented, would likely prove insightful.

Duration of second stage and labor overall were significantly shorter in women who used no pharmacologic analgesia, as compared to those using nitrous oxide and those using epidural only. Because, in our study, parity is highest in women laboring without pharmacologic analgesia and equivalent between the remaining two groups, it is likely that these trends may be explained by the shorter labors experienced by more parous women. Additionally, because more parous women experience shorter labors
and because of their familiarity with the course of labor, they may be more likely to choose to labor without pharmacologic pain management.

Consistent with nearly all previously published literature on the subject, there was no significant difference between neonatal Apgar scores or risk for NICU admission for the children of women who used nitrous oxide and those who did not. This affirms a confidence in the safety of nitrous oxide, which was expressed by several women in our study. As safety for the fetus was a commonly cited motivation for laboring with nitrous oxide, this provides pertinent information to include in counseling women regarding the method. While these findings regarding Apgar scores and NICU admission provide insight into fetal well-being in response to nitrous oxide, further research comparing umbilical cord gases would extend our understanding of the safety of the method.

Role of Race and Ethnicity in Labor Pain Management

Pain management in childbirth is heavily influenced by a parturient’s race and ethnicity. As has been extensively demonstrated, non-white women employ epidural analgesia less frequently than white women, with research suggesting that access to neuraxial analgesia is limited for women of color. However, when women of color choose to labor without pharmacologic pain management, they may be more strongly pressured into accepting medications than their white peers. For these reasons, it is critical that research regarding labor pain management evaluates potential racial and ethnic differences in the utilization of various means of pain management, while maintaining cultural sensitivity and recalling that cultural mores shape women’s perceptions of the labor experience.
It is therefore notable that in our study, women who used nitrous oxide did not differ significantly in race/ethnicity, from women who used no pharmacologic pain management or women who used epidural only. Similar results have been found in at least one other US-based study, however, it remains to be determined if racial and ethnic inequities in access to or utilization of nitrous oxide exist in other regions of the US. Lack of racial/ethnic differences in use of nitrous oxide may have significant implications because, as is demonstrated in the qualitative portion of this work, the method enhances some women’s feelings of control over labor, which are known to be subject to racial disparities.

Other demographic factors, including educational attainment and insurance coverage, also did not vary depending on method of labor analgesia employed, suggesting that, at least at our institution, access to this method of labor pain management is equitable.

**Conversion to Neuraxial Analgesia**

The qualitative portion of this work demonstrated that, for many women, interest in nitrous oxide is derived from a desire for a lower-intervention birth and, in some cases, particularly by a desire to avoid neuraxial analgesia. It is therefore important to know whether nitrous oxide is able to reliably delay the time to epidural placement or obviate need for it altogether. In our study, 34% of women labored with nitrous oxide, a rate higher than that found in other studies. This is likely due to our study being conducted at the primary delivery site for women receiving midwifery care through our tertiary medical center. Of the women using nitrous oxide, approximately half progressed to
neuraxial analgesia, which is relatively consistent with, or perhaps slightly lower than, those reported elsewhere in the literature.\textsuperscript{34,39,56,73} While previous studies have found, via surveys and medical record review, that oxytocin induction or augmentation of labor and inadequate pain relief are correlated with progression to epidural, no previous studies have solicited women’s own reflections on the transition.\textsuperscript{74–76} In our study, we found that inadequate pain control is largely responsible for the transition to epidural. However, exhaustion is a commonly reported motivation as well, with many women speculating that, had their labors been shorter, they may have used only nitrous oxide.

While previous research has examined whether use of nitrous oxide obviates the need for an epidural, no previous research has considered whether use of nitrous oxide delays initiation of epidural analgesia. By comparing dilation at time of epidural placement and duration of epidural use between women who used both nitrous oxide and epidural and women who used epidural only, we were able to discern that, in our sample, nitrous oxide does not delay time to epidural placement.

Taken in conjunction with the existing literature, our findings suggest that nitrous oxide does, indeed, provide inferior labor analgesia, when compared to epidural. However, our qualitative work maintains that nitrous oxide nonetheless contributes meaningfully to women’s birth experiences.

\textit{Experiences of Nitrous Oxide in Childbirth}

Data published in regions of the world in which use of nitrous oxide labor analgesia is common suggest that despite inferior pain relief, most women would choose to use the method again.\textsuperscript{53} That nitrous oxide provides inadequate or incomplete
analgesia, yet many women are satisfied with the method is perhaps counterintuitive; however an extensive body of literature suggests that satisfaction with childbirth is largely independent of effective pain relief.\textsuperscript{34,39,56,76} Several studies have found that adequate analgesia contributes less to satisfaction with labor than do feelings of control over labor and decision-making capabilities within labor.\textsuperscript{39,77–80} In fact, across a multitude of studies, feelings of control over labor are most closely associated with satisfaction with labor overall, a finding that is consistent across cultures and that has held true over decades.\textsuperscript{39,81–87} Because nitrous oxide is self-administered and easily and rapidly reversible, places few constraints on mobility, and requires no additional interventions, such as urinary catheters, it theoretically affords women a level of control over their analgesia that is unrivaled by any other method of pharmacologic pain management.

This was confirmed in our work. Nearly all interviewed women reported that nitrous oxide contributed to an enhanced sense of agency in childbirth. In some cases, this was expressed explicitly as increased feelings of control, while other women voiced appreciation for maintained mobility. Regardless of whether they proceeded to epidural analgesia, many women expressed appreciation of an additional option for managing labor pain.

Perhaps for the above reasons, several women expressed feeling empowered by the experience of laboring with nitrous oxide. These feelings were especially strong in the two interviewed women who labored only with nitrous oxide and who also expressed beliefs in physiologic birth. This finding is consistent with previous studies reporting lower-intervention births in women who accept pain as an inevitable and potentially beneficial component of labor.\textsuperscript{81,88–90}
Having found in our qualitative work that the use of nitrous oxide enhances women’s feelings of control in labor, it remains to be demonstrated whether these increased feelings of control correspond to measurable increases in satisfaction with childbirth. Future research quantitatively assessing for differences in perceived control in childbirth and satisfaction with childbirth between women who use nitrous oxide, women who use no pharmacologic analgesia, and women who use only epidural would contribute greatly to our understanding of women’s experiences with nitrous oxide labor analgesia.

**Limitations**

The most notable limitation to our work is that our sample size was relatively small. This prevented us from dividing the group of participants using nitrous oxide into those who progressed to neuraxial analgesia and those who did not, which would facilitate a more complete analysis of why women choose to discontinue laboring with nitrous oxide. Though we were able to address women’s self-expressed reasons for transitioning to an epidural, further quantitative analysis would likely be revealing.

Like many studies evaluating nitrous oxide labor analgesia, our findings may be confounded by potential suboptimal use of nitrous oxide. Some interviewed women expressed surprise when informed of the lag time between first inhaling nitrous oxide and reaching optimal analgesic concentrations, suggesting potential improper use. This is especially notable when considering that, in our study, half of women using nitrous oxide proceed to epidural due to inadequate pain management. In addition to drawing attention to the need for more effective coaching in the method, this complicates interpretation of
our results. However, because these patterns of usage are largely consistent with those reported in the literature, this potential suboptimal use of nitrous oxide should not inherently limit the generalizability of our work.

Finally, because births at the study site are attended by midwives, women delivering at this site may be more interested in a low-intervention birth and have lower-risk pregnancies than most women, potentially limiting the generalizability of this study in the US. Additionally, while all women who used nitrous oxide were eligible for interview and were invited to participate, the portion of women who consented to participation may over-represent women with polarized views of nitrous oxide and women who feel capable of articulating these beliefs.

**COVID-19 Addendum**

As initially conceived, this study included the administration of a validated scale assessing both perceived control in childbirth and satisfaction with childbirth, as a means of exploring the relationship between the unique properties of nitrous oxide, its theoretical ability to enhance feelings of control over labor, and thus its ability to increase satisfaction with labor. To perform this portion of the study well, a sample size of approximately 200 is required. Thus far, the scale assessing perceived control and satisfaction in childbirth has been administered to all study participants included in this work. However, due to the COVID-19 pandemic, per ACOG recommendations, nitrous oxide was unavailable for several months, during the time designated for completion of data collection. Therefore, data collection for this portion of the study has not been
completed, and this portion of the study has therefore not been included in this work. At this point, nitrous oxide is again being offered, and data collection has resumed.

Conclusion

This study provides valuable information regarding the factors behind nitrous oxide’s increasing popularity in the US as well as its influence on women’s labor experiences. The growing availability of nitrous oxide in the US prompts inquiry regarding the needs it does and does not fulfill for laboring women, in order to facilitate the discovery of additional means of fulfilling those needs and to ensure that this option is offered to the patients most likely to benefit.

Among women who received nitrous oxide, a desire for low-intervention birth was their primary motivation, though half of women in our study progressed to neuraxial analgesia as a consequence of inadequate pain control or exhaustion. Despite inferior pain control, most women interviewed in our study reported benefitting from the availability of nitrous oxide, with nitrous oxide augmenting their feelings of control over their labors and enhancing their ability to cope with labor.
References
8. Tunstall ME. OBSTETRIC ANALGESIA. The Use of a Fixed Nitrous Oxide and Oxygen Mixture from One Cylinder. Lancet 1961;278(7209).
20. Nitrous oxide may be a hazard after retinal surgery. BMJ 2002;325(7363).
44. Plenda M. Using Laughing Gas to Relieve the Pain of Childbirth. Atl 2014;
60. Shenouda C, Wijesooriya A, Toufeili A, Miller MR, Penava D, de Vrijer B.


79. Bramadat IJ, Driedger M. Satisfaction with Childbirth: Theories and Methods of