

**Passive and Active Sampling of Occupational Exposures to Nitrous Oxide Among
Indian Health Service Dental Employees and Possible Mitigating Factors**

by

LCDR John C. Hansen, REHS

Thesis submitted to the Faculty of the
Preventive Medicine and Biostatistics Graduate Program
Uniformed Services University of the Health Sciences
In partial fulfillment of the requirements for the degree of
Master of Science in Public Health, 2017



UNIFORMED SERVICES UNIVERSITY, SCHOOL OF MEDICINE GRADUATE PROGRAMS
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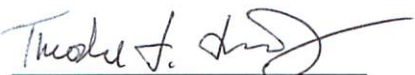
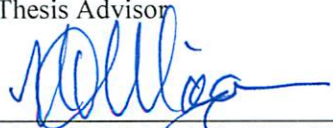
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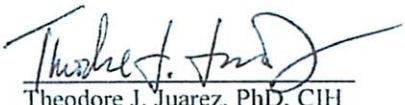
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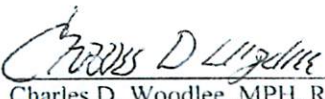
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Thank you all!

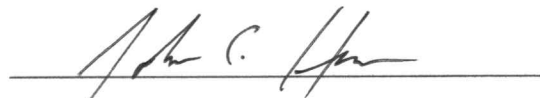
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A handwritten signature in black ink, appearing to read "John C. Hansen", is written over a horizontal line.

John C. Hansen

May 19, 2017

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ABSTRACT

Passive and Active Sampling of Occupational Exposures to Nitrous Oxide Among Indian Health Service Dental Employees and Possible Mitigating Factors

LCDR John C. Hansen, Master of Science in Public Health, 2017

Thesis directed by: Dr. Theodore J. Juarez, Assistant Professor, Department of Preventive Medicine and Biostatistics

Nitrous oxide is a commonly used gas in dental facilities and considered safe for patients undergoing dental procedures. However, epidemiological studies show that there are adverse health effects associated with chronic occupational exposure to nitrous oxide, including reproductive issues, neurologic, renal and liver disease. Indian Health Service reports have documented high levels of nitrous oxide during dental procedures. This study compared sampling using the Thermo Scientific™ Miran SapphIRe portable analyzer with the Advanced Chemical Sensor™ Passive Badge, and characterized dental personnel's exposure to nitrous oxide levels in the breathing zones during dental procedures.

Similar exposure groups were determined by job title (Dentist and Dental Assistant) and an ANOVA was used to explore the appropriateness of considering similarity of the groups across 6 dental clinics within the Indian Health Service. An independent *t*-test was used to determine if there was a mean difference of exposure between the similar exposed groups. A paired *t*-test was used to compare the similarity of the two sampling methods, and the Bland-Altman analysis was used to assess level of agreement between the two methods. Finally, this study looked at the effect of nitrous

oxide concentration/flow rate and room air exchange rates on exposure levels.

Excursion levels over the occupational exposure limit of 250 ppm_v were exceeded in 21 of 41 (51%) procedures in this study. Mean upper tolerance limit estimates for dental procedures were 1245 ppm_v for dentists and 802 ppm_v for dental assistants. Four passive 8-hour TLV-TWAs were over the 50 ppm_v occupational exposure limit, two for dentists (55.6 and 152 ppm_v) and two for dental assistant (81.3 and 56.0 ppm_v).

There was no significant difference between similar exposure group concentrations using either sampling method (Miran SapphIRe portable analyzer, 0.071; Advanced Chemical Sensor™ Passive Badge, *p*-value 0.106). However, both sampling methods showed a trend toward the dentist having an 81 to 86% higher exposure rate than the dental assistant.

When comparing sampling methods by job title, the dentist exposure group showed no difference (*p*-value of 0.058) while the dental assistant exposure group showed a difference (*p*-value of 0.019). Bland-Altman analysis showed that both sampling methods differed by more than 25% with 95% confidence when compared to each other.

The effect of nitrous oxide concentration and flow rate, and room air exchange rate did not show any significant association with observed nitrous oxide concentrations in the breathing zones of employees.

This study suggests there needs to be a focus to better control excursions above 250 ppm_v, which would also help lower procedural and 8-hour TLV-TWAs. Continued sampling should be conducted to increase sample size and overall power to better

characterize similar exposure groups. Lastly, laboratory studies designed to understand the difference in sampling methods should be accomplished.

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CHAPTER 1: Introduction

Statement of Purpose

“Characterize breathing zone levels of nitrous oxide among Indian Health Service dental clinic employees during dental procedures by job title and sampling method.”

The primary purpose of this study was to profile nitrous oxide concentrations in conjunction with three mitigating factors recommended by the American Dental Association (ventilation, percent nitrous oxide, and nitrous oxide flow rate). The study was specific to the dental clinics within the Indian Health Service (IHS). Of particular interest were concentrations that exceeded the recommended excursion limit. Excursion limits are short-term exposures to chemicals that do not have a threshold limit value-short-term exposure limit (TLV-STEL) and are intended to protect personnel from acute toxicological effects [1]. The observed excursions were then compared to IHS policy and American Conference of Governmental Industrial Hygienists (ACGIH) exposure limits and recommendations. An important area of concern was the variability of concentration between clinical personnel, as a result, exposures were grouped by similarity. Job titles were assumed to be appropriate for this purpose, and two similar exposure groups were investigated: dentist and dental assistant. Due to time constraints and logistical issues, the study was conducted in four of the twelve IHS Areas: Oklahoma, Albuquerque, Phoenix, and Navajo. Two different sampling methods were also investigated: a real-time detection method using the Thermo Scientific™ Miran SapphIRe portable analyzer (Miran) and the Advanced Chemical Sensor™ Passive Badge (ACS).

Background

Nitrous oxide is an odorless, tasteless, and colorless gas frequently used alone or in combination with other anesthetic gases or oxygen for surgical or dental procedures [2]. Chronic occupational exposure to nitrous oxide can be a long-term health concern [3], but it is presumed that healthy surgical patients could receive nitrous oxide without harm [4].

The main route of nitrous oxide exposure in occupational settings is inhalation, and it is rapidly absorbed upon inhalation. As a result of the lower tissue/blood partition coefficients, the equilibration of nitrous oxide in most tissues occurs rapidly and most of the inhaled nitrous oxide is rapidly eliminated through the lungs, with small amounts diffusing through the skin. Nitrous oxide is not known to be metabolized in the body [2].

Nitrous oxide inactivates vitamin B₁₂ and interferes with B₁₂- dependent conversion of homocysteine to methionine, which can be seen as gait ataxia, sensory loss, peripheral neuropathy and myelopathy [2]. Chronic exposure can cause megaloblastic erythropoiesis and neurological features similar to subacute combined degeneration of the spinal cord, and can cause neurological and hematological changes [2, 3]. Several human studies have also shown that occupational exposure to nitrous oxide may increase the risk of reduced fertility, spontaneous abortions, and neurologic, renal, and/or liver disease [3, 5]. Some key neurologic effects include acute decreases in mental performance, audiovisual ability, and manual dexterity [2].

If dentists and dental assistants experience the acute neurologic effects, there is a potential adverse impact to the safety of the patient (e.g. inability to control a drill or

inserting needle in the wrong location). In fact, it has been suggested by Shaw and Morgan (1998) that chronic low levels of anesthetic gases, like nitrous oxide, may impair the performance of staff working in these environments [6]. However, the proper use of ventilation and scavenging systems dramatically reduces the levels of nitrous oxide in the clinical environment [6] and are key components in mitigating dental employee exposure where nitrous oxide is used.

Animal studies have shown that exposure to nitrous oxide during gestation can produce adverse health outcomes in offspring and indicate that the toxic effects of nitrous oxide are concentration and time-dependent [5, 7]. These adverse health effects have been demonstrated with continuous exposures of 1,000 ppm_v or higher. However, at lower exposure levels or shorter intermittent exposure, increased fetal loss is not seen consistently. Increased fetal loss has been reported in rats exposed to as little as 100 ppm_v nitrous oxide for 8 hours a day from 4-9 days during gestation [8, 9].

Nitrous oxide is used extensively in dental facilities. Breathing zone samples of dental personnel have linked occupational exposure to nitrous oxide with a number of health problems and adverse reproductive outcomes [7]. Even so, there is not an occupational Permissible Exposure Limit (PEL) promulgated by the Occupational Safety and Health Administration (OSHA) for nitrous oxide. However, the National Institute for Occupational Safety and Health (NIOSH) has a Recommended Exposure Limit (REL) for nitrous oxide of 25 parts per million by volume (ppm_v) [10]. There is also an eight-hour threshold limit value-time-weighted average (TLV-TWA) recommended guideline for

nitrous oxide by the American Conference of Governmental Industrial Hygienists (ACGIH) of 50 ppm_v [1].

The occupational exposure limit (OEL) adopted by the Indian Health Service (IHS) is 50 parts per million by volume (ppm_v) for an 8-hour work day. In addition, current IHS policy follows ACGIH recommendations that excursion limits should not exceed three times the TLV-TWA (150 ppm_v) for no more than a total of 30 minutes during a workday, and under no circumstances should excursion limits exceed five times the TLV-TWA (250 ppm_v) [1, 11]. Excursions are short-term exposures that deviate above the normal path of concentration [12]. Excursions above the OELs allow high levels of the toxicant of concern, nitrous oxide, to reach the cellular level of the central nervous system increasing the concern for short-term and chronic exposures. Excursion limits apply to those TLV-TWAs that do not have a threshold limit value-short-term exposure limit (TLV-STEL), like nitrous oxide. A TLV-STEL is a 15-minute time weighted average exposure that should not be exceeded at any time during a work day, even if the 8-hour time weighted average is within the TLV-TWA [1].

There has been growing concern regarding employee exposures to nitrous oxide in IHS dental clinics, even though engineering and environmental controls like ventilation and active scavenging systems have been in place for many years. Several internal IHS air sampling reports using the Thermo ScientificTM Miran SapphIRe portable analyzer (Miran) have shown breathing zone concentrations of nitrous oxide that were well above the OELs. The exposures exceeded an average of 250 ppm_v during dental

procedures and several maximum readings were over 500 ppm_v. Figure 1 shows a conceptual model of how dental employees are exposed to nitrous oxide.

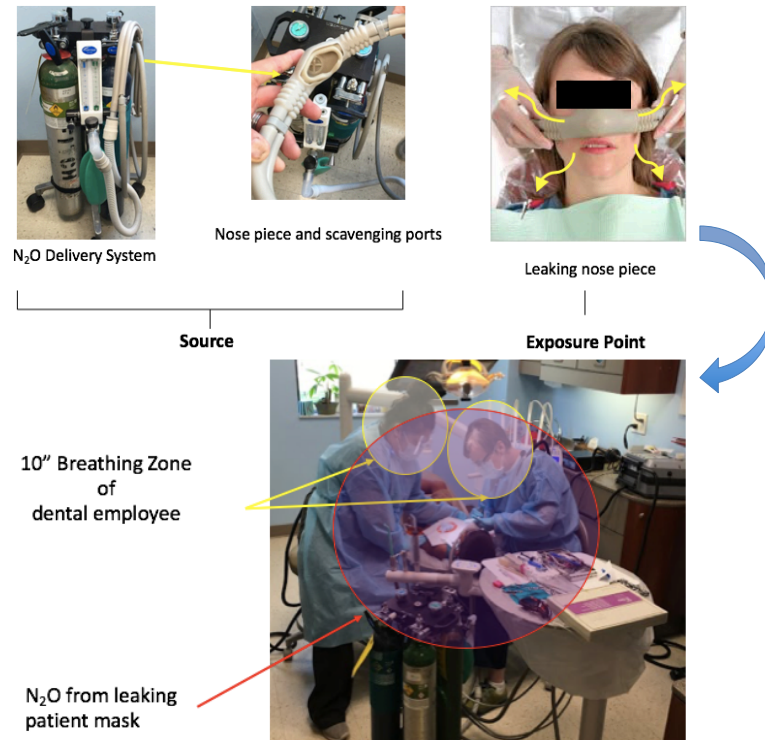


Figure 1: Conceptual model of how dental employees are exposed to nitrous oxide.

To help reduce the excursion, IHS dental clinics have revised their policy on the monitoring and control of nitrous oxide exposures of employees. The revised policy was based on the national IHS policy, but were restructured and enhanced to be more specific and user-friendly. For example, it included step-by-step guidelines (with pictures) to help guide employees through leak checks, maintenance and overall safety procedures. Air samples taken since the revised policy was instituted have shown nitrous oxide levels lower than before, indicating improvement. Nevertheless, some measurements remain above the TLV-TWA and excursions still occur.

A portable analyzer utilizing an infrared spectrometer for gas monitoring (Thermo ScientificTM Miran SapphIRe) will be used in this study, as it is commonly used in the field by IHS personnel to help determine nitrous oxide exposure. However, portable analyzers have limitations in the field as they are large, heavy, expensive to purchase/maintain, and are difficult/expensive to ship and use in remote locations common in the IHS. In addition, they require advanced technical training that reduces the number of personnel capable of performing the surveys and increases costs.

Comparatively more affordable, passive dosimeters are regularly employed to determine potential nitrous oxide exposures. Passive dosimeter badges are a popular method of sampling because they are compact and portable, require minimal manipulation, are low cost, and can be conveniently used for personal monitoring (breathing zone) [13-15]. However, with short duration samples the level of quantification (LOQ) for passive dosimeters may not adequately obtain accurate results. The limit of quantifications are the stated limiting values for the lowest and highest concentration that can be quantified with confidence [12]. For instance, the passive dosimeter used for this study has a minimum LOQ of 1 ppm_v for one hour and requires a minimum 30-minute sampling period. As a result, both validity and reliability issues become potential limitations with a 30-minute sampling period as some dental procedures take less than 30 minutes to complete. In addition, the passive dosimeter used in this study has a maximum LOQ of 500 ppm_v and results exceeding this limit, and associated 8 hour TLV-TWAs, will be considered an estimate of concentration. Furthermore, when compared to real-time detection devices that can average readings captured at intervals every few seconds, passive dosimeters are less likely to detect peak levels from

excursions, Figure 2.

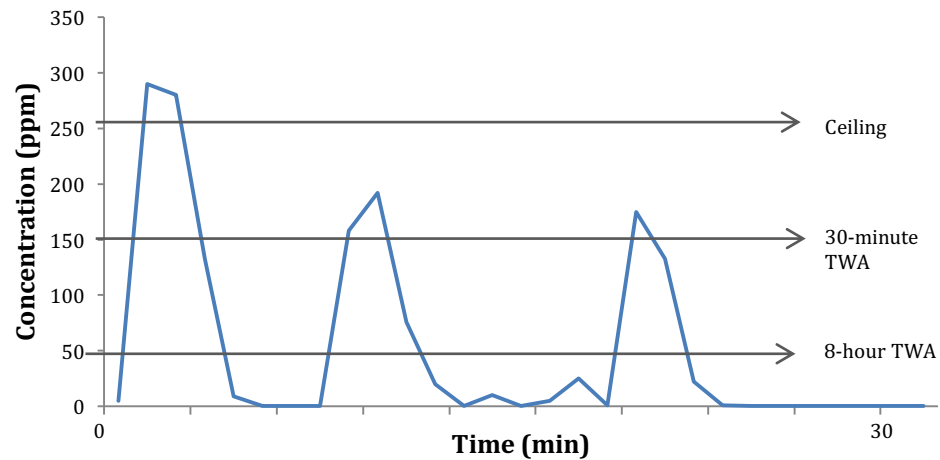


Figure 2: Hypothetical 30-minute nitrous oxide exposure profile. Brief excursions may occur that cannot be detected using a 30-minute averaging time provided by a passive dosimeter.

Comparing the two methods could help determine if they should be used in unison, if one's result can be used for both, or if one should not be used at all. This could provide the IHS with information to help guide policy to make staff more effective and efficient when determining dental employee nitrous oxide exposure in the future.

Specific Aims

The ultimate goal of this study is to determine if there is a nitrous oxide exposure concern. Additionally, this study seeks to identify possible mitigating factors to help prevent exposure. This study may also help determine if there is a difference in exposures between Dentists and Dental Assistants. This is of particular interest as Dunning, et al. (1996, 1997) found that dentist exposures were significantly higher than dental assistants, including higher excursion levels [16, 17]. With this in mind, the specific aims listed below were created to help guide this research. Focus will be on characterization of

airborne nitrous oxide concentrations, comparing active and passive sampling methods, and exploring potential mitigating factors identified by the American Dental Association [18].

- Characterize airborne nitrous oxide concentration levels during dental procedures using the Advanced Chemical Sensor Passive Badge and the Thermo ScientificTM Miran SapphIRe portable analyzer.
 - Compare results with the IHS/ACGIH excursion and threshold limit value-time weighted average exposure limits.
 - Compare Dentist and Dental Assistant concentrations using the independent *t*-test.
- Determine if the Advanced Chemical Sensors passive badge and the Thermo ScientificTM Miran SapphIRe portable analyzer time weighted average estimates are within the Occupational Safety and Health Administration (OSHA) minimum accuracy criteria of 25%_v, with 95% confidence, of each other using Bland Altman analysis.
- Characterize the number of air changes per hour, nitrous oxide flow rate, and the nitrous oxide percentage in each clinical exam room studied, and determine if there are any exposure concentration trends.

CHAPTER 2: Literature Review

Concern Regarding Chronic Employee Exposure to Nitrous Oxide

Becker and Rosenberg (2008) state that nitrous oxide is considered generally safe to use for dental patients and that nitrous oxide could be the safest of all the modalities available for sedation in dentistry. However, they also noted that chronic exposure to nitrous oxide could lead to adverse health effects, thereby putting dental employees at risk. Becker and Rosenberg further state that those connected with chronic adverse effects could possibly experience infertility, spontaneous abortion, blood dyscrasias, and neurologic deficits [4].

Szymanska (2001) further adds that dental employees chronically exposed to nitrous oxide are at serious risk. Although occupational effects are still uncertain, there are real potential adverse health effects on the reproductive, neurological, haematological, hepatic and renal systems. In addition, Szymanska observed a decrease in psychomotor performance on visual perception, immediate memory, cognition, and motor responses with human subjects receiving as little as 50 ppm_v nitrous oxide over a two-hour period [19]. This could be of some concern as patient safety would then be at risk.

According to Howard (1997), chronic exposure to nitrous oxide can produce irreversible toxic changes to dental employees utilizing nitrous oxide. Howard continues that chronic exposure to nitrous oxide has been associated with neurological, immunological, reproductive, hematologic, liver and kidney disorders. Howard also

found that exposure is dose and time dependent, increasing intensity of health effect with higher exposure [20].

Sanders, Weimann, and Maze (2008) state that although gas scavenging systems have drastically reduced nitrous oxide levels in operating rooms, peak nitrous oxide concentrations exceeding 1,000 ppm_v have been recorded [21]. These peak exposures, or excursions, are a concern as levels over 250 ppm_v should not be exceeded at any time when nitrous oxide is in use [1, 11]. Sanders, et al. also found evidence showing that nitrous oxide exposure can induce fertility defects through inhibition of methionine synthase; however, there is no evidence that this toxicity occurs with concentrations below the occupational exposure limits. Nevertheless, animal data suggests that doses of 500 ppm_v are a threshold for this toxicity, raising concerns for peak excursions above 250 ppm_v for chronically exposed employees [21].

Middendorf, et al. (1986) characterized dental employees' nitrous oxide exposure using active sampling method (Miniature Infra-Red Analyzer, 1A-CVF Gas Analyzer, Model 063-0015) so they could compare his findings to the National Institute of Occupational Safety and Health's (NIOSH) recommended time-weighted average of 25 ppm_v (for one operation). Although the Miran used by Middendorf, et al. is a different model, it uses the same infra-red technology as the Miran used in this study. Personal sampling results ranged from 132-880 ppm_v and were between 10-120 minutes per procedure. Their results were consistently higher than the NIOSH limit of 25 ppm_v [22].

Kugel, Norris, and Zive (1989) characterized dental employees' nitrous oxide exposure and ambient nitrous oxide levels using the Miran 101 (Miniature Infrared

Analyzer 101 Specific Vapor Analyzer manufactured by The Foxboro Company) when a scavenging system was employed and when one was not. Kugel, Norris, and Zive maximum nitrous oxide exposure results in the dentist breathing zone ranged from 15-1000 ppm_v with means ranging from 3-239 ppm_v. Maximum ambient nitrous oxide level results were taken at the foot of the dental chair (~6 feet) ranged from 0-320 ppm_v with means ranging from 0-213 ppm_v. These results show that scavenging systems alone may not be sufficient to protect dental employees from nitrous oxide exposure [23].

Dentist vs. Dental Assistant Exposure

Only two journal articles that compared dentist's nitrous exposure to dental assistant's nitrous exposure could be found during this literature review; both were written by the same authors using the same study. Dunning, McFarland, and Safarik (1996, 1997) measured the nitrous oxide exposure levels among 70 dentists and their primary dental assistant to determine risk of exposure. Results were compared using *t*-test comparisons of the means. They showed that dentist exposures were significantly higher than dental assistants (97 ppm_v vs 59 ppm_v, respectively), including higher excursion levels (1415 ppm_v vs 986 ppm_v, respectively). Samples were collected using the Landauer 40-hour passive dosimeters that were validated by OSHA. However, the excursion levels were calculated by the laboratory and not measured using active sampling. Excursion levels were estimated by taking the total minutes the monitor was worn divided by total minutes nitrous oxide was used and multiplied by the 40-hour TLV-TWA. [16, 17].

Active Sampling (Miran) for Personal Exposure Monitoring

Christensen, Vann, and Linville (1985) utilized Miran infrared spectrophotometer (Miran 1A, Wilks, South Norwalk, CT) to determine levels of nitrous oxide in dentist personal breathing zones while testing different scavenging system masks. The breathing zone in their study was 6-10 inches from the nose of the dentist [24]. This was based on the study conducted by Whitcher, et al. (1977) that showed overwhelming evidence that the breathing zones have the highest levels of nitrous oxide [25]. The Miran was used to determine time weighted averages and peak levels of nitrous oxide in the breathing zone of the dentist that participated in the study. They used the Miran during 80 dental procedures to determine results and showed a significant difference in the effectiveness of the two ADA scavenging systems [24] demonstrating that infrared technology can be used to determine ambient nitrous oxide levels during dental procedures.

Henry and Primosch (1991) used a Miran infrared spectrophotometer (Miran 1BD, Foxboro, South Norwalk, CT) to determine waste nitrous oxide concentrations in the personal breathing zones of dental personnel. They were also attempting to determine if the size of the operating room has any influence on scavenger effectiveness. Their characterization of nitrous oxide exposure concentrations included minimum, time weighted averages, and peak exposure levels. The breathing zone was defined as 50-56 cm from the nose directly above the patient's chest. The further distance away from the nose compared to the 6-10 inches used in this thesis and mentioned above was due to minimizing concerns regarding carbon dioxide as it has an infrared absorbance wavelength of 4.43 μm , very near to that of nitrous oxide absorbance of 4.54 μm . Water vapor was also a concern as they worried it could be a possible blocking/interfering

agent. These concerns have been indicated as limitations in the US Environmental Protection Agency publication 9360.8-17FS [26]. However, during the pilot study at 10 inches from the nose, nitrous oxide levels above 1800 ppm_v were noted, raising concerns of higher exposure rates when measured closer to the breathing zones of dental employees. [27].

Henry and Jerrell (1990) used a Miran infrared spectrophotometer (Miran 1B, Foxboro, South Norwalk, CT) in a similar approach as Henry and Primosch (1991). Their purpose was to accurately determine waste nitrous oxide levels during pediatric sedations in the dental personnel breathing zone, and to evaluate the effect of scavenging in reducing environmental exposure. This included minimum, time weighted averages, and peak exposure levels of nitrous oxide. Because similar concerns as reported by Henry and Primosch (1991) regarding carbon dioxide and water vapor, the breathing zone was defined as 22-24 inches from the nose directly above the patient's chest [28].

Similar to this thesis, Henry and Primosch (1991) and Henry and Jerrell (1990) had the manufacturer calibrate the Miran infrared spectrophotometer (Miran 1B, Foxboro, South Norwalk, CT), while zeroing of the instrument was accomplished prior to each use. Additional similarities included measuring nitrous oxide per procedure and using averaged 15-second intervals throughout each appointment [27, 28].

Passive Dosimeters for Personal Exposure Monitoring

Gorecki and Namiesnik (2002) argue that sampling is the most important step in analytical procedure, including personal exposure in workplace air. However, in many cases, it is necessary to perform additional operations prior to the final determination of

the sample, where errors cannot be corrected for later in the process. Many of these additional operations require numerous steps and can take hours to perform. Gorecki and Namiesnik state that it is obvious that the biggest gains in result times of an analytical system can be achieved by reducing the time required to process the samples. They further state that passive sampling addresses these issues as they combine sampling, analyte isolation and pre-concentration into a single step with little to no solvent required.

Gorecki and Namiesnik conclude that there are many advantages with passive sampling, including simplicity, low cost, no power requirements, unattended operation, and the ability to produce accurate results. However, they state that limitations may be difficult to overcome on the uptake of the analyte include possible effects from temperature, air movement, and humidity and that further research is warranted [29].

Mazur, et al. (1980) compared passive sampling in an operating room to a charcoal tube monitor that was exposed to the same gases at known concentrations at various lengths of time to determine the comparability of the passive sampler. The passive sampling results were then compared to the charcoal tube monitor results for correlation. Sampling time, concentration, and storage were all variables that were studied. Mazur, et al. concluded that the passive sampler was a reliable and convenient sampling method with relative standard deviations ranging from 0.8-15.4%. They also discuss the advantages of passive sampling. First, passive badges are more cost effective and easier to use. Second, passive badges do not require on-site assembly, and third, unlike active sampling, passive samplers are not subject to malfunction [30].

Active vs. Passive Sampling Methods

In the article by Yu, Morandib, and Weisela (2008), passive badge application in ambient indoor air monitoring and personal exposure studies using nitrogen dioxide (NO₂) are discussed. They compare the passive sample performance to active samplers to help determine if passive monitoring can be used in place of active monitoring. Their study indicates there is a measurement bias in NO₂ passive sampling results compared to active monitors. They suggest this bias could be due to other interfering compounds. Yu, Morandib and Weisela concluded that passive monitoring is potentially a viable alternative to active sampling, and that there is a need for field studies where the passive samplers are collocated with active sampling methods in realistic conditions [15].

Zabiegała, et al. (2010) state that there are many advantages for using passive sampling, especially in the field where it could be difficult to use larger, more cumbersome sampling methodologies. Some of the most compelling advantages discussed were reduced cost, ease of use, and the collection of long-term measurements, as they do not need a source of power. Zabiegała, et al. stressed that intrusive monitoring methods can impede the dentist or dental assistant from performing their duties effectively. Therefore, they contend that effective monitoring requires relatively non-intrusive monitoring strategies [14].

However, Zabiegała, et al. state that one needs to consider numerous variables when using passive sampling, including the choice of passive samplers, locations, duration of exposure, and issues surrounding quantification in the laboratory. The authors also state that there are still serious limitations to the application of passive sampling. Significant limitations include temperature, air humidity, and air movement on the

analyte uptake. Zabiegała, et al. further conclude that important factors to properly interpret data include knowledge of the source, quantity in the environment, and the analytical methods used for quantification. The authors conclude proper sample collection is of high importance if results are to be representative of exposure, and thus lead to correct data interpretation and conclusions [14].

Mukerjee, et al. (2004) compared passive NO₂ samplers to active continuous samplers to determine if there was a difference. They found that precise results (<5% relative standard deviation) were found for NO₂ measurements from collocated passive samplers when compared to active sampling results. However, the passive results did over predict when compared to the active sampling results due to the variability in the lack of a statistical fit test. Mukerjee, et al. conclude by stating that method evaluations should continue to be conducted to further establish passive sampling capabilities. Additionally, these method evaluations of passive samplers should be a routine quality assurance component when deployed in exposure assessment studies [31].

Bishop and Hossain (1984) compared two passive samplers (Solid State Sensor Monitor® and R.S. Landauer, Jr. and Co.) to conventional (active) sampling methods, the Miran 1-A® IR, to evaluate their use as passive monitors for fugitive nitrous oxide concentrations in medical, dental and veterinary facilities. The nitrous oxide passive sampler results were compared to the Miran between a range 4-330 ppm_v. Two-sided *t*-tests were performed to determine slope and the 95% confidence level. The Landauer passive sampler was determined to have ideal correlation with the Miran.

Effects of Percent and Flow Rate of Nitrous Oxide Used

Henry and Primosch (1991), in addition to using active sampling, also looked at any association between percent of nitrous oxide used and ambient nitrous oxide air levels in dental clinics. They showed a significant reduction of ambient waste nitrous oxide concentration when percent nitrous oxide administered was reduced from 50% to 30%. They stated that no actual evaluation had been conducted for comparison. However, the results of Henry and Primosch's study suggested that such a relationship does exist, further stating that low ambient nitrous oxide levels were influenced by the concentration delivered to the patient [27].

Borganelli, Primosch, and Henry (1993) studied effects air changes per hour in a closed dental operatory would have on ambient nitrous oxide levels. Their design used air exchange rates of 0, 5, 10, and 15 per hour. They delivered 40% nitrous oxide mixture with a total flow rate of 5 L/min to a mannequin. They then measured ambient levels of nitrous oxide at 0, 15.3, 30.7, and 61.4 cm from the nitrous oxide delivery mask using an infrared spectrophotometer (Miran 1B®, Foxboro, South Norwalk, CT). The authors found that operatory ventilation at all rates greater than zero air changes per hour produced a significant reduction in the ambient nitrous oxide levels observed. The highest exposure levels observed were with a zero-air exchange rate and were 177 ± 71.7 ppm_v and the lowest levels were achieved at an air exchange rate of 15 per hour reducing exposure levels to 16.3 ± 4.5 ppm_v. All exposure concentrations were measured at 61.4 cm from the nasal hood. However, this study was conducted in an ideal setting and further research should be conducted regarding real world scenarios [32].

CHAPTER 3: Methods

To measure nitrous oxide levels during each dental procedure, an active and passive sampling method was employed. A Thermo ScientificTM Miran SapphIRe Portable Analyzer (Miran) utilizing an infrared spectrometer for gas monitoring was used to actively determine nitrous oxide levels in the breathing zones of dental employees during individual dental procedures. The nitrous oxide passive dosimeter, (catalog no. N-10) manufactured by Advanced Chemical Sensors (ACS), was also used to obtain breathing zone samples. The ACS dosimeter has been validated for an 8-hour time weighted average exposure limit of 25 ppm_v (NIOSH time weighted average). Both sampling procedures are documented in NIOSH method 6600 for nitrous oxide. Each passive dosimeter was analyzed by an American Industrial Hygiene Association (AIHA)-LAP, LLC and New York Environmental Laboratory Approval Program (ELAP) accredited laboratory.

The nitrous oxide delivery and scavenging system was inspected prior to sampling at each location to ensure proper function. This was conducted by visual inspection of the equipment and by quantitative leak testing using the Miran. Two blank ACS passive dosimeter samples were used per location to help assess the extent to which actual samples may have been contaminated.

The sampling methods were based on the NIOSH 6600 analytical method for nitrous oxide. The passive dosimeter was used according to the manufactures instructions for sampling and shipment for analysis. The Miran was prepared according to NIOSH 6600 method [33]. The following steps were conducted:

1. Selected sampling mode for ambient air;

2. Set instrument parameters as required for analysis, allowing for sufficient warm-up time;
3. Calibration was conducted by the manufacture and calibration certificate was verified by the user for all portable analyzers used;
4. Routine maintenance was conducted as needed;
5. Sample collected;
6. Accessed data for analysis.

This sampling method is similar to Middendorf, et al. when they characterized occupational exposure to nitrous oxide in dental operatories in 1986. This also included purging and zeroing the active sampler with uncontaminated air [22]. In addition, the method for this study includes turning on the Miran at least 30 minutes before use, allowing the electronics to warm up. Once warmed up, the Miran was zeroed by measuring the nitrous oxide concentration of uncontaminated air, which is similar to the method used by Kugel, Norris, and Zive. [23].

To quantify any differences between the Miran and the ACS passive dosimeter, both sampling devices were co-located during exposure sampling. The active sampling probe was connected to sampling tubing and located within the breathing zone (e.g. clipped to a collar). The breathing zone is defined as the zone within a 10-inch radius of a worker's nose and mouth. It has been generally assumed that a contaminant in the breathing zone is homogeneous, and its concentration is equivalent to the concentration inhaled by the worker [34]. The passive dosimeter was also attached in the same breathing zone (e.g. clipped to the collar opposite the active sampling hose) of dental employees as shown in Figure 3.



Figure 3: Active and passive sampling devices and how they were positioned during the sampling process.

The sampling tube connected to the Miran was four meters in length to provide the dental employees ample room to move as needed to conduct the dental procedures. Each tube was connected to its designated Miran, with the particulate filter in place, as shown in Figure 4. Similar exposed groups (SEGs) were defined by job title, dentist and dental assistant, and sampled simultaneously and identically. Due to logistical limitations SEGs were not able to be randomized.

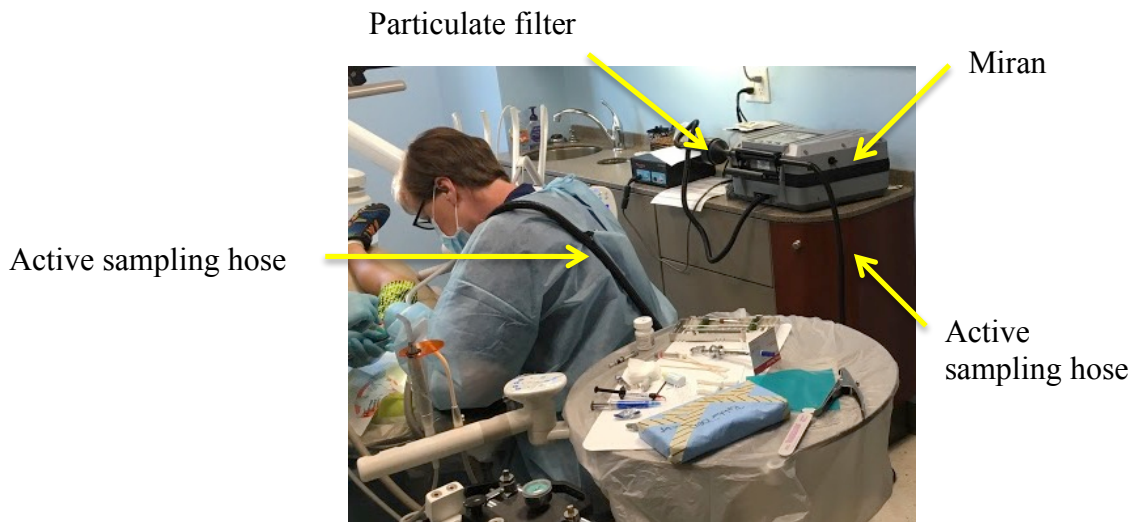


Figure 4: Miran and sampling hose connected to the dentist. The dental assistant had the same sampling train as well.

All operatories were of similar temperature, size, and overall working condition. They used similar standard operating procedures, and all facilities were built, owned, maintained and operated by the IHS. The only determined difference between the locations was atmospheric pressure. The Miran is sensitive to pressure differences and was corrected using manufacturer guidance prior to sampling at each site by manually entering the atmospheric pressure [35].

Each device sampled from the time nitrous oxide use began until the time the nitrous oxide supply mask was removed from the patient. After procedure completion, the ACS dosimeter was removed and maintained according to the manufacturer's directions for shipping and analysis and the Miran was stopped. A new ACS dosimeter was then donned, and the Miran reset before the next dental procedure that utilized nitrous oxide began. All comparisons of the TLV-TWAs between ACS dosimeter and Miran sampling methods used the same averaging time, be it per procedure or per 8-hour work day. Note, the maximum limit of quantification (LOQ) for the ACS passive

dosimeter is 500 ppm_v. All results exceeding the maximum LOQ will be recorded as 500 ppm_v for analysis as this is the best estimate of the actual result. The ACS dosimeter 8-hour TLV-TWA was provided by the accredited laboratory after analysis and the Miran 8-hour TLV-TWA was calculated using equation 1. This would be the cumulative average dose in an 8-hour day for each volunteer. The duration of the work day that had no exposure was assumed to be a concentration of zero:

$$\text{8-Hour TLV-TWA} = \frac{C_1T_1 + C_2T_2 + C_3T_3 + \dots}{8} \quad (1)$$

Where: C_x is Concentration of procedure
T_x is Time of procedure

Quality Control

Quality control was performed throughout this study to help ensure the integrity of the data for analysis. Quality control of each sampling method is detailed below.

Advanced Chemical Sensors™ (ACS) Passive Badge Quality Control

To ensure quality data, all Advanced Chemical Sensors™ (ACS) passive badges were only exposed to the atmosphere immediately prior to each procedure. At the completion of each procedure, the badges were immediately sealed from the atmosphere per manufacturer's instructions. In accordance with quality control procedures for NIOSH method 6600, at least one field blank was submitted for analysis from each sampling location. Samples and field blanks were stored at room temperature and shipped within one week of analysis, meeting manufacturer recommendations of shipping within two weeks of analysis. All samples and field blanks were analyzed within 48 hours by the

Advanced Chemical Sensors™ Laboratory, an AIHA LAP accredited laboratory in Boca Raton, FL (Lab # 102047).

Thermo Scientific™ Miran SapphIRe Portable Analyzer Method Quality Control

There were three Miran SapphIRe Portable Analyzers (Miran) used in this study. Each analyzer warmed up for 30 minutes prior to sampling per manufacturer recommendation. The same analyzer was used consistently with a particular similar exposure group. Miran 1 was used exclusively with Dental Assistants, and Miran 2 and Miran 3 were used with Dentists. Once in operation, the analyzer continuously recorded concentration levels of nitrous oxide. The time each ACS badge was exposed to the atmosphere was carefully recorded and matched to the Miran to ensure comparability of the data.

Each instrument calibration for nitrous oxide must be conducted annually by the manufacturer, and each instrument was verified as current prior to each sampling evolution.

Statistical Methods

To compare the Dentist SEG TLV-TWA concentrations with the Dental Assistant SEG TLV-TWA concentrations, the groups were tested for homogeneity using Levene's test, and for normality using the Shapiro-Wilk test. When the assumption of homogeneity was not met, Welch's *t*-test was used. When the assumption of normality was not met, the non-parametric alternative, the Mann-Whitney test, was used. Otherwise the Independent *t*-test was used.

For comparison of the Miran time-weighted concentrations with the ACS dosimeter time-weighted concentrations, the assumption of normality of the paired

differences was tested using the Shapiro-Wilk test. When the paired differences were found to be normally distributed, the paired t -test was used. When the assumption of normality was not met, the Mann-Whitney test was used.

According to Miltz, Mulhausen, and Damiano (2006), the distribution of industrial hygiene exposure data is known to be either normal or log-normal [36]. Log-normally distributed data was reported as geometric means and standard deviations. Log-normal data was tested using parametric statistical tests. Analysis of the results were conducted using IBM SPSS® Statistics, Version 22.0 with an alpha 0.05 as the level of statistical significance and according to guidance by Field, Miles and Field [37].

Descriptive Statistics

Descriptive statistics was used to characterize dental employee exposure to nitrous oxide by method and job title. TLV-TWAs and excursion levels were then compared to the IHS policy and ACGIH guidelines to determine if occupational exposure is a concern.

A mean sample result was used to determine if there is a difference between job titles (dentist vs. dental assistant) using an independent t -test. This could lead to a more focused preventative effort regarding procedure or employee role.

Method Comparison

A paired t -test and Bland Altman analysis was used to determine if there was a significant difference in the estimated time weighted average levels using the passive and active sampling methods determined time weighted averages by job title [38].

For measuring the degree of agreement between the two methods of analysis, Bland-Altman analysis was used [38]. The analysis compares methods quantitatively and

visually as a plot of percent difference relative to the mean difference between the methods vs. the mean value between the methods, equation 3.

$$\% \text{ Difference} = \frac{(M_1 - M_2)}{M^-} \times 100$$

Where: M_1 = Measurement from method 1
 M_2 = Measurement from method 2
 M^- = Mean of measurements of method 1 and method 2 (2)

To be consistent with typical OSHA accuracy criteria, the methods would be considered equivalent if the mean percent difference was within 25%_v with 95% confidence [39].

Exploration of Potential Explanatory Variable

To explore the effects of patient nitrous oxide flow rate and percent of nitrous oxide on the TLV-TWA, the exposure concentrations observed during a procedure were plotted against nitrous oxide flow rate or percent nitrous oxide used per procedure. In addition, characterization of air changes per hour in each operatory used during the study was compared with observed exposure concentrations. The measurements of the room air exchanges per a unit of time were determined using a balometer flow capture hood (Shortridge Air Hood Flowmeter®) or thermal anemometer (TSI VelociCalc®), where needed.

Study Power

The goal of this study was to collect enough samples to reach 80% power at the 0.05 level of significance. Based on previous IHS sampling, this study was expected to have a large effect size. Effect sizes are calculated to indicate the relative magnitude of the difference between means [40]. Table 1 shows the eta squared values that will be used

to determine the sample size and effect size for this study. Eta squared is a measurement of effect size. The calculations are based on 80% power, an alpha level of 0.05, and two-sided. This was conducted using computer software (G*Power 3.1) for power and sample size [41].

Table 1: Eta squared value and effect size for a given sample size.

Sample size (n)	Eta squared	Effect size
788	0.01	Small
128	0.06	Medium
52	0.14	Large

CHAPTER 4: Results

A total of 41 paired samples from seven different dental operatories at six different facilities were collected during 23 dental procedures using nitrous oxide. As normality was inconsistent throughout the data, all data was log-transformed to meet the assumption of normality for statistical analysis.

Quality Control

In accordance with quality control procedures for NIOSH method 6600, a minimum of one field blank was submitted for analysis from each sampling location, a total of 12 blanks (2 per location) were collected. All field blanks were below the method limit of detection. Any samples above the upper quantification range (500 ppm_v) of the passive method were entered as 500 ppm_v for the per-procedure time weighted average. All 8-hour time weighted averages provided by the laboratory were used.

Sampling Results by Location and Method

Sampling of dental personnel occurred at six different locations over 10 separate days and involved 8 dentists and 10 dental assistant volunteers. Sampling concentrations are reported as a threshold limit value – time weighted average (TLV-TWA) for the duration of each dental procedure and for the full workday (expressed as an 8-hour TLV-TWA). In some instances, an instrumentation error occurred so no concentration could be calculated. Tables 2 and 3 summarize the sampling results for each individual sampled by location and date.

Table 2: Dentist Sampling Summary.

Location	Date	Subject #	Sample Duration (hr)	Miran Concentration (ppm)	8-hour TWA Concentration (ppm)	ACS Badge Concentration (ppm)	8-hour TWA Concentration (ppm)
1	7/25/16	D1	0.38	Instrument Error		58	7.7
			0.30	Instrument Error		200	
			0.53	19.8	5.9	38	
			0.33	61.9		83	
			0.40	39.9		36	
	7/26/16		0.55	72.3	5.0	150	10
2	7/28/16	D2	0.62	6.4	20	7.1	13
			0.67	236.3		150	
	7/28/16	D3	0.45	89.4	7.7	60	4.7
			0.30	71.2		36	
3	8/9/16	D4	0.25	31.8	3.3	40	4.3
			0.27	47.6		50	
			0.40	14.7		27	
4	8/10/16	D5	0.42	4.9	3.3	10	8.0
			0.50	22.7		91	
			0.45	28.2		32	
5	9/12/16	D6	0.72	118	11	270	24
	9/13/16		0.60	292	22	88	6.6
	9/14/16	D7	0.57	242	17	500	152
6	11/16/16	D8	0.30	Instrument Error		210	7.9
			0.52	310	42	500	44.1
			0.52	340		500	55.6
	11/17/16		0.93	82.8	9.6	360	42

Among the Dentists, there were 151 excursions above 250 ppm_v using the Miran SapphIRe Portable Analyzer. All Miran 8-hour TWA concentrations were below 50 ppm_v. However, there were two ACS 8-hour TWAs above 50 ppm_v (55.6 and 152 ppm_v).

Table 3: Dental Assistant Sampling Summary.

Location	Date	Subject #	Sample Duration (hr)	MIRAN Concentration (ppm)	8-hour TWA Concentration (ppm)	ACS Badge Concentration (ppm)	8-hour TWA Concentration (ppm)
1	7/25/16	DA1	0.38	Instrument Error		41	8.8
			0.30	Instrument Error		81.8	
			0.53	14.0	1.7	32.1	
			0.33	19.4		39.1	
		DA2	0.40	20.1	1.5	61.1	4.8
			0.55	6.50		25.4	
2	7/28/16	DA3	0.62	4.80	21	3.7	14
			0.67	150		89.9	
			0.45	112		71.9	
			0.30	38.8		45.5	
			0.25	9.00		21.4	
3	8/9/16	DA4	0.27	35.7	2.2	61.5	3.6
			0.40	14.1		16.6	
			0.42	0.900		7.8	
4	8/10/16	DA5	0.50	6.00	1.0	7.8	1.5
			0.45	10.0		11	
			0.72	69.7		47.1	
5	9/12/16	DA6	0.60	105	7.9	500	81.3
	9/13/16		0.57	166	12	204	15
	9/14/16	DA7	0.60	17.6	1.3	66.6	5.0
6	11/16/16	DA8	0.52	47.1	10	72.2	16
			0.52	108		169.2	
			0.93	265		479	
	11/17/16	DA10					

Among the Dental Assistants, there were 53 excursions above 250 ppm_v using the Miran SapphIRe Portable Analyzer. All Miran 8-hour TWA concentrations were below 50 ppm_v. However, there were two ACS 8-hour TWAs above 50 ppm_v (81.3 and 56.0 ppm_v).

Out of the 41 total active samples collected, 21 of them had at least one excursion over 250 ppm_v. That equates to 51% of the procedures sampled not meeting the IHS policy or ACGIH guidelines for nitrous oxide excursions limits, Figure 5.

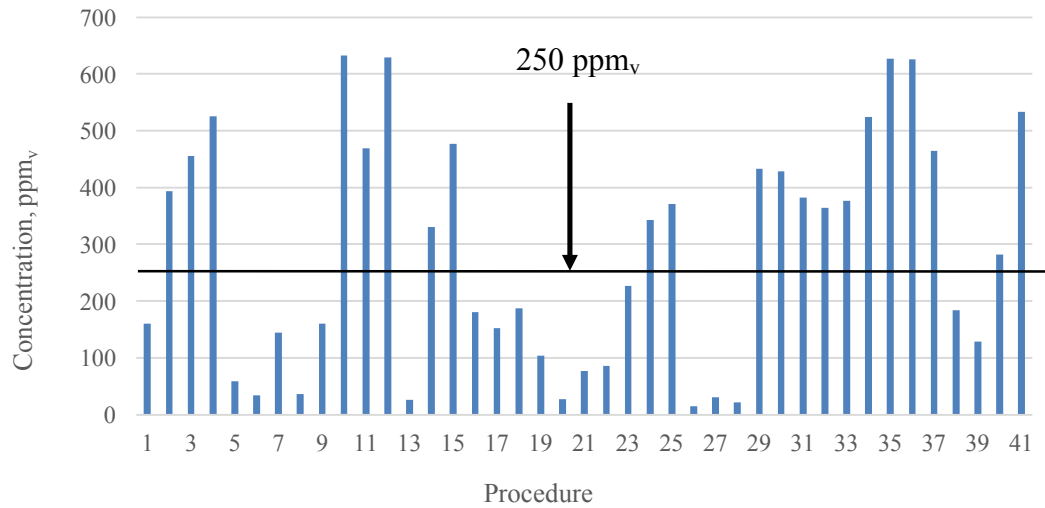


Figure 5: Maximum excursion levels per procedure. Maximum excursions can only be measured by an active sampler like the Miran.

Table 4 shows the upper tolerance limits (UTL) for the dentist and dental assistants by procedure. A UTL is the point estimate of an upper percentile in the exposure distribution and its upper confidence, allowing one to quantify confidence in a percentile estimate [42]. For example, the dentist’s mean UTL was 1245 ppm_v, meaning that one is 95% certain that 95% of the exposures are less than 1245 ppm_v. The UTLs were calculated using the American Industrial Hygiene Association’s Multilingual IHSTST+ software according to the methods described by Mulhausen and Milz [43].

Table 4: Upper Tolerance Levels by job title and procedure.

Dentist, ppm _v			Dental Assistant, ppm _v			Avg. Procedure Length, hour
<u>Miran</u>	<u>ACS</u>	<u>Mean</u>	<u>Miran</u>	<u>ACS</u>	<u>Mean</u>	
1140	1349	1245	787	816	802	0.49

Exploring the Appropriateness of Similar Exposure Groups

When designing this study, it was assumed that regardless of location, there were two different SEGs: Dentists and Dental Assistants. Although preliminary in nature, an analysis of variance (ANOVA) was conducted by location for each SEG to investigate the appropriateness of combining all dentists and all dental assistants into two large SEGs across all locations. Log-transformed data from both sampling methods were used to conduct an ANOVA. Table 5 shows the results of the ANOVA.

A p -value greater than 0.05 would indicate the locations could not be distinguished from one another. The ANOVA was statistically significant for dentist and dental assistant (p -value of .020 and 0.018; and .012 and 0.006, respectively). These results indicate that further observation and sampling is needed to determine if the SEG should be broken into subgroups by location. However, to ensure maximum power for this study to detect a difference, two SEGs by job title across all locations were used for all analysis in this study.

Table 5: ANOVA of SEGs across all locations by job title using Miran and ACS results.

Dentist				Dental Assistant			
Miran		ACS		Miran		ACS	
<i>F</i>	<i>P-value</i>	<i>F</i>	<i>P-value</i>	<i>F</i>	<i>P-value</i>	<i>F</i>	<i>P-value</i>
3.91	0.020	4.70	0.018	4.33	0.012	4.81	0.006

To compare dentist and dental assistant's exposure, independent t -tests comparing the means from the Miran and ACS dosimeters were conducted. Table 6 and Table 7 illustrate the results of the independent t -test for the passive and active samples, respectively. Both methods of sampling showed no significant difference in airborne exposure levels between the dentist and dental assistant, p -value of 0.106 and 0.071.

Although there no statistical difference between job titles was seen, dentists showed a higher mean result in both ACS dosimeter and Miran sampling results when compared to dental assistants (81.3% and 85.7%). No statistically significant difference may indicate that all dental employees can be combined into a single SEG. Nevertheless, the consistently higher exposure for dentists suggests further observations and sampling should be conducted to potentially refine these SEGs.

Table 6: Independent Samples T-Test of Passive Samples between Dentists procedural TLV-TWA mean and Dental Assistants procedural TLV-TWA mean, including Levene's test to ensure homogeneity (p -value >0.05).

Independent Samples T-Test – Passive							
n (dentist)	n (dental asst.)	Levene's Test for Equality of Variances		t-test for Equality of Means			
		F	p -value	p -value (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
						Lower	Upper
23	23	.049	.825	.106	.25647	-.05700	.56993

Table 7: Independent Samples T-Test of Active Samples between Dentists procedural TLV-TWA mean and Dental Assistants procedural TLV-TWA mean, including Levene's test to ensure homogeneity (p -value >0.05).

Independent Samples T-Test – Active							
n (dentist)	n (dental asst.)	Levene's Test for Equality of Variances		t-test for Equality of Means			
		F	p -value	p -value (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
						Lower	Upper
20	21	.592	.446	.071	.33851	-.03009	.70710

Comparability of Sampling Methods

Active and Passive Per-Procedure TLV-TWAs by Job Title

Tables 8 and 9 compare the Miran SapphIRe portable analyzer and the ACS Passive Badge determined exposure concentrations by job title. The dentist results

showed no difference when comparing the two sampling methods (p -value of .058).

However, the dental assistant results were different between the two sampling methods with a p -value of 0.019.

Table 8: Paired sample t -test of active vs passive procedure TLV-TWA means by job title, dentist.

n (paired)	Paired Differences – Dentist					Sig. (2-tailed)
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference		
				Lower	Upper	
20	.12832	.28419	.06355	-.00469	.26133	.058

Table 9: Paired sample t -test of active vs passive per-procedure TLV-TWA means by job title, dental assistant.

n (paired)	Paired Differences – Dental Assistant					Sig. (2-tailed)
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference		
				Lower	Upper	
21	.23199	.30382	.06630	.09369	.37028	.002

Method of Analysis Comparison

Whereas the t -test can determine if two means can be distinguished from one another, it does not consider differences that are externally determined to be significant. In this study, it was important that the methods be within 25%_v of each other with 95% confidence. To measure the agreement based on these criteria, the methods were compared using Bland Altman analysis. All dental procedure TWA concentrations that had a valid pair were used to compare the Miran SapphIRe Portable Analyzer and the ACS passive badge exposure concentrations. Figure 6 and Figure 7 show the amount of agreement between the two methods by similar exposure group using the percent differences and the mean of the method concentrations for each dental procedure. In both

instances, the methods differed by more than 25%_v with 95% confidence, demonstrating that the two methods are not the same.

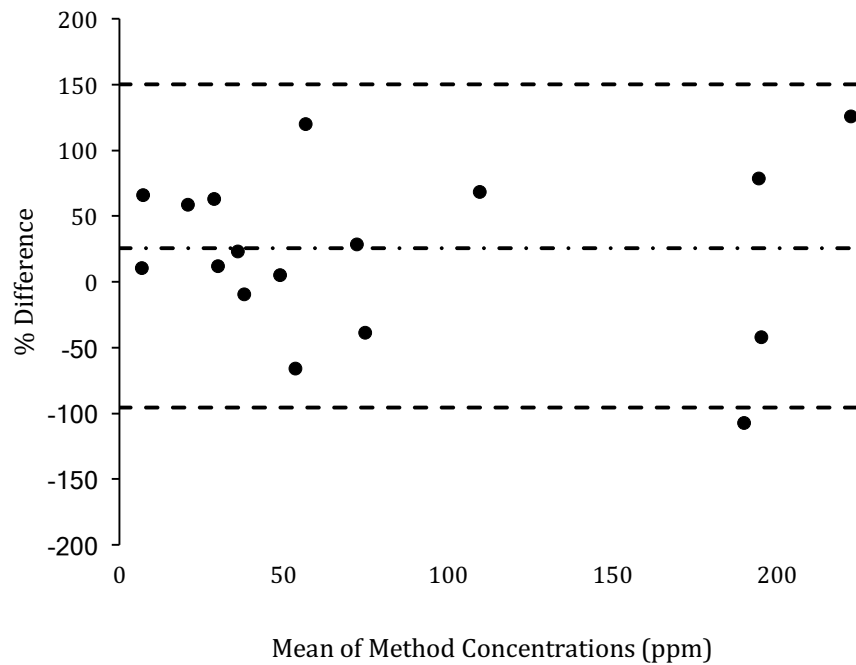


Figure 6: Dentist Similar Exposure Group Method Agreement. The mean percent difference and the 95% confidence interval are indicated by dashed lines. The distribution was log-normal and the geometric mean percent difference between methods is 26%_v with a 95% confidence limits of -95 – 150%_v. The methods differed by more than 25%_v with 95% confidence.

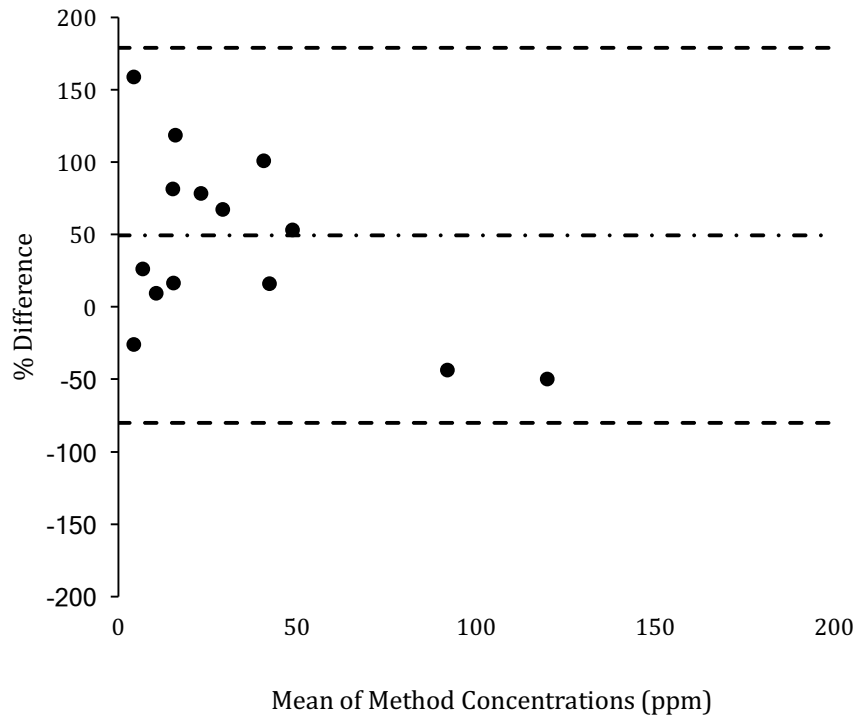


Figure 7: Dental Assistant Similar Exposure Group Method Agreement. The mean percent difference and the 95% confidence interval are indicated by dashed lines. The distribution was normal and the mean percent difference between methods is 49%_v with a 95% confidence limits of -80 – 180%_v. The methods differed by more than 25%_v with 95% confidence.

Exposure and Delivery of Nitrous Oxide and Room Ventilation Air Exchange Rates

The minimum of 12 air changes per hour for dental operatories using nitrous oxide is required and must be negative pressure [18]. Christensen, Vann, and Linville (1985) found that room air concentrations of nitrous oxide dramatically decreased as the number of room air changes and percentage of fresh air increased [24].

Table 10 provides the air changes per hour and if at least one excursion over 250 ppm_v occurred. All rooms met the required minimum air changes per hour (>12) when using nitrous oxide. Despite this, all but one had an excursion spike over 250 ppm_v. Operatory 4 had no excursion spikes above 250 ppm_v but had an air change per hour rate over 70, 5.9 times higher than the minimum.

Table 10: Air changes per hour, pressure of each dental operatory used during study and if a spike occurred.

Operatory	Air Changes per Hour	Excursion above 250 ppm_v
1	27.8	Yes
2	23.5	Yes
3	21.2	Yes
4	70.7	No
5	14.9	Yes
6	14.4	Yes
7	32.7	Yes

The percentage of nitrous oxide used with oxygen and flow rate for each procedure is presented in Figure 8. As some procedures used multiple levels of nitrous oxide, the concentration that was provided for the longest duration was used. Typical patients require 30-40% nitrous oxide to achieve ideal sedation for dental procedures. However, there can be many reasons for increasing the amount of nitrous oxide. For example, patients with higher anxiety may require higher levels [44]. In this study, 56.5% of the procedures used nitrous oxide at percentages higher than 40%.

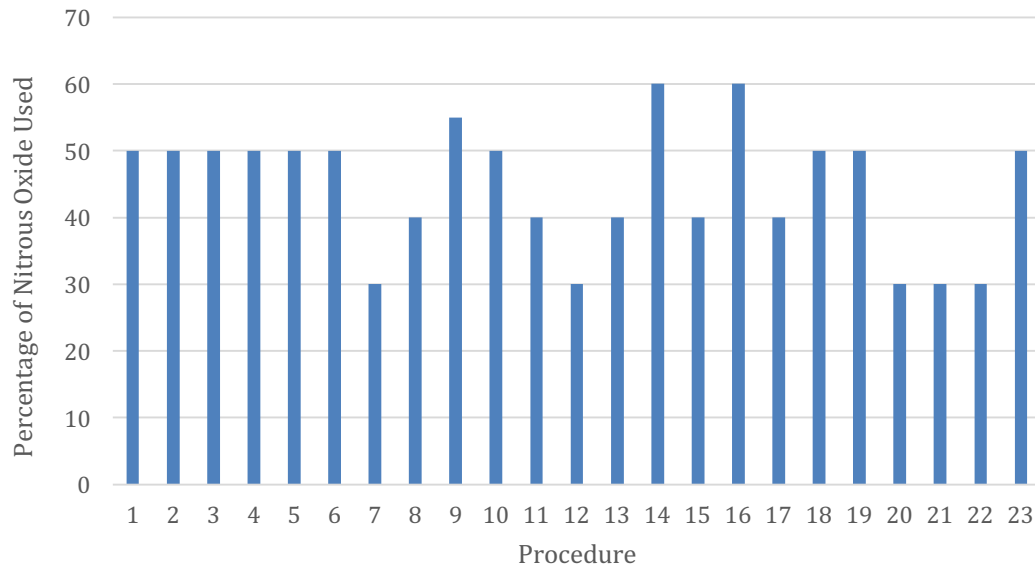


Figure 8: Percentage of nitrous oxide used during each procedure.

The nitrous oxide flow rate percentage breakdown is detailed in Figure 9. Flow rates ranged from 1-5 liters per minute. All flow rates met the recommendations of up to 5-6 liters per minute, which the American Academy of Pediatric Dentistry (AAPD) considers generally acceptable for most patients [45].

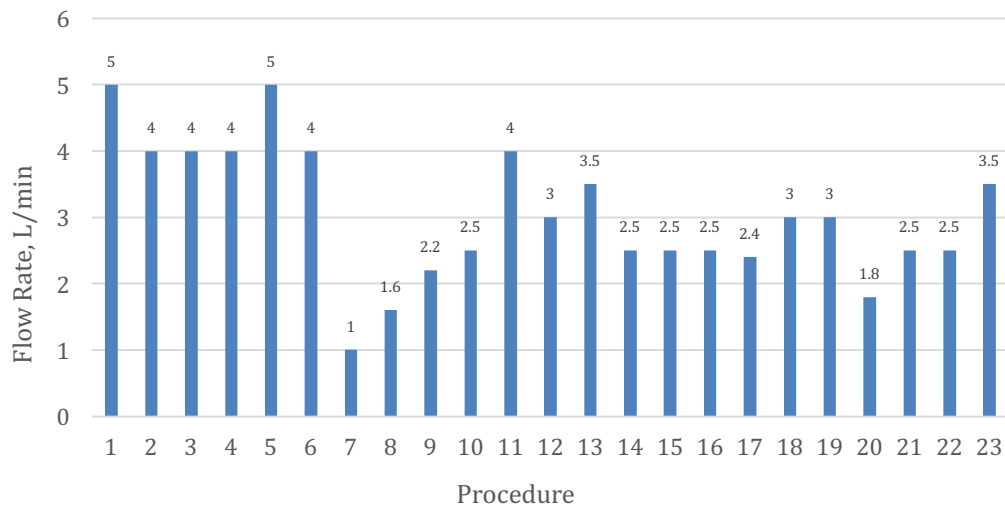


Figure 9: Flow rates of nitrous oxide per procedure.

To determine if the nitrous oxide generation rate (%Liter/minute) had an effect on the TLV-TWA, the data was plotted to determine if an association could be seen. However, no relationship was seen in this study. In addition, data was plotted to see if there was an association between air changes per hour and mean time-weighted averages. However, no association was found with these results either. All plot results can be found in Appendix A.

CHAPTER 5: Discussion

According to guidance from the ACGIH and IHS policy, nitrous oxide levels should not exceed 250 ppm_v at any point during a dental procedure. However, 51% of the 41 procedures had at least one excursion over this limit (151 excursions for dentists, 53 excursions for dental assistants). There are many variables that could contribute to these high levels of nitrous oxide in the breathing zone of dental employees, many of which are difficult to control. The variables include, but are not limited to:

- Ergonomic position of the dental employee
- Improper fit of patient delivery mask
- Nitrous oxide scavenging system not functioning properly
- Patient breathing excessively through their mouth
- Room ventilation system not functioning efficiently

These variables may not only contribute to high excursion levels and overall TLV-TWAs of the dental employees, but may also contribute to background nitrous oxide levels. Background levels of nitrous oxide continue to expose employees after a dental procedure is complete, and could accumulate with back to back procedures if the room is not ventilated completely between patients. Five samples collected with the ACS badge sampling method exceeded the 8-hour TLV-TWA during this study. If more back-to-back procedures occur, this could be a greater concern as indicated by the high mean upper tolerance limits found in this study (dentist – 1245 ppm_v, dental assistant – 802 ppm_v).

Comparing dentists to dental assistants showed no difference when using both the ACS Passive Badge and Miran SapphIRe portable analyzer sampling methods. This

result is not expected when compared to the literature [16, 17]. This could be caused by comparing the average of averages. By definition, a time-weighted average is an average of exposure over a period of time. In addition, a paired t-test compares the means (i.e. averages) of the time-weighted averages, therefore, averaging a set of averages. This further normalizes the results and can be misleading to the actual differences in the exposure levels of the volunteers. Furthermore, dentists had higher results in 81% of the ACS dosimeter results and in 86% of Miran results when compared to the dental assistants. This may be due to the proximity of the dentist to the patient, leaking nitrous oxide from the scavenging system and the patient breathing from the mouth as seen in Figure 1.

Data collected prior to conducting this study indicated 80% power to detect a statistically significant difference between exposure groups for the ACS passive badge and the Miran SapphIRe portable analyzer could be achieved with the number of samples collected during this study. The observed power, however, was 0.38 for the ACS Badge and 0.46 for the Miran SapphIRe portable analyzer. It may be that the exposure concentrations were more variable than the preliminary data had indicated.

The expectation was that there would be no difference between the Miran SapphIRe portable analyzer and the ACS passive badge, as both are validated sampling methods, which was the case when comparing the results of the dentist SEG (p -value of .155). However, it should be noted that the power of this comparison was only 51%. The paired mean difference between the two sampling methods, however, was found to be significant for the dental assistant SEG (p -value of 0.37).

Possible reasons for this difference include an insufficient number of samples, equipment failure, human factors (inadvertently blocking sampling device during routine dental activities), or outlier sampling results. Other studies have found that differences could occur through bias, including air flow, humidity, and temperature when used in the field, and conclude that additional active and passive sample comparison studies in the field should be conducted to improve understanding [14, 15]. Figure 10 is a graph demonstrating how an outlier may have caused the significant difference. The ACS Passive Badge result for procedure 12 was 8.7 times higher than the Miran SapphIRe portable analyzer result (7.8 ppm_v vs. 0.9 ppm_v respectively). When procedure 12 was removed, the *p*-value went from significant (0.002) to non-significant (0.085).

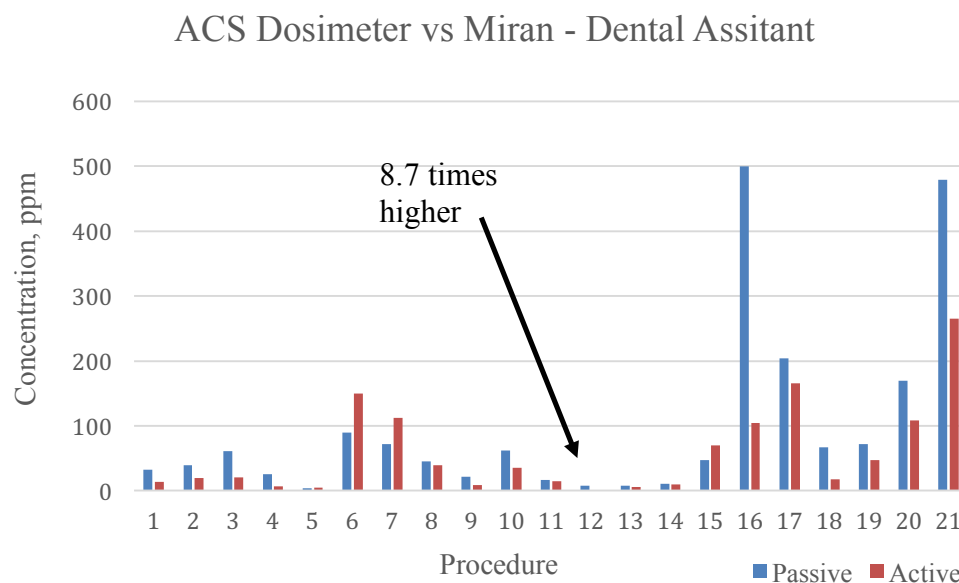


Figure 10: Sampling method comparisons per procedure for dental assistants.

The Bland-Altman analysis provided a wide confidence interval, greater than 25% with 95% confidence, for both dentist and dental assistant. This demonstrates that the two methods are not the same based on objective criteria used by OSHA for considering an

analysis to be accurate. Possible issues affecting the ACS passive badge could include temperature, air humidity, and air movement on the analyte uptake [14]. Conversely, the Miran SapphIRe portable analyzer could have sampling issues relating to carbon dioxide and water vapor interferences from the dental employees [27, 28]. Without controlling the variables that could affect the results, they are expected to have a wide range of confidence when using passive dosimeters in the field. Future studies should focus on controlling these variables in test chambers in a laboratory setting to explore potential causes of the observed difference.

According to Borganelli, Primosch, and Henry (1993), air changes per hour in closed dental operatories have a significant effect on ambient nitrous oxide levels in the breathing zone of dental employees [32]. However, their study was simulated with ideal conditions and not conducted in the field as this study was. Borganelli, Primosch, and Henry found that 15 air changes an hour dramatically reduced ambient nitrous oxide levels. Although, with air changes an hour as high as 32 in this study, excursions over 250 ppm_v were still noted.

The only dental operator that did not have an excursion over 250 ppm_v had over 70 air changes per hour. Air changes this high are not routine as the required minimum air changes per hour for rooms that use nitrous oxide is 12, almost six times less. However, this does suggest that higher ventilation rates may be helpful in controlling higher excursion levels than currently recommended and further studies should be conducted to further explore this relationship.

Association between nitrous oxide flow rate and percentage was explored. However, this study did not show a measurable relationship and is contrary to other

studies [27, 32]. This could be due to the high variability of the exposure concentrations and the narrow range of observed differences in air exchange rates (e.g. low study power).

Limitations

There were many limitations to this study as it was conducted in the field during actual dental procedures and controlling for all variables that could increase ambient nitrous oxide levels was implausible. This would include the ergonomic positioning of the dentists, possible short-circuiting of ventilation systems, ensuring proper mask fit on patients, and breathing patterns of patients (e.g. rapid or through the mouth).

Random sampling was not conducted due to logistics, number of volunteers available, and the limited amount of time available at each location. This is better defined as convenience sampling, which is common in more health research projects as researchers have to rely on volunteers or readily available subjects. However, generalizations have to be made on the basis of non-statistical considerations, which could produce results that are misleading [46]. This could indicate that the dental employees may be improperly grouped into their respective SEGs and that further observation and sampling should be used to further refine the SEGs.

Scavenging system flow rates were not taken during this study and is an important limitation. According to the NIOSH, the scavenging system flow rates should be at least 45 L/min to minimize leakage of nitrous oxide [25]. NIOSH also states that flow rates of less than 40 L/min may result in significant leakage around the mask [25]. If scavenging flow rates would have been measured during this study it could have helped clarify the issue of high ambient nitrous oxide levels during dental procedures. Future studies should

include scavenging flow rates to help determine effective scavenging rates when different air changes per hour are in use.

There were multiple ACS passive dosimeter results that were above the maximum LOQ (500 ppm_v). These results, when paired with the associated Miran results, are a source of error as the actual concentration is not known. This would also be the case with the associated 8-hour TLV-TWAs that were provided by the laboratory. The 8-hour TLV-TWAs are only estimates and are not actual observed concentrations and a source of error.

Where results were not significant, the power within that specific test was not above the target power level of 80%. There are multiple causes of low power results, including a wide standard deviation and low significance level. However, the limited sample size in this study is most likely the main cause for power levels below 80%. Additional samples from both sampling methods should be collected to increase power and to have more confidence in the results.

A study by the Pacific Northwest National Laboratory showed that the Miran SapphIRe Portable Analyzer is capable of 96% relative accuracy and 99% relative precision at 100 ppmv [42]. Ideally the Miran SapphIRe Portable Analyzer calibration would involve field calibration quality control checks. However, budgetary and logistical constraints made obtaining and traveling with a certified calibration gas standard impractical during this study. Future studies should include quality control checks on the Miran SapphIRe Portable Analyzer performance. This is particularly important for exploring and understanding the observed differences in concentrations between the two sampling methods studied.

CHAPTER 6: Conclusion

This study was conducted to determine ambient nitrous oxide levels in the breathing zones of dental employees. Excursion levels above the 250 ppm_v were found to be an important occupational exposure concern. Additionally, with the high UTLs seen in this study, 8-hour TLV-TWAs could also become a significant concern if multiple dental procedures utilizing nitrous oxide are conducted in succession. Further observation of this population should be conducted to confirm these findings and increase the study power (>80%).

Comparing the active to passive sampling methods did not compare with literature results and were not within 25% accuracy with 95% confidence that is typical of OSHA requirements. This could be due to the many limitations within this study that are related to sampling in active field conditions. Many variables that could affect nitrous oxide levels could not be addressed as they could in a laboratory or mock dental operatory setting. Further studies should focus on understanding the potential effect of interference from humidity, temperature, air velocity and CO₂ on the accuracy of each method of analysis.

Room ventilation rates should be further explored to determine what rates effectively reduce ambient nitrous oxide to levels that prevent excursions over 250 ppm_v and lower overall TLV-TWAs. In this study, only one dental operatory did not have an excursion over 250 ppm_v (70 air changes per hour), even though they were all over the 12 air changes per hour requirement (ranged from 14-70 air changes per hour). This suggests that higher ventilation rates may be helpful in controlling higher excursion levels than currently recommended and further studies should be conducted to determine this.

No association between nitrous oxide generation rate (%Liter/minute) or room air changes per hour on the TLV-TWAs levels were seen in this study. However, this was limited by logistics and further studies should be conducted to increase the amount of dental operatories included.

Although not studied in the project, to help address high ambient nitrous oxide levels during dental procedures, all scavenging system should also be inspected to ensure they have a continuous flow rate of at least 45 L/min at the patient. This should help limit the amount of nitrous oxide leaking from the delivery mask limiting the amount of ambient nitrous oxide that would have to be removed by the ventilation system. This may help explain why there are high levels of ambient nitrous oxide measured during dental procedures.

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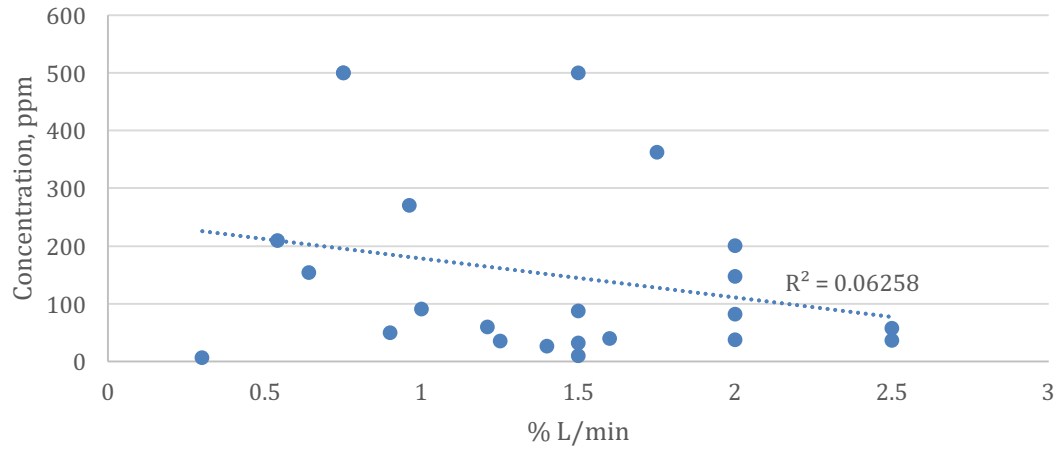
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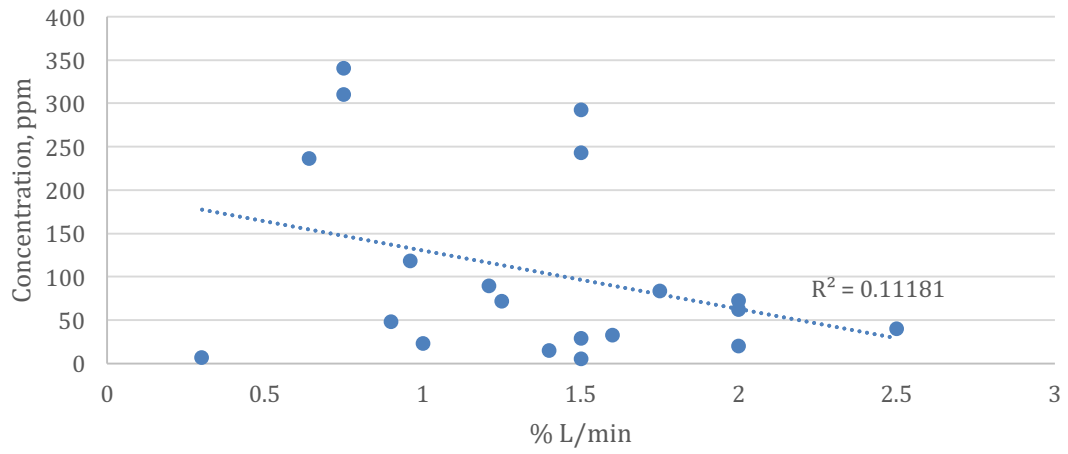
Appendix A

Nitrous Oxide Generation Rates per Procedure Graphs

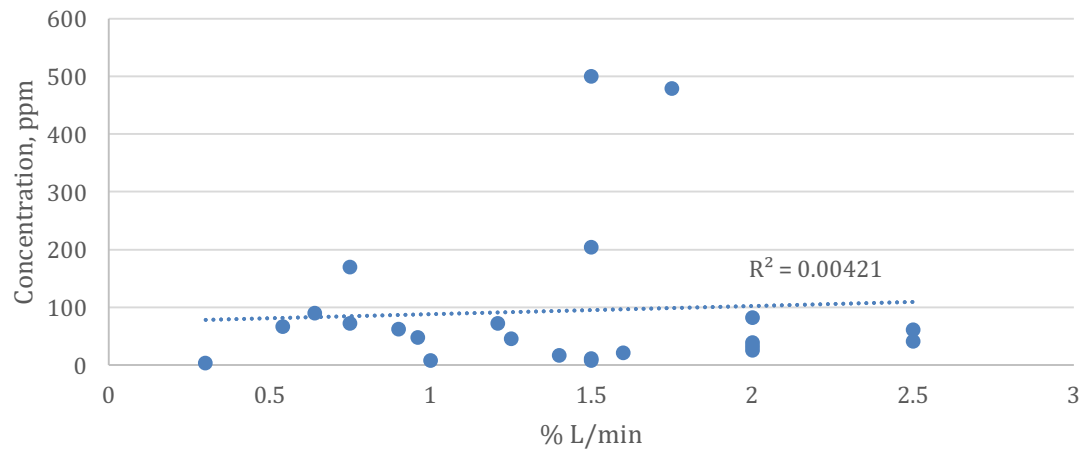
Dentist Passive TWA



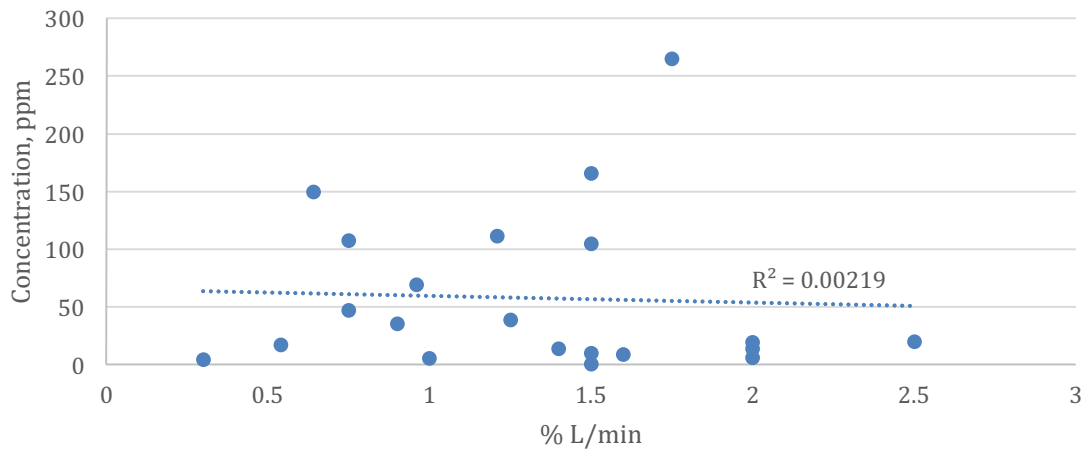
Dentist Active TWA



Dental Assistant Passive TWA

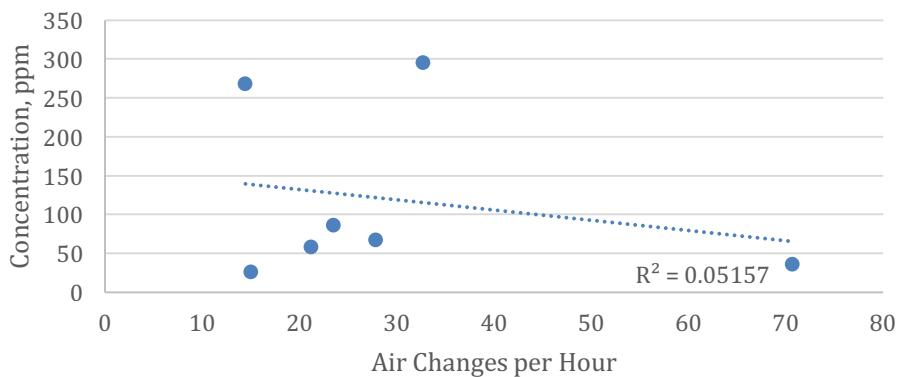


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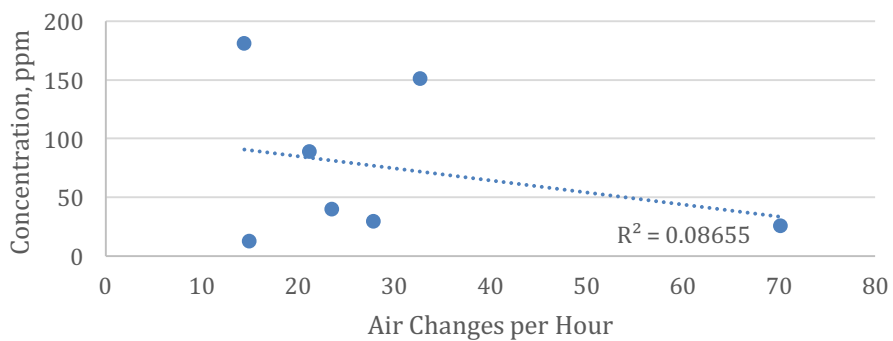


Mean Time Weighted Averages per Air Changes per Hour Graphs

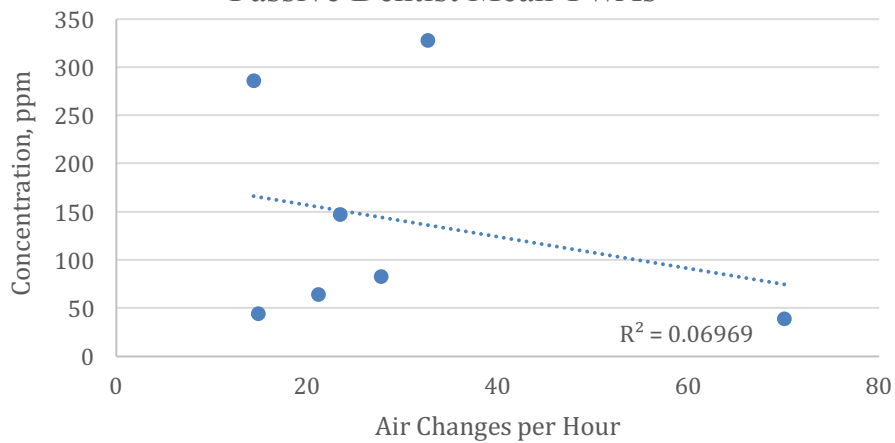
Passive All Mean TWAs



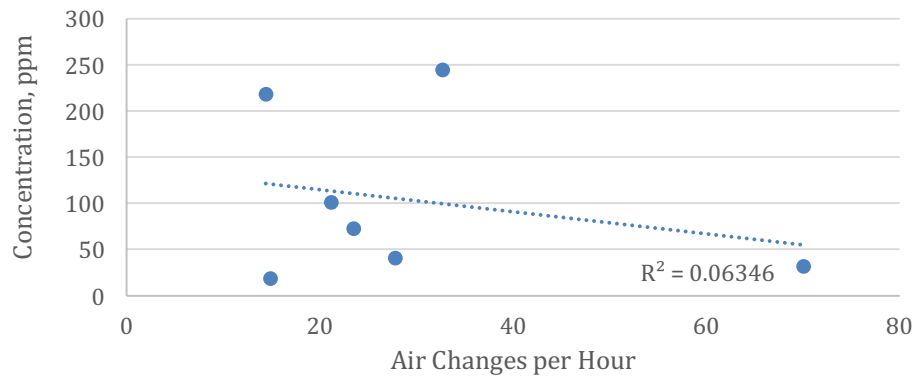
Active All Mean TWAs



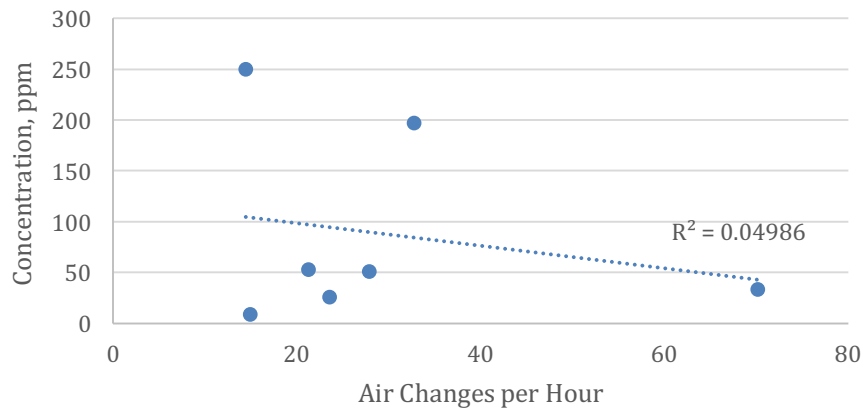
Passive Dentist Mean TWAs



Active Dentist Mean TWAs



Passive Dental Assistant Mean TWAs



Active Dental Assistant Mean TWAs

