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Potential of nitrous oxide sedation in pedodontics to reduce the need of dental general anesthesia

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1. Publication

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2. Short summary (English)

Aim: To investigate the possible reduction of the need for dental general anesthesia (DGA) through nitrous oxide sedation (NOS), when is used in combination with behavior management techniques among patients younger than 12 years of age referred to a specialized pedodontics practice due to the high dental treatment need and poor cooperation level.

Materials and methods: Retrospective analysis was performed of the digital medical records of all children treated under NOS in a specialized pedodontics clinic between 2012 and 2017. The potential reduction of the need for dental general anesthesia was assessed depending on the success rate of NOS on patient-level with relations to multiple related factors such as age, reason of referral and treatment need.

Results: out of 510 patients, 228 meet the inclusion criteria. Nitrous oxide was used in 406 dental treatment sessions on 228 pre-cooperative and/or anxious patients aged 3-12 years (mean 6.4±1.7; 43.4% female). 91.9% of the NOS sessions were successful in achieving the intended dental treatment. Complete oral rehabilitation was possible for 84% of the patients using NOS without the need of DGA. Regarding the age, DGA reduction among pre-school children was lower than in schoolchildren (77.8% and 87.9%, respectively).

Conclusion: A high fraction of anxious or semi-cooperative children with high dental treatment needs can be treated without the use of DGA when a comprehensive concept of caries management is combined with the use of NOS and behavior management techniques. NOS should, therefore, always be considered as an option for dental treatment of semi-cooperative children with high dental treatment needs before making a decision towards DGA.

Keywords: dental general anesthesia, nitrous oxide, pediatric dentistry, sedation, success rate

3. Kurzzusammenfassung (Deutsch)

Ziel: Untersuchung bezüglich der möglichen Reduktion einer zahnärztlichen Sanierung unter Vollnarkose durch Lachgassedierung in Kombination mit Verhaltensmanagementtechniken bei Patienten unter 12 Jahren, die aufgrund des hohen zahnärztlichen Behandlungsbedarfs und der mangelnden Kooperation bei zahnärztlichen Behandlungen in eine spezialisierte Praxis für Kinderzahnheilkunde überwiesen wurden.

Materialien und Methoden: Retrospektive Analyse der digitalen Patientenakten aller Kinder, die zwischen 2012 und 2017 in einer spezialisierten Kinderzahnklinik mit NOS behandelt wurden. Die Reduzierung des Bedarfs an zahnärztlicher Vollnarkose wurde in Abhängigkeit von der Erfolgsrate der Lachgassedierung auf Patientenebene und in Bezug auf mehrere damit zusammenhängenden Faktoren wie Alter, Grund der Überweisung und Behandlungsbedarf gemessen.

Ergebnisse: In 406 zahnärztlichen Behandlungssitzungen wurde Lachgas bei 228 präkooperativen und/oder ängstlichen Patienten im Alter von 3-12 Jahren (Mittelwert 6,4±1,7; 43,4% weiblich) eingesetzt. In 91,9 % der Lachgas-Sitzungen konnte die geplante zahnärztliche Behandlung erfolgreich durchgeführt werden. Eine vollständige orale Rehabilitation war bei 84 % der Patienten mit Lachgassedierung ohne Narkose möglich. Was das Alter betrifft, so war die Narkosereduktion bei Vorschulkindern geringer als bei Schulkindern (77,8 % bzw. 87,9 %).

Schlussfolgerung: Ein hoher Anteil ängstlicher oder semi-kooperativer Kinder mit hohem zahnärztlichem Behandlungsbedarf kann ohne Vollnarkose behandelt werden, wenn ein umfassendes Konzept der Kariesbehandlung mit dem Einsatz von Lachgassedierung und Verhaltensmanagementtechniken kombiniert wird. Lachgassedierung sollte daher als Option für die zahnärztliche Behandlung von semi-kooperativen Kindern mit hohem zahnärztlichem Behandlungsbedarf in Betracht gezogen werden, bevor eine Entscheidung für eine Zahnbehandlung unter Narkose getroffen wird.

Schlüsselwörter: zahnärztliche Allgemeinanästhesie, Lachgas, Kinderzahnheilkunde, Sedierung, Erfolgsquote

4. Introduction

Dental anxiety is considered to be one of the biggest challenges in the field of pediatric dentistry. About 10 - 30% of children and adults show fear of dental treatment [CED 2012, IDZ 2012].

Non- or low cooperative behavior due fear or anxiety is one of the biggest challenges general dental practitioners and pediatric dentists may face in dental treatments [Savanheimo and Vehkalahti, 2008]. This in particular relates to dental treatments that require injections for local anesthesia [Erten et al., 2006]. Dental fear or anxiety in children and adolescents is reported to reach a prevalence between 10% - 29.3% in different populations and using different scales [Cianetti et al., 2017]. A slightly lower prevalence of 3.3% - 15.3% is reported for adults with different severities of anxiety level [Silveira et al., 2021]. The use of basic and advanced behavior management techniques (BBMT and ABMT) is, therefore, essential to overcome this challenge and provide safe, efficient, and effective dental care [*Guideline on Behavior Guidance for the Pediatric Dental Patient*, 2015; American Academy of Pediatric Dentistry, 2020].

Despite the great decline in caries prevalence in many countries worldwide, caries remains a major burden [Bernabe et al., 2020]. Additionally, caries is distributed in a polarized manner leaving children with a high number of affected teeth along with a low care index while others have healthy dentitions [DPHEP, 2019; Team DAJ, 2017].

Remaining high levels of untreated caries lesions indicate, that the cooperation of these children is not sufficient to undergo dental treatments, or that treatments of such carious lesions especially in the primary dentition might be considered by the parents or even the dentists as unnecessary. Another factor, that could lead to high numbers of untreated carious lesions in children can be the poor training in Pediatric Dentistry in universities [Basner et al., 2012; Giacaman et al., 2018] and thus the "know-how" in this specialty is sometimes insufficient. For this reason and in case of an acute dental treatment need in many countries, uncooperative children especially under the age of 12 are often treated under general anesthesia (GA), even though other alternatives exist [Milnes, 2003]. Therefore, other (advanced) behavior management techniques (ABMT) such as sedation

should be applied to avoid dental GA's, due to the severe life-threatening complications that may accompany GA in children in rare cases [Roberts et al., 2020]. In Germany, the use of dental general anesthesia (DGA) to perform dental treatments in uncooperative children is often used as it is covered by the National Health System until the age of 12 years when justified with lack of compliance and treatment need [KZBV, 01/2022].

The sedation with nitrous oxide (NOS) for dental treatment is used commonly in many countries worldwide such as the USA, the UK or other European countries and is considered as an alternative option to DGA for performing (invasive) dental treatments for patients with dental fear or anxiety with high levels of patient or parental satisfaction [Arcari and Ferro, 2008]. Unlike those countries, NOS for dental treatment is not commonly used in Germany for treating patients/children as it is still not covered by the National Health System on the contrary to DGA.

The German Society of Anesthesiologists and the working group from multiple professional societies (DGAI, BDA, DGKiZ and DGZMK) published a statement supporting the use of NOS for minimal sedation in pediatric dentistry in 2013 [Philippi-Höhne et al., 2013]. Eight years later, in 2021 an updated statement was also published from the same working group encouraging the use of NOS in the dental practice when indicated [Höhne et al., 2021].

To my knowledge, few international published data and none for Germany have described the success rate of NOS for dental treatments. Moreover, there is little to no published scientific evidence describing the success rate of NOS for dental treatments for participants with dental fear or anxiety, that would otherwise be "DGA candidates" and would have needed to undergo dental treatments under DGA.

Therefore, the aim of this study is to investigate the success rate of NOS among patients younger than 12 years of age, referred to a pedodontics practice, who might be otherwise considered as likely candidates for dental treatments under GA, due to the high dental treatment need and a low level of cooperation with dental treatment.

5. Literature review

Despite the great success of caries prevention in Germany [IDZ, 2016; Team DAJ, 2017], there is still a huge need for dental treatment in the primary dentition, where Almost every seventh 3-year-old child and almost 45% of 6-7-year-olds had a teeth needs treatment [Team DAJ, 2017].

In the literature it was reported that dental fear potentially leading to non-cooperative behavior is most likely also associated with an increased level of caries [Esa et al., 2010; Esa et al., 2014]. Another study reported a twofold risk of untreated caries in children with high dental fear in comparison with children with low fear [Murthy et al., 2014]. The dental treatment of these patients remains as on o the biggest challenges in pediatric dentistry, Therefore, the use of basic behavior management techniques (BBMT) and advanced behavior management techniques (ABMT) plays an important role in dentistry and especially in pediatric dentistry [American Academy of Pediatric Dentistry, 2020]

Basic behavior management techniques (BBMT) include direct observation, tell-show-do, ask-tell-ask, voice control, nonverbal communication, etc. on the other hand, advanced behavior management techniques (ABMT) include the use of protective stabilization, sedation, and general anesthesia, these are commonly taught and used in advanced pediatric dental training programs [American Academy of Pediatric Dentistry, 2020].

Basic behavior management techniques alone may not always increase the cooperation of children sufficiently in order to perform the dental treatment [Al-Zahrani et al., 2009]. With the help of sedation, it is often possible to reduce the level of anxiety in these patients and create a more favorable treatment condition. Moreover, a long-term positive attitude towards dental visits may develop after positive dental experiences [Hallonsten et al., 2003]. However, even with the use of sedation there are still patients remaining that are not able to tolerate certain dental procedures and, therefore, may require alternative approaches, such as treatment under general anesthesia [Matharu and Ashley, 2006].

5.1 Sedation in (pediatric) dentistry

Sedation is considered on the advanced behaviour management techniques in dentistry [American Academy of Pediatric Dentistry, 2020]. It is a very helpful treatment option, which is used for treating anxious patients with low cooperation e.g. small children or patients with motor dysfunction or cognitive impairment who need an invasive or extensive dental procedure which is usually combined with local anesthetic [CDSBC, 2018].

Besides general anesthesia three levels of sedation were defined by the American Dental Association guidelines for the use of sedation and general anesthesia by dentists [American Dental Association, 2016].

5.2 Conscious sedation

Conscious sedation is a medically induced controlled state of minimally to moderate depression of consciousness in which the protective reflexes stay maintained. The patient stays capable of maintaining a patent airway without any help during the sedation and retains an appropriate response to verbal commands and tactile stimulation [American Dental Association, 2016; Attri et al., 2017].

5.2.1 Indications of conscious sedation in dentistry

Indications for conscious sedation as a potential adjunct for patient management include [Attri et al., 2017; Hallonsten et al., 2003]:

- patients/children with behaviour management problems,
- patients with dental anxiety and phobia,
- patients with a need for long, complicated invasive dental procedures,
- patients in whom stress potentially aggravates medical conditions,
- and in some cases, also to treat patients with special needs.

Table 1: Type of sedation and relating bodily functions [American Dental Association, 2016]

	minimal sedation	moderate sedation	deep sedation	general anesthesia
conscious depression level	minimally	moderate	patient cannot be easily aroused	loss of consciousness
depression produced by	pharmacological method	a drug induced depression	a drug induced depression	a drug induced depression
response to verbal commands	normal response	purposefully response, alone or accompanied by light tactile stimulation	purposefully response following repeated or painful stimulation	patient is not arousable, even by painful stimulation
ventilatory function	unaffected	no intervention is required	may be impaired	often impaired
maintaining a patent airway	independently and continuously	no intervention is required	may require assistance	require assistance
spontaneous ventilator	unaffected	adequate	may be inadequate	patient require a positive pressure
cardiovascular functions	unaffected	usually maintained	usually maintained	may be impaired

5.2.2 Inhalative conscious sedation with nitrous oxide

Nitrous oxide (N_2O) is the most commonly used inhalation sedative in dentistry [Mohan et al., 2015]. It has been used in dentistry for many decades. The first use reported was in December 1844 by Horace Wells [Haridas, 2013].

5.2.2.1 Characteristics of nitrous oxide

In the room temperature, N_2O is a colorless and odorless gas, which has a faint, sweet smell [Paterson and Tahmassebi, 2003]. Due to its analgesic and anxiolytic effect it causes depression and euphoria to the central nervous system with a minimum effect on the respiratory system and has a rapid onset and recovery due to its quick absorption of about two or three minutes [*Guideline on Behavior Guidance for the Pediatric Dental Patient*, 2015; Council of European Dentists, 2014].

N_2O considered to be a good sedative having a moderate analgesic effect. For this reason, local anesthesia is usually still required when invasive dental treatments are performed [Zier et al., 2010].

NOS is widely accepted and is considered a safe and effective sedation technique in dentistry [Hallonsten et al., 2003]. Therefore, and especially for pre-cooperative children (4–5-year-olds), it is very important to consider NOS as a treatment option before deciding for a dental treatment under general anesthesia. Similarly or even more effectively in adults, NOS may be a very helpful alternative to DGA [Hallonsten et al., 2003].

In different countries such as USA, UK [Bryan, 2002; Foley, 2005], Canada [Ramos-Jorge et al., 2015], Italy [Collado et al., 2006; Galeotti et al., 2016] and France [Collado et al., 2006; Hennequin et al., 2012] numerous studies were conducted regarding the use of conscious sedation with NOS.

While sedated the patient feels mostly calm, but sometimes euphoric with mental and physical/muscle relaxation [Becker and Rosenberg, 2008], but remains responsive. Breathing becomes calm and deep, the gag reflex usually disappears completely [Kaufman et al., 1988; Veaux et al., 2016; Yoshida et al., 2007]. Pain perception and reaction are reduced. Patients often have "positive experience," especially when the sedation is combined with behavior managements techniques or hypnotic communication [Schmierer 2013].

In the literature, it was reported that gases achieve tensions and equilibrate more rapidly when they have low solubility in blood and adipose tissue. This tension in blood results in a driving force for inhalation agents allowing them to enter the brain, where their anesthetic action occurs. For this reason, N_2O is considered to have the fastest onset among inhalation agents [Becker and Rosenberg, 2008; Tobias, 2013; Wang et al., 2002].

The half-life of N_2O is about 5 minutes, the sedation starts by giving pure oxygen for 2 to 5 minutes followed by a stepwise increase in N_2O concentration every second minute [Mohan et al., 2015]. The maximum concentration of N_2O allowed for the use of sedation in pediatric dentistry differs between the European countries (50 to 70%) and is determined by the national regulations [Hallonsten et al., 2003]. An administration of pure oxygen for 5 minutes at the end of the dental treatment is considered to be essential [Mohan et al., 2015; Patel et al., 1994].

5.2.2.2 Indications and contraindications for nitrous oxide sedation

Besides the general indications for conscious sedation, N_2O is indicated in patients with a strong gag reflex and in patients with muscular tone disorders such as cerebral palsy to avoid unintentional movements which makes the treatment impossible [Hallonsten et al., 2003].

NOS can be safely used for almost all patients (ASA I, II) in routinely performed dental treatment. Sedation with N_2O is considered as the safest of all the modalities available for sedation in dentistry [Becker and Rosenberg, 2008]. Nonetheless, it is very important to review the medical history of the patient, because and like any other pharmacologic agent, N_2O may not be suitable for some patients.

Nitrous oxide is contraindicated in:

- patients who are unable to use the nasal mask or cannot inhale adequately through the nose because of anatomic and/or chronic obstructive pulmonary diseases (COPD) [Becker and Rosenberg, 2008; Mohan et al., 2015],
- patients who are diagnosed with personality and psychiatric disorders especially those diagnosed with schizophrenia or bipolar disorder. In those patients NOS should be used carefully and a medical consultation is strongly recommended to avoid any unpredictable complications [Becker and Rosenberg, 2008],
- patients who have had a recent surgery of the ear and in case of any compromise in patency of the eustachian tube which may lead to pressure increases within the middle ear [Becker and Rosenberg, 2008],
- (first trimester of) pregnancy [American Academy of Pediatric Dentistry, 2018; Rowland et al., 1995],
- patients who are undergoing treatment with bleomycin sulfate [American Academy of Pediatric Dentistry, 2018; Fleming et al., 1988],
- patients who have Methylenetetrahydrofolate reductase deficiency [American Academy of Pediatric Dentistry, 2018; Selzer et al., 2003],

- and in patients who have vitamin b12 deficiency or blood anemia, knowing that the chronic exposure to N_2O induces b12 deficiency which may lead to a higher risk of complications [Brown and Sneyd, JR, 2016].

In some other medical conditions like (congestive heart failure, sickle disease [Ogundipe et al., 1999] acute otitis media, recent tympanic membrane graft [Fish et al., 2000], and acute severe head injury [Moss & McDowall 1979], a medical consultation from a specialist is considered to be essential before the administration of any sedative agent [American Academy of Pediatric Dentistry, 2018; Becker and Rosenberg, 2008].

5.2.2.3 Advantages and disadvantages of nitrous oxide sedation

According to Mohan et al. 2015, the use of N_2O as a sedative agent has a lot of advantages regarding the way of administration and its safety (Tab. 2).

Table 2: Most important advantages and disadvantages of nitrous oxide sedation in dentistry [according to Mohan et al. 2015].

nitrous oxide sedation	
Advantages	**disadvantages**
easy administration with a rapid onset of action/uptake time	expensive equipment
high safety of use and fast recovery time	sedation it just possible through the nose
titration is possible	difficulty of giving an injection in the anterior maxillary region because of the nasal mask
nausea and vomiting are uncommon	-
no preparation of patient is required	-
no need for any escort	-

5.2.2.4 Technique and equipment

In the dental practice, a titratable system should be favored in which the concentration of oxygen-nitrous oxide mixture can be modified (Fig. 1). The N_2O concentration usually ranges between 0-50% within the respiratory mixture. A minimum of 50% oxygen is included in the respiratory mixture at all times. In the case of an interruption of the oxygen flow, the N_2O flow must be automatically interrupted and a sufficient oxygen reserve must be available in order to ventilate the patient for a sufficiently long time.

The dental practice should be equipped with the following elements: Titratable N_2O system, adequate masks (small and large), N_2O and O_2 bottle or central system, external suction of the exhaled air, room ventilation, when possible, in the floor area, pulse oximeter and an emergency set (Fig. 1 - 5).

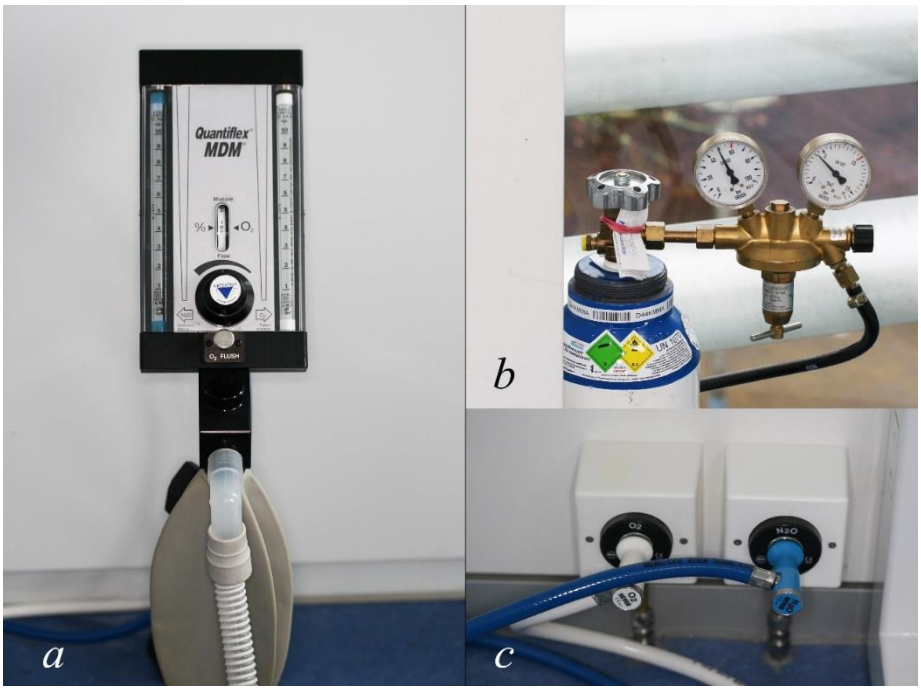

Figure 1: Titratable nitrous oxide system: Quantiflex MDM (a), rental cylinder for nitrous oxide and oxygen (b) and central system for nitrous oxide and oxygen (c)

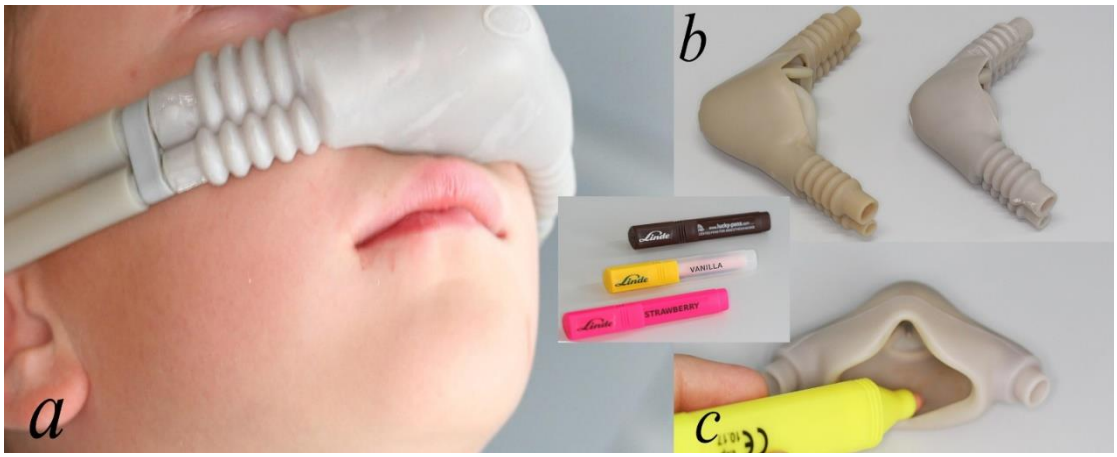

Figure 2: Nasal masks for the inhalative sedation with nitrous oxide

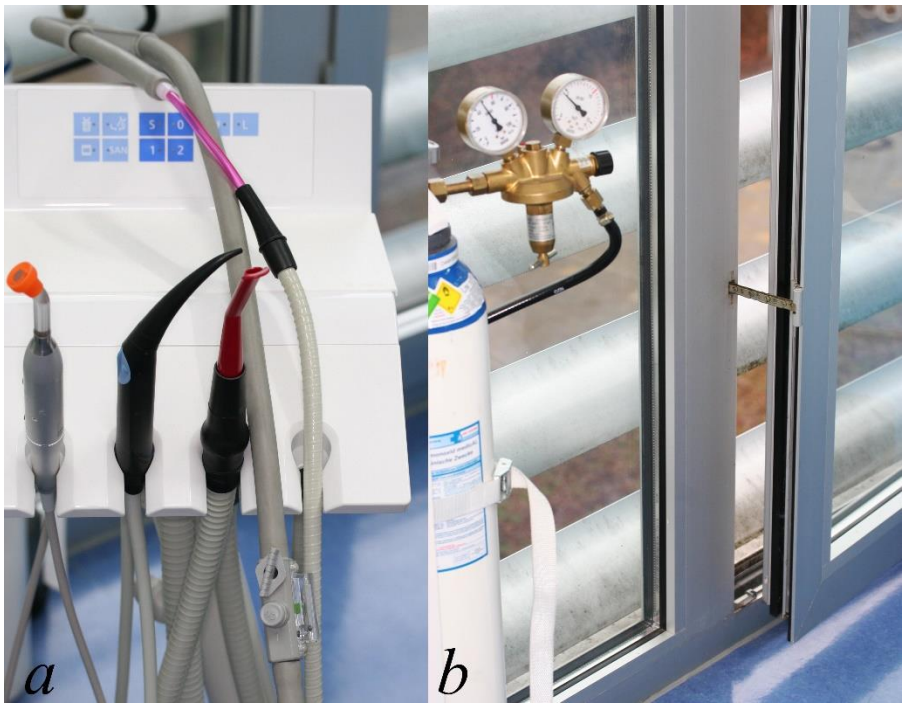

Figure 3: External suction for exhaled air to reduce workplace pollution by nitrous oxide is possible, for example, via the suction system of the treatment unit (a) and room ventilation in the floor area through a large floor window to reduce workplace pollution. Nitrous oxide is heavier than air and therefore sinks to the ground (b)

Figure 4: Pulse oximeter for monitoring heart rate and oxygen saturation

5.2.2.5 Steps in the clinical application

After a detailed medical, dental and social anamnesis, the patient must have no serious illnesses and no contraindications for sedation. In addition to the general medical history, an additional N_2O anamnesis directly prior its application is necessary asking about:

- if the patient has a cold or a restriction in his nasal breathing,
- a newly diagnosed lung disease or infection,
- if the patient was currently treated form or have (lung disease, eyes surgery, pregnancy, bowel obstruction, Vitamin B12 deficiency or anemia),
- the presence of a middle ear infection (otitis media),
- if the patient suffers under a new concussion injury, or psychological problems
- and in the end, it is important to know if the patient took any medication before the treatment appointment and make sure that it won't intervene with the sedation.

Furthermore, there must be sufficient cooperation and willingness of the patient to be placed on the chair, to breathe through the nasal mask, and a general emotional maturity for the conduct of the behavior. Patient' and parental consent is mandatory. This should include sufficient written information about N_2O and its effects, indications, contraindications, side effects, risks and costs.

It is advisable to inform the children and the adults about the usual expected experiences - in a positive way - at the appointment before the sedation, because some patients develop fear or feel insecure due to negative experiences, such as loss of control at the dentist. The use of perfume sticks (Fig. 5) especially in small children can increase the acceptance of the nasal mask and nasal breathing.

Figure 5: Pleasant smell obtained with smell pens can motivate you to breathe better through the nose mask. The child is allowed to choose his or her own favorite smell such as strawberry, chocolate or vanilla

A documentation of heart rate, oxygen saturation in the blood (e.g. with a pulse oximeter), the length of the procedure, the maximum dosage and the duration of treatment in the patient record is recommended [Hallonsten et al., 2003]. Practical experience has shown that in most patients a N_2O concentration of 30-40% is sufficient to achieve the optimal sedation depth [Council of European Dentists, 2014]. The use of rubber dam is recommended, when possible, to secure nasal breathing and to minimize the necessary amount of N_2O especially for long lasting treatments with an open mouth such as endodontic treatments.

At the beginning of the sedation, pure oxygen (100%) should first be inhaled through the nasal mask. Then the N_2O concentration can be incrementally titrated up to 30-50% to achieve the desired sedation depth. At the end of treatment and before removing the nasal mask, pure oxygen should be administered again for 3-5 minutes [Hallonsten et al., 2003]. Choosing a well-fitting nasal mask is very important to the success of the NOS.

At the first sign of overdose, for example, forehead wrinkles, increasing agitation, and cold sweat or if the patient does not respond to instructions, pure oxygen must be given immediately. NOS does not replace behavior management techniques such as tell-show-do, desensitization, or hypnotic communication. In case of combining NOS and the above maintained behavioral managements techniques, a significantly improved cooperation in children and in adults can be achieved [Schmierer 2013].

5.2.2.6 Certification for nitrous oxide sedation in Germany

To use NOS in a dental practice, the dentist should pass a certified theoretical and practical training according to the CED regulations [Council of European Dentists, 2014]. This is usually a two days course with practical exercises including an emergency management course which are certified by the DGKiZ [Deutsche Gesellschaft für Kinderzahnheikunde, 2022].

The theoretical knowledge base consists of Compulsory content of a 2-day theory course (10-14 hours) which includes the following topics:

- dental fear and behaviour management techniques
- technical aspects of various sedation devices
- chemical, physiological and biological aspects of N_2O
- emergencies and life-saving emergency measures

The practical training requires 5 times visitation, 5 times assistance and 5 times supervised performing a NOS.

5.3 General anesthesia in (pediatric) dentistry

Dental treatment for children under general anesthesia requires a complex decision-making process, since DGA poses vital health risks and is organizationally complex (multiple informed consents, require the presence of an anesthesiologist) and also expensive. Nevertheless, the reimbursement of the costs of anesthesia within the German insurance system for children up to 12 years of age may sometimes promote the decision to use anesthesia, since, in contrast, desensitization and also NOS laughing gas sedation must be paid for privately. Against the background of the caries polarization in the primary dentition described above, which correlates with the educational level of the parents, it is not surprising that parents sometimes advocate the apparently easier and, for them, "less expensive" path. As a practitioner and also as a parent, one should therefore always keep in mind that there is always the risk that a patient may die or suffer severe (brain) damage during such "elective anesthesia".

However, a potentially easy decision to treat under anesthesia for all parties involved must be questioned, and treatment under anesthesia is often even avoidable. The dentist should be aware that in the worst-case scenario, a patient may die or suffer severe long-term consequences (e.g., brain damage) during dental rehabilitation under anesthesia, even if the risk has decreased significantly in recent decades [Roberts et al., 2020]. In such a case, the dental indication and the information about the anesthesia as well as available alternatives are first questioned; the dentist thus bears primary responsibility and not the anesthesiologist.

6. Materials and methods

6.1 Study design and ethical approval

This study is a retrospective analysis of the digital medical records of all children treated under NOS between January 2012 and December 2017 at the Department of Preventive and Pediatric Dentistry at the University of Greifswald / Germany. This retrospective data is applied in different models in order to demonstrate the likely fractions of avoided DGA via the use of at least one NOS within a setting of specialist care in caries management and basic behavior management. Ethical approval was obtained from the Research Ethics Committee of the University of Greifswald under the protocol number (BB 028/16, date: 15.03.2016).

Information related to referral and treatment session(s), as well as related patient characteristics including age, gender, caries experience (dmft/DMFT), treatment need (dt/DT), sedation success/failure etc. were recorded.

6.1.1 Inclusion criteria

Referred children with dental treatment need, who without the treatment option of NOS would likely end up receiving a DGA, were included in the analysis in order to investigate the proportion of reducing DGA with the use of NOS. For the inclusion the following criteria was used:

- healthy patients (ASA I and ASA II) treated under NOS in the period between January 2012 and December 2017.
- patients aged between 3 and <12 years at the first nitrous oxide session. The maximum age was set at 12, because until this age according to the Federal Association of Statutory Health Insurance Dentists (KZBV), the costs of dental treatment under GA will be generally covered by the insurance system for children who cannot cooperate to perform a chairside dental treatment.
- referred patients with the reason of referral being either generally an uncooperative behavior, or specifically stating to be treated under general anesthesia, or specifically to be treated under NOS.

The study population was further divided into two age groups; pre-school children (3-5 years) and schoolchildren (6 - <12 years), as these two groups have a different potential and capability to cooperate with dental treatment and also with NOS.

6.2 Definition of referred patients

The University of Greifswald/School of Dentistry is the only facility in the region, which has a specialized dental clinic for pediatric dentistry, including NOS as well as GA opportunities for children and where specialized dentists certified by the German Association of Pediatric Dentistry (DGKiZ) work [DGKiZ, 2022]. Almost 200 patients are referred to the pedodontic clinic per year [Alkilzy et al., 2015].

Referral because of cooperation problems:

- all patients who had an official referral from another dentist due to dental anxiety,
- patients who previously visited another dentist, but the treatment was not performed because of a cooperation problem
- or the patients who came after a (very) bad experience at another dentist/dental visit.

Referred to be treated under DGA:

- all patients who had an official referral from another dentist for treatment under DGA.

Referred to be treated under NOS:

- all patients who had an official referral from another dentist for treatment under NOS.

Referred for further treatment and diagnostics:

- all patients who had an official referral from another dentist for further treatment and diagnostics without any cooperation problem; these patients were excluded.

6.3 Nitrous oxide success rate on the session-level

Based on the information provided in the digital medical-dental records; a treatment session with N_2O was considered a success when the planned dental treatment was successfully performed under sedation. For this part, the success rate was calculated regarding age group and gender.

6.4 Nitrous oxide success rate on the patient-level

The success rate on a patient-level allows us to identify cases, where the use of NOS as a treatment option, helped to avoid the need for a DGA.

6.4.1 Circumstances and assumptions for models analyzing DGA avoidance

As described in the literature, the use of basic behavior management techniques increases the patient's level of cooperation. Still, for some kind of treatments, and depending on the level of cooperation, it might be necessary to include advanced behavior management techniques in the dental treatment plan for complete dental rehabilitation of the patients.

As a part of the clinical standards used in the Department of Preventive and Pediatric Dentistry at the University of Greifswald, newly admitted patients undergo clinical and when necessarily radiological examinations to determine the treatment need and the level of cooperation. An additional desensitization session might also be planned to improve/assess the cooperation level of the patient before beginning with the (invasive) dental treatment. Depending on the patient level of cooperation and the treatment needed, chairside dental treatments are usually performed stepwise beginning with ''easy treatments'' (e.g. sealants) in the first appointments and ending with the most needed invasive ''difficult'' treatments (e.g. endodontic treatment and extraction) in a way that suits the patient´s level of cooperation with the use of NOS when required (Fig. 6).

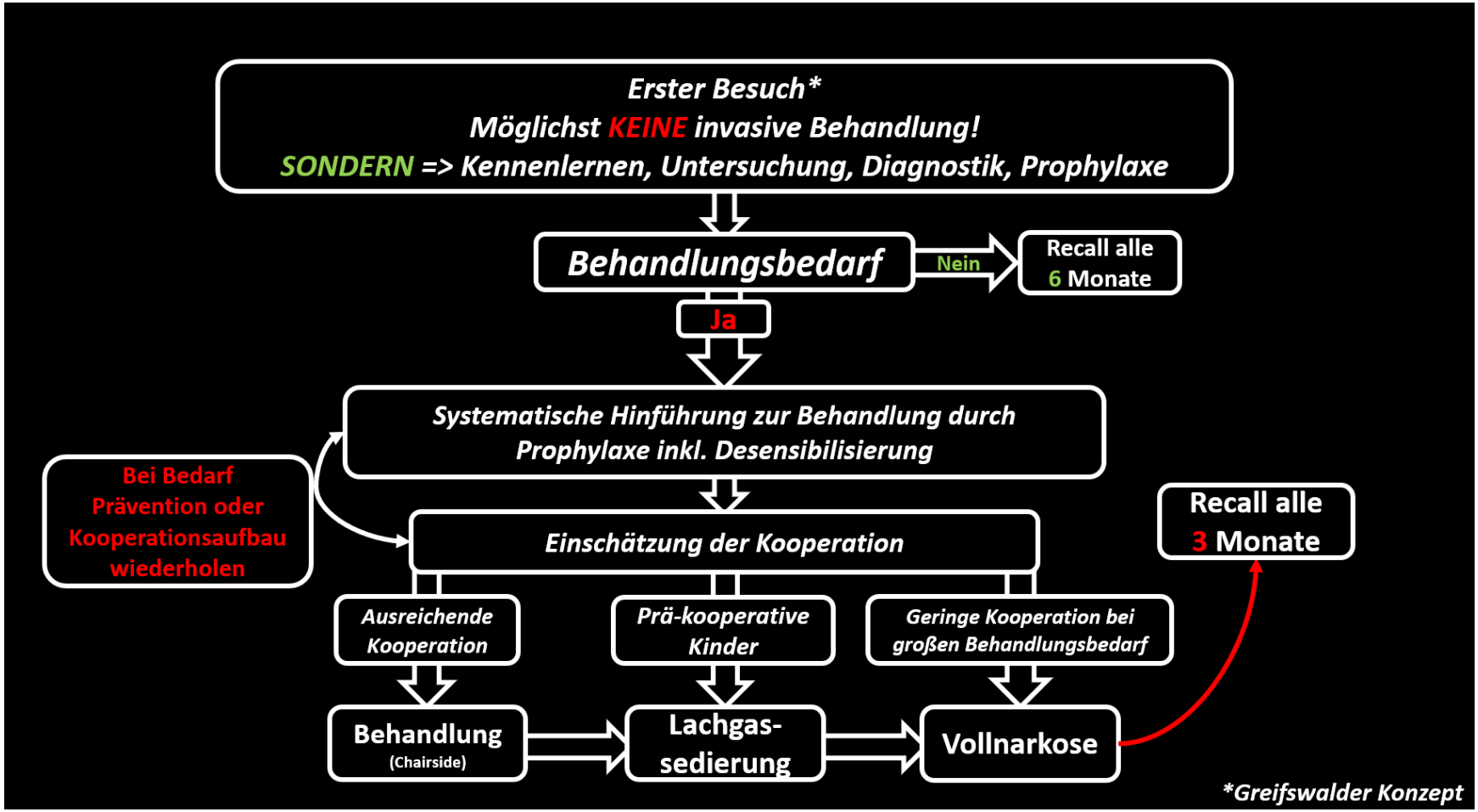

Figure 6: Greifswalder treatment concept for newly admitted patients in the Department of Preventive and Pediatric Dentistry at the University of Greifswald

Based on the information provided, the treatment with NOS was considered successful on the patient level when the children with dental treatment need had at least one treatment session under NOS and eventually had no remaining treatment need while no DGA was performed to achieve this status. In these cases, it is considered, that a DGA was successfully avoided, as these children would have otherwise probably received a DGA if no NOS had been performed.

To evaluate the success rate on the patient-level, which indicates a successful avoidance of DGA, only patients with available information on whether all teeth were treated or not after the last treatment session were included. Patients who didn't show up and weren't fully treated after a last "successful" NOS session with no clear reason, why they didn't show up to the next appointment were excluded. Although the last treatment session was successful, and due to the low level of clinical certainty behind why they didn't return for the next appointment, these patients were excluded from this analysis. Still, patients who had a failure in the last nitrous oxide session and didn't show up after the last appointment were included as a DGA would likely be the only remaining option to complete the dental treatments (Fig. 8 & Tab. 5).

6.5 Clinical standard procedure for dental treatment and nitrous oxide sedation

For high-quality medical care while treating the patients and ensure their safety, all sessions of dental treatments under NOS since its implementation in 2012 at the Department of Preventive and Pediatric Dentistry at the University of Greifswald are performed only by trained dentists, who have special training for NOS. The sessions follow a standard sequence of events starting with checking all the essential requirements including the suction system and ending with the release of the patient in the normal state. These standard procedures are always available in the treatment room in a clear and detailed checklist, which is designed following the international recommended standards (AAPD, EAPD).

All sedation sessions were performed using “MDM Quantiflex Flowmeter” combined with “Complete tube set with double mask – child” from Grodenta. The use of this device allows a titratable N_2O administration with the maximum used/possible concentration of N_2O of 50%. In all sedation sessions, patients were monitored using a finger clip pulse oximeter and received 100% oxygen for 3 to 5 minutes after the end of the dental treatment until the patient no longer exhibits any clinical signs of sedation.

All steps are listed in a checklist divided into four main phases shown in the following figures:

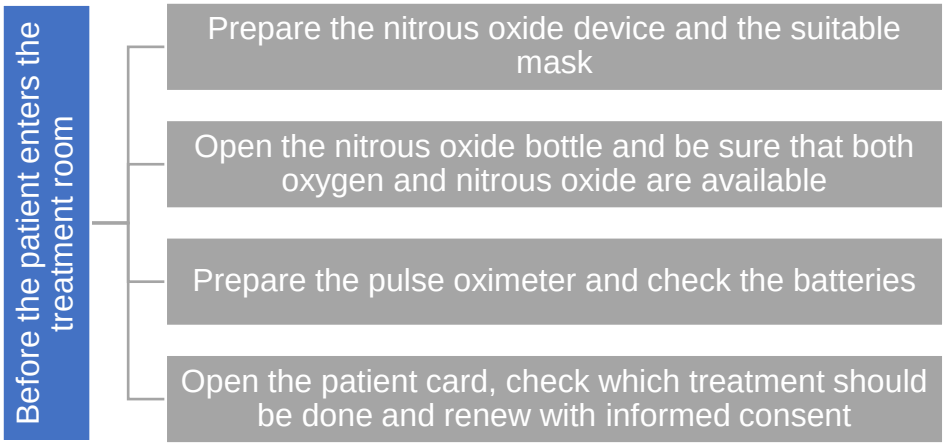

Figure 7a: Checklist part 1 - before the patient enters the treatment room for nitrous oxide sedation at the Department of Preventive and Pediatric Dentistry

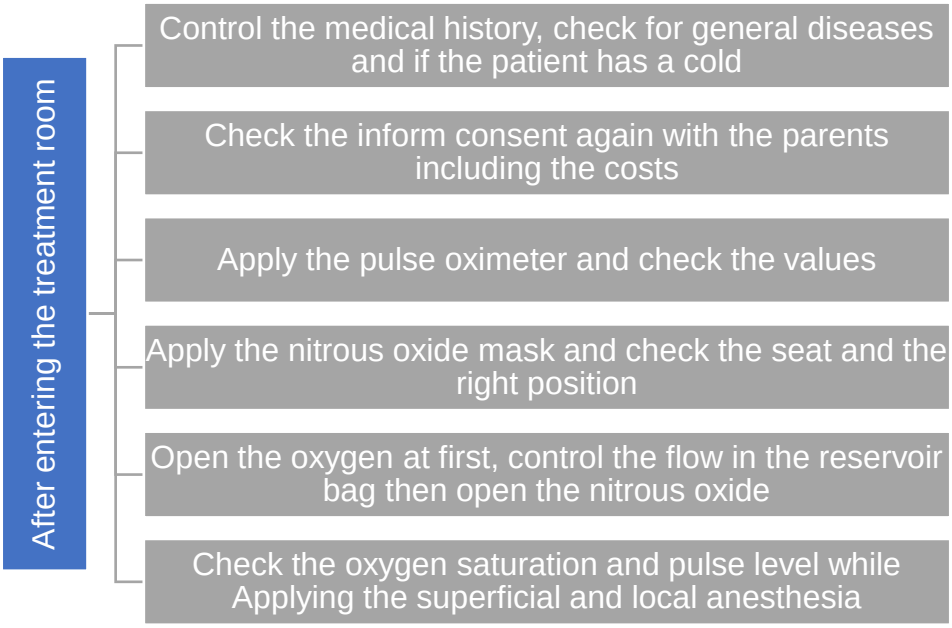

Figure 7b: Checklist part 2 - before the treatment under nitrous oxide sedation starts at the Department of Preventive and Pediatric Dentistry at the University of Greifswald

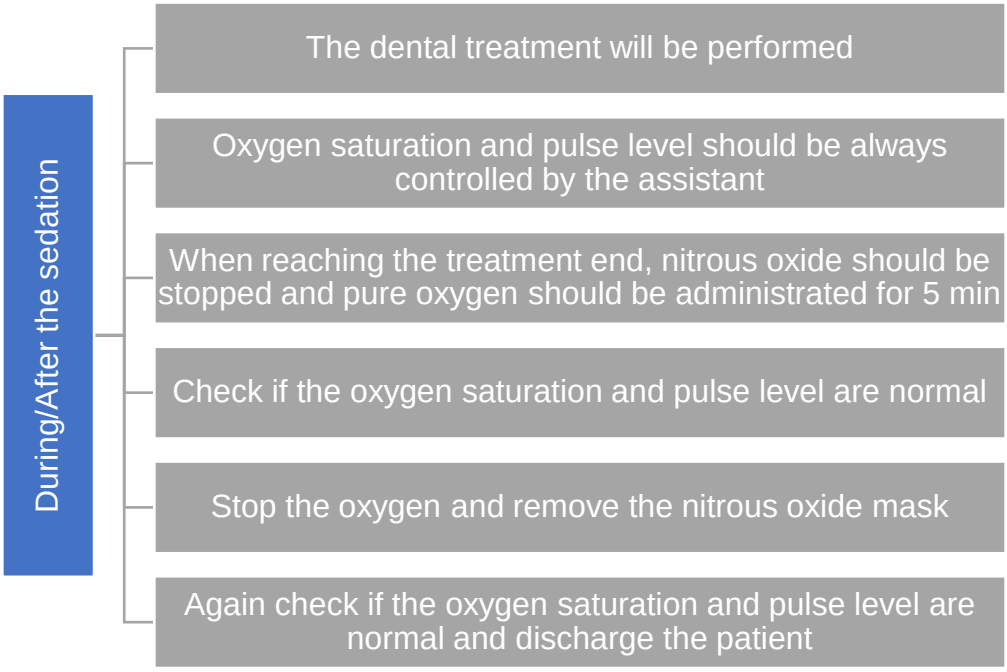

Figure 7c: Checklist part 3 - during treatment under nitrous oxide sedation till patient discharge at the Department of Preventive and Pediatric Dentistry at the University of Greifswald

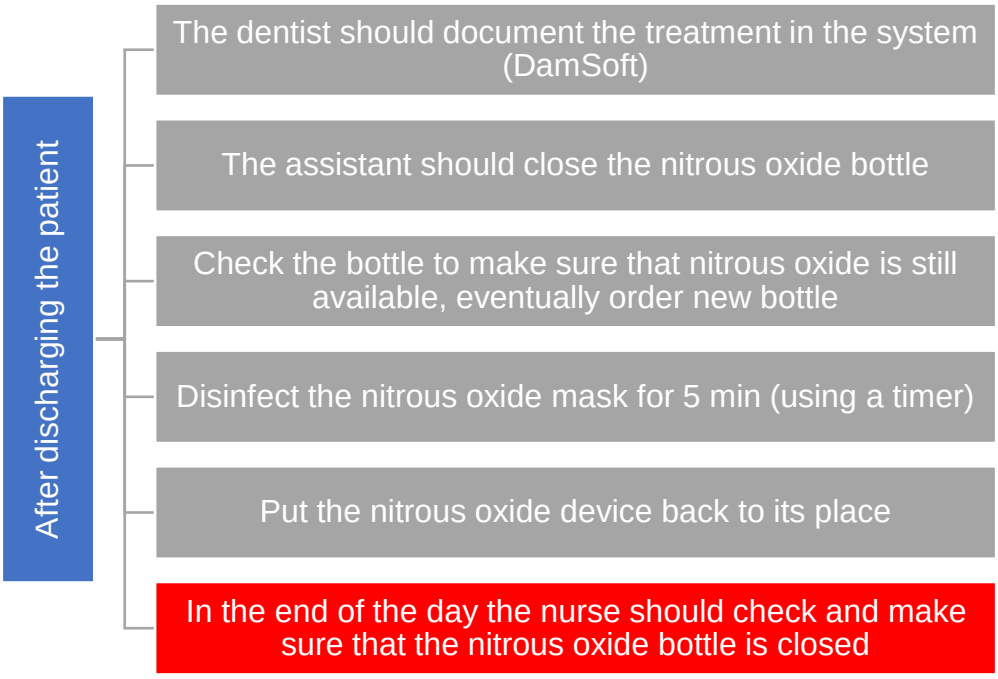

Figure 7d: Checklist part 4 - after discharging a treated patient under nitrous oxide sedation at the Department of Preventive and Pediatric Dentistry at the University of Greifswald

6.6 Data collection and statistical analysis

One author (MSM) was responsible for data collection from the patients' digital records. In cases of uncertainties, a second author was consulted (JS). Patients' data were excluded when the available information was not specific enough for data analysis. Patients' data were encoded, entered, and analyzed in SPSS for Windows (version 17.0, IBM). Descriptive statistics were performed to report the frequency distributions (mean and standard deviation) of the assessed variables.

Four different models/scenarios with slightly different age-dependent assumptions were used for all patients with sufficient data on follow-up to analyze the potential fraction of the reduction in DGA for the complete dental rehabilitation:

1st scenario: all 3 - <12 year-olds who received nitrous oxide sedation

2nd scenario: only 3 - 5 year-olds who received nitrous oxide sedation

3rd scenario: only 6 - <12 year-olds who received nitrous oxide sedation

4th scenario*: children with dt/DT ≥ age * who received nitrous oxide sedation

* In a study investigating the characteristics of children receiving treatment under DGA in Germany, it was found that the mean number of teeth needing treatment (dt) is higher than the mean age of the treated children [Takriti et al., 2019]. Such high untreated caries levels (dt) in children might justify the use of DGA for treating these young children. Other studies found high caries levels along with fear and dental anxiety among children treated under DGA [Alkilzy et al., 2015; Karim et al., 2008; Vinckier et al., 2001]. Depending on these facts and the author knowledge of the selection criteria of DGA patients in specialized dental practices in Germany, it can be assumed that when the number of teeth that need invasive dental treatments exceeds the age in years, children will probably need DGA for full oral rehabilitation.

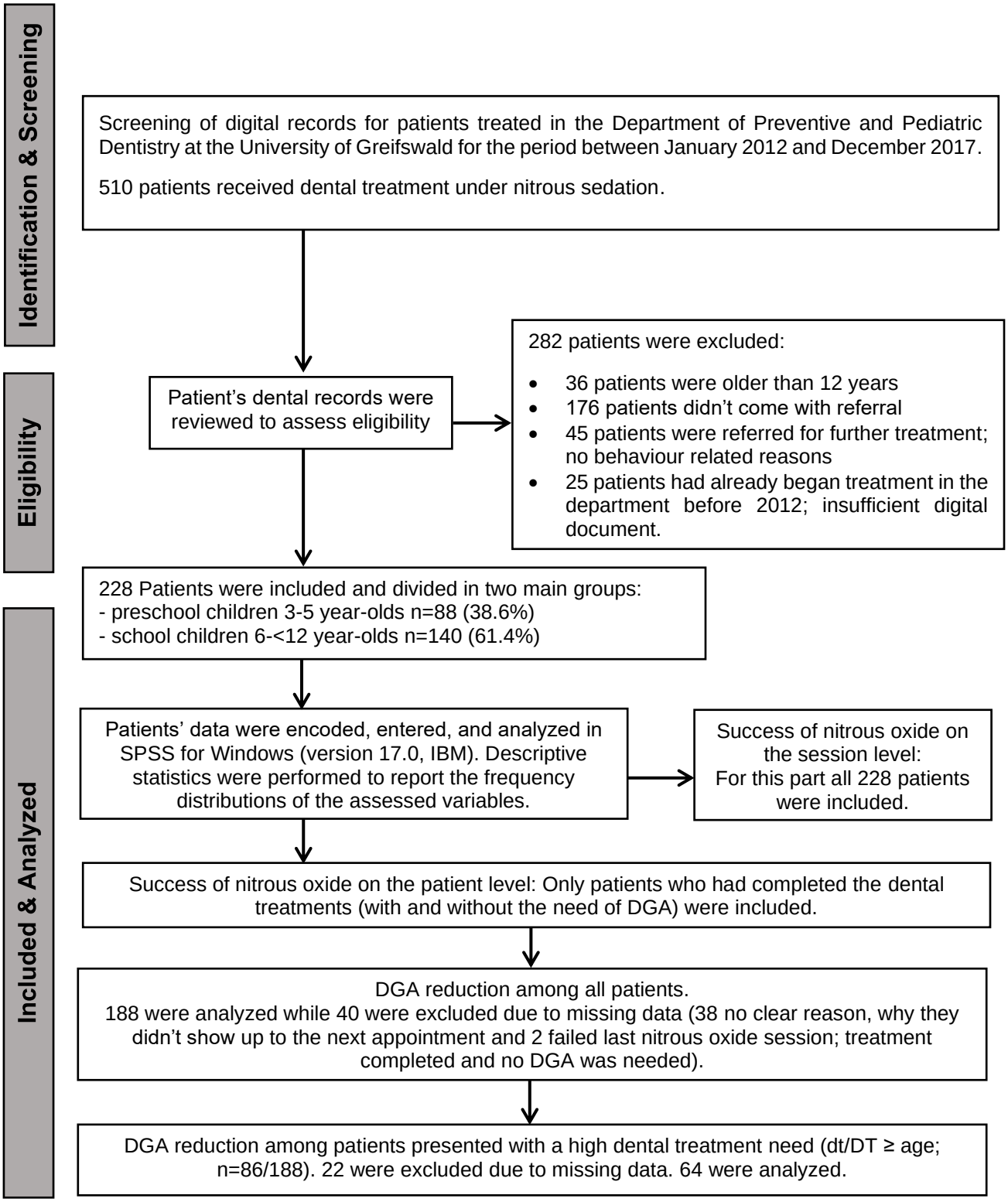

Figure 8: Flow-chart of the 6 years retrospective study assessing the reduction in the dental general anesthesia in children and success of nitrous oxide sedation in the Department of Preventive and Pediatric Dentistry at the University of Greifswald

7. Results

In total, 510 patients were treated under NOS in the period between January 2012 and December 2017 at the Department of Preventive and Pediatric Dentistry at the University of Greifswald/Germany. 228 patients aged 3 to 12 met the inclusion criteria of the study (Figure 1).

7.1 Characteristics of the study sample

Patients treated under NOS were mainly healthy patients (ASA I). Only 5.7% (n=13) had a mild controlled systematic condition (ASA II; e.g. Asthma, Diabetes, etc.). The distribution of the 228 patients (mean age 6.4±1.7 years) according to the age group is shown in (Tab. 3). 43.4% of the patients were females.

The mean caries experience (mean dmft) in the study sample revealed very high values for the pre-school and schoolchildren in the primary dentition (6.2±3.5 dmft, 4.9±3.3 dmft, respectively).

All patients included were referred to be treated in the Preventive and Pediatric Dentistry department. The main reason for referral was insufficient cooperation (IC) which led to difficulties in performing dental treatment by general practitioners (n=157; 68.9%). 22.8% (n=52) of the patients were specifically referred to be treated under DGA, whereas only 8.3% (n=19) were specifically referred to be treated under nitrous oxide sedation (NOS; Fig. 9).

Table 3: Baseline characteristics of included patients treated under nitrous oxide sedation from 2012-2017 in the Department of Preventive and Pediatric Dentistry

baseline characteristics on patient level				
group	3-5 year-olds	6- <12 year-olds	total	drop-out[1]
n (%)	88 (38.6%)	140 (61.4%)	228 (100%)	38 (16.6%)
mean age (yrs)	4.6 (±0.7)	7.5 (±1.7)	6.4 (±1.7)	6.5 (±2.1)
gender	**n (%)**	**n (%)**	**n (%)**	**n (%)**
male	46 (52.3%)	83 (59.3%)	129 (56.6%)	24 (63.2%)
female	42 (47.7%)	57 (40.7%)	99 (43.4%)	14 (36.8%)
dmft (SD)	6.2 (±3.5)	4.9 (±3.3)	5.4 (±3.4)	7.2 (±3.7)
dt (SD)	5.5 (±3.7)	3.7 (±3.0)	4.4 (±3.3)	6.0 (±3.6)
DMFT (SD)	-	0.9 (±1.8)	-	1.2 (±2.5)
DT (SD)	-	0.8 (±1.7)	-	1.2 (±2.5)

[1] Excluded patients from success rate analysis on patient-level (DGA reduction)

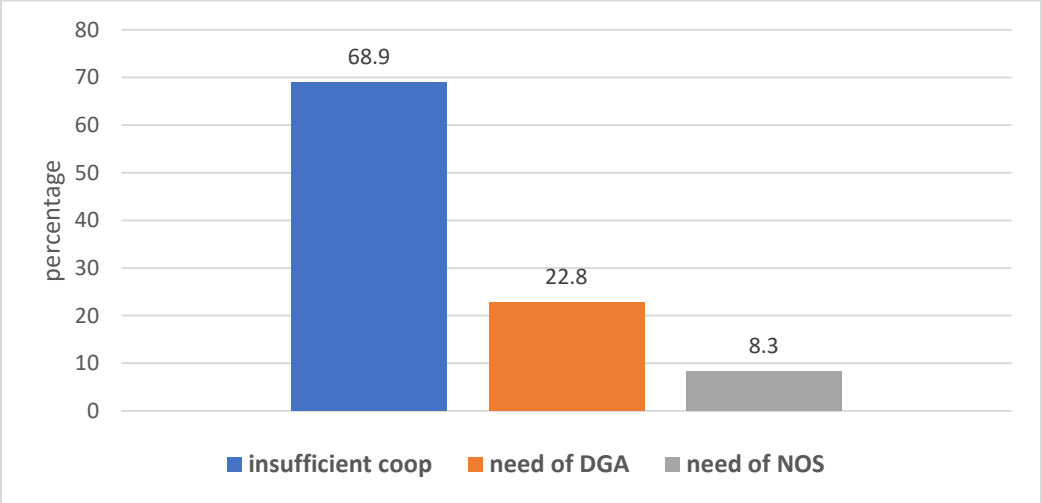

Figure 9: Proportion of children treated under NOS from 2012-2017 at the Department of Preventive and Pediatric Dentistry at the University of Greifswald according to the reason of referral

7.2 Nitrous oxide sedation success rate

7.2.1 Success rate on the session-level

In total 406 nitrous oxide sessions were performed for children up to the age of 12 in the time frame of 6 years. In 91.9% of the sessions (n=373), NOS and the planned dental treatment could be performed successfully (Tab. 4).

In 38.3% (n=143/373) of the successfully completed sessions more than on dental treatment (mean=2.2) was performed successfully.

Table 4: Baseline characteristics on session-level of patients treated under nitrous oxide sedation from 2012-2017 in the Department of Preventive and Pediatric Dentistry

baseline characteristics on session level			
	success	failure	Total
n (%)	373 (91.9%)	33 (8.1%)	406 (100%)
mean age (yrs ± SD)	6.6 (±2.0)	5.8 (±1.5)	6.5 (±2.0)
age groups			
3-5 year-olds, n (%)	136 (87.2%)	20 (12.8%)	156 (100%)
6- <12 year-olds, n (%)	237 (94.8%)	13 (5.2%)	250 (100%)
gender			
female, n (%)	158 (91.9%)	14 (8.1%)	172 (100%)
male, n (%)	215 (91.9%)	19 (8.1%)	234 (100%)

7.3 Success rate on the patient-level and DGA reduction

In 45/228 patients (19.7%) the dental treatment was not completed after the last session. 38 of the 45 patients had a successful last NOS session with no clear reason, why these patients didn't show up for the next appointment and were therefore excluded from the analysis, while 7 patients had a failed last nitrous oxide session and were included. In 2 cases, dental treatment was successfully completed without the need of DGA although a failure in the last NOS session was documented, these were also excluded from the analysis (Tab. 5).

From the total sample, 188 patients were included in the first scenario. In 84.0% (n=158) of the patients DGA was successfully avoided (Tab. 5).

7.3.1 DGA reduction according to age

Regarding the potential influence of age, a slightly lower rate of successful oral rehabilitation without DGA was achieved for pre-school (77.8%) than for schoolchildren (87.9%, Tab. 5 & Fig. 10).

7.3.2 DGA reduction according to treatment need

About one third (37.7%; 86/228) of the patients included in this study presented with an extremely high treatment need, where dt/DT ≥ age (years). 74.4% (64/86) of these patients were included in this analysis (Tab. 5). Among this group, the mean (dt/DT) revealed very high values (7.9±2.5 dt/DT; mean age 5.3 ±1.5 year-olds). Surprisingly even among this "high risk for DGA" group, 73.4% of the patients successfully completed the oral rehabilitation without the need of a DGA (Fig. 10).

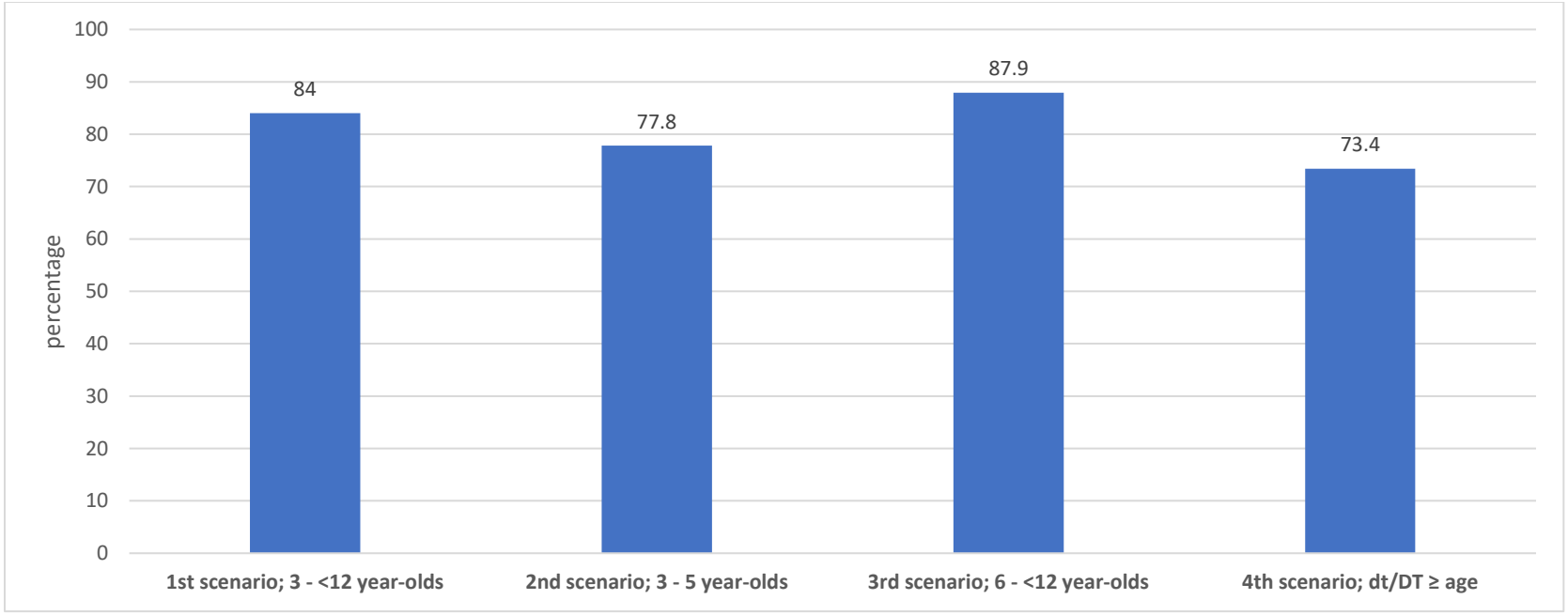

Figure 10: Potential of DGA reduction among the patients treated from 2012-2017 at the Department of Preventive and Pediatric Dentistry at the University of Greifswald according to the different scenarios

Table 5: Scenarios for successful completed oral rehabilitation with nitrous oxide sedation and proportions for avoiding dental treatment general anaesthia (DGA) with different age-specific inclusion criteria

scenario	characteristics	information about completed dental treatment available	information about completed dental treatment not available
1st scenario 3 - <12 year-olds; n=228	no DGA needed*[1]	158	-
	DGA needed*[2a/b]	23[2a]	7[2b]
	insufficient information to include	2[3]	38[4]
	Total	183	45
	included in the analysis; n (%)	188 (82.5%)	
	successful oral rehabilitation without DGA	**158/188 (84%)**	
2nd scenario 3 - 5 year-olds; n=88	no DGA needed*[1]	56	-
	DGA needed*[2a/b]	13[2a]	3[2b]
	insufficient information to include	1[3]	15[4]
	Total	70	18
	included in the analysis; n (%)	72 (81.8%)	
	successful oral rehabilitation without DGA	**56/72 (77.8%)**	
3rd scenario 6 - <12 year-olds; n=140	no DGA needed*[1]	102	-
	DGA needed*[2a/b]	10[2a]	4[2b]
	insufficient information to include	1[3]	23[4]
	Total	113	27
	included in the analysis; n (%)	116 (82.8%)	
	successful oral rehabilitation without DGA	**102/116 (87.9%)**	
4th scenario dt/DT ≥ age; n=86	no DGA needed*[1]	47	-
	DGA needed*[2a/b]	14[2a]	3[2b]
	insufficient information to include	-	22[4]
	Total	61	25
	included in the analysis; n (%)	64 (74.4%)	
	successful oral rehabilitation without DGA	**47/64 (73.4%)**	

[1] no DGA needed; successful oral rehabilitation including NOS without the need of dental DGA

[2a/b] a) DGA needed; failed last NOS session, dental DGA was needed to complete the oral rehabilitation; b) a failure in the last NOS session which indicates a possible need for dental DGA to complete the oral rehabilitation

[3] Excluded; failed last NOS session; treatment completed and no DGA was needed

[4] Excluded; no clear reason, why they didn't show up to the next appointment

7.3.3 DGA reduction according to the reason of referral

According to the reason of referral, the lowest success rate to avoid a GA was found for the patients originally and specifically referred for treatment under DGA. Still, for 65.7% (23/35) of these patients a successful complete oral rehabilitation could be achieved without DGA (Tab. 6 & Fig. 11).

Table 6: Successful complete oral rehabilitation with nitrous oxide sedation without the need of DGA according to the reason of referral

Referral due to	n	included in the analysis; n (%)	excluded from the analysis[1]; n (%)	successful oral rehabilitation without DGA
insufficient coop	157	134 (85.3%)	23 (14.7%)	**117/134 (87.3%)**
need of DGA	52	35 (67.3%)	17 (32.7%)	**23/35 (65.7%)**
need of NOS	19	19 (100%)	0	**18/19 (94.7%)**

[1] Excluded; failed last nitrous oxide session; treatment completed and no DGA was needed **or** no clear reason, why they didn't show up to the next appointment

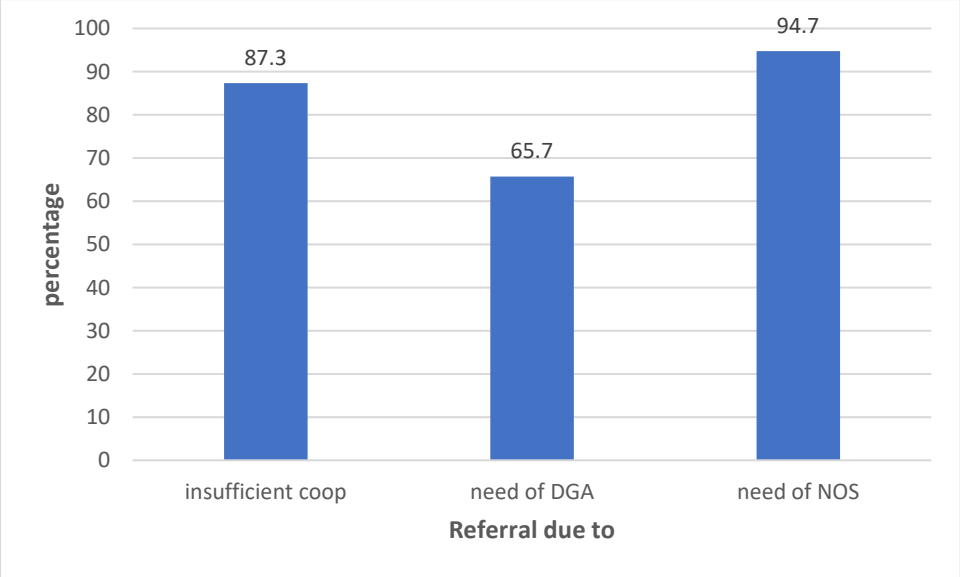

Figure 11: Potential of DGA reduction among the patients treated from 2012-2017 at the Department of Preventive and Pediatric Dentistry at the University of Greifswald according to the reason of referral

8. Discussion

8.1 Characteristics of the study sample

Despite a clear caries decline in the last couple of years in Germany shown by several national surveys and the increase of caries-free children [IDZ, 2016; Team DAJ, 2017], young children still present with a significant caries experience and high treatment need in specialist care setting [Santamaria et al., 2019; Schmoeckel et al., 2019; Team DAJ, 2017].

Compared with the most recent epidemiological studies in Germany [IDZ, 2016; Team DAJ, 2017], in which 1.7 dmft value was reported in 6-7-year-olds children, the population in this study had about 3-4 times higher dmft/DMFT values (Tab. 3). These can be considered to be comparable to the (SiCdmft/DMFT) values (4.8) for the German population representing a high caries risk group of patients.

According to the literature, dental anxiety could be a predictor of / associated with high levels of dental caries [Esa et al., 2014; Milgrom et al., 1988] and they are the key patients for specialized pediatric dentists. For these reasons, the dental treatment especially for this group of patients remains challenging and requires a very good knowledge of both BBMT and ABMT.

Besides the fact that risks of morbidity and mortality associated with DGA are considerably higher when it is compared to conscious sedation [Soldani et al., 2010], a proper knowledge of BMT and caries management is essential to provide the best dental care for pediatric patients.

Caries management techniques such as non-restorative caries control (NRCC), Hall-Technique (HT) and the application silver diamine fluoride (SDF) have been proven to be effective and viable treatment options in pediatric dentistry [Rosenblatt et al., 2009; Santamaría et al., 2020]. The application of these techniques combined with NOS, when needed, and implementing these options in the treatment concept might lead to DGA reduction among young patients with high treatment need.

8.2 Nitrous oxide sedation success rate

8.2.1 Success rate on the session-level

This study showed a 91.9% success rate of NOS in the children included in this study on the session-level, which highlights its importance as a viable ABMT option to reduce the number of DGA. These results underline previous findings in the literature on the potential of NOS sedation reporting success rates of 83.9%, 86.3% and 93.7%, respectively [Bryan, 2002; Collado et al., 2006; Collado et al., 2007; Galeotti et al., 2016; Hennequin et al., 2012]. The failure rate was not affected by the patients' gender (8.1% for females and males).

8.2.2 Success rate on the patient-level and DGA reduction

Despite that a 91.9% success rate on a session-level might be considered an important finding, clinically it is more important to examine the success rate on the patient level. This could be used as an accurate indicator regarding the reduction/avoidance of DGA.

One of the main findings of this study was that for the vast majority (84.0%) of patients complete oral rehabilitation could be successfully achieved without the need of DGA. This is in good agreement with Bryan 2002, where treatment plans in 83·9% of the treated children were successfully completed [Bryan, 2002]. Taking into account, that all the patients included in this study where young pre-cooperative patients with different cooperation related problems and referral reasons, this should be considered a remarkable finding.

8.2.3 DGA reduction according to age

As expected, schoolchildren showed higher success rates compared to pre-school children on both session and patient-level. Accordingly, multiple studies reported that those patients who successfully completed treatment were statistically significant older than those in whom treatment was not completed [Foley, 2005; Hennequin et al., 2012; Lyratzopoulos and Blain, 2003].

According to Hennequin et al. [2012], a high success rate was found in preschool children (91.7%, n=85) which is comparable with these results. Also patients with disability (87.3%, n=71), anxious/phobic patients (95.1%, n=269) and in patients with one-off indication (94.8%, n=213) showed a high success rate for treatment under NOS [Hennequin et al., 2012]. In contrast to this, Galeotti et al. [2016] reported no statistically significant difference between success and failure in relation to the mean age, possibly due to different categorization of the age groups [Galeotti et al., 2016].

Although the preschool children in the 2nd scenario (3 - 5 year-olds) showed the lowest success rate for complete oral rehabilitation without DGA (77.8%), it should still be considered to be high for the group itself. This can be still interpreted as an encouraging result, as it shows the importance of applying NOS also for pre-school children to avoid the risk of treatment under general anesthesia, especially as they usually are the largest group of patients with treatment needs (high caries levels, pulp symptoms and low cooperation) in a specialized pediatric practice.

8.2.4 DGA reduction according to treatment need

Different studies suggested, that high caries levels along with fear and dental anxiety were found among children treated under DGA [Alkilzy et al., 2015; Karim et al., 2008; Vinckier et al., 2001]. Another study investigating the characteristics of children receiving treatment under DGA in Germany found that the mean number of teeth needing treatment (dt) is higher than the mean age of the treated children [Takriti et al., 2019].

This study reveals a high dt values among all the treated children (mean = 4.4±3.3) and especially among the children included in the 4th scenario (mean = 7.9±2.5).

Such high untreated caries levels (dt) in children might justify the use of DGA for treating these young children. Depending on these facts and the experienced author knowledge of the selection criteria of DGA patients in specialized dental practices in Germany, it can be assumed that when the number of teeth that need invasive dental treatments exceeds the age in years, children will probably need DGA for full oral rehabilitation.

Interestingly and even among the “high risk of DGA” group in the 4th scenario (dt/DT ≥ age; n=86) the DGA reduction was still very high (74.3%). A DGA reduction among this group should considered to be a huge achievement and a proof of success of the overall treatment concept.

8.2.5 DGA reduction according to reason of referral

As a part of the clinical standards used in the Department of Preventive and Pediatric Dentistry at the University of Greifswald newly admitted patients undergo clinical and when necessarily radiological examinations. This helps determining the treatment need and whether the level of the cooperation is sufficient to perform the needed treatment or not. According to the reason of referral, the lowest success rate was among the DGA-group and the highest success rate was among the NOS-group, this might show that referring dentist have a tendency to be able to identify complicated cases requiring special care. Conversely, the high percentage of patients referred due to IC without specifying whether a DGA or NOS is needed might indicate to the lack of knowledge on ABMT. which might be due to the poor training in Pediatric Dentistry provided by the universities [Basner et al., 2012].

Although a lot of children are treated under NOS in the Department of Preventive and Pediatric Dentistry every year, about 90 sessions of DGA are performed every year to treat mainly very young children (1 to 4 year-olds) with very low levels of cooperation, where a chair-side dental treatment not possible or NOS is contraindicated.

8.3 Discussion of the drop-outs

Interestingly, the drop-outs (n=38; 16.6%) differed only slightly from the included patients revealing marginal higher caries rates and a slightly higher fraction of specific referrals for DGA. Not showing up for the next scheduled appointment might be considered under these circumstances a form of neglect, The failure of seeking dental treatment or completing a recommend course of treatment while having an adequate access to oral healthcare services raise the possibility of dental neglect [Bhatia et al., 2014; Kiatipi et al., 2021]. Therefore, it might be important to implement a concept to keep track of these patients to ensure that they receive the treatment required and when necessarily report to the appropriate authorities. With unclear reasons leading to not showing up for further treatments along with the fact, that the last NOS for these patients was a success, the missing data is not thought to be due to failure in the treatment concept with NOS. Consequently, the risk of bias due to missing data should be considered low.

8.4 Strengths and limitations

To my knowledge, this study is the first to describe the success rate and potential of DGA reduction for children under 12 years of age treated under NOS in Germany.

While the presented study has a retrospective design, which holds a potential risk of bias, the data showed and reflected a typical real life specialized pedodontic setting, where the pediatric dentists face the challenge to treat young children with high caries levels and mostly limited cooperation.

In order to provide a high treatment quality and for better quality management, a clear protocol for treating patients under NOS and documentation is used by all the dentists at the department, which minimizes the potential error in both documentation and the bias in case selection.

With a large sample size of 228 patients treated within a long time span of 6 years, the results should be considered highly plausible especially as certain key aspects and findings were comparable to other studies reported in the literature [Ferrazzano et al., 2020; Foley, 2005; Galeotti et al., 2016; Hennequin et al., 2012].

8.5 Clinical implications and further recommendations

A low number of DGA should be a major aim of a society to reduce risks for the children and costs for health care. In the light of the findings of this study regarding the possible high percentage of DGA avoidance/reduction when using NOS for treating pre-cooperative patients in pediatric dentistry it is very important for dental practices which offer DGA to have training and knowledge in BMT beside new caries management techniques like nonrestorative caries control, silver diamine fluoride, Hall technique and also ABMT such as sedation with N_2O. Otherwise, the proper indication of DGA would be highly questionable.

In Germany, sedation with N_2O for dental treatment in children is not paid for by the national health system in contrast to GA which are right now covered until the age of 12 years. Thus, it would be helpful that more studies, potentially even large-scale prospective trials, confirm the success of NOS and assess the cost effectiveness in order to encourage the national health system to cover the costs of sedation for dental treatment in children. This could be a decisive factor in reducing the number of DGA in Germany.

9. Conclusion

A high fraction of children with high dental treatment need can be managed without the use of DGA when a comprehensive concept of caries management is combined with the use of NOS and behavior management techniques. NOS should, therefore, be considered as an option for dental treatment of semi-cooperative children with high dental treatment need before making a decision towards DGA.

10. Acknowledgements

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Last but not the least; I would like to thank my parents, sisters, and brother for their infinite support through this journey and my life.

In the end, I would also like to thank the German Society of Dentistry and Oral Medicine (DGZMK) for their partial financial support of this study.

11. List of abbreviations

Abbreviation	Definition
AAPD	American Association of Pediatric Dentistry
ABMT	Advanced Behavior Management Techniques
ADA	American Dental Association
ASA	American Society of Anesthesiologists
BBMT	Basic Behavior management techniques
BDA	Berufsverband Deutscher Anästhesisten
CDSBC	College of Dental Surgeons of British Columbia
CED	Council of European Dentists
COPD	Chronic Obstructive Pulmonary Diseases
DAJ	Deutsche Arbeitsgemeinschaft für Jugendzahnpflege e. V.
DGA	Dental General Anesthesia
DGAI	Deutsche Gesellschaft für Anästhesiologie & Intensivmedizin
DGKiZ	Deutsche Gesellschaft für Kinderzahnheilkunde
DGZMK	Deutsche Gesellschaft für Zahn-, Mund- und Kieferheilkunde
DMFT	Decayed/Missing/Filled Teeth (permanent teeth)
dmft	decayed/missing/filled teeth (primary teeth)
EAPD	European Academy of Paediatric Dentistry
ECC	Early Childhood Caries
GA	General Anesthesia
HT	Hall Technique
IC	Insufficient Cooperation
MIH	Molar Incisor Hypomineralisation
N_2O	Nitrous Oxide
NOS	Nitrous Oxide Sedation
NRCC	Non Restorative Caries Control
SDAC	Standing Dental Advisory Committee
SPSS	Statistical Package for the Social Sciences
SSC	Stainless Steel Crown

12. References

Alkilzy M, Qadri G, Horn J, Takriti M, Splieth C: Referral patterns and general anesthesia in a specialized paediatric dental service. Int J Paediatr Dent 2015; 25:204–212.

Al-Zahrani AM, Wyne AH, Sheta SA: Comparison of oral midazolam with a combination of oral midazolam and nitrous oxide-oxygen inhalation in the effectiveness of dental sedation for young children. J Indian Soc Pedod Prev Dent 2009; 27:9–16.

American Academy of Pediatric Dentistry: Use of Nitrous Oxide for Pediatric Dental Patients 2018:338–343.

American Academy of Pediatric Dentistry: Behavior Guidance for the Pediatric Dental Patient. The Reference Manual of Pediatric Dentistry. 2020:292–310.

American Dental Association: Guidelines for the Use of Sedation and General Anesthesia by Dentists 2016.

Arcari S, Ferro R: Preschool children and relative analgesia: satisfaction grading through a verbal questionnaire. Eur J Paediatr Dent 2008; 9:18–22.

Attri JP, Sharan R, Makkar V, Gupta KK, Khetarpal R, Kataria AP: Conscious Sedation: Emerging Trends in Pediatric Dentistry. Anesth Essays Res 2017; 11:277–281.

Basner R, Hirsch C, Splieth CH: Lehre im Fach Kinderzahnheilkunde im Grundstudium Zahnmedizin in Deutschland, 2012.

Becker DE, Rosenberg M: Nitrous oxide and the inhalation anesthetics. Anesth Prog 2008; 55:124-30; quiz 131-2.

Bernabe E, Marcenes W, Hernandez CR, Bailey J, Abreu LG, Alipour V, Amini S, Arabloo J, Arefi Z, Arora A, Ayanore MA, Bärnighausen TW, Bijani A, Cho DY, Chu DT, Crowe CS, Demoz GT, Demsie DG, Dibaji Forooshani ZS, Du M, El Tantawi M, Fischer F, Folayan MO, Futran ND, Geramo YCD, Haj-Mirzaian A, Hariyani N, Hasanzadeh A, Hassanipour S, Hay SI, Hole MK, Hostiuc S, Ilic MD, James SL, Kalhor R, Kemmer L, Keramati M, Khader YS, Kisa S, Kisa A, Koyanagi A, Lalloo R, Le Nguyen Q, London SD, Manohar ND, Massenburg BB, Mathur MR, Meles HG, Mestrovic T, Mohammadian-

Hafshejani A, Mohammadpourhodki R, Mokdad AH, Morrison SD, Nazari J, Nguyen TH, Nguyen CT, Nixon MR, Olagunju TO, Pakshir K, Pathak M, Rabiee N, Rafiei A, Ramezanzadeh K, Rios-Blancas MJ, Roro EM, Sabour S, Samy AM, Sawhney M, Schwendicke F, Shaahmadi F, Shaikh MA, Stein C, Tovani-Palone MR, Tran BX, Unnikrishnan B, Vu GT, Vukovic A, Warouw TSS, Zaidi Z, Zhang ZJ, Kassebaum NJ: Global, Regional, and National Levels and Trends in Burden of Oral Conditions from 1990 to 2017: A Systematic Analysis for the Global Burden of Disease 2017 Study. J Dent Res 2020; 99:362–373.

Bhatia SK, Maguire SA, Chadwick BL, Hunter ML, Harris JC, Tempest V, Mann MK, Kemp AM: Characteristics of child dental neglect: a systematic review. J Dent 2014; 42:229–239.

Brown SM, Sneyd, JR: Nitrous oxide in modern anaesthetic practice. BJA Education 2016; 16:87–91.

Bryan RAE: The success of inhalation sedation for comprehensive dental care within the Community Dental Service. Int J Paediatr Dent 2002; 12:410–414.

CDSBC: Minimal and Moderate Sedation Services in Dentistry 2018.

Cianetti S, Lombardo G, Lupatelli E, Pagano S, Abraha I, Montedori A, Caruso S, Gatto R, Giorgio S de, Salvato R: Dental fear/anxiety among children and adolescents. A systematic review. Eur J Paediatr Dent 2017; 18:121–130.

Collado V, Hennequin M, Faulks D, Mazille M-N, Nicolas E, Koscielny S, Onody P: Modification of behavior with 50% nitrous oxide/oxygen conscious sedation over repeated visits for dental treatment a 3-year prospective study. J Clin Psychopharmacol 2006; 26:474–481.

Collado V, Nicolas E, Faulks D, Hennequin M: A review of the safety of 50% nitrous oxide/oxygen in conscious sedation. Expert opinion on drug safety 2007; 6:559–571.

Council of European Dentists: Anwendung der inhalativen Lachgassedierung in der Zahnmedizin. Stomatologie 2014; 111:188–190.

Deutsche Gesellschaft für Kinderzahnheikunde: Lachgaszertifizierung. https://www.dgkiz.de/lachgaszertifizierung.html, 2022.

DGKiZ: Behandler-/Kinderzahnarztsuche - DGKiZ. https://www.dgkiz.de/kinderzahnarztsuche.html?querry=17491, 2022.

DPHEP: National Dental Epidemiology Programme for England: oral health survey of five-year-old children 2015 A report on the prevalence and severity of dental decay 2019.

Erten H, Akarslan ZZ, Bodrumlu E: Dental fear and anxiety levels of patients attending a dental clinic. Quintessence Int 2006; 37:304–310.

Esa R, Ong AL, Humphris G, Freeman R: The relationship of dental caries and dental fear in Malaysian adolescents: a latent variable approach. BMC Oral Health 2014; 14:19.

Esa R, Savithri V, Humphris G, Freeman R: The relationship between dental anxiety and dental decay experience in antenatal mothers. Eur J Oral Sci 2010; 118:59–65.

Ferrazzano GF, Quaraniello M, Sangianantoni G, Ingenito A, Cantile T: Clinical effectiveness of inhalation conscious sedation with nitrous oxide and oxygen for dental treatment in uncooperative paediatric patients during COVID-19 outbreak. Eur J Paediatr Dent 2020; 21:277–282.

Fish BM, Banerjee AR, Jennings CR, Frain I, Narula AA: Effect of anaesthetic agents on tympanometry and middle-ear effusions. J Laryngol Otol 2000; 114:336–338.

Fleming P, Walker PO, Priest JR: Bleomycin therapy: a contraindication to the use of nitrous oxide-oxygen psychosedation in the dental office. Pediatr Dent 1988; 10:345–346.

Foley J: A prospective study of the use of nitrous oxide inhalation sedation for dental treatment in anxious children. Eur J Paediatr Dent 2005; 6:121–128.

Galeotti A, Garret Bernardin A, D'Antò V, Ferrazzano GF, Gentile T, Viarani V, Cassabgi G, Cantile T: Inhalation Conscious Sedation with Nitrous Oxide and Oxygen as Alternative to General Anesthesia in Precooperative, Fearful, and Disabled Pediatric Dental Patients: A Large Survey on 688 Working Sessions. Biomed Res Int 2016; 2016:7289310.

Giacaman RA, Muñoz-Sandoval C, Neuhaus KW, Fontana M, Chałas R: Evidence-based strategies for the minimally invasive treatment of carious lesions: Review of the literature. Adv Clin Exp Med 2018; 27:1009–1016.

Guideline on Behavior Guidance for the Pediatric Dental Patient. Pediatr Dent 2015; 37:57–70.

Hallonsten A-L, Jensen B, Raadal M, Veerkamp J, Hosey M, Poulsen S: EAPD Guidelines on Sedation in Paediatric Dentistry 2003.

Haridas RP: Horace wells' demonstration of nitrous oxide in Boston. Anesthesiology 2013; 119:1014–1022.

Hennequin M, Collado V, Faulks D, Koscielny S, Onody P, Nicolas E: A clinical trial of efficacy and safety of inhalation sedation with a 50% nitrous oxide/oxygen premix (Kalinox™) in general practice. Clin Oral Investig 2012; 16:633–642.

Höhne C, Daubländer M, Becke K, Splieth CH, Beck G: Empfehlung Einsatz von Lachgas zur minimalen Sedierung von Kindern in der Zahnheilkunde. Gemeinsame wissenschaftliche Mitteilung des Wissenschaftlichen Arbeitskreises Kinderanästhesie der DGAI und des Interdisziplinären Arbeitskreises Zahnärztliche Anästhesie von DGAI, BDA, DGKiZ und DGZMK 2021.

IDZ: Fünfte Deutsche Mundgesundheitsstudie (DMS V). Köln, Deutscher Zahnärzte Verlag DÄV, 2016.

Karim ZA, Musa N, Noor SNFM: Utilization of dental general anaesthesia for children. Malays J Med Sci 2008; 15:31–39.

Kaufman E, Weinstein P, Sommers EE, Soltero DJ: An experimental study of the control of the gag reflex with nitrous oxide. Anesth Prog 1988; 35:155–157.

Kiatipi M, Davidopoulou S, Arapostathis K, Arhakis A: Dental Neglect in Children: A Comprehensive Review of the Literature. J Contemp Dent Pract 2021; 22:199–204.

KZBV: Vollnarkose beim Zahnarzt – Wann zahlt die Krankenkasse? https://www.kzbv.de/kzbv2021-pi-vollnarkose.download.68527610c984873a13996098757c79f3.pdf, 01/2022.

Lyratzopoulos G, Blain KM: Inhalation sedation with nitrous oxide as an alternative to dental general anaesthesia for children. J Public Health Med 2003; 25:303–312.

Matharu L, Ashley PF: Sedation of anxious children undergoing dental treatment. Cochrane Database Syst Rev 2006:CD003877.

Milgrom P, Fiset L, Melnick S, Weinstein P: The prevalence and practice management consequences of dental fear in a major US city. J Am Dent Assoc 1988; 116:641–647.

Milnes AR: Intravenous procedural sedation: an alternative to general anesthesia in the treatment of early childhood caries. J Can Dent Assoc 2003; 69:298–302.

Mohan R, Asir VD, Shanmugapriyan, Ebenezr V, Dakir A, Balakrishnan, Jacob J: Nitrousoxide as a conscious sedative in minor oral surgical procedure. J Pharm Bioallied Sci 2015; 7:S248-50.

Murthy AK, Pramila M, Ranganath S: Prevalence of clinical consequences of untreated dental caries and its relation to dental fear among 12-15-year-old schoolchildren in Bangalore city, India. Eur Arch Paediatr Dent 2014; 15:45–49.

Ogundipe O, Pearson MW, Slater NG, Adepegba T, Westerdale N: Sickle cell disease and nitrous oxide-induced neuropathy. Clin Lab Haematol 1999; 21:409–412.

Patel R, Lenczyk M, Hannallah RS, McGill WA: Age and the onset of desaturation in apnoeic children. Can J Anaesth 1994; 41:771–774.

Paterson SA, Tahmassebi JF: Paediatric dentistry in the new millennium: 3. Use of inhalation sedation in paediatric dentistry. Dent Update 2003; 30:350-6, 358.

Philippi-Höhne C, Daubländer M, Becke K, Reinhold P, Splieth CH, Beck G: Gemeinsame Stellungnahme: Einsatz von Lachgas zur minimalen Sedierung von Kindern in der Zahnheilkunde. Anästhesiologie & Intensivmedizin 2013; 54:323–326.

Ramos-Jorge J, Alencar BM, Pordeus IA, Da Soares MEC, Marques LS, Ramos-Jorge ML, Paiva SM: Impact of dental caries on quality of life among preschool children: emphasis on the type of tooth and stages of progression. Eur J Oral Sci 2015; 123:88–95.

Roberts GJ, Mokhtar SM, Lucas VS, Mason C: Deaths associated with GA for dentistry 1948 - 2016: the evolution of a policy for general anaesthesia (GA) for dental treatment. Heliyon 2020; 6:e02671.

Rosenblatt A, Stamford TCM, Niederman R: Silver diamine fluoride: a caries "silver-fluoride bullet". J Dent Res 2009; 88:116–125.

Rowland AS, Baird DD, Shore DL, Weinberg CR, Savitz DA, Wilcox AJ: Nitrous oxide and spontaneous abortion in female dental assistants. American journal of epidemiology 1995; 141:531–538.

Santamaria RM, Schmoeckel J, Basner R, Schüler E, Splieth CH: Caries Trends in the Primary Dentition of 6- to 7-Year-old Schoolchildren in Germany from 1994 to 2016: Results from the German National Oral Health Surveys in Children. Caries Res 2019; 53:659–666.

Santamaría RM, Abudrya MH, Gül G, Mourad MS, Gomez GF, Zandona AGF: How to Intervene in the Caries Process: Dentin Caries in Primary Teeth. Caries Res 2020; 54:306–323.

Savanheimo N, Vehkalahti MM: Preventive aspects in children's caries treatments preceding dental care under general anaesthesia. Int J Paediatr Dent 2008; 18:117–123.

Schmoeckel J, Santamaría RM, Basner R, Schüler E, Splieth CH: Introducing a Specific Term to Present Caries Experience in Populations with Low Caries Prevalence: Specific Affected Caries Index (SaC). Caries Res 2019; 53:527–531.

Selzer RR, Rosenblatt DS, Laxova R, Hogan K: Adverse effect of nitrous oxide in a child with 5,10-methylenetetrahydrofolate reductase deficiency. N Engl J Med 2003; 349:45–50.

Silveira ER, Cademartori MG, Schuch HS, Armfield JA, Demarco FF: Estimated prevalence of dental fear in adults: A systematic review and meta-analysis. J Dent 2021; 108:103632.

Soldani F, Manton S, Stirrups DR, Cumming C, Foley J: A comparison of inhalation sedation agents in the management of children receiving dental treatment: a randomized, controlled, cross-over pilot trial. Int J Paediatr Dent 2010; 20:65–75.

Takriti M, Alhakim D, Splieth C: Dental characteristics and according treatments of children under GA in Germany. Eur Arch Paediatr Dent 2019; 20:617–622.

Team DAJ: Epidemiologische Begleituntersuchungen zur Gruppenprophylaxe 2016. Bonn, Deutsche Arb.-Gemeinsch. f. Jugendzahnpflege, 2017.

Tobias JD: Applications of nitrous oxide for procedural sedation in the pediatric population. Pediatr Emerg Care 2013; 29:245–265.

Veaux CKE de, Montagnese TA, Heima M, Aminoshariae A, Mickel A: The Effect of Various Concentrations of Nitrous Oxide and Oxygen on the Hypersensitive Gag Reflex. Anesth Prog 2016; 63:181–184.

Vinckier F, Gizani S, Declerck D: Comprehensive dental care for children with rampant caries under general anaesthesia. Int J Paediatr Dent 2001; 11:25–32.

Wang CY, Chiu CL, Har KO, Chan C, Rahman ZAA: A comparative study of sevoflurane sedation with nitrous oxide sedation for dental surgery. Int J Oral Maxillofac Surg 2002; 31:506–510.

Yoshida H, Ayuse T, Ishizaka S, Ishitobi S, Nogami T, Oi K: Management of exaggerated gag reflex using intravenous sedation in prosthodontic treatment. Tohoku J Exp Med 2007; 212:373–378.

Zier JL, Tarrago R, Liu M: Level of sedation with nitrous oxide for pediatric medical procedures. Anesth Analg 2010; 110:1399–1405.

13. Declaration of authorship

I hereby certify that this doctoral thesis "**Potential of nitrous oxide sedation in pedodontics to reduce the need of dental general anesthesia**" has been composed by me and is based on my own work, unless stated otherwise. No other person's work has been used without acknowledgement in this thesis. All references and verbatim extracts have been quoted, and all sources of information, including graphs and data sets, have been specifically acknowledged.

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"Whenever you feel like criticizing anyone … just remember that all the people in this world haven't had the advantages that you've had."

The Great Gatsby, F. Scott Fitzgerald