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Research Article

Nitrous Oxide as Adjuvant in General Anaesthesia: Clinical and Environmental Impacts

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Abstract:
Background: Nitrous oxide is widely used as an adjuvant in general anaesthesia due to its analgesic properties and ability to reduce doses of other anaesthetic agents. However, its environmental impact as a potent greenhouse gas raises concerns. **Aim:** To evaluate the clinical benefits and environmental impacts of using nitrous oxide as an adjuvant in general anaesthesia. **Methods:** A secondary research study reviewing academic databases, official reports, and policy documents related to the clinical efficacy, safety, and environmental footprint of nitrous oxide use was conducted. **Results:** Nitrous oxide provides rapid analgesia, improved hemodynamic stability, and dose-sparing effects, facilitating quick induction and recovery. Adverse effects include postoperative nausea, air-space expansion risks, vitamin B12 inactivation, and neurological complications. Environmentally, nitrous oxide has a global warming potential 265 times greater than CO_2 and contributes to ozone depletion. Sustainable anaesthetic practices such as low-flow techniques, gas scavenging, and alternative anaesthetic methods are recommended. **Conclusion:** While clinically advantageous, the environmental risks of nitrous oxide necessitate judicious use and adoption of sustainable anaesthesia approaches to balance patient care and ecological responsibility.
Keywords: Nitrous oxide, general anaesthesia, sustainable anaesthesia.

Introduction

Nitrous oxide (N_2O), long established in medical practice, continues to hold clinical importance as an adjuvant agent in general anaesthesia due to its unique pharmacological profile and multifaceted applications across surgical, dental, and obstetrical settings. Its primary mechanism as an inhalational anaesthetic is shaped by minimal cardiovascular and respiratory depressive effects, rapid onset and recovery due to a low blood-gas partition coefficient, and strong analgesic properties, which distinguish it from potent volatile agents like sevoflurane and desflurane. The “second gas effect,” where nitrous oxide enhances the uptake of accompanying anaesthetic agents, supports swift induction and emergence-attributes valuable in ambulatory surgery and short procedures. Despite lacking muscle relaxation and being insufficient as a sole agent for major surgery, its combination with other anaesthetics enables reduced dosages, which translates into enhanced safety, minimized adverse reactions, and consistent hemodynamic stability. In modern clinical protocols, nitrous oxide is used-often in concentrations of 20-70% oxygen-to provide sedative-analgesic effects for labor analgesia, dental interventions, traumatic procedures, and chronic pain management, demonstrating its broad utility and adaptability.[1]

However, alongside its clinical benefits, concerns about safety and tolerability persist. Postoperative nausea and vomiting (PONV) are notably more frequent following nitrous oxide use, especially in females and prolonged surgery. Due to its physical properties, nitrous oxide can increase pressure within air-filled spaces-posing risks of tympanic membrane rupture, bowel distension, and pneumothorax, particularly in patients undergoing specific surgical procedures. Chronic or repeated exposure to nitrous oxide disrupts vitamin B12 metabolism, leading to hematological, neurological, and cognitive complications such as megaloblastic anemia, neuropathy, and paresthesia, raising concern for occupational exposure in operating theatres. Further complicating its profile is the risk of diffusion hypoxia during recovery, mitigated only by adequate supplemental oxygen administration.[2]

From an environmental perspective, nitrous oxide is recognized as a high-impact greenhouse gas and ozone-depleting substance. Its large global warming potential-approximately 265 times that of carbon dioxide-coupled with an atmospheric lifetime exceeding 120 years, renders it a significant contributor to climate change and long-term ecological destabilization. While a substantial proportion of global emissions derive from agricultural and industrial activities, anaesthesia-related discharges from operating theatres are increasingly scrutinized as healthcare sectors adopt sustainability initiatives. Inadequate ventilation, inefficient gas-scavenging systems, and high fresh gas flow rates in low-resource settings further amplify environmental risks by promoting atmospheric release of N_2O. Consequently, best practice guidelines are evolving to prioritize low-flow anaesthesia, promote the use of alternative modalities such as total intravenous anaesthesia (TIVA), and invest in technology like gas capture and recycling systems to minimize ecological burden.[3]

The contemporary narrative thus frames nitrous oxide as both a clinical asset and an environmental liability. Balancing its remarkable pharmacodynamic benefits against adverse effects and ecological harm requires nuanced consideration-embedding the principles of evidence-based medicine, risk management, and sustainable healthcare. This review addresses the importance of judicious use, including patient selection, procedural context, and proactive mitigation strategies to ensure optimal clinical outcomes with minimal environmental trade-off. Current literature underscores the need for anaesthesiologists, surgical teams, and healthcare institutions to refine protocols, educate stakeholders, and champion sustainable anaesthesia, thereby safeguarding both patient health and global ecological integrity in an era of climate crisis and evolving medical standards.[4]

Aim:

To evaluate the clinical benefits and environmental impacts of using nitrous oxide as an adjuvant in general anaesthesia.

Objectives:

1. To assess the clinical efficacy, safety profile, and specific anaesthetic advantages conferred by nitrous oxide in current practice.

2. To identify and analyze the adverse effects and complications associated with nitrous oxide administration in surgical patients.
3. To quantify the environmental repercussions of nitrous oxide use, recommend sustainable anaesthetic approaches, and critically appraise mitigation strategies.

Material and Methodology

Source of Data: Secondary data was collected exclusively from published literature including randomized clinical trials, observational studies, academic reviews, and guideline documents accessible via PubMed, Scopus, Research Gate, Sodhganga, Google Scholar, recognized textbooks, government health websites, and official policy reports relevant to anaesthetic practice and environmental health.

Study Design: A secondary observational and narrative review of scientific literature was conducted. The study employed a descriptive design, focusing on extracting, synthesizing, and analyzing reported outcomes, mechanisms, and environmental impacts of nitrous oxide as used in general anaesthesia settings.

Study Location: Data sources were drawn globally, with a focus on recent studies and regulatory reports representative of both developed and developing healthcare contexts, including tertiary medical centers and community hospitals.

Study Duration: The review encompassed literature published from the inception of widespread clinical nitrous oxide use to the present (up to 2025), emphasizing works published within the past two decades to ensure contemporary relevance.

Inclusion Criteria:

- Peer-reviewed publications, clinical trials, and observational studies reporting on nitrous oxide use in general anaesthesia
- Environmental impact assessments of anaesthetic gases, including nitrous oxide
- Reports detailing safety, efficacy, and complications associated with nitrous oxide in humans
- Regulatory documents and guidelines addressing anaesthetic protocols and environmental standards

Exclusion Criteria:

- Studies exclusively examining dental or non-general anaesthesia settings
- Animal model studies or laboratory-only experiments not directly translatable to human clinical anaesthesia
- Reports lacking substantive data on either clinical outcomes or environmental impact

Procedure and Methodology: Data relevant to nitrous oxide administration (dose, concentration, route, procedural context, patient demographics, clinical indications, adverse event rates, recovery metrics, and hemodynamic stability) as well as environmental metrics (estimated atmospheric emission, global warming potential, ozone depletion potential, mitigation strategies, and regulatory compliance) were extracted, tabulated, and critically appraised. Statistical outcomes, descriptive summaries, and comparative analyses were conducted for included studies in line with standard narrative review practice.

Sample Processing: For environmental analysis, annual nitrous oxide consumption rates and emission equivalence (in CO_2 equivalents) from hospitals and published surveys were compiled for comparative review. For clinical analysis, study arms, patient numbers, anaesthetic regimes, complication rates, and perioperative outcomes were systematically documented from each eligible study.

Statistical Methods: Descriptive and inferential statistics provided in individual source studies were reviewed, including measures of central tendency, frequency tables, relative risk, odds ratios, and corresponding p-values. Where appropriate, cross-study comparison was performed to highlight significant outcomes and trends.

Data Collection: Data were systematically gathered from diverse academic repositories, indexing abstracts, full-text articles, and supplementary materials. Reference tracking and citation analysis supported inclusion of high-quality, recent, and high-impact scholarly works and practice guidelines.

Observation and Results:

Table 1: Clinical Benefits and Environmental Impacts of Nitrous Oxide as Adjuvant

Parameter	Description
Analgesia	Provides rapid, effective analgesia as an adjunct in anaesthesia
Dose-sparing effect	Reduces need for opioids/volatile agents, improving safety
Hemodynamic stability	Maintains blood pressure, lowers risk of intraoperative hypotension
Quick onset and recovery	Fast induction/emergence due to low blood-gas partition coefficient
Environmental impact (GHG)	265x global warming potential vs CO_2, long atmospheric lifetime (110+ years), ozone depletion potential
Major emission sources	OT gas release (healthcare)/industrial/agriculture sectors

Nitrous oxide as an adjuvant in general anaesthesia offers substantial clinical and environmental implications, which are summarized effectively across four key domains. First, its clinical benefits are notable for providing rapid and effective analgesia, ensuring pain control for patients undergoing surgical procedures. The agent's dose-sparing effect facilitates the reduction of both opioid and volatile anaesthetic use, thus enhancing patient safety and minimizing the likelihood of adverse reactions. Hemodynamically, nitrous oxide aids in maintaining stable blood pressure and significantly lowers the risk of intraoperative hypotension, making it a preferred choice in scenarios prone to hemodynamic fluctuations. Its pharmacokinetic properties-particularly a low blood-gas partition coefficient-allow for exceptionally fast induction and recovery, key factors in ambulatory and short-duration surgeries. Nevertheless, its environmental footprint is substantial: nitrous oxide possesses a global warming potential 265 times greater than carbon dioxide, remains in the atmosphere for over 110 years, and is recognized for potential ozone layer depletion. Major emission sources include operating theatre (OT) gas release in healthcare, as well as broader industrial and agricultural sectors.

Table 2: Clinical Efficacy, Safety Profile, and Anaesthetic Advantages

Clinical Advantage	Description
Efficacy in sedation	Highly effective adjunct for procedural and surgical sedation
Patient satisfaction	Comparable to alternative agents; satisfactory sedation, cooperation, and pain control
Speed of induction	Onset within 2-5 minutes; rapid recovery post-procedure

Safety profile	Minimal cardiovascular/respiratory depression, not linked to malignant hyperthermia
Paediatric and adult usability	Well-tolerated across age groups, used in paediatric, obstetric, and general surgery

In assessing clinical efficacy and safety, nitrous oxide proves to be a highly effective adjunct for procedural and surgical sedation, providing reliable patient comfort and positive procedural outcomes. Patient satisfaction scores frequently match or exceed those for alternative agents due to excellent sedation, cooperation, and pain control. The agent's speed of induction-with anaesthesia achieved in 2-5 minutes-and rapid recovery provide operational advantages in busy clinical settings. Its safety profile is robust, as it induces only minimal cardiovascular and respiratory depression and is not correlated with malignant hyperthermia, allowing use in a wide range of patient populations. Moreover, nitrous oxide is well-tolerated across age groups, finding utility in paediatric, obstetric, and general adult anaesthesia practice.

Table 3: Adverse Effects and Complications Associated with Nitrous Oxide

Adverse Effect or Complication	**Description**
Postoperative nausea and vomiting	PONV risk increased, especially in females and lengthy procedures
Air-filled space expansion	May cause bowel rupture, ear trauma, pneumothorax
Vitamin B12 inactivation	Linked to megaloblastic anemia, neuropathy, cognitive deficits
Neurological impairment	Paresthesia, memory loss, motor dysfunction on chronic exposure
Diffusion hypoxia	Occurs post-procedure; requires supplemental O_2
Rare major complications	Laryngospasm, aspiration in exceptional cases
Dizziness and headache	Mild, transient, self-limited in most patients

Despite these positives, nitrous oxide administration carries certain adverse effects and complications. Among these, postoperative nausea and vomiting (PONV) is a significant concern, especially for female patients and those undergoing lengthy procedures. Expansion of air-filled spaces-such as the bowel, middle ear, and pleura-may result in serious complications like rupture, trauma, or pneumothorax. Prolonged or chronic exposure leads to inactivation of vitamin B12, with downstream consequences including megaloblastic anemia, neuropathy, and cognitive deficits. Neurological impairments such as paresthesia, memory loss, and motor dysfunction may occur, while diffusion hypoxia post-procedure mandates supplemental oxygen administration for safety. Rare but serious complications-like laryngospasm and aspiration-can present, although most are mild and self-limited, such as transient dizziness or headache.

Table 4: Environmental Repercussions, Sustainable Approaches, and Mitigation Strategies

Environmental Issue/Strategy	**Description**
Greenhouse gas emissions	N_2O potent GHG (265x CO_2), contributes significantly to climate change
Ozone layer depletion	N_2O removal depletes stratospheric ozone

Low-flow anaesthesia	Reduces wastage, lower fresh gas flow/optimized delivery, decreases emissions
Gas scavenging/capture devices	Technology to mitigate atmospheric discharges of N_2O and other agents
Alternatives to N_2O (TIVA, RA)	Total intravenous anaesthesia, regional anaesthesia minimize environmental impact
Avoid high-impact agents	Reduce/replace N_2O, desflurane with agents of lower GWP (sevoflurane)

Environmental repercussions from nitrous oxide use are significant but actionable. As a potent greenhouse gas, its emission substantially contributes to climate change and, upon removal, depletes stratospheric ozone. Best practice involves the adoption of low-flow anaesthesia protocols to reduce wastage and minimize gas emissions, alongside optimized fresh gas delivery. Implementation of gas scavenging and capture devices in operating theatres can further mitigate atmospheric discharge of nitrous oxide and similar agents. Alternatives such as total intravenous anaesthesia (TIVA) or regional anaesthesia (RA) dramatically decrease environmental impact, while avoiding high-impact agents like nitrous oxide and desflurane in favor of lower global warming potential agents (e.g., sevoflurane) aligns anaesthetic practice with modern sustainability standards.

Discussion:

The clinical and environmental profile of nitrous oxide as an adjuvant in general anaesthesia is extensively documented in recent studies, corroborating the findings summarized in the presented tables. The agent's rapid and effective analgesic property is universally recognized, supporting its use for both major and minor procedures, as highlighted by Gupta N et al.(2022)[5] and Morgan G et al.(2024)[6], who emphasize nitrous oxide's synergistic effect in reducing perioperative pain and improving patient comfort. Its dose-sparing effect is substantiated by Guimarães MC et al.(2021)[7], showing that nitrous oxide, when combined with other agents, minimizes the necessity for higher doses of opioids and volatile anaesthetics, enhancing safety and decreasing adverse reactions. The maintenance of hemodynamic stability, especially among vulnerable patient groups, is supported by large-scale observational data, indicating lowered risk of hypotension and cardiac events.

Furthermore, nitrous oxide's rapid onset and fast recovery are a function of its low blood-gas partition coefficient, a property evident in paediatric, ambulatory, and obstetric cases, with studies reporting average induction times of 2-5 minutes and swift emergence from anaesthesia. However, the considerable environmental impact of nitrous oxide use in healthcare has been the focus of climate studies; it possesses a global warming potential approximately 265 times that of CO_2, with an atmospheric residence time surpassing one century, and substantial ozone depletion potential according to Wang Z et al.(2023)[8]. Major emission sources are operating theatre gas release-often elevated by inefficient scavenging and high-flow methods-alongside broader industrial and agricultural sectors.

Examining efficacy and safety further, comparative meta-analyses and systematic reviews confirm nitrous oxide's high effectiveness for procedural sedation, with patient satisfaction scores comparable to or higher than alternative agents owing to satisfactory sedation, cooperation, and pain control. Patient-centred outcomes demonstrate reliable safety profiles, including minimal cardiovascular and respiratory depression and no links to malignant hyperthermia or severe arrhythmic events. Clinical reports document successful application across paediatric, obstetric, and general surgery, highlighting its versatility and tolerance in various age groups. Biyani G et al.(2022)[9]

Regarding adverse effects, large clinical datasets and case analyses confirm a higher risk of postoperative nausea and vomiting (PONV), especially in females and complex or prolonged cases, supporting the findings of Friedericy HJ et al.(2025)[10] and other risk analyses. Expansion of air-filled spaces remains a key concern; nitrous oxide's physical properties may precipitate bowel rupture, tympanic membrane trauma, or pneumothorax in susceptible patients, prompting cautious selection. Chronic or repeated administration is associated with vitamin B12 inactivation, leading to megaloblastic anemia, neuropathy, and cognitive deficits as reported by several occupational health studies. Diffusion hypoxia is a recognized, though preventable, risk that underscores the need for supplemental oxygen following nitrous oxide administration, while rare complications like laryngospasm and aspiration have been described in isolated case reports. Most side effects-such as dizziness and headache-are mild and self-limited, occurring infrequently in contemporary sedation protocols. Seglenieks R et al.(2022)[11]

Environmental repercussions have driven a shift in practice towards sustainable anaesthesia. Nitrous oxide is a potent greenhouse gas with significant climate impact, and its use is increasingly scrutinized for ozone depletion, prompting active intervention by international regulatory bodies. Adoption of low-flow anaesthesia practices and gas scavenging/capture technology has shown tangible emission reductions in clinical audits and environmental sustainability studies. Alternatives-such as total intravenous anaesthesia (TIVA) and regional anaesthesia-are being strongly promoted to minimize environmental footprint, as is the replacement of high-impact agents like nitrous oxide and desflurane with lower GWP options such as sevoflurane. Kampman JM et al.(2025)[12]

Conclusion:

Nitrous oxide remains a valuable adjuvant in general anaesthesia, offering substantial clinical benefits including rapid and effective analgesia, dose-sparing effects for other anaesthetic agents, hemodynamic stability, and swift induction and recovery. Its broad applicability across age groups and varied surgical contexts underscores its versatility and safety profile. However, the environmental implications of nitrous oxide use are significant, given its potent global warming potential, long atmospheric lifetime, and ozone-depleting properties. These ecological concerns necessitate the adoption of sustainable anaesthetic practices such as low-flow techniques, gas scavenging, and increased use of alternatives like total intravenous anaesthesia and regional anaesthesia. Balancing the clinical advantages with environmental responsibility is imperative to ensure patient safety and minimize healthcare's ecological footprint.

Limitations of Study:

This study is limited by its secondary research design relying solely on published literature, which may introduce selection and publication biases. The heterogeneity of study designs, patient populations, and outcome measures across sources restricts direct quantitative synthesis. Environmental impact assessments vary in methodologies, and real-time clinical emission data specific to individual institutions are often unavailable. Additionally, advances in anaesthetic technology and evolving clinical practice patterns over time may not be fully captured. Further prospective, multicentric clinical and environmental research is warranted to provide higher-quality, generalizable evidence.

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