## **Recreational Nitrous Oxide Use**

Subjects: Health Policy & Services

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Nitrous oxide ( $N_2O$ ) is a dissociative anaesthetic that is sometimes used recreationally. The prevalence of  $N_2O$  use is difficult to quantify but appears to be increasing. Research on  $N_2O$  harms and application of harm reduction strategies are limited. The disparate body of research on recreational nitrous oxide use to inform harm reduction approaches tailored for young people was collated and synthesised.

Keywords: nitrous oxide; N2O; nangs; systematic review; harm reduction; drug use; substance addiction; health risks; psychological harm

#### 1. Introduction

The pleasurable and intoxicating effects of psychoactive substances result in widespread use. However, deaths and injury from psychoactive substance use, particularly among young people, are a global public health problem [1][2]. Harm reduction is an evidence-based approach to reducing adverse consequences from the use of psychoactive substances, recognising eliminating use is not necessarily realistic or desirable [3]. Harm reduction strategies can be applied in different ways. For example, at a policy level such as the funding of supervised drug consumption sites, at a service level such as gender-specific services or information in different languages; and at an individual level with personalised advice according to the drug used and patterns of use. Drug use occurs on a spectrum ranging from occasional experimentation through to using multiple times a day when highly dependent on a substance. Understanding the benefits and problems associated with different drugs and patterns of use is an important part of creating contextually and physiologically relevant harm reduction strategies [4]. Psychoactive substances vary greatly in the way they change mental states and in potential harms including those caused while intoxicated and others because of regular or prolonged use.

Nitrous oxide ( $N_2O$ ) is a dissociative anaesthetic that is sometimes used recreationally. Once inhaled,  $N_2O$  is quickly absorbed into the bloodstream through the lungs; then, it travels rapidly to the brain and the rest of the body. The gas produces a rapid rush of euphoria, heightened consciousness, disassociation, and feelings of floating and excitement, lasting approximately one minute <sup>[5]</sup>.  $N_2O$  is used within the medical and dental fields for anaesthetic, sedation, and pain relief purposes. Beyond its medical use,  $N_2O$  is used as a fuel booster in the racing industry and in the food industry as an aerosol spray propellant <sup>[6]</sup>.

 $N_2O$  is readily available at supermarkets and convenience stores in small metal bulbs used to produce whipped cream. It is cheap to purchase—each bulb costs approximately \$1 AUD. Legalities around the sale of  $N_2O$  vary between countries. For example, there are no legal measures to control the sale of  $N_2O$  in Amsterdam because it is considered relatively safe and moderately used  $^{[Z]}$ . In contrast, Australia's states and territories have made it an offence to supply canisters that hold  $N_2O$  to anyone suspected of using it for recreational purposes. However, it is not an offence to inhale it  $^{[g]}$ . Australian legal systems have difficulty monitoring the selling or purchasing of  $N_2O$  for recreational use  $^{[g]}$ . In the UK, plans to criminalise the use of  $N_2O$  are being discussed because of concerns that use and related harms are growing  $^{[\underline{10}]}$ .

The prevalence of  $N_2O$  use is difficult to quantify but appears to be increasing. Misuse among medical and dental professionals because of easy access and methods of controlled administration has been documented [11]. Media reports regarding  $N_2O$  use are common and are fuelling the UK parliament's concerns about rising prevalence and harms [12]. For example, a 'Google' news search on  $N_2O$  brings up 2790 results of news stories related to  $N_2O$  recreational use between 2018 and 2021. The news stories range from high-profile celebrities being caught on camera using  $N_2O$  to young people dying in situations where  $N_2O$  use is implicated (e.g., [13][14]). There are frequent reports in UK local media about parties and events resulting in  $N_2O$  canisters littering public areas.

Most research reporting  $N_2O$  prevalence has used self-selected samples of people who use drugs such as the Global Drug Survey [15] and in Australia, the National Ecstasy and Related Drugs Reporting System [9]. However, both these sources report year on year increases in use of  $N_2O$  and that young people are the most frequent users. It is important to

note that  $N_2O$  use can be under-reported due to its short-lived effects, inability to be detected through drug testing and because it is often used with other drugs [16]. However, the observed upward trend is concerning because not only is  $N_2O$  easy to access at a low cost and sold in bulk but because of a lack of information for people using the drug [17].

Research on  $N_2O$  harms and patterns of use are limited. Some studies have identified both minor and chronic harms associated with  $N_2O$  use including death by asphyxiation, psychiatric sequelae such as psychosis and physical symptoms, such as burns or frostbitten skin and the depletion of B12 levels from prolonged use of  $N_2O$  resulting in neurological damage [18][19][20][21]. Other harms are related to intoxication: for example, falling over or losing consciousness whilst under the influence of  $N_2O$  [18]. However, patterns, benefits and social factors related to  $N_2O$  use have not been explored in detail. The lack of information readily available to decision-makers, practitioners, educators, and young people makes it difficult to provide contextualised harm reduction strategies to minimise any risks involved in  $N_2O$  use.

### 2. Policy Implications

There was limited inclusion of policy or legislative responses in any published studies. Three studies identified ease of purchase as a factor in increasing prevalence including availability in retail shops  $^{[22]}$  and online  $^{[23]}$  even after the UK's psychoactive substances legislation. In the EU, restrictions on N<sub>2</sub>O purchase were imposed because of health concerns rather than a relationship to drug-related crime  $^{[24]}$ . One study noted the risks of N<sub>2</sub>O use were underestimated in policy and legislative responses to drug use. For example, there was no mention of volatile substance abuse (VSA) including N<sub>2</sub>O, in the UK Government's 2017 Drug Strategy, although VSA caused the same number of deaths as MDMA  $^{[25]}$ . Only one publication suggested harms were overstated  $^{[26]}$ . However, this publication was an opinion piece with a weak rating. Drug Science  $^{[26]}$  concluded that media campaigns are driving concern, and the problem to be addressed by policy or legislation is canisters littering party sites rather than the use of N<sub>2</sub>O.

That conclusion about lack of harms was not shared. Several studies highlighted that the prevalence appears to be increasing worldwide (e.g.,  $\frac{[24][27][28]}{[28]}$ ) and therefore is an issue for policy makers to consider because a small proportion of heavy users are at risk of acute harms  $\frac{[17][29]}{[29]}$ . Nabben  $\frac{[30]}{[29]}$  reported an increase in nitrous oxide-related traffic accidents in the Netherlands, noting that most users believe the drug is safe and has no lasting effects and therefore not understanding the risks of driving during or after N<sub>2</sub>O use.

# 3. Service Delivery—Assessment, Treatment and Education

 $N_2O$  use risks are generally underestimated. For example, the majority (91.6%, n = 99) of those who had heard of  $N_2O$  were not aware of any side effects associated with its use and believed the drug was safe  $\frac{[Z][3O][31]}{[Z][3D][31]}$ . However, Ehirim et al.  $\frac{[31]}{[Z][3D][31]}$  was the only study with a strong quality rating. Formal assessment of  $N_2O$  use rarely occurs in treatment services. When identified, reports of  $N_2O$  misuse do not fit the criteria for substance dependence and therefore may be underestimated because only two to three DSM-5 criteria are identified during assessment. However, Criterion 1 (Taking the substance in larger amounts or over a longer period than was intended) is positive in 98% of cases included in the review by  $\frac{[32]}{[32]}$ . The capacity of services to respond to people who use  $N_2O$  is complicated by the lack of a formal screening tool and  $N_2O$  use presenting with other drug use  $\frac{[33]}{[25]}$ . Furthermore, one study suggests people who inhale volatile substances including  $N_2O$  rarely access treatment services  $\frac{[25]}{[25]}$ . Leigh and Maclean  $\frac{[25]}{[25]}$  suggest mental health services might be first point of contact for vulnerable solvent users rather than drug and alcohol services.

Information for young people or clinicians about  $N_2O$  harms appears to be limited or unavailable. Three studies noted  $N_2O$  is not included in drug education programs  $^{[\mathcal{I}][22][34]}$ , and another high-quality study reported young people believe more information/education is needed to raise awareness of harms  $^{[31]}$ . The majority of respondents in that study (60%, n = 86) chose the scale value of 10 (extremely important) as to how important it is to educate young people about the effects of  $N_2O$   $^{[31]}$ . In relation to where to intervene, one study suggested that because  $N_2O$  is most often consumed via balloons at festivals and in clubs, this is the best type of intervention site  $^{[29]}$ . Another study recommended using influencers in media campaigns with the aim to decrease the risks of heavy nitrous oxide use and improve treatment access  $^{[30]}$ . Because driving is impaired for up to 30 min after exposure to  $N_2O$ , information for  $N_2O$  users about risks of traffic accidents was recommended  $^{[\mathcal{I}]}$ .

# 4. Individuals

Recreational nitrous oxide use is popular with young people. In one study, most respondents (77.1%, n = 108) had heard of N<sub>2</sub>O and 27.9% (n = 39) had taken N<sub>2</sub>O in the past 12 months  $\frac{[29]}{N_2}$ . Three studies  $\frac{[22][31][34]}{N_2}$  found males were more likely

to use  $N_2O$  than females. For example,  $N_2O$  was more popular among males at 39.0% (n = 16) compared to females at 24.7% (n = 23) [31], and in another survey, 15% of men and 9% of women in NZ had used  $N_2O$  [34]. However, no statistically significant association between age and  $N_2O$  use was found [31]. That is,  $N_2O$  is not exclusively a young person's drug. Leigh and Maclean [25] identified an increasing prevalence of deaths from volatile substances including  $N_2O$  and that the age profile of those dying is older than the typical user profile [25]. One high-quality study investigating substance use disorders found that while most users use infrequently, and their use is not associated with significant harm,  $N_2O$  was 'overused' by men, adolescents and young adults [32]. Another study confirmed that frequent  $N_2O$  use is associated with hallucinations and confusion and persistent numbness and accidental injury [29]. The quantity associated with problematic  $N_2O$  use varies. Studies identified 300 canisters per week [23], 40–60 per day [35] and 50–100 bulbs taken per session by heavy users to remain intoxicated [1]. Worryingly, regular users appear to be increasing the amount they use both in days of use per month and amount used at each session [9][27]. However, patterns of  $N_2O$  use have not been thoroughly investigated nor have the benefits that prompt use.

The case reports found  $N_2O$  use was typically overlooked, and that people deny using it  $\frac{[36]}{3}$ . In some cases, serious degeneration and limb paralysis is observed before  $N_2O$  problems are identified  $\frac{[37]}{3}$ , suggesting scope for earlier identification and intervention. Common presentations indicating problematic  $N_2O$  use include muscle weakness, stumbling and spinal cord problems  $\frac{[38][39]}{3}$ . One person was in a wheelchair for a year before the problem of  $N_2O$  use was diagnosed  $\frac{[37]}{3}$ . Ng  $\frac{[34]}{3}$  suggested that with an increasing proportion of vegetarianism, many young people have a higher risk of nutritional deficiencies, further increasing their risk of subacute combined degeneration of the spinal cord. Other case studies reported strokes  $\frac{[40]}{3}$  and thrombosis  $\frac{[41]}{3}$ . Neuropsychiatric symptoms were also identified  $\frac{[36]}{3}$ . One case study made a connection to psychosis and schizophrenia, concluding that  $N_2O$  use may be a causative factor in the development of psychotic symptoms  $\frac{[42]}{3}$ . However, this was only one study and a speculative finding.

Addressing  $N_2O$  harms for individuals currently relies on medical intervention particularly B12 injections. There was one report of an individual who injected themselves with B12 on the advice of a friend, which resolved their symptoms [43]. However, one-third or 29% of people with  $N_2O$  problems will not have B12 deficiency [44]. The most significant limitation of the case reports is that the outcome of medical interventions is not reported. The follow-up of individuals in case reports is rare and was identified as difficult when people do not return for check-ups [37]. Therefore, ongoing symptoms of misuse and success of interventions is unknown.

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