



# Nitrous Oxide (N<sub>2</sub>O)

## A briefing for professionals

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**1. Background to current situation:** Nitrous oxide (N<sub>2</sub>O for short) is a colourless, slightly sweet smelling, non-flammable gas, first discovered in 1772. N<sub>2</sub>O became a popular recreational drug because of its euphoric effects and much later came to be widely used in dentistry and during childbirth for its mild anaesthetic and analgesic effects (Gilman, 2019; Ruston, 2022).

The contemporary resurgence in recreational use of N<sub>2</sub>O has predominantly revolved around the sale of single-use finger-length steel cartridges containing 8 grams of pressurised gas, disingenuously sold from shops and websites for making whipped cream (fig 1). The recent availability and popularity of much larger 600+ gram tanks containing over 80 times the amount of N<sub>2</sub>O, along with reports of an increase in neurological and other problems are currently causing concern.

**2. Common names:** Nitrous oxide is commonly known as *Laughing Gas*. When mixed 50/50 with air and used medically (*Etonox*) it is commonly known as *Gas and Air*. When used as an additive in drag racing engines it is commonly known as *NOS (Nitrous Oxide System)*. *NOS* or *Noz* are also nicknames for it as a street drug, although it is also known by other street names such as *balloons* and (mainly by journalists) as *Hippy Crack*.

**3. Pharmacology:** N<sub>2</sub>O is classed as a dissociative, putting it in the same drug class as ketamine (Adley/ DrugWatch, 2021). Despite its long-term medical use, the pharmacology of N<sub>2</sub>O is not fully understood. It has been suggested that *opioid receptors* are responsible for its analgesic properties (Savage, Ma, 2014) while its dissociative effects are probably caused by preventing the normal action of the *NMDA receptor* (NEPTUNE, 2015), the anti-anxiety effect is produced by the blocking *GABA<sub>A</sub> receptors*, while euphoria felt when the drug is taken is due to the release of *dopamine*. N<sub>2</sub>O's effects occur at lower concentrations and may be produced by alterations in brain blood flow similar to those produced when sniffing poppers (Drug Science, 2019).

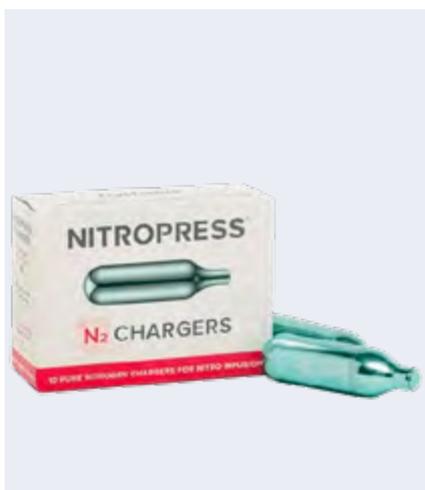
**4. Effects:** A single inhalation will result in effects starting almost immediately, peaking about 10-30 seconds after inhalation and then rapidly diminishing. It produces a euphoric, pleasant, joyful, empathogenic and sometimes hallucinogenic effect, and causes a deep 'silly' voice. If the dose is repeated, effects reach a plateau about 30-60 seconds after the first breath. Whilst the user often

feels back to 'normal' within about 1-5 minutes after the last inhalation, some users report that effects such as a sense of well-being can be felt for up to 30 minutes after last use. Short term temporary side effects include pins and needles, numbness, dizziness, dissociation, disorientation, loss of balance, impaired memory and cognition and weakness in the legs (van Amsterdam, Nabben, & van den Brink, 2015; The Vaults of EROWID, 2022; PsychonautWiki, 2022; NEPTUNE, 2015).

**4.1 N<sub>2</sub>O use with other drugs:** Anecdotal reports suggest an increase in the effects of N<sub>2</sub>O when combined with alcohol, and it may briefly enhance the effects of psychedelic drugs like LSD and ketamine. When used at the same time as stimulant drugs it may have a greater effect on blood pressure and heart rate. As it is not metabolised by the liver, the potential for drug interactions with other agents, including antiretrovirals, is very low (NEPTUNE, 2015). Anecdotal reports suggest when combined with alcohol, GHB/GBL or opioids there is greater loss of co-ordination and balance and increased sedation leading to unexpected loss of consciousness at high doses (PsychonautWiki, 2022).

**5. Methods of recreational N<sub>2</sub>O use:** In order to produce its effects N<sub>2</sub>O must be inhaled. Serious damage can be done to the lungs by inhaling any pressurised gas directly from cylinders or the nozzle of a whipped cream dispenser, added to that when discharged N<sub>2</sub>O is freezing cold and can cause ice burns (LiPuma, Wellman, & Stern, 1982). Inhaling through a mask, respirator, via a bag over the head or in an enclosed space such as a car, runs the risk of asphyxia as the N<sub>2</sub>O displaces oxygen in a closed space (Wagner, Clark, Wesche, Doedens, & Lloyd, 1992). Users will drop a balloon filled with N<sub>2</sub>O if they are getting too **hypoxic** (a deficiency of oxygen) or lose consciousness, so inhaling from balloons is the least risky way of using N<sub>2</sub>O for recreational purposes. Balloons come in both standard and extra-large sizes.

**6. Small chargers and larger tanks:** The single-use finger-length steel whipped cream chargers containing 8 grams of N<sub>2</sub>O, are known as *whippets*, *chargers* or *nangs* etc (fig 1). An 8g charger is inserted into a device called a *cracker* (fig 2) and a balloon is attached and filled with N<sub>2</sub>O. Alternatively, an 8g charger is fitted into a whipped cream dispenser and when the lever is pressed the balloon fills with N<sub>2</sub>O [fig 3] (The Vaults of EROWID, 2022; Drug Science, 2019).



(Fig 1). 8g chargers or 'Whippets'



(Fig 2). An 8g charger is fitted inside a device called a 'Cracker'



(Fig 3). An 8g charger can also be used with a whipped cream dispenser

**6.1 Larger sized tanks:** Although the UK recreational N<sub>2</sub>O market has been dominated by 8g chargers (*whippets*), the market appears to have recently changed with the advent and wide-spread availability from mainstream and specialist websites, social media vendors and other retail outlets of much larger 600+ gram tanks. According to a recent VICE article the two largest companies supplying the UK are Dutch and were formed in 2018/2019 (Hiller, 2022). It is unclear exactly when this market change first occurred in the UK, but a recent Dutch study indicates that the large tanks first appeared in Amsterdam around 2017/2018 (Nabben, Weijs, & van Amsterdam, 2021).

The larger 640g sized tanks (fig 4) come with a small nozzle for directly filling the balloon (fig 5). Even larger tanks containing 2,000 grams (equal to 250 x 8g chargers) are now also being advertised [fig 6] and are commonly used by heavy users in Holland (Creme Deluxe (a), 2022; Nabben, Weijs, & van Amsterdam, 2021). There is currently no UK data on the volume of N<sub>2</sub>O sales for catering/recreational use or for the market share of larger tanks.



(fig 4) 640g tanks



(fig 5) A small release nozzle



(fig 6) 2,000g tank

**7. Prevalence:** N<sub>2</sub>O use by young adults in England in Wales was first recorded in 2013-14 when 7.6% of those aged 16-24 reported using the drug in the past year. Prevalence peaked at 9.0% in 2016-2017, and despite N<sub>2</sub>O's inclusion in the *Psychoactive Substances Act* (PSA), estimated use of N<sub>2</sub>O by 16–24-year-olds was 8.7% in the year ending March 2020<sup>1</sup>, making it the second most prevalent drug after cannabis (Home Office, 2018; ONS, 2020).

Despite media coverage of discarded 8g N<sub>2</sub>O chargers leading to a short-lived moral panic and a parliamentary debate (Hansard, 2020), there was little evidence of an increase in N<sub>2</sub>O use during lockdown. The Release online survey found just 1 person out of 2,621 had used N<sub>2</sub>O during the lockdown period<sup>2</sup> (Release, 2021), while the GM-TRENDS survey of 500 young people in contact

<sup>1</sup> The Crime Survey for England and Wales (CSEW) was suspended during lockdown and has not reported since.

<sup>2</sup> Note: as the researchers point out, this may have reflected respondents not considered nitrous oxide a drug and/or the question not being directly asked in the survey.

with treatment services in Greater Manchester found N<sub>2</sub>O use decreased from 4.1% pre-lockdown to 2.1% post-lockdown (MMU/GMCA, 2021). In 2021 the use of N<sub>2</sub>O was reported by 1.8% of pupils aged 11-15 years in England in the last year, down considerably from 4.1% in 2018 (ONS (a), 2022). However, the current (as yet unpublished) 2022 GM-TRENDS survey of young people in contact with services suggests that in Greater Manchester there has been a notable post-lockdown rise in N<sub>2</sub>O use: increasing from 2.1% (2021) to 14.5% of young people surveyed in 2022 (this equates to 52 young people). Almost a quarter (23.1%) of these young people reported using for the first time during the past year (MMU/GMCA, 2022).

**8. Prices:** According to advertising by one supplier the 640g of N<sub>2</sub>O in a large tank (equal to 80 single 8g chargers) is sold at a price equivalent to 50 x 8g chargers, representing a cost saving (Creme-deluxe (b), 2022). Prices of large tanks vary and they are also sold in bulk at a discount. Prices for one of the leading brands ‘Smart Whip’ on the UK supplier ‘Smart Chef Store’ website (based in Bolton) are below (Smart Chef Store, 2022). As with any heavy drug habit, cost and debt are likely to be an issue and debt problems have been reported in Dutch research with heavy users (Nabben, Weijts, & van Amsterdam, 2021).

Brand and size	Price	Total of N <sub>2</sub> O	Price per gram of N <sub>2</sub> O
Smartwhip 8g x 24 pack	£10.99	192g	5.8p per g
Smartwhip 8g x 120 pack	£50.99	960g	4.2p per g
Smartwhip 640g x 1 pack	£29.99	640g	4.6p per g
Smartwhip 640g x 6 pack plus free gift of 24 x 8g pack	£139.99	3,840g + 192g <b>Total = 4,032g</b>	3.5p per g

**9. Risk and harms of infrequent recreational use:** It is commonly thought that the vast majority of those people who use N<sub>2</sub>O are infrequent, episodic users. Infrequent use of lower doses of N<sub>2</sub>O is considered lower risk compared to that of other illicit substances, with few short-term adverse effects other than headaches (NEPTUNE, 2015; ACMD, 2015; Winstock & Ferris, 2020). A recent paper compared N<sub>2</sub>O to 20 well know drugs, with N<sub>2</sub>O scoring as the second least harmful drug. However, the authors acknowledge that in their model:

*“Drugs with low scores may on occasion cause significant harm to a small minority of users, but when considering policy and regulation the factor that carries the most weight should be harm on a population-based level” (Ferreira, et al., 2022).*

Most commonly, harms from N<sub>2</sub>O use are likely to result from falling over and accidental injury. However, accidental injury is dose related (Kaar, et al., 2016), so if the widespread use of larger tanks has led or leads to an increase in the amount used in a session, a corresponding increase in accidental injury may occur. There is no available data on falling over or accidental injury as a result of N<sub>2</sub>O use.

**9.1. Accidental asphyxiation as a result of method of use:** When N<sub>2</sub>O is inhaled it displaces the air in the lungs, thus temporarily preventing oxygen from entering the bloodstream and causing the side effects described in section 4. Deaths associated with N<sub>2</sub>O use are usually a result of its method of use and thought due to accidental asphyxiation often resulting in **arrhythmias** (abnormal heart beat) and **seizures**. Although N<sub>2</sub>O does not depress the respiratory drive significantly, the normal physiological response to **hypoxia** (*deficiency of oxygen*) is blunted when N<sub>2</sub>O is taken. Deaths are often associated with bags being put over the head in order to facilitate inhalation, or inhalation in cars, as N<sub>2</sub>O displaces oxygen in a closed space (NEPTUNE, 2015; Winstock & Ferris, 2020; Wagner, Clark, Wesche, Doedens, & Lloyd, 1992; Knuf & Maani, 2022).

**9.2. Fatalities:** There were 56 N<sub>2</sub>O deaths registered in England and Wales between 2001 and 2020; 45 of those having been registered since 2010 [4½ per year between 2010 to 2020] (ONS (b), 2022).

**9.3. Arrhythmia:** People with heart conditions or abnormal blood pressure may be at higher risk of harm as the drop in oxygen levels caused by inhaling N<sub>2</sub>O raises the heart rate and can cause arrhythmias. This could lead to cardiac arrests in susceptible people (Drug Science, 2019).

**9.4. Ice burns:** N<sub>2</sub>O canisters become ice cold as the gas is discharged and may cause ice burns when coming into contact with skin. Sometimes these ice burns may not be noticed due to the anaesthetic effect of N<sub>2</sub>O. Some users get blisters in the mouth, and on the tongue, arms and legs (Nabben, Weijs, & van Amsterdam, 2021). Some of these wounds are very deep and can require multiple surgeries and result in scars. Burns can look superficial, but can rapidly develop into third-degree burn wounds (Quax, Van Der Steenhoven, Bronkhorst, & Emmink, 2022; Stone, Roberts, & Anwar, 2021). There are recent local anecdotal reports suggesting the valves of larger tanks can burst causing gas to leak and ice burn injury (MMU/GMCA, 2022). *The British Burn Association* has reported an increase in deep cold burns following the use of N<sub>2</sub>O canisters held between the legs, however no detail or additional data is available (British Burn Association, 2022). For minor ice burns it is recommended to immerse in warm water, but as more serious burns can appear superficial, medical assistance or advice should be sought by dialling **NHS 111** (NHS, 2022).

**10. Amount used per session and frequency of use:** Although the practice of putting two 8g chargers into a single balloon (known as *double ballooning*) is well known, the introduction of 640g tanks means it is far harder to regulate the amount in an individual balloon, particularly with the introduction of XL balloons, which are even sold as a package with N<sub>2</sub>O *crackers* on mainstream websites e.g Amazon (Amazon, 2022). 8g chargers are usually purchased in packs of 10 or more and multiple doses are often used in a session. Although data is limited and the typical amount reportedly used in a single session varies, it is generally thought most people use N<sub>2</sub>O less than 10 times per year with less than 10 balloons per session. Whilst it has long been acknowledged that there is a sub-population of N<sub>2</sub>O users who are heavy users, there is a paucity of information on the percentage of the overall population of N<sub>2</sub>O users frequently using very large amounts. One survey showed 14% of respondents using N<sub>2</sub>O more than 100 times and 17% using more than 25 whippets in an average session (van Amsterdam, Nabben, & van den Brink, 2015; NEPTUNE, 2015; Ferreira, et al., 2022).

Although there are no quantitative data or large-scale studies, according to a Dutch paper (which although small scale is one of the few ethnographic studies of heavy use), the availability of larger tanks has led to an increase in the amount and frequency of N<sub>2</sub>O use.

*“The advent of large kilo tanks, provided by ambitious 24/7 delivery services, has been a dramatic game-changer. From that moment on, due to easier tapping of the gas, the rapidly increasing habituation, and the possibility to inhale nitrous oxide non-stop, repeated dosing seems unlimited.”* (Nabben, Weijs, & van Amsterdam, 2021, page 13)

**10.1. Amounts used by chronic, heavy users:** There is no available data on the prevalence of or even a definition of what constitutes heavy or chronic use. *Marsden et al* suggest that (from a point of view of diagnosis of chronic toxicity) a rough guide is the daily use of 100 x 8g cartridges for at least a month (Marsden, Sharma, & Rotella, 2022). This equates to daily use of 800g of N<sub>2</sub>O, or just under one and a half 640g tanks per day for a sustained period. One medical case study reported the use of 400 x 8g cartridges of N<sub>2</sub>O per day (Ickowicz, Brar, & Nolan, 2020), however by their nature medical case studies report on extremes or unusual cases. The Dutch research into heavy street users, referenced heavily in this briefing, suggests that chronic use inevitably becomes an isolated solo activity, with binges on 2-3 x 2,000g tanks at least 3 times a week, with one reportedly using 8 x 2,000g tanks in a day-long session.

*“A considerable group of unsuspecting users gradually inhale themselves longer and deeper into an unknown world without a bottom, ceiling, and perspective. Some of them increasingly get lost in hypnotically repetitive and long-lasting nitrous oxide sessions starting from once a week, to a few times a week to sometimes every day. Compared to other substances, nitrous oxide is different in that it can be used for hours and sometimes even days (binge) and the user is not aware when he/she has to stop”.* (Nabben, Weijs, & van Amsterdam, 2021, page 13)

**11. Dependency and chronic, heavy use:** There is no evidence of significant withdrawal symptoms apart from cravings to use more, and little evidence<sup>3</sup> of physical dependence to N<sub>2</sub>O. However there is anecdotal evidence of psychological dependence and tolerance developing with heavy use, and a subpopulation of heavy users *‘who may be using in a dependent pattern’* (van Amsterdam, Nabben, & van den Brink, 2015; Malamed & Clark, 2003; NEPTUNE, 2015; Kaar, et al., 2016). Anecdotal reports from treatment services rarely mention heavy N<sub>2</sub>O use and no adults or young people in treatment during 2020-21 were recorded as having a problem<sup>4</sup> with N<sub>2</sub>O (OHID, 2021; OHID, 2022). However, if N<sub>2</sub>O use is taking place within populations where its use is taboo, access to treatment may be limited, and treatment numbers may not accurately reflect problems associated with the drug.

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<sup>3</sup> One study of mice claimed that chronic exposure results in physical dependence which resembles alcohol and not opiate dependence (Milne, Cervenko, & Jhamandas, 1981), another 2020 study suggested the ‘opiate like effects’ of N<sub>2</sub>O ‘addiction’ can be treated with the opiate agonist naltrexone (Ickowicz, Brar, & Nolan, 2020).

<sup>4</sup> When young people enter treatment, they can record up to 3 substances that they have a problem with. The absence of N<sub>2</sub>O mentions may be a result of the numbers being so low that they were recorded under ‘other/NPS’ and/or they did not see their use of N<sub>2</sub>O as a problem.

**12. Acute intoxication:** The toxic dose of N<sub>2</sub>O is not established. Advice on occupational exposure limits ranges from 25 to 100 parts per million. This is thought to be far below the level of common heavy use, however may provide an indication of the level at which harms can occur in recreational users (NEPTUNE, 2015). According to NEPTUNE the evidence of acute harms associated with recreational use is limited, consisting mainly of case reports, with occasional experimental studies into acute effects. NEPTUNE provides a summary chart [below] (NEPTUNE, 2015).

Features of acute intoxication with nitrous oxide (NEPTUNE, 2015)		Simple definition of medical terms
<b>Respiratory effects</b>	Asphyxia and Hypoxia	<i>Hypoxia</i> = a term used to indicate a deficiency of oxygen. <i>Asphyxia</i> refers to the physiological results of hypoxia.
<b>Neurological and psychiatric effects</b>	CNS depression Convulsions Psychiatric symptoms Headache Polyneuropathy Myeloneuropathy Dizziness, Excitement, Paraesthesia Paralysis Psychosis	<i>Myeloneuropathy</i> = damage of the tracts of the spinal cord and peripheral nerves in the lower limbs. <i>Polyneuropathy</i> = the simultaneous malfunction of peripheral nerves throughout the body. <i>Paraesthesia</i> refers to a burning or prickling, tingling sensation or numbness that is usually felt in the hands, arms, legs, or feet, but can also occur in other parts of the body.
<b>Cardiovascular effects</b>	Hypertension Cardiac dysrhythmias Megaloblastic anaemia Leukopenia Anoxia	<i>Hypertension</i> = raised blood pressure. <i>Cardiac dysrhythmias</i> = irregular heartbeats. <i>Megaloblastic anaemia</i> = a type of vitamin B12 deficiency. <i>Leukopenia</i> = lower than normal white blood cells. <i>Anoxia</i> = when your body or brain completely loses its oxygen supply. Anoxia is usually a result of hypoxia
<b>Metabolic features</b>	Thrombocytopenia	<i>Thrombocytopenia</i> = deficiency of platelets in the blood. This causes bleeding into the tissues, bruising, and slow blood clotting after injury.
<b>Gastrointestinal symptoms</b>	Nausea and vomiting	

**12.1 B12 deficiency and neuropathic damage:** The toxicity of N<sub>2</sub>O is based on its interaction with **vitamin B12** and was first reported in 1968 (Banks, Henderson, & Pratt, 1968). The inactivation of vitamin B12 as a result of heavy N<sub>2</sub>O use manifests as the respiratory, psychiatric, cardiovascular, metabolic and neurological features outlined in the chart above. N<sub>2</sub>O-induced damage to the nerves (**neuropathy**) was first recognized in the 1970s (Layzer, Fishman, & Schafer, 1978). While infrequent, episodic users are not at risk, a minority of heavy users are at dose-dependent risk of developing these serious neurological consequences (Marsden, Sharma, & Rotella, 2022; Winstock & Ferris, 2020). Vegans, dependent drinkers and patients with pernicious anaemia are more susceptible to B12 deficiency (Society of Hospital Medicine, 2015, Fragasso, Mannarella, Ciancio, & Sacco, 2009).

N<sub>2</sub>O-induced vitamin B12 deficiency can manifest as **myeloneuropathy**. *Myeloneuropathy* is characterized by simultaneous damage of the tracts of the spinal cord and peripheral nerves in the lower limbs. The earliest symptoms are usually the presence of tingling or numbness, in hands and legs (starting in fingers and toes, usually on both sides at same time), skin crawling, or itching, numbness in hands and legs and later staggering uncoordinated walk, lower limb weakness, muscles stiffen or tighten, overactive or overresponsive bodily reflexes such as twitching etc. Standard treatment is cessation of N<sub>2</sub>O use, along with vitamin B12 supplementation. This can result in improvement and, in some cases, complete resolution of symptoms occurring, although this can take months (Campdesuner, Teklie, Alkayali, Pierce, & George, 2022; NEPTUNE, 2015; Eftimova, Sholjakova, Mirakovski, & Hadzi-Nikolova, 2017; Nabben, Weijs, & van Amsterdam, 2021).

It has been suggested in some online user forums that taking vitamin B12 supplements may mitigate against B12 deficiency for those using large amounts of N<sub>2</sub>O (reddit forum, 2020). There is no evidence that taking over the counter oral supplements works. One paper suggests this is futile as B12 has very low oral absorption so severely deficient people need B12 intramuscular injections (Blair, Tremonti, Edwards, Haber, & Halmagyi, 2019).

**12.2 Reproductive risks:** Before health exposure limits were introduced, evidence from professionals working in dental and midwifery practices exposed to high levels of N<sub>2</sub>O, indicated reproduction effects that included congenital anomalies, spontaneous abortion and reduced fertility rates in females. Recreational users of N<sub>2</sub>O, may repeatedly expose themselves to (very) high doses of N<sub>2</sub>O, greatly exceeding the health exposure limits. There is therefore a risk, especially in heavy N<sub>2</sub>O users, pregnant users or those who intend to become pregnant (van Amsterdam & van den Brink, 2022).

**12.3 Psychiatric symptoms:** Current literature suggests that psychosis associated with N<sub>2</sub>O use is transient and resolves upon cessation and treatment of vitamin B12 deficiency. However, in a recent review approximately half of the cases that presented with N<sub>2</sub>O-induced psychiatric complaints did not show neurological symptoms, and their vitamin B12 concentration was often within the hospital's reference range (Paulus, Wijnhoven, Maessen, Blankensteijn, & van der Heyden, 2021; Roberts, Farahmand, & Wolkin, 2020).

**12.4. Clinical guidelines:** UK clinical guidelines were produced by *NEPTUNE* in 2015 and current advice is available from *TOXBASE* for medical professionals (NEPTUNE, 2015). A recent Australian review paper suggested a guide for diagnosis of chronic N<sub>2</sub>O toxicity (see chart below):

<b>A suggested approach for the diagnosis of chronic nitrous oxide toxicity (Australia)</b> (Marsden, Sharma, & Rotella, 2022).	
<b>Clinical</b>	<ul style="list-style-type: none"> <li>• Young patient (usually in 20s).</li> <li>• Reported use of &gt;100 bulbs (8g cartridges) per day.</li> <li>• At least months of use.</li> <li>• Presence of neurological disturbances such as sensory changes and gait ataxia weakness.</li> </ul>
<b>Biochemical</b>	<ul style="list-style-type: none"> <li>• Elevated serum homocysteine and/or methylmalonic acid prior to commencement of any treatment.</li> <li>• Serum total and active Vitamin B12 may be normal.</li> </ul>
<b>Imaging and other tests</b>	<ul style="list-style-type: none"> <li>• Dorsal column abnormalities in cervical spine other segments (diagnostic).</li> <li>• Peripheral neuropathy on nerve conduction studies (supportive).</li> </ul>

Note: "A suggested approach to diagnosis is offered but requires validation in prospective studies. Further research exploring the efficacy of B12 and methionine therapy is required to refine management" (Marsden, Sharma, & Rotella, 2022).

**12.5. Prevalence of acute intoxication presentations:** Although there is a lack of available data, there is enough anecdotal evidence to suggest there has been a rise in cases seen by hospitals. Some UK neurologists have claimed that the common availability of larger tanks have been responsible for the ‘*epidemic*’ of young people seen with neurological injuries (The Independent, 2022). Doctor David Nicholl, a consultant neurologist at Queen Elizabeth Hospital in Birmingham, has stated that he and his colleagues are seeing ‘*large numbers of young people*’ coming into hospital after taking N<sub>2</sub>O (Sky News, 2022; Hussain, 2022). However, as no data is available from the NHS on the number of incidents involving chronic use of N<sub>2</sub>O, quite what ‘*large numbers*’ or ‘*epidemic*’ equates to is unclear.

Local data is being sought by the current *GM-TRENDS* study. A number of local hospital staff have anecdotally reported a rise in serious incidents involving N<sub>2</sub>O, although they could not provide data. One NHS service covering 4 local authority areas of Greater Manchester, who see referrals from young people admitted to hospital for alcohol and drug related incidents, reported 2 recent incidents, where none had been seen the previous year (MMU/GMCA, 2022).

The Dutch Poisons service reported an annual average of 6 poisonings per year between 2010-2015, which rose to 144 in 2020. They associated this increase with a shift from heavy and frequent use of 8g cartridges to large canisters and cylinders (van Riel, et al., 2022). According to the 2020-2021 UK *National Poisons Information Service* (NPIS) annual report there was an 3,600% increase in telephone enquiries about N<sub>2</sub>O, equating to an increase from 1 to 37 calls (NPIS, 2021). An article in *The Independent* stated that the (as yet unpublished) 2021/2022 report shows a further 257% increase (The Independent, 2022).

**13. Driving:** Although N<sub>2</sub>O is very short-acting it affects coordination and awareness and reduces psychomotor skills, thereby increasing the likelihood of road traffic accidents (NEPTUNE, 2015; Moyes, Cleaton-Jones, & Lelliot, 1979). Unlike alcohol there are no national statistics on road traffic deaths involving drugs. However, experimental data indicates that in Great Britain in 2019 ‘*Drugs of abuse*’ were detected in 117 deceased drivers (compared to 143 involving alcohol). There is no breakdown of the types of ‘*Drugs of abuse*’ involved (Dept for Transport, 2022). Reports from Dutch police indicate that between 2019-2021, 63 people were killed in road traffic accidents involving N<sub>2</sub>O (NL Times, 2021). Dutch research describes a street culture of risk taking and driving while inhaling N<sub>2</sub>O balloons:

*“... (internet) clips of artists surrounded by hip-swaying girls with balloons and cool guys who give extra throttle with balloons behind the wheel are often shared by (street) youngsters... You do not want to perform worse than others and you surpass the others with even more balloons. As such, the risks are sought out rather than avoided”.* (Nabben, Weijs, & van Amsterdam, 2021, page 14)

There have been a number of local media reports of inhaling balloons while in or driving cars, and of N<sub>2</sub>O-related road traffic accidents (MEN (a), 2022; MEN (b), 2022). Data from City Centre Manchester indicates that there have been 71 reported incidents in 2021/2022 of drivers inhaling from balloons (sometimes while in the act of driving), an increase from 31 reported incidents during 2020/2021 (GMP, October 2022).

**14. Aggression and violence:** The association of N<sub>2</sub>O with aggression and violence is not new. A wood engraving from 1840 entitled 'An Exhibition of the Laughing Gas' states:

*"It is named Laughing Gas on account of the very exhilarating emotions produced in those who respire it for a short time; laughing, dancing, jumping, acting, reciting and (last but not least) fighting are amongst the prominent effects displayed by persons under its influence."* (Ruston, 2022)



Although there are reports of *"high tension, quarrels and sometimes violence between users or toward friends, partners and parents"* among heavy users (Nabben, Weijs, & van Amsterdam, 2021, p. 10), this is commonly reported among people who use commonly-used drugs such as alcohol and cocaine and is nearly always reported when new drugs or drug trends appear. Given the large numbers of people who use N<sub>2</sub>O, there is little evidence to suggest that the vast majority are likely to become aggressive or violent, any more than they are likely to start *acting or reciting*. However, researchers involved in fieldwork cautioned against disturbing people who are under the influence of the drug, describing them as being *"in their self-created time capsule... a rough disturbance can lead to aggressive behaviour"* (Nabben, Weijs, & van Amsterdam, 2021, p. 10).

**15. Litter:** Abandoned nests of 8g chargers are a common site on UK streets, although as with many N<sub>2</sub>O related issues, there is no available national prevalence data. One recycling, and waste management company claims to have seen *"...an extraordinary increase in the number of gas canisters being thrown out as general waste"* (Vaclavova, 2022).

N<sub>2</sub>O depletes the ozone layer, and while it may have a significant impact on global warming, this overwhelmingly involves its use in agriculture (Shankman, 2019). Although non-flammable, N<sub>2</sub>O will support combustion to the same extent as oxygen does. Used chargers and tanks should never be thrown into fires as they may explode (Knuf & Maani, 2022). Smaller 8g chargers, and a more recent trend for larger tanks, are often put into mixed recycling bins [often your neighbours] (MEN (c), 2022) but may explode when going through an 'Energy from Waste facility' [EfW] (Vaclavova, 2022). Recycling advice is often mixed and confusing. Although not all recycling centres accept smaller 8g chargers, they are recyclable and some specialist recycling centres (in theory) will accept them. Larger tanks should be placed with the other large gas cylinders at local recycling centres (Recycle for Greater Manchester, 2020).

Several local authorities have tried to tackle the N<sub>2</sub>O anti-social/litter issue with initiatives involving education, public reporting, street cleaning, enforcement and dispersal (Middlesbrough Council, 2022), but there are no available evaluations for the effectiveness of this approach.

**16. N<sub>2</sub>O and the law:** N<sub>2</sub>O was included within the *Psychoactive Substances Act (PSA)* in 2016. It can be sold legally, for instance as a propellant in whipped cream, but is an offence under the PSA to supply N<sub>2</sub>O for the purpose of intoxication. Possession of N<sub>2</sub>O is not an offence unless in a custodial institution (Home Office, 2018). N<sub>2</sub>O is legally available in large tanks designed for modified car engines, but this is not suitable for human use because it contains sulphur dioxide and other impurities (The Vaults of EROWID, 2022). Large medical grade hospital tanks are classed as medicinal products, and supply or administration without *MHRA* authorization is a criminal offence under the *Human Medicines Regulations 2012* (UK Statutory Instruments, 2012). The 600g+ tanks are not classed as medicinal products and they can be legally sold for ‘*catering purposes*’, however they are covered by the PSA if sold for the purpose of intoxication (Fortson, 2022).

On September 3rd 2021, the then Home Secretary asked the *ACMD* to review the legal status of N<sub>2</sub>O, in light of “...concern, in particular, over the long-term effects caused by the inactivation of vitamin B12” (*ACMD*, 2021). In 2015 the *ACMD* had concluded that N<sub>2</sub>O was not sufficiently harmful to warrant it becoming a controlled drug (*ACMD*, 2015). Quite how the *ACMD* will recommend resolving the N<sub>2</sub>O legal loophole and if this will be any more successful than the PSA, which appears to have had no impact on prevalence (Home Office, 2018), is presently unknown. *The British Compressed Gases Association* have recently called for a ban on all direct consumer sales (*BCGA*, 2022).

**16.1 Offences:** During 2021 the number of N<sub>2</sub>O seizures increased from 256 to 373 (GMP made 39 seizures). The quantity of N<sub>2</sub>O seized by police forces was 30% higher and Border Forces 693% higher [a total of 2.05 million doses] (Home Office, 2022). Data from city centre Manchester suggests reports of people using N<sub>2</sub>O in public spaces increased to 23 (2021/2022) from 16 incidents the previous year. There were 13 offences recorded in relation to N<sub>2</sub>O supply in the City Centre [2 offences of supply, and 11 offences of possession with intent to supply] (GMP, October 2022).

**17. Harm reduction advice:** The following advice may be useful to those using N<sub>2</sub>O.

#### Burns

- Nitrous oxide tanks can become freezing cold when the gas is released and there has been a rise in ice burns when people hold the large tanks between their legs.
- Nitrous oxide released directly from the tank can cause ice burns, sometimes these ice burns are not noticed due to the anaesthetic effect of nitrous oxide. Some of the burns are very deep and require multiple surgeries and result in scars. Burns can look superficial, but can rapidly develop into third-degree burn wounds. If you get nitrous oxide on your skin rinse it in cold water. If you get an ice burn, seek medical attention from a doctor or at a hospital.

#### Asphyxiation (suffocation)

- Do not inhale directly from the tank, cracker or whipped cream dispenser, it’s so cold that it could seriously damage the throat and lungs. Always inhale nitrous oxide through a balloon.
- Do not use nitrous oxide with a bag over your head or with a mask attached to cylinders. About five people a year die as a result of breathing nitrous oxide continuously without breathing air as the body becomes starved of oxygen and they suffocate.
- Do not continuously breath nitrous oxide in a confined space like a car. Nitrous oxide displaces air in a confined spaces depriving the body of oxygen. Several deaths have been associated with these methods of use.

## Accidents

- Driving under the influence of nitrous oxide is an offence and has resulted in a number of fatal car crashes.
- When using nitrous oxide, use in a safe location (e.g., sitting on a sofa or the floor) so that any lack of coordination or temporary unconsciousness does not result in falling or other accidents. Do not smoke or hold drinks or anything sharp when inhaling nitrous oxide. The more nitrous oxide you use, the higher the risk of falls or accidents.

## Effects on physical health

- People with heart conditions or abnormal blood pressure may be at higher risk as the drop in oxygen levels caused by inhaling nitrous oxide raises the heart rate, which could cause problems in these individuals.
- Avoid mixing nitrous oxide with other drugs, especially stimulants, as effects on blood pressure and heart rate could be unpredictable.

## Mental Health

- Use of nitrous oxide may induce psychotic symptoms in people with underlying mental ill health.

## Pregnancy

- If pregnant, breast-feeding or planning on becoming pregnant then you should avoid nitrous oxide as this can harm the baby.

## Addiction

- There has been an increase in the use of larger 640g tanks and extra-large balloons. This has led to some people using very large amounts on a regular basis. Some people are using compulsively and may have become dependent on nitrous oxide. There are confidential services who can help you.

## Nerve Damage

- Because of the increased use of larger tanks and extra-large balloons, there has been a significant increase in people being seen at hospitals with nerve damage as a result of using large amounts of nitrous oxide on a regular basis.
- Using large amounts of nitrous oxide on a regular basis can lead to vitamin B12 deficiency, which can cause serious damage to the nerves and spine, resulting in some people being unable to walk. In some cases, this can last for months or years, or may even be permanent.
- Taking B12 supplements, will not prevent B12 deficiency as a result of heavy prolonged nitrous oxide use. You may be treated with B12 supplements at hospital or your GP, but this is given by injection and you have to stop using nitrous oxide for this treatment to be effective.
- The earliest symptoms of B12 deficiency are usually the persistence of tingling, skin crawling or itching, numbness in hands and legs and later a staggering uncoordinated walk, lower limb weakness, muscle stiffness or twitching.
- If you have been using large amounts of nitrous oxide and are experiencing any of these symptoms please see your doctor or go to the A&E department of the hospital as soon as possible.

## Poisons

- Because they are both gases used to fill balloons, nitrous oxide is sometimes confused with helium. Helium causes a high 'silly' voice, whereas nitrous oxide causes a deep 'silly' voice. The two gases are not related.
- Nitrous oxide is not the same as nitric oxide. Nitric oxide is a poisonous gas.

## What to do in emergency?

- If there are serious adverse effects call 999 and tell emergency services what has been taken.
- Seek medical attention if experiencing any negative side effects.
- Always place an unconscious person in the recovery position (see illustration below).

1. Put the right hand by the head (as if they were waving)



2. Put the left arm across the chest, so that the back of the hand rests against the cheek



3. Hold the hand in place and lift up the left knee



4. Turn them on their side by pushing down on the knee



## Recycling

- Dispose of empty containers responsibly. Whippets can be recycled and larger tanks can be placed with other large gas cylinders at a recycling centre.

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## Where to get help

Anyone experiencing issues from nitrous oxide or other substances should seek medical support via their GP or the NHS. There are a wide range of young persons services who can offer confidential support and help:

**England:** <http://www.talktofrank.com/need-support>

**Scotland:** <https://www.scottishdrugservices.com/>

**Wales:** <http://dan247.org.uk>

**Northern Ireland:** <http://www.publichealth.hscni.net/publications/drug-and-alcohol-directories-services>

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**Note:** There is limited data available on use, and much of the anecdotal reports in this briefing are drawn from a single source (Nabben, Weijs, & van Amsterdam, 2021). The current young persons focus of the 2022 GM-TRENDS study is on the problematic use of N<sub>2</sub>O. This briefing will be updated accordingly when the study is available towards the end of 2022.

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