Exploring the Confluence of Animal Medicine and its Implications for Human Health: A Systematic Literature Review

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Abstract

The abuse of veterinary drugs has emerged as a concerning trend, with global fatalities on the rise. Our understanding of this phenomenon remains limited. This study aims to identify the veterinary drugs being misused, the reasons behind their misuse, and the means by which they are obtained. Utilising PubMed, Scopus, and Web of Science databases, along with related grey literature, we applied the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) framework for data collection. Screening and cross-referencing yielded 66 relevant articles, encompassing case reports, surveys, reports, and systemic literature reviews. The analysis identified 28 distinct veterinary drugs being misused in humans, primarily falling into categories e.g. α-2- and β-2-adrenergic receptor agonists, GABAergic receptor modulators, opioid receptor agonists, non-steroidal anti-inflammatory drugs (NSAIDs), and N-methyl-D-aspartate (NMDA) receptor antagonists. These drugs were used for various purposes including recreational use, weight loss, bodybuilding, pain relief, and self-medication for stress-related symptoms. Routes of administration predominantly included parenteral, oral, and inhalation methods. Veterinary workers/assistants and individuals connected to animals were identified as contributors to the misuse of these medications. Motivations for their utilisation ranged from affordability and accessibility to the ease of obtaining multiple prescriptions from various veterinary sources, often in conjunction with other illicit substances. Dependence and addiction were common outcomes to the misuse of veterinary medicines by humans. Overall, this systematic review underscores the increasing popularity of veterinary prescription drug misuse, despite being under-reported with limited available data. Healthcare professionals are urged to remain vigilant to potential overdose events involving these medications.

Keywords: veterinary medicines, animal medicines, substance use, diversion of medicines, drug misuse

Introduction

As the global crisis of prescription drug misuse continues to escalate, individuals grappling with substance use are relentlessly seeking new avenues to satisfy their cravings. According to the National Survey on Drug Use and Health (NSDUH), diversion of prescription medicines is defined as 'use without a prescription or in ways not intended by the prescriber' (Schepis et al., 2020). The diversion of veterinary and human medicine is gaining prominence as a pivotal focal point. Veterinarians, who annually treat numerous animals and have the authority to prescribe controlled substances, are often overlooked as potential contributors to prescription drug misuse (Anand & Hosanagar, 2021). A survey conducted in 2023 explored the perspectives of UK veterinarians regarding the potential misuse of veterinary prescription medications (VPMs). The findings revealed that 88% of participants recognised the risk of abuse associated with certain VPMs. Furthermore, 30% of respondents reported suspicions of pet owners misusing VPMs, while 20% expressed concerns about misuse among veterinary staff (Lehnus et al., 2023). The growing inclination towards acquiring medications through healthcare providers, such as veterinarians, is a familiar trend owing to the perception of these drugs being safer than those obtained through illicit channels, as well as being more cost-effective (Health Canada, 2006). Additionally, the purchase of veterinary medicines online in the UK is reportedly on the rise (VMD, 2014). The practice of "vet shopping" involves soliciting veterinarians for prescription medications intended for animals, without the intention of administering them to the animals in question (AVMA, 2019). This behaviour significantly contributes to the escalating global issue of substance misuse, as individuals gain access to additional drug supplies through veterinarians. A study conducted in 2022 revealed a threefold increase between 2014 and 2019 in the number of clients obtaining prescriptions for any class of controlled substances from four or more veterinarians (Chua et al., 2022). The surge in acquiring medications through veterinarians prompted the United States Food and Drug Administration (US FDA) to express concerns in 2018, highlighting the significant risk posed by the prescription of opioids by veterinarians. Similar to opioid medications intended for human use, these drugs hold the potential for addiction, abuse, and overdose when diverted for personal use (FDA, 2020). News articles have reported novel methods employed by individuals to access these controlled substances, such as harming their pets to obtain analgesics (Herzog, 2018) and training their dogs to simulate symptoms to receive hydrocodone cough syrup (Burke, 2002).

The issue extends beyond the misuse of prescription drugs approved for human use; there has been a concerning increase in the misuse of medications exclusively approved for animal use. This trend is alarming as drugs approved solely for animal use have not undergone testing on humans, potentially resulting in a range of adverse effects due to anatomical, physiological, and pharmacokinetic differences. Unlike in human development, pre-clinical trials for animal medicine are not necessarily utilised, meaning human safety is not a focus (reference). The administration of larger doses in animals, owing to variations in hepatic metabolism (LeBourgeois et al., 2002), increases the risk of toxic effects when these medications are misused in humans. For example, veterinary ketamine formulations can be ten times stronger than human formulations (reference). Recreational ketamine use and associated fatalities are on the rise (Corkery et al., 2021), with the prevalence of ketamine use in the last year increasing by 3.8% (ONS, 2023). Conversely, carfentanil, approved only for animal use due to its potency being 100 times higher than fentanyl (Swanson et al., 2017), was the second most frequently reported synthetic opioid in the United States between 2016 and 2017 (Zawilska et al., 2021), prompting the World Health Organisation to declare it a serious threat to public health.

Given that prescription drug misuse in veterinary settings remains an underestimated and under-researched area (Anand & Hosanagar, 2021), this study aims to enhance understanding regarding the types of veterinary medications that are misused, the intentions behind their misuse, and the methods of acquisition.

Methodology

A systematic review involves a meticulous analysis of well-defined research questions employing a systematic and explicit methodology to identify, select, and critically evaluate pertinent research, as well as to analyse the data derived from the studies incorporated (Moher, 2019). To ensure objectivity

and rigor in study selection, a systematic and structured approach was adopted. Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Moher et al., 2009) were adhered to, providing consistency and transparency in the collection of suitable studies. This method facilitated a clear and structured approach to data collection. In November 2023, a systematic search was conducted using PubMed (NCBI), Web of Science (Clarivate), and Scopus (Elsevier) databases. The aim was to identify the most appropriate scientific databases for this study. As Falagas et al. (2008) noted, PubMed was praised for its convenience, speed, and user-friendliness, particularly significant for clinicians and researchers. The study also affirmed that Scopus covers a broader range of journals compared to PubMed and Web of Science. Additionally, it highlighted Google Scholar's utility in retrieving less mainstream information, albeit with the drawback of infrequent updates.

Boolean operators (AND/OR) were utilised to combine two groups of words into the final string utilised in all three databases. An iterative process of optimisation and refinement was utilised to ensure the retrieval of pertinent and comprehensive articles. Initially, various combinations of the search thread were explored to determine their effectiveness in capturing relevant literature. Further adjustments were made to the search strategy until a final search thread was determined. The string (("veterinary drug" OR "veterinary medication" OR "veterinary prescription drug") AND ("misuse" OR "abuse")) was entered into the three scientific databases. We established clear inclusion and exclusion criteria to ensure a selection of papers relevant to our research questions and the aims of the study. Specifically, we included articles that addressed the misuse or diversion of veterinary medicine regarding human consumption. This encompassed literature reviews, case studies, and reports focusing on the unauthorised use, misuse, or non-medical consumption of veterinary drugs. Conversely, we excluded papers that did not explicitly reference the misuse or diversion of veterinary pharmaceuticals in humans. A thematic approach was employed to analyse the existing literature. This type of analysis aided in the identification of specific themes present within the literature. Following a systematic review of all articles, the data was organised based on categories including drug class, classification as human or animal drugs, and controlled substance status. The search was not restricted by time or geographical limitations, and all languages were included in the search results. Identification of grey literature was conducted between November and December 2023, involving examination of government reports and manual scrutiny of supplementary articles through Google Scholar. Microsoft Excel (Version 16.79.1 (23111614)) served as a tool to eliminate duplicate articles. A supplementary cross-reference search was conducted on the remaining studies to mitigate the risk of overlooking relevant articles in the systematic search.

Results

Initially, a total of 338 records were identified, encompassing both database searches and various sources of grey literature. Following the completion of the screening process, 66 articles were found to be relevant to the current study. Within this body of literature, 28 distinct veterinary drugs were identified as being misused by humans or posing a risk to human health. Figure 1 provides a summary of the process through which records were identified, screened, and assessed for eligibility. Subsequently, each remaining article underwent further analysis, and the main findings from the selected articles and reports were summarised in Supplementary Information (SI) (Table 1). This Table (in SI) provides an insight into the off-label use/ indication for each of the diverted veterinary medicines being identified in this literature review, the dose consumed, the routes of administration and where each medicine was obtained from.

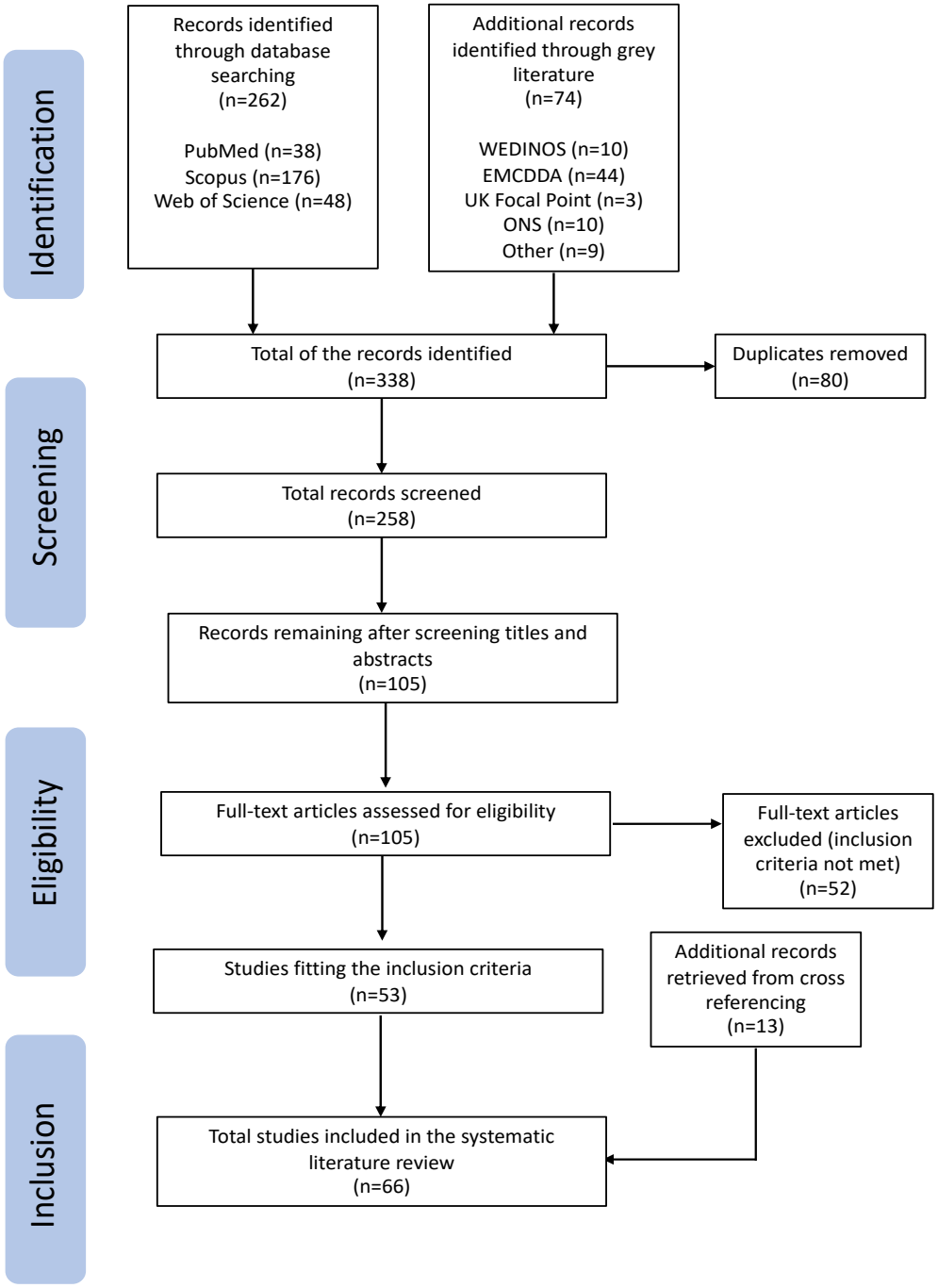

Figure 1- PRISMA flow diagram of included studies assessing the effects of veterinary medication use by humans on their health (*Welsh Emerging Drugs and Identification of Novel Substances (WEDINOS), European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), Office for National Statistics (ONS)).

One of the primary objectives of the systematic literature review was to identify the types of veterinary medications susceptible to misuse by humans or currently being misused. The primary classes of drugs identified included α-2- and β-2-adrenergic receptor agonists, NMDA antagonists, opioid receptor agonists, GABAergic receptor modulators, and non-steroidal anti-inflammatory drugs (NSAIDs). Table 1 provides a summary of the veterinary drugs obtained from the literature, along with the primary reasons for their misuse in humans.

Table 1 - Drugs identified through systematic literature search and their potential reasons for their misuse in humans.

Drug Class	Name of Drug	Reason for Misuse in Humans
Adrenergic Receptor Agonists		
	Xylazine	Sedation/Analgesia
	Medetomidine	Sedation/Analgesia
	Dexmedetomidine	Sedation/Analgesia
	Clenbuterol	Performance Enhancement
NDMA Antagonists		
	Ketamine	Analgesia/Dissociation/Sedation
	Telazol (Zolazepam/Tiletamine)	Anaesthesia/Sedation/Sedation
Opioid Receptor Agonists		
	Carfentanil	Analgesia/Euphoria
	Tramadol	Analgesia/Sedation/Euphoria
	Butorphanol	Analgesia/Sedation/Euphoria
GABAergic Receptor Modulators		
	Diazepam	Sedation/Muscle Relaxation
	Clorazepate	Sedation/Muscle Relaxation
	Pentobarbital	Suicidal Indications/Sedation
	Phenobarbital	Sedation/Anticonvulsant/Hypnotic Effects
Other Drugs		
	Acepromazine (Phenothiazines)	Sedation/Muscle Relaxation
	Levamisole (Anthelminthic)	Bulking agent
	Pheniramine (Antihistamine)	Sedation
	Stanozolol (Anabolic Steroid)	Performance Enhancement
	Levothyroxine (Thyroid Hormone)	Weight loss Supplement
	Furosemide (Loop Diuretic)	Weight loss Supplement
	Amitriptyline (Tricyclic Antidepressant)	Antidepressant Properties
	Tilmicosin (Macrolide Antibiotic)	Suicidal Indications
	Embutramide/Mebezonium (Euthanasia Compound)	Suicidal Indications
	Dinoprost (Prostaglandin)	Abortion
	Cloprostenol (Prostaglandin)	Abortion
	Phenylbutazone (NSAID)	Analgesia/Anti-Inflammatory
	Flunixin (NSAID)	Analgesia/Anti-Inflammatory
	Carprofen (NSAID)	Analgesia/Anti-Inflammatory
	Vitamin ADE Compound	Performance Enhancement

Among the drugs identified, those approved exclusively for animal use constituted 53.6% of the total drugs retrieved from the literature (15 out of 28). The remaining 13 drugs were approved for both human and animal use, although some were administered at higher doses were approved solely for animal use. Table 2 outlines the approved/ licensed usage of each veterinary drug identified, and its legal classification in both the UK and the US.

Table 2 - The veterinary drugs identified from the literature review, their licensed usage and legal classification in both the UK and US.

Drug Name	Approved Usage (Humans or Animals)	Status: UK	Status: FDA
Xylazine	Animals	Not Controlled	Not Controlled
Medetomidine	Animals	Not Controlled	Not Controlled
Dexmedetomidine	Both	Not Controlled	Not Controlled
Clenbuterol	Both	Class C, Schedule 4	Not Controlled
Ketamine	Both	Class B, Schedule 2	Schedule III
Telazol (Zolazepam/ Tiletamine)	Animals	Not Controlled	Not Controlled
Carfentanil	Animals	Class A	Schedule II
Tramadol	Both	Class C, Schedule 3	Schedule IV
Butorphanol	Both	Not Controlled	Schedule IV
Diazepam	Both	Class C, Schedule 4	Schedule IV
Clorazepate	Both	Class C, Schedule 4	Schedule IV
Pentobarbital	Animals	Class B, Schedule 3	Schedule II
Phenobarbital	Both	Class B, Schedule 3	Schedule IV
Acepromazine (Phenothiazines)	Animals	Not Controlled	Not Controlled
Levamisole (Anthelminthic)	Animals	Not Controlled	Not Controlled
Pheniramine (Antihistamine)	Both	Not Controlled	Not Controlled
Stanozolol (Anabolic Steroid)	Both	Class C, Schedule 4	Schedule III
Levothyroxine (Thyroid Hormone)	Both	Not Controlled	Not Controlled
Furosemide (Loop Diuretic)	Both	Not Controlled	Not Controlled
Amitriptyline (Tricyclic Antidepressant)	Both	Not Controlled	Not Controlled
Tilmicosin (Macrolide Antibiotic)	Animals	Not Controlled	Not Controlled
Embutramide/Mebezonium (Euthanasia Compound)	Animals	Not Controlled	Not Controlled
Dinoprost (Prostaglandin)	Animals	Not Controlled	Not Controlled
Cloprostenol (Prostaglandin)	Animals	Not Controlled	Not Controlled
Phenylbutazone (NSAID)	Animals	Not Controlled	Not Controlled
Flunixin (NSAID)	Animals	Not Controlled	Not Controlled
Carprofen (NSAID)	Animals	Not Controlled	Not Controlled
Vitamin ADE Supplement	Animals	Not Controlled	Not Controlled

Among all medicines identified as misused by humans, 68% (19 out of 28) are not classified as controlled substances. Examination of the regulatory status of these drugs in both the UK and the US reveals significant similarities, with only two drugs having different classifications between the two countries. Specifically, while clenbuterol is not considered a controlled substance in the US, it falls under controlled status in the UK. Conversely, butorphanol is not classified as a controlled substance in the UK. Notably, only 13% (2 out of 15) of drugs approved strictly for animal use only (carfentanil and pentobarbital) are classified as controlled drugs in both countries.

Discussion

The primary objective of this systematic review was to delve into the spectrum of veterinary medications prone to misuse or capable of fostering drug-seeking behaviour and dependence in humans, while also exploring the motivations behind individuals resorting to substances intended for animal use. To our knowledge, this marks the first systematic literature review analysing the harms associated with veterinary drug misuse in humans.

Of all drugs identified as misused by humans, over half (57% (n=15/28)) are exclusively approved for animal use. Through comprehensive literature review, we identified 28 distinct veterinary medications being misused by humans. Among these, 15 were solely approved for animal use, while the remaining 13 held approval for both species. Despite certain drugs being approved for both humans and animals, distinct dosages are mandated for each species due to variable biochemical and functional systems, thereby altering the pharmacokinetics of different drugs (Nair & Jacob, 2016). Drug metabolism, a crucial aspect of pharmacokinetics, is influenced by the variation in expression and activity of drug-metabolising enzymes between humans and animals, thereby necessitating tailored doses for different species.

Among the 28 drugs identified, their primary effects are attributed to analgesic and sedative properties, indicating potential for misuse. The main drug classes identified in the literature include α-2- and β-2-adrenergic receptor agonists (n=4 drugs), GABAergic receptor modulators (n=4 drugs), opioid receptor agonists (n=3 drugs), NSAIDs (n=3 drugs), and NMDA receptor antagonists (n=2 drugs). Literature findings reveal that veterinary drugs are primarily obtained by individuals working in veterinary settings or those with easy access to the drugs (Alleva et al., 2015; de la Peña and Cheong., 2016; Perrin, 2014; Ruiz-Colon et al., 2014), as well as through the practices of "vet shopping" and malingering by using animals as proxies (LeBourgeois et al., 2002; Russel et al., 2018). Parenteral injection emerged as the primary route of administration for veterinary drugs, followed by oral ingestion and inhalation by humans. Only 32% of identified veterinary drugs fall under the category of controlled substances (in the UK), with the remaining 68% not subject to the stringent regulations, monitoring, and legal restrictions applied to the prescribing and supply of controlled drugs. The absence of such strict oversight may contribute to increased accessibility and growing misuse of these non-controlled drugs.

The α-2-adrenergic agonists, particularly xylazine, have emerged as a potential contributor to increasing drug-related deaths globally. Xylazine, known for its central nervous system (CNS) depressant effects, is commonly used for sedation, muscle relaxation, analgesia, and anaesthesia in veterinary practice (Greene & Thurmon, 1988). However, its misuse, often in conjunction with opioids, has potentially led to a surge in fatalities, drawing attention to its alarming presence as an adulterant in illicit drug markets. Studies have documented a sharp increase in xylazine-related deaths by 276% in the US, particularly in combination with illicitly-manufactured fentanyl (IMF), indicating a concerning trend in substance misuse (Sibbesen et al., 2022). The co-consumption of xylazine and opioids can lead to synergistic effects, exacerbating CNS depression and increasing the risk of fatalities (Acosta-Mares et al., 2023). Recent data underscore the growing prevalence of xylazine in drug-related fatalities, prompting public safety alerts in several countries (CDC, 2023a; United States DEA, 2022). Notably, xylazine-associated deaths have been reported in the UK and Europe, indicating its infiltration into the European illicit drug supply (Rock et al., 2023). Kacinko et al. (2022) found that stimulants were present in 53% of xylazine-positive cases, cannabinoids in 30% and benzodiazepines in 26%. Other drugs detected in xylazine-related deaths cases include morphine, cocaine, paracetamol, pregabalin, THC, diazepam, methadone, alcohol, and heroin (Johnson et al., 2021; Rock et al., 2023). Other drugs identified in xylazine-positive syringes included protonitazene, metonitazene, isotonitazene, and carfentanil (EMCDDA, 2023a; EMCDDA, 2023b). The new mixtures of novel benzodiazepines and opioids, with xylazine, have been reported in Estonia (EMCDDA, 2023f) and have the potential to seriously impact public health (EMCDDA, 2023e).

Xylazine misuse encompasses various scenarios, including recreational use, adulteration of other drugs, drug-facilitated crimes, and intentional poisoning (Teoh et al., 2022). Its combination with opioids,

termed "tranq dope," has been reported to enhance the euphoric effects of fentanyl and prolong its duration of action (Friedman et al., 2022). Moreover, physical dependence on xylazine, coupled with withdrawal symptoms, have been observed, further complicating its misuse dynamics (Torruella, 2011). Synergistic effects of the combination of opioids with xylazine have been reported to enhance sedation and analgesia in the veterinary setting (Leonardo et al., 2016), where greater sedation is observed using the combination than the α-2-agonist alone. Known by inducing painful ulcers, xylazine misuse has been fuelled by its ability to alleviate pain from injection site ulcers it causes, creating a negative cycle. Research shows α-2 adrenergic agonists, like xylazine, can partially block withdrawal symptoms in opioid users. This suggests individuals may combine xylazine with opioids to manage withdrawal discomfort. Similarly, clonidine, another α-2 agonist, is used to treat withdrawal from various substances by modulating noradrenergic activity. This inhibition of norepinephrine release may explain why xylazine is misused with other drugs. The route of administration for xylazine primarily involves parenteral injection, with males being disproportionately affected by xylazine-related overdoses and fatalities (CDC, 2023b; Forrester, 2016; Ruiz-Colon et al., 2014).

Medetomidine and dexmedetomidine, α-2-adrenergic agonists primarily used for sedation and analgesia in dogs, have recently emerged as substances of misuse. While dexmedetomidine is approved for both human and animal use, medetomidine is restricted to veterinary use. A toxic adulterant alert in December 2023 identified medetomidine in drug samples containing fentanyl, xylazine, heroin, and cocaine, raising concerns due to its potency and selectivity as an agonist. While xylazine was previously the primary drug in this class associated with diversion and abuse, recent misuse of medetomidine and dexmedetomidine has been observed. Like xylazine, these drugs diminish opioid withdrawal symptoms, potentially explaining their misuse alongside opioids. Additionally, α-2-adrenergic receptors, targeted by these drugs, play a role in modulating symptoms of nicotine and alcohol withdrawal syndromes. Notably, there are no further documented instances of medetomidine or dexmedetomidine misuse in humans beyond the mentioned alert.

Clenbuterol, a **β-2-adrenergic receptor agonist**, activates adenylyl cyclase and thus, protein kinase A (PKA) to promote the relaxation of smooth muscles (Witkowska-Piłaszewicz et al., 2021). It is primarily used as a bronchodilator in horses (Wingert et al., 2008) and asthma treatment in humans (Lust et al., 2011), has seen a surge in misuse, particularly in the context of weight loss and bodybuilding. Despite its exclusive veterinary approval in the US, clenbuterol has become prevalent in illegal markets, marketed as a weight loss supplement. The dosages consumed by athletes often far exceed therapeutic levels, reaching up to 200mg daily, posing significant health risks (Moriarty & Attar, 2020). The addictive potential of clenbuterol misuse stems from its ability to activate the brain's reward system, leading to dopamine release and habit formation (NIDA, 2022). Moreover, the physical effects associated with bodybuilding, such as enhanced athletic performance, increase the rate of muscle protein deposition and reduced appetite, contribute to its addictive behaviour (Lust et al., 2011; Moriarty & Attar, 2020). Salbutamol, a similar β-2 agonist, is also misused for performance enhancement, although clenbuterol exhibits a higher abuse potential due to its potency and pharmacokinetic properties (Milano et al., 2018).

In addition to its misuse in bodybuilding, clenbuterol is increasingly being mixed with opioids and benzodiazepines, posing grave health risks. The concurrent use of clenbuterol with depressants like opioids and benzodiazepines can lead to unpredictable interactions, exacerbating cardiovascular and respiratory complications (Wingert et al., 2008). Furthermore, co-ingestion with stimulants like cocaine heightens the risk of cardiovascular distress and central nervous system overstimulation (Wingert et al., 2008). The widespread availability of clenbuterol online has also fuelled its misuse, with reports of increased exposure to poison control centres (Brett et al., 2014; Schifano et al., 2018). The alarming trend of clenbuterol intoxication showed the presence of heroin, cocaine, fentanyl, benzodiazepines and methadone (Wingert et al., 2008). Opioids and benzodiazepines depress both cardiovascular and respiratory functions while inducing sedation in the CNS. In contrast, clenbuterol has opposing effects, boosting heart and respiratory rates while triggering anxiety and tremors in the CNS. Such differing effects can result in unpredictable interactions and heightened risks when these substances are used together. Conversely, cocaine shares similar stimulating effects on the cardiovascular and CNS systems

with clenbuterol, escalating the chances of heart complications and CNS overstimulation when these substances are co-consumed.

For the **NMDA receptor agonists/antagonists**, Telazol, a veterinary anaesthetic (licensed for cats and dogs) compound composed of an equal ration of zolazepam, a benzodiazepine, and tiletamine, an NMDA receptor antagonist, has raised concerns regarding its misuse in humans despite its safe use in veterinary medicine (de la Peña & Cheong, 2016). The potent nature of tiletamine, akin to ketamine, combined with zolazepam's benzodiazepine properties, poses a risk of misuse and dependence (Lin et al., 1992). Instances of Telazol misuse, resembling recreational drugs like ketamine and diazepam, underscore its potential for abuse, particularly among those with easy access to veterinary settings (de la Peña & Cheong, 2016). Despite its controlled status in the US, Telazol remains unregulated in the UK, amplifying concerns regarding its public health impact (EMCDDA, 2009). In 2003, the UK's Threat Assessment of Serious and Organised Crime raised concern about the rising abuse of ketamine and further stated that its restriction may lead to Telazol being used as a replacement in the future (NCIS, 2003). Most cases involved individuals with easy access to the veterinary drug combination, indicating a heightened risk within veterinary settings. Telazol misuse by a veterinarian to reduce heroin consumption (Lee et al., 2009) corroborates with research showing that most Telazol abusers also use other psychoactive drugs, often through cross-addiction, wherein users are more likely to misuse drugs with similar anaesthetic/ depressant effects that act on the NMDA/GABA receptors (de la Peña & Cheong, 2016). This pattern of polydrug misuse was evident in a case where a patient was found unresponsive, with Telazol, benzodiazepines, and cannabinoids detected in urine analysis (Quail et al., 2001). Tiletamine (a component of Telazol) exhibits significantly higher potency than ketamine, and zolazepam (the other component of Telazol) is 5-10 times more potent than diazepam (Chung et al., 2000). Tiletamine, an NMDA receptor antagonist, produces rewarding and reinforcing effects, potentially leading to dependence and addiction (Bryan et al., 2012). Similar to ketamine, tiletamine induces hallucinogenic, dissociative effects, possibly contributing to its recreational misuse (Lee et al., 2009). Furthermore, NMDA receptor antagonists stimulate the mesolimbic dopamine system and directly inhibit dopamine reuptake, highlighting the role of the reward pathway in drug dependence (Bryan et al., 2012; Smith et al., 1977). Exposure to zolazepam also increases dopamine levels by hyperpolarising GABA neurons, leading to dopamine neuron inhibition (Tan et al., 2011).

Although ketamine is widely known to be a veterinary anaesthetic, its diversion from medical settings is a contributing factor to its recreational use (EMCDDA, 2002). The misuse of ketamine 'pink cocaine' has been associated with increased levels of serotonin, dopamine, and norepinephrine (Lindefors et al., 1997; EMCDDA, 2023b), possibly driving its misuse as individuals seek mood enhancement and altered states of consciousness fuelled by the heightened activity of these neurotransmitters. Despite its therapeutic potential in pain management and depression treatment, ketamine's recreational misuse remains a significant health concern (Gao et al., 2016). The escalating prevalence of ketamine misuse, highlighted by its emergence as a prevalent substance in drug markets, underscores the urgent need for public health interventions (GOV.UK, 2021; EMCDDA, 2022b). The poly-drug misuse of ketamine, particularly in combination with stimulants like cocaine and MDMA, poses grave risks, including cardiovascular complications and serotonin syndrome (Francescangeli et al., 2019). Ketamine's pharmacokinetic characteristics include a broad hepatic CYP P-450 induction, which may potentiate the toxicity of other drugs in the hepatobiliary system by increasing the production of harmful metabolites (Lee et al., 2009). Despite its therapeutic benefits, ketamine's accessibility, low cost, and potent dissociative effects contribute to its widespread misuse (Beerten et al., 2023).

Opioid agonists identified include carfentanil, tramadol and butorphanol. Despite its exclusive approval for veterinary use, carfentanil has emerged as a prevalent opioid misused by humans, often disguised as heroin in illicit drug markets (DEA, 2016). Its potency, estimated to be thousands of times greater than morphine, poses severe health risks, contributing to numerous deaths and poisonings worldwide (Bever et al., 1976). Carfentanil's increasing presence in illicit drug markets, combined with its potency, makes it particularly dangerous, with users often unaware of its inclusion in street drugs (EMCDDA, 2018). The mixture of carfentanil with other substances like cocaine exacerbates these risks, leading to unintended side effects and fatalities (Prekupec et al., 2017). The lack of data on its

abuse liability and dependence potential underscores the urgent need for further research and public health interventions (Wei et al., 2023).

Tramadol, a controlled substance approved for both human and animal use, is susceptible to misuse, particularly due to its accessibility through veterinary prescriptions (Anand & Hosanagar, 2021). Its relatively low cost compared to other opioids and its dual action as an opioid agonist and serotonin-norepinephrine reuptake inhibitor (SNRI) contribute to its abuse potential (Russell et al., 2018; Miotto et al., 2017). Tramadol's unique pharmacological profile results in distinctive withdrawal symptoms and an increased risk of dependence (Miotto et al., 2017; Babalonis et al., 2013). Despite its partial agonist and antagonist activity, making dependence less likely than with traditional opioids, butorphanol misuse has been documented, often through deceptive means such as malingering by animal proxy (Heel et al., 1978; LeBourgeois et al., 2002). In contrast to other opioids abused by humans, butorphanol demonstrates partial agonist and antagonist activity (Heel et al., 1978), potentially resulting in a reduced likelihood of dependence compared to opioids like morphine. Limited information exists on butorphanol misuse, highlighting the need for further research and surveillance in veterinary settings.

GABAergic receptor modulators/ positive allosteric modulators identified include diazepam, clorazepate, phenobarbital and pentobarbital. While not commonly discussed in the context of misuse, diazepam stands out as the most prescribed benzodiazepine in veterinary settings (Anand & Hosanagar, 2021). Its accessibility in veterinary medicine raises concerns about potential misuse by pet owners, given its addictive properties and associated withdrawal symptoms. Instances of "vet shopping" and malingering by animal proxy have been documented, illustrating the acquisition of clorazepate from veterinary sources for personal use (LeBourgeois et al., 2002). As a controlled substance with addictive potential, monitoring its use in veterinary settings is essential, particularly in light of the growing concern over benzodiazepine misuse (Votaw et al., 2019). Used primarily for seizure management in both humans and animals, phenobarbital has been misused, leading to fatal overdoses in some cases (Alleva et al., 2015). Its accessibility in veterinary medicine poses a risk, especially when individuals with substance use disorders seek to alleviate withdrawal symptoms (Alleva et al., 2015). Similar to phenobarbital, pentobarbital misuse has been reported, particularly among individuals associated with veterinary practices (Perrin, 2014). Its potential for habit formation and toxic effects underscores the need for vigilance, especially in professions where access to veterinary medications is common (Johnson & Sadiq, 2021). Recent cases of pentobarbital adulteration in counterfeit fentanyl tablets highlight the potentially lethal consequences of combined drug use (CFSRE, 2024).

Several veterinary medications, not fitting into previously mentioned categories, have been identified for misuse by humans. Among these are acepromazine, pheniramine, and others.

Acepromazine emerged as a notable focus in five retrieved papers (Algren & Ashworth, 2014; Anand & Hosanagar, 2021; Erramouspe et al., 2002; de Lima & de Araujo, 2023; Perrin, 2014). This commonly used phenothiazine tranquiliser is administered to mitigate stress and excitement during various veterinary procedures (Schneiders et al., 2012). Originally approved for treating schizophrenia in humans, acepromazine is now exclusively licensed for veterinary use, although it is not classified as a controlled substance. Its pharmacological profile includes antagonistic effects on dopaminergic and serotonin receptors, as well as antagonism of histamine, muscarinic acetylcholine, and α-1 receptors (Algren & Ashworth, 2014). A case study detailed a woman who intentionally ingested 950mg of her dog’s acepromazine, with a medical history notable for depression, anxiety, and hypothyroidism. Despite several reports of acepromazine poisonings, including instances of drug-facilitated sexual assaults and suicides, detection remains challenging due to rapid metabolism (de Lima & de Araujo, 2023). Erramouspe et al. (2002) outlined a case where a survey of veterinary practitioners revealed misuse of veterinary acepromazine for stress management. In these cases, acepromazine misuse appeared associated with mental health conditions such as stress, anxiety, and depression, possibly linked to its antagonism of dopamine and serotonin receptors. Two additional suicide cases involving acepromazine were documented (Perrin, 2014), both involving female individuals. One case involved a veterinary worker, while the source of acepromazine for the other patient remained unclear. In both

instances, acepromazine was implicated in completed suicides, with one dose totalling 2500mg. To our knowledge, the misuse of its analogue promazine has not been documented and is not known.

Pheniramine, an antihistamine, is approved for use in both humans and animals, primarily targeting allergic conditions. Antihistamines, easily accessible over the counter, rank among the most abused drugs (Kamath et al., 2022). A study revealed that 14.7% of overdose deaths in the US between 2019 and 2020 involved antihistamines, with opioids implicated in 82.8% of these cases (Dinwiddie et al., 2022). However, despite this concerning trend, the UK has not conducted an analysis of antihistamine-related mortalities in over 40 years (Oyekan et al., 2021), and reports on pheniramine misuse are scarce. Notably, a high proportion (79.9%) of patients hospitalised due to pheniramine poisoning had a history of drug or alcohol abuse, with 60.5% exhibiting antihistamine abuse history (Buckley et al., 1994). Although not a controlled substance, one documented case highlights veterinary-grade pheniramine misuse, where a user intravenously mixed 100mg of heroin with 15ml of injection pheniramine, 4-5 times daily, in an attempt to manage sleep issues (Tyagi et al., 2022). Co-administration of pheniramine with opioids like heroin can lead to life-threatening outcomes, given the additive effects of antihistamines with CNS depressants (Oyekan et al., 2021). In this case, the user exhibited signs of heavy pheniramine addiction, experiencing withdrawal symptoms such as insomnia, restlessness, and tremors upon attempts to reduce dosage (Tyagi et al., 2022). Psychological tolerance and physical withdrawal symptoms to pheniramine misuse have been documented (Tyagi et al., 2022). It remains unclear how the veterinary-grade pheniramine was obtained in this case, but a 100ml bottle labelled "NOT FOR HUMAN USE. FOR ANIMAL TREATMENT ONLY" was reported. Given its source outside traditional pharmacies, it's plausible that this veterinary product was purchased online. A study addressing the illicit veterinary medicine market highlighted the distribution of such medications through illegal online pharmacies, online marketplaces, and social media platforms, posing significant regulatory and enforcement challenges (Pons-Hernandez et al., 2022).

Stanozolol, an anabolic steroid, holds licenses for use in both human and veterinary medicine and is classified as a Class C controlled substance (Home Office, 2022). It ranks among the most commonly abused anabolic androgenic steroids (AAS), particularly among young adults and professional athletes, often sought to enhance physical appearance and performance (Ozcagli et al., 2018). A case study documented an individual's attempt to procure stanozolol, without an accompanying animal, from a veterinary facility (LeBourgeois et al., 2002). While the extent of the individual's dependence on the AAS remains unclear, studies have indicated the potential for dependency due to the self-administration stimulation observed in animal models (Kanayama et al., 2010). Although users do not experience immediate intoxication, dependence on AAS may develop, particularly in individuals grappling with body image disorders like "muscle dysmorphia" (Kanayama et al., 2009).

Both levothyroxine and furosemide were found to be utilised inappropriately for weight loss (Erramouspe et al., 2002; LeBourgeois et al., 2002). Levothyroxine, typically prescribed for hypothyroidism, was acquired from a veterinary source by a veterinary worker for off-label use as a weight loss aid. It was apparent that in this instance, the individual engaged in 'vet shopping', obtaining multiple prescriptions for levothyroxine from different veterinary clinics. Similarly, misuse of furosemide, a loop diuretic, was reported by veterinarians to be misused for weight management (Erramouspe et al., 2002). Furosemide has been recognised for its misuse in sports due to its ability to induce rapid weight loss (Cadwallader et al., 2010).

A single case of veterinary amitriptyline misuse was identified. Amitriptyline, a tricyclic antidepressant, is licensed for use in both humans and animals. LeBourgeois et al. (2002) detailed an incident wherein an anxious pet owner specifically requested amitriptyline for her dog. The prescribed three-week medication supply was depleted within a mere 10 days, prompting suspicion of misuse by the owner. Notably, a study revealed that 25% of amitriptyline users aimed to achieve euphoria (Cohen, 1978), highlighting the potential for dependence and abuse. This may be attributed to the drug's synergistic antihistamine and anticholinergic effects (Umaharan et al., 2021).

Two articles documented the misuse of the veterinary antibiotic tilmicosin. While this antibiotic serves as a calcium-channel blocker and lacks approval for human use, it has been implicated in suicide cases. Tilmicosin poses a significant risk to certain animal species, including pigs, primates, and horses, due to its cardiotoxicity (Lust et al., 2011). However, it is deemed appropriate for treating specific infectious diseases in cattle and sheep. Despite many exposures being accidental, there have been 25 recorded deaths, with 16 suspected suicides (AVMA, 2017). The primary exposure route in all tilmicosin cases was parenteral (Perrin, 2014), with intentional misuse in humans attributed to its widespread availability. In 2017, the FDA issued a warning regarding the dangers of tilmicosin, noting its lack of antidote and its toxic effects on the heart (AVMA, 2017).

The use of Tanax® has been implicated in suicide cases. Tanax® is a veterinary drug comprising three ingredients: embutramide (a general anaesthetic), mebezonium iodide (a neuromuscular blocking agent), and tetracaine hydrochloride (a local anaesthetic), known to potentially encourage abuse due to its hypnotic effects (Lajtai et al., 2016). Prior to 2014, eight documented fatalities resulted from self-administration of mebezonium and embutramide (Perrin, 2014). Notably, 50% of these cases involved individuals with convenient access to euthanasia agents, including veterinarians. Forensic and clinical toxicological analyses revealed embutramide in two cases in 2013 (Lajtai et al., 2016). In the first case, embutramide was detected in the urine of a man who had murdered his ex-wife, along with alprazolam. The second case involved a 16-year-old hospitalised for severe symptoms, experiencing recurrent episodes of unconsciousness, bradycardia, and diplopia over several months. While research by Lajtai et al. (2016) indicated that this drug combination had not previously been associated with abuse, both cases underscored the need for heightened attention to the misuse of veterinary medications.

Dinoprost and cloprostenol are both classified as veterinary medications with potential hazards for humans. Dinoprost, a synthetic form of prostaglandin F2 alpha, is not approved for human use and is primarily employed for inducing abortion in cattle (Lust et al., 2011). However, concerns have been raised regarding its potential misuse for terminating unwanted pregnancies in humans. Erramouspe et al. (2002) reported a case of dinoprost misuse for this purpose. In contrast, Lust et al. (2014) noted that human exposure to dinoprost is typically accidental, often occurring through occupational exposure. Similarly, cloprostenol, another synthetic prostaglandin used in veterinary medicine, is not licensed for human use and shares concerns about potential misuse for inducing abortion.

Interestingly, phenylbutazone emerged as the most frequently misused veterinary medication, constituting 57% of all reported cases involving non-steroidal anti-inflammatory drugs (NSAIDs). While primarily intended for animal use, phenylbutazone is approved for treating ankylosing spondylitis in humans. However, its human usage is associated with gastrointestinal toxicity, renal dysfunction, and aplastic anaemia (Erramouspe, 2002). Concerningly, instances of phenylbutazone adulterating illicit drugs, particularly those containing heroin, fentanyl, and/or fentanyl derivatives, have been on the rise (CFSRE, 2023a). This trend is troubling given that phenylbutazone was largely discontinued for human consumption due to associated fatalities. Since 2016, Pennsylvania alone has reported 116 positive samples containing phenylbutazone as an adulterant (CFSRE, 2023a). Flunixin, another NSAID, was identified as a medication misused in a study analysing veterinarians' perceptions of the misuse of veterinary medications in humans (Erramouspe, 2002). While NSAIDs were the most frequently reported class of drugs in this study, flunixin accounted for 24% of these cases. Adverse outcomes associated with flunixin's misuse in humans, including gastrointestinal toxicity and renal dysfunction, were documented (Erramouspe, 2002). The study highlighted the potential for severe human overdose due to the oral formulations of flunixin used for horses. Similarly, carprofen, another veterinary NSAID, was recognised as being misused by humans in the same study by Erramouspe (2002). Although NSAIDs were the most commonly misused drug class identified, carprofen ranked as the third most misused drug within this category (13%). However, no additional reports of flunixin or carprofen misuse were found in the literature. In general, over-the-counter NSAIDs are known with increasing potential for their misuse (Hudson, 2019). This is because of their availability and overuse, the lack of knowledge e.g. taking multiple NSAIDs simultaneously or exceeding the recommended doses, non-adherence to instructions e.g. taking doses sooner than instructed, and self-medication e.g. for pain management (Well, 2019).

Finally, the misuse of a veterinary vitamin supplement containing vitamins A, D, and E for the purpose of enhancing muscle volume served as a primary motivation behind this misuse, with the oily vehicle of the supplement contributing to this effect (Ronsoni et al., 2017). Over a four-month period preceding the case presentation, a parenteral application of 150 mL, containing 20,000,000 IU of vitamin A, 5,000,000 IU of vitamin D3, and 6,800 IU of vitamin E per 100 mL vial, was administered. Despite being restricted for veterinary use only, this vitamin combination is becoming increasingly popular in Brazil due to its non-anabolic classification, easy accessibility, and affordability (Ronsoni et al., 2017). Although not inherently addictive, users may misuse the supplement due to observable physical changes and may develop psychological dependence to achieve fitness goals. Several other studies also document the misuse of the veterinary ADE supplement for bodybuilding purposes (De Francesco Daher et al., 2017; Rocha et al., 2011). However, all reported cases are from South America, and it remains unclear whether similar misuse occurs in the UK.

The findings presented shed light on a concerning trend of increasing misuse of veterinary medications, reflecting a complex interplay of factors driving this phenomenon. While the majority of data primarily focuses on misuse in the US and UK, there are significant reports of carfentanil misuse across Northern Europe (EMCDDA, 2023h). Additionally, the detection of xylazine has extended to Estonia, Latvia, and France (EMCDDA, 2024), demonstrating that this issue is potentially spreading into multiple countries. The accessibility and affordability of these drugs, coupled with lax prescribing oversight, have rendered them attractive to a diverse range of users for various purposes, from recreational use to self-medication and even illicit drug adulteration. However, the underreporting of such instances highlights a significant gap in our understanding of the scope and implications of veterinary drug misuse. Furthermore, the diverse motivations behind this misuse, including recreational, therapeutic, and criminal intents, underscore the need for multifaceted interventions to address this issue effectively. Strengthening monitoring protocols within the veterinary industry and enhancing public awareness and education are crucial steps towards mitigating the risks associated with veterinary drug misuse. Additionally, healthcare professionals must remain vigilant to the unique challenges posed by poly-substance use involving veterinary medications, necessitating the development of targeted treatment and intervention strategies. Ultimately, concerted efforts across multiple sectors are essential to address this emerging public health concern and safeguard both human and animal welfare.

Conclusions

This comprehensive literature review aimed at evaluating the prevalence and motivations underlying the misuse of veterinary medications reveals a troubling trend. Veterinary drugs are increasingly appealing to drug users due to their affordability and ease of access, stemming from less rigorous prescribing oversight. However, despite this surge in usage, instances of veterinary medication misuse remain largely underreported, with scant data available for research. The review revealed various rationales driving this misuse, ranging from recreational use to pain relief, self-medication, suicide, drug-facilitated crimes, pregnancy termination, bodybuilding, and weight loss. Of particular concern is the frequent use of veterinary drugs as adulterants in illicit drug samples, often unclaimed to consumers, leading to unintended exposures and potential health hazards.

There exists an urgent need for veterinary professionals to bolster monitoring protocols for their products, aiming to curtail overdose incidents among staff and associated personnel, while also ensuring that animal owners procure these drugs for legitimate purposes. Concurrently, healthcare practitioners must exercise heightened vigilance regarding the diverse effects that may manifest in emergency room scenarios due to poly-substance use, exacerbated by the lack of necessary antidotes for many veterinary products. To effectively address these challenges, a multi-pronged approach is imperative. This includes bolstering public awareness and education efforts to elucidate the risks associated with veterinary medications. Furthermore, stricter regulatory measures are warranted alongside the development of more robust treatment and intervention strategies to mitigate the burgeoning misuse of these medications.

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Supplementary Information: Table 1 - All articles included within the systematic literature review.

Type of publication	Main Findings	Specifics - illicit indication	Dose	Route	Source	References
Case Study https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4371025/	950mg of a woman's dog's acepromazine was ingested intentionally, resulting in central nervous system and respiratory depression. Her past medical history included depression, anxiety and hypothyroidism.	Potential self-medication to treat anxiety/depression	950mg	Oral	Pet's own prescription	Algren & Ashworth, 2014
Case Study https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9249150/	A 29-year-old male reported misuse of injected 100mg heroin mixed with 15ml veterinary-use pheniramine maleate, 4-5 times a day. Misuse started due to sleep problems and decreasing the dose lead to insomnia, restlessness, and tremulousness. The likelihood for addiction potential is due to stimulation of dopamine. Case report concluded pheniramine has a dependence potential.	Initially misused for sleep problems	100mg heroin with 15ml pheniramine	Parenteral injection	Online Source	Tyagi et al., 2022
Case Study https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7473675/	Myocardial injury is one of the life-threatening complications due to the misuse of clenbuterol. Although used in veterinary medicine, it's misuse has been increasing due to the illegal marketing as a weight loss supplement. There is no reported antidote for clenbuterol misuse.	Anabolic effects for bodybuilding	40mg (dosing frequency unknown. Most commonly dosing regimen in athletes if up to 200mg, 1-3 times daily	Oral	N/A	Moriarty & Attar, 2020

Case Study https://pubmed.ncbi.nlm.nih.gov/18713522/	Discussed 12 clenbuterol cases of intoxication. Heroin was present in 8/12 cases with the remaining 4 cases indicating a history of heroin misuse due to the presence of morphine. Multi-drug use was popular with fentanyl present in 3 cases, cocaine in 4, ethanol and benzodiazepines in 2, and methadone present in 1 case.	Anabolic effects for bodybuilding	Case 1 - 76 ng/mL (Blood) Case 2 - Present (Urine), Trace (Blood) Case 3 - 7.6ng/mL (Blood) Case 4 - Present (Urine), Trace (Blood) Case 5 - Present (Urine), ND (Blood) Case 6 - 10ng/mL (Blood) Case 7 - 5.5ng/mL (decomposition fluid), 12ng/g (Spleen) Case 8 - Present (Urine), ND (Blood) Case 9 - Present (Urine), Trace (Blood) Case 10 - Present (Urine), ND (Blood) Case 11 - Present (Urine), 6.3ng/mL (Blood) Case 12 - Present (Urine), 20ng/mL (Blood)	N/A	N/A	Wingert et al., 2008

Case Study https://onlinelibrary.wiley.com/doi/10.1111/1556-4029.13010	1/3 of Tanax's components, Embutramide, was identified in the urine of a man who murdered his ex-wife, along with alprazolam. The second case study reported a 16-year-old who was hospitalised, where embutramide, drotaverine (antispasmodic) and alprazolam was found. This patient suffered with severe symptoms and was hospitalised 4 more times in the following 4 months due to the same symptoms, being periods of unconsciousness, bradycardia and diplopia.	Suicide attempt (case 1) & general drug misuse (case 2)	2.36 µg/mL (in urine (case 1)) & 2.83µg/mL (in urine (case 2))	Case 1 - N/A Case 2 - Inhaled	Case 1 - User was a veterinarian so had own access Case 2 - N/A	Lajtai et al., 2016
Case Study https://pubmed.ncbi.nlm.nih.gov/29319776/	Veterinary concentrations of vitamin A, D and E were misused and injected into patient's arms twice a month. This veterinary vitamin combination is popular in Brazil due to its availability and low cost, and due to not being classed as an anabolic steroid.	Muscle swelling for body building	150mL of vitamin ADE (20,000,000 IU Vitamin A, 5,000,000 IU Vitamin D3, 6,800 Vitamin E per 100mL vial) in the previous 4 months	Parenteral injection	N/A	Ronsoni et al., 2017
Case Study https://www.sciencedirect.com/science/article/pii/S0735675709000102?via%3Dihub	A 35-year-old veterinarian was hospitalised with movement disorder due to the misuse of Zoletil (Telazol) - a fixed ratio combination of zolazepam (tranquiliser) and tiletamine (anaesthetic). The accessibility of scheduled drugs and health care professionals was highlighted in this case.	To reduce the amount of heroin misused	N/A	N/A	User was a veterinarian so had own access	Lee et al., 2009
Case Study file:///C:/Users/2009986/Downloads/Phenobarbitaltoxicityfromahighlyconcentratedveterinaryformulation-	Case of intoxication of a high concentration of veterinary acquired phenobarbital, complicated by ethanol abuse. The co-ingestion caused significant central nervous system depressants.	Patient had a history of substance misuse	124mcg/mL initial serum concentration (consumption amount unknown)	N/A	User was an assistant horse trainer with access to equine phenobarbital	Alleva et al., 2015

reviewandcasereport%20(1).pdf						
Case Study https://academic.oup.com/jat/article/25/4/245/779255?login=true	The dose of xylazine used for animals ranges from 0.5-5.0mg/kg. A 27-year-old farmer attempted suicide with an ~75mL 2% aqueous solution xylazine by intramuscular injection.	Suicide attempt	75mL 2% aqueous solution	Intramuscular	User was a farmer	Hoffmann et al., 2001
Case Study https://pubmed.ncbi.nlm.nih.gov/12539907/	5 cases of malingering my animal proxy were reported by veterinarians. Case 1 involves a dog noise phobia case in order to receive clorazepate (benzodiazepine) for the owner's use. Case 2 includes a false reporting of malnutrition in a dog to obtain stanozolol. In case 3, the client was seeing multiple veterinary clinics to misuse levothyroxine for weight loss. Case 4 involved falsely reporting a dog's cough to receive opioids. Case 5 involved amitriptyline for the owner to misuse as an antidepressant.	Case 1 - Benzodiazepine (Clorazepate) misuse Case 2 - Anabolic steroid use for body building Case 3 - Levothyroxine misuse for weight loss Case 4 - Opioid (Tobuterol) misuse Case 5 - Self-medication for anxiety using amitriptyline	Case 1 - 7.5mg Case 2 - N/A Case 3 - N/A Case 4 - 7- to 10-day 5mg Case 5 - 30mg every 12 hours for 21 days	Case 1 - Oral Case 2 - N/A Case 3 - N/A Case 4 - Oral Case 5 - Oral	Prescribed from veterinary clinic	LeBourgeois et al., 2002
Case Study https://pubmed.ncbi.nlm.nih.gov/29098704/	Describes three cases where xylazine was used in human poisoning events with criminal intent via drink spiking. This report suggests xylazine should be classified as a controlled drug.	Intentional poisoning with criminal intent	Case 1 - N/A Case 2 - 0.294 µg/mL (urine) & 0.057 µg/mL (serum) Case 3 - 0.533 µg/mL (urine)	Oral ingestion	N/A	Krongvorakul et al., 2017
Case Study https://pubmed.ncbi.nlm.nih.gov/11527235/	A 30-year-old zoo employee, found unresponsive, tested positive for benzodiazepines and cannabinoids and revealed a history of Telazol misuse.	Patient revealed history of Telazol recreational misuse	N/A	Parenteral injection	User was a veterinary worker	Quail et al., 2001

Case Study https://pubmed.ncbi.nlm.nih.gov/10872580/	A 22-year-old male was found dead with 28 needle marks where it was suspected illicit drugs were used. Upon analysis, tiletamine and zolazepam were identified. This drug combination is common in veterinary medicine as an anaesthetic.	N/A	Exact doses unknown Concentration in blood = 0.85mg/L (tiletamine) & 3.3mg/L (zolazepam) Concentration in tissue injection site = 25.2mg/L (tiletamine) & 23.3mg/L (zolazepam)	Parenteral injection	N/A	Chung et al., 2000
Case Study https://pubmed.ncbi.nlm.nih.gov/12670006/	A case study in which xylazine was detected on its own in a suicide by hanging.	Suicide due to history of depression	The detected xylazine concentrations were as follows: 2.3 mg/L in heart blood, 2.9 mg/L in peripheral blood, 6.3 mg/L in bile, 0.01 mg/L in urine, 6.1 mg/kg in the liver, and 7.8 mg/kg in the kidney.	Parenteral injection	User was a veterinary worker	Moore et al., 2003
Case Study https://pubmed.ncbi.nlm.nih.gov/37236142/	The first drug-related death in the UK/Europe associated with Xylazine was reported to the National Programme on Substance Abuse Deaths (NPSAD) on the 31/12/22. Other drugs present in urine/blood samples of the deceased included cocaine, fentanyl, morphine, paracetamol, pregabalin, THC, diazepam, methadone and alcohol.	Illicit drug misuse - also found cocaine, fentanyl, diazepam and alcohol in tissue	Exact dose unknown Blood concentration of xylazine = 38ng/ml and urine = 135ng/ml	N/A	N/A	Rock et al., 2023
Government Article https://www.gov.uk/government/publications/controlled-drugs-list--2/list-of-most-commonly-encountered-drugs-currently-controlled-under-the-misuse-of-drugs-legislation	A compilation of the frequently encountered drugs currently regulated by the misuse of drugs legislation, indicating their classifications under both the Misuse of Drugs Act 1971 and the Misuse of Drugs Regulations 2001.	N/A	N/A	N/A	N/A	Home Office, 2022

Government Report https://www.gov.uk/government/publications/united-kingdom-drug-situation-focal-point-annual-report/uk-drug-situation-2019-summary	The current rate of ketamine use among adults in England and Wales is the highest ever recorded, reaching 0.8%.	N/A	N/A	N/A	N/A	GOV.UK, 2021
Informative poster https://www.avma.org/sites/default/files/2019-11/Opioids_Vet-Shopping-Drug-Diversion_Guide-for-Veterinarians_flyer.pdf	Describes behaviour associated with 'vet shoppers' and ways to minimise drug diversion in a veterinary setting.	N/A	N/A	N/A	N/A	American Veterinary Medical Association, n.d.
Journal Article https://pubmed.ncbi.nlm.nih.gov/27341080/	Reviewed 7 cases of human exposure to the veterinary tiletamine-zolazepam combination. In 6/7 cases, administration was intentional and the use of the drug combination in 5/7 cases was for recreational purposes. It was shown that human misuse of veterinary medications is more prevalent than previously thought. The majority of people who misuse the TZ combo also use or abuse other psychoactive substances.	Case 1 - Recreational use Case 2 - Substitute for heroin Case 3 - To get high Case 4 - N/A Case 5 - To get high Case 6 - Suicidal purposes Case 7 - Recreational use	Case 1 - 200mg-100mg tiletamine, 100mg zolazepam Case 2 - N/A Case 3 - 500mg Case 4 - 875mg tiletamine, 875mg zolazepam Case 5 - 1125mg tiletamine, 1125mg zolazepam (over 9 days) Case 6 - N/A Case 7 - N/A	Case 1 - Injection Case 2 - N/A Case 3 - Ingestion Case 4 - Injection Case 5 - Injection Case 6 - Injection Case 7 - Injection	2/7 patients were veterinarians, 1/7 works in a veterinarian's office, 1/7 is a zoo employee	de la Peña & Cheong, 2016
Journal Article https://pubs.rsc.org/en/content/articlelanding/2023/ay/d3ay00815k#!	Acepromazine poisonings have been reported, including suicide reports and drug-facilitated sexual assaults, however it is difficult to detect due to rapid metabolism.	N/A	N/A	N/A	N/A	de Lima & de Araujo, 2023

Journal Article https://medic.upm.edu.my/upload/dokumen/2022071815362726_MJMHS_1600.pdf	Xylazine can be misused in several ways including as a recreational drug, an adulterant, in drug-facilitated crime/sexual assault and as a source of accidental and intended poisoning.	Recreational drug, adulterant, drug facilitated crime and sexual assault, doping agent in animal sport	N/A	Inhaled/snorted/ injected	N/A	Teoh et al., 2022
Journal Article https://pubmed.ncbi.nlm.nih.gov/20221861/	Levamisole, an anti-parasitic is used as an adulterant in a high percentage of cocaine samples. This may be because it is a bulky white powder, similar to cocaine. Other theories include to increase profit and the idea of levamisole adulterated cocaine effecting the ability to be detected by dogs/analytical methods. It was reported that levamisole was found to affect the endogenous opiate levels, including codeine and morphine.	Adulterant	N/A	N/A	N/A	Wiegand, 2010
Journal Article https://pubmed.ncbi.nlm.nih.gov/33403403/	Currently, there is insufficient information regarding veterinary prescription drug misuse to estimate the severity. 398 veterinarians reported in a study that they suspected 23% of pet owners misuse animal drugs on themselves. A different study found that 13% of veterinarians were conscious of an animal owner that injured their pet to gain opioids, and 12% were aware of staff opioid misuse. Opioid prescribing is increasing in the veterinary setting.	N/A	N/A	N/A	Veterinary setting	Anand & Hosanagar, 2021

Journal Article https://jamanetwork.com/journals/jama/fullarticle/2805530	Xylazine was found in every street opioid sample tested by the Philadelphia Department of Public Health in January 2023. The FDA have issued an import alert, restricting unlawful importation of xylazine, in February 2023. In April 2023, the White House Office of National Drug Control Policy declared xylazine mixed with fentanyl as an "emerging threat to the United States".	N/A	N/A	Injection	Illicit drug supply	Rubin, 2023
Journal Article https://pubmed.ncbi.nlm.nih.gov/20045604/	There is a need for increased awareness of the potential hazards of veterinary medications in humans. The veterinary products with significant health hazards to humans are carfentanil, clenbuterol, ketamine, tilmicosin, testosterone/estradiol, dinoprost and cloprostenol.	N/A	N/A	N/A	N/A	Lust et al., 2011
Journal Article https://pubmed.ncbi.nlm.nih.gov/25404261/	Examined which veterinary compounds are misused in human suicide. The drugs found were veterinary-grade pentobarbital, xylazine, tilmicosin (antibiotic), acepromazine and euthanasia preparations (mebezonium and embutramide).	Pentobarbital - Suicide Acepromazine - Suicide	Lethal blood concentration of 2mg/L of pentobarbital reported, 2500mg acepromazine, 21mg/kg tilmicosin	Parenteral/oral consumption	50% of cases involved either veterinarian/those who had easy access due to their employment. Reports of people with no association with veterinary medicine being able to successfully buy veterinary-	Perrin, 2014

					grade pentobarbital.	
Journal Article https://pubmed.ncbi.nlm.nih.gov/29733092/	In America, veterinarians are a unique source of prescription opioid analgesics as many states do not need to report their prescribing of them. There are no limits on the amounts of opioids veterinarians can prescribe, influencing diversion/misuse. 75% of a sample (of US veterinarians) were aware of working with someone with a substance abuse problem.	N/A	N/A	N/A	Veterinary setting	Russell et al., 2018
Journal Article https://pubmed.ncbi.nlm.nih.gov/12135152/	Analgesic, anti-inflammatory, anti-arthritis, systemic antibiotics and topical corticosteroids were the most frequently reported veterinary drugs misused. Veterinarians stated the most likely reason for veterinary drug misuse include lower cost, convenient availability and the belief that veterinary medications are stronger than comparable human medications.	Low cost and the belief that veterinary medications are stronger than comparable human medications	N/A	N/A	People involved in animal sport, those who work in healthcare	Erramouspe et al., 2002
Journal Article https://pubmed.ncbi.nlm.nih.gov/21481268/	There is a notable gap in the understanding of how xylazine was diverted into the illicit drug market, the specific context of its use, and the chronic health implications associated with its consumption. It was common for consumers in Puerto Rico to be able to control the ratio of heroin:xylazine themselves, as it was usually sold not mixed. 'Speedball' was a mix of heroin, xylazine and cocaine and when sold, each substance was kept separate so the user could tailor to their own liking. Skin ulcers, due to xylazine,	N/A	N/A	Parenteral injection	N/A	Torruella, 2011

	promoted further xylazine use to help manage the pain.					
Journal Article https://www.sciencedirect.com/science/article/pii/S0736467916303547	There were 76 cases of xylazine exposures reported to Texas poison centres between 2000-2014. 93% of patients were over the age of 20 and 54% were male. Injection accounted for 51% of exposures and ingestion for 28%. 64% of exposures were unintentional and 32% were intentional. Drowsiness/lethargy (47%), bradycardia (20%), hypotension (11%), hypertension (9%), puncture/wound (8%) and slurred speech (8%) were the most common clinical effects.	31.6% of exposures were intentional, of which 15.8% were suspected suicide attempt, 13.2% were drug abuse	N/A	Parenteral injection (51.3%), Ingestion (15.8%), Dermal Route (14.5%), Ocular Route (2.6%), Inhalation (2.6%).	N/A	Forrester, 2016
Journal Article https://pubmed.ncbi.nlm.nih.gov/24769343/	From 1966 to 2013, 43 cases of intoxication were reported, of which 51% resulted in fatalities. Of the 22 fatal instances, 17 had xylazine usage as a contributing factor. Males made about 60% of the intoxication cases. In 82% of cases, xylazine deaths were accidental, whereas 9% were suicide-related. Xylazine was employed in 17/18 unintentional occurrences as an adulterant. Parenteral (intramuscular, subcutaneous, and intravenous) administration was the primary mode of delivery. 33% of intoxications were individuals that had easy access to the drug, including veterinarians (and assistants), farmers and horse trainers.	Horse doping agent, a drug of abuse, for attempted sexual assault, as a source of accidental or intended poisonings	Doses to produce toxicity and fatality vary from 40 to 2400ng	Inhaled, intramuscular, intravenous, ocular exposure, oral administration, subcutaneous, self-administration	Individuals who had easy access (veterinarians /farmers/horse trainers)	Ruiz-Colon, 2014

Journal Article https://pubmed.ncbi.nlm.nih.gov/37009344/	Of the 59 documented occurrences of xylazine intoxication, 21 had fatal results; of these, 17 included the combination of xylazine and other substances. 1,200mg was the average fatal dose, 525mg was the average dose in non-fatal cases.	Drug abuse	525mg = non-fatal average dose 1,200 mg = fatal average dose Doses ranged from 40mg-4300mg	Intravenous, subcutaneous, intramuscular, inhalation	N/A	Ayub et al., 2023
Journal Article https://pubmed.ncbi.nlm.nih.gov/35770859/	Every stimulant-containing xylazine-positive case also included an opioid. Stimulants were present in 53% of cases, cannabinoids in 30% and benzodiazepines in 26%. Xylazine's geographic distribution and prevalence grew during the study period.	N/A	450mg (injected) - for one case studied	Injection Inhalation Dermal Exposure Ingestion	N/A	Kacinko et al., 2022
Journal Article https://injuryprevention.bmj.com/content/injuryprev/27/4/395.full.pdf	Between 2010 and 2015, xylazine was found in less than 2% of fatal heroin and/or fentanyl overdose cases; in 2019, it was found in 262 (31%) of the 858 cases of fatal heroin and/or fentanyl overdose. Of the 262 fatal cases, 76% were male. 100% of these fatal cases in 2019 were positive for fentanyl, as well as xylazine.	People stated eurphoric effects lasted longer, like heroin before it was replaced with fentanyl	N/A	Injection	N/A	Johnson et al., 2021
Journal Article https://pubmed.ncbi.nlm.nih.gov/30485426/	In Kentucky, cocaine and methamphetamine were the main controlled substances and levamisole was the most prevalent adulterant detected (17.5%). Xylazine was present as a cutting agent in 4.6% of heroin samples, 11% of fentanyl samples and 2.6% of cocaine samples.	As an adulterant	N/A	N/A	N/A	Fiorentin et al., 2018

Journal Article https://www.sciencedirect.com/science/article/pii/S2772632023000582	In 2023, xylazine addiction has rapidly grown into a global concern and misuse has increased alarmingly. Serious repercussions have been seen in 2023 due to xylazine quickly growing into a global concern. Between 2019-2021, fatal overdoses in New York increased by more than 80%.	Drug of abuse, drug of sexual assault attempt, accidental/ intentional poisoning	N/A	Oral administration, inhaled, sniffed, injected	Online Source	Debnath and Chawla, 2023
Report https://www.cfsre.org/images/content/reports/public_alerts/Medetomidine_Public_Health_Alert__Final.pdf	A toxic adulterant alert sent out in December 2023 due to medetomidine/dexmedetomidine being identified as an adulterant in illicit drug material. Medetomidine (potent veterinary anaesthetic) has frequently been observed in samples containing fentanyl and xylazine and also heroin and cocaine.	N/A	N/A	N/A	N/A	CFSRE, 2023b
Retrospective, Secondary Data Analysis https://pubmed.ncbi.nlm.nih.gov/36504413/	An increase of xylazine deaths in West Virginia have gone from 1% (2019) to 5% (2021). Deaths involving xylazine had more coin toxicants, compared to non-xylazine deaths. 98% of xylazine deaths involved fentanyl. There was a greater history of drug/alcohol use with xylazine decedents.	N/A	N/A	N/A	N/A	Sibbesen et al., 2022
Journal Article https://pubmed.ncbi.nlm.nih.gov/37700329/	Xylazine-related overdoses in the United States have been escalating rapidly and show little indication of decelerating, posing a significant public health crisis. The 'speedball' mixture of heroin, cocaine and xylazine is obtainable for $8. Monthly rates of fentanyl mixed with xylazine overdose deaths increased nearly fourfold (from 2.9% to 10.9%) between January 2019 - June 2022.	N/A	N/A	Injection (84.5%), inhalation (14.1%), smoking (1.4%)	N/A	Zhu, 2023

Report https://www.dea.gov/sites/default/files/2022-12/The%20Growing%20Threat%20of%20Xylazine%20and%20its%20Mixture%20with%20Illicit%20Drugs.pdf	The prevalence of xylazine is increasing although limited scientific research has been conducted on the effects of the drug in the body. The Centre for Disease Control and Prevention does not include xylazine-positive overdose deaths meaning it's prevalence is widely underestimated. A significant jump in xylazine deaths in the US from 2020-2021 has been reported. Northeast US has experienced a 103% increase, South - 1127% increase, Midwest - 516% increase and West - 750% increase.	N/A	N/A	N/A	N/A	DEA, 2022a
Report https://www.cdc.gov/mmwr/volumes/72/wr/mm7226a4.htm	In 21 US jurisdictions, the monthly percentage of deaths involving xylazine in the context of illicitly manufactured fentanyl (IMF) increased by 276%, rising from 2.9% in January 2019 to 10.9% in June 2022.	N/A	N/A	N/A	N/A	CDC, 2023a
Report https://blogs.cdc.gov/nchs/2023/06/30/7408/	Males were at least twice as likely to die from overdoses involving xylazine each year from 2018 to 2021. The highest rate of overdose deaths involving xylazine in 2021 were among the 35-44 age group.	N/A	N/A	N/A	N/A	CDC, 2023b
Report https://www.dea.gov/alert/dea-reports-widespread-threat-fentanyl-mixed-xylazine	Public Safety Alert was announced in November 2022 warning the public of the increasing reports of fentanyl mixed with xylazine, stating that will be the deadliest drug threat the US has ever faced. The Drug Enforcement Administration reported the seizure of xylazine-fentanyl mixture in 48 of 50 states.	N/A	N/A	N/A	N/A	DEA, 2022b

Report https://www.emcdda.europa.eu/publications/european-drug-report/2023/drug-situation-in-europe-up-to-2023_en	Ketamine seizures remain high, often found in MDMA mixtures. The rise of 'Pink cocaine'—ketamine mixed with other synthetics—reflects growing consumer interest.	N/A	N/A	N/A	N/A	EMCDDA, 2023g
Report https://www.emcdda.europa.eu/publications/risk-assessments/ketamine_en	Hospitals, veterinary clinics and pharmaceutical distribution are ways ketamine is diverted for recreational use as sources have concluded the synthesis of ketamine as difficult. 12 deaths where ketamine had been identified occurred between 1987 and 2000. Concerns are present due to the 'near death' experiences and the unpredictability of the drug.	N/A	N/A	N/A	N/A	EMCDDA, 2002
Report https://www.emcdda.europa.eu/publications/data-factsheet/syringe-residues-analysis-data-escape-project_en	Carfentanil was frequently identified in syringes from Vilnius (92%) and Riga (29%). Xylazine was found in 13% of syringes from Riga, often co-occurring with isotonitazene, metonitazene, or carfentanil.	N/A	N/A	N/A	N/A	EMCDDA, 2023h
Report https://www.emcdda.europa.eu/publications/european-drug-report/2023_en	Quantity of ketamine seized and reported to EU Early Warning System remains relatively high in recent years, suggesting it is consistently available in national drug markets, where it has been found in mixtures sold as 'pink cocaine'. A seized mixture in 2022 from Estonia included a mixture of protonitazene, metonitazene and xylazine.	N/A	N/A	N/A	N/A	EMCDDA, 2023b

Report https://www.emcdda.europa.eu/publications/european-drug-report/2023/injecting-drug-use_en	In Riga, Xylazine was found in 13% (25/194) of syringes. It was consistently mixed with isotonitazene or metonitazene in all 25 syringes and co-occurring with carfentil in 3 syringes. Carfentanil was commonly found in syringes from Vilnius (92%) and Riga (29%).	N/A	N/A	N/A	N/A	EMCDDA, 2023a
Report https://www.emcdda.europa.eu/publications/rapid-communication/new-psychoactive-substances-global-markets-glocal-threats-and-covid-19-pandemic_en	In 2019 there was 234 seizures of carfentanil (10044.2g). 17kg of new opioids were seized with 12kg being in the form of powders - 84% was carfentanil. In 2018, the total quantity to be seized was 1.9kg.	N/A	N/A	N/A	N/A	EMCDDA, 2020
Report https://www.emcdda.europa.eu/publications/european-drug-report/2023/harm-reduction_en	Increasing polydrug consumption adds to the challenges of developing effective responses to reduce drug overdose deaths and drug-related poisonings. Mixtures containing novel benzodiazepines, novel opioids and the tranquiliser xylazine, has been reported in Estonia.	N/A	N/A	N/A	N/A	EMCDDA, 2023f
Report https://www.emcdda.europa.eu/publications/european-drug-report/2023/drug-induced-deaths_en	Xylazine was identified in one fatality in 2022.	N/A	N/A	N/A	N/A	EMCDDA, 2023c
Report https://www.emcdda.europa.eu/news/2023/european-drug-report-2023-highlights_en	The increasing diversity in drug supply and usage poses novel challenges for drug policy and healthcare in Europe. The mixtures of novel benzodiazepines and opioids,	N/A	N/A	N/A	N/A	EMCDDA, 2023e

	with xylazine, has the potential to impact European health.					
Report https://www.emcdda.europa.eu/ews25_en	In 2020, approximately 1.2 tonnes of seized material consisted mainly of aryl cyclohexylamines, with ketamine making up the vast majority at 1.1 tonnes (93%). In 2020, carfentanil made up 52% of opioid seizures. Argentina has reported the adulteration of cocaine with carfentanil, leading to deaths and non-fatal poisonings.	N/A	N/A	N/A	N/A	EMCDDA, 2022b
Report https://www.emcdda.europa.eu/publications/risk-assessments/carfentanil_en	Carfentanil is mainly seized as a powder but has been seen as a liquid, although in Europe it is typically administered via intravenous injection. Carfentanil misuse may be under-reported due to not being part of most routine drug screening. There is limited information regarding the dose regimens of carfentanil and the abuse liability in humans.	N/A	N/A	N/A	N/A	EMCDDA, 2018
Report https://www.emcdda.europa.eu/publications/european-drug-report/2023_en	Around 930 new psychoactive substances were being monitored by the EMCDDA by the end of 2022. Ketamine has gained prominence as a preferred drug among certain demographics.	N/A	N/A	N/A	N/A	EMCDDA, 2023d
Report https://www.emcdda.europa.eu/publications/edr/trends-developments/2022_en	Belgium and the Netherlands announced the dismantling of laboratories producing ketamine. 1600 seizures and 240kgs of ketamine was reported by 16 EU countries. 13% of people who used drugs in the last 12 months used ketamine, from the European Web Survey on Drugs.	N/A	N/A	N/A	N/A	EMCDDA, 2022a

Report https://www.emcdda.europa.eu/publications/edr/trends-developments/2021_en	Until 2021, there was inadequate monitoring of ketamine, which restricted the comprehension of its usage and its impact on public health. Denmark reported a last year prevalence of ketamine of 0.6% in 2017, and Romania 0.8% in 2019.	N/A	N/A	N/A	N/A	EMCDDA, 2021
Report https://www.emcdda.europa.eu/publications/joint-reports/carfentanil_en	Until 2017, the EMCDDA had 755 seizures of carfentanil reported by seven Member States. Seizures reported carfentanil was mixed with other opioids or the synthetic cathinone alpha-PHP. 48 deaths were reported to the EMCDDA up until 2017 - 85% were male and 15% female.	N/A	N/A	N/A	N/A	EMCDDA, 2017
Report https://www.wedinos.org/resources/downloads/Annual-Report-22-23-English.pdf	In 2022/2023, ketamine was the 5th most identified psychoactive. Ketamine was the 7th most intended purchased drug but was 6th most common drug identified post analysis. Ketamine was the second most common drug identified (206) from the 1112 samples analysed from 22 Nighttime Economy Venues and 2 festivals. 204 samples of ketamine were submitted during 2021-2022, with 6% of these containing no ketamine. The initial sample of xylazine was received in January 2020, followed by 10 subsequent samples containing xylazine. Among the 9 samples received between April 2022 and March 2023, none were submitted with xylazine listed as the intended purchase.	N/A	N/A	N/A	N/A	WEDINOS, 2023

Report https://www.wedinos.org/resources/downloads/Annual-Report-21-22-English.pdf	Ketamine was the 4th most identified psychoactive substance. 213 samples of ketamine were identified from the 1102 samples from 24 Nighttime Economy Venues and 3 festivals - making it the second most identified substance after cocaine. 160 samples were submitted as ketamine, with 8% containing no ketamine.	N/A	N/A	N/A	N/A	WEDINOS, 2022
Report https://www.wedinos.org/resources/downloads/Annual-Report-20-21-English.pdf	Ketamine was the 3rd most prevalent drug submitted by individuals aged 0-17 years. Ketamine was the 7th most intended purchased drug but was the 10th most common drug identified post analysis.	N/A	N/A	N/A	N/A	WEDINOS, 2021
Report https://www.wedinos.org/resources/downloads/PHILTRE-AR-Eng-19-20.pdf	Ketamine was the 4th most identified psychoactive substance. Ketamine was the 6th most intended purchased drug but the 8th most common identified drug post analysis. From the 1048 samples received from Nighttime Economy and Festivals, ketamine was the 3rd most common drug identified, after cocaine and MDMA.	N/A	N/A	N/A	N/A	WEDINOS, 2020
Report https://www.wedinos.org/resources/downloads/Annual_Report_201819.pdf	Ketamine was the 3rd most prevalent substance identified, after cocaine and MDMA. From the 339 samples identified from Nighttime Economy and Festivals, ketamine was the most prevalent drug.	N/A	N/A	N/A	N/A	WEDINOS, 2019
Report https://www.wedinos.org/resources/downloads/Philtre_Annual_Report_2017-18.pdf	Ketamine was 5th most identified NPS. A sample submitted with intent to be ketamine was identified as beta-hydroxy fentanyl.	N/A	N/A	N/A	N/A	WEDINOS, 2018

Report https://www.wedinos.org/resources/downloads/Philtre_Annual_Report_2016-17.pdf	Ketamine was the 6th most identified NPS. Ketamine bought by users were analysed and sampled to be cocaine or furanylfentanyl.	N/A	N/A	N/A	N/A	WEDINOS, 2017
Report https://www.wedinos.org/resources/downloads/WEDINOS_Annual_Report_2015-16_FINAL.pdf	Ketamine was a new entry and was the 3rd most identified NPS.	N/A	N/A	N/A	N/A	WEDINOS, 2016

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