THE ABUSE AND MISUSE OF PRESCRIPTION AND OVER THE COUNTER DRUGS

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ABSTRACT:

A growing number of reports have surfaced about the recreational abuse of several prescription and over-the-counter (OTC) medicines. Psychoactive pharmaceutical usage and "pharming" are two recent, popular practices that include the recreational use of OTC and prescription medications for non-medical purposes in order to produce psychoactive effects, either alone or in conjunction with other substances.

This article gives a general overview of the subject and focusses on a variety of medications, including over-the-counter medications like loperamide, dextromethorphan, benzydamine, promethazine, chlorphenamine, diphenhydramine, and hyoscine butylbromide and prescription medications like quetiapine, gabapentinoids, Z-drugs, bupropion, and venlafaxine, which have been identified as being misused and diverted or have already been documented in the literature and on websites maintained by drug users that document new trends and experiments in drug abuse.

Pharmacies, psychiatry, public health, and drug control regulations face challenges in light of this quickly evolving drug landscape. Additionally, there has been a change in drug availability and usage patterns, which may be related to the COVID-19 epidemic. This has led to a change in behaviours for both prescription and over-the-counter medications. Healthcare practitioners should be aware of probable diversion of prescription medicines, be able to identify instances of misuse, take into account the risk of polydrug abuse, and take steps to avoid it. Pharmacists should be active in evidence-based initiatives to identify, comprehend, and prevent drug diversion activities as well as the negative impacts of drug usage. They can also prevent and minimise drug addiction.

KEYWORDS: Pharmacists, prescription, drug misuse, over-the-counter, drug abuse.

INTRODUCTION:

The advent of new psychoactive substances (NPSs) and the recreational use of medications have caused an evolution in drug misuse situations in recent years. 1,2,3,4 Prescription drug misuse is a rising health concern that involves not only the hazards associated with the individual medications but also the environment in which they are used (e.g., social situations, mental diagnoses, concurrent consumption of other substances with synergistic effects). 4,5,6,7,8 There has been a noticeable rise in the general population's use of prescription medications recently. Nevertheless, there has been no correlation between this rise and better health. The World Health Organisation (WHO) reports that about 50% of people misuse these medications, which raises morbidity and death rates, and that over 50% of medications are prescribed or delivered improperly globally. 10,11

Data from the United Nations Office on Drugs and Crime (UNODC) indicate that prescription medication abuse and related deaths are becoming more commonplace globally. ^{12,13,14} Healthcare professionals, women, elderly persons, and adolescents and young adults are vulnerable populations more likely to misuse drugs. ¹⁵

Patients can obtain over-the-counter (OTC) medications without a prescription from a doctor. They are often prescribed for a wide variety of mild ailments, such as heartburn, musculoskeletal discomfort, headaches, and colds. ¹⁶

OTC medications have a comforting safety record, but they are not innocuous, and abusing them—that is, taking them for purposes other than those prescribed by a doctor—can result in serious side effects including addiction or even death. Furthermore, improper usage of over-the-counter medications, which happens when these drugs are used for legitimate medical conditions but are administered incorrectly, can have a negative impact on patient outcomes.¹⁷

Since there are no authorised medications or vaccinations for the treatment of COVID-19, the epidemic has had an impact on the use of medications worldwide and the incidence of self-medication, particularly in its early stages. ^{18,19}More precisely, the usage of over-the-counter medications has skyrocketed during the pandemic due to the infection's symptoms, which included fever, headache, exhaustion, and cough. In addition, the availability of over-the-counter medications, anxiety about being sick, and worry about being placed in quarantine might all lead to the use of OTC medications during the pandemic. In addition, people may turn to over-the-counter medications when they are unable to access medical treatment because of financial or practical barriers. ¹⁸

Research has indicated that a variety of cultural, political, and environmental variables impact the use of self-medication to cure or prevent symptoms and illnesses. Self-medication is most frequently used to treat the following medical conditions: headache, joint pain, fever, cold and cough, allergy, heartburn, and diarrhoea. If health literacy is not improved, increased access to medications raises the possibility of abuse. ^{20,21}

PRESCRIPTION DRUGS MISUSE:

Abuse of prescription drugs has emerged as a worrying scourge in modern times. ^{22,23,24}This is particularly true for young people and adolescents, whose use of marijuana has outpaced all other illicit drug usage. ^{25,26}While opioids, benzodiazepines, and stimulants have historically been the focus of attention, other commonly prescribed medications may also be abused, misused, or diverted for non-medical uses. ²⁷Prescription drug use among young individuals is often done for recreational (getting "high"), anxiety or relaxation relief, or academic performance enhancement. ^{5,7,8,28}Drugs can be purchased over the internet, from friends or family, from drug dealers, or directly prescribed by a physician. ^{2,29,30}The frequency of prescription drug usage among young people in the UK is not well-documented nationally, although there are emerging reports that indicate the issue is becoming more widespread. ³¹

EXAMPLES OF MISUSED PRESCRIPTION DRUGS:

1. Quetiapine:

Because of its sedative, relaxing, and anxiolytic properties, quetiapine seems to be the most widely reported second-generation antipsychotic that is abused, according to the literature. 32,33 There have been reports of high rates of quetiapine-related ambulance attendances and emergency department visits. Data from the Drug Abuse Warning Network (DAWN) regarding the frequency of quetiapine-related ED visits among the general US population between 2005 and 2011 showed an increase from 35,581 ED visits to 67,497 ED visits. 34 Similar statistics pertaining to rising rates of ambulance attendances for quetiapine have been documented in Australia. These data have been linked to mental disorders, history of heroin and alcohol usage, and concomitant toxicity from opioid replacement treatment and heroin. 35

Additionally, drug-seeking activities have been noted, including the distribution of illegal drugs and a rise in the availability of quetiapine on the black market. ³⁶Those with a history of substance abuse, mental health patients, prisoners, and opioid addicts are the groups most vulnerable to substance abuse. ^{37,38}Lastly, the intranasal and intravenous administration methods have been explained. ³⁹

2. Gabapentinoids:

The authorised therapies for neuropathic pain syndromes and epilepsy include gabapentin and pregabalin. 40,41,42Both drugs' potential for abuse has been documented more frequently; but, due to pregabalin's increased potency, quicker start of effect, and quick absorption, it is thought to have a larger potential for abuse. Harms associated with both gabapentinoids include death, physical dependency, and a tendency to promote depression of the central nervous system (CNS), particularly when taken in conjunction with opioids and sedatives. Those with previous or ongoing substance use disorders, primarily those who use opioids and other polydrugs, are the main group at risk for addiction. 43,44,45,46Opioid users often misuse pregabalin to self-treat physical pain, to achieve a desired psychoactive effect (e.g. potentiate the effects of heroin/cocaine), and combat opioid withdrawal symptoms. 44,45,47,48

Furthermore, during the past ten years, rates of ambulance attendances associated to pregabalin usage have significantly grown (for example, in Australia, from 0.28 instances per 100,000 population in the first half of 2012 to 3.32 cases per 100,000 in the second half of 2017). Consequently, it was discovered that pregabalin and gabapentin may be abused, become addicted, or cause overdoses. Alaka, and alaka, the Misuse of Drugs Advisory Council recommended that both be classified as Class C substances under the Misuse of Drugs Act 1971 and scheduled as Schedule 3 under the Misuse of Drugs Regulations 2001 to avoid preventing their lawful prescription use. This recommendation came after safety warnings and an increase in deaths associated with their use.

3. Z-Drugs:

The Z-drugs, also known as hypnotic medicines (zolpidem, zaleplon, and zopiclone), were first made available for the short-term treatment of insomnia in the 1980s. ⁴⁰Since they had better pharmacokinetic qualities and receptor selectivity than benzodiazepines, it was thought that they had a safer and more favourable profile. ⁵¹They have strong hypnotic effects that include a decrease in sleep latency and an enhancement in the quality of sleep via increasing the transmission of γ-aminobutyric acid (GABA) at the same GABA-type A receptor as benzodiazepines.

Concerns over their safety have increased recently due to problems with abuse and dependency,^{52,53}sexual assaults aided by drugs and risky sleep-related activities (such as eating, driving, and sleepwalking). Males and young individuals who use high dosage drugs recreationally have been reported to have problematic use of hypnotic substances. They are frequently misused via intravenous or intranasal injection in combination with other legal and illegal substances.⁵⁴

Study participants included long-term users, patients with co-occurring mood/neurotic disorders and SUDs, and elderly patients taking Z-drug hypnotics for insomnia who were unable to reduce the dosages required to control withdrawal symptoms. ^{55,56}Both zolpidem and zopiclone showed the same risk of dependency; however, zopiclone was more relevant in cases of overdose adverse drug reactions and its sale on the illicit market. ^{52,57}Similarly to benzodiazepines, since 2013, Z-drugs have been controlled as Class C and Schedule 4 substances under the Misuse of Drugs Act and Regulations, respectively. ^{58,59}

4. Bupropion:

Bupropion's dopaminergic, stimulant-like properties among antidepressants may account for its potential recreational utility. It is a selective catecholamine (dopamine and noradrenaline) reuptake inhibitor, a type of second-generation antidepressant. It is only authorised as a smoking cessation therapy in the UK. Solding drug bupropion instances were reported to the National Poison Data System (NPDS) over a 14-year period, with "intentional abuse" listed as the classified cause for exposure in cases involving people 13 years of age and older.

Between 2000 and 2012, there was a 75% rise in the prevalence of misuse, with the majority of cases being teenagers and young adults who reported tachycardia, seizures, and agitation/irritability as clinical consequences. There have been reports of persons abusing the substance for recreational purposes by oral, nasal, or intravenous methods in order to get a "high" that is comparable to that of other stimulants, including cocaine. (62,63,64,65,66)

5. Venlafaxine:

A member of the serotonin-norepinephrine reuptake inhibitor class of antidepressants is venlafaxine. ⁴⁰Its reuptake inhibition is linked to its recreational use; at low doses (150 mg/day), it has dose-dependent effects on selective serotonin (5-HT) transmission; at moderate levels (>150 mg/day), it has effects on both 5-HT and norepinephrine systems; and at high doses (>300 mg/day), it has effects on dopamine. ⁶⁷Large doses of venlafaxine may be taken to achieve effects similar to those of amphetamine and ecstasy. It has been reported that euphoria and enhanced sociality coexist with dissociative effects, such as a warped sense of time and "numbness." ^{62,68}It seems that patients having a history of SUD (such as opioid addiction or dependency) were more susceptible to venlafaxine overuse. ^{67,69}

Many overdose occurrences have resulted in fatalities, along with symptoms like tachycardia, seizures, coma, and serotonin syndrome; also, long-term usage has been linked to dependency problems. A retrospective analysis of venlafaxine exposures reported to the NPDS between 2000 and 2016 found that of the total 85,621, there were 752 deliberate venlafaxine exposures; the proportion of these exposures decreased from 107/10,000 in 2000 to 59.3/10,000 in 2016. With a median age of 23, half of the population was female. 90.8% of patients took venlafaxine via ingestion, whereas 4.7% took it by inhalation or intrasal delivery. The most often reported clinical symptoms were agitation (11.5%), sleepiness (20.7%), and tachycardia (33.9%). The authors proposed a number of explanations for the decline in purposeful abuse exposures in the research, including as underreporting or a potential decline in the incidence of venlafaxine misuse when patients switch to other medicines; however, they eliminated changes in venlafaxine prescription trends.

OVER THE COUNTER DRUGS:

Medications that may be acquired over-the-counter (OTC) do not require a prescription. By obtaining over-the-counter (OTC) medications from pharmacies, people can treat their symptoms on their own. For over-the-counter (OTC) pharmaceuticals, there are store brand names, generic names, and brand names (similar to prescription treatments). Generic, store, and brand labels all have the same active components and work on the body in the same way if the concentration of those substances is the same. The most often misused over-the-counter medications are covered in this article along with some of its negative consequences. An extensive range of conditions and symptoms, including pain, colds and coughs, diarrhoea, nausea, and more, are treated using over-the-counter medications. OTC medications are becoming more and more popular since they may be misused at higher-than-recommended dosages and because it's possible to divert them to produce centrally psychoactive effects. OTC medications are used to treat and prevent a wide range of conditions, such as heartburn, headaches, musculoskeletal pain, allergies, and tobacco addiction. To

Prescription drug abuse (i.e., using drugs to get high) includes taking a medicine in a method or dose that is different from what is prescribed, getting a prescription from someone else, even if it is for a valid medical condition like pain, and taking a medication to feel euphoric. Non-medical use of prescription drugs is the term used to describe several kinds of abuse. The three categories of drugs that are most frequently abused are as follows: Opioids are often used to relieve central nervous system [CNS] pain. Stimulants: frequently used to treat attention-deficit hyperactivity disorder, and depressants: used to treat anxiety and sleep disorders, including tranquillizers, sedatives, and hypnotics.⁷³

Over 80% of elderly people (57 to 85 years of age) use one or more prescription medications daily, and over 50% take five or more prescription medications or supplements daily. If you take a prescription medication in a method not recommended by a doctor or if you use it for purposes other than what it was designed to do. The use of medications (and other substances) is riskier in older people than in younger individuals as a result of the high prevalence of many (comorbid) chronic illnesses, age-related changes in medication metabolism as well as the potential for drug interactions. ⁷⁴In addition, a large number of elderly people take nutritional and herbal supplements, over-the-counter medications, and other non-medical drug usage, which may worsen any potential health risks. In addition, a lot of elderly people use nutritional and herbal supplements in addition to over-the-counter medications, which may worsen any side effects from non-prescription drug use. ⁷⁵

Misuse of opioid drugs:

Opioids are medications that work on opioid receptors in the brain and spinal cord to reduce the intensity of pain signals. Additionally, they have an impact on the emotional regulation regions of the brain, which can further reduce the intensity of painful stimuli. For thousands of years, they have been used to treat pain, diarrhoea, and cough. These days, the most prevalent usage of opioids is for the relief of acute pain.⁷⁶

Hyperalgesia, a condition where individuals become more sensitive to pain or their pain worsens as a result of taking opioid medication, affects some people. Crucially, opioids not only reduce pain but also activate brain reward regions, producing a euphoric feeling known as a "high" that may trigger relapses and drug abuse disorders. Overdosing is dangerous because opioids interact with parts of the brain stem that regulate breathing. suffocating from an opioid overdose can occur if the user experiences respiratory suppression to the point of suffocating.

Naloxone can reverse an overdose (and save death) if it is administered promptly. Codeine is usually provided for mild discomfort, while morphine is usually advised for severe pain both before and after surgical procedures. In addition to treating pain, several of these drugs—like codeine and diphenoxylate—are also used to treat severe diarrhoea and coughs. ^{76,77,78}

Effects of Opioids on brain and body:

Opioid receptor proteins on nerve cells in the brain, spinal cord, gastrointestinal tract, and other organs are bonded to by opioids, and this is how they function. These drugs block the transmission of pain signals when they attach to their receptors. Opioids can also result in pleasure because they act on reward-related brain areas, but they can also produce drowsiness, mental confusion, nausea, constipation, and respiratory depression. This is

especially true when taking larger-than-recommended dosages or using them in ways that are not intended.⁷⁹

• Commonly misused CNS depressants:

CNS depressants are drugs that slow down brain activity. This class of drugs includes hypnotics, sedatives, and tranquillizers. They can be used to treat anxiety and sleep issues because of this characteristic.⁸⁰

- I. <u>Benzodiazepines:</u>Benzodiazepines including diazepam, clonazepam, and alprazolam are occasionally used to treat anxiety, acute stress responses, and panic attacks. Clonazepam is also used to treat insomnia and seizure disorders. More sedating benzodiazepines, such triazolam and estazolam, are used to treat short-term sleep problems. In light of the significant potential for tolerance, dependence, or addiction, long-term prescriptions for benzodiazepines are uncommon.
- II. <u>Non-benzodiazepine sleep medications:</u>Z-drugs, such as zolpidem, eszopiclone, and zaleplon, function on the same GABA type A receptors in the brain as benzodiazepines while having a distinct chemical structure. They should be less likely to cause addiction and have fewer side effects than benzodiazepines.
- III. <u>Barbiturates:</u>It is less frequent to utilise medications like mephobarbital, phenobarbital, and pentobarbital sodium to treat anxiety and sleep disorders because of their increased overdose risk when compared to benzodiazepines. Nevertheless, they continue to be used in surgery and seizure management.

• Effects of CNS depressants on the brain and body:

The majority of CNS depressants function by increasing activity at inhibitory neurotransmitter receptors called gamma-aminobutyric acid receptors (GABA). Although CNS depressants function differently in different ways, they all provide a soothing or drowsy effect that is medically helpful for people with anxiety or sleep difficulties because they increase GABA transmission, which increases the inhibition of brain activity. 80

• Consequences of CNS depressant misuse:

Notwithstanding their beneficial medicinal benefits, barbiturates and benzodiazepines should only be taken as directed by a doctor.

Z-drugs, or non-benzodiazepine sleep aids, have not been well examined, although certain signs have led to worries about their potential for abuse. Rapid reduction or cessation of intake may cause dependency and withdrawal symptoms. Since CNS depressants lower brain activity, stopping them suddenly may induce a rebound effect that might lead to seizures or other undesirable effects.

Withdrawal from barbiturates can be lethal, whereas withdrawal from benzodiazepines is rarely deadly, despite the possibility of difficulty. Therefore, anybody thinking about stopping a CNS depressive or going through withdrawal symptoms after stopping one should speak with a doctor or get help right once.⁸⁰

• Misuse of stimulants:

Stimulants increase energy, alertness, and attention in addition to raising blood pressure, heart rate, and respiration. In the past, stimulants have been used to treat a variety of ailments, including obesity, neurological disorders, asthma, and other respiratory issues. These days, stimulants are only used to treat a small number of illnesses, including narcolepsy, ADHD, and occasionally treatment-resistant depression.⁸¹

Effects of stimulants on brain and body:

Dextroamphetamine and methylphenidate are stimulants that affect the brain's monoamine neurotransmitter systems, which include dopamine and norepinephrine. ⁸²The effects of these substances are enhanced by stimulants. These medications' effects on norepinephrine create euphoria via increasing blood pressure, heart rate, blood vessel constriction, blood glucose elevation, breathing tube opening, and dopamine signalling from stimulant usage that is not prescribed. ⁸³

EXAMPLES OF MISUSED OTC DRUGS:

1. <u>Loperamide:</u> A typical anti-diarrhea medication is loperamide, which binds to $\beta\mu$ -opioid receptors in the gastrointestinal tract to increase sphincter tone and decrease peristalsis. ⁶⁷ Loperamide does not produce cross-central opioid effects at therapeutic levels (e.g., 2 mg, with a maximum dosage of 16 mg); nevertheless, at large dosages (e.g., 50–800 mg), it may be misused recreationally to produce a euphoric condition known colloquially as "lope high." ⁸⁴ It might be applied to control and alleviate the symptoms of opioid withdrawal. ^{7,84,85,86}

Loperamide toxicity can have potentially fatal effects on the nervous system, respiratory system, heart, and lungs. It can also cause ventricular dysrhythmias and abnormalities in the electrocardiogram, torsades de pointes, prolonged such as OT. ORS widening. 67,87,88,89,90,91,92,93,94,95 Exposures to loperamide that were reported to the NPDS consistently showed deliberate abuse and misuse. The number of reported exposures increased by 91% between 2010 and 2015, totalling 201 and 383 exposures in each year, respectively. The majority of these instances included the misuse of single-agent loperamide and cardiotoxicity. 96,97

The Food and Drug Administration (FDA) has restricted the size of loperamide packages since September 2019 in an effort to decrease improper usage. 98 There are currently few

pharmacies that control its sale, and there are no laws against buying from non-pharmacy web retailers. Pharmacies that are interested can put procedures in place to limit excessive access and stop damage. Collateral buying, however, may still happen at pharmacies or other retail establishments.⁹⁹

- 2. <u>Dextromethorphan:</u>Several cough and cold medications include dextromethorphan, a semisynthetic morphine derivative and codeine analogue. Dextromethorphan has negligible analgesic and antitussive effects when taken in therapeutic amounts. When taken in large quantities, it blocks N-methyl-D-aspartate receptors, which results in the desired hallucinogenic and dissociative effects for recreational use. A mild to moderate stimulation with restlessness and euphoria (at 100–200 mg doses) to a dissociated state marked by hallucinations, paranoia, perceptual distortions, delusional beliefs, ataxia, and out-of-body experiences (at doses higher than 1,000 mg) are the range of neurobehavioural effects that are dose-related. We call these events "robo-ing," "robo-copping," or "robo-tripping."^{7,100,101,102,103}
- 3. <u>Benzydamine:</u>BZY is used topically to relieve oral and vaginal mucosal inflammations. It has analgesic and antipyretic properties. Misuse of BZY at high doses (i.e., 500–3,000 mg) to achieve stimulant effects on the central nervous system (e.g., euphoria, hyperreactivity, insomnia, abnormal behaviour, and psychotic symptoms, including paranoia and visual hallucinations) has been reported in a number of countries, including Brazil, Italy, Romania, Poland, and Turkey. 104,105,106,107,108,109,110 Problems with BZY diversion might include youth and alcohol/cannabis usage concurrently. 111,112,113

Although the precise chemical process responsible for the intoxicating and strengthening effects of BZY remains unclear, a primary cannabinoid mode of action has been proposed. ^{100,114}Informal self-reports, disseminated through social media and online drug forums, have played a role in the spread of BZY abuse by disseminating details about dosages, preparation methods, and routes of administration from commercial products. They have also offered recommendations for other psychotropic substances that can be used in conjunction with BZY to maximise its positive effects and mitigate its negative ones. ^{111,112,113}

• ANTIHISTAMINE DRUGS:

1. **Promethazine:** Promethazine, a histamine (H)1 receptor antagonist, is frequently used to treat symptoms of the common cold, motion sickness, allergic reactions, and nausea and vomiting. Its misuse potential appears to be connected to its soothing and sedative action, as well as the augmentation of other co-ingested chemicals, such as benzodiazepines and opioids. It is frequently offered with codeine as popular cough suppressants. 114,100,115

Because of its euphoric effects and ease of accessibility, promethazine misuse combined with soft drinks, candies, and in some cases, purple-colored alcohol (also known as "purple drank") has become popular among young people. 116,117,118 Promethazine has been reported to be misused among people with an SUD or opioid dependence as a substitute for another drug (e.g., if the desired drug is unavailable or too costly) or to augment the effects of inadequate opioid dosing (i.e., to delay the onset of opioid withdrawal), despite being preferred to other substances, such as

benzodiazepines, for the treatment of anxiety and sleep disorders in substance-dependent patients. 119,120,121,122

2. <u>Chlorphenamine:</u>Chlorphenamine is a first-generation H1-receptor antagonist that is used as an inexpensive anxiolytic or sleep aid. ¹²³Strong antimuscarinic qualities in chlorphenamine have been linked to euphoric highs that encourage drug abuse and the risk of drug dependence, but in susceptible people (such as those with mental illnesses or those who abuse other drugs concurrently), chlorphenamine abuse may also result in psychotic symptoms. ¹²⁴

When used concurrently with serotoninergic medications or dextromethorphan in cough and cold suppressants, it may result in severe serotonin poisoning. ^{102,125,126,127} There has been one recorded death with the concurrent use of chlorphenamine and an opioid. ¹²⁸ Data gathered from the Texas Poison Centre Network Toxic Exposure Surveillance System have been used to characterise the misuse of chlorphenamine, and it shows that both its intended usage and abuse are on the rise, especially among youth. ¹²⁹

3. <u>Diphenhydramine:</u> Diphenhydramine is an over-the-counter medication that reduces allergy symptoms by acting on peripheral and central H1 receptors, respectively. ¹³⁰A strong competitive antagonist on muscarinic receptors that causes sinus tachycardia, xerostomia, mydriasis, blurred vision, ileus, urine retention, CNS depression, agitation, hyperactivity, or psychosis is one of the many possible mechanisms of action linked to diphenhydramine abuse. ^{102,130}

Diphenhydramine can produce stimulatory effects in children and young adults, such as raised mood, increased activity, and moderate euphoria, instead of the sedating qualities found in adults, when used at high dosages and concurrently with other substances (such as alcohol, cannabis, and stimulants). The mesolimbic pathway's increased dopaminergic neurotransmission is assumed to be the source of rewarding traits and drug-seeking behaviour. There are no instances of at-risk populations where this usage occurs. ^{102,130}

4. Hyoscine Butylbromide: Hyoscine butylbromide, sometimes referred to as scopolamine butylbromide, is an anticholinergic substance produced from plants that is frequently used as an antispasmodic medication. A dosage of at least 10 mg is used as a premedication for anaesthesia, to relieve the symptoms of irritable bowel syndrome, and to regulate spasms of the digestive tract and other smooth muscles. Young people have previously been documented to use and misuse it as a psychoactive drug; they get it via proprietary goods (e.g., Buscopan [Sanofi]). ¹³¹It exerts strong central nervous system (CNS) effects at supratherapeutic dosages (1.2 mg as a single dose; adults should take one to two tablets of 0.3 mg as a single dose). These effects include excitement, euphoria, restlessness, irritability, disorientation, and typical delirium-like states with auditory, visual, and tactile hallucinations, altered mood, insomnia, and cognitive dysfunctions. ^{131,132,133}Although it hasn't been formally reported as an NPS, the European Monitoring Centre for Drugs and Drug Addiction issued an alert warning in 2016 about 17 intoxications with cocaine containing scopolamine. ^{134,135}

ABUSE OF DRUGS DURING THR COVID-19 PANDEMIC

Public health policies have been put to the test by the COVID-19 epidemic because of new worries about drug users and those with SUDs. 136,137 Those who fall into this vulnerable category may also be at risk for psychological comorbidities (such as mood and anxiety disorders, psychoses), physical problems (such as neuropathies, obesity, cardiovascular diseases, and hepatic/renal dysfunctions), homelessness, incarceration, economic hardships, and other socioeconomic problems resulting from drug addiction. 137,138,139,140,141,142 Also affecting the pharma markets is the COVID-19 epidemic. There have been reports of price rises for users on the black market, losses in quality, and shortages of certain medications (such as opioids) at the street level. 137,138,143 These problems, together with a general decline in income, may lead to changes in drug-using habits that are riskier, such the following:

- Use of pharmaceuticals made in the country;
- usage of over-the-counter and prescription medications;
- mixing with less expensive medications (such "street benzos") and synthetic cannabinoids 143

Quarantine, social isolation, and other restrictive measures implemented to curb the spread of COVID-19 impair access to drug services. ^{137,138,139,141,144} Furthermore, community pharmacies are facing difficulties related to a lack of staff, disorganised services, and self-isolation. As a result, there is an urgent need to expand the availability of drug services in order to safeguard vulnerable populations and prevent further strain on the healthcare system. ^{137,141,145}

CONCLUSION:

In comparison to the incidence of acute or chronic disorders and the use of prescription medications, the study population has a relatively high OTC drug consumption rate. OTC drug users are most likely to be members of the non-formal education or university education demographics. Analgesics are the most often used over-the-counter medication category, followed by antitussives and cold remedies. To optimise the use of OTC pharmaceuticals and prevent adverse effects related to inadequate information about their usage, national health policies pertaining to drug use should specifically target these demographics and drug categories.

Global public concern over prescription and over-the-counter drug addiction is growing. Pharmacists and healthcare professionals are facing significant challenges due to the current medication situations, especially in light of the Covid-19 outbreak. It is advised that these medical experts be watchful and devise plans to guarantee continuity of care for drug users and those suffering from drug use disorders, as well as to stop potential medication abuse and diversion.

REFERENCES:

- 1. Graddy R, Buresh ME & Rastegar DA. New and emerging illicit psychoactive substances. *Med Clin North Am* 2018;102(4):697–714.
- 2. Hughes GF, McElnay JC, Hughes CM & McKenna P. Abuse/misuse of non-prescription drugs. *Pharm World Sci* 1999;21(6):251–255.
- 3. Schifano F. Recent changes in drug abuse scenarios: the new/novel psychoactive substances (NPS) phenomenon. *Brain Sci* 2018;13;8(12)pii:E221.
- 4. Schifano F, Chiappini S, Corkery JM & Guirguis A. Abuse of prescription drugs in the context of novel psychoactive substances (NPS): a systematic review. *Brain Sci* 2018;22;8(4)pii:E73.
- 5. Chiappini S & Schifano F. What about "pharming"? Issues regarding the misuse of prescription and over-the-counter drugs. *Brain Sci* 2020;10,736.
- 6. Lessenger JE & Feinberg SD. Abuse of prescription and over-the-counter medications. *J Am Board Fam Med* 2008;21:45–54.
- 7. Levine DA. "Pharming": the abuse of prescription and over-the-counter drugs in teens. *Curr OpinPediatr* 2007;19(3):270–274.
- 8. Wood D. Drug diversion. AustPrescr 2015;38:164–166.
- 9. Esher A., Coutinho T. Uso racional de medicamentos, farmaceuticalização e usos do metilfenidato. *CiênciaSaúdeColetiva*. 2017;**22**:2571–2580.
- 10. WHO: World Health Organization . *The Safety of Medicines in Public Health Programmes: Pharmacovigilance an Essential Tool.* WHO; Geneva, Switzerland: 2006. [(accessed on 1 March 2020)]. Quality Assurance and Safety of Medicines Team.
- 11. Costa C.M.F.N., Silveira M.R., Acurcio F.D.A., Junior A.A.G., Guibu I.A., Costa K.S., Karnikowski M., Soeiro O.M., Leite S.N., Costa E.A., et al. Use of medicines by patients of the primary health care of the Brazilian Unified Health System. *Rev. SaúdePúb.* 2017;**51**:18.
- 12. Advisory Council on the Misuse of Drugs. Diversion and illicit supply of medicines. 2016.
- 13. United Nations Office on Drugs and Crime. The non-medical use of prescription drugs. Policy direction issues. 2011.
- 14. United Nations Office on Drugs and Crime. World drug report 2019. 2019.
- 15. National Institute on Drug Abuse. Drug misuse and addiction. 2020.
- 16. Cooper RJ. Over-the-counter medicine abuse a review of the literature. *J Subst Use*. 2013;18(2):82-107.
- 17. Hughes GF, McElnay JC, Hughes CM, McKenna P. Abuse/misuse of non-prescription drugs. *Pharm World Sci.* 1999;21(6):251-255.
- 18. Quincho-Lopez A, Benites-Ibarra CA, Hilario-Gomez MM, Quijano-Escate R, Taype-Rondan A. Self-medication practices to prevent or manage COVID-19: a systematic review. *PLoS One*. 2021;16(11):e0259317.
- 19. Karlsson P, Nakitanda AO, Löfling L, Cesta CE. Patterns of prescription dispensation and over-the-counter medication sales in Sweden during the COVID-19 pandemic. *PLoS One*. 2021;16(8):e0253944.
- 20. Fereidouni Z., Morandini M.K., Kalyani M.N. Experiences of self-medication among people: A qualitative meta-synthesis. *DARU J. Pharm. Sci.* 2019;**27**:83–89.

21. Doomra R., Goyal A. NSAIDs and self-medication: A serious concern. *J. Fam. Med. Prim. Care.* 2020;**9**:2183–2185.

- 22. Hernandez SH & Nelson LS. Prescription drug abuse: insight into the epidemic. *Clin Pharmacol Ther* 2010;88(3):307–317.
- 23. Lipari RN, Williams M & Van Horn SL. Why do adults misuse prescription drugs? In: The CBHSQ report. Rockville (MD): substance abuse and mental health services administration (US). 2017.
- 24. McCabe SE, Cranford JA & West BT. Trends in prescription drug abuse and dependence, co-occurrence with other substance use disorders, and treatment utilization: results from two national surveys. *Addict Behav* 2008;33(10):1297–1305.
- 25. Fortuna RJ, Robbins BW, Caiola E *et al.* Prescribing of controlled medications to adolescents and young adults in the United States. *Pediatrics* 2010;126(6):1108–1116.
- 26. Kelly BC, Wells BE, Leclair A *et al.* Prescription drug misuse among young adults: looking across youth cultures. *Drug Alcohol Rev* 2013;32(3):288–294.
- 27. D'Souza RS & Eldrige JS. Prescription drug monitoring program. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2020.
- 28. JouanjusE, Guernec G, Lapeyre†• Mestre M & the French Addictovigilance Network. Medical prescriptions falsified by the patients: a 12†• year national monitoring to assess prescription drug diversion. Fundam ClinPharmacol 2018;32(3):306–322.
- 29. Soussan C, Andersson M & Kjellgren A. The diverse reasons for using novel psychoactive substances: a qualitative study of the users' own perspectives. Int J DrugPolicy 2018;52:71–78.
- 30. Sukkar E & Osborne K. Pharmacists can help prevent misuse of prescription drugs by young people. *Pharm J* 2017;298:7902.
- 31. Advisory Council on the Misuse of Drugs. Diversion and illicit supply of medicines. 2016.
- 32. Evoy KE, Teng C, Encarnacion VG *et al.* Comparison of quetiapine abuse and misuse reports to the FDA adverse event reporting system with other second-generation antipsychotics. *Subst Abuse* 2019;13:1178221819844205.
- 33. Klein L, Bangh S & Cole JB. Intentional recreational abuse of quetiapine compared to other second-generation antipsychotics. *West J Emerg Med* 2017;18(2):243–250.
- 34. Mattson ME, Albright VA, Yoon J & Council CL. Emergency department visits involving misuse and abuse of the antipsychotic quetiapine: results from the Drug Abuse Warning Network (DAWN). *Subst Abuse* 2015;9:39–46.
- 35. Heilbronn C, Lloyd B, McElwee P *et al*. Trends in quetiapine use and non-fatal quetiapine-related ambulance attendances. *Drug Alcohol Rev* 2013;32(4):405–411.
- 36. Kim S, Lee G, Kim E *et al*. Quetiapine misuse and abuse: is it an atypical paradigm of drug seeking behavior? *J Res Pharm Pract* 2017;6(1):12–15.
- 37. Chiappini S & Schifano F. Is there a potential of misuse for quetiapine? Literature review and analysis of the European Medicines Agency/European Medicines Agency adverse drug reactions database. *J Clin Psychopharmacol* 2018;38(1):72–79.
- 38. Vento AE, Kotzalidis GD, Cacciotti M *et al.* Quetiapine abuse fourteen years later: where are we now? A systematic review. *Subst Use Misuse* 2020;55(2):304–313.
- 39. Reeves RR & Brister JC. Additional evidence of the abuse potential of quetiapine. *South Med J* 2007;100(8):834–836.

40. Stahl SM & Grady MM. Stahl's Essential Psychopharmacology: Prescriber's Guide. Cambridge: Cambridge University Press; 2017.

- 41. Electronic medicines compendium. Gabapentin 2020.
- 42. Electronic medicines compendium. Pregabalin. 2020.
- 43. Bonnet U &Scherbaum N. How addictive are gabapentin and pregabalin? A systematic review. *EurNeuropsychopharmacol* 2017;27(12):1185–1215.
- 44. Schifano F & Chiappini S. Pregabalin: a range of misuse †related unanswered questions. *CNS Neurosci Ther* 2019;25:659–660.
- 45. Chiappini S & Schifano F. A decade of gabapentinoid misuse: an analysis of the European Medicines Agency's 'suspected adverse drug reactions' database. *CNS Drugs* 2016;30(7):647–654.
- 46. Schifano F. Misuse and abuse of pregabalin and gabapentin: cause for concern? *CNS Drugs* 2014;28(6):491–496.
- 47. Baird CR, Fox P & Colvin LA. Gabapentinoid abuse in order to potentiate the effect of methadone: a survey among substance misusers. *Eur Addict Res* 2014;20(3):115–118.
- 48. Buttram ME & Kurtz SP. Preliminary evidence of pregabalin misuse among prescription and/or illicit opioid (mis)users. *J Psychoactive Drugs* 2020;52(2):172–175.
- 49. Crossin R, Scott D, Arunogiri S *et al.* Pregabalin misuse-related ambulance attendances in Victoria, 2012–2017: characteristics of patients and attendances. *Med J Aust* 2019;210(2):75–79.
- 50. Advisory Council on the Misuse of Drugs. Addendum to advice on the anticonvulsant drugs pregabalin and gabapentin. 2018.
- 51. Gunja N. The clinical and forensic toxicology of Z-drugs. J Med Toxicol 2013;9(2):155–162.
- 52. Schifano F, Napoletano F, Chiappini S *et al.* New emerging psychoactive substances and associated psychopathological consequences. *Psychol Med* 2019;22:1–13.
- 53. Lähteenmäki R, Neuvonen PJ, Puustinen J *et al.* Withdrawal from long-term use of zopiclone, zolpidem and temazepam may improve perceived sleep and quality of life in older adults with primary insomnia. *Basic Clin PharmacolToxicol* 2019;124(3):330–340.
- 54. Hockenhull J, Black JC, Haynes CM *et al.* Nonmedical use of benzodiazepines and Z-drugs in the UK. *Br J Clin Pharmacol* 2020.
- 55. Griffiths RR & Johnson MW. Relative abuse liability of hypnotic drugs: a conceptual framework and algorithm for differentiating among compounds. *J Clin Psychiatry* 2005;66 Suppl 9:31–41.
- 56. Rousselet M, Feuillet F, Gerardin M *et al*. The French addictovigilance network clinical assessment: Z-drugs, true false twins. *Expert Opin Drug Saf* 2017;16(9):1063–1069.
- 57. Jaffe JH, Bloor R, Crome I *et al.* A postmarketing study of relative abuse liability of hypnotic sedative drugs. *Addiction* 2004;99:165–173.
- 58. Advisory Council on the Misuse of Drugs. Advice on the control of Z-drugs (zaleplon, zolpidem and zopiclone). 2013.
- 59. Marsden J, White M, Annand F *et al.* Medicines associated with dependence or withdrawal: a mixed-methods public health review and national database study in England. *Lancet Psychiatry* 2019;6(11):935–950.
- 60. Electronic medicines compendium. Zyban 150mg prolonged release tablets. 2019.

61. Stassinos GL & Klein-Schwartz W. Bupropion "abuse" reported to US poison centers. *J Addict Med* 2016;10(5):357–362.

- 62. Evans EA & Sullivan MA. Abuse and misuse of antidepressants. *Subst Abuse Rehabil* 2014;5:107–120.
- 63. Hu LY, Lu T & Chen YT. Have we underestimated the possibility of bupropion sustained-release addiction? *Aust N Z J Psychiatry* 2016;50,925–926.
- 64. McCormick J. Recreational bupropion abuse in a teenager. *Br J Clin Pharmacol* 2002;53(2):214.
- 65. Reeves RR & Ladner ME. Additional evidence of the abuse potential of bupropion. *J Clin Pyschopharmacol* 2013;33,584–585.
- 66. Stall N, Godwin J& Juurlink D. Bupropion abuse and overdose. CMAJ 2014;186(13):1015.
- 67. Schifano F & Chiappini S. Is there such a thing as a 'lope' dope? Analysis of loperamide-related European Medicines Agency (EMA) pharmacovigilance database reports. *PLoS One* 2018;13(10):e0204443.
- 68. Francesconi G, Orsolini L, Papanti D *et al.* Venlafaxine as the 'baby ecstasy'? Literature overview and analysis of web-based misusers' experiences. *Hum Psychopharmacol* 2015;30: 255–261.
- 69. Namdari B. Venlafaxine abuse in a patient with schizophrenia and prior history of substance dependence: a case report. *J Addict Dis* 2013;32(4):393–395.
- 70. Bosse GM, Spiller HA & Collins AM. A fatal case of venlafaxine overdose. *J Med Toxicol* 2008;4(1):18–20.
- 71. Leonard JB & Klein-Schwartz W. Characterization of intentional-abuse venlafaxine exposures reported to poison control centers in the United States. *Am J Drug Alcohol Abuse* 2019;45(4):421–426.
- 72. OTC introduction= https://en.wikipedia.org/wiki/Over-the-counter_drug.
- 73. Hernandez SH, Nelson LS. Prescription drug abuse: insight into the epidemic. Clin Pharmacol Ther. 2010;88(3):307-317.
- 74. Lipari RN, Williams M, Van Horn SL. Why Do Adults Misuse Prescription Drugs? In: The CBHSQ Report. Rockville (MD): Substance Abuse and Mental Health Services Administration (US); July 27, 2017.1-10.
- 75. McCabe SE, Cranford JA, West BT. Trends in prescription drug abuse and dependence, cooccurrence with other substance use disorders, and treatment utilization: results from two national surveys. Addict Behav. 2008;33(10):1297-1305.
- 76. Substance Abuse and Mental Health Services Administration. COVID-19 and opioid treatment programs. 2020. https://www.samhsa.gov/sites/default/files/sample-otp-covid-19-faqs.pdf (accessed November 2020) ABUSE pharmacist role
- 77. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain— United States, 2016.; 2016. https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm. Accessed September 18, 2018.
- 78. Lee M, Silverman SM, Hansen H, Patel VB, Manchikanti L. A comprehensive review of opioid induced hyperalgesia. Pain Physician. 2011;14(2):145-161.
- 79. Hart C, Ksir C. Drugs, Society, and Human Behavior. 15 edition. New York, NY: McGraw-Hill Education; 2012.

80. Gunja N. The clinical and forensic toxicology of Z-drugs. J Med Toxicol Off J Am Coll Med Toxicol. 2013;9(2):155-162.

- 81. Scammell TE. Narcolepsy. N Engl J Med. 2015;373(27):2654-2662. doi:10.1056/NEJMra1500587
- 82. Santosh PJ, Sattar S, Canagaratnam M. Efficacy and tolerability of pharmacotherapies for attention deficit hyperactivity disorder in adults. CNS Drugs. 2011;25(9):737-763.
- 83. McCabe SE, West BT. Medical and Nonmedical Use of Prescription Stimulants: Results From a National Multicohort Study. J Am Acad Child Adolesc Psychiatry. 2013;52(12):1272-1280.
- 84. Reeves RR, Ladner ME, Perry CL *et al.* Abuse of medications that theoretically are without abuse potential. *South Med J* 2015;108(3):151–157.
- 85. MacDonald R, Heiner J, Villarreal J &Strote J. Loperamide dependence and abuse. *BMJ Case Rep* 2015;2015:bcr2015209705.
- 86. Powell JW & Presnell SE. Loperamide as a potential drug of abuse and misuse: fatal overdoses at the Medical University of South Carolina. *J Forensic Sci* 2019;64(6):1726–1730.
- 87. Ali M, Mujahid A, Bulathsinghala CP & Surani S. Cardiac arrhythmia secondary to loperamide abuse and toxicity. *Cureus* 2020;12(2):e6936.
- 88. Antoniou T & Juurlink DN. Loperamide abuse. CMAJ 2017;189(23):E803.
- 89. Atoot A, Sholem S, Khaddash I & Zuberi J. Transient brugada pattern induced by loperamide abuse. *Cureus* 2020;12(5):e8037.
- 90. Katz KD, Cannon RD, Cook MD *et al*. Loperamide-induced torsades de pointes: a case series. *J Emerg Med* 2017;53(3):339–344.
- 91. Marraffa JM, Holland MG, Sullivan RW *et al.* Cardiac conduction disturbance after loperamide abuse. *Clin Toxicol (Phila)* 2014;52(9):952–957.
- 92. Nattel S. An emerging malignant arrhythmia epidemic due to loperamide abuse: underlying mechanisms and clinical relevance. *JACC Clin Electrophysiol* 2016;2(7):790–792.
- 93. Rasla S, Parikh P, Hoffmeister P *et al*. Unexpected serious cardiac arrhythmias in the setting of loperamide abuse. *R I Med J* (2013). 2017;100(4):33–36.
- 94. Stefek B, Wolfe LT & Cohen M. Brugada syndrome associated with adolescent loperamide abuse. *Pediatrics* 2018;142(4):e20181423.
- 95. Wightman RS, Hoffman RS, Howland MA *et al*. Not your regular high: cardiac dysrhythmias caused by loperamide. *Clin Toxicol (Phila)* 2016;54(5):454–458.
- 96. Vakkalanka JP, Charlton NP & Holstege CP. Epidemiologic trends in loperamide abuse and misuse. *Ann Emerg Med* 2017;69(1):73–78.
- 97. Eggleston W, Marraffa JM, Stork CM *et al.* Notes from the field: cardiac dysrhythmias after loperamide abuse New York, 2008–2016. *MMWR Morb Mortal Wkly Rep* 2016;65(45):1276–1277.
- 98. Food and Drug Administration. FDA limits packaging for anti-diarrhea medicine loperamide (Imodium) to encourage safe use. 2019.
- 99. Feldman R & Everton E. National assessment of pharmacist awareness of loperamide abuse and ability to restrict sale if abuse is suspected. *J Am Pharm Assoc*. 2020;S1544–3191(20)30264-8.

100. Zaprutko T, Koligat D, Michalak M et al. Misuse of OTC drugs in Poland. Health Policy 2016;120(8):875–881.

- 101. Martinak B, Bolis RA, Black JR *et al.* Dextromethorphan in cough syrup: the poor man's psychosis. *Psychopharmacol Bull* 2017;47(4):59–63.
- 102. Sansgiry SS, Bhansali AH, Bapat SS & Xu Q. Abuse of over-the-counter medicines: a pharmacist's perspective. *Integr Pharm Res Pract*. 2017;6:1–6.
- 103. Schwartz RH. Adolescent abuse of dextromethorphan. *Clin Pediatr* (*Phila*) 2005;44(7):565–568.
- 104. Acar YA, Kalkan M, Cetin R *et al.* Acute psychotic symptoms due to benzydamine hydrochloride abuse with alcohol. *Case Rep Psychiatry* 2014;290365.
- 105. Anand JS, Lukasik-GlÄTMbocka M & Korolkiewicz RP. Recreational abuse with benzydamine hydrochloride (tantum rosa). *Clin Toxicol* 2007;45(2):198–199.
- 106. Ballesteros S, Ramón MF &MartÃnez-Arrieta R. Ingestions of benzydamine-containing vaginal preparations. *Clin Toxicol (Phila)* 2009;47(2):145–149.
- 107. Can B, Oz I, Ozer H & Simsek T. Hallucinations after ingesting a high dose of benzydamine hydrochloride. *Clin PsychopharmacolNeurosci* 2016;14(4):407–408.
- 108. Doğan M, Yılmaz C, Çaksen H & Güven AS. A case of benzydamineHCL intoxication. *East J Med* 2006;11(1):26–28.
- 109. Gürü M, Åžafak Y, Cengiz GF & Kuru E, Örsel S. Chronic psychosis related to benzydamine hydrochloride abuse. *Neurocase* 2019;25(3–4):156–158.
- 110. Rotolo MC, Pellegrini M, Solimini R *et al.* 'Smart drugs', the new drugs on the web: two cases of acute intoxication. *Biochim Clin* 2014;38(3):268–271.
- 111. Opaleye ES, Noto AR, Sanchez Zv *et al.* Recreational use of benzydamine as a hallucinogen among street youth in Brazil. *Braz J Psychiatry* 2009;31(3):208–213.
- 112. Opaleye ES, Sanchez ZM, Moura YG *et al.* An anti-inflammatory as a recreational drug in Brazil. *Addiction* 2011;106(1):225.
- 113. Schifano F, Corazza O, Marchi A *et al*. Analysis of online reports on the potential misuse of benzidamine. *RivPsichiatr* 2013;48(3):182–186.
- 114. Avvisati R, Meringolo M, Stendardo E *et al*. Intravenous self-administration of benzydamine, a non-steroidal anti-inflammatory drug with a central cannabinoidergic mechanism of action. *Addict Biol* 2018;23(2):610–619.
- 115. Jensen LL, RÃ, msing J & Dalhoff K. A Danish survey of antihistamine use and poisoning patterns. *Basic Clin Pharmacol* 2017;120:64–70.
- 116. Tsay ME, Procopio G, Anderson BD & Klein-Schwartz W. Abuse and intentional misuse of promethazine reported to US poison centers: 2002 to 2012. *J Addict Med* 2015;9(3):233–237.
- 117. Burns JM & Boyer EW. Antitussives and substance abuse. *Subst Abuse Rehabil* 2013;4:75–82.
- 118. Agnich LE, Stogner JM, Miller BL & Marcum CD. Purple drank prevalence and characteristics of misusers of codeine cough syrup mixtures. *Addict Behav* 2013;38(9):2445–2449.
- 119. Miuli A, Stigliano G, Lalli A *et al.* "Purple drank" (codeine and promethazine cough syrup): a systematic review of a social phenomenon with medical implications. *J Psychoactive Drugs* 2020;1–10.

120. Chiappini S, Corkery JM, Schifano F & Guirguis A. Beyond the purple drank. Study of promethazine abuse according to the European Medicines Agency (EMA) adverse drug reactions (ADR) reports. *J Psychopharmacol* 2020; In press.

- 121. Clatts M, Giang Le M, Goldsamt L & Colón-López V. Nonmedical use of promethazine hydrochloride among heroin injectors in Vietnam: unrecognized risks and unintended consequences. *Subst Use Misuse* 2010;45(4):515–527.
- 122. Lynch KL, Shapiro BJ, Coffa D *et al.* Promethazine use among chronic pain patients. *Drug Alcohol Depend* 2015;150:92–97.
- 123. Shapiro BJ, Lynch KL, Toochinda T *et al.* Promethazine misuse among methadone maintenance patients and community-based injection drug users. *J Addict Med* 2013;7(2):96–101.
- 124. Cooper RJ. Over-the-counter medicine abuse: a review of the literature. *J Subst Use* 2013;18(2):82–107.
- 125. Banerji S & Anderson IB. Abuse of coricidin HBP cough & cold tablets: episodes recorded by a poison center. *Am J Health Syst Pharm* 2001;58(19):1811–1814.
- 126. Dickerson DL, Schaepper MA, Peterson MD & Ashworth MD. Coricidin HBP abuse: patient characteristics and psychiatric manifestations as recorded in an inpatient psychiatric unit. *J Addict Dis* 2008;27(1):25–32.
- 127. Kirages TJ, Sulé HP &Mycyk MB. Severe manifestations of coricidin intoxication. *Am J Emerg Med* 2003;21(6):473–475.
- 128. Monte AA, Chuang R &Bodme M. Dextromethorphan, chlorphenamine and serotonin toxicity: case report and systematic literature review. *Br J Clin Pharmacol* 2010;70:6:794–798.
- 129. Kinoshita H, Tanaka N, Jamal M *et al.* A fatal case due to cough syrup abuse. *Soud Lek* 2012;57(4):69–70.
- 130. Baker SD & Borys DJ. A possible trend suggesting increased abuse from coricidin exposures reported to the Texas Poison Network: comparing 1998 to 1999. *Vet Hum Toxicol* 2002;44(3):169–171.
- 131. Saran JS, Barbano RL, Schult R *et al*. Chronic diphenhydramine abuse and withdrawal. A diagnostic challenge. *Neurol Clin Pract* 2017;7(5):439–441.
- 132. Kummer S, Rickert A, Daldrup T & Mayatepek E. Abuse of the over-the-counter antispasmodic butylscopolamine for the home synthesis of psychoactive scopolamine. *Eur J Pediatr* 2016;175(7):1019–1021.
- 133. Jalali F, Afshari R & Babaei A. Smoking crushed hyoscine/scopolamine tablets as drug abuse. *Subst Use Misuse* 2014;49(7):793–797.
- 134. Cheng SW, Hu WH, Hung DZ & Yang DY. Anticholinergic poisoning from a large dose of Scopolia extract. *Vet Hum Toxicol* 2002;44(4):222–223.
- 135. Ham S, Tae KK, Kim K *et al.* Drug abuse and psychosis: new insights into drug-induced psychosis. *Exp Neurobiol* 2017;26(1):11–24.
- 136. Lakstygal AM, Kolesnikova TO, Khatsko SL *et al.* DARK classics in chemical neuroscience: atropine, scopolamine, and other anticholinergic deliriant hallucinogens. *ACS Chem Neurosci* 2019;10(5):2144–2159.
- 137. Enforcement Administration. COVID-19 information page. 2020.

138. European Monitoring Centre for Drug and Drug Addiction. The implications of COVID-19 for people who use drugs (PWUD) and drug service providers. 2020.

- 139. Chiappini S, Guirguis A, John A *et al.* COVID-19: the hidden impact on mental health and drug addiction. *Front Psychiatry* 2020;11:767.
- 140. Department of Health and Social Care and Public Health England. COVID-19: guidance for commissioners and providers of services for people who use drugs or alcohol. 2020.
- 141. Pfefferbaum B & North CS. Mental health and the covid-19 pandemic. *NEJM* 2020;383(6):510–512.
- 142. Volkow ND. Collision of the COVID-19 and addiction epidemics. *Ann Intern Med* 2020.
- 143. Zhu S, Wu Y, Zhu CY *et al*. The immediate mental health impacts of the COVID-19 pandemic among people with or without quarantine managements. *Brain BehavImmun* 2020;pii:S0889–1591(20)30601-2.
- 144. United Nations. COVID-19 causes some illegal drug prices to surge, as supplies are disrupted worldwide. 2020.
- 145. Volkow ND. Coping with the collision of public health crises: COVID-19 and substance use disorders. 2020.
- 146. Green TC, Bratberg J & Finnell DS. Opioid use disorder and the COVID 19 pandemic: a call to sustain regulatory easements and further expand access to treatment. *Subst Abus* 2020;41(2):147–149.