Briefing Paper

Treatment, prevention and harm reduction interventions for different forms of ATS use

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List of Acronyms

4-FA	4-Fluoroamphetamine ($C_9H_{12}FN$), also known as para-fluoroamphetamine (PFA)
4-MA	4-Methylamphetamine ($C_{10}H_{15}N$)
ADHD	Attention Deficit Hyperactivity Disorder
ATS	Amphetamine Type Stimulants
ATTUNE study	Understanding Pathways to Stimulant Use: a mixed-methods examination of the individual, social and cultural factors shaping illicit stimulant use across Europe
CDU	Currently Dependent User
CNU	Non-dependent Current frequent User
EMCDDA	The European Monitoring Centre for Drugs and Drug Addiction
EU	European Union
FDU	Formerly Dependent User
FFU	Formerly Frequent User
MDA	3,4-Methylenedioxyamphetamine ($C_{10}H_{13}NO_2$), also known as sassafras or sass
MDAI	5,6-methylenedioxy-2-aminoindane ($C_{10}H_{11}NO_2$)
MDMA	3,4-Methylenedioxymethamphetamine ($C_{11}H_{15}NO_2$), also known as ecstasy
NFU	Non-Frequent Users
NPS	New Psychoactive Substances
NU	Exposed Non-User
PFA	Para-fluoroamphetamine, also known as 4-Fluoroamphetamine (4-FA)
PMA	Paramethoxyamphetamine ($C_{10}H_{15}NO$)
PTSD	Post-Traumatic Stress Disorder
STI	Sexually Transmitted Infection
UK	United Kingdom of Great Britain and Northern Ireland

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Introduction

Amphetamine-Type Stimulants (ATS) are the second most commonly used illicit drugs worldwide as well as in Europe (1,2). In Europe, the highest last-year prevalence for amphetamine use among young adults aged 15-34 years is found in Germany (2.9%) and for MDMA in the Netherlands (6.9%) (1). Methamphetamine has been a main drug of use for over four decades in the Czech Republic, and increasing use has been reported in Cyprus, (eastern) Germany, Slovakia and Spain, as well as in parts of Northern Europe (3).

Long term ATS use can lead to physical (4,5), mental (6) and social (7) harms, including (psychological) dependence (8,9). Harms may include cardiovascular complications, neurological damage, liver damage and intoxication (10) and memory impairment (11). Mental health issues, such as induced paranoia and psychosis (12), as well as sleep disorders, depressed mood and persistent anxiety (13) are also reported by ATS users. Besides, people who use ATS are more likely than those who use opioids to engage in risky sexual activities, increasing their risk for contracting various sexually transmitted infections (STIs) (7).

No single intervention can address the variety of issues experienced by people who use ATS. Any comprehensive package needs to consider the specificity of different ATS substances and patterns of use. Contextual variations, such as social, cultural, and legal aspects, also define the type and feasibility of interventions.

Despite the increasing use of ATS and the specificities related to these substances, most interventions directed to prevent, treat or reduce the harms of illicit drug use currently focus on (injected) opioids (14,15). Yet people who use ATS usually do not identify with (problematic) opioid use, often belong to different user networks and do not perceive opioid-focused services as relevant to them (16). They are likely to develop different trajectories of drug use, face different drug-related harms, and have different needs than those using opioids, thus requiring specific or adapted services (17).

This policy brief aims at contributing to the reduction of the harms of ATS use by describing different trajectories of ATS use and offering a set of evidence-based interventions for different groups of ATS users. The different ATS trajectories are based on qualitative findings of large multinational research, the ATTUNE study, conducted between February and August 2017 in five European countries – the Netherlands, UK, Germany, Poland and the Czech Republic. The evidence-based interventions recommended in this brief are based on a literature review. In this document, we combine both ATS trajectories and interventions from previous studies/programmes to propose tailor-made recommendations for peop-

le who use ATS and those providing services to them. The following sections in this brief describe:

1. The different types of ATS and the context of their use in Europe;
2. The various ATS use trajectories that ATTUNE study participants have experienced;
3. A set of evidence-based interventions to prevent, treat and reduce the harms caused by ATS use; and,
4. Recommendations for policymakers, practitioners and others working with drug-related services.

ATS types and use in Europe

Amphetamine-type substances (ATS) are a group composed of synthetic stimulants. All ATS have an amphetamine base, but each ATS type has specific characteristics and effects. Their occurrence varies in the different regions and countries of Europe:

Amphetamine

Also called speed, amphetamine is a central nervous system stimulant, as are all other forms of ATS. Amphetamine generally comes in the form of a white or yellow powder but can also come in tablet form. It can generally be swallowed, snorted or injected.

Amphetamine is the most prevalent form of ATS used in Western and Central Europe. Since 2009, its use has been relatively stable in most countries of this region, except in Germany and the Netherlands which have reported an increase (2). Long-term and injecting amphetamine use have, historically, been most evident in northern European countries (1). The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) estimates that 12.3 million adults in the European Union (EU) (aged 15-64 years) have used amphetamines at least once in their lifetime (1).

Methamphetamine

Also called crystal meth, ice, crystal, meth, shabu or Tina. It is similar to amphetamine in its structure but is more potent and has, in general, longer effects. It is available in the form of crystalline hydrochloride, formulated tablets, and powder (18) and it can be taken orally, intranasal, through inhalation, smoked as a vapour or injected.

The Czech Republic is the only country in Europe where methamphetamine has been a main drug of use for over four decades (19). Nevertheless, increasing use of the drug has also been reported in countries such as Cyprus, (eastern) France, Germany, Slovakia, Spain and Turkey, as well as in parts of Northern Europe (3). Use of methamphetamine is reported as rising especially among people who practice chemsex (1).

Amphetamine-like NPS

New Psychoactive Substances (NPS) can include stimulants, depressants and hallucinogen substances. Stimulants make up the biggest group (36%) of all NPS (2). Examples of amphetamine-like NPS include synthetic cathinones (such as mephedrone, methylone, methedrone, butylone, MDAI,

buphedrone, and flephedrone), 4-FA, 4-MA, MDA and PMA (20). These drugs can be administered orally, rectally, intramuscularly, intravenously, or by inhalation (21). Synthetic cathinones are the largest group of stimulant NPS reported to the EU early warning system (1). NPS are sometimes preferred by users to more traditional drugs due to their "legal" status.

Amphetamine-type prescription drugs

Since the 1920s, amphetamine has been used as a legal prescription to treat asthma, depression, and to combat fatigue in soldiers during the World War II. Restrictions were enforced in the 1970s, allowing amphetamine in certain medicines. Nowadays, amphetamines and amphetamine derivatives are used in the treatment of narcolepsy (a sleep disorder) and attention deficit hyperactivity disorder (ADHD) (3). Medical use of amphetamines and amphetamine derivatives (such as Ritalin) has increased steadily over the past decade, yet nonmedical use of these substances has also increased, especially among university students (22). Motives for nonmedical use of prescription stimulants generally include improved concentration and to perform better at university (23).

MDMA

Also known as ecstasy, MDMA is a popular recreational drug particularly associated with nightlife and dance settings. MDMA is traditionally available in pills but, since 2010, its forms have diversified to include high-purity powder and crystals, also commonly used in Europe. MDMA is usually ingested orally and its use is relatively higher among younger people (2). In the past, MDMA has been used as a psychotherapeutic drug to improve communication and helping to achieve greater insights (24). Nowadays, the use of MDMA in a therapeutic setting has been increasingly debated and studied (25–27).

An estimated 13.6 million people, or 4.1% of adults (aged 15-64 years) in the European Union have used MDMA at least once in their lifetime. In Europe, the prevalence of past-year use of ecstasy is higher in Western and Central Europe (0.8%) (2). The higher estimates are in the Netherlands where 6.9% of the adult population have ever used MDMA (1). Both the Netherlands and the United Kingdom reported a decreasing trend of MDMA use in the last year, while Germany has reported an increasing trend (2).

ATS trajectories

The types of harms faced by people who use ATS can vary by the type of ATS substance, the context whereby drug use takes place, and personal characteristics. These will also lead to different trajectories of ATS use. There are four key phases in drug use trajectories: initiation, continuation, increase/relapse and decrease/abstinence (28).-In each phase, individual, social and environmental influences may shape the entrance to, continuation of, or exit from, the phase (28). The ATTUNE study aimed at mapping different trajectories and the factors influencing them through the targeting of six different groups of people who use(d) ATS:

1. Currently dependent[1] users (CDU);
2. Formerly dependent users (FDU);
3. Non-dependent current[2] frequent[3] users (CNU);
4. Formerly frequent users (FFU);
5. Non-frequent users (NFU); and,
6. Exposed non-users (NU)[4].

A total of 279 people who use(d) ATS were interviewed in the Czech Republic, Germany, the Netherlands, Poland and the UK. To better focus on ATS, people reporting to have an opioid dependence were excluded from the study. Only people of 18 years of age and above were included. Each of the boxes below describe a fictitious person, representing common stories of the different people within each ATS trajectory according to the experiences reported by ATTUNE participants.

GROUP 1
Currently dependent users (CDU)

Bob is 32 years old. He grew up in a small village with both his parents and his brother. His youth was quite average but he dropped out of school when he was 16 as he had difficulties with concentration and he preferred handing out with his peers. He lives with room-mates in a big city and since he lost his job in a convenience store some months ago, he has been on welfare. He uses amphetamine almost daily, usually by 'bombing' it after he wakes up. That kickstarts his day and gives him some energy and motivation to do his daily household chores. It also helps him to feel less depressed. He started using ATS when he was 16. He first initiated ecstasy use in a club but, soon thereafter, discovered he preferred the effects that amphetamine gave him. As he partied more often with peers, his use increased from monthly to weekly rather fast, and in the first years of his ATS career, weekends of 3 days in a row partying and using drugs were common. Soon, his social network, including on-and-off romantic partners, consisted mainly of other frequent speed users, and that remained unchanged. They often use speed together, combined with large amounts of alcohol. Side effects of his speed use includes memory loss, troubles with his daily functioning and sleep problems. To sleep easier, he usually smokes cannabis before he goes to bed. Bob went into treatment once, mainly out of financial debts that he wanted to deal with. He managed to quit using speed for some time, but relapsed.

1 Dependence on ATS was assessed using the severity of dependence scale (GOSSOP, et al., 1995) with the recommended cut-off for ATS of ≥ 4 points (Bruno, et al., 2009).
2 Current use referred to ATS use in the past 12 months.
3 Frequent use was defined as > 10 consumption days in 12 months.
4 Exposure to ATS use was operationalised as having opportunities to take ATS due to being present when peers, partners, and/or family members were using ATS.

GROUP 2
Formerly dependent users (FDU)

Carl came out of treatment for his speed and alcohol dependence a year ago. He is 33 years old and it was the third time he had been in treatment, yet this time he feels he succeeded better as it gave him new insights into his reasons for use. While it started recreationally when he was 18, generally at home with peers, he now recognises that his ATS use was also driven by the desire to forget his problems and as a way of coping with difficult situations and emotions in his life. His parents divorced when he was 15 and the years beforehand were characterised by many fights. He didn't see his father often between the age of 15 and 20 and entered the squat scene after finishing school. There he lived with many ATS users, including some who dealt drugs, and his use increased rapidly to (almost) daily. That negatively impacted his daily functioning in different areas such as social relationships and work; he experienced difficulties getting out of bed, feelings of depression and sometimes paranoid. At a certain point he realised he had lost control, but his ATS-using environment made it difficult for him to decrease or quit using ATS, and his mental health went downhill. The turning point was when a friend of his suddenly died, making him realise that he wanted to change and feel better about himself. During the last treatment sessions, he made specific plans to reorganise his daily life, including steps to move to his own place and change his social network. He has used ATS a few times in the past year and is not sure he will never use again, but no longer feels dependent on it.

GROUP 3
Currently frequent non-dependent ATS users (CFU)

Mia is 29 years old and a true party animal. She is always game for a fun night and known for being the last to leave a party. Her perfect night combines friends with music, dancing and meeting new people. She likes a drink, but prefers ATS to make a night out even better. Depending on the context, she commonly starts the night with ecstasy, which she takes to feel energetic, talkative and happy. During the night, she takes some speed or cocaine to refresh her energy and ends with cannabis to come down. Since she tried ATS for the first time when she was almost 19, she tries to stick to the informal rule of using not more than every 6 weeks, but not always successfully. Most of her friends also go out a lot and use ATS quite frequently. They take into account 'suicide Tuesday' by not planning much on that day, eating healthy and going to bed early after ATS use. She is a part-time student and works three days a week in a café. She sometimes skips a class if her hangover is very bad. She tried Ritalin a few times to focus on a study assignment but it wasn't her thing. She lives in a student house with 7 others and goes to her parents for the weekend once a month. While she is, and always has been, on good terms with them, they are not aware of her party lifestyle and she prefers to keep it that way. While she is quite open about her drug use and has mentioned it once, she doesn't feel like it is something to share with her parents.

GROUP 4

Formerly frequent non-dependent ATS users (FFU)

Adam is 32 years old. He lives with a partner and their 2-year-old son in a medium-sized city. He grew up as an only child and his parents divorced when he was 8 years old. He was 17 when he initiated ATS use which was at a party with a friend who had used ecstasy several times before. His friend offered it to him, he was curious and took it. He had a great night dancing and socialising. Since then, his ATS use increased and, on average, he used ATS every six-to-eight weeks at parties and festivals, mainly ecstasy but sometimes also amphetamine and NPS. At one of those parties, he met his current partner and they also used ATS together. His use has varied a bit over the years, usually using more in summer than in winter. After finishing his studies, he found a job he liked and strived for promotion. Simultaneously, his use decreased slowly but steadily as he partied less often and more frequently associated with colleagues from work who happened to be non-ATS users. Also, the effects of ATS began to wear off and the side effects no longer outweighed the positive effects it used to bring him. Since his son was born, his lifestyle changed somewhat as it became more concentrated on his family. When meeting with his friends, he now usually likes to talk instead of dance together. He hasn't used ATS since, and while he doesn't want to pledge that he will never use it anymore, he hasn't felt the need to use again.

GROUP 5

Non-frequent ATS users (currently and formerly) (NFU)

Tom works full-time as a social worker and is 31 years old. He lives alone in a small city not far from his parents. In his leisure time he likes to play football, go to a café with friends and or just chill at home and watch tv series. When he was 19, he and his best friend bought ecstasy from a dealer and, after searching for information on the internet, they tried it at home. He found the effects mediocre; but when, some years later, he took it again at a festival, he had a great time, feeling sociable, talkative and secure. Since then, he uses drugs irregularly, generally ecstasy twice a year and magic mushrooms once a year. The effects of ATS are varying, sometimes positive but he also had some negative experiences where he felt anxious, almost panicky and uncomfortable, waiting for the effects to diminish. In addition, he finds the side effects quite tough as he usually needs a week to get back on track, making it difficult to combine it with his job and responsibilities. Therefore, he keeps his drug use to special occasions.

GROUP 6
Exposed non ATS users (NU)

Eva is a 29-year-old female. She grew up with loving parents and a younger sister in a village close to a big city. She was a fast learner and finished her studies some years ago. After that, she started working as a teacher. She lives on her own and is single. She spends her leisure time mainly by going out for dinner and drinks with her friends. She has both ATS-using and non-using friends. When clubbing, some of them use ATS and they have offered it to her several times to try. However, she's never been interested, and while her peers usually seem to enjoy the effects, she refrains from it. She likes to stay in control and you never know how the effects will work out. For a year she dated a girl who used ATS every now-and-then, but that didn't work out. Eva drinks alcohol when going out, and while she has used cannabis periodically, she has never really been into drugs. While she never felt pressured to try ATS, she sometimes decides to not join her friends at a festival when she knows they will use ATS, or she makes sure there are other non-users she can hang out with.

Protective and risk factors of different phases

As one can see from the stories of Bob, Carl, Mia, Adam, Tom and Eva, not only the type of substance used is important to indicate if someone will become dependent, a frequent user, or only use occasionally. The life context, the surroundings and the personal characteristics are also crucial to define how someone will relate to a substance (29).

From the stories above, we can see that a *risk factor* possibly leading to **initiation** of ATS use is hedonism - curiosity, pleasure seeking or staying awake at a party - as in the case of Mia, for example. Risk factors leading to **continuation** of use include functional reasons (improving work/study/sexual performance); using for coping with difficulties or mental health problems; experiencing positive effects (alertness, connectedness and no hunger); and having friends or who (frequently) use ATS. *Protective factors*, on the other hand, can be the willingness to keep a clear mind, and fear of losing control, or of unpredictable effects, such as in the case of Tom or Eva (who never even tried). Experiencing negative effects can also prevent people in the initial phases from continuing or increasing use.

In **continuing or increasing phases** of ATS use, *risk factors* can include the desire to preserve the positive effects of ATS and by frequenting settings where ATS use is normalised (such as being involved in the party scene as with Mia); and having a network of friends who use ATS, as was the case for Carl. Becoming a more experienced user and being willing to experiment with multiple drugs - in general to counter or balance their effects, such as with Mia - is also a risk factor leading

to increased ATS use. Using ATS is also related to to coping with demands of everyday life, to lose weight or to feel more energetic. Engagement in chemsex practices also offers a higher risk of increased ATS use, especially methamphetamine.

Dependent phases of ATS use, such as in the cases of Bob and Carl, were observed mostly for methamphetamine and amphetamine. *Risk factors* to become dependent on ATS use, as reported by ATTUNE participants, include having underlying mental health problems, such as Bob who needed to use to be able to start the day and feel less depressed. Having alcohol dependence was also a risk factor. A rapid increase in frequency of use, as in the case of Carl, led more frequently to a dependent pattern of use. *Protective factors*, both for dependent phases and increasing phases, included experiencing (other) side effects or health problems related to ATS use, such as Bob's experiences of paranoia and depression. Increasing life responsibilities and changing life priorities (such as having a family or a job, as with Adam) also acted as a protection, leading to decreasing or quitting use.

Interventions for ATS use

In the last decades, an increasing body of studies has analysed and proposed prevention, treatment and harm reduction interventions for people who use ATS. Researchers have studied, for instance, substitution treatment for ATS (30), interventions to reduce the harms of MDMA use (31), and forms of preventing dependent use on different ATS substances (32). A few overviews of recommended interventions are also provided by different organisations in the harm reduction and drug policy field (12, 33, 34, 77).

Studies usually investigate the effectiveness of interventions for a specific substance, or form of administration. Less attention is paid to the phase of ATS use in which such interventions can be beneficial. This gap can be filled by combining the different ATS trajectories and experiences of use as found in the ATTUNE study with the scientific literature around interventions for ATS use. Below, evidence-based interventions are described which can be beneficial to reduce the harms of ATS use in different phases of ATS consumption.

Evidence-based information

Providing evidence-based information for ATS use(rs) about substances and their effects, and how to reduce the potential harms of its use, can be beneficial in several phases of ATS use.

In the case of MDMA, for instance, important aspects to consider when choosing which information to provide are the motivations of specific groups for using MDMA as well as the perceived risks that users associate with its use (35). Known desired effects include: sense of relaxed euphoria, decreased inhibition, and elevated mood and sociability, as mentioned by Mia. Sexual arousal, heightened perceptions, and vivid hallucinations can also be desired effects (13). However, desired effects can vary according to the phase and the years of experience someone has using MDMA. Considering the reasons people have to not use MDMA or other ATS, and targeting these in prevention messages, can also help to curb or delay initiation (36). Often, as was the case for Eva, reasons for not using ATS include the willingness to stay in control, mainly related to uncertainties of how the effects will work out, and to keep a clear mind.

In any phase of use, it is also important to include the potential consequences of mixing ATS with other drugs. Several ATTUNE participants mentioned poly-drug use to manage their energy and counter the effects of ATS; Mia, for instance, started the party night with MDMA, used cocaine or speed to boost her energy, and ended with cannabis to help coming down. Warning about the effects of mixing substances also includes adverse outcomes due to the concomitant use of ATS with alcohol (37) (as mentioned by Bob) and energy drinks (38). The possibility of engaging in high-risk sexual behaviours after taking MDMA should also be addressed (39). It is also known that some intimate partners use MDMA to revitalise their connection, and in a few cases this might develop into emotionally unhealthy patterns (40). Engaging with the motives of people for using MDMA as a relationship "aid", and helping them to distinguish forms of emotional harm entangled in a couple's use of it, is recommended.

Other important preventive messages include: warning users about potential sleeping and sleep deprivation problems; and educating people about the potential dangers of hyperthermia, hydration and water intoxication (41, 42).

Internet-based prevention programmes have also shown positive results to reduce the harms of ATS use. An online school-based prevention programme implemented in secondary schools in Australia, for example, focused on NPS and MDMA use and showed a reduction in the intent of students to use NPS as their knowledge on both MDMA and NPS improved (32).

When sharing information, but also when providing other interventions, it is important to meaningfully involve peers - people with lived experience of ATS use and, preferably, part of the same sub-groups of ATS users for whom the intervention is planned. Several ATTUNE participants mentioned the importance of peers in influencing their initiation, continuation and decrease in ATS use. Peer-based interventions are a very effective way of sharing honest harm reduction education and information among people who use drugs (43, 44). Peers are more effective in engaging with users (45) and more easily trusted as they share experiences and background. Peer outreach work is particularly effective for safer drug use education (46).

Self-management of drug use

People who use drugs, including those using various types of ATS, are often able to control their drug use to varying levels of success (29, 47, 48). Take, for example, the patterns of consumption of frequent non-dependent users, such as Mia, or non-frequent users, like Tom. Studies have shown that self-management of drug use can lead to less problematic patterns of use (49) and increase the chances of becoming and staying abstinent from drugs (50), as was the case for Adam.

While self-management can be learned, it must build upon the ability of users, empowering the skills and competencies that they already use to control their use and reduce their risks (51). Previous literature (33) has mapped some of the methods already often used by people who use stimulant drugs to self-manage their use. They include the creation of (informal) rules for use according to perceived risk and triggers that include:

- only using when feeling well;
- using only with friends;
- only use during weekends;
- not using when at work or before work, when this is going to negatively impact the productivity of the user; and,
- establishing a maximum amount or frequency of use.

To be effective, any methods and training in self-regulation should be developed together with people who use ATS. In these self-management processes, peers could also play a supportive role.

Mental health support

Several people who use ATS do so to cope with difficulties and existing mental health problems (52, 53). That was the case, for example, for Carl. Frequent ATS use may also lead to mental harms (6) such as depression, psychotic symptoms (hallucinations) and paranoid thoughts (6, 54). Evidence shows that frequent and extended use of methamphetamine may cause long-term psychiatric and neurological sequels (55). Moreover, chronic users have high levels of psychiatric comorbidity (such as depression, post-traumatic stress disorder (PTSD), ADHD, eating disorders and suicidal thoughts/attempts) (7, 56). Mental health support, therefore, can be used in initial phases to help people cope with stressful life events and prevent increased/uncontrolled use (57), or in dependent or continued trajectories to help tackle the mental harms (partly) due to extended drug use.

Drug checking services

Drug checking services are a harm reduction strategy usually associated with people using drugs in nightlife settings and with less problematic patterns of consumption (58). Nevertheless, these services can be useful to reduce the harms of people also in continuation and increasing phases of ATS consumption.

The illegal status of ATS often leads to unknown dosages and contents, increasing the risk of overdose as well as of other harms. In this context, drug checking can help to detect adulterants in substances, thereby decreasing the intent of the user to consume potentially dangerous substances and help inform harm reduction efforts. These services can also be crucial for issuing preventative warnings (in case of dangerous adulterants), helping to avoid further harm. Nevertheless, drug checking alone might be insufficient, especially for less frequent users who may require education about adulteration and drug-checking and referral to support services and drug education that are important facilitators of harm reduction interventions (59–62).

Safer social settings

The pleasurable effects of "party-drugs" such as MDMA may be perceived as compensating the unwanted effects caused by use, leading users to a low desire to decrease use or to get help (63). In that context, interventions that are placed in, and adapted to, party settings can be very useful to engage ATS users in reducing harms, especially users at initial phases of ATS consumption, but also those continuing or increasing use.

Chill-out rooms, for instance, can help MDMA users to increase their fluid intake and prevent hyperthermia, as well as warning users of the potential harm of overconsumption of fluids (24). Other practices can be promoted at the premises where party drugs will be consumed. These include temperature control at the venue and adequate ventilation; adequate provision of free cold water; staff training to understand and manage drug-related risks and emergencies; adequate emergency provision; and a harm reduction focus for security when targeting people in possession of drugs for personal use (64).

Substitution therapy

Substitution therapy is an intervention used, in general, for a dependent pattern of drug use, such as experienced by Bob. Substitution therapy for ATS follows a similar rationale as substitution therapy for opiates: replacing the use of one drug with another based on its perceived safety, level of addictive potential, effectiveness in relieving symptoms, as well as access and level of acceptance (65). Whereas opiate drugs, such as methadone and buprenorphine, have been widely acknowledged as effective to substitute heroin, there is limited evidence of the benefit of pharmacotherapy for reducing ATS use. So far, studies have demonstrated only limited benefits for a few drugs, such as methylphenidate, bupropion, modafinil, and naltrexone (30).

Despite the low evidence given the lack of studies, some also advocate for a "plant-based substitution" of ATS. Cathinone is the main psychoactive ingredient in the leaves of Khat, traditionally chewed in the Horn of Africa and Yemen. Some advocate that the plant could be a potential substitute for amphetamine given its milder effects (66). In practice, some people who use ATS choose to use plant-based stimulants that are legal in their country (such as ephedra, betel, kava, or kratom) instead of using illegal ATS (67). Such a strategy can be useful in the earlier phases of ATS use and might help both in reducing harms (such as legal risks) and the increased consumption of stronger substances (33). Finally, another much used (self-medication) strategy is to use cannabis to reduce cravings and minimise psychological harms such as anxiety, aggression and paranoia ('coming down'). While the use of cannabis to ease comedown is much more widespread for those using cocaine and crack cocaine (56, 68), it has also been often reported by respondents using MDMA in the ATTUNE study (such as by Mia), and in the literature concerning mephedrone users (69). Such forms of use of other drugs might be helpful to enhance self-regulation.

Abstinence-based treatment and counselling

For those who are dependent on ATS and/or are willing to quit its use, abstinence-based treatment and supportive counselling can be recommended.

A few specific abstinence-based treatments have been developed for ATS. An example is the Matrix model. This model combines different therapeutic interventions and has been proven effective for methamphetamine use (70). Specific, structured brief counselling has been developed for regular methamphetamine users that has proven to help increase abstinence and manage the risks of tobacco smoking, polydrug use, risky injecting behaviour, criminal activity, and psychiatric dis-

tress (71) . Brief interventions, such as motivational enhancement therapy, have shown to help reduce MDMA use and severity of MDMA-related problems (72) and promote readiness to change (73). In any chosen treatment, follow-up after treatment completion is crucial. As in the case of Carl, many ATS users repeatedly enrol in drug treatment and, without adequate aftercare, may quickly relapse to older habits.

To help people who use ATS to cope with the process of abstinence, non-mental health professionals can also offer counselling for supported withdrawal (33). Possible strategies include: providing oral and written information around the withdrawal process (duration, symptoms); helping to identify protective and risky factors in previous withdrawals; and helping identify key social supports (74). Finding and focusing on pleasant activities, and maintaining a healthy diet and routine, can also help with strengthening self-regulation (12). This strategy was mentioned by ATTUNE participants, such as Mia, who set boundaries for use and choose specific days to eat healthy, sleep early and not to consume. Here again, peers can be relevant during the process of abstinence in either maintaining abstinence or contributing to handle relapse episodes, as happened to Carl in his previous attempts to quit.

Support in case of acute or chronic harms

ATS use may also bring acute or chronic harms. ATS use, in general, can cause wakefulness and altered attention, an elevated mood and increased optimism and impulsiveness, as well as reduced appetite (11). Despite the fact that these might be desired effects for people consuming ATS, heavy or chronic consumption can elevate such effects to cause unintended harms. Frequent MDMA use may cause liver damage and intoxication (10), besides induced memory impairment (20) and sleeping problems as mentioned by dependent users such as Bob. Sleep deprivation can cause impaired driving (18) and, in chronic cases, amphetamine associated seizures (55). Potentially life-threatening effects due to MDMA use include: hyperpyrexia (>40°C), serotonin syndrome, hyponatremia (due to overconsumption of fluids) and cerebral oedema (75, 76). Lighter ATS effects include tachycardia, anxiety, prolonged 'hangover' or 'comedown', as well as bruxism (grinding teeth) (24). Bruxism was especially mentioned by ATTUNE participants dependent on ATS (speed/meth), leading to damage and loss of teeth.

While more severe harms need medical care, some preventative or supportive interventions can be done by non-medical staff. Liver damage and toxicity cases require medical and nursing care and treatment, but non-medical staff may warn users of the possible effects and how to identify them on time. Anxiety and agitation may require specialised mental health assistance or medication but interventions such as chill-out rooms, or immediate mental health support, can be done by harm reduction workers in a variety of low-threshold settings. In case of elevated temperature, simple cooling measures can be applied such as use of water and a fan, and applying ice packs to the groin and axilla. Non-medical workers can also educate recreational users about the potential dangers of hyperthermia and sleeping problems.

Recommendations

People who use ATS are a very diverse group with various and shifting patterns of use. Therefore, not all of them will benefit from interventions or support. The table below presents recommendations for people who use ATS, and those providing services to them, on how to reduce the harms of ATS use in the different trajectories of such use. Given the need for multidisciplinary care, a general recommendation for service providers is to work with partnerships to provide integrated care.

ATS trajectory	Potential support and interventions
Initial phases	• Information about the effects and harms of ATS use • Peer-led outreach and drug education • Drug checking services • Promote safer social settings
Continuation	• (Peer-led) harm reduction information and counselling • Drug checking services • Mental health support to help people cope with stressful life events • Foster self-management and control of drug use
Increase	• Mental health support to prevent increased/uncontrolled use • Skills-building, education and vocational training • Foster self-management and control of drug use • Drug checking services • Assistance with basic symptomatic detoxification and withdrawal
Decrease/abstinence	• Online support mechanisms and apps to support controlled drug use or abstinence • Ongoing therapeutic support • Skills building, education and vocational training • Follow-up support after treatment (continuum of care)
Dependent phase	• Harm reduction • Services related to social integration, rehabilitation and care (e.g. housing services, work integration, activation programmes, debt control) • Family and partner support services • Specialised, voluntary drug dependence clinical treatment • Follow-up support after treatment (continuum of care) • Mental health support to help tackling problems (related to drug use) • Medication assisted withdrawal programmes • Substitution therapy if available and approved

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Correlation
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