TE POU

Substance withdrawal management

Guidelines for medical and nursing practitioners

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This guideline is one of a series that were developed to provide information about safer withdrawal management. Each set of guidelines has been designed to provide readily accessible and appropriate information for the specialist addiction sector, the general addiction and allied workforces and for people who use substances and their whānau and support people.

Disclaimer

The opinions expressed herein are the views of the authors and do not necessarily reflect the official position of the Ministry of Health.

The guidelines in this document should not be considered exhaustive, exclusive or substitutes for individualised care and treatment decisions.

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Withdrawal management reference group 2019

Steph Anderson: Addiction Nurse Specialist, Nelson Marlborough DHB *

Raewyn Birkett: Senior Withdrawal Management Nurse, Christchurch City Mission

Dr Grant Christie: Child and Adolescent Addiction Psychiatrist, Waitemata DHB Altered High

Michelle Fowler: Project Manager, Werry Workforce Whāraurau *

Moira Gilmour: Nurse Practitioner, Capital and Coast DHB Addiction Service *

Truusje Hewson: Charge Nurse, Canterbury DHB Kennedy Detox Unit *

Terry Huriwai: Kaiwhakahaere: Te Hau Mārire, Te Rau Ora

Dr Vicki Macfarlane: Lead Clinician, Waitemata DHB CADS

Sheridan Pooley: Regional Consumer Advisor, Waitemata DHB CADS

Simon Rouch: Service Supervisor, Christchurch City Mission

Dr Fraser Todd: Senior Clinical Advisor, Matua Raki *

*Member of Withdrawal management reference group 2011

The 2011 Withdrawal management reference group also included:

Shelley Andrews: Clinician, Rongo Atea Youth Alcohol and Drug Treatment Service

Dr Susanna Galea: Clinical Director / Consultant Psychiatrist, Waitemata DHB CADS

Dr Helen Liley: Lead Clinician, Auckland Methadone Service, Waitemata DHB

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Withdrawal management

In the context of addiction treatment 'withdrawal' is used to describe the process and the acute symptoms, physical and psychological, that can accompany the cessation or reduction of use of any substance or combination of substances that have been used regularly over a prolonged period of time.

The purpose of 'withdrawal management' is to ensure the safety of the person, and others, as they stop or reduce substance use, and where possible to address withdrawal symptoms to alleviate acute distress and cravings. Specific objectives include:

- Preventing or managing severe medical complications such as seizures or delirium
- Preventing or managing severe psychiatric complications such as psychosis or agitation.

Planned withdrawal management also serves to:

- Engage the person in ongoing specialist addiction treatment (eg counselling, pharmacotherapy, and or residential treatment), and mental health and primary care services
- Involve the person in psychosocial support: including, financial, health and welfare services
- Interrupt periods of heavy use driven by neuroadaptation
- Support pharmacotherapy reduction or stabilisation.

Appropriate withdrawal management planning depends on an accurate assessment of the person's:

- patterns of substance use; what, how much, how often and last use
- withdrawal risks, risks to self and others, history of withdrawal
- coexisting problems; mental and physical health
- social, personal and community support systems; including family, whānau and friends
- motivation; goals and resilience
- immediate environment; support available and safety
- external sources of stress.

Withdrawal management can be provided in a wide range of settings, including the person's own home, general practices, hospitals, respite facilities, residential treatment, police cells and prisons.

The focus of these guidelines is on substances which carry a significant physical and or mental health risk for people when in withdrawal. The list of substances covered is not exhaustive and nicotine, for instance, has not been included as adequate guidance exists elsewhere; https://www.medicalnewstoday.com/articles/323012 and https://www.health.govt.nz/your-health/healthy-living/addictions/smoking/stop-smoking/stop-smoking-medicines.

Unplanned withdrawal management

There is a clear consensus that withdrawal management is not in and of itself an effective stand-alone treatment for severe substance use disorders.

Withdrawal management does not address core issues and stressors that contribute to substance use and when provided in isolation it is likely to simply be a brief interruption in a pattern of ongoing substance use. Repeated interruptions in substance use without concurrent treatment may carry significant risks for the person due to lowered tolerance, and the subsequent risk of overdose, and the physical impact of withdrawal.

Managed withdrawal needs to occur in the context of ongoing treatment, which may include residential treatment, medication assisted treatment, outpatient counselling/therapy and integrated care for coexisting problems, including mental and physical health, housing and employment.

When a person with a severe substance use disorder indicates that they wish to reduce and or stop using substances withdrawal management needs to be a component of a long-term treatment plan that may take some time to line up. For instance, if requested and it is considered that the person is likely to benefit from residential treatment following managed withdrawal the timing of this will be dependent on availability of a place at the residential facility.

Unplanned withdrawal management may however occur for a variety of reasons. It is not unusual for a person with a severe substance use disorder to make a decision to stop using their substance of choice and proceed without contacting their General Practitioner (GP) and arranging support until withdrawal symptoms emerge. This places significant pressure on the GP to medically manage the acute symptoms of withdrawal. It can seem counterintuitive to try to slow the process down and take the time to arrange ongoing care for the person, however, for the reasons stated above, it is important to ensure that the person develops an ongoing treatment plan with a specialist addiction service as soon as possible.

There are also significant risks with providing suitable medication to manage withdrawal symptoms in the community. These include the risk of overdose as benzodiazepines, one of the main medications used in withdrawal management, do not prevent people from ‘craving’ or using their substance of choice. If that substance is a central nervous system (CNS) depressant and they use that substance while on even relatively modest doses of benzodiazepines they will be at significant risk of overdose and death.

For these reasons it is strongly recommended that no one is prescribed over 40mg diazepam (or diazepam equivalent, excluding oxazepam and lorazepam), if over 20 years old and 20mg under 20 years old, if undergoing unplanned withdrawal management in a community setting.

While many people will stop or reduce substance use by choice others will have this imposed on them through admission to hospital or prison. In these situations people may not disclose substance use or may not be aware of the risk of withdrawal themselves. To provide appropriate care clinicians across a range of disciplines and settings need to be able to screen for substance use disorders and recognise the features of withdrawal from a range of substances and tailor responses accordingly. Where possible specialist addiction services should be involved and provide both immediate support and advice to ensure the person’s immediate safety and help arrange appropriate after care and treatment for the substance use disorder.

Planned withdrawal management

Assessment

When a person presents to an addiction service requesting help to stop using a substance or substances the first step is to identify the substances used and assess immediate risk, i.e. does the person have withdrawal symptoms and what risks are associated with this? If the person is not at immediate risk and is not severely intoxicated a comprehensive assessment should be carried out. This will provide the information needed to develop a treatment plan that suits the needs and situation of that person, including a plan for withdrawal management if needed.

A comprehensive assessment generally includes:

- presenting issues
- detailed substance use history and patterns of substance use over time
- current substance use including frequency, amounts, how used and last use
- impact of substance use and risk-taking behaviour
- evidence of withdrawal, historical and current
- what the person identifies as problematic, if anything, about their substance use and their goals for treatment
- what the person identifies as their strengths/resources to support their goal of stopping substance use
- gambling history
- developmental history, whānau background and relationships, parenting responsibilities
- current living circumstances
- whānau substance use history and physical and mental health history
- cultural assessment and formulation, social connectedness and needs
- education and employment history
- history of trauma and adverse childhood experiences (ACEs); physical, emotional and psychological
- physical health history and current issues, noting any traumatic brain injuries (TBI), blood borne virus history and risks and results of cognitive screening
- mental health history with current mental health status
- prescribed and over the counter medication
- forensic history and current or pending justice involvement
- risk assessment; self-harm and harm to others including safety of children
- diagnoses
- formulation of issues
- treatment and recovery goals, what the person wants to achieve
- a collaborative treatment or management plan.

For more information about comprehensive assessment see:
https://www.tepou.co.nz/resources/mental-health-and-addiction-screening-and-assessment

Withdrawal specific risk assessment, management and safety planning

The primary aim of withdrawal management is to keep people safe during the process. To do this it is necessary to assess imminent and medium to long term risk as an integral part of assessment and ongoing treatment. Depending on the substance or substances the person has been using there are specific risks to the person and or others that are associated with withdrawal. Potential risks include:

- exacerbation of coexisting mental health problems
- exacerbation of coexisting physical health problems
- low mood and suicidality
- anxiety and panic attacks
- irritability and anger
- aggression
- disturbed sleep and insomnia
- confusion
- dehydration due to vomiting and or diarrhoea
- elevated blood pressure
- arrhythmias
- delusions and psychosis
- hallucinations
- brain damage
- seizures
- death.

In the context of withdrawal management, it is important to assess the risk to the person and or others of supporting the person through the withdrawal process in their own home, in a respite and or supported withdrawal management facility or in a hospital setting. Most people going through withdrawal can be supported through the process, with or without medication, in the community or in their own home. The decision to admit the person into a respite and or supported withdrawal management facility or a hospital depends very much on the outcome of the risk assessment and the degree of support the person would have available to them in the community.

Providing people with information about the risks associated with withdrawal and ways to minimise these risks is essential as is working with them to develop a plan for how to keep themselves safe through the withdrawal process.

Engaging whānau in the process and providing clear information, both verbally and in writing, about the withdrawal process, what to expect, potential risks and how they can support the person through withdrawal and ongoing treatment can significantly improve outcomes. Involving peer support throughout the withdrawal process can also help to demystify withdrawal and reassure people and whānau that it is a safe process and encourage long term engagement in treatment.

Driving

Where withdrawal management is carried out in the community the issue of safety to operate a motor vehicle must be addressed with the person. People need to be advised that the physical and or psychological effects of substance withdrawal may make it unsafe for them to drive any motor vehicle. People prescribed medication as part of withdrawal management should be strongly encouraged not to drive a vehicle at all while on medication. The continuation of withdrawal management and or medication should be reviewed if people do not follow this advice.

Where it appears that people are continuing to drive a motor vehicle while impaired or potentially impaired, either by withdrawal effects or medication, it may be necessary to inform the Police or

Waka Kotahi NZ Transport Agency of the risks to the community of the person driving. The person planning on undertaking a managed withdrawal should be informed of these possible outcomes before embarking on the process.

For a more detailed description of a model of assessment refer to *Mental Health and Addiction Screening and Assessment guideline,* Matua Raki 2016, and *Te Ariari o te Oranga: the Assessment and Management of People with Coexisting Mental Health and Substance Use Problems,* Todd 2010**.**

Where the person is in acute withdrawal, and it is inappropriate to carry out a full comprehensive assessment, effort should be made to identify:

- recent substances used and how used
- last use
- current withdrawal symptoms
- current coexisting problems
- current risks and safety.

Specialist addiction services may also carry out a range of physical examinations that could include:

- breathalysing the person for alcohol
- saliva testing to screen for recent substance use
- urine drug screening
- blood tests screening for physical impact and or confirmation of substance use
  - GGT
  - LFT
  - Albumin
  - ALT
  - AST
  - MCV
  - FBC
  - CDT
  - INR
  - Folates
  - Vit B12
  - Glucose
  - Electrolytes and Urea
  - Magnesium, Phosphate and Potassium
  - HBV
  - HCV
  - HIV
- blood pressure
- pulse/heart rate, EEG
- checking for injection sites
- general physical examination
- neuropsychological assessment/screening
- appropriate withdrawal scale if available.

Coexisting mental and physical health problems

The presence of coexisting problems can make the withdrawal process more distressing and riskier for people who stop or reduce substance use. Clinicians will need to be aware of potential problems and adapt treatment to manage significant risks and possible consequences beforehand. Particular care needs to be taken prescribing medication for withdrawal management when people are prescribed medication for coexisting problems. Combining certain medications may inhibit or enhance each other's effects. This also includes some foodstuffs and complementary or natural therapies.

Refer to Appendix 8 (from Todd, 2010) for a guide to some known and potential drug-drug and drug-medication interactions. Also see resources section for links to online sites to complement the information in Appendix 8. Where no interactions are indicated, it is wise to check multiple sources as no one source can be exhaustive or completely up to date.

Practitioners and clinicians need to be mindful of the existence of chronic pain problems through the withdrawal process. These may be pre-existing and could have contributed to the development of substance use disorders or could emerge during withdrawal. Chronic pain problems need to be treated in consultation with pain specialists to reduce the chances of causing distress or undermining the withdrawal management process.

Ongoing monitoring of coexisting problems is necessary to enhance safety and the likelihood of a successful withdrawal process. It is possible that ongoing substance use has masked a coexisting issue that can emerge in withdrawal and require appropriate treatment.

Coexisting problems of particular concern during the withdrawal process can include:

- depression
- bipolar disorder
- anxiety
- psychosis
- borderline personality disorder
- conduct disorder
- anti-social personality disorder
- neurological disorders
- brain injuries
- chronic pain
- dental problems
- malnutrition
- gastrointestinal disorders
- infection
- liver disorders
- cardiac disorders
- epilepsy
- respiratory disorders.

Special populations

Older people

Older people can experience a more severe and protracted withdrawal and metabolise some medications less effectively, especially longer acting benzodiazepines such as diazepam. As a consequence older people may experience benzodiazepine toxicity during withdrawal using diazepam.

Older people prescribed diazepam are also at greater risk of injury due to falls and fractures. Close monitoring and possible adjustment of benzodiazepine doses and or choice of benzodiazepine is necessary when supporting withdrawal in older people.

Diazepam can be replaced with lorazepam or oxazepam, neither of which have active metabolites and are less likely to accumulate to toxic levels.

Young people

Most young people going through substance withdrawal can be safely managed in the community unless there are significant concerns related to their mental health or other safety issues. Young people are developmentally more likely to be impulsive and reactive and the psychological symptoms of withdrawal, in particular anxiety, may trigger challenging behaviour and or suicidality.

Most young people will not need specific medical input into their managed withdrawal as the key intervention is support. However, where available, referral to a specialist service for young people is recommended to provide support and ongoing therapeutic follow-up post withdrawal. Admission to an inpatient, respite or residential setting may be necessary to provide a substance free environment as often the main barrier to successful withdrawal management is ongoing access to and exposure to substance use. Other reasons for admission include significant neuroadaptation and concerns around self-harm and suicidality. Medication is seldom required to manage withdrawal symptoms but may be beneficial for managing coexisting low mood, agitation, anxiety and or aggression. Consultation with an addiction medicine specialist, physician or psychiatrist is recommended.

See *Guidelines for the Management of Acute Substance Withdrawal in Young People - 2017 update* (Grant Christie & Helen Temperton) for more information.

Pregnant women

Pregnant women may go into sudden withdrawal when they realise they are pregnant and immediately stop using substances. Abrupt cessation of substance use, especially central nervous system (CNS) depressants such as alcohol, opioids, gamma hydroxybutyrate (GHB) and benzodiazepines, during pregnancy can carry significant risks for the fetus. This is particularly the case in the first and third trimesters of pregnancy. Risks include infant mortality, miscarriages and low birth weight.

Prior to commencing any withdrawal management with a pregnant woman consult an addiction medicine specialist, physician or psychiatrist.

However, generally if a woman has been using opioids, opioid substitution treatment is the safest option throughout the pregnancy (see section on opioids).

In the case of neuroadaptation to alcohol the risks to the fetus of continued drinking are very high and rapid commencement of a withdrawal management plan is recommended (see section on alcohol).

If a woman has neuroadaptation to benzodiazepines then maintaining a 'controlled' dose of these throughout the pregnancy is usually the safest option (see section on benzodiazepines).

See Appendix 9 for list of 'safer' medications for use in pregnancy and the WHO guidelines (https://www.who.int/publications/i/item/9789241548731) for more information about the management of substance use disorders in pregnant women.

Secure facilities and prison inmates

Admission into a secure facility or incarceration with no access or very limited access to substances can precipitate involuntary withdrawal. The combination of loss of freedom and substance withdrawal can compound mood disorders and the risk of self-harm and suicidality. Medical and nursing practitioners in secure facilities and prisons need to be aware of the possibility of people developing acute withdrawal and be competent in managing the symptoms appropriately. At times it can be difficult to distinguish between withdrawal and some mental health issues and careful assessment and monitoring is needed to decide on an appropriate treatment plan.

Withdrawal management settings

Community and home-based withdrawal management

Many specialist addiction services offer a community-based withdrawal management service. This involves specialist addiction practitioners visiting people in their own home during the acute withdrawal period to provide supervision, encouragement, support and medication as needed. Along with an assessment of specific withdrawal risks addiction practitioners also assess the appropriateness of the person's supports, their physical environment and general safety. When people have responsibility for the care of other people, either for children or dependent adults, negotiating alternative care arrangements for the duration of the managed withdrawal may be necessary.

When carried out in the community addiction practitioners visit people in their own homes as often as needed during acute withdrawal. When medication is used as part of withdrawal management this is supervised by specialist withdrawal management nurses.

Addiction medicine specialists, physicians or psychiatrists are available for consultation as needed.

Withdrawal management may or not require prescribed medication. Alternative and complementary therapies may also be offered by some services (see Appendix 10).

Respite service withdrawal management

Respite withdrawal management services are mostly located in the main centres and provide a safer, supervised environment away from community and peer influences. Staff members are available for support and encouragement twenty-four hours a day. Specialist nursing and medical staff members are available on call for consultation.

Methamphetamine withdrawal management beds

A number of dedicated beds are available in residential treatment services nationally to assist those with methamphetamine use disorders to have time out as a one-off opportunity or a lead-in to residential treatment.

Specialist inpatient and hospital withdrawal management

Aotearoa New Zealand has two specialist facilities providing inpatient withdrawal management. Full 24 hour medical supervision is provided by nurses and addiction medicine specialists to avoid or reduce the medical complications associated with withdrawal.

Where specialist facilities are unavailable general hospital based withdrawal management is appropriate for people with severe substance use disorders and or complicating factors. This includes:

- serious coexisting mental or physical health problems
- significant other substance use
- a history or high risk of withdrawal related seizures
- a history or apparent withdrawal related complications such as dehydration or delirium
- physical frailty
- risks to the individual or community.

Rongoā Māori

Rongoā Māori has been described as a holistic range of approaches to health and wellbeing that traditionally included "ritenga and karakia (incantations and rituals involved with healing), rongoā (physical remedies derived from trees, leaves, berries, fruits, bark and moss), mirimiri (similar to massage/ physiotherapy), wai (use of water to heal), and surgical interventions." (Ahuriri-Driscoll et al., 2008).

At times whānau undergoing withdrawal might utilise mirimiri, rongoā and karakia to improve general health and wellbeing, and to relieve distress and withdrawal symptoms. The cultural assessment included in the comprehensive assessment should provide indications for how these adjuncts might complement the whole managed withdrawal process. Being supportive of these techniques may help engagement and retention in the process of withdrawal management, ongoing treatment and continuing care. Supporting the use of traditional therapies may also help with engaging whānau who may wish to support tāngata whai ora through acute and protracted substance withdrawal.

For a description of Rongoā Māori and more detail of Rongoā rākau, or plant remedies, that may have potential applications in withdrawal management:
http://www.bpac.org.nz/magazine/2008/may/docs/bpj13_rongoa_pages_32-36_pf.pdf

For a list of Ministry of Health funded rongoā providers:
https://www.health.govt.nz/our-work/populations/maori-health/rongoa-maori-traditional-maori-healing

Addiction treatment

Withdrawal management is a component of addiction treatment for many people with severe substance use disorders. It is often the first experience many people have of addiction treatment and for this reason it is important that practitioners involved with withdrawal management focus on engagement and developing a therapeutic relationship with the person. Where possible withdrawal management should be part of a planned process to engage a person in treatment, which may include ongoing counselling, medication and or residential addiction treatment. As many people with severe substance use disorders also have coexisting physical and mental health issues along with homelessness, unemployment and relationship problems these issues will also need to be actively addressed in collaboration with the person as soon as possible. Where available partners, friends, family and whānau need to be involved in this planned process.

Alcohol

These guidelines have been developed to assist nursing and medical practitioners to identify alcohol withdrawal symptoms and to provide safe withdrawal management strategies for people who have a severe alcohol use disorder.

The active ingredient in alcohol is ethanol, also called ethyl alcohol. Ethanol has depressant effects on the central nervous system.

Acute alcohol exposure can inhibit the action of N-methyl-D-aspartate (NMDA) and kainite at glutamate receptors, inhibit voltage sensitive Ca^{2+} channels and enhance the action of gamma-aminobutyric acid (GABA) at inhibitory GABA A receptors. Alcohol also enhances the action of serotonin (5-HT) and acetylcholine at 5-HT3 and nicotinic acetylcholine receptors, increasing excitatory neurotransmission at these receptors.

Even in people with significant neuroadaptation to alcohol the risks of impulsive behaviour need to be considered in the context of withdrawal management. Impulsivity may contribute to impulsive unplanned withdrawal and suicidal behaviour. Unplanned and or repeated cycles of withdrawal and relapse have significant risks for the person. These include an increasing vulnerability to the risks associated with withdrawal such as seizure and cognitive impairment.

Assessment

A comprehensive assessment is the first step in managing withdrawal with the priority being to identify and define any risks.

A specific alcohol use history also includes:

- type and strength (% alcohol per volume) currently using
- time of last drink
- average number of standard drinks (std) a day over time
- early morning drinking or drinking when waking through the night
- needing to control shakes by using alcohol
- history of seizures
- history of medicated withdrawal
- history of hallucinations
- coexisting physical and mental health problems
- current goals relating to use.

Withdrawal from commercially available methylated spirits, which has not contained methanol since 2007, should be dealt with as with alcohol. If the person has been using high concentration industrial methanol for a period of time it will be necessary for them to be stabilised on alcohol for two or three days prior to initiating a planned withdrawal.

Alcohol withdrawal

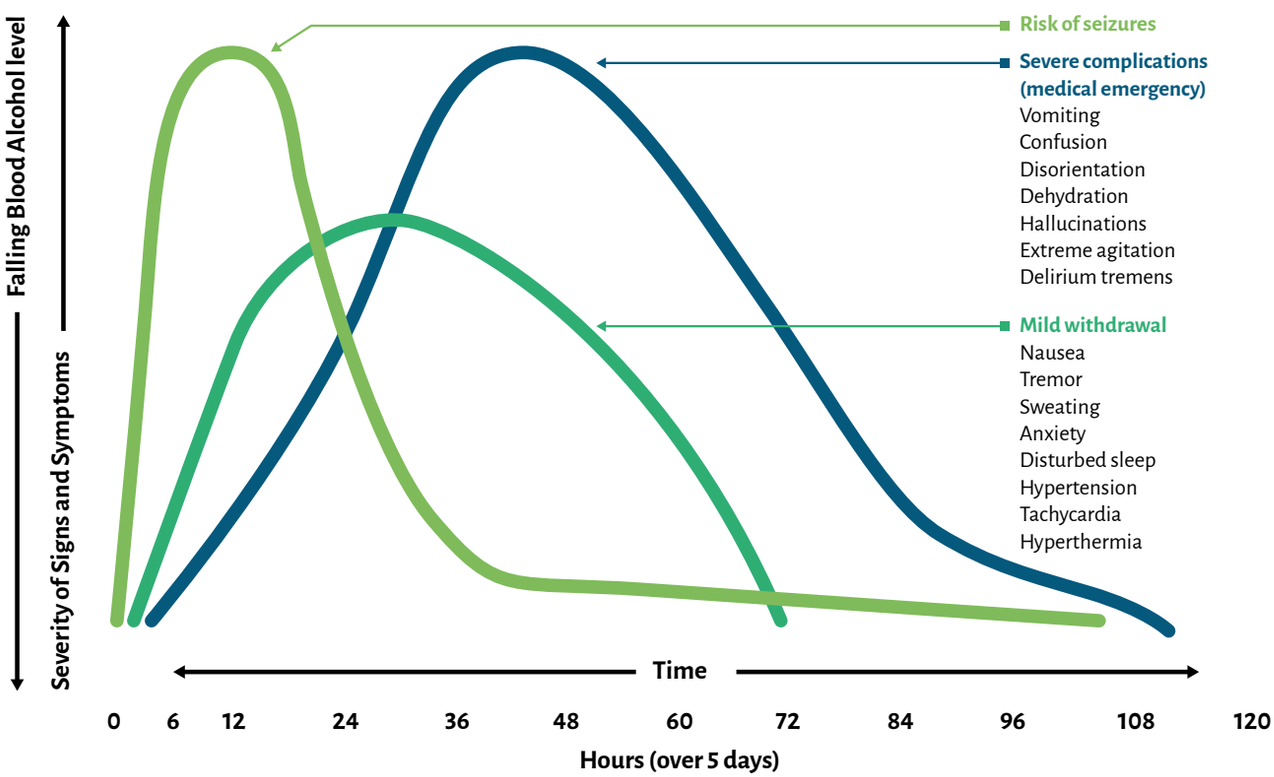
In mild withdrawal the only evidence of physiological withdrawal symptoms may be one to two days of sleep problems and mild irritability.

People who have a more severe alcohol use disorder may experience symptoms of withdrawal before their blood alcohol level reaches zero. This can follow abrupt cessation or a marked reduction in consumption levels. Withdrawal symptoms can occur within a few hours of their last use of alcohol as blood plasma levels fall, triggering the consumption of alcohol to relieve symptoms. Early morning drinking occurs in some cases as the person is woken in the night by withdrawal symptoms.

Alcohol withdrawal can be associated with significant health risks and early identification of symptoms using the Clinical Institute Withdrawal Assessment of Alcohol Scale Revised (CIWA-Ar) tool (see 'Severity of withdrawal' below), along with prompt tailored treatment reduces complications and the duration of withdrawal.

Figure 1: Progress of alcohol withdrawal from time of last drink

Symptoms and duration of alcohol withdrawal



Adapted and used with permission: Frank, L. and Pead, J. (1995), *New concepts in drug withdrawal: A resource handbook*, Services for alcohol and drug withdrawal, Monograph No.4, Victoria, Australia

Figure 2: Symptoms of alcohol withdrawal

Mild	Moderate	Severe
restlessness irritability anxiety agitation sleep problems intense dreaming nightmares	poor concentration impaired memory and judgment increased sensitivity to sound, light, and tactile sensations tremor (shakiness) elevated heart rate increased blood pressure anorexia nausea, vomiting	hallucinations delusions grand mal seizures hyperthermia (high fever) delirium with disorientation fluctuation in level of consciousness problems with eye movements
Daily consumption **less than 10** standard drinks a day	Daily consumption **between 10 and 20** standard drinks a day	Daily consumption **more than 20** standard drinks a day

Features of complicated withdrawal

Hallucinations

- occur in up to 25% of people with severe alcohol use disorders
- are generally more common in the first 48 hours but can occur up to day five
- are usually visual and tactile and are occasionally auditory
- can occur while the person is still orientated without delirium.

Seizures

- occur in 2-5% of people with severe alcohol use disorders
- risk increases if the person has had a previous withdrawal seizure
- generally occur within the first 48 hours
- are classically single, generalised grand mal tonic seizures without focal features or loss of consciousness
- status epilepticus is rare
- long term prophylaxis with anticonvulsants is ineffective in preventing seizure recurrence related to alcohol withdrawal.

Note: Other potential causes of seizure should always be considered. These include:

- associated idiopathic epilepsy
- hypoglycaemia
- hypocalcaemia
- hypomagnesaemia
- subdural haematoma.

Delirium tremens (DTs)

Delirium tremens is the most severe form of alcohol withdrawal syndrome and is a medical emergency. It is usually seen in people who have a severe disorder with physical complications. It is unlikely to occur if people are adequately screened and provided an appropriate managed withdrawal. The greatest risks for delirium tremens are:

- a long history of a severe alcohol use disorder
- a prior episode of delirium tremens
- being over 60 years
- coexisting acute medical illness
- presenting in severe withdrawal
- having significant withdrawal symptoms with elevated breath or blood alcohol levels
- seizure during current withdrawal.

Features include:

- autonomic hyperactivity with fluctuations in blood pressure or pulse
- disturbance in fluid balance/electrolytes/hyperthermia
- gross tremor
- paranoid ideation
- hallucinations
- confusion and disorientation
- extreme agitation or restlessness.

Other risks associated with alcohol withdrawal

Complications of prolonged heavy alcohol use that can lead to high mortality include:

- dehydration leading to cardiac arrhythmias
- hypotension
- renal failure
- pneumonia
- infection.

Thiamine

Amongst daily or near daily users of alcohol poor diet and nutrition exacerbated by impaired absorption, due to gastritis, liver damage, vomiting and diarrhoea and an increase in metabolic demand, can cause vitamin deficiencies. These include vitamins B1 (thiamine), B6 (pyridoxine) and C (ascorbic acid).

Wernicke's encephalopathy

Wernicke's encephalopathy is a brain injury resulting from a deficiency in Vitamin B1. If not treated rapidly it can lead to permanent brain damage and memory loss, i.e. Wernicke-Korsakoff syndrome.

Symptoms of Wernicke's encephalopathy include:

- confusion
- confabulation
- agitation
- nystagmus, diplopia, with or without ophthalmoplegia
- ataxia or inability to stand without assistance
- peripheral neuropathy (can be present in up to 80% of people with Wernicke's encephalopathy).

Note: Wernicke's encephalopathy can be difficult to diagnose in an intoxicated person as ataxia, confusion and nystagmus may also be attributed to intoxication.

Prevention and treatment

Thiamine or Pabrinex should be prescribed as an intravenous injection (IV) to people at high risk of developing Wernicke's encephalopathy:

- the malnourished or at risk of malnourishment
- those with decompensated liver disease
- in acute alcohol withdrawal
- before and during planned alcohol withdrawal.

Local District Health Board IV administration protocols and guidelines should be followed for administration of IV thiamine.

Recommended thiamine dosage

For prevention of Wernicke's: Thiamine 200mg IV daily, or one pair of ampoules 1 and 2 Pabrinex IV daily, for at least three days at which time it is replaced by oral thiamine, 50mg four times a day (qid) or 100mg two times a day (bd). Oral thiamine should be continued for at least one month.

If IV access is not possible then thiamine 200mg by intramuscular injection (IMI)* may be given as an alternative to Pabrinex for the prevention of Wernicke 's encephalopathy.

*IMI injections are contraindicated if the platelet count is less than 50 or the INR is above 1.5.

In suspected and confirmed Wernicke's: Thiamine 200mg IV three times daily (tds), or two pairs of ampoules 1 and 2 Pabrinex IV every 8 hours (q8h), for at least three days. If there is no improvement discontinue treatment. If symptoms respond continue Pabrinex 2 pairs IV twice daily for a further 5 days or as long as improvement continues. Oral thiamine, 50mg four times a day (qid) or 100mg twice daily (bd), should be continued for at least one month.

Treatment of confirmed or suspected Wernicke's encephalopathy requires admission to a hospital or specialist unit for IV therapy.

Note: To reduce the risk of precipitating or worsening Wernicke's encephalopathy IV thiamine and IV Pabrinex must be given prior to administration of carbohydrates (e.g., glucose) to people in alcohol withdrawal (McClintock, A.D. et al. 1999). In an emergency situation where IV glucose is necessary and there may be a time delay before admission to hospital, administration of glucose prior to thiamine and Pabrinex may be a safer treatment option.
http://emedicine.medscape.com/article/819502-treatment and https://nzf.org.nz/nzf_70372

For more information on precautions and other information prior to administration of thiamine and Pabrinex: https://dailymed.nlm.nih.gov/dailymed/druglnfo.cfm?setid=af3f9344-f743-4bad-b319-53b96e13fee2

Nutrition and hydration

Food and fluid intake need to be monitored during withdrawal from alcohol. Dehydration from vomiting, sweating and diarrhoea is a risk that could induce further complications. Fluids should be encouraged and electrolytes monitored, including magnesium and potassium, as part of medical management of alcohol withdrawal.

People presenting in withdrawal often have loss of appetite and education about healthy eating should be part of withdrawal management and post withdrawal treatment. People with compromised physical health due to liver damage, gastric inflammation, dental problems, low albumin or general poor health, should be referred for specialist dietary advice and support.

Pregnancy

There is no safe level of alcohol use in pregnancy and pregnant women who have an alcohol use disorder and who agree to withdrawal management should be admitted to a specialist withdrawal unit if available. The use of benzodiazepines for alcohol withdrawal in pregnant women should be discussed with an addiction medicine specialist.

Management of alcohol withdrawal

The following are general principles for treatment planning for use in settings appropriate to the severity of withdrawal and or risk assessment.

Monitoring of withdrawal requires ongoing assessment and clinical judgement.

Risks in alcohol withdrawal management

A key cause of death in the management of alcohol withdrawal is related to the unsupervised prescription of benzodiazepines in current drinkers. Alcohol and diazepam when taken together can act synergistically and cause respiratory depression. People who are prescribed diazepam to support withdrawal in the community may drink alcohol impulsively or take more diazepam than prescribed putting them at risk of overdose. To mitigate this risk, those undergoing managed withdrawal in the community without specialist support should only be prescribed 'Close Control' medication, i.e. as low dose daily pick up from the pharmacy, or have consumption supervised by a professional or reliable informed support person.

Alcohol withdrawal management

Unplanned withdrawal

The AUDIT-C (https://www.alcohol.org.nz/sites/default/files/documents/AUDIT-C%20tool.pdf) and information about the amount of alcohol consumed daily can be easily used to screen for the risk of possible alcohol withdrawal in a non-specialist setting or in unplanned withdrawal management. This information can also be used as a general guide to providing appropriate medication support in the absence of immediate addiction specialist advice.

AUDIT-C score:

- under 3 - no medication needed, offer brief advice if drinking over 'safer' drinking limits, taking into account age and coexisting physical and mental health issues
- between 3 and 10 – no medication needed apart from oral thiamine 50mg qid or 100mg bd and refer to specialist addiction service with person's consent
- over 10 – carry out blood tests as above and, depending on results*, provide thiamine 200mg IV or Pabrinex 250mg IV:
  with a history of or evident withdrawal symptoms (shakes, agitation and sweaty), if drinking:
  - up to 10 standard drinks a day with mild withdrawal symptoms - provide 20mg oral diazepam and 200mg IV thiamine, reduce dose of diazepam by 5mg a day over four days
  - between 10 and 20 standard drinks a day with moderate withdrawal symptoms - provide 40mg oral diazepam and 200 mg IV thiamine, reduce dose of diazepam by 10mg a day over five days
  - over 30 standard drinks a day with moderate to severe withdrawal symptoms - provide IV thiamine. **Contact specialist service for urgent advice.** As the risk of withdrawal seizures is high at this level of consumption withdrawal management should only be carried out in a hospital or specialist setting.

*see note above about use of IV thiamine and IV Pabrinex

Planned community withdrawal management

Where community home based withdrawal management services are available the majority of people withdrawing from alcohol, particularly those with low to moderate CIWA-Ar scores, can safely be managed and cared for in their own homes or in supported/respite accommodation. A maximum dose of 40mg diazepam a day is considered safe for use in community based managed withdrawal.

Planned inpatient and hospital withdrawal management

The availability of 24 hour specialist nursing and medical supervision allows for the safer management of risks associated with alcohol withdrawal than in a community setting. This is particularly true for people with a known history of severe withdrawal, coexisting moderate to severe physical health problems, seizures and CIWA-Ar scores over 15.

Severity of withdrawal

Tremor, nervousness and sweating are the most sensitive markers of alcohol withdrawal and should be used as primary indicators of withdrawal severity. They are indicative of acute withdrawal. Diazepam should be commenced promptly, or the withdrawal management regime reviewed urgently, where these symptoms are present. See Appendix 2 for an alcohol withdrawal management medication regime.

The most commonly used rating scales to measure the severity of alcohol withdrawal are the Clinical Institute Withdrawal Assessment for Alcohol (Revised) Scale (CIWA-Ar) and the Alcohol Withdrawal Scale (AWS). Rating scales are not diagnostic instruments and assessment can be difficult if the practitioner using the tool is inexperienced assessing alcohol withdrawal or the person is medically unwell. The use of withdrawal rating scales may result in under-treatment of alcohol withdrawal if the practitioners are not familiar with their use.

The CIWA-Ar (Appendix 1) is the best-validated tool to assess alcohol withdrawal and is widely used in both inpatient and community settings because of its high level of inter-assessor reliability and ease of use. For clinicians trained in its use the CIWA-Ar provides a structured format to record the severity of withdrawal symptoms. The scale consists of 10 items and can be administered in about 5 minutes. A CIWA-Ar score of less than 10 indicates mild withdrawal, 10 to 15 moderate to severe withdrawal, and more than 15 very severe withdrawal. Alongside its usefulness in initial assessment of withdrawal symptoms the CIWA-Ar can be used to monitor changing withdrawal symptoms and the efficacy of withdrawal management over time.

Figure 3: Alcohol withdrawal severity and management

Indicators	Features	Withdrawal management setting
Mild withdrawal		**Community or home withdrawal management**
Drinking up to 10 standard drinks a day Mild to moderate substance use disorder severity on assessment Person has no significant coexisting physical or mental health problems No apparent significant risks of complicated withdrawal	mild rise in temperature mild hypertension mild anxiety slight tremor mild sweating nausea, vomiting mild dehydration headaches tachycardia dyspepsia sleep problems	Requires monitoring by community withdrawal management nurse in consultation with GP and or addiction service clinician/ practitioner Stable accommodation and commitment/support from appropriate whānau member or friend.
Moderate withdrawal		**Community 24 hr supervised residential setting**
Drinking between 10-20 standard drinks a day Repeated unsuccessful attempts to withdraw at home Person may have mild to moderate coexisting physical and or mental health problems Geographic isolation from a community withdrawal management nurse Unstable home or living environment No past history of complicated withdrawal	mild rise in temperature e.g., 37˚C mild –moderate hypertension (diastolic reading of 100-110Hg) mild tremor weakness dehydration headache moderate sweating dyspepsia nausea, vomiting diarrhoea anorexia moderate anxiety (will respond to reassurance) hyperventilation and panic attacks restlessness, agitation insomnia, nightmares	Requires 24 hr supervision by support workers with training in substance withdrawal and or use of CIWA-Ar scale. Up to date CPR training 24 hr access to medical practitioner Access to community withdrawal management nurse and addiction medicine specialist, physician or psychiatrist for consultation Medications blister packed and managed by residential support workers with support from community withdrawal management nurse during day.

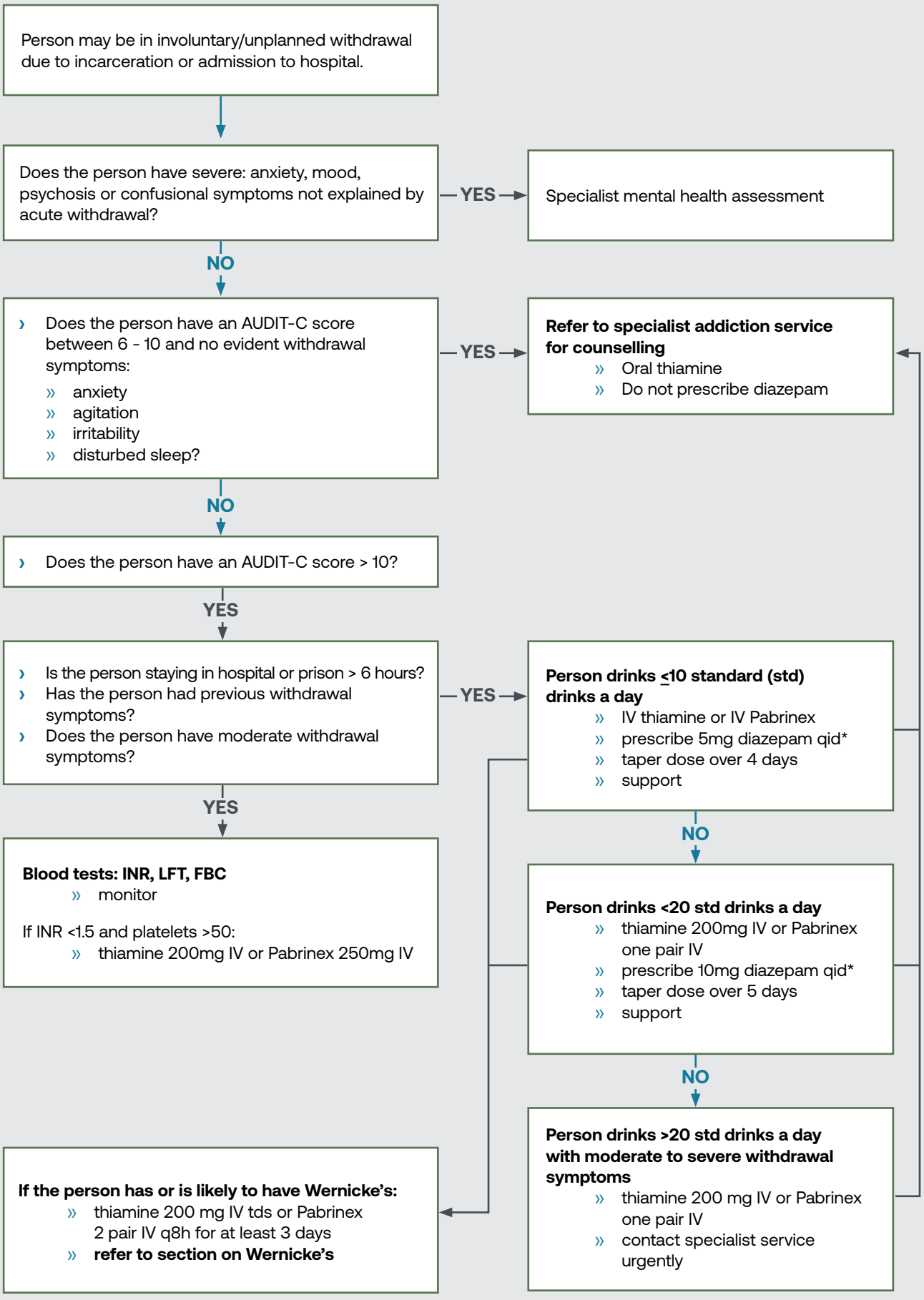
Indicators	Features	Withdrawal management setting
Severe		**Inpatient medical withdrawal management**
Drinking 20 or more standard drinks daily. (Blood alcohol level of 150mg/100mls) Past history of complicated withdrawal symptoms Serious coexisting physical and or mental health problems Older	hypertension (danger sign is diastolic pressure ≥ 120mmHg) or hypotension raised temp ≥ 37˚C marked tremor withdrawal seizures or history of seizures dehydration excessive sweating diarrhoea nausea, vomiting acute anxiety (may or may not respond to reassurance) restlessness and or aggression hypersensitivity to stimulation hallucination severe depressive disorder or severely depressed mood psychosis related to substance use	24 hr care from experienced nursing and medical staff Treatment for dehydration Treatment for altered electrolyte states Assessment of nutritional deficits Resuscitation capability

See Appendix 2 for an alcohol withdrawal management medication regime.

Note

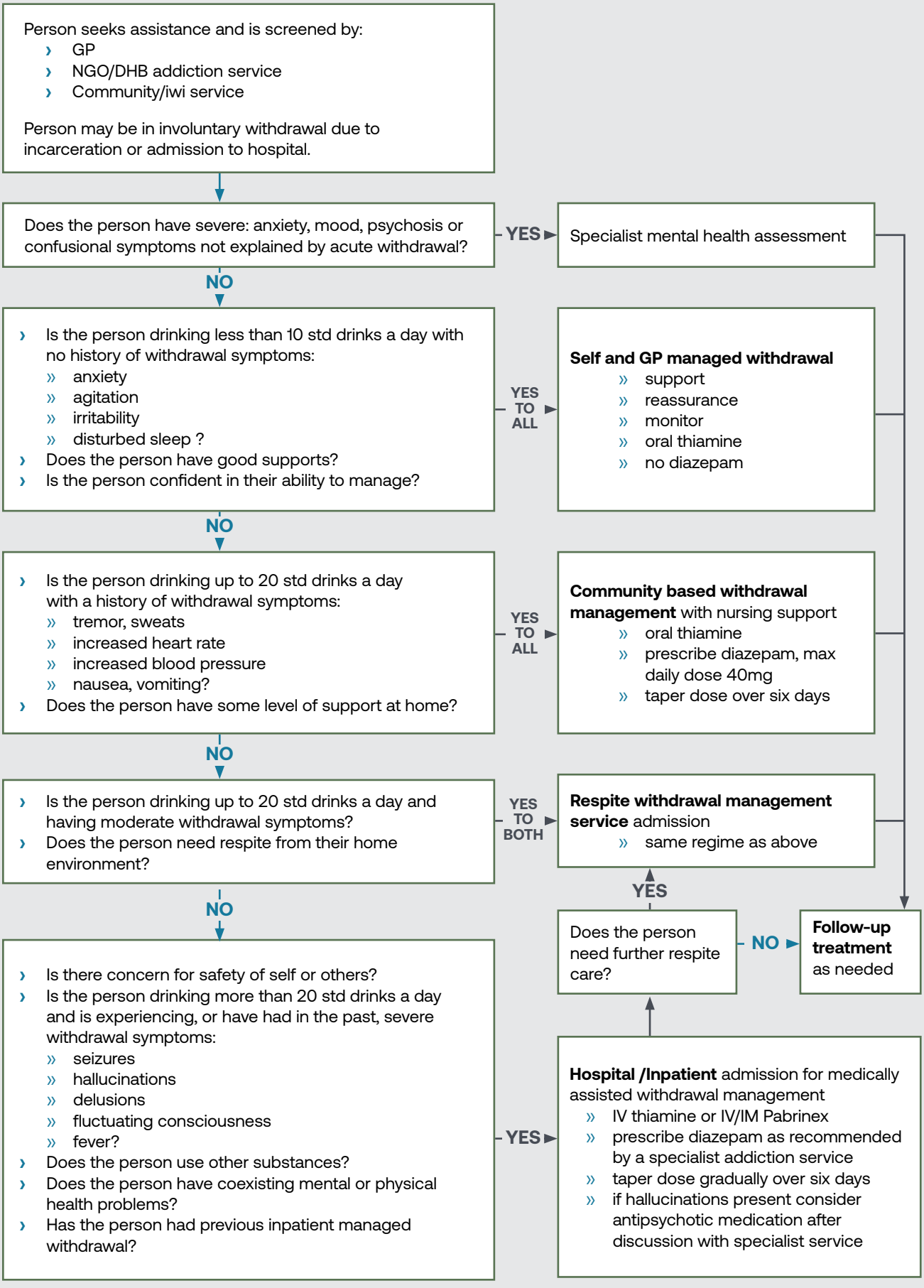
- do not exceed stated maximum diazepam doses in a twenty four hour period without consulting a medical practitioner, addiction medicine specialist, physician or psychiatrist
- if the person is older and or has severe liver dysfunction consider replacing diazepam with lorazepam or oxazepam which have no active metabolites and are less likely to accumulate to toxic levels
  - when using oxazepam or lorazepam the rate of reduction will need to be slower over a period of seven to ten days
- antipsychotic medication can reduce seizure threshold and there is a greater risk of adverse effects in those who are elderly, who have lower body weight or are dehydrated
- use of antipsychotic medication if the person is having distressing hallucinations should only be considered in consultation with an addiction medicine specialist, physician or psychiatrist.

Figure 4: Unplanned alcohol withdrawal management pathways



*If person is >65, or has liver impairment or is at risk of respiratory depression use oxazepam in preference to diazepam

Figure 5: Planned alcohol withdrawal management pathways



Amphetamine-type stimulants (ATS)

These guidelines have been developed to assist nursing and medical practitioners to identify amphetamine-type stimulant withdrawal symptoms and to provide safe withdrawal management strategies for people who have stimulant use disorders.

Amphetamine-type stimulants (ATS) are a group of substances consisting of synthetic stimulants including: amphetamine, dexamphetamine, methamphetamine, methcathinone, methylphenidate (Ritalin), methylenedioxymethamphetamine (MDMA or ecstasy-type substances), methylenedioxyamphetamine (MDA), piperazines (BZP, TFMPP etc), methylmethcathinone (mephedrone) and many other substances chemically related to amphetamine.

ATS are central nervous system stimulants that appear to be similar to the neurotransmitters dopamine, noradrenaline and serotonin and act by promoting their release from nerve terminals and blocking their re-uptake.

Assessment

A comprehensive assessment is the first step in managing withdrawal with the priority being to identify and define any risks.

A specific ATS use history includes:

- names and types of ATS used
- route of use and documentation of injecting sites
- average frequency and quantity of use, in milligrams, over time
- time of last use
- context of use
- periods of abstinence
- experience of withdrawal symptoms and how managed, e.g., self-sourced quetiapine
- other substances used concurrently, including frequency and amounts
- current or recent psychosis symptoms
- initial reasons for starting to use ATS
- current goals relating to use.

ATS withdrawal

The severity of ATS withdrawal symptoms generally depends on how much, how long and how a person has been using ATS. However, withdrawal symptoms can occur following heavy episodic (e.g., weekend) use. Smoking and intravenous use of methamphetamine in particular is associated with greater withdrawal symptom severity. Personality differences and pre-existing conditions can also impact on the severity of withdrawal.

Most people who use ATS also use a range of other substances at the same time. These include gamma hydroxybutyrate (GHB), alcohol, benzodiazepines, cannabis and opioids. Managing ATS withdrawal is often complicated by other substance withdrawal symptoms emerging and it is important to continue to monitor for these over time.

Risks associated with ATS withdrawal

- ATS withdrawal is not physically dangerous
- most people will complete withdrawal with only mild to moderate symptoms
- a past history of violence and aggression may indicate a risk of aggressive behaviour which could place other people at risk
- symptoms of psychosis may develop both when intoxicated and when in withdrawal
- underlying mental health issues may emerge during withdrawal
- medication is likely to be appropriate with those people with severe withdrawal symptoms and or coexisting problems
- while unlikely in withdrawal, serotonin toxicity may occur due to elevated serotonin levels, especially if the person is also prescribed a selective serotonin reuptake inhibitor (SSRI) or selective norepinephrine reuptake inhibitor (SNRI).

In an acute setting it is important to distinguish between methamphetamine toxicity, serotonin syndrome and withdrawal symptoms. Methamphetamine toxicity is marked by severe agitation, arrhythmia, fluctuating blood pressure, hyperthermia, metabolic and electrolyte abnormalities and on occasion seizures. Serotonin syndrome is marked by agitation, hyperreflexia, diaphoresis, hypertension, tachycardia, hyperthermia and potentially delirium and seizures. If the person has been taking serotonergic medication (SSRI's, SNRI's, tramadol) remove access to the medication and manage symptomatically. Where there is significant cardiovascular instability or a change in consciousness refer person to the Intensive Care Unit. As both conditions are potentially fatal collateral evidence may be required to distinguish between these states.

The St Vincent's Hospital brief *Guidelines for the Acute Assessment and Management of Amphetamine-Type Stimulant Intoxication and Toxicity* is a useful resource to have available in acute settings. https://www.svhm.org.au/ArticleDocuments/2140/ATSIntoxicationWithdrawalflowchartNov2014.pdf.aspx?embed=y

Onset and duration of withdrawal

After stopping use many people who use ATS 'crash', sleeping long hours and feeling fatigued and restless when awake. The 'crash' can last for up to three days. It is important to ensure that people are adequately hydrated and nourished through this period and this can require waking them up to drink fluids and eat food. Following the 'crash' withdrawal proper begins. Most symptoms peak between days two and ten but some symptoms can persist for several months, especially sleep and mood problems.

Figure 6: Symptoms of ATS withdrawal

Mild	Moderate	Severe
› restlessness › lethargy › low energy › irritability › agitation › sleep problems › low mood	› poor concentration and memory › mood swings › anxiety › anger › diarrhoea › aches and pains › hunger › insomnia › cravings	› depression › hallucinations › paranoia › psychosis

Management of ATS withdrawal

The following are general principles for treatment planning for use in settings appropriate to the severity of withdrawal and or risk assessment.

Monitoring of withdrawal requires ongoing assessment and clinical judgement.

Outpatient withdrawal management

Generally ATS withdrawal is not life threatening or physically risky and the function of withdrawal management is to provide support and reassurance through the withdrawal. If the person has only been using ATS there is rarely any need for medication such as benzodiazepines through the withdrawal process. Engagement in ongoing treatment and relapse prevention is the main goal.

To increase the likelihood of engagement:

- assume the person has cognitive problems and repeat information as often as needed to ensure understanding
- address health issues that could be causing pain
- monitor mood states and suicidal ideation closely
- provide dietary advice about the need for sustained healthy eating and multivitamin use following likely poor nutrition while using ATS
- involve mental health services if anxiety, depression or psychosis emerge as problems post withdrawal.

Inpatient withdrawal management

Inpatient ATS withdrawal management is rarely required unless people are using other substances that have a complicated withdrawal, such as alcohol, GHB and or benzodiazepines, or they have a serious coexisting physical or mental health disorder. When people meet these criteria the specific needs of people in ATS withdrawal include:

- enough space for people to move around freely
- access to a range of activities to help with distraction and relaxation
- not panicking or reacting in a challenging manner
- a low stimulus environment with minimal noise and environmental stressors
- ready access to beds for rest and sleep
- ready access to a variety of nutritious food.

Respite withdrawal management beds

The Government's Tackling Methamphetamine 2009 initiative made available 30 beds nationally to assist those with methamphetamine use disorders to have time out as a one-off opportunity or a lead-in to residential treatment.

Medication for ATS withdrawal

To date no specific pharmacotherapy has been identified as being effective for treatment of ATS withdrawal.

Benzodiazepines (e.g., diazepam) can help to manage severe anxiety, agitation and irritability and sleep disturbances in the week or two after the initial 'crash' that follows stopping ATS use. This however needs to be managed under supervision from a specialist addiction service or a GP.

On an outpatient basis:

- following the 'crash' 'Close Control' supervised diazepam, 5mg, three to four times daily for four to seven days
- dose and duration is dependent on each individual presentation
- low dose quetiapine as needed (prn) for sleep and irritability
- provide paracetamol for fever
- monitor and ensure adequate hydration
- provide antiemetics as required
- discuss and review with an addiction medicine specialist, physician or psychiatrist.

On an inpatient basis:

- medicate as necessary for withdrawal from other substances
- monitor closely and adjust as appropriate
- low dose quetiapine 'prn' for sleep and irritability
- provide paracetamol for fever
- monitor and ensure adequate hydration
- provide antiemetics as required.

Benzodiazepines should not be used for ATS withdrawal management for longer than one week and use should be monitored daily.

Adjunctive medication

Some ATS withdrawal symptoms may need to be treated with specific medications. What medication is appropriate to use should be discussed with an addiction medicine specialist, physician or psychiatrist.

Antidepressants

- can be helpful in combating the depressive symptoms frequently seen in methamphetamine withdrawal
- most antidepressants are not fully effective for some weeks so are not useful to treat acute low mood
- care also needs to be taken in case people have elevated serotonin levels as they will have an increased risk of serotonin syndrome.

Antipsychotics

- may help with sleep disturbances, agitation and anxiety at low doses
- can be prescribed by a GP in consultation with a specialist service as there may be contraindications with some antipsychotic medication
- are useful to manage psychoses that occur in ATS intoxication and withdrawal
- olanzapine has been shown to be better tolerated than haloperidol but both medications have been shown to be helpful in managing symptoms of psychosis.

Melatonin

Melatonin is a synthetic supplement that mimics natural melatonin and helps with sleep disturbances:

- evidence is limited for the effectiveness of melatonin when used in withdrawal management
- melatonin can be prescribed by a GP but is not funded by PHARMAC.

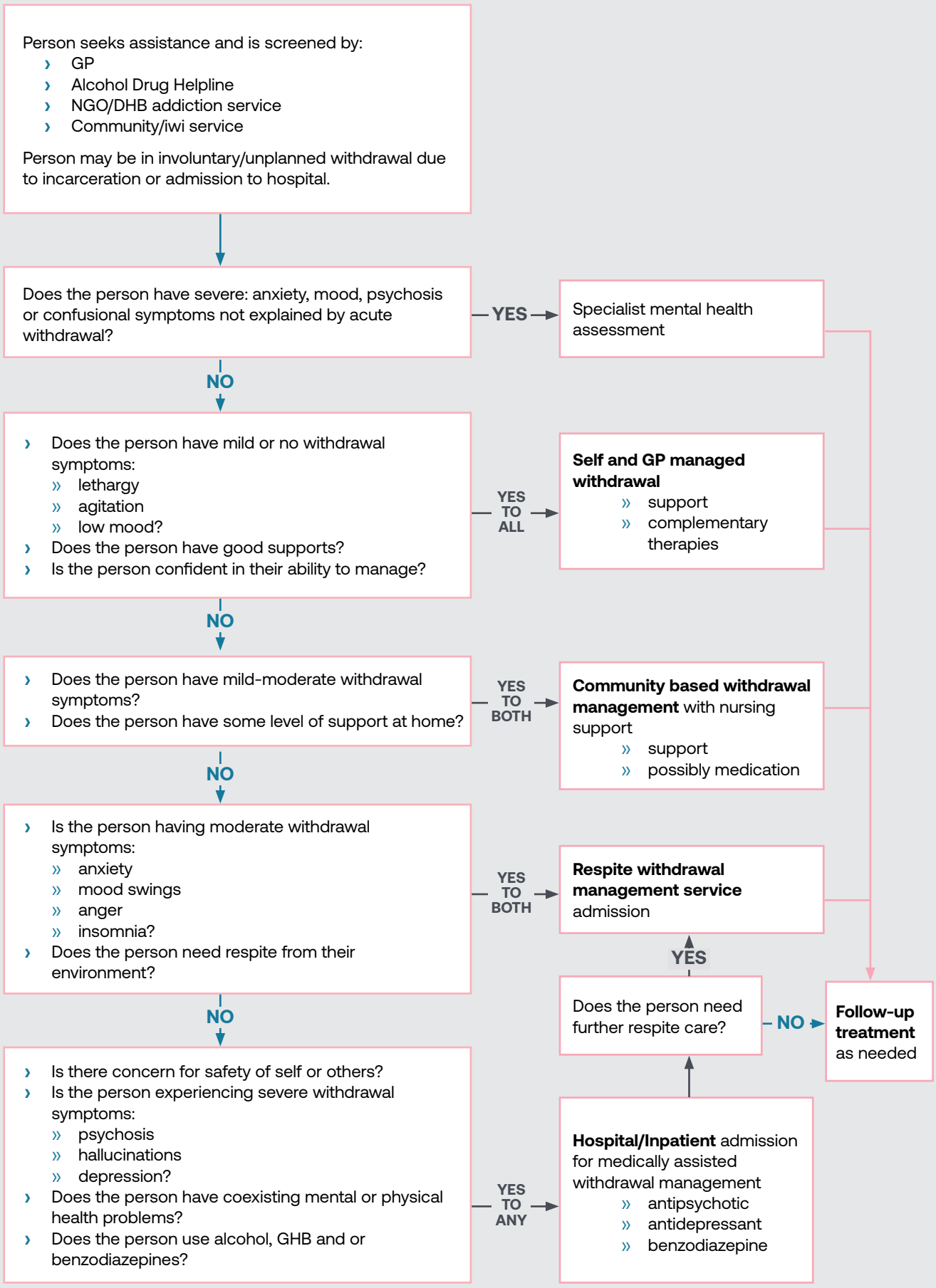
Complementary therapies

There is no reliable evidence to support the use of natural alternatives or complementary therapies for use in managing ATS withdrawal. However natural alternatives, see Appendix 10, can help with:

- anxiety
- sleep difficulties
- muscles aches
- relaxation
- irritability.

Note: St John's Wort needs to be used with caution in people with possibly elevated serotonin levels because of the risk of developing serotonin syndrome. See Appendix 8.

Figure 7: Amphetamine-type stimulant withdrawal pathways



Benzodiazepines and zopiclone

These guidelines have been developed to assist nursing and medical practitioners to identify benzodiazepine withdrawal symptoms and to provide safe withdrawal management strategies for people who have benzodiazepine use disorders.

Benzodiazepines (BZD) belong to the sedative-hypnotic group of substances which have depressant effects on the central nervous system. Zopiclone is included in this category as though it is chemically very different from the benzodiazepines it works in similar ways on the gamma-amino butyric acid (GABA) system and similar withdrawal symptoms are evident on discontinuation.

Benzodiazepines and zopiclone enhance the effect of the neurotransmitter GABA which results in varying sedative, hypnotic (sleep-inducing), anxiolytic (anti-anxiety), anticonvulsant, muscle relaxant and, depending on the type of benzodiazepine, amnesic action.

Assessment

A comprehensive assessment is the first step in managing withdrawal with the priority being to identify and define any risks.

A specific benzodiazepine use history includes:

- name of the benzodiazepine(s) or if zopiclone used
- average quantity of use, dose (in milligrams), over time
- time of last use
- is the benzodiazepine prescribed or non-prescribed
- initial reasons for starting to take benzodiazepines
- past history of seizures
- current goals relating to use.

There are two main types of benzodiazepine use disorders observed in people who present for treatment. The most common in general practice is low dose neuroadaptation to benzodiazepines or zopiclone that has developed over many years in people who have been prescribed them for a range of issues. This is seen most often in women and older people. High dose benzodiazepine use disorders also occur and are often seen in association with polysubstance use or a history of polysubstance use.

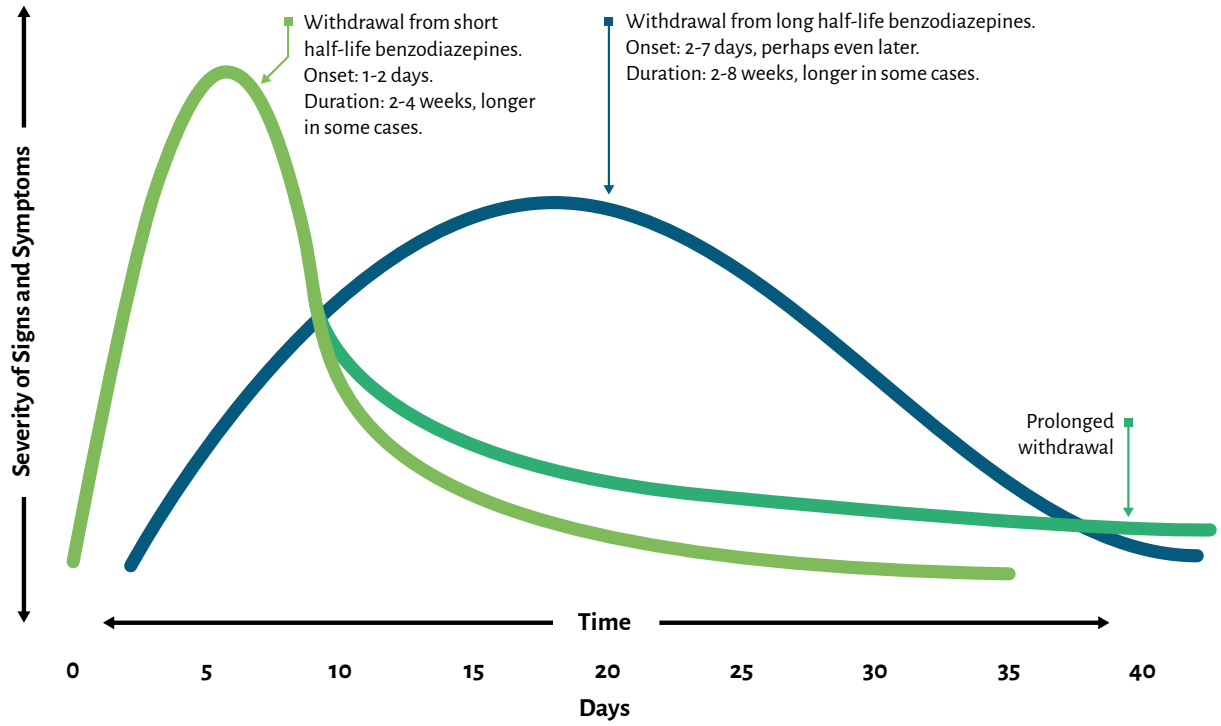
Benzodiazepine withdrawal

The primary aim of managed withdrawal is safety, with the person reducing or stopping use without major complications such as delirium, seizures or serious mental health consequences such as suicidality. Many people who have been prescribed benzodiazepines and zopiclone over the course of many years may wish to stay on their current dose and this will need to be discussed with them, especially if there are known risks, e.g., falls, associated with continuing on that dose.

Withdrawal is enhanced by having a clear management plan, effective communication, and stabilisation and a slow withdrawal using a long acting benzodiazepine. Close controlled daily dispensing may also be considered necessary for safety reasons if people have been consuming high doses of benzodiazepines.

Developing a good therapeutic relationship, along with reassurance and a gradual dose reduction, appears to improve outcomes for people undergoing benzodiazepine withdrawal.

Figure 8: Onset and duration of benzodiazepine withdrawal:



Symptoms and duration of benzodiazepine withdrawal

Adapted and used with permission: Frank, L. and Pead, J. (1995), *New concepts in drug withdrawal: A resource handbook*, Services for alcohol and drug withdrawal, Monograph No.4, Victoria, Australia

Onset and duration of benzodiazepine withdrawal

- the onset of withdrawal from short-acting BZD, marked by rebound insomnia and anxiety, generally occurs within one to two days after stopping use
- the onset of withdrawal from long-acting BZD generally starts two to seven days after stopping use
- withdrawal from short-acting BZD typically produces a quicker and more intense onset of symptoms than longer acting BZD
- the use of "therapeutic doses" of BZD or zopiclone for as short a period as four weeks can result in neuroadaptation and a withdrawal syndrome that may last from one to six weeks on stopping use
- not all individuals stopping BZD will experience withdrawal symptoms and for those who do the symptoms are not always disabling
- BZD withdrawal syndrome may last from six months to a year for those people who have been using BZD on a long-term basis and most will benefit from psychological support through this process
- using high doses of BZD over a prolonged period of time is more likely to result in severe withdrawal symptoms
- withdrawal symptoms may also be more severe for those that are using more than one BZD at a time.

Figure 9: Symptoms of benzodiazepine withdrawal

Common	Less common	Uncommon severe symptoms
› anxiety › insomnia, disturbed sleep › restlessness › agitation › irritability › depression › poor memory › poor concentration › muscle tension › aches and twitching › sweating	› headache › nightmares › tremor › fatigue › weakness › appetite/weight change › tingling › dizziness, poor balance › blurred/double vision › feelings of unreality › dry mouth › increased sensory perception - metallic taste › flushing/sweating › palpitations › gastrointestinal upset › urinary difficulties › menstrual changes › skin rashes, itching	› delusions › paranoia › hallucinations › confusion › persistent tinnitus › seizures

Management of benzodiazepine withdrawal

The following are general principles for treatment planning for use in settings appropriate to the severity of withdrawal and or risk assessment.

Monitoring of withdrawal requires ongoing assessment and clinical judgement. Benzodiazepine withdrawal scales have not proven to be reliable and useful in treatment planning.

Outpatient withdrawal management

- diazepam is used for withdrawal management as it has a long half-life, reducing the need for multiple daily doses to prevent the emergence of withdrawal symptoms
- if the person is older and or has severe liver dysfunction replace diazepam with clonazepam or oxazepam which have no active metabolites and are less likely to accumulate to toxic levels and or contribute to the risk of falls and fractures
- convert the average daily dose into an 'equivalent' dose of diazepam using conversion chart (see Appendix 3)
- prescribe 'equivalent' dose in two to four divided doses per day, guided by the person's reported symptoms and monitoring for signs of toxicity due to long half-life of diazepam
- stabilise person on 'equivalent' dose for at least 4 weeks before starting reductions
- initial conversion and stabilisation from high doses may need to be carried out in an inpatient setting
- a typical guideline for reduction of dose is between 10-20% at fortnightly intervals
- if the person is on doses above 40mg of diazepam reduce by 5mg-10mg every two weeks until the dose reaches 40mg and then reduce as above
- the lower rate of dose reduction will allow for neuroadaptation to the new dose of diazepam and reduce withdrawal severity
- regularly review and titrate the dose of diazepam to the severity of apparent and self-reported withdrawal symptoms

- in general a reducing regime will take six to eight weeks
- depending on the person and their circumstances some reducing regimes may need to take months or even years
- initiate therapeutic support to address issues, e.g., trauma, insomnia or anxiety, that contributed to the initiation of BZD use as soon as the person is able to engage in the process
- if there is significant or distressing withdrawal symptoms that emerge at any time during the reduction the dose may be held steady until the symptoms improve
- raising the dose in response to distress is never recommended
- providing ready access to talking therapies during the process will support the person experiencing distress
- the effectiveness of the withdrawal management process may be improved by slowing down the rate of reduction when the person is on a lower dose, such as below 15mg diazepam.

Low dose iatrogenic neuroadaptation can be safely managed by a GP with support and follow up from a specialist addiction service. In many areas community withdrawal management nurses may be available to support the withdrawal process and or monitor symptom severity as needed.

For people that present needing assistance for withdrawal from zopiclone, unless taking low doses at night (i.e. no more than 3 tablets), it is recommended to follow the same general principles as for benzodiazepine withdrawal. Zopiclone should be converted to diazepam (see Appendix 3) and then slowly reduced over time, guided by the person's symptoms. Zopiclone tablets can be hard to break into lower doses and due to the very short half-life and rebound anxiety some people may require assistance from a specialist service.

Inpatient withdrawal management

The availability of 24 hour specialist nursing and medical supervision allows for a more rapid and safe conversion and stabilisation process than in a community setting for people assessed as having severe withdrawal risks and or severe coexisting mental and or physical health problems. This can include people who have coexisting substance use problems and or are engaged in Opioid Substitution Treatment.

- convert the average daily BZD dose into equivalent dose of diazepam using conversion chart (Appendix 3)
- divide the equivalent dose into three or four divided doses/day
- once stable on the dose of diazepam the person can be transferred and managed by a specialist service in an outpatient setting if appropriate.

Caution:

While diazepam is recommended for benzodiazepine withdrawal management it needs to be used with extreme caution and may be contraindicated in older people and in certain conditions such as respiratory failure and or liver disease. If there are medical conditions that are negatively affected by long acting benzodiazepines then use of a short acting benzodiazepine should be considered.

Adjunctive medication

There is insufficient evidence based research to recommend specific alternative pharmacological treatment(s) for management of benzodiazepine withdrawal. However some medications that could be helpful can be considered on an individual basis following discussion with an addiction medicine specialist, physician or psychiatrist.

Antidepressants

- can be helpful for people with persistent features of depression and or anxiety with a pre-existing DSM5 diagnosis
- if not already available assessment by a GP or psychiatrist should be considered
- SSRI's and SNRI's are the most commonly used antidepressants
- low dose tricyclic antidepressants have also been used as an aid for sleep difficulties (Ashton, 2002).

Antipsychotics

- may help with sleep disturbances, agitation and anxiety at low doses
- generally not recommended.

Beta blockers

- can be used in the rare cases of withdrawal where severe palpitations, muscle tremors or motor jerks are causing significant problems
- may be useful at the end of the withdrawal process to treat anxiety
- can be prescribed regularly in low doses for a short period of time or taken on an as needed (prn) basis (Ashton, 2002)
- should be prescribed in consultation with an addiction medicine specialist, physician or psychiatrist.

Melatonin

- a synthetic supplement that mimics natural melatonin and helps with sleep disturbances
- evidence is limited for the effectiveness of melatonin when used in withdrawal management
- melatonin can be prescribed by a GP but is not funded by PHARMAC.

Complementary therapies

There is no reliable evidence to support the use of natural alternatives or complementary therapies for use in managing benzodiazepine withdrawal. However natural alternatives, see Appendix 10, can help with:

- anxiety
- sleep difficulties
- muscles aches
- relaxation.

Special populations

Older people

For older people the benefits of withdrawal can include:

- improved cognition
- alertness
- mobility
- reduced risk of incontinence
- a reduced risk of falls and fractures.

The effectiveness for older people of a managed withdrawal, i.e. gradually tapering doses of benzodiazepines, is apparently similar to the outcomes with younger people (Ashton, 2002), but should be guided by an analysis of the risks and benefits for the person of continuing to take benzodiazepines and discontinuing benzodiazepines.

People with chronic physical illness

Similar to older people many people with physical illnesses may be unable to metabolise benzodiazepines efficiently and accumulation can occur. Following a risk and benefit analysis and if a reduction is initiated it is recommended that withdrawal is monitored closely and doses adjusted to the needs of the individual or a different long acting benzodiazepine is used for a reducing dose.

Pregnant women

Abrupt cessation of benzodiazepines is not recommended for pregnant women who have a benzodiazepine use disorder. If the woman is able to tolerate it, a gradual reduction regime under medical supervision is essential for safety. On occasion it may be necessary to stabilise a pregnant woman on a controlled dose of diazepam during the pregnancy to ensure the safety of the fetus. It is likely that the baby will need specialist support for neonatal abstinence syndrome (NAS) when born and this will need to be arranged ahead of time.

Neonates

Babies born with benzodiazepine intoxication and or withdrawal can present with symptoms which can last for weeks after birth. These include:

- respiratory depression
- poor sucking
- hypotonia
- poor temperature regulation.

Abrupt benzodiazepine withdrawal at birth has been shown to result in:

- neonatal irritability
- hypertonia
- seizures
- diarrhoea.

Neonatal abstinence syndrome (NAS)

Onset may occur one to ten days after delivery and can last from seven days to one month.

- babies born to women who have a benzodiazepine use disorder should be observed in hospital for one week before discharge
- following this they should have weekly outpatient reviews for at least one month
- the Finnegan scale (Appendix 5) may be used to identify neonatal abstinence syndrome associated with benzodiazepines.

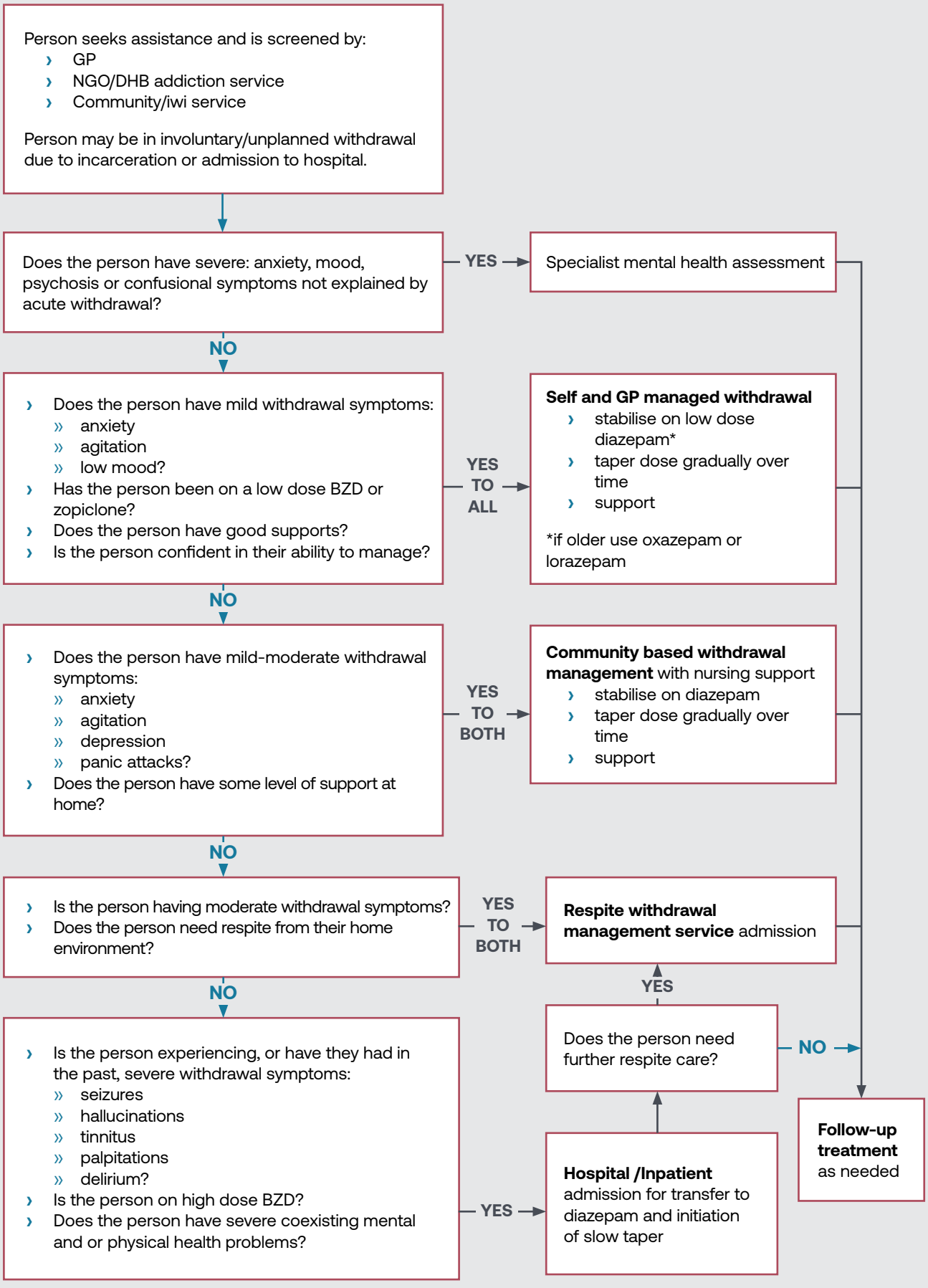
Breastfeeding

- breastfeeding is not recommended for women who are using higher than therapeutic doses of benzodiazepines
- breastfeeding should be postponed if a mother appears sedated or the mother should be securely sitting in a chair with the baby well supported.

For more detailed guidance please refer to: *Clinical Guidelines for the Management of Substance Use During Pregnancy, Birth and the Postnatal Period* (2014)

This is available at: https://www.health.nsw.gov.au/aod/professionals/Publications/substance-use-during-pregnancy-guidelines.pdf

Figure 10: Benzodiazepine withdrawal management pathways



Cannabis

These guidelines aim to assist nursing and medical practitioners with the assessment and identification of cannabis withdrawal symptoms in order to be able to provide safer withdrawal management.

The main active ingredient of cannabis is Delta-9 tetra-hydrocannabinol (THC). Cannabidiol (CBD) is another significant active ingredient of cannabis. THC is thought to exert its effect by binding to cannabinoid CB1 receptors on pre-synaptic nerve terminals in the brain, activating G-proteins that activate/inhibit a number of signal transduction pathways.

The major effects of cannabis are on the central nervous, gastrointestinal and cardiovascular systems.

See below for information on synthetic cannabinoids.

Assessment

A comprehensive assessment is the first step in managing withdrawal with the priority being to identify and define any risks.

A specific cannabis use history includes:

- quantity of use, amount consumed, type of cannabis and potency
- duration, pattern and frequency of use
- mode of administration (smoked or eaten, mixed with tobacco)
- time and amount of last use
- past history of aggression and violence
- goals relating to use.

Cannabis withdrawal

People wanting to withdraw from cannabis should be provided with a menu of intervention options. This may include the choice of sudden cessation, with or without symptomatic medication, or a supported gradual reduction using psycho-social interventions.

Risks associated with cannabis withdrawal

- cannabis withdrawal is not physically dangerous
- most people will complete withdrawal with only relatively mild symptoms
- a past history of violence and aggression may indicate a risk of aggressive behaviour which could place other people at risk
- underlying mental health issues may be unmasked during withdrawal
- suicidality and self-injury may be a risk factor for people with a coexisting mood disorder or psychosis
- people with severe withdrawal symptoms and or coexisting problems may require appropriate medication.

Onset and duration of withdrawal

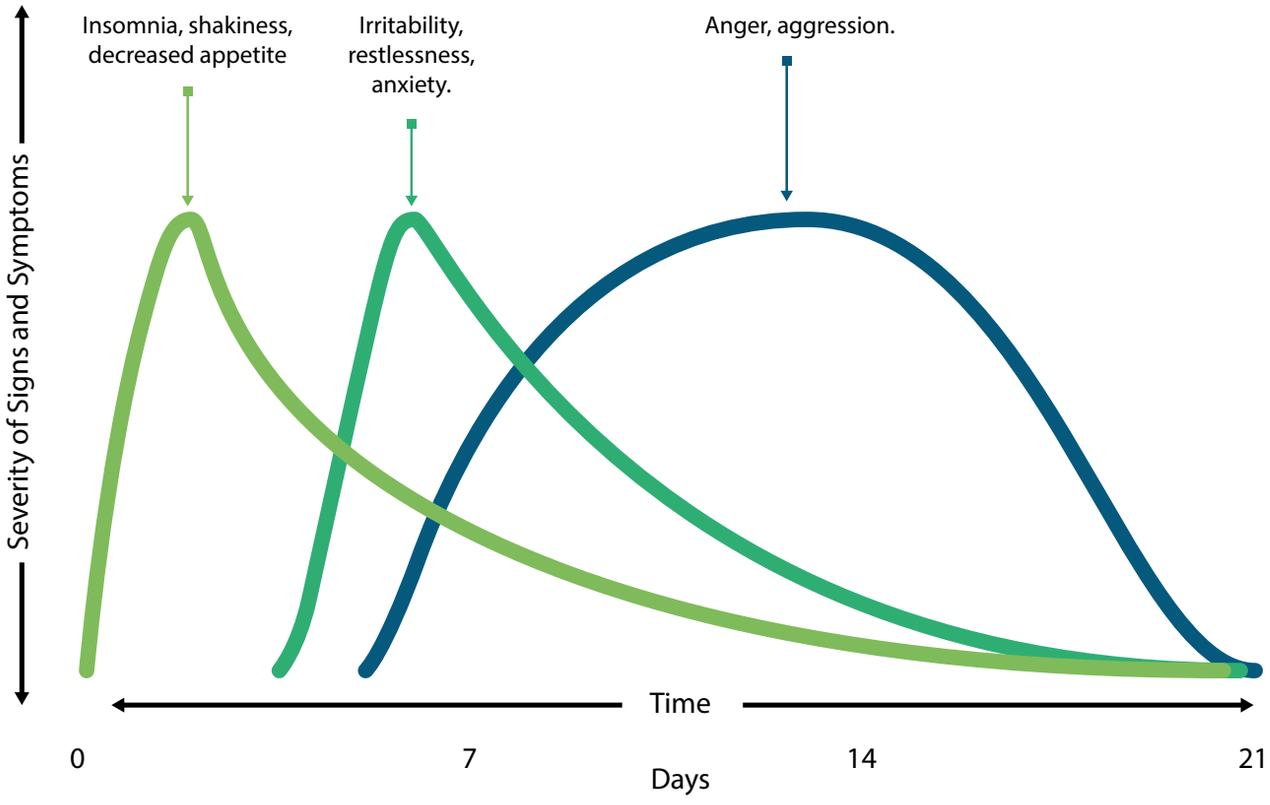
Onset of cannabis withdrawal usually occurs one to two days after last use. Most symptoms peak between days two and six. It is important to note that withdrawal severity and duration will be dependent on the individual and the following variables:

- the amount, frequency and strength of cannabis used
- duration of current patterns of use
- stopping suddenly or reducing levels of use over time

- other substance use
- coexisting mental health problems
- coexisting physical health problems including chronic pain
- history of aggression or violence
- outpatient or inpatient setting.

Note: The emergence of problems with aggression and anger may be delayed and can be evident for up to two to three weeks after stopping use. The duration and intensity of withdrawal symptoms tends to be correlated with the potency and amounts of cannabis used over time.

Figure 11: Cannabis withdrawal symptoms over time



Symptoms and duration of cannabis withdrawal

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Figure 12: Symptoms of cannabis withdrawal

Mild	Moderate	Severe
› restlessness › irritability › nervousness › anxiety › agitation › sleep problems	› poor concentration › mild depressive symptoms › nausea › loss of appetite › increased appetite › anger › intense dreaming › nightmares › craving	› aggression › exacerbation of existing mood disorder › suicidality › headaches › insomnia › vomiting › heavy sweating

Management of cannabis withdrawal

For the majority of people comprehensive assessment, treatment planning and supportive counselling are the main strategies for managing cannabis withdrawal and can be safely provided in the community. Medication and or admission into a respite withdrawal management facility are rarely required apart from those people with coexisting problems, including other substance use, a history of aggression and or inappropriate home environments.

There is currently no validated assessment tool for monitoring the severity of cannabis withdrawal however the Cannabis Withdrawal Scale (Allsop et al., 2011) may be useful in clinical practice (Appendix 6).

Medication for management of cannabis withdrawal

To date no specific pharmacotherapy has been proven to significantly help with managing cannabis withdrawal.

Atypical antipsychotic medication, e.g., quetiapine, has been used short-term to help manage agitation, anxiety and sleep problems in cannabis withdrawal. There is limited evidence to date to support this practice and anecdotal reports of efficacy. Use of antipsychotic medication for this purpose should be only considered in consultation with an addiction medicine specialist, physician or psychiatrist.

Benzodiazepines (e.g., diazepam) may help with managing very severe withdrawal symptoms such as extreme anxiety, agitation, irritability and aggression and prolonged sleep difficulties. This however needs to be managed under supervision from a specialist addiction service.

If the person is in a respite setting 'Close Control' zopiclone can also be helpful for sleep for the first two to three days.

On an outpatient basis:

- 'Close Control'- supervised daily dispensing - diazepam 5 to 10mg, two to four times daily for four to seven days
- dose and duration is dependent on each individual presentation
- discuss and review with an addiction medicine specialist, physician or psychiatrist.

Benzodiazepines should not be considered a treatment of choice for cannabis withdrawal management and if used should not be prescribed for longer than two weeks and use should be monitored on a daily basis.

Adjunctive medications that may be helpful in managing some withdrawal symptoms include:

- chlorpromazine – restless leg
- paracetamol - headaches, muscular aches, sweating, chills and pain
- nonsteroidal anti-inflammatory drugs (NSAID's) - headaches, muscular aches and pain (contraindicated if person is dehydrated)
- magnesium – headaches and muscular aches
- ondansetron – nausea
- capsaicin - hyperemesis
- antihistamines – nausea, nasal congestion
- metoclopramide – nausea
- prochlorperazine – nausea, nasal congestion.

(Winstock and Lea, 2009)

Complementary therapies

In the absence of evidence based medication to assist with the management of cannabis withdrawal symptoms, many addiction services use or recommend the use of alternative therapies, see Appendix 10, for sleep disturbances and agitation.

Note: Ongoing monitoring of the person's wellbeing and mental health status post withdrawal is recommended as mental health symptoms may have been masked by ongoing cannabis use.

Special populations

Pregnant women

There is some limited research into the effects of cannabis on fetal development which indicates a raised risk of low birth weight and possible developmental delays. Pregnant women should be advised to stop cannabis use and supported to do so, without the use of medication if possible. Reducing levels of use over time may be a helpful strategy.

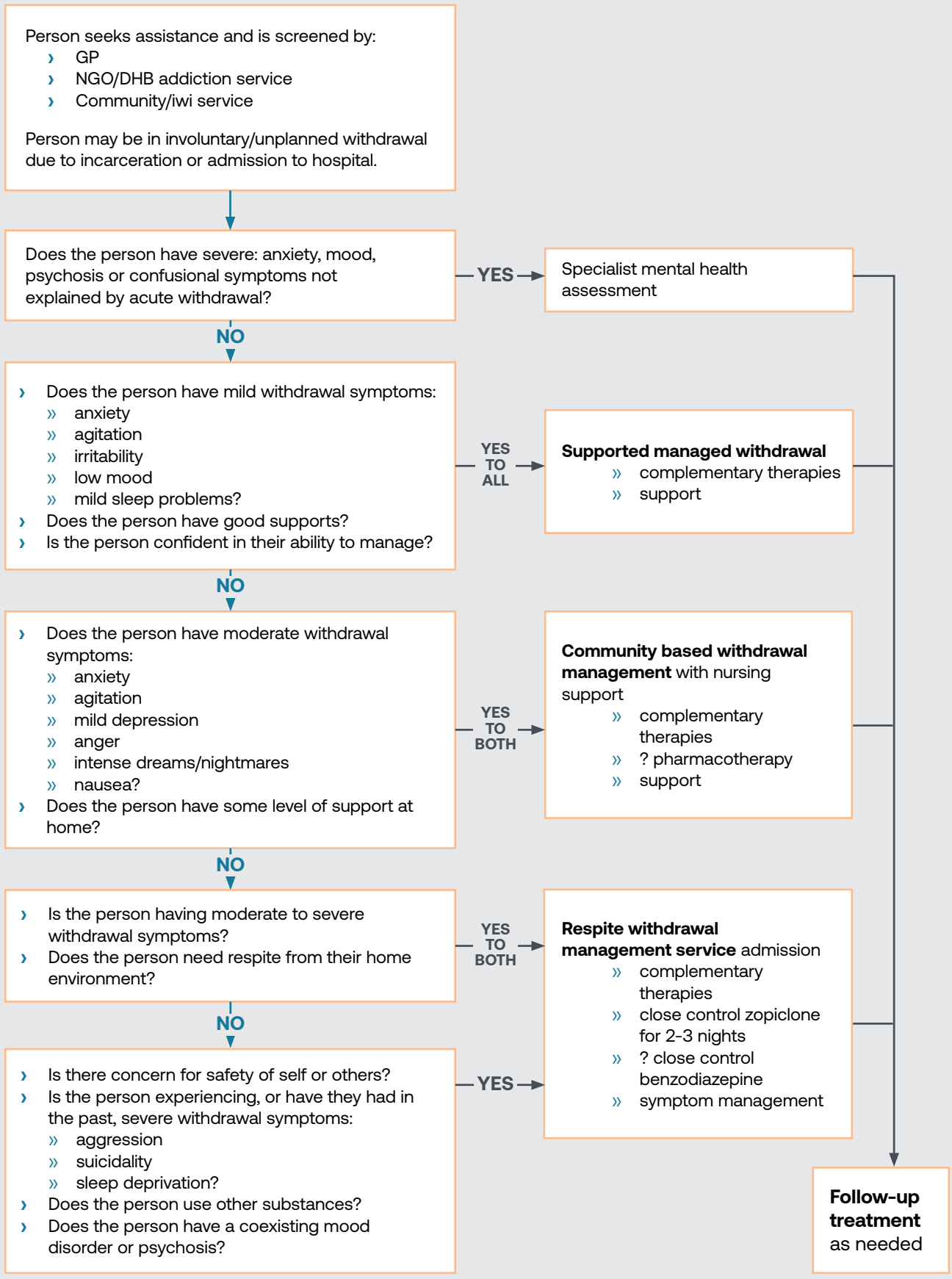
Neonate

There is some evidence that neonates may experience mild withdrawal from cannabis following birth. The most common features that have been observed are:

- restlessness
- agitation and crying
- not settling
- poor sucking.

Often withdrawal symptoms will not become apparent until at least the second week postnatal. Supportive settling techniques are the only recommended treatment.

Figure 13: Cannabis withdrawal management pathway



Gamma-hydroxybutyrate (GHB)

These guidelines have been developed to assist nursing and medical practitioners to identify gamma-hydroxybutyrate acid withdrawal symptoms and to provide safe withdrawal management strategies for people who have a GHB use disorder.

Gamma-hydroxybutyrate acid (GHB) and its analogues, 1, 4-butanediol (1, 4-BD) and gamma-butyrolactone (GBL), are endogenous inhibitory neurotransmitters and anaesthetics, with a similar action to benzodiazepines. GHB is believed to possess partial agonist activity at the GABA-B receptor, and further activity may be related to conversion of GHB to GABA. GHB also has effects on dopamine, acetylcholine, serotonin, glutamate and opiate neurotransmission (Wojtowicz et al., 2008). The action of GHB on the central nervous system is known to be highly dose dependent. In high doses, profound sedation and seizures can occur (Cape et al., 2002).

Polysubstance use along with GHB is common. Attention should be focused on other central nervous system depressants such as alcohol, benzodiazepines and opioids as the person may require close monitoring to assess and identify the risks of central nervous system depression.

Assessment

A comprehensive assessment is the first step in managing withdrawal with the priority being to identify and define any risks.

A specific GHB use history includes:

- average quantity (usually in “mls” as consumed as a liquid) and frequency of use over time
- time of last use
- other central nervous system depressants used concurrently
- history of seizures
- cognitive deficits and history of trauma
- peer affiliations
- initial reasons for starting to use GHB
- current goals relating to use.

GHB withdrawal syndrome has been well documented, however there is little in the way of international evidence or guidelines documenting withdrawal management strategies. Predicting the course of GHB withdrawal is difficult. Studies reviewing the available literature report that severe neuroadaptation, as reflected in high frequency of use (every 1 to 2 hours) and daily amount (over 20mls a day), is associated with the need for medicated withdrawal management. Use of over 30mls a day will require withdrawal management in an inpatient setting.

Withdrawal from GHB can be associated with a severe, potentially life threatening withdrawal state that requires vigorous clinical management (McDonough et al., 2004).

GHB withdrawal

Withdrawal severity appears to be dependent on frequency of use and amounts used. Mild withdrawal may occur after occasional use but is more likely to occur after several weeks of daily use. Severe withdrawal tends to be associated with using GHB several times a day over an extended period of time. Withdrawal symptoms do not always progress from mild to severe in a predictable way.

Figure 14: Symptoms of GHB withdrawal

Mild	Moderate	Severe
› anxiety › sweating › restlessness › insomnia › mild hypertension	› tremor › tachycardia › nausea › vomiting › abdominal cramps › diarrhoea	› tachycardia (may present as transient spikes) › hallucinations (visual, auditory, tactile) › delusions or paranoia › psychosis in clear consciousness › delirium › hypertension › rhabdomyolysis › seizures

Management of GHB withdrawal

The following are general principles for treatment planning in settings appropriate to the severity of withdrawal and or risk assessment.

Monitoring of withdrawal requires ongoing assessment and clinical judgement.

As the use of GHB is a relatively new phenomenon and withdrawal is apparently rare, withdrawal scales have not as yet been developed for use in treatment planning.

The onset of withdrawal symptoms can be rapid (one to six hours after the last dose) and symptoms prolonged (five to fifteen days). There is a possibility that chronic use of GHB can contribute to the development of Wernicke's encephalopathy and accordingly people should be provided prophylactic thiamine as in alcohol withdrawal (Friedman et al., 1996).

Outpatient withdrawal management

Community or supported outpatient withdrawal management is suitable for most people using less than three times or less than 30ml* of GHB a day.

- provide thiamine as outlined in alcohol withdrawal guide
- on the first day dispense up to 40mg of diazepam orally till settled (as in mild to moderate alcohol withdrawal regimes)
- monitor physical state on daily basis
- if symptoms are not alleviated or worsen admit for inpatient withdrawal management
- on the second day of managed withdrawal maintain on the same dose of diazepam, split into four doses (qid), as was adequate to manage symptoms on day one
- reduce to zero over seven days.

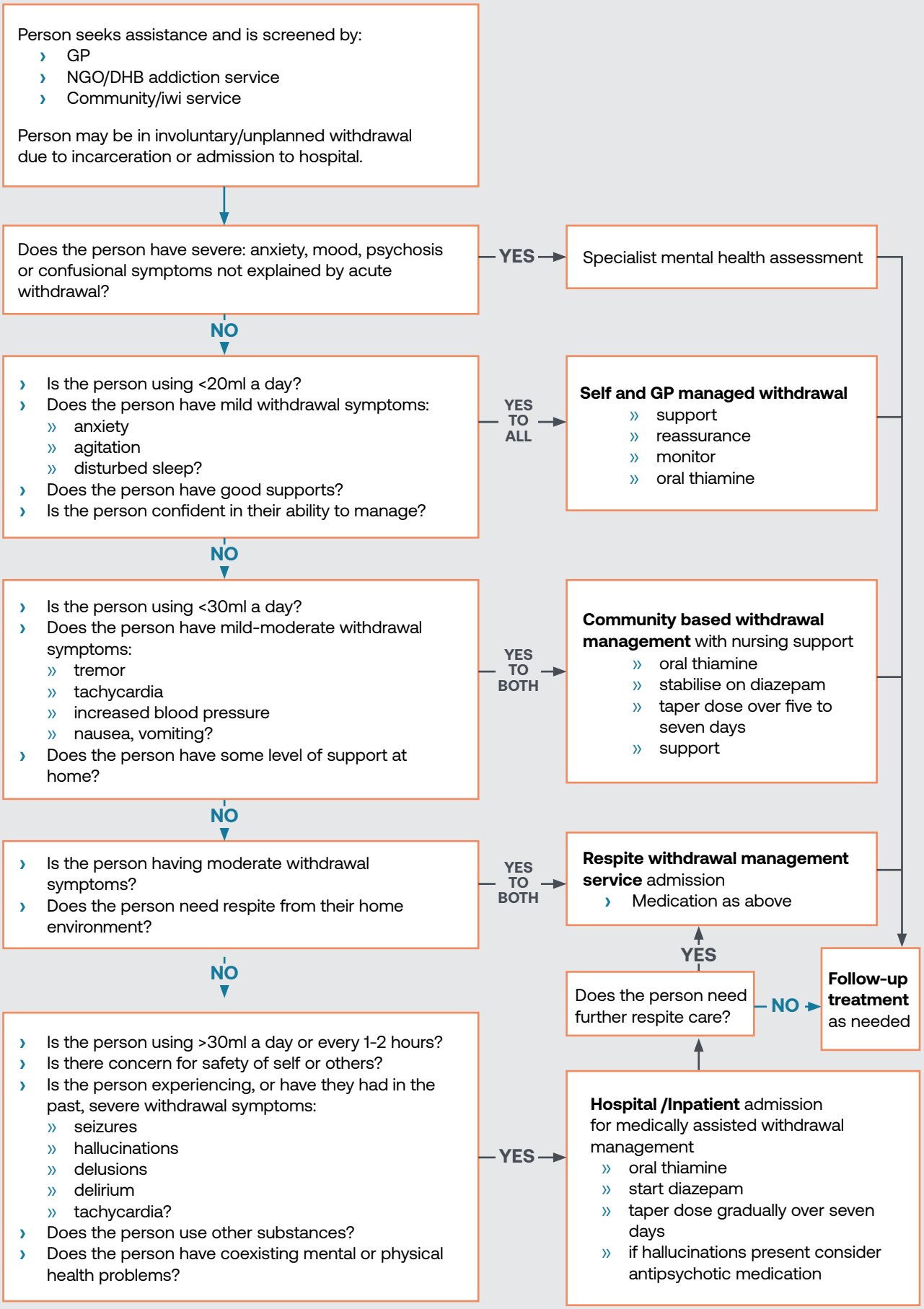
*Note: converting the persons reported levels of use from "ml's" into grams can only be approximate as more than 1gm of sodium GHB can be dissolved in 1ml of water.

Inpatient withdrawal management

The availability of specialist nursing and medical supervision allows for the safer management of risk than in a community setting. This is particularly true for people with a known history of severe withdrawal, seizures and very high levels of GHB use, i.e. over 30ml a day.

- provide thiamine as outlined in alcohol withdrawal guide
- in the absence of delirium provide up to 50mg of diazepam until settled
- if familiar with the CIWA-Ar use it to guide medication choices
- in the presence of delirium people may require up to 150mg of diazepam orally or intravenously
- do not exceed 150mg unless in consultation with addiction medicine specialist, physician or psychiatrist and only if airway support is available
- if the person is older and or has severe liver dysfunction consider using oxazepam or lorazepam as they have no active metabolites and are less likely to accumulate to toxic levels
- reduce diazepam, lorazepam or oxazepam doses over five to seven days or as symptoms persist
- if the person in withdrawal is having distressing hallucinations consider the use of an antipsychotic medication in consultation with an addiction medicine specialist, physician or psychiatrist
- where more severe symptoms emerge admission into intensive care may be necessary.

Figure 15: GHB withdrawal management pathway



Inhalants

These guidelines have been developed to assist nursing and medical practitioners to identify inhalant withdrawal symptoms and to provide safe withdrawal management strategies for people who use inhalants regularly and may have an inhalant use disorder.

The term inhalant is used to describe the wide range of volatile substances whose chemical fumes can have psychoactive effects when inhaled.

Commonly used products include:

- liquids: glue, petrol, contact cement (rubber cement), thinners, lacquers, nail-polish remover, dry-cleaning fluids, amyl nitrite
- aerosols: spray paints, lighter fluid, cooking sprays, cosmetics, hairspray, toiletries, deodorants
- gases: butane, LPG, nitrous oxide.

Chemicals found in inhalants include the following:

- propane
- butane
- n-hexane
- trichloroethylene
- freon
- benzene
- toluene
- xylene
- acetone
- methyl isobutyl ketone
- chlorinated hydrocarbons.

The majority of inhalants used as intoxicants are central nervous system depressants with effects similar to alcohol. Effects include slurred speech, lack of coordination, euphoria, and dizziness. Inhalant use may also lead to light-headedness, hallucinations, and delusions. As the effects are short lived many people try to prolong them by repeated use over a short period of time and this can result in disinhibited behaviour. The chemicals in different types of inhalants may also produce side effects such as palpitations, burns, confusion, nausea, or vomiting.

Assessment

A comprehensive assessment is the first step in managing withdrawal with the priority being to identify and define any current risks and risk of relapse.

A specific inhalant use history includes:

- type or types of inhalant used
- average quantity and frequency of use over time
- duration of regular inhalant use
- time of last use
- other central nervous system depressants used concurrently
- history of seizures
- cognitive deficits and history of trauma
- physical health issues
- peer affiliations
- initial reasons for starting to use inhalants
- current goals relating to use and relapse risks including income, history of brain injury and peers.

Inhalant withdrawal

Inhalant withdrawal syndrome is not well recognised or documented in the international literature and there is limited evidence or guidelines for managing withdrawal symptoms. It is apparent however that long term inhalant use may result in withdrawal symptoms when use is stopped.

Withdrawal severity appears to be dependent on frequency and intensity of use and symptoms can occur within hours of stopping use. Withdrawal symptoms appear to peak two to five days after stopping use of inhalants.

Figure 16: Symptoms of inhalant withdrawal

Mild	Moderate	Severe
› tremor › disturbed sleep › tiredness › nausea › anxiety › irritability › low mood › sweating	› tingling sensations › restlessness › chills › cramps › agitation › headache › abdominal pain › intense craving	› tachycardia › hallucinations › delirium › seizures

Management of inhalant withdrawal

The following are general principles for treatment planning in settings appropriate to the severity of withdrawal and or risk assessment.

Monitoring of withdrawal requires ongoing assessment and clinical judgement.

As the use of inhalants is usually time and age limited and people rarely develop an inhalant use disorder withdrawal is relatively rare. Inhalant withdrawal scales have not as yet been developed for use in treatment planning.

Medication for management of inhalant withdrawal

As the risk of immediate harm from the use of inhalants is so high managing withdrawal symptoms that might trigger use is a priority. The threshold for use of medication needs to be lower than in other circumstances, particularly when treating young people. While an evidence base for treating inhalant withdrawal does not exist the following medications have been used to help with symptomatic relief of inhalant withdrawal:

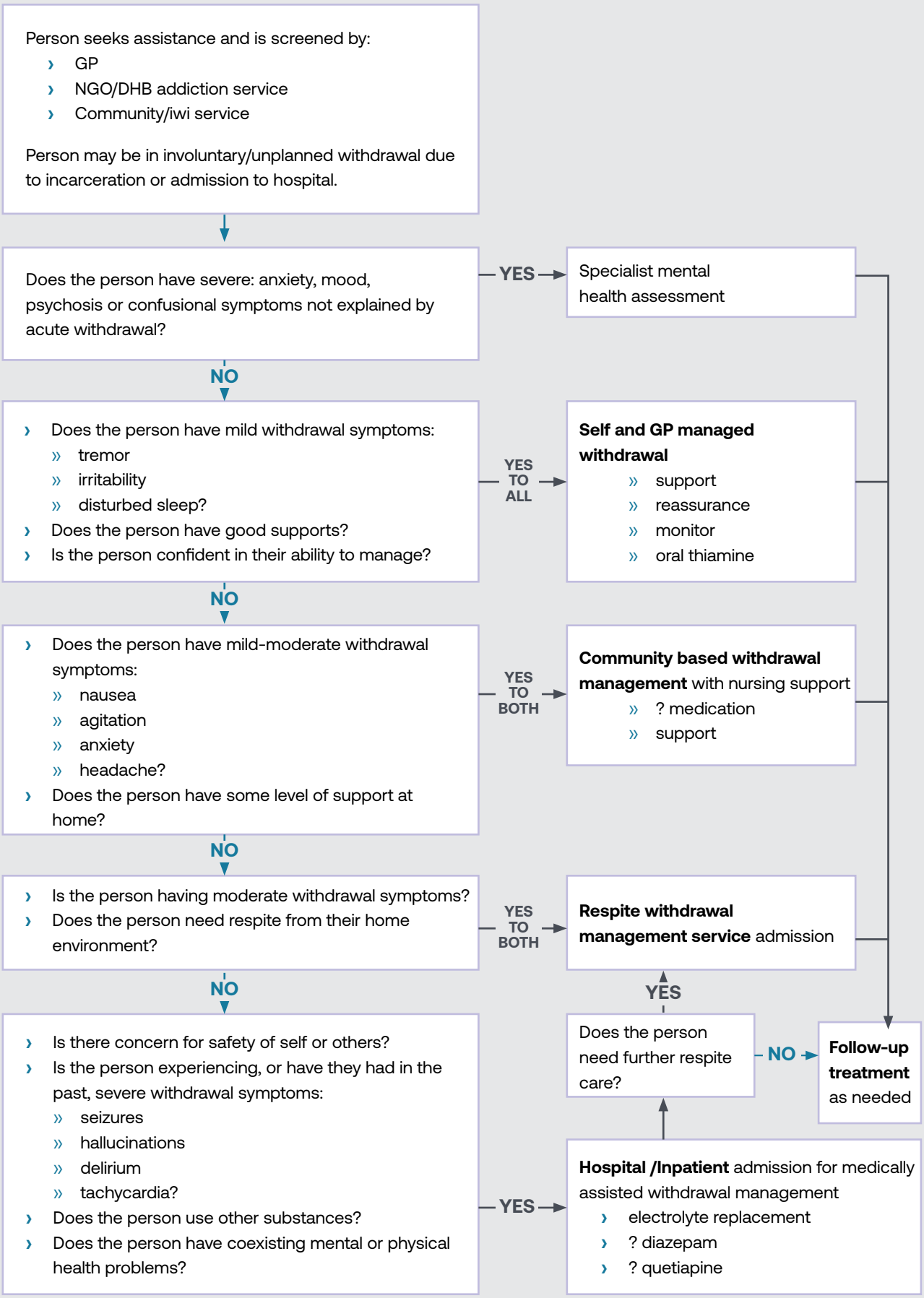
- diazepam helps with agitation and sleep disturbances, but doses should be based on presenting symptoms and this requires close monitoring
- quetiapine can also help with agitation and sleep
- electrolyte, potassium and phosphorus replacement may help improve muscle strength (hypocalcaemia is frequently encountered during fluid and electrolyte replacement).

Inpatient withdrawal management

The availability of specialist nursing and medical supervision allows for the safer management of risk than in a community setting. This is particularly true for people with:

- health complications due to inhalant use including cardiac problems, peripheral neuropathy and liver or kidney damage
- cognitive deficits due to inhalant use including memory loss, delusions and irritability
- a known history of severe withdrawal
- a history of seizures.

Figure 17: Inhalant withdrawal management pathway



Opioids

These guidelines have been developed to assist nursing and medical practitioners to identify opioid withdrawal symptoms and to provide safe withdrawal management strategies for people who have an opioid use disorder.

An opioid is any agonist substance with morphine-like activity that acts as a central nervous system depressant. Opioids produce their pharmacological actions, including analgesia, by acting on receptors located on neuronal cell membranes. The presynaptic action of opioids to inhibit neurotransmitter release is considered to be their major effect in the nervous system. There are three types of opioid receptor; mu, delta and kappa which are coupled to intracellular mechanisms via G-proteins.

An opiate is a naturally occurring opioid, i.e. a substance derived from the juice of poppies. Other opioids are semi-synthetic chemical derivatives of morphine (e.g., heroin) and some are fully synthetic (e.g., pethidine, fentanyl, tramadol and methadone).

With the scarcity of imported heroin in Aotearoa New Zealand people use a variety of opioids, including over the counter (e.g., Panadeine and Nurofen plus) medications, depending on their personal preference and what is readily available to them.

Assessment

A comprehensive assessment is the first step in managing withdrawal with the priority being to identify and define any risks.

A specific opioid use history includes:

- names of the opioids used
- prescribed or non-prescribed use
- route of use and documentation of injecting sites
- average quantity of use, morphine sulphate (MST) dose equivalence (in milligrams), over time
- time of last use
- peer affiliations
- periods of abstinence
- initial reasons for starting to use opioids
- current goals relating to use.

Opioid substitution treatment (OST) is the preferred treatment for most people with an opioid use disorder. See the *New Zealand Practice Guidelines for Opioid Substitution Treatment 2014* for further information. Managed opioid withdrawal has significant risks and there is a high rate of relapse and heightened risk of overdose post treatment. Opioid substitution is evidence based treatment that has been shown to reduce many of the short and long term risks associated with an opioid use disorder. For this reason referral to opioid substitution treatment should be the first option offered to people with a significant opioid use disorder and managed withdrawal should not routinely be offered unless the person has a mild opioid use disorder.

Indications that managed withdrawal is appropriate include:

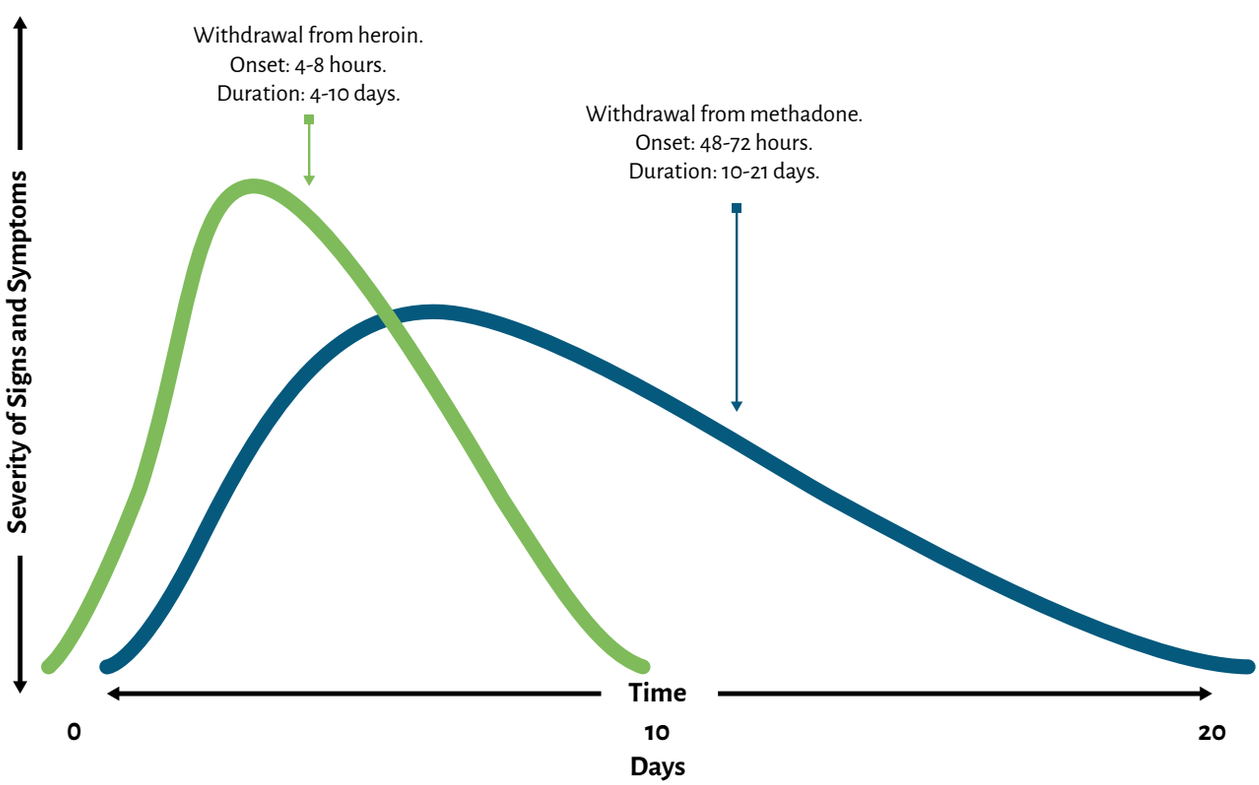
- limited duration of use
- iatrogenic/low dose neuroadaptation (due to long term prescribing for pain)
- amounts, mode and frequency of use have been relatively controlled and consistent over time
- positive supports
- engagement in appropriate post withdrawal treatment
- evidence of capacity to manage withdrawal symptoms
- no other substance use issues
- well managed or no coexisting physical and or mental health problems.

Opioid withdrawal

The primary aim of a managed opioid withdrawal is to reduce the acute physical and psychological discomforts that are the major symptoms of stopping opioid use. If carried out on the person's express wishes the process needs to be carried out as a slow taper as when withdrawal symptoms are not managed well over adequate time the rate of relapse is extremely high.

Opioid withdrawal is best managed with a clear management plan, effective communication and stabilisation and progressive withdrawal using a long acting oral opioid. Those people who do not wish to start OST should be engaged in post-withdrawal support and close monitoring to reduce the risks of relapse and overdose. Supervised daily dispensing is recommended during withdrawal to reduce the risk of diversion.

Figure 18: Opioid withdrawal symptoms over time



Symptoms and duration of opioid withdrawal

Reproduced with permission from NSW Dept of Health (2008).

Onset and duration of opioid withdrawal

- opioid withdrawal is influenced by the type of opioid and dose that the person has been using, how long they have been using and tolerance
- the onset of withdrawal from short acting opioids such as codeine, morphine and oxycodone, typically occurs between eight to twelve hours after last use
- withdrawal symptoms from short acting opioids will usually abate within five to ten days
- the onset of withdrawal from long acting opioids, such as methadone, tends to occur between twenty four to forty eight hours after last use
- long acting opioids will have a more protracted withdrawal of ten to twenty days, due to their long half-life
- the severity of withdrawal is also influenced by other substances that people may be using, including benzodiazepines.

Figure 19: Symptoms of opioid withdrawal

Common	Less common
disturbed sleep	fear
yawning	irritability
muscle aches	anorexia/ weight loss
abdominal and back pains	elevated blood pressure
sweating	headaches
cramps	urinary frequency
piloerection/goose bumps	dysphoria
fatigue	hot and cold flushes
dilated pupils	lacrimation
diarrhoea	twitching
runny nose	itching
craving	light sensitivity
nausea	restless legs
vomiting	
restlessness	
agitation	
anxiety	

Management of opioid withdrawal

The following are general principles for treatment planning in settings appropriate to the severity of withdrawal and or risk assessment.

Monitoring of withdrawal requires ongoing assessment and clinical judgement.

Opioid withdrawal severity can be measured with the Clinical Opiate Withdrawal Scale (COWS, Appendix 7)

Outpatient withdrawal management

Buprenorphine and methadone can be used to support people through opioid withdrawal. Specialist addiction treatment providers are the only providers gazetted to prescribe opioids for the treatment of opioid use disorders and should be contacted to manage opioid withdv-rawal. See the NZ Practice Guidelines for Opioid Substitution Treatment (OST) for further information.

Prescribing controlled drugs to treat addiction issues needs to be carried out by a prescriber gazetted to do so by the Ministry of Health.

Specialist addiction treatment withdrawal management

Buprenorphine* has been shown to be as effective in opioid withdrawal as methadone and may shorten the duration of withdrawal. Buprenorphine is a partial agonist with a high affinity for receptors but lower activity compared to most opioids.

Buprenorphine can precipitate withdrawal in patients who are using high doses of opioids, especially methadone.

To reduce the risk of precipitated withdrawal buprenorphine should not be prescribed until people are showing objective signs of withdrawal (COWS >12).

Precipitated withdrawal can occur with lower COWS so initiation of buprenorphine should be carried out cautiously on a case by case basis. In the event of precipitated withdrawal people should be treated symptomatically with adjunctive medication. They should not be prescribed any opioid until the next scheduled dose of buprenorphine.

Buprenorphine may be tapered by reducing an initial dose of 4-8mg daily by 10-20% every one to two days as necessary.

Using methadone to manage opioid withdrawal symptoms is an alternative option when the person is using up to 40mg methadone or an equivalent amount of other opioids. The initial dose should be no more than 40mg (Ministry of Health, 2014).

Caution: People prescribed methadone must be reviewed four hours after their first dose and again on the fourth day as methadone is known to accumulate in the liver and stable plasma levels on a set dose may not be achieved for up to five days. The NZ Practice Guidelines for Opioid Substitution Treatment contains full information about the risks and benefits of prescribing methadone.

It is useful for the person to stabilise on methadone for up to two weeks prior to commencing a reduction. The rate of reduction can be individually tailored and reviewed as needed. It is reasonable to support a slow reduction (1 to 2mg week) while withdrawal remains an appropriate and or desired form of treatment.

*A risk exists of triggering serotonin syndrome when people are prescribed one of the buprenorphine naloxone formulations (e.g., Suboxone) available in Aotearoa New Zealand.

Other opioids

Occasionally withdrawal from opioids such as codeine based medications can be managed by first stabilising and then reducing the dose, using an alternative opioid agonist such as dihydrocodeine (DHC). Withdrawal from high doses of tramadol can also be complicated by serotonin discontinuation withdrawal symptoms, i.e. dizziness, insomnia, nausea, anxiety, psychosis, mood swings and depression (see Matua Raki 2017 for more information).

Adjunctive medication

Adjunctive medication can be indicated either as a standalone treatment, potentially useful in custodial settings, or to support withdrawal along with opioid agonists. The following medications can be prescribed for symptomatic relief of symptoms of withdrawal.

Figure 20: Adjunctive medications

Medication	Dosage	Indication
Clonidine (use only if BP>100mm Hg systolic, 60mmhg diastolic) Check BP and pulse prior to each dose	› 25-150mcg tds for up to three days › reduce by a quarter of the third day's dose over the next three days › or › patches, typically tts1/2 › one patch weekly	relieves many symptoms of withdrawal, chart regular
Ondansetron	› 4-8mg tds (po/pr) prn for up to three or four days	nausea and vomiting
Metoclopramide	› 10mg tds for up to three or four days	nausea and vomiting
Prochlorperazine	› 5mg tds for up to three or four days	nausea and vomiting
Loperamide	› 4mg stat › 2mg with each loose motion › max 16mg in 24 hours › 2mg 1-2 times daily for up to five days	diarrhoea for ongoing diarrhoea post-acute withdrawal
Quetiapine	› 25-50mg tds prn › max 200mg daily	agitation and irritability
Zopiclone	› 7.5mg › if no effect within 2 hours another 7.5mg › max 15mg in 24 hours › for up to two weeks	insomnia
Paracetamol	› 1g qid (Q4 hours) › max of 4000mg in 24 hours › max 2000mg in 24 hours with impaired liver functions and or liver disease	headaches, myalgia, arthralgia
Ibuprofen (unless contraindicated)	› 400mg tds (close control)	headaches, myalgia, arthralgia
Buscopan	› 10-20mg prn qid for up to three or four days	abdominal cramps

These medications should not be prescribed without consultation with an addiction medicine specialist, physician or psychiatrist.

Nutrition and hydration

Fluid loss through sweating, vomiting and diarrhoea can lead to dehydration. People should be encouraged to drink 2 to 3 litres of fluids daily and to eat light and healthy meals as able.

Inpatient opioid withdrawal management

There is very little evidence to support admission to an inpatient setting for opioid withdrawal management. Inpatient withdrawal management should only be considered for people living in high risk environments, with moderate to severe coexisting physical health disorders, with moderate to severe coexisting mental health disorders and pregnant women. If carried out, part of discharge planning should include specific harm reduction advice and take home naloxone to reduce the risk of overdose.

Opioid withdrawal management in an inpatient setting is similar to management in the community or at a social withdrawal management service.

Complementary therapies

There is no reliable evidence to support the use of natural alternatives or complementary therapies for use in managing opioid withdrawal. However natural alternatives can help alleviate some withdrawal symptoms such as anxiety, sleep difficulties and muscle aches and can also promote relaxation (see Appendix 10). Complementary therapies should not be used as an alternative to a planned and managed withdrawal process.

Special populations

Pregnant women

Abrupt cessation of opioids is not recommended for pregnant women who have an opioid use disorder. Opioid withdrawal during the first and third trimester of pregnancy is associated with a higher risk of spontaneous abortion and premature delivery. Stabilisation on methadone as soon as possible, preferably in the first trimester, for the duration of the pregnancy is the recommended treatment. Use of buprenorphine is also appropriate in some cases. If the woman insists on undergoing withdrawal this should preferably be carried out in the second trimester under medical supervision with small dose reductions at any one time to reduce the stress on the fetus (Ministry of Health, 2014).

Neonates

Babies born with opioid intoxication and or withdrawal can present with symptoms which can last for several days after birth. These include:

- respiratory depression
- poor sucking
- hypotonia
- poor temperature regulation.

Neonatal abstinence syndrome (NAS)

Abrupt opioid withdrawal at birth has been shown to result in:

- high-pitched crying
- irritability
- tremor/jittering
- sleeping difficulties
- stuffy nose
- sneezing
- feeding difficulties due to sucking problems
- tense arms, legs and back
- poor weight gain
- vomiting/diarrhoea
- rapid breathing
- skin irritation.

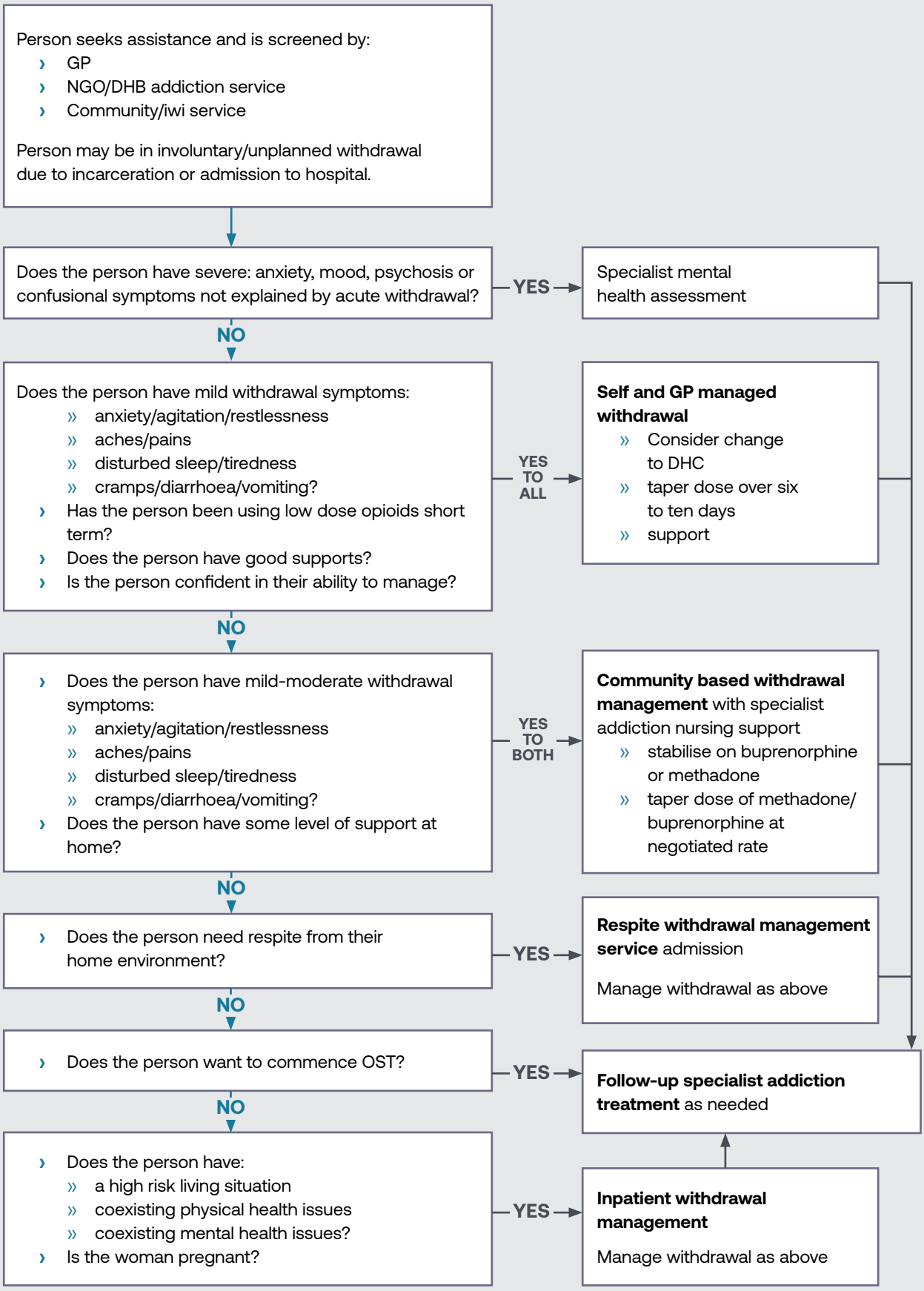
NAS (Neonatal abstinence syndrome) onset may occur one to ten days after delivery and can last from seven days to a month.

- babies born to women with an opioid use disorder should be observed in hospital for a reasonable length of time before discharge
- following discharge babies should have weekly outpatient reviews for at least one month
- the Adapted Finnegan scale (Appendix 5) is used to identify neonatal abstinence syndrome associated with opioids.

Breastfeeding

- breastfeeding is recommended for women who are on a stable dose of methadone or Suboxone (or equivalent) except in the presence of maternal HIV
- breastfeeding should be discontinued if a baby appears overly sedated.

Figure 21: Opioid withdrawal management pathway



Synthetic cannabinoids

These guidelines aim to assist nursing and medical practitioners with the assessment and identification of synthetic cannabinoid withdrawal symptoms in order to be able to provide safer withdrawal management.

There is limited research into the nature and treatment of synthetic cannabinoid withdrawal. As such, it is difficult to be prescriptive, but the information below is considered current expert best practice.

Over the past ten years synthetic cannabinoids have emerged as a significant risk factor for premature mortality, exacerbation of coexisting mental health issues, such as psychoses, the development of severe substance use disorders and associated withdrawal symptoms. Synthetic cannabinoids are chemicals with no relationship to 'natural cannabis' but are considered cannabinoids as they bind to cannabinoid receptors in the body. THC is thought to exert its effect by binding to cannabinoid CB1 receptors on pre-synaptic nerve terminals in the brain and over 200 synthetic cannabinoids have been synthesised with many being strong CB1 agonists, unlike THC which is a relatively weak partial agonist.

This significant difference in affinity for cannabinoid receptors means that most synthetic cannabinoids are many times more potent that natural cannabis, with accompanying severe withdrawal symptoms, many of them similar to cannabis but more intense and occurring rapidly, on cessation of use. The use of the more potent synthetic cannabinoids has been associated with seizures and deaths in Aotearoa New Zealand.

With over 200 synthetic cannabinoids available people are very unlikely to know which synthetic cannabinoid(s) they are using and how concentrated and or potent they are.

As with cannabis the major effects of synthetic cannabinoids are on the central nervous, gastrointestinal and cardiovascular systems.

Assessment

A comprehensive assessment is the first step in managing withdrawal with the priority being to identify and define any risks.

A history of synthetic cannabinoid use should include:

- quantity of use, amount consumed, type of synthetic cannabinoid (as far as is known) and potency
- duration, pattern and frequency of use
- time and impact of last use
- past history of aggression and violence
- goals relating to use
- DSM5 substance use disorder symptoms.

Synthetic cannabinoid withdrawal

People wanting to withdraw from synthetic cannabinoids should be provided with a menu of intervention options. This may include the choice of sudden cessation, with or without symptomatic medication and support in a respite withdrawal management facility, or a supported gradual reduction using psycho-social interventions and or transfer to natural cannabis.

Risks associated with synthetic cannabinoid withdrawal

- abrupt synthetic cannabinoid withdrawal may be physically dangerous
- withdrawal can be unpredictable and vary from presentation to presentation given the wide range of synthetic cannabinoids and the rapid changes in the types that are available in the community
- depending on frequency of use and product used withdrawal may have debilitating symptoms
- people consuming over 5gms a day are at highest risk
- a past history of violence and aggression may increase the risk of aggressive behaviour associated with withdrawal and this could place other people at risk
- underlying mental health issues may be unmasked or exacerbated during withdrawal
- the risk of suicidality and self-injury may be a risk factor for people vulnerable to these experiences, including those with a coexisting mood disorder or psychosis
- people with severe withdrawal symptoms and or coexisting problems may require appropriate medication and support in a respite withdrawal management facility or hospital.

Onset and duration of withdrawal

Onset of synthetic cannabinoid withdrawal may begin within 1-6 hours of last use. Most symptoms peak between 2-6 days after cessation but may last for several weeks. It is important to note that the intensity of withdrawal and possible complications will be dependent on the individual and the following variables:

- the amount, frequency and the synthetic cannabinoid used
- duration of current patterns of use
- stopping suddenly or reducing levels of use over time
- other substances used
- coexisting mental health problems
- coexisting physical health problems including chronic pain
- history of aggression or violence
- outpatient or inpatient setting.

Synthetic cannabinoid withdrawal symptoms can include;

- cravings
- headache
- ongoing vomiting
- constipation
- severe anxiety
- insomnia
- irritability
- memory problems
- confusion
- extreme agitation
- mood swings
- heavy sweating
- elevated body temperature
- severe dehydration
- palpitations
- tachycardia
- chest pain
- shortness of breath
- seizures, though this is observed more often in the context of intoxication.

Management of synthetic cannabinoid withdrawal

In many cases withdrawal symptoms can be managed in the community.

On occasion agitation is so extreme and the risk of dehydration is so high withdrawal management may need to be provided in a respite setting or an inpatient setting. Indications for inpatient withdrawal management include:

- history of seizures
- history of severe withdrawal symptoms
- potential risk factors for self-harm and harm to others
- physical health complications, e.g., severe dehydration.

Quetiapine and benzodiazepines (e.g., diazepam) may help with managing very severe withdrawal symptoms such as extreme anxiety, agitation, irritability and aggression and prolonged sleep difficulties. This however should be managed with support from a specialist addiction service where available.

In addition, consider:

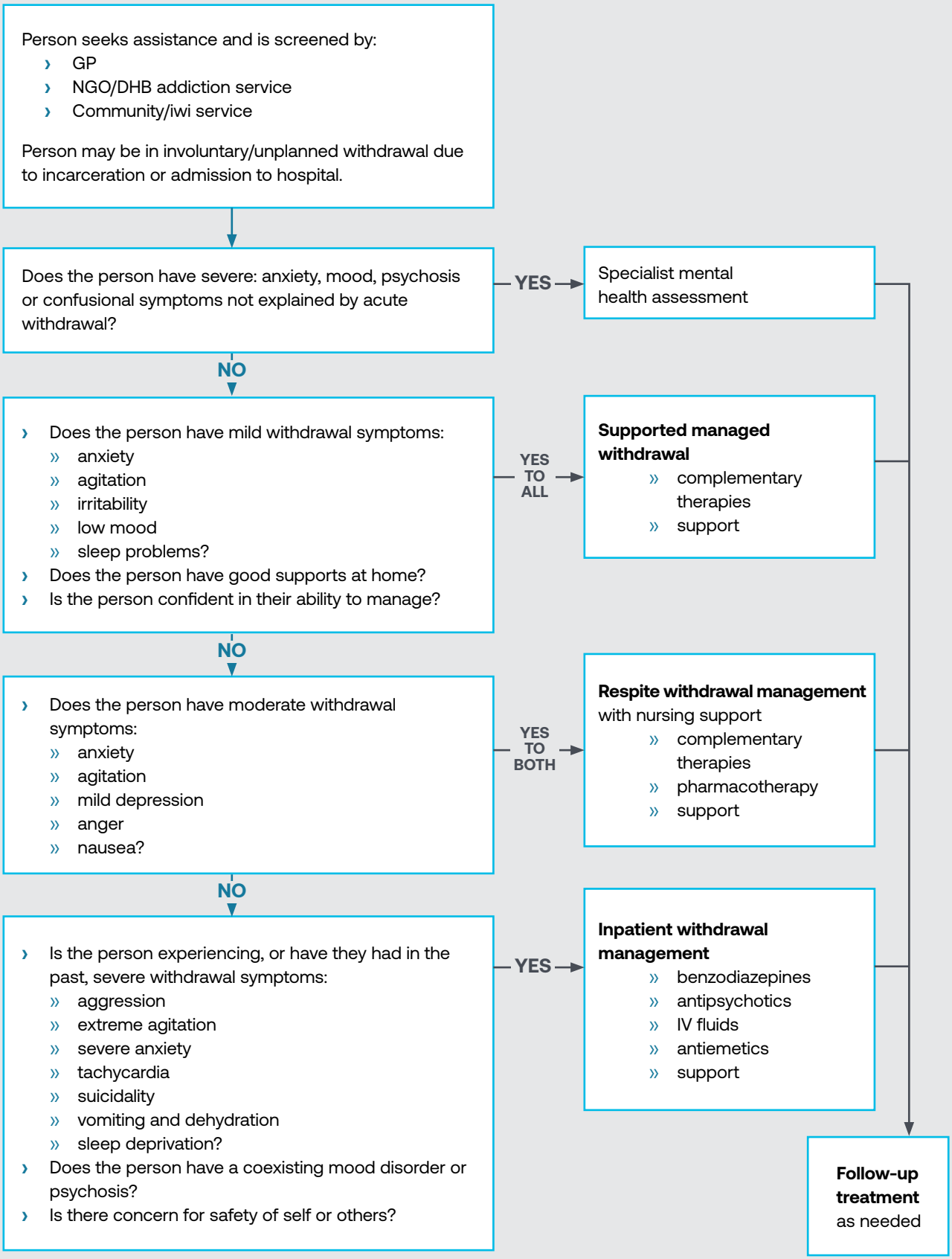
- nutritional supplementation
- fluids, possibly IV
- appropriate antipsychotic medication (e.g., quetiapine)
- antiemetics, e.g., metoclopramide, ondansetron or prochlorperazine.

Benzodiazepines should not be considered a treatment of choice for synthetic cannabinoid withdrawal management and if used outside of an inpatient setting use should be monitored on a daily basis. Due to the potential for rapid neuroadaptation to benzodiazepines duration of prescribing should be guided by symptom severity with the aim to prescribe for as brief a period as is appropriate.

For milder synthetic cannabinoid withdrawal adjunctive medications that may be helpful in managing some withdrawal symptoms include:

- paracetamol - headaches, muscular aches, sweating, chills and pain
- NSAID's - headaches, muscular aches and pain – **contraindicated if person severely dehydrated**
- magnesium – headaches and muscular aches.

Figure 22: Synthetic cannabinoid withdrawal management pathway



Resources

For a list of CYP450 substrates and enhancers and inducers which indicate the potential for interactions between medications and some other substances: https://drug-interactions.medicine.iu.edu/MainTable.aspx

For quick reference to complement the above resource and the drug-drug drug-medication interactions described in Appendix 8: http://reference.medscape.com/drug-interactionchecker?cid=med

Pharmacon Media. (2010). Drug-drug interactions in opioid maintenance: a focus on buprenorphine & methadone. 5th Edition. Pharmacon Media UK Ltd.

References

Ahuriri-Driscoll, A., Baker, B., Hepi, M. & Hudson, M. (2008). *Rongoa Maori Wellbeing and Sustainability.* A Report for Te Kete Hauora, Ministry of Health, Wellington, New Zealand.

Addolorato, G., Leggio, L., Ferrulli, A., Cardone, S., Vonghia, L., Mirijello, A., Abenavoli, L., D'Angelo, C., Caputo, F., Zambon, A., Haber, P. S., & Gasbarrini, G. (2007). Effectiveness and safety of baclofen for maintenance of alcohol abstinence in alcohol-dependent patients with liver cirrhosis: randomised, double-blind controlled study. *Lancet* 370, 1915–1922.

Allsop, D. J., Copeland, J., Norberg, M. M., Fu, S., Molnar, A., Lewis, J., & Budney, A. J. (). (2012). Quantifying the clinical significance of cannabis withdrawal. *PloS one*, 7(9), e44864. doi:10.1371/journal.pone.0044864

Ashraf, H. H. (2010). Neonatal Abstinence Syndrome Clinical Presentation. [Electronic version]. Medscape Reference. Retrieved May 11, 2011, from: https://emedicine.medscape.com/article/978763-clinical#a0217

Ashton, C. (2002). *Benzodiazepines: How they work and how to withdraw.* University of Newcastle. United Kingdom. Retrieved May 2, 2011, from: http://www.benzo.org.uk.

Astolfi, H., Leonard, L., & Morris, D. (1998). *GP Drug & Alcohol Supplement No. 10 –Cannabis Dependence and Treatment.* Central Coast Health Service.

Christie, G., & Temperton, H. (2017) *Guidelines for the Management of Acute Substance Withdrawal in Young People - 2017 update.* Available at: https://optforwellbeing.org/sites/default/files/pdfs/CEP/2017-Guidelines-Management-of-Acute-Substance-Withdrawal-in-Adolescents-Christie-Temperton.pdf

Cooper, Z. D. (2016). Adverse Effects of Synthetic Cannabinoids: Management of Acute Toxicity and Withdrawal. *Current Psychiatry Reports, 18(5),* 52. Retrieved July 1, 2019, from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4923337/

Day, E., & Strang, J. (2011). Outpatient versus inpatient opioid detoxification: A randomized controlled trial. *Journal of Substance Abuse Treatment*, 40: 56-66. Retrieved May 27, 2011, from: https://www.sciencedirect.com/science/article/abs/pii/S0740547210001893

De Crespigny, C., Talmet, J., Modystack, K., Cusack, L., & Watkinson, J. (2003). *Alcohol, Tobacco & Other Drugs Guidelines for Nurses and Midwives: Clinical Guidelines Version 2.* South Australia, Drug and Alcohol Services Council.

Dyer, J., Roth, B., & Hyma, B. (2001). Gamma-hydroxybutyrate withdrawal syndrome *Annals of Emergency Medicine,* 37: 147-153.

Friedman, J., Westlake, R., & Furman, M. (1996). "Grievous bodily harm:" gamma hydroxybutyrate abuse leading to a Wernicke-Korsakoff syndrome.*Neurology,* 46: 469-471.

Hulse, G. White, J., & Cape, G. (2002). *Management of Alcohol and Drug Problems*. Victoria, Australia: Oxford University Press.

Johnson, B. A. (2008). Update on Neuropharmacological treatments for Alcoholism: Scientific basis and clinical findings. *Biochemical Pharmacology,* 75, 34-56. Retrieved April 25, 2011, from: www.sciencedirect.com

Kamal, R.M., van Noorden. M.S., Wannet, W., Beurmanjer, H., Dijkstra, B.A., Schellekens, A. (2017). Pharmacological Treatment in-Hydroxybutyrate (GHB) and -Butyrolactone (GBL) Dependence: Detoxification and Relapse Prevention. *CNS Drugs*. 2017;31(1):51-64. doi: 10.1007/s40263-016-0402-z

Kenny, P., Swan, A., Berends, L., Jenner, L., Hunter, B., & Mugavin, J. (2009). *Alcohol and other Drug Withdrawal: Practice Guidelines, 2009*. Fitzroy, Victoria. Turning Point Alcohol and Drug Centre.

Kosten, T., & O'Connor, P. (2003). Management of Drug and Alcohol Withdrawal. *The New England Journal of Medicine,* 348, 1786-1795. Retrieved June 9, 2011, from: http://www.nejm.org/doi/full/10.1056/NEJMra020617

Leggio, L., Kenna, G. A., & Swift, R. M. (2008). New developments for the pharmacological treatment of alcohol withdrawal syndrome. A focus on non benzodiazepine GABAergic medications. *Progress in Neuropsychopharmacology and Biological Psychiatry,* 32, 1106-1117. Retrieved April 25, 2011, from: www.sciencedirect.com

Matua Raki. (2016). *Mental Health and Addiction Screening and Assessment Guideline.* Matua Raki. Wellington.

Matua Raki. (2017). *A guide to reducing or stopping mental health medication.* Matua Raki. Wellington.

Matua Raki. (2017b). *A guide to reducing or stopping mental health medication- notes for prescribers.* Matua Raki. Wellington.

McClintock, A., Woods, D., Kendall, P., McRae, G., Chalmers, G., Orange, A., & Little, S. (Eds). (1999). *Notes on Injectable Drugs.* NZ HealthCare Assoc. Wellington, New Zealand.

McDonough, M., Kennedy, N., Glaspe, A., & Bearn, J. (2004). Clinical features and management of gamma-hydroxybutyrate (GHB) withdrawal: a review. *Drug and Alcohol Dependence,* 75: 3-9. Retrieved June 10, 2011, from: www.elsevier.com/locate/drugalcdep

Ministry of Health. (2014). *New Zealand Practice Guidelines for Opioid Substitution Treatment 2014*. Ministry of Health: Wellington, New Zealand.

National Addiction Centre. (2003). *Drug Manual A guide to drug mechanisms and effects*. NAC. University of Otago, Christchurch.

National Institute for Health and Clinical Excellence. (2003). *Drug Misuse Opioid detoxification 2003.* Retrieved May 20, 2011, from: www.nice.org.uk

NSW Health Department. (1999). *NSW Detoxification Clinical Practice Guidelines.* Gladesville: New South Wales Health Department.

NSW Health Department. (2006). *National Clinical Guidelines for the Management of Drug Use during Pregnancy, Birth and the Early Development Years of the Newborn.* NSW Health Department. Sydney. Retrieved May 2, 2011, from: http://www.health.nsw.gov.au/pubs/2006/pdf/ncg_druguse.pdf

NSW Department of Health. (2008). *Drug and Alcohol Withdrawal Clinical Practice Guidelines – NSW*. NSW Department of Health. Retrieved May 2, 2011, from: http://www.health.nsw.gov.au/policies/gl/2008/pdf/GL2008_011.pdf

New Zealand Drug Foundation. About a drug: *GHB:* Retrieved June 19, 2019, from: https://www.drugfoundation.org.nz/matters-of-substance/february-2016/about-a-drug-ghb/

Perron, B.E., Glass, J.E., Ahmedani, B.K., Vaughn, M.G. Roberts, D.E. & Wu, L.T. (2011). The prevalence and clinical significance of inhalant withdrawal symptoms among a national sample. *Substance Abuse Rehabilitation*, April, 69–76. Retrieved July 19th, 2011, from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3123390/?tool=pubmed

Schuckit, M. A. (1995). *Drug and Alcohol Abuse*: *A clinical guide to diagnosis and treatment (4th ed.).* New York: Plenum Press.

Strobbe, S., Brower, K. & Galen, L. (2003). Predicting completion of outpatient opioid detoxification with clonidine. *The American Journal of Addictions*, 12: 260-269.

Sullivan, J. T., Sykora, K., Schneiderman, J., Naranjo, C.A. & Sellers, E. M. (1989). Assessment of alcohol withdrawal: The revised Clinical Institute Withdrawal Assessment for Alcohol scale (CIWA-Ar). *British Journal of Addiction*, 84: 1353-1357.

Todd, F. C. (2010). *Te Ariari o te Oranga: the Assessment and Management of People with Co-existing Mental Health and Substance Use Problems*. Ministry of Health: Wellington, New Zealand.

Victoria Police. (2001). *Custodial Drug Guide: Medical Management of People in Custody with Alcohol and Drug Problems*. Centreforce. Victoria, Australia.

Weaver, M., & Hopper, J. (2011). *Treatment of opioid use and dependence*. *UpToDate*. Retrieved June 10, 2011, from: www.uptodate.com

Wesson, D.R., & Ling, W. (2003). The Clinical Opiate Withdrawal Scale (COWS). *Journal of Psychoactive Drugs*, 35(2), 253-259.

Winstock, A., & Lea, T. (2009). Management of cannabis withdrawal. National Cannabis Prevention and Information Centre (ncpic). Retrieved July 6, 2011, from: http://ncpic.org.au/static/pdfs/background-papers/management-of-cannabis-withdrawal.pdf

Wojtowicz, J.M., Yarema, M.C., & Wax, P.M. (2008). Withdrawal from gamma-hydroxybutyrate, 1, 4-butanediol and gamma-butyrolactone: a case report and systematic review. *Canadian Journal of Emergency Medicine*, 10, 69-74. Retrieved June 14, 2011, from: http://www.cjem-online.ca/v10/n1/p69

Appendices

Appendix 1: Clinical institute withdrawal assessment of alcohol scale revised (CIWA-Ar)

CIWA - Ar Alcohol Withdrawal Assessment Flowsheet									
Date									
Time									
Pulse									
Resps									
O2 sat									
BP									
Temp									
BAL									
Nausea/Vomiting (0-7) 0 - none, 1 - mild nausea no vomiting, 4 - intermittent nausea, 7 - constant nausea, frequent dry heaves and vomiting.									
Tremors (0-7) 0 - no tremor, 1 - not visible but can be felt, 4 - moderate with arms extended, 7 - severe even with arms not extended.									
Anxiety (0-7) 0 - none, ease, 1 - mildly anxious, 4 - moderately anxious or guarded, 7 - equivalent to acute panic.									
Agitation (0-7) 0 - normal activity, 1 - somewhat normal activity, 4 - moderately fidgety and restless, 7 - passes or constantly thashes about.									
Paroxysmal Sweats (0-7) 0 - no sweats, 1 - barely perceptible sweating, palms moist, 4 - beads of sweat obvious on forehead, 7 - drenching sweat.									
Orientation (0-4) 0 - oriented, 1 - uncertain about date, 2 - disoriented to date by no more than 2 days, 3 - disoriented to date by > 2 days, 4 - disoriented to place and/or person.									
Tactile Disturbances (0-7) 0 - none, 1 - very mild itch, P&N, numbness, 2 - mild itch,P&N, burning, numbness, 4 - moderate hallucinations, 5 - severe hallucinations, 6 - very severe hallucinations, 7 - continuous hallucinations.									
Auditory Disturbances (0-7) 0 - not present, 1 - very mild harshness / ability to startle, 2 - mild harshness / ability to startle, 3 - moderate harshness / ability to startle, 4 - moderate hallucinations, 5 - severe hallucinations, 6 - very severe hallucinations, 7 - continuous hallucinations.									
Visual Disturbances (0-7) 0 - not present, 1 - very mild sensitivity, 2 - mild sensitivity, 3 - moderate sensitivity, 4 - moderate hallucinations, 5 - severe hallucinations, 6 - very severe hallucinations, 7 - continuous hallucinations.									
Headache (0-7) 0 - not present, 1 - very mild, 2 - mild, 3 - moderate, 4 - moderately severe, 5 - severe, 6 - very severe, 7 - extremely severe.									
Total CIWA - Ar score:									
PRN Med (circle one) Diazapam Lorazepam	Dose given (mg):								
	Route								
Time of PRN medication administration:									
Total daily dose (over the last 24 hours)									
RN Initials									

Signature / Title	Initials	Patient Identifier Sticker

Alcohol withdrawal assessment scoring guidelines (CIWA-Ar)

Nausea and Vomiting Ask "do you feel sick to your stomach? Have you vomited?" and observe. 0 - No nausea and no vomiting 1 - Mild nausea with no vomiting 2 - 3 - 4 - Intermittent nausea with dry heaves 5 - 6 - 7 - Constant nausea, frequent dry heaves and vomiting	**Tremor** Observe patients arms extended and fingers apart. 0 - No tremor 1 - Not visible but can be felt in fingertip 2 - 3 - 4 - Moderate with patients arms extended 5 - 6 - 7 - Severe, even with arms not extended
Anxiety 0 - No anxiety, at ease 1 - Mildly anxious 2 - 3 - 4 - Moderately fidgety and restless 5 - 6 - 7 - Equivalent to acute panic attack as seen in a severe delirium or acute schizophrenic reaction	**Agitation** 0 - Normal activity 1 - Somewhat more than normal 2 - 3 - 4 - Moderately fidgety and restless 5 - 6 - 7 - Paces back and forth during most of the interview, or constantly thrashes about.
Paroxysmal Sweats 0 - No sweat visible 1 - Barely perceptible sweating, moist palms 2 - 3 - 4 - Beads of sweat obvious on forehead 5 - 6 - 7 - Drenching sweat	**Orientation and Clouding of Consciousness** Ask "What day is it? Where are you? Who am I?" 0 - Oriented and can do serial additions 1 - Cannot do serial additions or is unclear about the date 2 - Disoriented by date by no more than two calendar days 3 - Disoriented by date by more than two calendar days 4 - Disoriented to place and person
Tactile Disturbances Ask "Do you have any itching, pins and needles, burning or numbness? Do you feel crawling under your skin?" 0 - None 1 - Very mild itching, pins and needles, burning or numbness 2 - Mild itching, pins and needles, burning or numbness 3 - Moderate itching, pins and needles, burning or numbness 4 - Moderetely severe hallucinations 5 - Severe hallucinations 6 - Extremely severe hallucinations 7 - Continuous hallucinations	**Auditory Disturbances** Ask "Are you more aware of sounds around you? Are sounds harsh or frightening to you? Are you hearing anything disturbing or that you know is not there?" Observe. 0 - Not present 1 - Very mild harshness or ability to frighten 2 - Mild harshness or ability to frighten 3 - Moderate harshness or ability to frighten 4 - Moderately severe hallucinations 5 - Severe hallucinations 6 - Extremely severe hallucinations 7 - Continuous hallucinations
Visual Disturbances Ask "Does the light appear to be too bright? Is its colour different? Does it hurt your eyes? Are you seeing anything that is disturbing to you? Are you seeing things you know are not there? Observe. 0 - Not present 1 - Very mild sensitivity 2 - Mild sensitivity 3 - Moderate sensitivity 4 - Moderately severe hallucinations 5 - Severe hallucinations 6 - Extremely severe hallucinations 7 - Continuous hallucinations	**Headache, Fullness in Head** Ask "Does your head feel different? Does it feel like there's a band around your head?" Do not rate for dizziness or light headedness. Otherwise rate severity. 0 - Not present 1 - Very mild 2 - Mild 3 - Moderate 4 - Moderately severe 5 - Severe 6 - Very severe 7 - Extremely severe

Procedure:

1. Assess and rate each of the 10 criteria of the CIWA scale. Each criterion is rated on a scale from 0 to 7, except for "Orientation" which is rated on a scale 0 to 4. Add up the scores for all ten criteria. This is the total CIWA-Ar score for the patient at that time. Prophylactic medication should be started for any patient with a total CIWA-Ar score of 8 or greater (ie. Start on withdrawal medication). If started on scheduled medication, additional PRN medication should be given for a total CIWA-Ar score of 15 or greater.
2. Document vitals and CIWA-Ar assessment on the Withdrawal Assessment Sheet. Document administration of PRN medication on the assessment sheet as well.
3. The CIWA-Ar scale is the most sensitive tool for assessment of the patient experiencing alcohol withdrawal. Nursing assessment is vitally important. Early intervention for CIWA-Ar scores of 8 or greater provides the best means to prevent the progression of withdrawal.

TEMPERATURE, PULSE AND BLOOD PRESSURE RECORDINGS NEED TO BE DOCUMENTED ON OBSERVATION CHART IN CONJUNCTION WITH THE CIWA-Ar ASSESSMENT

Original reference: Sullivan, J.T., Sykora, K., Schneiderman, J., Naranjo, C.A., & Sellers, E.M. (1989). Assessment of alcohol withdrawal: The revised Clinical Institute Withdrawal Assessment for Alcohol scale (**CIWA-Ar**). *British Journal of Addiction*, 84, 1353-7

Appendix 2: Alcohol withdrawal management medication regime

CIWA-Ar Score	Less than 8	8-15	15 and over	
Drinks	**Less than 10 std drinks a day with no withdrawal symptom history**	**Up to 10 std drinks a day with a history of or apparent withdrawal symptoms with no other risk factors**	**Between 10 to 20 std drinks a day with a history of or apparent withdrawal symptoms with no other risk factors**	**20 std drinks a day or more with a history of withdrawal symptoms or with other risk factors**
Setting	**Community/Home**	**Community or Respite**	**Community or Respite with 24 hr supervision**	**Inpatient only**
Day	**Provide oral thiamine, 50-100mg 4 times a day**	**Provide oral thiamine, 50-100mg 4 times a day, and consider thiamine 200mg IV/IM or Pabrinex one pair once daily for 3 days**	**Provide oral thiamine, 50-100mg 4 times a day, and consider thiamine 200mg IV/IM or Pabrinex one pair once daily for 3 days**	**Provide IV thiamine or Pabrinex for 3 days and oral thiamine 50-100mg 4 times daily**
1	› reassure › support › repeat CIWA-Ar four hourly › if CIWA-Ar exceeds 8	› 5mg diazepam four times daily › repeat CIWA-Ar four hourly › if CIWA-Ar exceeds 8	› 10mg diazepam 4 times daily * › repeat CIWA-Ar four hourly › may require additional diazepam if CIWA-Ar remains above 8	› 20mg diazepam 2 hourly till CIWA-Ar falls to below 8 or sedated › maximum dose 80mg in first 24 hours unless discussed with addiction specialist › repeat CIWA-Ar two hourly › monitor respiration rate and oxygen stats
2	› as above	› 5mg diazepam three times daily › if CIWA-Ar is less than 8 over three consecutive screens reduce screening to six hourly	› 10mg diazepam four times daily › repeat CIWA-Ar four hourly once symptoms reduce	› same dose of diazepam that reduced withdrawal symptoms on Day 1 dispensed in four doses (qid) › maximum dose 80mg › repeat CIWA-Ar four hourly once symptoms reduce
3	› as above	› 5mg diazepam bd	› 5mg diazepam four times daily (qid)	› half previous days dose of diazepam › dispense in four doses (qid)
4	› as above	› 5mg diazepam nocte	› 5mg diazepam twice daily	› half previous days dose of diazepam › dispense in four doses (qid)
5	› as above	› nil	› 5mg diazepam nocte	› half previous days dose of diazepam › dispense in two doses (bd)
6	› as above	› nil	› nil	› half previous days dose of diazepam › dispense in one dose

***All doses of diazepam over 40mg in one day require regular close monitoring of level of sedation, oxygen and respiration rates (>11) due to the risks of respiratory depression. Throughout the withdrawal process, make and document routine observations of blood pressure, pulse, respiratory rate and pupil size.**

Appendix 3: Absorption rates, half-life and equivalent daily doses of common benzodiazepines*

Generic Name	Trade Name	Equivalent dose to 5mg diazepam	Time to peak concentration	Elimination half life	Duration of action
Diazepam	Valium	5mg	30-90min	20-48 hours	Long
Alprazolam	Xanax	0.5-1.0mg	60 min	6-25 hours	Short
Clonazepam	Rivotril	0.5mg	2-3 hours	22-54 hours	Long
Lorazepam	Ativan	0.2-0.5mg	2 hours	12-16 hours	Short
Oxazepam	Serepax	10mg	2-3 hours	4-15 hours	Short
Nitrazepam	Mogadon	2.5-5mg	2 hours	16-48 hours	Long
Temazepam	Normison	10-20mg	30-60 min for tablets or 2 hours for capsules	5-15 hours	Short
Flunitrazepam	Rohypnol	1-2mg	1-2 hours	20-30 hours	Intermediate
Triazolam	Halcion	0.25	1-3 hours	2-5 hours	V. Short
Zopiclone	Imovane	7.5mg		5 hours	V. Short

Note: * These conversion figures are not intended to be absolutes and conversion should be guided by the symptoms the person experiences on conversion

- Elimination half-life: Time for the plasma drug concentration to decrease by 50%
- Duration of action (approx.):
  - Very short < 6 hours
  - Short < 12 hours
  - Intermediate < 24 hours
  - Long > 24hours.

Adapted from: Drug and Alcohol Withdrawal Clinical Practice Guidelines (NSW Department of Health, 2008).

Appendix 4: Example of a three times daily (tds) low dose diazepam reduction regime

	0800hrs	1400hrs	2000hrs	Total diazepam equivalent
Stage 1 (5mg tablets)	5mg	5mg	5mg	15mg
Stage 2 (5mg tablets)	5mg	2.5mg	5mg	12.5mg
Stage 3 (5mg tablets)	5mg	2.5mg	2.5mg	10mg
Stage 4 (2mg tablets)	4mg	2mg	2mg	8mg
Stage 5 (2mg tablets)	3mg	2mg	2mg	7mg
Stage 6 (2mg tablets)	2mg	2mg	2mg	6mg
Stage 7 (2mg tablets)	2mg	1mg	2mg	5mg
Stage 8 (2mg tablets)	2mg	1mg	1mg	4mg
Stage 9 (2mg tablets)	1mg	1mg	1mg	3mg
Stage 10 (2mg tablets)	1mg	-	1mg	2mg
Stage 11 (2mg tablets)	1mg	-	-	1mg
Stage 12	-	-	-	0 mg

Appendix 5: Adapted Finnegan scale

Systems	Signs and symptoms	Score	AM 2	4	6	8	10	12	PM 2	4	6	8	10	12	Daily WT.
Central Nervous System Disturbances	High Pitched Cry Continuous High Pitched Cry	2 3													
	Sleeps < 1 Hour After Feeding Sleeps < 2 Hours After Feeding	3 2													
	Hyperactive Moro Reflex Markedly Hyperactive Moro Reflex	2 3													
	Mild Tremors Disturbed Moderate Severe Tremors Disturbed	2 3													
	Mild Tremors Undisturbed Moderate Severe Tremors Undisturbed	1 2													
	Increased Muscle Tone	2													
	Excoriation (specify area:_____)	1													
	Myoclonic Jerks	3													
	Generalised Convulsions	3													
Metabolic Vasomotor/Respiratory Disturbances	Sweating	1													
	Fever < 101˚F (39.3˚C) Fever > 101˚F (39.3˚C)	1 2													
	Frequent Yawning (> 3-4 times/ interval)	1													
	Mottling	1													
	Nasal Stuffiness	1													
	Sneezing (> 3-4 times/interval)	1													
	Nasal Flaring	2													
	Respiratory Rate > 60/min Respiratory Rate > 60/min with Retractions	1 2													
Gastrointestinal Distubances	Excessive Sucking	1													
	Poor Feeding	2													
	Regurgitation Projectile Vomiting	2 3													
	Loose Stools Watery Stools	2 3													
Summary	Total Score														
	Scorer's Initials														
	Status of Therapy														

Adapted from Finnegan, L. (1986). Neonatal abstinence syndrome: assessment and pharmacotherapy. In F.F. Rubatelli, & B. Granti (Eds.), *Neonatal Therapy: An update* (pp.122-146). Elsevier Science Publishers B.V. (Biomedical Division). Retrieved May 11, 2011, from: http://emedicine.medscape.com/article/978763-clinical#a0217

Appendix 6: Cannabis withdrawal scale (CWS)

Allsop, D.J., Norberg, M.M., Copeland, J., Fu, S., Budney, A.J. (2011). The Cannabis Withdrawal Scale development: Patterns and predictors of cannabis withdrawal and distress, *Drug and Alcohol Dependence*, Vol 119, 123–129.,

For a copy of this scale go to: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3458862/

Note this scale is copyrighted by Elsevier

The cannabis withdrawal scale.

	Not at all Moderately Extremely											Negative Impact on daily activity (0–10)
1	The only thing I could think about was smoking some cannabis	0	1	2	3	4	5	6	7	8	9	10
2	I had a headache	0	1	2	3	4	5	6	7	8	9	10
3	I had no appetite	0	1	2	3	4	5	6	7	8	9	10
4	I felt nauseous (like vomiting)	0	1	2	3	4	5	6	7	8	9	10
5	I felt nervous	0	1	2	3	4	5	6	7	8	9	10
6	I had some angry outbursts	0	1	2	3	4	5	6	7	8	9	10
7	I had mood swings	0	1	2	3	4	5	6	7	8	9	10
8	I felt depressed	0	1	2	3	4	5	6	7	8	9	10
9	I was easily irritated	0	1	2	3	4	5	6	7	8	9	10
10	I had been imagining being stoned	0	1	2	3	4	5	6	7	8	9	10
11	I felt restless	0	1	2	3	4	5	6	7	8	9	10
12	I woke up early	0	1	2	3	4	5	6	7	8	9	10
13	I had a stomach ache	0	1	2	3	4	5	6	7	8	9	10
14	I had nightmares and/or strange dreams	0	1	2	3	4	5	6	7	8	9	10
15	Life seemed like an uphill struggle	0	1	2	3	4	5	6	7	8	9	10
16	I woke up sweating at night	0	1	2	3	4	5	6	7	8	9	10
17	I had trouble getting to sleep at night	0	1	2	3	4	5	6	7	8	9	10
18	I felt physically tense	0	1	2	3	4	5	6	7	8	9	10
19	I had hot flashes	0	1	2	3	4	5	6	7	8	9	10

Instructions: This version of the CWS asks about symptoms experienced over the last 24 hours, and can be administered by an interviewer OR by self report.

The following statements describe how you have felt over the last 24 hours. Please circle the number that most closely represents your personal experiences for each statement. For each statement, please rate its negative impact on normal daily activities on the same scale (0=Not at all to 10=Extremely), writing the number in the right hand column.

Score by summing each items value to a maximum withdrawal score of 190 (you can derive two scores from the scale: one for withdrawal intensity and one for the negative impact of withdrawal – each separate score has a theoretical maximum of 190).

Reprinted from Drug and Alcohol Dependence, Vol 119, Allsop, D.J., Norberg, M.M., Copeland, J., Fu, S., Budney, A.J. The Cannabis Withdrawal Scale development: Patterns and predictors of cannabis withdrawal and distress, 123–129., Copyright (2011), with permission from Elsevier (License number 2872801116106).

Appendix 7: Clinical opioid withdrawal scale (COWS)

<table>
<tr><td>Patient's Name:</td><td>Date and Time:_____/_____/_____</td></tr>
<tr><td colspan="2">Reason for this assessment:</td></tr>
<tr><td>Resting Pulse Rate: _____ beats/minute
Measured after patient is sitting or lying for one minute.
0 - pulse rate 80 or below
1 - pulse rate 81 - 100
2 - pulse rate 101 - 120
4 - pulse rate greater than 120</td><td>GI Upset: over last 1/2 hour.
0 - no GI symptoms
1 - stomach cramps
2 - nausea or loose stool
3 - vomiting or diarrhea
5 - multiple episodes of diarrhea or vomiting</td></tr>
<tr><td>Sweating: over past 1/2 hour not accounted for by room temperature or patient activity.
0 - no report of chills or flushing
1 - subjective report of chills or flushing
2 - flushed or observable moistness on face
3 - beads of sweat on brow or face
4 - sweat streaming off face</td><td>Tremor: observation of outstretched hands.
0 - no tremor
1 - tremor can be felt, but not observed
2 - slight tremor observable
4 - gross tremor or muscle twitching</td></tr>
<tr><td>Restlessness: Observation during assessment.
0 - able to sit still
1 - reports difficulty sitting still, but is able to do so
3 - frequently shifting or extraneous movements of legs/arms
5 - unable to sit still for more than a few seconds</td><td>Yawning: Observation during assessment.
0 - no yawning
1 - yawning once or twice during assessment
2 - yawning three or more times during assessment
4 - yawning several times/minute</td></tr>
<tr><td>Pupil size
0 - pupils pinned or normal size for room light
1 - pupils possibly larger than normal for room light
2 - pupils moderately dilated
5 - pupils so dilated that only the rim of the iris is visible</td><td>Anxiety or Irritability
0 - none
1 - patient reports increasing irritability or anxiousness
2 - patient obviously irritable or anxious
4 - patient so irritable or anxious that participation in assessment is difficult</td></tr>
<tr><td>Bone or Joint aches: If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored.
0 - not present
1 - mild diffuse discomfort
2 - patient reports severe diffuse aching of joints/ muscles
4 - patient is rubbing joints or muscles and is unable to sit still because of discomfort.</td><td>Gooseflesh skin
0 - skin is smooth
2 - piloerrection of skin can be felt or hairs standing up on arms
5 - prominent piloerrection</td></tr>
<tr><td rowspan="2">Runny nose or tearing: Not accounted for by cold symptoms or allergies.
0 - not present
1 - nasal stuffiness or unusually moist eyes
2 - nose running or tearing
4 - nose constantly running or tears streaming down cheeks</td><td>Total Score:
The total score is the sum of all 11 items.</td></tr>
<tr><td>Initials of person completing assessment:</td></tr>
</table>

Score: 5-12 = mild; 13-24 = moderate; 25-36 = moderately severe; more than 36 = severe withdrawal. Wesson, D.R., & Ling, W. (2003). The Clinical Opiate Withdrawal Scale (COWS). *Journal of Psychoactive Drugs*, 35(2), 253-259.

Appendix 8: Drug-drug and drug-medication interactions

This appendix is copied from *Te Ariari o te Oranga: the Assessment and Management of People with Co-existing Mental Health and Substance Use Problems* (Todd, 2010) and accompanies the text in Section 4.6.4 (pp. 118-9).

This is intended to be a guide to drug-drug and drug-medication interactions. Interactions between psychoactive substances are potentially important, though much is unknown, especially for interactions between prescribed medications and illicitly taken substances. This section highlights some key interactions to be aware of, but it is not comprehensive. Note that the absence of an interaction described here does not mean it does not exist and therefore the combination is safe.

Interactions may arise through a number of mechanisms, including synergistic effects on neurotransmitter systems, augmentation of side-effects and alterations in the metabolism of a drug. Alterations in metabolism are potentially complex and often involve the cytochrome (CYP450) system in the liver. There is a wide range of cytochromes, and where drugs taken at the same time are metabolised by the same cytochrome, metabolism may be affected by either inhibition or induction of the enzymes. The main cytochromes of relevance for CEP are CYP2D6 and CYP3A4. A table of CYP450 interactions is available at: https://drug-interactions.medicine.iu.edu/MainTable.aspx

As noted, there are likely to be important interactions that are not mentioned, and many of the interactions that are mentioned are theoretical or based on a small number of case reports. There is also considerable interpersonal variation in these interactions. This section should therefore be used as a guide to possible interactions, and in most cases drugs that interact should still be prescribed, but cautiously, and the effects monitored.

There are several potentially severe and fatal interactions. The combination of the following medications and drugs is best avoided:

- lorazepam and alcohol, which has been associated with significant respiratory and cardiac depression (this appears to be more likely with lorazepam than with other benzodiazepines)
- amyl nitrate and sildenafil (Viagra) or tadalafil (Cialis), which have been associated with potentially fatal hypotension
- ecstasy and ritonavir, which has been associated with fatalities reported
- ecstasy and monoamine oxidase inhibitors, including moclobemide, which have been associated with fatalities
- amphetamines and monoamine oxidase inhibitors, including moclobemide, which have been associated with a severe hypertensive crisis.

Nicotine

The main effect of nicotine on other drugs is via the polycyclic aromatic hydrocarbons in tobacco smoke and their induction of certain CYP450 enzymes. This increases the metabolism and reduces serum levels of a range of drugs, though there are other mechanisms that may be involved. The dosage of such medications may need to be increased in smokers and reduced upon cessation of smoking to avoid the emergence of side-effects.

Reduced blood levels may occur with the combination of tobacco use and the following drugs:

- alprazolam and other benzodiazepines
- beta-blockers, especially propranolol
- caffeine
- chlorpromazine
- clozapine (reduction in blood levels may be marked)
- corticosteroids
- haloperidol
- heparin
- inhaled insulin (currently unavailable; causes a significant increase in insulin levels, contraindicated in current or recent tobacco users)
- mexiletine
- olanzapine (mild effects, so may not need dose adjustment)
- pentazocine
- theophylline
- tricyclic antidepressants (especially imipramine and nortriptyline).

In addition, it should be noted that through other mechanisms, there may be an increased risk of myocardial infarction when tobacco smokers take oral contraceptives.

Figure 23: Interactions between alcohol and medications

Medication class	Medication	Effects
Anaesthetic agents	Fluothane, propofol	Risk of liver damage; higher doses needed to induce anaesthesia
Analgesics - non opioid	Aspirin and NSAIDs	Increased risk of gastric bleeding
Antibiotics	Metronidazole and tinidazole (antabuse-type reaction), griseofulvin, quinacrine	Reduced effectiveness, nausea/vomiting, headache, seizures
Anticoagulants	Warfarin	Increased clotting time with acute alcohol use; reduced clotting time with chronic use
Antidepressants	Tricyclic antidepressants	Increased sedation,impaired motor skills
	Monoamine oxidase inhibitor	Tyramine-rich drinks (beer, red wine) may cause severe hypertension and, rarely, cardiac arrhythmias
	Serotonin-specific re-uptake inhibitors (fluoxetine, citalopram, paroxetine)	May enhance the intoxicating effects of alcohol
Antidiabetic agents	Tolbutamide	Acute intoxication increases and chronic consumption reduces tolbutamide availability
Antihistamines	Diphenhyramine (Benadryl)	Increased sedation and dizziness, especially in elderly
Antipsychotics		Enhanced side-effects, especially sedation, hypotension, impaired judgement and motor incoordination; possible increase in akathisia and dystonic reactions (small case series)
Anticonvulsants	Phenytoin	Increased phenytoin levels with acute alcohol consumption
Antiulcer drugs	Ranitidine, cimetidine	May increase alcohol levels
Cardiovascular meds	Nitroglycerin, reserpine, methyldopa, hydralazine, guanethidine	Possible increased postural hypotension
Mood stabilisers	Lithium	Increased motor incoordination; lithium may slightly reduce intoxicating effects of alcohol in some
	Valproate	Increased sedation, especially in early phases of valproate treatment
Opioids		Increased sedation, possible respiratory depression, risk of overdose
Sedatives	All benzodiazepines	Sedation, motor incoordination
	Lorazepam	Respiratory and cardiac depression (avoid in acute intoxication)

Sources:

- NIAAA Alcohol Alert January 1995, no. 27 PH 355 publication
- Alcohol-drug Interactions, University Health Service (UHS) Health Promotion Office, Rochester University.

As noted, the interaction between lorazepam and alcohol may lead to possible cardiac and respiratory depression and should be avoided.

Where sedation and incoordination are noted, tāngata whai ora should be advised not to drive and to avoid using machinery.

Advice about not combining alcohol with specific medications should be given carefully, especially where the risk or severity of complications is mild. Tāngata whai ora are as likely to stop medication as alcohol, if advised not to combine them. This is especially the case in the treatment of mood problems, especially bipolar disorder, where mood stabilisers are likely to reduce alcohol consumption and the potential complications are usually mild.

Cannabis

Much of the information on cannabis interactions comes from research into the synthetic tetrahydrocannabinol (THC) analogue dronabinol. It should be noted that cannabis has a number of extra actions due to the large number of other compounds it also contains.

Figure 24: Interactions between cannabis and medications

Other medication	Effects
Amphetamines, cocaine, other sympathomimetics	Hypertension, tachycardia, possibly cardiotoxicity
Atropine, scopolamine, antihistamines and other anticholinergenics	Tachycardia, drowsiness
Amitriptyline, amoxapine, desipramine, other tricyclic antidepressants	Additive tachycardia, hypertension, drowsiness
Disulfiram (antabuse)	Possible hypomania (single case)
Benzodiazepines, alcohol, lithium, opioids, buspirone, antihistamines, other CNS depressants	Additive drowsiness and CNS depression
Theophylline	Increased theophyline metabolism, similar to the effects of smoking tobacco
Fluoxetine	Possible hypomania (single case)
Naltrexone	Intoxication enhanced by naltrexone

Note: **CNS** = central nervous system

There is some evidence that THC intoxication is enhanced by naltrexone (Haney et al., 2003), though other studies contradict this (Wachtel and de Wit, 2000).

Prior recent exposure to nicotine may enhance some of the effects of cannabis, especially in males (Penetar et al., 2005), though it has been shown that THC ameliorates acute nicotine withdrawal and that the cognitive effects of nicotine withdrawal (memory) are greater in cannabis users (Viveros et al., 2006).

Stimulants

Stimulants are drugs that are both prescribed and used illicitly. Amphetamines are metabolized by CYP2D6 and inhibitors of this enzyme such as paroxetine and fluoxetine. The concomitant use of methylphenidate (Ritalin) and monoamine oxidase inhibitors is contraindicated due to the risk of hypertensive crisis. Methylphenidate may decrease the effectiveness of medications used to treat high blood pressure and may increase levels of warfarin and tricyclic antidepressants.

Methamphetamine has many potential interactions. The following are the major interactions that can occur; in combination with:

- selegiline – hypertensive crisis (contraindicated)
- bupropion – increased risk of seizures
- tramadol – seizures
- SSRIs and venlafaxine – potential increase in amphetamine activity, potential serotonin syndrome with some (e.g., dexamphetamine)
- linezolid (a new antibiotic) – has monoamine oxidase inhibitor actions (contraindicated)
- sibutramine (Reductil) – contraindicated due to adrenergic and serotonergic reuptake inhibition.

Other medications with stimulant actions, especially those affecting the adrenergic system, can lead to increased blood pressure and pulse rate (e.g., chlorpheniramine, phenylephrine, dextromethorphan and brompheniramine, which are often found in cough mixtures). Antacids can increase amphetamine absorption and therefore actions.

MDMA (ecstasy)

MDMA is potentially hepatotoxic, and liver function should be monitored when prescribing other medications that are also hepatotoxic, such as naltrexone and sodium valproate. It also releases large amounts of serotonin and is mainly metabolised by CYP2D6. There is therefore a risk of serotonergic syndrome, especially in combination with drugs like fluoxetine, citalopram, paroxetine, venlafaxine buproprion and pethidine.

The most serious combinations include:

- ecstasy and MAOIs, including moclobemide (which has been associated with fatal interactions)
- ecstasy and ritonavir (fatalities have been reported).

Inhibition of metabolism via CYP2D6 inhibition can occur with:

- fluoxetine
- paroxetine
- buproprion
- methadone
- haloperidol
- quinidine
- ritonavir (antiviral agent).

Enhanced serotonergic effects can occur with:

- amphetamines
- St John's wort
- tramadol
- venlafaxine
- lithium
- clomipramine.

(Oesterheld et al., 2004)

Benzodiazepines and other sedatives

Benzodiazepines differ in terms of their metabolism. Most are metabolised by the CYP450 system in the liver and therefore are affected by other medications that increase or decrease the activity of that system. Medications that induce CYP450, such as St John's wort, carbamazepine, phenytoin and rifampicin, therefore decrease the action of these benzodiazepines. Medications that reduce the activity of CYP450, and therefore increase the effects of benzodiazepines, include oral contraceptives, antibiotics, antidepressants and antifungal agents. Benzodiazepines that are not metabolised by the CYP450 system, and therefore are not affected by these interactions, include lorazepam, oxazepam and temazepam.

Opioids

Pethidine

Pethidine has the potential to induce a serotonin syndrome when used together with other drugs including:

- dextromethorphan
- pentazocine
- tramadol
- tricyclic antidepressants
- selective serotonin reuptake inhibitors (SSRIs)
- monoamine oxidase inhibitors (MAOIs), including moclobemide.

Pethidine can increase risk of seizures in combination with the following drugs:

- theophylline
- tricyclic antidepressants
- fluoroquinolones (which can potentiate the seizure potential of pethidine).

Methadone

The tendency for methadone to prolong the QT interval may be enhanced by other drugs that do the same. A list of these can be found at: https://crediblemeds.org/index.php/drugsearch

Precipitation of opioid withdrawal

This can result from:

- buprenorphine
- pentazocine
- naltrexone
- naloxone
- tramadol.

Unpredictable interactions

These can result from combining opioids with:

- antiretroviral drugs
- benzodiazepines
- cannabis
- cyclizine
- interferon + ribavirin
- methylphenidate
- opioids
- promethazine
- tricyclic antidepressants.

Decreased methadone effects

This can result from combining methadone with:

- some antiretroviral drugs
- alcohol
- carbamazepine
- phenytoin
- rifampicin
- St John's wort
- tobacco
- urinary acidifiers.

Increased effects of methadone

These can be induced by combining methadone with:

- cimetidine
- some antiviral drugs
- diazepam
- dihydroergotamine
- alcohol
- erythromycin
- fluconazole
- grapefruit
- moclobemide
- omeprazole
- serotonin-specific reuptake inhibitors
- verapamil
- cyclizine.

(Leavitt, 2005)

Morphine

Morphine may interact with monoamine oxidase inhibitors to cause serotonin syndrome.

Tramadol

Tramadol may interact with SSRIs to cause serotonin syndrome.

Solvents and volatile substances

Solvents may sensitise the heart to adrenaline, and this has been associated with sudden cardiac death when adrenaline is co-administered. This usually only occurs in emergency medicine situations.

Other commonly prescribed medications

Naltrexone

- opioid antagonist, precipitates opioid withdrawal in those with physiological dependence on opioids
- otherwise known significant drug interactions.

Serotonin-specific reuptake inhibitors (SSRIs) (fluoxetine and citalopram)

The use of SSRIs with monoamine oxidase inhibitors is contraindicated. SSRIs may lower the seizure threshold and should be used cautiously with other drugs that do the same. Serotonin syndrome may occur when SSRIs are used with other drugs that enhance serotonin activity, or with drugs that inhibit SSRI metabolism.

Antipsychotics (risperidone, quetiapine, olanzapine, clozapine, chlorpromazine)

Antipsychotics may be associated with an increased risk of seizures and cardiac arrhythmias especially in those with QT prolongation. This risk may be enhanced with other drugs that have similar effects, particularly amphetamines.

Bupropion (Zyban)

The use of bupropion and monoamine oxidase inhibitors is contraindicated. The metabolism of bupropion may be inhibited by paroxetine, sertraline and antiretroviral agents, increasing its blood levels. Bupropion inhibits the CYP2D6 isoenzyme and may increase blood levels of drugs metabolised by this enzyme, including most antidepressants (e.g., nortriptyline, imipramine, desipramine, paroxetine, fluoxetine, sertraline), antipsychotics (e.g, haloperidol, risperidone, thioridazine), beta-blockers (e.g., metoprolol) and antiarrhythmics, and antipsychotics. Bupropion can also lower the seizure threshold and should be used with other drugs that act similarly only with great caution. This is especially so in tāngata whai ora with bulimia or anorexia nervosa due to possible increases in seizure risk in this population.

Varenicline

There are no known or predictive drug interactions of significance.

References

Haney, M., Bisaga, A., & Foltin, R. W. (2003). Interaction between Naltrexone and oral THC in heavy marijuana smokers. *Psychopharmacology.* 166: 77-85.

Leavitt, S.B. (2005). Methadone-drug interactions. *Addiction Treatment Forum.* November 2005.

National Institute on Alcohol Abuse and Alcoholism. (1995). Alcohol Alert. No. 27. PH 355. January 1995. Retrieved online from: http://pubs.niaaa.nih.gov/publications/aa27.htm

Nelson, E.M., & Philbrick, A.M. (2012). Avoiding serotonin syndrome: the nature of the interaction between tramadol and selective serotonin reuptake inhibitors. *The Annals of Pharmacotherapy*. 46(12):1712-6

Oesterheld, J. R., Armstrong, S. C., & Cozza, K. L. (2004). Ecstasy: pharmacodynamic and pharmacokinetic interactions. *Psychosomatics*. 45: 84-87.

Penetar, D. M., Kouri, E. M., Gross, M. M., McCarthy, E. M., Rhee, C. K., Peters, E. N., & Lukas, S. E. (2005). Transdermal nicotine alters some of marihuana's effects in male and female volunteers. *Drug and Alcohol Dependence*. 79: 211-223.

University of Rochester. (2011). Alcohol-drug Interactions. University Health Service (UHS). Health Promotion Office. Retrieved online from: http://www.rochester.edu/uhs/healthtopics/Alcohol/interactions.html

Viveros, M. P., Marco, E. M., & File, S. E. (2006). Nicotine and cannabinoids: parallels, contrasts and interactions. *Neuroscience & Biobehavioral Reviews,* 30: 1161-1181.

Watchel, S. R., & de Witt, H. (2000). Naltrexone does not block the subjective effects of oral delta-9-tetrahydrocannabinol in humans. *Drug and Alcohol Dependence*. 59 (3): 251-260.

Source:

Todd, F. C. (2010). *Te Ariari o te Oranga: the Assessment and Management of People with Co-existing Mental Health and Substance Use Problems*. Ministry of Health, Wellington, New Zealand.

This document is available in hard copy and is downloadable from: https://www.health.govt.nz/publication/te-ariari-o-te-oranga-assessment-and-management-people-co-existing-mental-health-and-drug-problems

Appendix 9: Medication safer to use in pregnancy

Prescribing in pregnancy

(adapted from and used with thanks to Canterbury DHB Pharmacy)

Many medications (drugs) can have harmful effects on the embryo or fetus at any time during pregnancy. It is important to bear this in mind when prescribing for a woman of child-bearing age.

During the first trimester drugs can produce congenital malformations (teratogenesis), and the period of greatest risk is from the third to the eleventh week of pregnancy.

Folic acid 5mg daily is recommended for high-risk patients or folic acid 0.8mg daily for all other patients during the first trimester. Potassium iodate 253mcg daily is recommended for the duration of pregnancy.

During the second and third trimesters drugs can affect the growth or functional development of the fetus, or they can have toxic effects on fetal tissues.

Drugs given shortly before term or during labour can have adverse effects on labour or on the neonate after delivery.

Not all the damaging effects of intrauterine exposure to drugs are obvious at birth, some may only manifest later in life. Such late-onset effects include adverse effects on intellectual, social, and functional development.

Drugs should be prescribed in pregnancy only if the expected benefit to the mother is thought to be greater than the risk to the fetus, and all drugs should be avoided if possible during the first trimester. Drugs which have been extensively used in pregnancy and appear to be usually safe should be prescribed in preference to new or untried drugs; and the smallest effective dose should be used.

Few drugs have been shown conclusively to be teratogenic in humans, but no drug is safe beyond all doubt in early pregnancy. Screening procedures are available when there is a known risk of certain defects.

Absence of information does not imply safety

Categorisation of a drugs proposed safety in pregnancy (using the Australian system)- medications listed in the New Zealand Formulary carry this categorisation.

It is important to note that:

- Human data are lacking or inadequate for drugs in the B1, B2 and B3 categories
- Subcategorisation of the B category is based on animal data
- The allocation of a B category does not imply greater safety than a C category
- Medicines in category D are not absolutely contra-indicated during pregnancy (e.g., anticonvulsants).

For pharmaceutical products containing two or more active ingredients, the categorisation of the combination is based on the active ingredient with the most restrictive pregnancy categorisation.

Category A- Drugs which have been taken by a large number of pregnant women and women of child-bearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the fetus having been observed.

Category B1- Drugs which have been taken by only a limited number of pregnant women and women of child-bearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed.

Studies in animals have not shown evidence of an increased occurrence of fetal damage.

Category B2- Drugs which have been taken by only a limited number of pregnant women and women of child-bearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed.

Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of fetal damage.

Category B3- Drugs which have been taken by only a limited number of pregnant women and women of child-bearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed.

Studies in animals have shown evidence of an increased occurrence of fetal damage, the significance of which is considered uncertain in humans.

Category C- Drugs which, owing to their pharmacological effects, have caused or may be suspected of causing, harmful effects on the human fetus or neonate without causing malformations. These effects may be reversible. Information sheets should be consulted for further details.

Category D- Drugs which have caused, are suspected to have caused or may be expected to cause, an increased incidence of human fetal malformations or irreversible damage. These drugs may also have adverse pharmacological effects. Information sheets should be consulted for further details.

Category X- Drugs which have such a high risk of causing permanent damage to the fetus that they should not be used in pregnancy or when there is a possibility of pregnancy.

Commonly prescribed withdrawal management medicines

Note: Please always contact a pharmacist for advice when prescribing any medications that are not category A in pregnancy as some medications have different safety profiles depending on which trimester of pregnancy they are used in.

Paracetamol- safe to use. **Category A**

Docusate and senna- safe to use. **Category A**

Metoclopramide- safe to use. **Category A**

Loperamide- limited human data, animal data suggests low risk. Due to limited data, use only if potential benefit outweighs the potential risk to the foetus. **Category B3**

Quetiapine- Maternal use of antipsychotic drugs during the third trimester of pregnancy has been associated with an increased risk of neonatal extrapyramidal and/or withdrawal symptoms following delivery. Can be used if benefit outweighs risk to the foetus. Recommend low doses. **Category C**

Zopiclone- best avoided in the first trimester as it has been associated with congenital malformations. Avoid in the third trimester close to delivery as it may cause neonate hypothermia, hypotonia and respiratory depression. Could be used sparingly in the second trimester at low doses (3.75mg). **Category C**

Hyoscine butylbromide- very limited data. Consider risk vs benefit. Recommend low doses. **Category B2**

Promethazine- considered low risk. Sometimes used as an antiemetic in pregnancy. **Category C**

Chlorpromazine- considered safe to use occasionally in low doses. Avoid near-term due to the danger of maternal hypotension and adverse effects in the newborn. **Category C**

Prochlorperazine- considered safe to use occasionally in low doses. **Category C**

Ondansetron- Human data suggests low risk. Has been used post 10 weeks gestation. **Category B1**

Diazepam/oxazepam- Studies have suggested that the use of benzodiazepines during the first trimester of pregnancy is associated with an increased risk of congenital malformations. If pregnancy occurs during chronic use, the patient should be advised of the desirability of discontinuing the drug and of possible consequences to the fetus. If given, prescribe as monotherapy in the lowest effective dosage, for the shortest duration possible, and in divided doses to avoid high peak concentrations.

Category C

Ibuprofen- Best to avoid (Highest risk in 1st and 3rd trimesters). **Category C**

Sodium valproate- Avoid. **Category D**

References:

New Zealand Formulary: http://nzformulary.org/

Micromedix: https://www.micromedexsolutions.com/home/dispatch/ssl/true

Briggs, G.G., Freeman, R.K., and Yaffe, S.J. (2014). *Drugs in pregnancy and lactation: A reference guide to fetal and neonatal risk*: Tenth edition. Wolters Kluwer Health, Philadelphia

Appendix 10: Alternative and complementary therapies

There is no reliable evidence to support the use of natural alternatives or complementary therapies for use in managing substance withdrawal. However, as an adjunct to withdrawal management some addiction services support the use of:

- acupuncture
- massage and mirimiri
- sensory modulation
- aromatherapy
- yoga
- vitamin, mineral and some herbal supplements
- homeopathic remedies.

Useful dietary supplements include:

- vitamin C
- zinc
- magnesium.

Products helpful for stress reduction, relaxation and sleep assistance include:

- DL-Phenylalanine
- valerian
- kava
- Rescue Remedy (homeopathic remedy)
- natural melatonin (tart cherry).

Products potentially helpful for nausea and vomiting include:

- ginger
- Nux Vomica or Vomiplex (homeopathic remedies)
- peppermint.

Products possibly helpful for joint pain:

- calcium
- fish oils
- flax seed oil
- magnesium.

Complementary therapies should not be used as an alternative to a planned and managed withdrawal process as the risks of doing so include:

- progression to severe withdrawal
- risk of injury to self and others due to altered mental state
- risk of dehydration or electrolyte imbalance
- seizures
- the person having a coexisting illness that is masked or mimicked by withdrawal
- accidents due to side effects such as hypotension.

Practical strategies and 'over the counter' or non-prescription medication that can be helpful to support managed withdrawal:

- Disturbed sleep
  - reducing coffee, tea, cola and energy drinks during the day and having none after 2 pm
  - eating 3 meals a day and avoiding heavy, spicy meals late at night
  - avoiding napping during the day and keeping to regular bed and wake times
  - exercising regularly (in the day, not after 6 pm)
  - using relaxation techniques
  - avoiding doing things (i.e. tough phone calls) that might be stressful before going to bed
  - having a bath in the evening.

- Sweating/hot and cold flushes
  - having regular showers or baths
  - Paracetamol - as directed on the packet.
- Muscle cramps and aches
  - having a bath
  - using a heat rub/wheat bag
  - doing gentle exercise e.g., walking
  - massage
  - Paracetamol –as directed on the packet
  - Ibuprofen – as directed on the packet.
- Poor appetite
  - eating small meals and snacking often
  - avoiding heavy, greasy, sweet or rich foods
  - drinking 6- 8 glasses of water a day
  - nutritional supplements e.g., Complan
  - multivitamins may be helpful if the person has not been eating well for some weeks.
- Constipation/diarrhoea
  - drinking plenty of fluids - 6 - 8 glasses of water a day
  - eating regular meals
  - having a high fibre diet
  - for severe constipation eating fresh fruit, prunes or kiwifruit
  - for severe diarrhoea try loperamide (Imodium) –as directed on the packet.
- Nausea/vomiting
  - eating small meals and snacks often
  - drinking plenty of water
  - trying small sips of liquid, or sucking an ice cube, if vomiting.
  - having a small amount of food once person has kept fluids down for a few hours
  - using rehydration/sports/isotonic drinks such as 'Powerade'
  - avoiding citrus and caffeine on an empty stomach.
- Anxiety/restlessness
  - using relaxation audios
  - reducing caffeine intake
  - having a bath
  - doing some gentle exercise.