Opioids and benzodiazepines combined misuse in clinical settings

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Thesis declaration form

I confirm that the work presented in this thesis is my own. Wherever information has been derived from other sources, I confirm that this has been indicated in the thesis.

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Overview

This thesis is comprised of three parts and explores the co-misuse of opioids and benzodiazepines in clinical settings.

Part one consists of a conceptual introduction summarising the current and most central research about the misuse of each drug and their combination; giving background and characterising these subtypes of users. Specifically, it focuses on the subpopulation of co-users of both opioids and benzodiazepines, which is consistently described in the literature as more complex in terms of their presentation, mental health difficulties, drug use related behaviours, risk and adverse childhood experiences. It also describes the current framework of treatment and complications in its employment.

Part two is an empirical qualitative research paper focusing on the co-misuse of these two drugs, aiming to explore the ways in which this subgroup of users is experienced and conceptualised by clinicians in substance misuse services. It is a qualitative study utilising eighteen semi-structured interviews with clinicians from different disciplines. Analysis produces 13 themes and 4 sub-themes grouped under two main domains and five sub-domains. One main domain describes clinicians' attempts to empathise with patients' attachment to the benzodiazepine and understand their desperate need for it in order to be able to function. The second reflects clinicians' difficulties working and making progress with them, which is attributed to (1) the very addictive nature of the benzodiazepines and the objective difficulty detoxing from in, (2) difficulties around engagement, assessment and prescribing and lastly (3) a feeling that this work requires a specific and different skillset as well as additional resources, mainly training and psychology. Lastly, clinicians' attitudes reflect a dissonance between these two main aspects of their experience- empathising and making progress with these patients, which often leads to a feeling of frustration and hopelessness.

Part three presents a critical appraisal of reflections made following the empirical research undertaken in part two. It summarises some of the dilemmas arising during the process of conducting this research and the ways in which they were resolved and affected the outcome. It concludes with some personal notes on the process from the writer's clinical perspective.

Impact statement

This thesis explores clinicians' experiences of working with opioids and benzodiazepines co-dependant users in substance misuse services. Using qualitative methodology, the empirical chapter aims to develop a deeper understanding of clinicians' perspectives on the ways in which this subpopulation of users presents in treatment, how this is conceptualised by clinicians and how it might affect their work.

There is currently a large amount of research on this subpopulation of users, however truly little of this research is qualitative. Moreover, only a limited amount focuses on clinicians' perspectives. This study therefore provides a unique perspective into the perceptions and conceptualisations of clinicians from different disciplines and their reflections of their work with this population, in their own words. It is hoped that this primary study will inspire future ones to better inform clinical care of these service users.

Additionally, the findings from this thesis provide clinical recommendations as well as ones concerning service structure that can be applied by a range of clinical mental health services in the U.K., specifically but not exclusively in substance misuse ones. The results will be shared with all participants and clinicians involved in the study, and hopefully will be published.

This study also highlights the importance of using qualitative research to improve health care and demonstrates how this approach can lead to research which aims to benefit the lives of individuals affected by its outcomes. Furthermore, the recommendations from this study can be included to develop and/or amend existing training opportunities for clinicians working with service users presenting with complex drug dependence.

It is hoped that the findings of this thesis will be disseminated via various platforms, to direct further research, enhance clinical practice, impact training delivered to mental health professionals and influence public policy design.

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Part 1: Conceptual introduction

The misuse and co-misuse of opioids and benzodiazepines

Abstract

This literature review is a conceptual introduction to the misuse of opioids and benzodiazepines, independently and combined. It reviews the most central current literature describing main findings in this field, thus focusing on presentation, prevalence, characteristics of users, adverse effects and current treatment. It sets a profile for patients who seek treatment for this specific sub type of drug-dependence and points to a lack of qualitative research in this field and the absence of research focusing on clinicians' perspectives.

Introduction

This conceptual introduction will examine the most central and relevant literature on the misuse and combined misuse of opioids and benzodiazepines. It will focus on mechanisms of effect, risks and complications that this subpopulation of service users presents with in treatment. It will also present the rationale for exploring the experiences and conceptualisations of clinical staff working with these service users to inform their management and care in specialist substance misuse services.

First, this review will provide a general introduction to the epidemiology, terminology, theoretical conceptualisation and treatment frameworks in the field of substance misuse. It will then expand on the non-medical use of opioids and benzodiazepines, focusing on the mechanism of effect, extent of use, adverse effect and treatment of each drug independently and the co-misuse of both.

Substance use disorders

Statistics

In the last year (2019-2020) 9.4% of adults between the ages of 16 to 59 years old had used drugs. Only 2.1% of them, approximately 712,000, were frequent users, using more than once a month- a decrease from the year ending March 2015 counting 3.1%; around 1 million adults (Stripe, 2020).

In 2018, 114,752 individuals entered drug treatment in the UK- another decrease from over 122,000 in 2015 (Public Health England, 2021). In addition, there were 234,101 people in treatment for drug dependency in England and Wales at any time during 2018. That year in Great Britain, treatment was sought most commonly for help with addiction to heroin, followed by cannabis.

Terminology

The accepted definition of "drug misuse" in the context of prescription drugs encompasses all patterns of intentional use of a medication with intoxicating properties which exceeds medical prescription for a specific medical condition. This excludes accidental misuse (Compton & Volkow, 2006).

Tolerance and withdrawal

Tolerance refers to an adaptation to repeated exposure to a drug such that the pharmacological response to the substance is diminished. This leads to either a need for substantially larger doses of the substance to achieve the desired effect (Boscarino et.al., 2011); or a reduction in the desired effect achieved, leading to increased symptomizing. Withdrawal symptoms tend to be opposite to the initial drug effects and begin as the drug is removed from the body through metabolism and excretion (Iverach et al., 2011). Often, to alleviate symptoms of withdrawal, reintroduction of the drug itself at a low and tapering dose, or alternatively, an introduction of a substitute is required.

Dependence and abuse

Due to changes of terminology in this field throughout the past decades it is important to distinguish between dependence and abuse. Physical dependence is a state in which withdrawal symptoms occur as a physiological response to reducing or stopping continuous use (Crawford et.al., 2017). Substance abuse, however, has a similar definition to misuse, and refers to any use that exceeds the intended medical/prescribed one, either in dosage or purpose (Baldessarini et.al., 2013).

The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) is the first to combine substance abuse and dependency into one single diagnosis of substance use disorder (SUD) (Hasin et.al., 2013). DSM-5 defines 11 criteria for diagnosis of SUD, which can be roughly divided into four categories of behaviours related to the substance

used: impaired control, social impairment, risky use behaviours and tolerance / withdrawal. It was decided to use the number of criteria met (from two to eleven) as the overall indicator of severity. Severity of SUD can therefore be mild (two to three criteria), moderate (four to five), or severe (six or more) (American Psychiatric Association, 2013).

Psychological theories of addiction and current framework of treatment

Scientific efforts in the past decades were unable to unveil one single factor able to explain why some people can use substances without developing SUD while others are unable to and develop a dependence as result.

There are many theoretical frameworks that were used to explain the psychological aspect of drug dependence: behavioural models which emphasise learning and conditioning as well as cognitive and motivational theories.

Behavioural

Behaviourist models of addiction posit that a behaviour (in this instance drug use) is maintained when there is positive reinforcement as a direct result of that behaviour (West & Farr, 1989). Drug self-administration is an example of an instrumental behaviour where the action of the person causes a pleasurable effect. Reinforcement in this context is biological (through activity in the mesolimbic dopamine pathway) as well as social and environmental in the form of attention or social acceptance (Altman et al., 1996).

Accordingly, it was found that classical conditioning plays a central part in the development and maintenance of addictive behaviours (Heather & Greeley, 1990; Westbrook et al., 1991). Cue exposure theory for example, based on classical conditioning theory, centralises cues in the development and maintenance of addictive behaviours (Drummond et al., 1995; Heather & Greeley, 1990). According to this theory, an environmental or internal cue that has previously been associated with drug consumption will likely elicit a conditioned

response in future exposure. This is referred to as "cue reactivity" and is thought to cause the sense of craving.

Supporting this further, it was also found that as drug addiction develops, the changes that occur in the brain are caused by behaviour, environmental and social circumstances associated with obtaining and using the drug, in addition to the drug itself (Childress et al., 1986; Hyman & Malenka, 2001; Hyman & Nestler, 1996; Narita et al., 2001; Nestler, 2001; Self & Nestler, 1998; Sell et al., 2008). These form a powerful memory imprint, like all conditioning responses, that are difficult to extinguish, even after drug cessation (Hyman & Malenka, 2001; Morris, 1997; O'Brien et al., 2006; Robinson & Berridge, 1993; Self & Nestler, 1998; Sell et al., 2000; Shaham et al., 2000) and contribute to the cycle of maintenance.

These models therefore underpin treatment which aims to enhance the value of non-drug rewards. Contingency Management (CM) is a behavioural intervention developed based on these principles, where abstinence, rather than drug use, is reinforced with incentives (Higgins et al., 1991; Petry, 2006). CM interventions often include three basic tenets (Higgins et al., 1994a; Higgins et al., 1994b). First, the clinician arranges the patients' environment in a way which makes the target behaviours (e.g., drug abstinence, medication compliance etc.,) easily detected. Second, tangible reinforces are introduced and provided when the target behaviour is demonstrated; and lastly, incentives are withheld when the target behaviour does not occur.

Cognitive

Self-regulation has been argued to be a defining factor in the development and maintenance of drug addictions. It was defined as an executive capacity to plan and execute flexible behaviour according to the external circumstances (Diaz & Fruhauf, 1991; Miller & Brown, 1997). These abilities relate to the difficulty many individuals encounter in resisting habitual drug use once established and explain the maintenance of drug use behaviour (Everitt

et al., 2007; Goldstein & Volkow, 2011; Porrino et al., 2007). The inhibitory and executive control functions, concentrated primarily in the prefrontal and parietal cortices, are crucial to the individual's ability to override a pre-potent 'impulsive' response, such as drug use behaviour in response to drug related cues (Sarter et al., 2006).

Cognitive Behavioural Therapy (CBT) in the context of substance misuse therefore teaches specific strategies, skills and coping mechanisms to reduce the need for and use of substances (Carroll et al., 1994; Marlatt & George, 1984). These include self-awareness (e.g., of cravings and sensitivity to environmental cues), self-instruction, planning and problem-solving and well-practiced behavioural strategies around risk reduction and increase of positive enjoyable sober activities. In addition, they also include methods of responding effectively to one's dysfunctional beliefs about oneself and the need for the drug etc.

One of the central guidelines for cognitive therapy of SUD is described as seven main areas of potential psychological vulnerability, contributing to the development and maintenance of SUD, and suggesting a potential focus for intervention (Beck et al., 1993). These include:

1. High-risk situations or cues, both external (e.g., people and places) and internal (e.g., distress/ certain mood states).
2. Dysfunctional beliefs about the drugs, drug use, oneself, and about one's "relationship" with the drugs.
3. Automatic thoughts in response to cues- these increase arousal and the intention to drink and/or use.
4. Physiological cravings and urges to use.
5. Permission-giving beliefs that one holds which justify their substance use.
6. Rituals and behaviours linked to the usage of substances.

7. Adverse psychological reactions to a lapse or relapse which lead to a vicious cycle of use.

Motivational

It has been hypothesized that the lack of motivation to change plays a central role in noncompliance with treatment and lack of engagement (Troop et al., 1996). According to the transtheoretical motivational model of behavior change (Prochaska & DiClemente, 1982), the intentions and motivations of the drug user are a critical part of the recovery process. Motivation for change plays a central role in the process of change and affects all aspects: from recognizing the need for change, through seeking treatment, and to achieving as well as maintaining change. Motivations can be both intrinsic and extrinsic, and change can be both imposed and intentional. Readiness for change versus readiness for treatment are also assessed as two separate aspects (Markland et.al., 2005).

Inspired by this theory, Motivational Interviewing (MI) is an intervention in which interviews are conducted in a style which is non-judgmental and explorative, to raise awareness and insight, as well as motivate and harness the individuals' capacity for change (Hettema et al., 2005). Rooted in client centred therapy (Rogers, 1959), MI combines a supportive and empathic counselling style with a consciously direct method for resolving ambivalence and facilitating change. It is aimed at helping people work through ambivalence around behavioural change and motivate them to commit to it. Drawing on self-perception theory (Bem, 1972) which posits that people tend to become more committed to what they hear themselves defend, MI aims to explore the client's own generated arguments for change. Clients thus hear themselves explain their own motivations for change followed by hearing them reflected back to them by the counsellor (Miller & Rollnick, 2012).

MI has often been combined with feedback from assessment, and this combination is referred to as Motivational Enhancement Therapy (MET) (Miller et al., 1992). In MET, the

therapist uses structured feedback of the patient's problems which are associated with the target behaviour, as well as feedback regarding each symptom compared to the norms. It was found that using brief motivational interventions, such as MI or MET, significantly increases treatment utilization and effectiveness among substance-abusers (Carroll et al., 2001; Carroll et al., 2006; Martino et al., 2000; Swanson et al., 1999).

Current framework of treatment

The current bio-psychosocial conceptualisation of addiction which integrates all the above aspects posits that biological-genetic, personality-psychological, cognitive, social-cultural and environmental factors interact between them to enable an individual to develop substance use disorder. Accordingly, an intervention program must target these multiple aspects in treatment (Skewes & Gonzalez, 2013).

Furthermore, the UK guidelines on clinical management of drug misuse and dependence centralise the importance of building a strong therapeutic alliance with key workers and employing psychological interventions in caring for service users (Department of Health and Social Care, 2017). This is done while addressing practical social-environmental factors which contribute to the development and maintenance of SUD. In compliance with the bio-psychosocial model, the guidelines specify that these core interventions also support the effectiveness of pharmacological management of patients and their detox, which remains the main route to treating SUD.

Interestingly and accordingly, effect sizes remain modest for most behavioural therapies and outcomes vary widely across individuals (Dutra et al., 2008), suggesting a need for further exploration of moderating effects of these treatments in the form of potential individual differences between service users.

Opioids

Opioids are a family of drugs which include natural (e.g., morphine, codeine, salvia divinorum), semi-synthetic (e.g., heroin, oxycodone, hydromorphone, hydrocodone, salvanorin A) and synthetic (e.g., methadone, buprenorphine, and fentanyl-derivatives;) opioids. Opioid drugs interact with opiate receptors of cell membranes, thus creating the opioid's physiological and psychological effects (Gaynor, & Muir, 2014). Opioids are known to have multiple effects: they cause sedation and depress respiration, can alter body temperature and can produce either euphoria or dysphoria. In addition, they were also found to increase appetite, decrease gastrointestinal transit and affect urinary output (Broekkamp et al., 1984; Wise, 1989).

Mechanism of effect

Opioids interact with one or more of the subclasses of the three opiate receptors, designated as mu (μ), delta (δ) and kappa (ƙ), to create their effect (Lord et al., 1977).

Prescription opioid analgesics (morphine, hydrocodone, and oxycodone hydrochloride) and illicit opioid drugs (heroin and its analogues) act primarily as agonists at the μ-opioid receptor leading to a rewarding effect of analgesia and euphoria (Contet et al., 2004; Le Merrer et al., 2009). This is due to the high concentration of these opioid receptors in regions that are part of the pain and reward networks where they increase the activity of dopamine neurons in the ventral tegmental area and increase dopamine release in the nucleus accumbens (Kosten & George, 2002). They are also located in regions that regulate emotions, which explain the frequent association between long-term opioid exposure and depression and anxiety (Wilson & Junor, 2008). In addition, they can be found in regions within the brainstem that regulate breathing, underlying the mechanism of respiratory depression when over-used, which is the main mechanism responsible for death from opioid overdoses (Imam et.al., 2018).

Abuse potential

Abuse potential of a drug is the extent to which it produces reinforcing effects, including positive subjective feelings. Opioid receptor agonist substances are therefore known to be addictive (Ewan & Martin, 2013; Treisman & Clark, 2011) and μ-receptors were found to mediate the abuse potential of many opioid drugs (Bertalmio & Woods, 1989; Matthes et al., 1996; Negus et al., 1993). Accordingly, heroin, as well as μ-receptor-selective prescription opioid drugs (e.g., morphine, hydrocodone, hydromorphone, fentanyl, buprenorphine and oxycodone) have consistently demonstrated significant abuse liability in humans (Comer et al., 2008; Middleton et al., 2011; Walsh et al., 2008; Zacny & Lichtor, 2008).

Extent of use

The UK has the largest portion of opioid users in Europe. Estimates of the prevalence of opioids use in the UK suggest an eight-fold increase between 1970 and 2000 (De Angelis et al., 2004). More recent numbers show that in the UK during 2017, 57,430 people began treatment for primary opioid use, which was 35% of all treatment seeking patients in Europe (Kmietowicz, 2018). The overall number of people in treatment for opiate dependency in the UK in 2018 remained stable compared to the year before (141,189 to 139,845- 1% decrease) with this group still making up the largest proportion of subpopulation in treatment for substance use disorders (52%) in the UK.

Similarly to the UK and on a larger scale, in the US, opioids are increasingly becoming a major problem with almost 11 million American adults (aged 18 years and over) misusing opioids in 2016 and more than 2 million Americans diagnosed with opioid use disorder (OUD) in that same year (Welty et.al, 2016).

Prescribed use of opioids

Opioid prescribing for chronic pain more than doubled in the period between 1998 and 2018 in the UK; and this has been referred to as an 'opioid epidemic' in the UK (Ashaye et.al., 2018).

Opioids are normally prescribed for pain alleviation and are found to be effective for treating severe and acute pain. However, evidence of their effectiveness in treating chronic pain have been less conclusive (Reuben et al., 2015). This is because tolerance seems to rapidly develop to their analgesic effects, leading to use of increasingly higher doses and therefore increasing risk or addiction, respiratory depression and fatal overdose. High dosage can also lead to hyperalgesia, where pain is exacerbated instead of alleviated (Roeckel et al., 2016).

A study assessing DSM-5 criteria for OUD among patients receiving opioid medications for chronic pain found that 28.1% had mild OUD, 9.7% had moderate OUD, and 3.5% had severe OUD (Reuben et al., 2015). Interestingly, a recent meta-analysis found the following factors as predictive of outpatient prescribed opioid misuse: any current or previous substance use, any mental health diagnosis, younger age and male sex (Cragg et.al., 2019).

Illicit use of opioids

It was found that the ongoing proliferation of prescribing as well as diversion of prescribed opioids in the past decades (McCabe et al., 2008) was accompanied by an increased abuse among youth (Catalano et al. 2011; McCabe et al., 2007) as well as adults (Compton & Volkow 2006).

A common and repeatedly recognised route to dependence on illicit opioids begins with prescription opioids. For example, it was found that 75% of heroin users seeking treatment for OUD had begun their drug use in the 2000s with prescription opioids (Cicero et.al., 2014). Another study found that over a third of heroin users reported being "hooked on" prescription-type opioids before initiating heroin use and dependence (Peavy et. al., 2012). This study also

indicated that younger age was associated with prescription-type opioids dependence prior to heroin use.

In terms of acquiring the drugs illicitly, there is evidence to suggest that opioid misusers often do so through forging prescriptions, obtaining them from relatives or emergency rooms with false complaints of pain; or purchase them off the street (Ballantyne & LaForge, 2007; Fishbain et al., 1992).

Adverse effects

Withdrawal

Opioid withdrawal is known to be acute and painful with clinical indicators in patients with OUD including abdominal cramps, diarrhoea, bone and muscle pain, insomnia and anxiety (Herridge & Gold, 1988).

Mortality

Long term opiate use is consistently found to be correlated with a high risk of mortality (Darke et al., 1996; Darke & Hall, 1997; Davoli et al., 1997) and morbidity (Hagan et al., 2001). It was also found to be related to lost productivity and family disruption, as well as increased costs to health care and crime and law enforcement (Mark et al., 2001).

Opioids users have a high risk of death, with annual estimated death rates of about 1%, which is more than 10 times that of the general population, contributing to over 10% of adult mortality *(*Bargagli et al., 2006; Gossop et.al., 2002*)*. In 2017, opioids were implicated in around 80-90% of drug-induced deaths registered in each country in the UK (European Monitoring Centre for Drugs and Drug Addiction, 2019). In addition, it was found that in 2018 there was an increase in deaths of people in treatment for all substances, and the overall increase was driven by individuals in treatment for opioids use (1,712 to 1,897, or 1.4% of adults in treatment for OUD) (European Monitoring Centre for Drugs and Drug Addiction, 2019).

Overdose

Most deaths among opioids users are the result of overdose, and opioids are the most common among controlled drugs to cause poisoning *(*Gossop et.al., 2003; Morgan et al., 2006a*;* Morgan et.al., 2006b; Morgan et.al., 2008).

Respiratory depression was found to be the primary mechanism of opioid overdose fatality (Imam et al., 2018; White & Irvine, 1999). Respiration is controlled primarily through respiratory centres in the medulla with peripheral input from chemoreceptors. Opioids use inhibits these chemoreceptors via μ receptors and the medulla via μ and lambda (ƛ) receptors (White & Irvine, 1999), thus causing respiratory depression.

In the US, the term 'epidemic levels' was used to describe the rate at which Americans are overdosing and often dying from prescribed opioids. Opioid prescription drugs are a more significant cause of death than car accidents and are killing users more than cocaine and heroin combined (Huang et al., 2018). It is estimated that deaths secondary to prescription opioid overdose in the US have quadrupled over a period of 15 years, reaching almost 19,000 per year (Compton et al., 2016).

Treatment

Treatment principles are based on the bio-psychosocial model and include assessing and treating according to amount and frequency of use within the context of the patients' social, cultural and psychological lives. Accordingly, guidelines specify that the management of withdrawal symptoms is not a treatment on its own, but often the first step in many forms of longer-term treatments. There is also an emphasis on reducing risky substance consuming behaviours (e.g., sharing needles). These are addressed by services in combination with pharmacologic management in the form of prescription drugs tapering which is considered the main and most helpful form of treatment (Department of Health and Social Care, 2017).

Two opioid drugs are primarily used as substitute treatments in OUD: Methadone- a full μ opioid agonist, and buprenorphine, a partial μ opioid agonist. Buprenorphine does not stimulate μ opioid agonists to the same degree as full agonists (such as methadone) and is therefore less likely to cause respiratory depression or euphoria (Fudala et. al., 2003). These are used to treat people with OUD as they reduce withdrawal as well as craving symptoms (Connock et.al., 2007), which reduces the likelihood of increasing intake for the purpose of alleviating withdrawal symptoms. The evidence suggests that people are less likely to relapse when prevented from experiencing uncomfortable feelings (Joseph et al., 2000); and patients who use methadone or buprenorphine as a replacement thus experience less withdrawal and craving symptoms during the treatment period.

In addition, Naloxone is a specific opioid antagonist that targets μ, δ and ƙ opioid receptors, and is therefore used to treat opioid overdose, rapidly reversing this effect (Clark et al., 2014).

Though current medications have proven to reduce withdrawal and craving symptoms, relapse and remission are still a common risk among opioid users, heightened by increased tolerance to opioids and subsequent neurobiological changes in the brain.

Benzodiazepines

During the 1970s and early 1980s, benzodiazepines (BZD) were the most frequently prescribed psychotropic drugs in the world (Coach, 1990). They are prescribed for their sedative, muscle relaxant, anticonvulsant, and anxiolytic properties. They are therefore most often prescribed for anxiety or insomnia, but also other mental health difficulties such as: depression, obsessive-compulsive disorder and post-traumatic stress disorder. In addition, they are also prescribed to treat seizures and withdrawal symptoms from other drugs, as well as for sedation prior to medical procedures (Olkkola & Ahonen, 2008; Page et al., 2002).

Mechanism of effect

BZDs can affect nearly every aspect of brain function, as they have an impact on multiple sites: the spinal cord, cerebellum, brain stem, cerebral cortex and limbic system (Ford & Law, 2014; Lader, 2011; Rudolph et al., 1999).

The natural inhibitory neurotransmitter gamma-amino butyric acid (GABA) acts to reduce the excitability of neurons in these regions, leading to a feeling of relaxation in the brain (Kerr & Ong, 1995). By enhancing the release of GABA via BZD receptors, BZDs cause a feeling of mental and physical relaxation (Carter et al., 2010). Additional effects include mild physical sedation, unsteadiness and disorientation which can be long-lasting (Baldwin et al., 2013; Griffin et al., 2013).

Furthermore, since the brain-stem controls vital functions such as heartbeat regulation, breathing and blood pressure (Nicholls & Paton, 2009), these are also significantly slowed down as result of the use of BZDs (Bandelow et al., 2017), and this is the mechanism underlying the sense of relief when struggling with first signs of panic (Stahl, 2002).

Extent of use

Despite the recommendations that BZDs should be prescribed for a maximal period of four weeks, long term prescribing remains common, with 300,000 long term users in the UK (Davies et al., 2017). In recent years, there have been numerous media reports in the UK of teen Xanax (alprazolam) misuse, with some stating children as young as 11 are taking this BZDs for anxiety (Reuben et al., 2015). This is a particularly worrying problem because alprazolam is the most potent of all prescribed BZDs causing amnesia, sedation and falls (Curran, 1991).

Prescribed use of benzodiazepines

Research has shown that non-psychiatrist doctors tend to prescribe BZDs more frequently than psychiatrists (Simon et al., 2001; Young et al., 2001). For example, one study

conducted in the US found that 55% of BZD prescriptions were given by family care physicians and only 16% by psychiatrists (Cascade & Kalali, 2008).

A study looking at the prevalence of prescriptions and attitudes of prescribers in the UK found that 18.7% of in-patient BZD prescriptions were for psychiatric reasons. Anxiety accounted for 50% of the prescriptions, aggression for 25.6% and agitation for 14.4% (Haw et al., 2007). The study also found that prescribers were more concerned with BZD's abuse and diversion potential than with their inherent addictive nature. Interestingly, most consultants believed the UK committee on the safety of medicine (CSM) guidance was too restrictive and their clinical practice indicates a need for modification in this sense.

Illicit use of benzodiazepines

Abuse of BZDs is typically defined as recreational, non-medical use for the purpose of becoming intoxicated or "high" (Griffiths & Johnson, 2005). Yet, there is an on-going debate concerning whether the abuse of BZDs is mainly recreational or medically adjunctive in its nature, i.e., associated with the therapeutic utility of the drug (Rosenbaum, 2005).

Numerous studies looking at the characteristics of BZD misuse have found that the potential for misuse increases with age, dosage and polydrug use, particularly alcohol (Maxwell et al., 2010). Kapil et al. (2014) discovered that 55.2% (n=64) of benzodiazepine using respondents were prescribed the drug and 39.7% (n=46) obtained them through friends and/or family. Online purchases accounted for 26.7% (n=31) and 19.8% (n=23) were purchased from the streets through dealers. Lastly, 11.2% (n=13) of respondents sourced them from outside the UK.

In the US, it was found that BZDs are the most commonly sold controlled prescription drugs on the internet, with 89% of the purchases obtained illicitly without a prescription (National Centre of Addiction and Substance Abuse at Columbia University, 2006). Interestingly, this study revealed that 70% of sites which require a prescription permitted the

prescription to be faxed, thus allowing for the possibility of forging, modifying or sending the same prescription to multiple sites.

Motivations for illicit use of benzodiazepines

Boyd et al. (2006) identified two main motivations for non-prescribed BZD use: self-medication and recreational use. Self-medication was for purposes of sleep and anxiety (see Andersson et al., 2017; Pederson & Lavik, 1991; Rigg & Ibañez, 2010). Recreational use was mainly to "get high" (Andersson et al., 2017; Kapil et al., 2014; Mateu-Gelabert et al., 2017; Rigg & Ibañez, 2010; Vogel et al., 2013; Weaver, 2015), and to "come down" from stimulant substances (Beharry & Gibbons, 2016; Kapil et al., 2014; Mateu-Gelabert et al., 2017; Rigg & Ibañez, 2010) especially after excessive cocaine use (Bardhi et al., 2007; Motto-Ochoa et al., 2017).

In addition, adverse or traumatic childhood experiences are known to be associated with an increased risk for SUD in general (Douglas et al., 2010, Dube et al., 2002, Dube et al., 2003, Pilowsky et al., 2009, Wu et al., 2010). However, they were also found to be especially associated with increased prescription of psychotropic drugs, and particularly anxiolytic ones like BZDs (Anda et al., 2007). These findings suggest that illicit BZD use may sometimes occur as self-medication for distressful psychological states related to early childhood traumatic experiences.

Adverse effects

Research has identified many potential adversities as result of misuse of BZDs and identified them to have an addictive potential (Covi et al., 1973; De las Cuevas et al., 2003; Hollister et al., 1961).

On a cognitive-physical level, long-term benzodiazepine use has proven to have significant and detrimental effects on processing speed, problem solving abilities, verbal memory skills, psychomotor skills and attention span (Barker et al., 2004; Block & Berchou,

1984;). These were also found to be related to increased risk of accidental injuries (Oster et al., 1987), e.g. falls, impaired driving (Bramness et al., 2002) and impaired everyday tasks (Kozená et al., 1995; Verster et al., 2002). It can also lead to serious accidents (Friedman, 2006; Ravera et al., 2011). BZDs have also been known to cause significant memory loss and impairments (Bond et al., 1991; Ford & Law, 2014; Griffin et al., 2013; Curran, 1991) which may remain in the long-term (Curran, 1986; Curran et al., 1994).

On an emotional level, prolonged BZD use and increased dosage were found to cause paradoxical effects (contradictory in their nature to the original intended effect), leading to feelings of anxiety and hyperactivity (Gardner & Cowdry, 1985; O'Sullivan et al., 1994). They were also found to cause feeling of emptiness, dysphoria, agitation and even rage when used long term (Ashton, 2002; Hollister et al., 1961; Lader, 2014; Paton, 2002). Furthermore, these were sometimes found to lead to erratic and violent behaviour (Ashton, 2002). In addition, a recent study looking at the recreational BZD use among students in the UK found that BZDs often caused users to feel 'invincible', leading to irrational and erratic behaviour on their part (Bloomfield, 2019).

Withdrawal

Symptoms of BZD withdrawal include autonomic instability, increased anxiety, fear, dread, agitation, confusion and panic attack. The key signs of withdrawal are perceptual sensitivities, especially to light and sound (Baldwin et.al., 1993) and abrupt BZD withdrawal can result in fatal refractory seizures (Durbin, 1994).

Interestingly, BZD withdrawal often has a paradoxical effect characterized by aggressive rebound symptoms which are contradictory in their nature to the initial therapeutic effects. Long-term users therefore may suffer with symptoms like rebound anxiety, depression, psychotic tendencies and agitation, in addition to loss of appetite, distorted perceptions of reality, abnormal body sensations and even seizures (Hollister et al., 1961; Pétursson, 1994).

For example, it was found that upon halting opioid type insomnia medication, the sleeping disorder can return with increased severity, causing a distorted and shorter sleep as well as increased difficulty falling asleep (Lader, 2012).

Overdose

Deaths involving BZDs have risen by 90% over a decade, from 207 deaths in 2007 to 391 in 2017 (Office for National Statistics, 2019). As mentioned, BZDs have anxiolytic, sedative, hypnotic, muscle relaxant, anticonvulsant and amnesic properties, and are therefore known to be effective during alcohol withdrawal (Amato et al., 2010; Ford & Law 2014;). However, evidence suggest that BZDs decrease cerebral blood flow and brain oxygen consumption, and can inhibit respiration (Forster et al., 1982; Olkkola & Ahonen, 2008). Therefore, increased dosage intake as well as in conjunction with other central nervous system (CNS) depressant drugs like opioids, alcohol, ketamine and cannabis can be fatal (Schmitz, 2016;) as the individual's heart rate may be suppressed to the extent that it can stop completely.

Treatment

To prevent symptoms of benzodiazepine withdrawal, the UK guidelines suggest continuation of prescription with the dose gradually reduced to zero (Department of Health and Social Care, 2017). It instructs that doses of more than 30mg diazepam equivalent per day must only be prescribed very rarely and only for the purpose of detoxification. This should only occur where there is decisive evidence of BZD dependence. This includes incredibly careful consideration of the patient's history, clinical records, observed symptoms of withdrawal and current as well as historical, drug testing. The aim is prescribing a reducing script for a limited agreed upon period. In practice, the particular BZD used is changed to a low potency BZD first in equivalent dosage and then reduced over time.

Co-misuse of benzodiazepines and opioids

BZDs and opioids are two of the most frequently abused psychoactive drug classes in the world (Grytten, 1998; Joranson et al., 2000). Furthermore, there is consistent evidence from the past four decades of the misuse of BZDs among patients treated for OUD while maintained on opioid agonists such as methadone and buprenorphine (Barnas et al., 1992, Brands et al., 2008; Kleber & Gold, 1978; Lavie et al., 2009).

Prescribed opioids and BZDs are thought to be safer than street drugs because they are manufactured to a high standard and do not contain adulterants (Friedman, 2006; Fleary et al., 2013; Kapil et al., 2014) and are therefore more socially accepted (Bettinardi-Angres et al., 2012). Accordingly, it was found that users often do not view their misuse of prescription drugs as a problem, since they are often able to maintain daily function psychosocially as well as occupationally (Chandler et al., 2014). It was also found that individuals who believe prescription drugs pose little potential harm are approximately 10 times more likely to misuse (Arria et al., 2008).

Extent of use

Research has identified the prevalence of BZD use among methadone-maintained patients to be consistent for decades and range between 51% and 70% of patients (Gelkopf et al., 1999; Hartog and Tusel, 1987; San et al., 1993; Stitzer et al., 1981). Similar rates were also reported for buprenorphine-maintained patients (Lavie et al., 2009; Nielsen et al., 2007; Thirion et al., 2002) as well as among active heroin users (not in treatment) (Darke et al., 1992, 1995).

A more recent survey conducted among methadone-maintained patients found that 47% of the respondents had a history of BZD use and 39.8% had used BZDs without a prescription. Half of the BZD users (54%) started using BZDs after entering the methadone program, and 61% of previous BZD users reported increased or resumed use after entering the MMT (Bouvier et. al., 2018). Furthermore, it was found that 40% of service users seeking inpatient

opioid detoxification had used BZDs in the month before (Stein et al., 2016), and 70% of opioid users receiving medication-assisted treatment also used BZDs (Nielsen et al., 2007). Furthermore, it was found that between 18% and 54% of new admissions onto the methadone programs presented with co-dependence on BZDs (Gelkopf et al., 1999; Rooney et al., 1999; Specka et al., 2011).

Darke and colleagues (1993) reported that 26.6% of methadone patients admitted to daily BZD use, and in another study, 41% of heroin users reported having used BZDs weekly (or more) within recent months (Ross et al., 1996). More recent studies found that one third of heroin users had obtained a prescription for a BZD drug in the preceding month (Darke et al., 2003).

These findings suggest consistent and significant levels of BZD dependence among opioid users as well as in treatment of OUD. The effects of different maintenance agonists on the prevalence of BZD use were investigated but remain unclear. There is some evidence to suggest there is no difference in BZD use between methadone and buprenorphine-maintenance (Mattick et al., 2004).

Motivation for co-use

Park and colleagues (2015) found that clinicians tend to prescribe both opioids and BZDs when pain and anxiety co-occur, despite the increased risk of overdose.

Regarding illicit use, several studies were conducted aiming to identify the reasons behind the combined abuse of these two drugs. It was found, for example, that 72% of methadone-maintained patients who regularly co-used diazepam reported that it was used to enhance the effects of their daily methadone dose (Stitzer et al., 1981). Similarly, Strang (1984) found that the addition of intravenous flurazepam increased and prolonged the intensity and duration of the heroin effect. Stein and colleagues (2016) also found that among methadone-maintained patients with a history of BZD use, 45.5% reported that they were used to: “get

high", "have a good time" or "produce an intense, exciting experience" as well as decrease symptoms of opioid withdrawal.

Lintzeris and colleagues (2007) found that co-administration of diazepam (40 mg) with methadone or buprenorphine was linked with higher reported "strength of drug effect" and "sedation" in comparison to each of the opiate's agonists independently. Interestingly, these findings were consistent with administration of lower doses of diazepam (10, 20 mg; Lintzeris et al., 2006). Spiga and colleagues (2001) found that pre-treatment with diazepam produced dose-related increases in subjective ratings of drug "liking," "high," "strength of drug effect," and "good effects," as well as increased self-administration of methadone by methadone-maintained participants.

There is also evidence to suggest that non-prescription BZDs use may also occur as self-medication of anxiety symptoms and insomnia among people with OUD and to alleviates distress (Gelkopf et. al., 1999; Lavie et al., 2009; Posternak & Mueller, 2001; Vogel et al., 2013). It was found for example that 87% of BZDs users who kept using throughout a year of MMT, used them as self-medication for emotional problems (Bleich et al., 1999; Gelkopf et al., 1999), rather than recreationally. This finding along with the elevated levels of psychological distress and psychopathology found in this sub-population of users supports a self-medication hypothesis (Khantzian, 2003), according to which use of BZDs in addition to opioids is a compensatory means to self sooth distressing psychological states.

Characteristics of co-users

Personal preference

Research has found that opioid-dependent populations have a preference for a particular BZD drug. A preference for diazepam seems common (Du pont, 1988; Iguchi et al., 1993), as well as for midazolam (Bruce et al., 2008) and alprazolam (Fernández-Sobrino et al., 2009).

The most frequently overall sought as well as prescribed BZD was found to be oxazepam, followed by diazepam (Bramness & Kroner, 2007).

Demographics

A recent study (Bouvier et. al., 2018) found that compared to the 75 participants who did not regularly use BZDs while methadone maintained, participants who reported regular BZD use were more likely to be white (66.3% vs. 58.0%, p = 0.03) (see, e.g., Cropsey et al., 2015, Tucker et al., 2016), have a history of incarceration (52.8% vs. 37.3%, p = 0.04; also found in Tucker et al., 2016), and prior diagnoses of psychiatric disorders (bipolar: 29.6% vs. 16.0%, p = 0.04; anxiety: 56.8 vs. 36.0%, p = 0.01; also found in Chen et al., 2011, Lavie et al., 2009; McHugh et al., 2017; Vogel et al., 2013). This study also found that among a sample of non-medical opioids users, 86% reported lifetime BZD use, with age at first BZD non-medical use ranging between 9 to 28 years. Additional studies concluded that for those who misuse opioids, benzodiazepine co-use was also associated with being female (Cropsey et al., 2015, Stein et al., 2017a) and older age (Stein et al., 2017b).

Life events

As mentioned previously, prolonged use of BZDs is also associated with childhood trauma in opioid-maintained patients. A recent study found that among patients prescribed opioids or treated for opioid dependency, BZD use was prevalent (61%) as were reported experiences of childhood trauma (67%). Participants reported at least one trauma of moderate-to-severe level. In addition, the Childhood Trauma Questionnaire (CTQ)-subcategories of "emotional abuse", "emotional neglect" and "physical neglect" were significantly associated with prolonged BZD use among this population (Vogel et. al., 2011).

Drug use behaviours

It was found that BZDs users tend to report a longer history of opioid use and prior opioid detoxifications as well as increased risky substance use behaviour such as: higher doses

of opioids used; higher frequency of injected drug use, needle sharing, co-occurring use of alcohol and cocaine; and greater criminal activity (Darke et al., 2010; Rooney et al., 1999; Ross & Darke, 2000).

There is also evidence that compared to individuals who only abuse opioids, BZD and opioid users not only have been using opioids for a significantly longer period and used higher doses of opioids but are also more likely to abuse other psychotropic drugs together with these drugs (Meiler et al., 2005; Rooney et al., 1999; Ross et al., 1996, 2000).

For example, Meiler et al. (2005) reported that among methadone-maintained patients, regular BZD users tended to abuse alcohol more and received higher daily methadone doses. Similarly, it was found that heroin users with a diagnosis of BZD dependence were more likely to have had a diagnosis of alcohol dependence (83% vs. 60%) and cocaine dependence (23% vs. 4%), in comparison to heroin users who did not present with BZD dependence (Ross and Darke, 2000).

Lastly, BZD use among methadone maintained patients was also found to be predictive of poorer treatment outcomes (e.g., withdrawal, health, legal problems, alcohol misuse) (Brands et al., 2008; Eiroa-Orosa et al., 2010), HIV infection (Ickowicz et al., 2015), and hepatitis C virus infection (Bach et al., 2016).

Perception of adverse effects of BDZs among opioid dependent individuals

It was found that people presenting with OUD tend to underestimate the risk of opioid induced overdose (Frank et al., 2015; Wilder et al., 2016); and opioids and BZDs co-dependant users display an optimistic bias and further underestimate the risk of overdosing (Rowe et al., 2016).

A recent study examining the beliefs about BZD use among opioid dependant patients (Stein, et. al., 2017a) found that they had an overall accurate perception of BZD adverse effects. They were nearly unanimously conscious of the addictive nature of BZDs, and acknowledged

their potential to muddle one's thinking, cause fatigue as well as driving accidents, contribute to the overdose risk and cause aversive withdrawal symptoms. However, they were less likely to believe that BZD use was correlated with worsening depressive symptoms and poorer treatment outcomes, in comparison to non-BZD opioids users.

Risk and adverse effects

In addition to the potential for worsening various drug-related harms, opioid and BZD co-abuse is further complicated by the possibility of co-dependence and simultaneous withdrawal (Puntillo et al., 1997).

Increased risky substance use behaviours

BDZs in some cases have the potential to cause acute disinhibiting effects (Van der Bijl, 1991) which can lead to partaking in increased risky behaviours. As mentioned, opioid users who co-use BZDs were found to display behaviours associated with increased risk of contracting human immunodeficiency virus (HIV) and hepatitis C (HCV). These include more frequent injections and needle sharing as well as sharing with more people (Breen et al., 2004; Darke et al., 1992, 1995; Forsyth et al., 1993; Kintz et al., 2001; Klee et al., 1990). These effects are hypothesised to be mediated by several drug mechanism factors described earlier, including: (1) reduced inhibition of impulse control which leads to more chaotic drug use and behaviours; (2) episodic and working memory loss, and (3) for some individuals, paradoxical effects of BZDs discussed earlier.

Other forms of risky behaviours have been less researched. In clinical practice, there is anecdotal evidence that methadone-maintained service users will take a BZD before going shop lifting to mask their physical signs of anxiety; one man referring to his Valium as his personal ‘Harry Potter invisibility cloak’ (H V Curran, pers. comm).

Overdose and death

Furthermore, BZDs were consistently found in the bodily fluids of 50–80% of heroin-related deaths (Grass et al., 2003; Oliver & Keen, 2003; Stenhouse & Grieve, 2003; Ward & Barry, 2001); and similarly, opioids were found to be involved in an estimated 75% of overdose deaths involving BZDs (Jones & McAninch, 2015).

One recent study conducted among opioids users found that those co-using BZDs were at an increased risk for overdose (Curtin & Heritier, 2017), and another study found an increase in BZDs involvement in opioid overdoses over the last two decades (Jones & McAninch, 2015). Between 2004 and 2011, the rate of deaths as result of overdose involving both BZDs and opioids increased from 11.0 to 34.2 per 100,000. Another study found that nearly one-third of opioid related fatalities were correlated with concurrent BZD use (Chen et al., 2014).

In the US, between the years 1996 and 2013, deaths as result of opioid overdose involving BZDs increased at a faster pace than the number of people filling BZDs prescriptions as well as the dosages filled (Bachhuber et al., 2016).

Overdose and death in treatment

There is consistent evidence showing that BZDs use among opioid agonist-maintained clients is associated with drug-related deaths in addition to poorer treatment outcomes, such as worsening psychosocial functioning, ongoing substance misuse and psychiatric as well as somatic comorbidities (Bleich et al., 1999; Ghitza et al., 2008; Di Marzo et al., 2009; McCowan et al., 2009; Peles et al., 2009; Schreiber et al., 2008; Wedekind et al., 2010).

Concomitant use of BZDs and opioids was found to be associated with the occurrence of both fatal as well as non-fatal opioid overdoses (Darke et al., 2000; Schmidt-Kittler et al., 2001); and BZD use was found to be independently associated with non-fatal overdose among injection drug users (Kerr et al., 2007). Interestingly, Bouvier and colleagues (2018) found that although the association was only marginally significant, users who were prescribed their

BZDs were at higher risk of accidental overdose in comparison with illicit users (41.9% vs. 24.4%, p = 0.06). Furthermore, it was found that methadone-maintained patients who are co-dependant on BZDs had an eightfold increased risk of death compared with those who were not co-dependent on BDZs (Caplehorn, 1996).

Moreover, a study looking at Emergency Department (ED) visits during buprenorphine treatment revealed twice as many ED visits among those with a BZDs prescription as those without ($p < 0.001$); BZD abuse history however had no effect (Kaufmann, Alexander, Rutkow & Mojtabai, 2017). Another study found that the odds of an accidental injury-related ED visit during MMT were greater among those with a BZD prescription, with an enhanced effect among females (Schuman-Olivier et.al., 2013). This study also found a relative risk ratio of 3.7 of BZD-related medical events among buprenorphine-maintained patients. Interestingly, a study conducted in 1990 by Oster et al., found the ratio to be 1.15, which suggests an increase of over twice within two decades in the likelihood of an accidental injury-related ED visit during opioid treatment to also be related to BZD use.

Treatment

In a similar way to treating each drug dependence alone, the primary focus of treatment is pharmacological. Traditional therapeutic approaches to the treatment of BZD dependence that have been utilized with opioid co-users include tapered detoxification with barbiturates (although very risky when mixed with alcohol), long-acting BZDs, and rarely antiepileptics (Bleich, 2002). The most used method however is administration of a long-acting BZD at first, followed by a switch to a less potent long-acting BZD, and then gradual tapering (Curran & Clark, 2003).

The guidelines for treating drug dependence, in compliance with the bio-psychosocial approach, suggests careful assessment of the patient's needs and adjustment of treatment (Department of Health and Social Care, 2017). This includes historical factors, consideration

of dosage used, ways of obtaining the drug, social and environmental factors contributing to and facilitating use and the function of drug use for each patient.

For example, if the patient is also opioid dependant and receiving a long-term methadone prescription, then methadone dose should not be changed throughout the BZD reduction period. Simultaneous detoxification from both is to be avoided, especially in a community setting. Furthermore, in these cases the initial focus should be on stabilisation of physical and psychological health, particularly for those with a primary BZD dependence, as well as in presence of a severe comorbidity (such as with depression and anxiety),

There is no specific protocol for the psychological treatment of opioids and BZDs co-dependant patients. However, guidelines instruct that the psychological focus while still working to achieve pharmacological stabilization should be around psychoeducation and group work, to develop awareness and insight into the reasons for use and the cycle of dependence (Department of Health and Social Care, 2017). Later on, and once stabilisation and engagement are established, complimenting psychological interventions as described above, such as MI, CI and CBT are recommended. Importantly, as clients progress through treatment they will take part in role play or discussions of how to deal with risky situations which might trigger a relapse to renewed drug use. They should therefore be encouraged to develop and practice skills for dealing with risky situations. In addition, and according to the current bio-psychosocial model, other aspects of the person's life should be addressed as well, such as their housing situation, social support network etc.

Conclusions

Opioids and BZDs are two drugs widely used to treat patients in physical and/or mental health settings all over the world, and are two of the most commonly misused drugs, frequently co-misused as well. The co-misuse of BZDs and opioids has been studied for decades, suggesting this subpopulation of substance misuse service users present with increased risk and

complexity. This has repeatedly raised issues around the best way to support and care for these patients, and there remains a lack of evidence base to suggest clear guidelines regarding how these added difficulties of combined use should be managed in services. Although several studies were conducted to explore the patterns and reasons for co-misuse, as well as treatment paths and added risks, no known study has so far explored the conceptualisations and experiences of clinicians who are treating individuals who co-misuse opioids and BDZs.

This study therefore aims to explore this. Specifically, the ways in which clinicians view and address the additional complexity of these clients and their opinions on how to improve treatment and care. It will explore their thought process around adjusting treatment and the way in which this population is experienced by them. This is done qualitatively through interviews with clinicians working in specialist substance misuse services in London.

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Part 2: Empirical study

Clinicians' experiences of working with service users presenting with co-dependency on opioids and benzodiazepines in substance misuse services

Abstract

Background: Current literature points to the added complexity characterising substance misuse service users presenting with co-dependency on opioids and benzodiazepines. However, there is no previous research focusing on clinicians working with these clients.

Aim: This study aims to explore the perspectives and conceptualisations of clinicians working with individuals who are co-dependent of opioids and benzodiazepines to better inform clinical management.

Method: Eighteen semi-structured interviews with clinicians experienced with working with this population in substance misuse services were conducted. Their responses were analysed using a Thematic Analysis.

Results: Thirteen main themes and four sub-themes were identified and were grouped into two main domains and five sub-domains. Participants described their understanding of these patients and attempted to empathise with what they perceive as a unique attachment to benzodiazepines among this group (main domain 1). Secondly, they identify them as more difficult to work with than other clients and harder to make progress with (main domain 2). They also express a sense of frustration as a result of the combination of these two aspects of their experience.

Conclusions: This study emphasises the importance of psychoeducation and ongoing psychological support for these patients as well as for their clinicians, and their sense that a more rigid treatment plan is needed in these cases.

Introduction

The aim of this study is to explore clinicians' experiences and conceptualisation of working with service users who are co-dependant on opioids and benzodiazepines (BZD) in substance misuse services. In practice, this sub-population of service users is normally treated in services for opioid use disorder (OUD) in the methadone maintenance treatment program (MMT); Therefore, this study will focus on the experiences of clinicians working with MMT patients presenting with co-dependency on BZD.

Prevalence

Benzodiazepines are commonly misused in conjunction with other drugs, most frequently opioids (Crane & Nemanski, 2004; Substance Abuse and Mental Health Services Administration, 2011). Recent investigation found that 10% of opiate dependent clients in treatment in the UK over 2017-2018 also presented with BZD dependence- the 3rd highest co-dependence (with opioids) after alcohol and cannabis, respectively (National Drug Treatment Monitoring System, 2018).

Characteristics of methadone-BZD co-users

Presentation and risk

Research has repeatedly identified BZDs users on MMT as more complex and at higher risk than non-BZD users for a series of conditions. These co-dependent users are likely to present with a more severe history of drug use (Chutuape et al., 1997; Darke et al., 1993), higher levels of psychological distress (Brands et al., 2008; Darke, 1994), a higher prevalence of antisocial personality disorder (Chutuape et al., 1997), poorer health and social functioning as well as a higher incidence of hepatitis C (Darke et al., 1994; van den Hoek et al, 1990). BZD users were also previously found to engage in more HIV/HCV risk-taking behaviours than non-users (Darke, 1994) and this was not due to concurrent heroin abuse.

A research study following MMT patients over a year of treatment (Bleich, et. al, 1999), found that BZD using patients were more frequently single, jobless, more often served time in prison and more often had one parent with a history of substance addiction or mental illness compared to non-BZD abusing MMT patients. This subgroup of MMT patients reported an earlier onset of heroin and cocaine use, but not earlier onset of BZD or cannabis use. Furthermore, BZD use during treatment was correlated with continued heroin, cannabis and cocaine abuse following one year in treatment. These patients also used higher methadone dosages in comparison with non-BZD users and were found to have significantly more mental health difficulties, especially depression, obsessive compulsive disorder, paranoia, psychoticism, phobias and interpersonal hostility as well as higher psychological distress.

Increased mortality

A systematic review found MMT participants with co-dependency on BZD to have higher mortality rates in general compared to non-BZD using opioids users (Charlson et al., 2009; Webster, 2011), and there is further evidence suggesting this subgroup has up to an eight-fold higher mortality risk compared to other MMT patients (Caplehorn et al., 1996). Accordingly, BZD poisoning was found to be present among 17% of the opiate deaths in U.S. (Warner et al., 2009) and BZD prescriptions were even found to be associated with non-overdose opioids related deaths (Abrahamsson et al., 2017).

Motivation for use of BZD when treated with methadone

Drugs become addictive because they have the ability to alleviate psychological distress. Accordingly, BZD misuse is often considered an attempt to self-medicate and alleviate distress. For example, it was found that 87% of BZDs users in treatment for opioid dependance reported using them as self-medication for emotional problems rather than recreationally (Bleich et al., 1999).

In addition, there is an evidence base suggesting BZDs are also used when treating for opioid dependency for the purpose of intensifying and prolonging the effect of the opioid substitute (Stitzer et.al., 1981; Strang, 1984); as well as "getting high" and alleviating symptoms of opioid withdrawal (Stein et al., 2016).

Treatment of BZD abuse in the context of MMT

Retention in treatment and mortality rates:

Current BZD treatment was recently found to be an independent predictor of non-response to MMT (Alcaraz et. al., 2018). In addition, a study investigating the patients' perspective of reasons why they are getting stuck in MMT (Moran et al., 2018) found not only increased adverse childhood experiences and early exposure to illicit drug use, but also increased rates of mental illness and concurrent benzodiazepine use disorder. Use of BZDs among this group was also found to be associated with lower rates of opioids abstinence (Kamal et al., 2007).

In addition, a 20-year latitudinal study found that BZD abuse upon entry to MMT predicted lower retention in treatment as well as shorter actual survival (Peles et al., 2014). Interestingly, this study concluded that high and low rates of BZD abuse may also be attributed to staff tolerance of this abuse; thus, recommended a strict attitude by staff in order to reduce these patients' harm.

Complications in treatment of co-dependent patients

It was found that patients receiving buprenorphine frequently requested quite early in treatment a BZD prescription for the purpose of alleviating anxiety and insomnia symptoms (Lintzeris & Nielsen, 2010). In this context, it was argued that BZDs hinder the development of psychological coping strategies and therefore prescribing them should be avoided in these settings (Otto et al., 2005; Soyka, 2010). It was also found that they can sabotage the

psychological process of healing in addition to the known risk of misuse (Brunette et al., 2003, Chen et al., 2011) and increase the risk of relapse (Brands et al., 2008).

In contrast, there is evidence that use of long-acting BZDs can be useful as a maintenance strategy for individuals with OUD in opioid agonist maintenance treatments (Weizman et al., 2003); especially with people who have co-occurring severe anxiety disorders (Bleich et al., 2002; Liebrenz et al., 2010).

Clinicians' attitudes toward users

There is no previous research looking at mental health clinicians' attitudes towards co-users of BZD and opioids. However, a study (Merrill et al., 2002) looking at the relationship between illicit opioid users and the medical staff involved in their care in an A&E, from both perspectives, found three main themes characterising these interactions from clinicians' perspective. First, it revealed mistrust towards these patients and a feeling that it is difficult to determine whether their displayed need for opioids was medically necessary for physical pain alleviation or motivated by a pre-existing addiction. Secondly, there was an expressed need for a standard approach for assessing and treating these patients, especially as their reports were perceived as unreliable. Lastly, they expressed discomfort and uncertainty in their approach to treating these patients.

Other studies exploring clinicians' attitudes towards their complex and emotionally demanding patients suffering from other clinical problems can be drawn upon due to the similarity of high emotional intensity they can provoke withing their clinicians. In one study looking at nurses' attitudes towards clients who deliberately self-harm, complex and multidimensional approaches were found (McAllister et al., 2002). Although this is a different clinical problem, self-harming patients and substance using patients can be paralleled in the sense that they trigger complex and ambivalent feelings of care professionals. That study identified three dimensions that help explain variations in nurses' attitudes towards self-

harming patients: (1) their perceived confidence in the process of assessment and referral; (2) ability to deal effectively with clients, or an empathic approach; and (3) ability to cope effectively with the systemic constraints- legal and hospital regulations that guide practice. Nurses scoring higher on these dimensions were more likely to feel positively toward their patients who self-harm and the care they provide.

Similar clinicians' reports were found in other studies looking at clinicians' attitudes towards their patients of other treatment resistant clinical problems; and these can be drawn upon due to this similarity. For example, a literature review examining clinicians' reactions to their patients with eating disorders (ED) found many to have negative reactions, mainly frustration, hopelessness, a sense of lack of competence, and worry (Thompson-Brenner et. Al., 2012). In that study, negative reactions to patients with ED were associated with patients' lack of improvement and personality pathology as well as with clinicians' stigmatizing beliefs, and inexperience.

It is therefore likely to assume that mental health staff will have similar attitudes towards BZD-opioids co-users, although additional themes are also likely to arise.

Current study

Although there is pre-existing literature about the characteristics of service users who are co-dependent on opioids and BZDs, there is no specific information about clinicians' perspectives and experiences of working with these clients. As this population is consistently described in literature as presenting with additional complexity in terms of risk, presentation and adherence to treatment, it is of interest to explore how this is experienced and managed by clinicians, their thoughts and reflections of their work.

This exploratory study therefore aims to give a broad and initial account of the experiences of clinicians and their understanding of this population and working with them. Data was collected in semi-structured interviews, and participants were asked to discuss their

experiences of working with this population and their views about what might help them as clinicians and their services to better care for BZD dependent users in MMT.

Method

Design

The study used a qualitative methodology and focused on clinicians' experiences and conceptualisations of working with opioids and BZD co-dependant service users.

Participants were clinicians who were recruited from substance misuse services in London. Thematic analysis was selected to understand the experiences of clinicians due to its ability to encode and interpret patterns across a data set, thus enabling a description of subjective experiences (Pistrang & Barker, 2010). It is also recommended for exploratory studies, such as this one, as this is the first study of its kind. Data was therefore analysed qualitatively using thematic analysis in compliance with the guide for thematic analysis in psychology by Braun & Clarke (2006).

Ethical approval

Approval was gained through University College London's Ethics Committee in October 2019 (see appendix A for approval letter).

Participants

Participants were purposively recruited from substance misuse services in London. The sample comprised 18 clinicians from various backgrounds- medical doctors in training and GPs, psychiatrists, general nurses, mental health nurses, recovery practitioners and managers. Inclusion criteria required that each had at least one year of experience working in substance misuse services and experience working directly with opioid and BZD co-dependant service users.

Those eligible were identified by staff members and approached either in team meetings or their places of work. They were provided with information on the study and asked to contact

the researcher by email if interested in participating. Upon meeting them they were given an information sheet (see appendix B) and informed consent forms (see appendix C) and were informed of their right to withdraw consent at any point. They were then interviewed and were given space to ask any question or share their thoughts before and during the last stage of the interview. They were compensated with £20 pounds for their time and efforts. No one dropped out of the study.

Table 1

Participants by role in the service

Qualification/role	**N**
Recovery practitioners	5
Mental health nurses	4
General nurses	2
Psychiatrists	2
Trainee medical doctor	1
GP	1
Managers	2
Assistant psychologist	1
Total	18

Data collection- Interviews

Interviews took place during mid-late 2019 to early 2020 in the community/workplaces of the clinicians and lasted between twenty-five and fifty minutes. Semi-structured interviews were used (see appendix D for interview schedule) and included direct questions around areas of interest as well as prompting questions aimed to expand on the content participants shared. They were designed and conducted as a guided conversation (Qu & Dumay, 2011).

Interviews started with the question: "Can you please tell me about your experience of working with the subpopulations of service users who are co-dependant on opioids and benzodiazepine?" and continued with follow up questions, depending on the content of their

responses, prompting them to expand. This was aimed to encourage free association to elicit spontaneous responses and tap latent patterns of thoughts and feelings around this topic (Bollas, 2002). Participants were asked follow-up questions to prompt them to expand upon their answers.

Questions were designed to address key points identified in previous research as particular to this population. They were phrased in an open-ended manner to focus on the clinicians' perspectives, their thoughts and experiences with risk and detox. They were also asked about the thinking process around treating these service users. Importantly, these questions were asked to prompt participants to discuss their perspectives and feelings around these experiences, and the researcher remained aware of not adding any leading content in their prompting questions.

Participants were then asked what they would find helpful when working with this population, as a way of informing future care. Finally, they were offered an opportunity to ask any questions or add any thoughts they might have.

Figure 1

Interview questions excluding prompts

1. *Can you please tell me about your experience of working with the subpopulations of service users who are co-dependant on opioids and benzodiazepines?*
2. *Can you please tell me about your experiences with them around detox?*
3. *Can you please tell me about the thought process around treatment plan with these service users? What would be considered?*
4. *Can you please tell me about your thoughts around risk with these patients?*
5. *What would be helpful for you as a clinician working with this population?*
6. *Is there anything you would like to add/ bring up/ reflect upon/ ask?*

Interviews were digitally recorded and transcribed by the researcher and then sent to a transcription service to be amended. This was because the researcher is not a native English speaker and some of the data were unintelligible to them. Recordings, transcriptions and other confidential/participant-identifiable data were held on a password-protected USB stick.

Method of data analysis

Transcripts were explored using thematic analysis (TA; Braun & Clarke, 2006). This is a widely used 7-step method (detailed below) for analysing qualitative data and identifying recurring themes within it. This method instructs that once transcriptions are made and the researcher is familiar with the written data, they create a coding system which is based on both semantic and conceptual elements. These codes are then constructed into themes, repeatedly checked, and finally contextualized into a coherent narrative.

Other methods were considered, but this method was chosen because unlike other qualitative methodologies, it is not bound to, influenced by or aiming to create a specific theoretical framework (Braun & Clarke, 2006; King, 2004). Furthermore, TA can be used both inductively (data-driven) and deductively (theory-driven) and can capture both manifest (explicit) and latent (underlying) meanings. It was therefore chosen for this study as it allows the inductive analysis of the data, maintaining a strong link between the process of coding and analysis to the data rather than the theoretical interest of the researcher (Braun & Clarke 2006, p. 83). Moreover, and importantly, it also encompasses a deductive identification of detailed semantic patterns and accounts for complex interpretative analyses of the data when appropriate (Clarke et. al., 2013).

Since the researcher has not been able to find any previous studies which employed a qualitative approach to addressing similar questions among clinicians, nor quantitative research focusing on clinicians' experiences, this flexible method was deemed more appropriate in this initial stage of investigation.

Analysis

Coding

Interviews were first listened to by the researcher. Upon the second round of listening, interviews were transcribed by the researcher and then double-checked by a university-approved transcription service. Interviews were then read and listened to simultaneously and repeatedly to achieve total immersion in the data.

The first coding was done manually with notes taken in the margins of the text (Braun & Clarke, 2006). This was done inductively with the smallest units of meaning emerging from the data and coded semantically without adding any meaning or interpretation. These were initially kept within the original paragraph, to maintain context throughout the analysis (Bryman, 2001), and were only extracted at the more advanced stage of choosing extracts for write up.

At the second coding, the researcher used the online program NVivo which does not code but aids in organising the codes and references and creating visual aids. When coding, the researcher created a separate folder and coded data they felt might be important, but they were unsure of how to code them or that they were indeed relevant to the research question. This level of coding generated dozens of codes which were fine-tuned upon a third coding round, in which the extracts in the separate folder were recoded into the more general themes or discarded. The program also allows the identifying and coding of a relationship between two concepts, and this was done for one theme (‘frustration’) in the third coding round when refining, as the researcher repeatedly noticed this connection arising from the data.

A reliability check was performed with an independent external coder (see below) and codes were then organised into a thematic framework which was systematically reapplied to the entire data set upon a fourth coding round. The analysis was sequential, with the data appearing to hit saturation before the final interview.

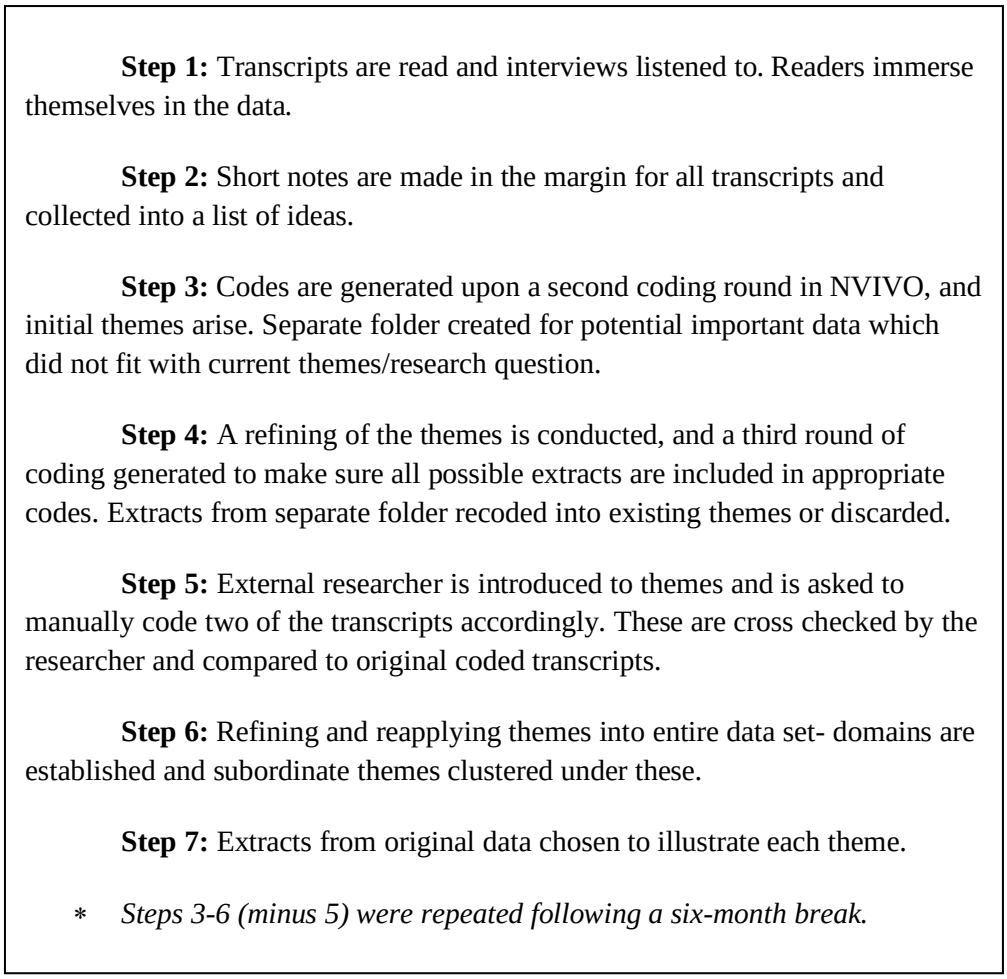
Recurring themes were then labelled as main or subordinate themes and clustered into coherent domains. This involved multiple meetings with the project's supervisors to discuss the relevance of themes to clinical practice as well as the current literature and to assure internal homogeneity (cohesiveness) and external heterogeneity (independence) of the themes (Patton, 2003). They were then rechecked against the original interviews to ensure that the original data was vivid and meaningful, and nothing was missed.

A fifth round of coding and re-grouping into main themes and domains was conducted approximately six months later, as the researcher was unable to proceed at the time due to personal reasons. This was redone as a method of both re-immersion in the data as well as a credibility check- as the codes and themes identified the first time reappeared similarly six months later. In both processes, when refining, they were grouped under three main groups (See appendix E for evolution of themes map).

Lastly, a document with a table containing themes, descriptions and examples was created. Between 3 and 6 extracts were then identified under each theme as representative of that theme and inserted into the table. The number of extracts was then reduced again when extracting from the table into the final write up to comply with word limitation guidelines.

Figure 2

Summary of data analysis



Reliability check

It is recommended that the evaluation of inter-coder reliability/agreement is made part of the development of coding schemes for qualitative data (Hruschka et al. 2004; Krippendorff 2004; Miles & Huberman 1984; Weber 1990). Accordingly, once the coding scheme was established following the third round of coding, the percentage of agreement between two coders to assess the reliability of data analysis was calculated. This was done by allowing for two randomly selected transcripts to be coded by an external coder (Barbour, 2001; Campbell et al., 2013; Hallgren, 2012; Kurasaki, 2000; Marques & McCall, 2005), a DClinPsy graduate

who undertook a thematic analysis thesis themselves. The external coder randomly selected two numbers between 1 and 18 and those were the two interviews they coded.

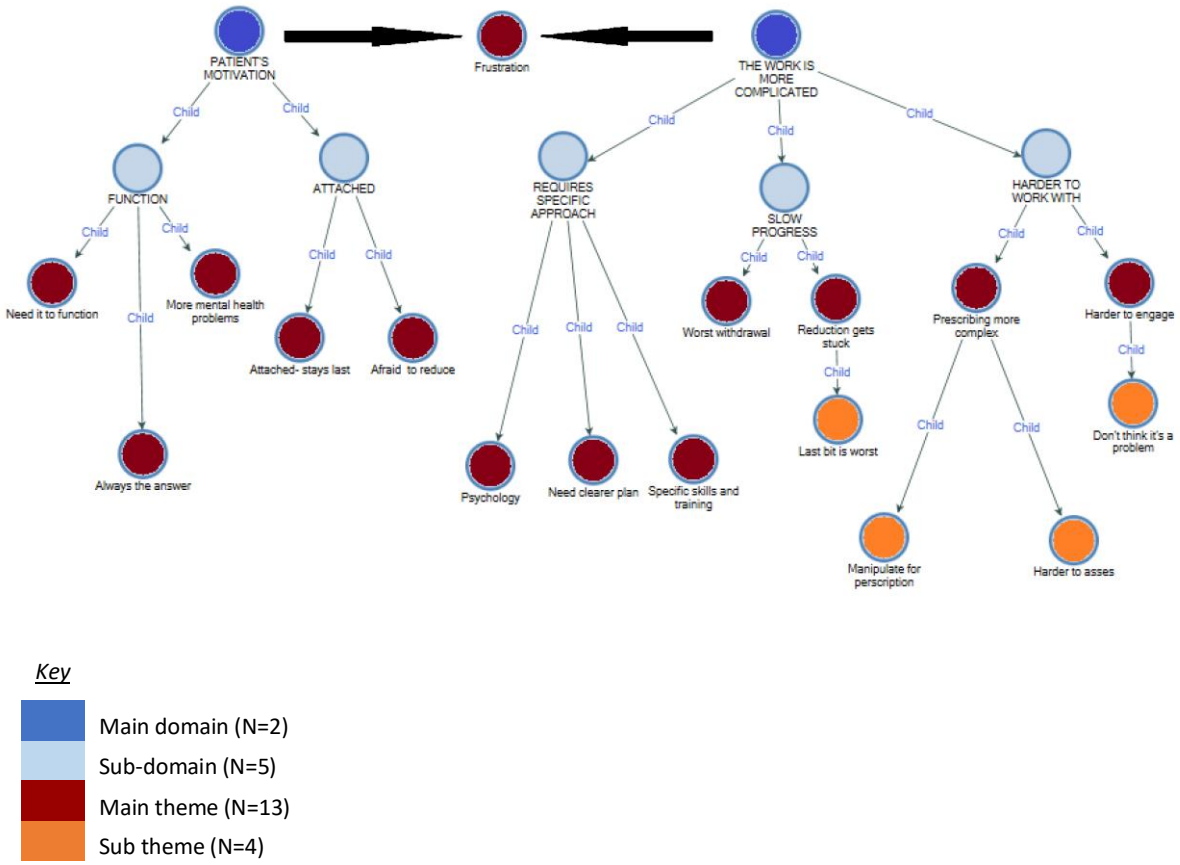
A meeting was held whereupon standardized units of data were introduced to the external coder (Campbell et al., 2013), and the developed themes were reviewed and explained to them. After the external coder coded the two transcripts, coding was compared, and level of agreement by percentage calculated using the methods described by Campbell et al. (2013). For purposes of calculation percentages of agreement, segments of text which were coded into more than one code were regarded as different and independent units (for example, if the researcher coded one segment of the data into two codes, that segment was regarded to as two different units of text and meaning). An agreement rate of 78% between the two coders for the double coded transcripts was calculated, which the literature regards to as either acceptable or high (Campbell et al., 2013).

Results

The analysis generated thirteen main themes and four sub-themes . Twelve themes were organised into 5 sub-domains, which group into two main domains (patients' motivation; the work is more complicated). The last (thirteenth) theme, frustration, remained independent, connecting the two main domains, as graphically described within a map (Figure 3; see appendix E for evolution of theme map).

Figure 3

Final theme map



The first main domain- patients' motivation, describes clinicians' attempt to understand, empathise and reflect upon the patients' own experiences and motivations and includes the sub-domains of 'attached' and 'function'. The second main domain- the work is more complicated, reflects clinicians' own perceptions and experiences of working with this population, and contains the sub-domains of 'specific approach', 'harder to work with', and 'hardest drug to come off'. The thirteenth theme, 'frustration', remains independent, as it reflects an emotional experience that is the result of clinicians' attempt to compromise between

the two main domains of experience- understanding these patients' difficulty and trying to make progress working with them.

Interestingly, although the researcher tried to avoid contradictions and allow a variety of opinions, participants generally held similar views about their experiences and how they perceived the BZD using service users in MMT and working with them.

Table 2

Frequency of themes by each participant and total number of participants endorsing each theme

	P1	**P2**	**P3**	**P4**	**P5**	**P6**	**P7**	**P8**	**P9**	**P10**	**P11**	**P12**	**P13**	**P14**	**P15**	**P16**	**P17**	**P18**	**N**
More mental health problems						x				x	x	x							4
Need it for function	x	x								x		x	x	x	x	x		x	9
Always the answer				x				x						x					3
Afraid to reduce	x	x		x	x	x	x	x	x	x	x	x	x	x		x	x	x	16
Attached- stay last	x				x	x		x	x			x	x	x			x		9
Worst withdrawal		x				x		x	x	x	x		x	x					8
Reduction gets stuck	x	x		x		x			x	x	x	x		x		x	x		11
Last bit is worst											x	x		x			x		4
Prescribing more complex		x	x	x	x	x			x	x			x	x	x	x	x	x	13
Harder to assess	x		x	x	x	x	x	x	x	x	x	x	x			x		x	14
Manipulate for prescription				x	x			x	x		x	x	x		x				8
Harder to engage	x		x		x	x	x	x	x	x	x	x	x	x		x	x	x	15
Do not think it is a problem	x	x			x	x	x	x	x		x		x						4
Specific skills and training	x	x			x	x	x	x	x	x	x	x		x			x		12
Need a clearer plan		x	x	x		x	x	x	x	x						x	x	x	11
Psychology	x		x		x	x	x	x	x		x	x	x			x		x	12
Frustration		x		x	x	x	x	x	x	x			x	x		x			11

The following is an exploration of these themes, organised by domains. Direct quotes from participants are used to support the findings by grounding them in participants' accounts and provide resonance with readers' understandings (Spencer et al., 2003).

Patient's motivations (main domain 1)-

This domain describes the clinicians' perceptions of the patients' states of mind, their understanding of patients' motivations and behaviours and their attempt to empathise with them.

[Different] Function (sub domain 1)-

This domain groups together clinicians' perceptions of the function of the drug for the patients.

More mental health problem (main theme 1)-

Participants expressed a feeling that co-dependency on these two specific drugs suggests a deeper psychological complexity:

> *"So, when somebody has to take opiates and benzos at the same time it suggests that emotionally they're in quite a challenging position… I think they have more trauma to deal with, more emotional pain to deal with, more psychological interference" (P11).*

Others noted that it is specifically the BZDs that suggest the added complexity:

> *"I think there's probably a higher proportion of maybe anxiety and maybe paranoia and psychosis in the people who are also using benzos… paranoia or worries about people around them, I think. So that might prompt a bit more benzodiazepine use. I feel like there's more mental illness in people who tend to also use benzodiazepines…" (P10)*

Need it to function (main theme 2)

In the context of increased mental health difficulties, BZDs were referred to as a coping mechanism, a way of self-medicating for anxiety and trauma, allowing them to function throughout the day:

> *"I think that diazepam is almost as, and more important sometimes than the methadone to them, in terms of their functioning… it's a way of life for a lot of people because of their high levels of anxiety… diazepam will be the way they function, the way they get themselves out of the house in the morning… So, actually they feel unable to cope without them, that's their main coping mechanism… It'll have a different function for them I think than, you know, other drugs that they're using. I suppose it's like being an asthmatic and needing your inhaler, almost. You know, you need your inhaler. That's what you do" (P1).*

They also reflect this specific function of the BZDs in addition to the opioids- the first enables function through the second's sedation of the emotional pain:

> *"So, the opiates can block out for a certain amount of time, but they have to function during the daytime, and I think benzos helps them to cope from hour to hour. Benzos, I think, help them cope with anxiety and function during the daytime. And people who have extreme benzo use tend to want to block out all of the emotional feelings to the point of the emotional pain is so great, you can hardly bear to be conscious with it" (P11).*

Always the answer (main theme 3)

Clinicians talked about a feeling that the patients not only depend on the BZDs to function, but also see them as a magical drug almost, that can make anything better:

> *"And a lot of clients feel that they want something else to take the edge off, and so they ask for something to take the anxiety away, something to make them feel calm, to make them feel good, and they think that diazepam is going to be the answer… I'm just aware of the problematic nature of benzodiazepines and how people really grab onto this as some kind of drug that is going to somehow make them feel good" (P4)*

Some also described it as the patients' 'solution' (or 'answer') when other drugs are reduced or not available:

> *"I've got a client who's coming down on his methadone and will not stop asking for more diazepam because he just sees that's the answer. Everything else comes down, so whack the diazepam up. It's the answer to everything" (P8).*

Attached [to the drug] (sub-domain 2)

Afraid to reduce (main theme 4)

Participants' spoke about the patients' fear of the anxiety returning when coming off BZDs, leading to a reluctance to reduce:

> *"…and they say, "Well, if you make me come off diazepam, I'm going to be anxious," and they come up with all kinds of, "I'm going to have fits and I'm going to –" They get extremely anxious, not just slightly anxious, but extremely anxious about the idea of coming off…It's even the idea of coming off. They think that it's just going to cause them all kinds of problems and anxieties and they're going to start fitting and*

they're just not going to be able to cope, and they say, "I might become angry and I'm going to be this, and I'm going to react in this way if I don't have diazepam," not really understanding that it's the whole fear of coming off from and the fact that diazepam – it's mainly the fear of coming off." (P4)

Another participant described:

"Anxiety. Anxiety is always the answer when you ask people about their benzo use, and "Do you want to come off it?" "No, no, no. I need that for my anxiety. I was anxious before I started using. If I stop it all, I'll just go back to being anxious. So, I'll stop all the bad stuff, the heroin and blah blah blah. but I'll keep my anxiety medication." It's always the answer". (P8)

Attached- last drug to come off (main theme 5)

Clinicians described a sense of attachment to the BZDs, leading them to prefer reducing any other drug but not the BZDs:

"Because certainly the clients I've worked with are just so attached to it. We're always having that chat but actually, as I said, they would rather reduce everything else before they reduce the diazepam" (P1).

Another described this attachment as their baby:

"With benzo clients, I just find them quite challenging to want to reduce…it's like their baby, they're not coming off that one for love nor money. They don't want to come off that. They'll look at all the other stuff. They're happy to address certain things, but when it comes to benzos…" (P5)

This attachment leads to the BZDs always staying last after all other drugs were addressed:

> *"Also, there are some users who've come off heroin, who've come off methadone, who've come off everything, and they're still on Valium… in my experience usually they're the last drug that anyone ever tackles… I have never seen it where someone gives up their benzos first. It's always the other way around, and that seems to be the way it goes. Some people give up all the rest of their drugs, and just stay on benzos alone" (P14).*

The work is more complicated [demanding for clinicians] (main domain 2)

This domain refers to the clinician's accounts of what they felt is an added difficulty this population presents with in treatment.

Slow progress (sub-domain 3)

This domain groups together themes that relate to the BZD's withdrawal symptoms and complicate the work.

Worst withdrawal (main theme 6)

Clinicians described their experience of patients' withdrawal from BZDs as the hardest of all drugs, psychologically and physically, and takes the longest time:

> *"Methadone doesn't give the same high as heroin, but it does help people stabilise. It prevents very uncomfortable withdrawal. With benzos, there's going to be an uncomfortable withdrawal. It's a very unpleasant experience, and in my experience over the years, I would say it's probably the most difficult and the worst drug to try and come off". (P5)*

They also spoke about the uniquely long process of coming off BZDs in comparison to other drugs:

> *"…the diazepam detox was the worst of all the drugs…You have to do it very, very, very slowly. And the anxiety is horrendous, it's really bad… Different levels, but definitely paranoia, emotions all over the place. People seem to struggle the most with diazepam detox. It makes a methadone detox look easy, it really does" (P8).*

Reduction gets stuck (main theme 7)

Moreover, clinicians described a pattern in which patients struggle with reduction and quite often ask to increase the dose or buy illicitly on top, saying they cannot bear the anxiety returning:

> *"And it's quite difficult to do some kind of progress with the benzodiazepines, even if you make reduction with the client and you make the plans, quite often you arrive to some point and people straightaway they want to see the doctor and to have the review, because they are afraid to be without benzodiazepines. So, most of the time it's very, very slow progress, and I think it's more difficult than methadone, to be honest." (P2)*

This is described as an ongoing pattern, lasting years:

> *"So, there are lots of medical reviews around saying "I can't. I'm getting anxious, and I'm getting angry and my emotions are all over the place and I can't sleep. Can you please go up again?" And then the medication goes up and then it goes up and then we start again, and then the same thing happens. We've had people on this pattern for years and I mean, years, you know, still prescribed methadone, but also this*

diazepam. They go up and then go on a low dose and then, "I'm buying again, I'm buying on top". (P4)

Last bit is worst (sub-theme 1):

Furthermore, clinicians identified the last few milligrams as the hardest for patients to let go of psychologically:

"And, all of a sudden they get to the last couple of milligrams, it's psychologically the worst part, the most difficult, because it means at some stage they'll be without a prop. And the last couple of milligrams can be doing them very, very little at all, but psychologically that last little bit is the toughest to deal with". (P11)

Harder to work with [and make progress] (sub-domain 4)

Prescribing more complex (main theme 8)

Participants spoke about the thinking process behind prescribing, and the added complexity as result of the additional factors they need to consider with this population; needing to make sure that clients are truly motivated, and the prescription will not be abused or diverted:

"If somebody is saying that they're using diazepam, more engagement is necessary before jumping in to giving them a prescription because there is such a high risk that people will just be using the prescription of diazepam on top of whatever they're going to take and they're not really motivated to make any changes with their diazepam use". (P3)

In addition, the testing and monitoring process was described as more complicated with BZDs, adding to this struggle:

"It's also harder, I think, to monitor their recovery from kind of chaotic benzo use or using one type of prescription for diazepam that you might

give because we can't test for it….whereas somebody who's coming in for treatment for their heroin addiction, you can give them a methadone prescription or prescription for buprenorphine and you can monitor how they're doing in terms of stabilising on that prescription by doing a test to see if they're still taking opiates. In addition to that, you could do a urine test for that. Whereas somebody who is presenting with benzo use, whether it's dependency or chaotic use, if I give them a prescription for diazepam, I've got no way of knowing if they're using additional diazepam on top of what I'm giving… I can't check for it, so I have to work on what they say and it's difficult to know, and people use in a variety of different ways. So, it's more tricky to monitor and assess people's progress on a diazepam prescription than it is to do the same on a methadone prescription". (P16)

Harder to assess [the severity of dependence] (sub theme 2)

In this context, they also spoke about the difficulty achieving accuracy of the amount as well as types of BZDs used, as due to the nature of this drug market, patients often hide, or do not even know what exactly they are taking:

"I've never been able to see kind of – because people don't know what and how much they're taking. So, it's quite difficult to find out exactly how much they are taking. They'll be like, "I take about three or four pills," and you don't know what the strength is, and so it's just becomes really difficult and really complicated". (P9)

Another described:

"*A lot of people, they do they buy prescribed ones from someone who's selling them, but a lot of people are just buying them from the internet.*

Who knows what they are? They'll tell you, "Oh I've been buying these diazepam." I'll be like, "OK. What dose?" "Don't know," because they're a different colour from the ones in the UK. I mean, it's just terrifying". (P8)

Manipulate for prescription (sub theme 3)

Another factor identified by clinicians as contributing to the difficulty of working with this population is their desperation for the BZDs, which is felt to lead them to manipulate in order to get the prescription*:*

"Our clients do manipulate, and they will come and try and manipulate… They could say that they need to go up. They will say sometimes, "Oh I need to go up." They'll come out with some stories, believe me... They'll just demand that they want to go up or they've been buying illicit street diazepam. That's another way they'll come, and, "Oh, I've got this habit," again, try and look for another 5mls or 10mls, you know." (P5)

This pattern was repeatedly attributed to the increased anxiety as result of dosage decrease:

"They start feeling anxious and then they start saying, "Well, I'm just going to go and use on top." So, they start using those kinds of threats, and tactics in order to remain on the same dose…" (P9)

Hard to engage (main theme 9)

In addition to the difficulty assessing, clinicians spoke about the challenges of engaging these patients and discussing BZDs reduction:

"You find what you'll get is clients will not – I've had clients not want to talk about that, "We'll talk about everything else, but we're not

talking about my benzos," because they're fearful we want to then try and work about how to reduce. So, yes, there's a couple of clients in mind. Yes, absolutely won't want to talk about it. So, we can talk about anything but that. Well, it's then of course trying to work with them around that. It's impossible" (P13)

They describe a deep reluctance to even discuss the topic of BZDs reduction and how this affects them as well as their ability to work with these co-dependant patients:

"So, in some ways you would do the same work, but I think convincing people around the benzos and coming off the benzo is more difficult and does take longer, much longer…They are difficult clients to work with, partly because they are in a huge amount of distress, and that's difficult to watch and it's difficult, I think, at times to say, "Now we're going to cut it down again," and go negotiate that". (P6)

Do not think it is a problem (sub-theme 3)

In this context participants identified one of the reasons for patients' reluctance to engage is that they simply do not see the BZDs as a drug. They do not think it is a problem, since it is a medication prescribed by doctors:

"When clients are on methadone and diazepam, they don't see diazepam as a problem… They don't see as a big problem compared to heroin and methadone… I think because it's prescribed. I think that has a big impact on what people believe, "It's okay because it's prescribed by a doctor, therefore, it can't be doing anything harmful". Lots of people take it. It's normal. I think that's the difference" (P8)

In addition, it does not bring with it the lifestyle that street drugs do:

"I think there's also the kind of look on a benzodiazepine that because it's a tablet, it's almost clean, it's a pharmaceutical… whereas street heroin isn't OK. And street heroin brings a whole lifestyle with it that people want to get away from when they go to detox and rehab… whereas benzos don't necessarily bring that." (P13)

Requires specific approach (sub-domain 5).

All these added complexities which are without exception attributed to the BZDs addition to the opioids, are also reflected in clinicians' repeated claims that this work, in fact, requires specific approach; different to those employed with patients who are dependent on any of the other drugs.

Specific skills and training (main theme 10)

Participants spoke about a feeling that this type of work is more complex and different in its nature to the work with other patients they see, and so it requires special skills. Some clinicians described that they would seek advice on these cases from clinicians who have a lot of experience with this population:

"I think the fact that there is a specialized clinic now is great, and there was evidently kind of a need for that specialism… I would tend to speak to my colleagues who are running the service and just say…". *(P14)*

Others expressed their need for further training directly:

"I think a bit more training, actually, for myself personally, specifically with benzo clients, because I think they are slightly more unique at times, because they're more complex…" (P5)

And some described their sense that some clinicians might feel they lack the skill to work with this population:

"I think some clinicians don't feel skilled enough… but I think some people don't feel comfortable with dealing with both benzos and methadone… Because they feel they haven't got the experience of dealing with someone who's got that kind of dual presentation… Sometimes I get referrals off people who do not want to see people on both of them, and just want to see someone who's just on one medication. There is a training need there" (P14).

Need a clearer plan (main theme 11):

Similarly, another recurring theme was a feeling that there is a need for a clear plan and more strict guidelines when working with BZD and opioid co-dependent patients, as the lack of a strict regime makes it more complicated for them to make progress:

"And I think when people started on a high dose that sometimes it feels it's not that strict in terms of, "Right we're going to put you on this dose, but the plan is, this is what we're going to do." It's down to the individual key workers to kind of do that, and when you've taken on a new client who was previously working with someone else that had just been on that dose for a long time, they become really, really reluctant. So I think it would be really helpful if we were to just start prescribing someone on benzos and make it clear to them it's for a short period of time, and that they would be required to reduce, and I don't think that always happens here. Hence why a lot of people come in to say that they're using benzos and they need to get on a script, because they know that they'd be able to get a script." (P9)

This was repeatedly attributed to a lack of uniform approach and policy, putting key workers and nurses in a difficult position in front of the clients:

"Stop prescribing it unless it's an emergency. I think the doctors at the top, the ones who are prescribing in here in drug services, need to talk to the clients about it and be a bit stronger like, about saying, "Right, we need to start reducing this." Because when it's just left to the nurse they just, "Oh whatever." They don't Listen." (P8)

Psychology (main theme 12)

They also described the need for ongoing support and psychology for these individuals to be able to make progress with the BZD reduction:

"The difficult thing we struggle with is that there is not much psychological support to recognise these people. In a way, the psychological support is also around that trauma, but they are not going to get – often they will get stuck in the detox because they can't go further. We have one psychologist here, but it's not really a psychology service… But there are people who could probably stably go through a detox more successfully if they could also have psychological input halfway through, and I think that would help people come off the benzos more" (P18).

And this again, links the added psychological complexity they see in the BZDs users among their opioid dependant clients, with the difficulty in making progress; leading to a greater need for psychological input:

"But the issue is more psychological. It's more that they're not comfortable, there's something there, they're anxious, they're socially awkward. So, it's not always the drug. The drug just suits how they are. So that's why we have psychology and it's to do that together, benzo and psychology, because it is a big part psychology of how they feel…

and I do think they just need that psychological input. They really do, because they all say the same thing, that they feel very anxious about benzos, they feel very socially awkward. There's a lot of psychology involved in that and it's a long-term treatment as well." (P13)

Frustration (main theme 13):

The final theme which occurred throughout the data describes the emotional impact of working with this population on the clinicians. When coding, these extracts were initially coded into multiple codes, and on the third coding round and when refining, it was recoded as a relationship code, and included the extracts with emotional impact. This relationship was interpreted as the result of their attempts to empathise and contain the patients' distress on one hand and make progress with their work on the other:

"They're so much harder sometimes to work with. Those that are getting it consistently, those that are using it almost daily, it's just very difficult to ever… It's heart-breaking, and then they become quite resistant to engage with you because they're scared. You're trying to help them get towards coming off benzos. They get scared. They don't want to acknowledge that they're using them. Yes, it's so difficult. There's been a few cases over the years where I've just – yes, I just can't see how because it's there". (P13)

Another clinician described*:*

"They are difficult clients to work with, partly because they are in a huge amount of distress, and that's difficult to watch… And as I say, for some – key workers have got a large caseload of people, the anxiety is, as I said, you know, it's contagious. I think people can feel quite stressed

after working with people with benzo dependency as well. They can be quite demanding and, in the end, persuasive… ". (P5)

And lastly:

"I think there's a general feeling of, "This person will not want to change." You know, someone that's just on heroin or whatever, it can be quite hopeful. You can do it, but, yes, in conversation it's like, "Oh, nothing much is going to change, and it'll be a battle to even start a conversation about it" … So, yes, it is frustrating. You don't get the results that make you feel good. You know, "We've detox them," and that's satisfying. It is really hard to get that with diazepam, benzo clients. So, yes, bit soul destroying". (P8)

Discussion

Summary and implications

Service users in substance misuse services, presenting with co-dependence on opioids and benzodiazepines, are consistently described in the literature as more complex psychologically as well as in terms of risk and adherence to treatment. This led to the interest in exploring the way in which mental health clinicians working with them experience and conceptualise this work, and how it might be affected by these experiences. Complimenting existing research, this was the first study known to the researcher examining this population of substance misusers from mental health clinicians' perspectives.

This study shows that this sub-population of service users is perceived by clinicians as more complex psychologically, in their presentation and attachment to the BZDs and indeed, more difficult for clinicians to work with. In addition, there seems to be a general feeling of lack of systemic containment for these patients- evident in clinicians' expressions of difficulty

working with them and their feeling that they lack appropriate skills and more consistent guidelines. These results complement existing research, suggesting that more psychoeducation and containment is needed for service users and clinical staff about the nature and costs of this addiction and recovery process.

Many of the findings derived from this population are congruent with other studies investigating this subpopulation of service users from other perspectives. For example, a recent study examining the barriers to progressing through a methadone maintenance treatment programme from the perspectives of the clients found that an overwhelming proportion of users were dually addicted to benzodiazepines (Moran et al., 2018). Thematic analysis revealed that often clients were buying these on the city's black market. Moreover, as result of the high local demand for BZDs, the market was becoming more dependent on external foreign suppliers and purchasing BZDs from the internet became increasingly common. Clients had no idea what they were purchasing, as these tablets were illegally manufactured and therefore did not resemble known prescribed BZDs in shape, size or potentially chemical composition; and they are indeed often laced with other drugs. This was repeatedly mentioned in this current study as well and was perceived by clinicians as an added barrier to assessing and prescribing these patients (main theme- harder to assess).

Moreover, clients' own suggestions for improving their journeys through treatment included educating themselves, their families, the public and allied health care professionals on all aspects of OUD and its treatments. Interestingly, when clients were not progressing appropriately, they themselves suggested enforcing a 'time-limit' on engaging with the programme or for their treatment to be postponed (Moran et. al., 2018). In this current study, clinicians expressed a feeling that people end up staying in treatment for years not making any progress, linking it to the lack of clear, unequivocal guidelines and need for a more restrictive approach.

Another important finding is that clinicians seem to struggle to reconcile between an attempt to make sense of their patients' experiences and empathise with them and their complex needs on one hand, while making progress with their work with them toward recovery, on the other. This struggle appears to lead at times to feelings of frustration, hopelessness and even apprehension regarding working with service users, as represented under the theme of frustration.

Similar struggles have been identified in previous research. For example, in a study exploring medical cultural response to curricular addition of communication skills training, a gap was found between the rhetoric of ''patient-centred communication'' and ''empathy", and the traditional concerns of medical authority, efficiency, and scientism (Raz & Fadlon, 2006). That study however, unlike this one (although conducted in different settings and populations), did not yield staff's emotional responses to this dissonance.

In this study, elements of confidence in their own skills, empathy towards their patients and perceived systemic constrains were prominent elements in clinicians' experience of working with these clients. These compliment earlier findings (Merrill et al., 2002) of clinicians' mistrust towards these patients, a discomfort and uncertainty in their approach to treating them and their reported need for a standard approach for assessing and treating these patients, as result. Furthermore, and similarly to our findings, aspects of clinicians' experience of working with complex self-harming patients which were found to impact their feelings towards them were their confidence in the treatment plan, an empathic approach and ability to adapt to the system (McAllister et al., 2002).

However, a causal analysis was not included in this study, nor a correlational one, and therefore a link cannot be made between the attitudes found among clinicians regarding their perceived skills and empathy, to the actual effectiveness of treatment.

In terms of making sense of their patients' struggles, participants repeatedly described their patients as psychologically more highly distressed in comparison to other service users, linking this specifically to the benzodiazepines being added to the opioids. They describe a unique attachment to this drug and their understanding of its origin being in its ability to allow a state of emotional numbness, enabling them to function, in addition to the feeling of high caused by the opioids. This, in addition to what clinicians perceive as a sense among these users that BZDs can solve any problem, leads to a deep fear of coming off these drugs, as well as to their prolonged misuse. Moreover, they describe how often a patient will detox from all drugs yet keep taking BZDs- considering themselves recovered.

This naturally complicates the work with these patients, and indeed clinicians report increased difficulty in all aspects of the work- from engagement through assessment to prescribing. This increased difficulty is attributed to the BZD use rather than any other drug involved. This manifests in their attachment and desperation about it, the nature of these specific drugs and their detox, the market for the drug and the fact that it is a drug prescribed by doctors. Participants describe a much longer process of working with these patients, with multiple relapses involved as well as what they feel is manipulation on the patients' part.

Lastly, participants expressed a feeling that as result of this increased difficulty, a specific approach is needed when treating these patients. This includes more psychological atonement and increased support, clearer guidelines and specific training for staff.

Practice recommendations

These findings yield clear practice recommendations based on clinicians' perceived needs- both their own and their patients'.

First, based on clinicians' repeated reports of their felt lack of training, it is evident that such training which encompasses psychoeducation of this specific population and their needs is needed for clinicians. It is also indicated that psychoeducation in needed for patients- as they

seem to lack insight into the addictiveness of the drug and tend to view their use of benzodiazepine as medicinal, in contrast to misuse or dependence.

In this context, it is also indicated that there is a great need for psychological input for these patients, and a lack of psychologists in these services to comply with this demand. It is also recommended, although this was concluded rather than explicitly said in the interviews, that some additional containment might be helpful for clinicians working with these patients, evident by their sense of frustration and difficulty working with them. This can be achieved by creating a peer support group or specific group supervision for staff members working with these patients.

Another important implication is a felt need for clearer guidelines- this was a frequently repeated theme and arose in previous research as well, interestingly- from patients' perspectives (Moran et. al., 2018). This would include prescribing only for the purpose of reducing and enforcing a 'time-limit' on engagement, in addition to reviewing and explaining the plan to the patients by the prescribing doctor rather than the key workers.

Limitations and future research

There are three main limitations to this study. The first- subpopulations of clinicians were not separated into groups and differences between these groups were not explored. Since this is the first research exploring mental health clinicians' attitudes, clinicians from all disciplines were recruited- psychiatrists, recovery practitioners, mental health nurses and assistant psychologists. As the study progressed the researcher felt it could have been of interest to explore potential group differences, ideally using more specific questions aiming to explore these differences. It would be of special interest to explore the correlation between length of experience and attitudes, considering prior evidence of such difference from other clinical populations. For example, in the earlier described review of clinicians' attitudes towards ED patients, Thompson-Brenner et. Al., (2012) found that less experienced clinicians held more

negative attitudes toward ED patients, but more experienced ones did not. However, due to time limitations and complications around recruiting further, this was not explored in this study and can be done in future studies based on the results of this one.

Secondly, since the nature of this topic is very delicate, the researcher had the sense while interviewing that some participants held back or had more to say than they did. One participant said, off the record, that if the interview was not recorded, they would have said more than they did. This should be thought of in future research and methodology should be aimed to address this difficulty- perhaps with anonymous questionnaires rather than recorded interviews. Nevertheless, these findings show that many of the respondents were able to convey self-criticism and frustration both about their patients and about themselves.

Lastly, an inherent limitation of thematic analysis when compared to other methods of conversation analysis is that it does not allow researchers to make claims about language use (Braun & Clarke, 2006). This led to leaving out phatic expressions, for example, and can be approached in future research through more specific techniques of conversation analysis. However, since this is a preliminary study, the researcher took a more semantic approach to data analysis, weighing the costs and benefits for this approach and prioritising precision of conclusions over potential depth of interpretation.

Conclusion

This study, complimenting existing research in the field, is a qualitative one exploring the experiences and conceptualisations of clinicians in substance misuse services, of working with service users who are co-dependant on benzodiazepines and opioids. It explored how the added difficulties this sub-population of users present with in treatment is experienced and handled by clinicians, and their thoughts of how this can be better approached.

Analysis concluded three main ideas- a perception of clinicians of the unique attachment this population has to BZDs and a sense that they are more complex to work with,

and finally, a sense of frustration as a result of empathising with their difficulties in combination with the difficulty making progress in treatment. Finally, limitations of this study were detailed, and recommendations made for future research based on this.

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Part 3:

Critical appraisal

Introduction

Reflexivity in terms of the 'self' is encouraged in qualitative research (Ortlipp, 2008). Reflexivity refers to the close attention paid to the researcher's role in all stages of qualitative research (Fontana, 2004). It involves a continuous process of reflection on the researcher's values, preconceptions, assumptions and experiences and how these may influence the findings of a study, either intentionally or unintentionally (Jootun et al., 2009).

Accordingly, throughout the process of conceptualizing and writing the empirical chapter in this thesis, I kept a reflection journal in which I wrote notes and comments for myself to consider during different stages in this process. Some of the content of this critical appraisal expands these notes, written following further reflection, at the final stages of write up.

In this section I will discuss my thoughts and reflection of the process of data collection, coding and analysis. I will also discuss my personal orientation and how it affects the work, some broader systemic issues implied by the results, and end with some personal notes on the process.

Reflection on the process

Interviews

First and foremost, it is worth thinking about the research question. This was my first experience with qualitative methodology. When identifying the question, my aim was to keep a broad spectrum of potential content, given that this was a preliminary study and the first of its kind as far as I am aware. Therefore, it made sense to keep the questions open, allowing content to arise spontaneously and inductively. However, in retrospect, this, in combination with my lack of experience with qualitative interviewing, created some complications.

First, I did not realise how broad the potential content was, and how unfocused interviewees were on the questions asked. This was evident in the amount of interview data which was related but not directly relevant to this study. For example, one participant spoke at

length about their family member who was prescribed at the time both opioids and benzodiazepines, and when stopped the BZD prescription- they experienced mild psychotic symptoms as result. Others spoke often about their experiences with BZDs users, who were not also addicted to opioids. This was difficult to monitor and stop during the interview as both myself and participants were very engaged with the content, and therefore required rigid exploration of the data at the coding level and determining what was and was not relevant to the question. Trying to keep participants on track proved to be more complex than I expected, resulting in quite a lot of data being discarded during analysis. Upon reflection, I wonder if I had been better able to do this empathically, I might have kept them on track long enough to produce more relevant content instead.

Another issue I wondered about during the interviews phase, was whether I made a good decision offering to interview participants at their place of work. My thinking was to make it easy for them to participate. In retrospect, however, I wonder whether some may have been distracted by their work and wanted to keep the interview brief or were less concentrated on the questions as I imagine I might have been if I were in their shoes.

In addition, participants often seemed to think and come to new conclusions during the interview itself. It would often happen that a participant took their time with an answer or could not find the specific words to express what they wanted. I later wondered if giving them some time to reflect on my questions beforehand would have helped with this and allowed them to provide broader answers to my questions and/or be more precise in their responses.

Interestingly, my final interview question [“Anything else you would like to ask or add before we finish? Any thoughts, ideas, questions? Anything you want to bring up?”] which was added mainly as a courtesy, ended up producing significant data. It was then for example, that a few of the participants noted their difficulty balancing risk issues with the reduction plan, and their broader thoughts around issues with prescribing. Interestingly, when asked earlier in the

interview directly about risk, the same issues were at times not expressed. This is the clearest example of a phenomenon I noticed when participants did not answer my question directly but did answer it indirectly on different questions later. This made me think about the way my questions were asked, and whether I could have asked them differently to produce more content. I attribute this as well to my lack of prior experience with qualitative interviewing.

My conduct during interviews

I often wondered, listening to the recordings, whether I had stayed quiet long enough for participants to come up with answers before I offered prompts. I wonder what would have happened if I had waited longer. In contrast, at other times I found myself wondering if I prompted them enough, thinking I could have encouraged them to take their answers further. For example, I could have asked more about how they coped with their feelings towards their patients, taking the question beyond the original interview schedule. Writing this now, I find myself thinking if this might be in part a result of a qualitative stance which does not use strict specific methods but rather demands thoughtful decision making and awareness throughout the process.

Another thing I noticed was that when interviewing, participants made their meaning obvious quite often without words. I realized this non-verbal communication mid interviewing and started asking them to put their gesture into words when needed, but some of the earlier interviews contained information which due to my lack of awareness was missed, for this reason. This again highlights the dilemma and costs and benefits of semantic vs. interpretive analysis, as semantic coding technique of thematic analysis does not allow for interpretations of language use or the functionality of talk (Braun & Clarke, 2006).

Coding and six months break

My coding phase lasted many, many months. For personal reasons I was unable to work on the project for several months and this happened at the final stage of analysis. By then, I had gone through four rounds of coding and organising my themes into three main domains.

Upon my return to work on the project, I felt quite disconnected to it, and after a couple of weeks of struggling with the data and making no progress, I decided to start from zero and code all over again. This proved to be a very wise decision, even though it meant additional time-consuming coding work. There were two main reasons for this; first, and I could only see this in retrospect, there was too much data to keep fresh in my mind for all this time. The process of recoding was like diving straight into the knowledge I already had and so it was much, much easier than the first-time. In addition, it was as if the time that passed allowed for some unconscious consolidation of the data in my mind. At that point, it felt as if the themes almost organised themselves, and appeared with more clarity and sense. This made me feel more confident in my outcome and conclusion, especially in combination with the high percent agreement rate between coders.

Reflections on the results

Potential group differences

There were two main differences across interviews that I had noticed during the thematic analysis. First, some interviews were much shorter than others, with much less content. It might have been interesting to run a quantitative analysis on participants' data (age, profession, years of experience etc.) to gain an understanding of this gap and the reasons for it. Are some clinicians less knowledgeable? Less experienced? Clearly this study was not powered to allow for such analysis and time limitations as well as important participant confidentiality meant this type of data was not gathered.

Secondly, I did notice a gap between the few very experienced participants and the others in terms of their views and what was and was not mentioned. For example, none of the experienced participants spoke about their personal difficulty working with these patients, but did however, acknowledge how it can be difficult for some (other) clinicians to work with these service users and expressed an understanding of why that is. In future studies, it could be interesting to test a hypothesis regarding experience as well as qualification and discipline as potential moderating factors to the difficulty working with this population as well as difficult feelings around it. Alternatively, this can also be done qualitatively.

Broader systemic issues

Several times during the interview stage, participants stopped to re-confirm that the interview was confidential. One explicitly said to me before I started recording, that they would have been more open and literal if the interview was not being recorded. As all participants were working in the same NHS service, it was understandable that some may not want their work colleagues to know their views on treating this group of clients. In future it would be interesting to compare findings with unrecorded interviews and/or data from anonymous questionnaires.

Another issue I became aware of was that some participants may have held some internal implicit criticisms toward the system. Surprisingly, the question regarding confidentiality was asked in context of speaking about prescribing (with what they felt was lack of a clear plan for reduction), and not, as might be expected, the patients and their feelings towards them. At times, I felt there was more to say on this subject that was not said, based on the timing of this questions as well as some participants' tone when they spoke of this; and again, sticking to the guidelines of semantic analysis- this was left out. Moreover, some criticism towards the system was made during interviews, however this was more often not

specific to our population of interest as well as the research question and therefore was left out of analysis.

In addition, there seems to be an issue of information not well communicated within the system. Again, this was not explicitly said and therefore was excluded from analysis, but participants often described not being clear on why the service keeps prescribing benzos for a long time rather than reducing promptly and restricting prescriptions to 4 weeks (Baldwin, et. Al., 2012). However, there were a small number of more senior clinicians who seemed to be noticeably clear on this, not referring to it is an issue at all. It would be interesting to know whether this reflects their greater experience with these clients or a lack of internal systemic communication or training where some clinicians have less knowledge and understanding than others in the same service. One way or another, to me, there is indeed a "need for a clearer plan" in how BDZs should be managed during opioid substitution treatments.

Personal orientation

This was an interesting project for me, as I had no prior experience working in substance misuse services or with addictions in other contexts. I had only learned about the issues involved with these two drugs as well as gained knowledge of theories and treatment of addictions during my work on the project. For this reason, I had no prior conceptions or orientation to guide me through the process of data collection, analysis and conclusion drawing. This has both advantages and disadvantages. On the one hand, I felt it made it more difficult for me to study this new area without experiencing it as a trainee or assistant myself. It made the process of deciding upon the questions included in the questionnaire schedule more complex, as I felt I could not be independent, but rather draw not only on the literature but also the knowledge of supervisors within the NHS as well as at UCL. One example of where I encountered a difficulty was when participants used language which one would be familiar

with when working in the field. Throughout the interviews I have improved at identifying when this happens and asking for clarification.

This process has led, I believe, to the biggest advantage, which was my neutrality and curiosity throughout. As participants spoke, I felt I was genuinely interested and surprised by their answers. It was easy for me to explore the content of their responses from an unbiased stance, as I had limited prior knowledge and no biases that I was aware of. More importantly, it reduces the threat of my own conceptions influencing the outcomes of this study, thus increasing its validity.

Final notes

During the interview stage, I was undergoing my speciality placement in a psychodynamic oriented service. I think that this experience influenced my state of mind and made me more susceptible to unconscious communication which was present during the interview. In psychodynamic theory, the therapist often feels what is projected onto them by the patient, in a process called "projective identification" (Klein, 1946), thus experiencing the emotion originating in the patient themselves. I was aware, during many of the interviews, of feeling a growing sense of anxiety. Reflecting on this, I think a lot of this feeling originated in my interviewees, arising and increasing during the interview, as they were talking about their very anxious co-dependant patients. Anxiety was mentioned many times by participants and was a theme on its own in the initial stage of the analysis, later incorporated into the theme of "more mental health problems". And indeed, anxiety was very much present in most of the interviews, as one of the participants stated: "it is almost contagious, the anxiety".

In this context, when participants spoke so often about how these patients needed more-psychology, more time and more containment, I wondered if they were also speaking about themselves, almost projecting their own needs onto their patients. I felt as if they, the clinicians themselves felt they needed more of these things- more containment around their work with

these patients, and more ongoing support with this work, as the clinicians said- it is harder and more complex.

In terms of my own journey, I began the UCL Doctorate in Clinical Psychology as an overseas trainee with English as my second language and my culture hugely different to the one in the UK. This has put some added difficulty to my experiences on the course, both clinical and research, but also gave me a different angle on both. In addition, my entire clinical and research experience was gained in a separate health system which is structured very differently. Now as that journey ends and my thesis is complete, I have been able to reflect on this process and I realise how much I learned. I feel, for example, that my interest in a qualitative methodology, in which language is the data as well as method of data collection has required me to be twice as tenacious when working on this project. My insecurity around the potential of misunderstanding or missing something important that was said made me double check everything.

I would be interested in undertaking another project in the future and deepening my experience with qualitative methods as I learned, that in the field of psychology that is all about people and their interpretations of the external world- language and expression is so central to understanding people's experiences. I would be interested in experiencing with a more interpretive method of qualitative analysis and broadening my learning in this method of using language and gestures as data.

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Appendix A

Letter of ethical approval

UCL RESEARCH ETHICS COMMITTEE
OFFICE FOR THE VICE PROVOST RESEARCH

24 October 2019

Prof. Valerie Curran and Dr Sunjeev Kamboj
Clinical, Education and Health Psychology
UCL

cc. Efrat Chudin

Dear Prof. Curran and Dr Kamboj

Notification of Ethics Approval Project ID/Title: 15219/001: Clinicians' experience of working with Benzodiazepine users on methadone maintenance treatment (MMT) for opioids dependency

I am pleased to confirm in my capacity as Chair of the UCL Research Ethics Committee (REC) that I have ethically approved your study until **30 November 2020.**

Ethical approval is granted subject to the following conditions:

Notification of Amendments to the Research
You must seek Chair's approval for proposed amendments (to include extensions to the duration of the project) to the research for which this approval has been given. Each research project is reviewed separately and if there are significant changes to the research protocol you should seek confirmation of continued ethical approval by completing an 'Amendment Approval Request Form' http://ethics.grad.ucl.ac.uk/responsibilities.php

Adverse Event Reporting – Serious and Non-Serious
It is your responsibility to report to the Committee any unanticipated problems or adverse events involving risks to participants or others. The Ethics Committee should be notified of all serious adverse events via the Ethics Committee Administrator (ethics@ucl.ac.uk) immediately the incident occurs. Where the adverse incident is unexpected and serious, the Joint Chairs will decide whether the study should be terminated pending the opinion of an independent expert. For non-serious adverse events the Joint Chairs of the Ethics Committee should again be notified via the Ethics Committee Administrator within ten days of the incident occurring and provide a full written report that should include any amendments to the participant information sheet and study protocol. The Joint Chairs will confirm that the incident is non-serious and report to the Committee at the next meeting. The final view of the Committee will be communicated to you.

Final Report

At the end of the data collection element of your research we ask that you submit a very brief report (1-2 paragraphs will suffice) which includes in particular issues relating to the ethical implications of the research i.e., issues obtaining consent, participants withdrawing from the research, confidentiality, protection of participants from physical and mental harm etc.

Office of the Vice Provost Research, 2 Taviton Street
University College London
Tel: +44 (0)20
7679 8717 Email:
ethics@ucl.ac.uk
http://ethics.grad.ucl.ac.uk/

In addition, please:

- ensure that you follow all relevant guidance as laid out in UCL's Code of Conduct for Research:
https://www.ucl.ac.uk/srs/file/579
- note that you are required to adhere to all research data/records management and storage procedures agreed as part of your application. This will be expected even after completion of the study.

With best wishes for the research.

Yours sincerely

Professor Lynn Ang
Joint Chair, UCL Research Ethics Committee

Appendix B

Participant's information sheet

Clinicians' experiences of working with BZD and opioids co-dependant service users

YOU WILL BE GIVEN A COPY OF THIS INFORMATION SHEET

Name and Contact Details of the Researcher:
Efrat Chudin
e.chudin.17@ucl.ac.il

Name and Contact Details of the Principal Researcher:
Valerie Curran- v.curran@ucl.ac.uk
Sunjeev Kamboj- sunjeev.kamboj@ucl.ac.uk
Dominic O'Ryan- Dominic.O'Ryan@Candi.nhs.uk

We would like to invite you to participate in this research project. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Aim
The project aims to explore the experiences and opinions among clinicians who have been working with Methadone Maintained (treated for opioids dependency) service users presenting with co-dependency on Benzodiazepines (BZD).
We aim to both understand this subgroup of service users better as well as inform clinical interventions.

Participants
For this purpose, we are looking to recruit 12-18 clinicians of any disciplines who have experienced working with this client group, for one session of interview which should take around 30-40 minutes. Participants will be rewarded with 20£.

Taking part in the study is entirely voluntary and that refusal to agree to participate will involve no penalty or loss of benefits to which the participant is otherwise entitled. If you choose to participate, *you can withdraw your consent at any time without giving a reason and without it affecting any benefits that you are entitled to.* If you decide to withdraw you will be asked what you wish to happen to the data, you have provided up that point.

What does participation require
Participation in this project will include being interviewed by the researcher personally and anonymously. Interviews will be recorded and transcribed by the researcher and information will be analysed anonymously. Any identifying information will be kept separately from the data itself on a secure server and will not be analysed. It will only be

seen by the main researcher alone. No other use will be made of them without your written permission, and no one outside the project will be allowed access to the original recordings.

Risks and benifits

There are no risks or disadvantages associated with participation. Interviews will be conducted at a time and place convenient to participants and they will be reimbursed with £20 for their time.

Confidentiality

All the information that we collect about you during the course of the research will be kept strictly confidential. You will not be able to be identified in any ensuing reports or publications.

Please note that confidentiality will be maintained as far as it is possible, unless during our conversation I hear anything which makes me worried that someone might be in danger of harm, I might have to inform relevant agencies of this.

the data collected during the course of the project might be used for additional or subsequent research in the future, but any identifying information will remain strictly confidential.

Local Data Protection Privacy Notice

The controller for this project will be University College London (UCL). The UCL Data Protection Officer provides oversight of UCL activities involving the processing of personal data, and can be contacted at data-protection@ucl.ac.uk

Your personal data will only be collected to maintain information on who participated, but will not be analysed nor processed. Your data from this study will be stored in locked cabinets or electronically in password-protected files. Data will be labelled with a numbered code and will be stored separately from your name and contact details. Only researchers directly involved in the study have access to your name and contact details. Pseudo-anonymised data may be shared with other researchers at UCL or with collaborators at other institutions, to help answer new research questions, but they will never be given your name or contact details

You have certain rights under data protection legislation in relation to the personal information that we hold about you. These rights apply only in particular circumstances and are subject to certain exemptions such as public interest (for example the prevention of crime). They include:

- The right to access your personal information.
- The right to rectification of your personal information;
- The right to erasure of your personal data;

- The right to restrict or object to the processing of your personal data;
- The right to object to the use of your data for direct marketing purposes;
- The right to data portability;
- Where the justification for processing is based on your consent, the right to withdraw such consent at any time;
- The right to complain to the Information Commissioner's Office (ICO) about the use of your personal data.

The categories of personal data collected will be as follows:

Name
Telephone number
Email
Job title

If you are concerned about how your personal data is being processed, or if you would like to contact us about your rights, please contact UCL in the first instance at data-protection@ucl.ac.uk.

This research is organized and funded by UCL.

If you have any further enquiries, please feel free to contact us on e.chudin.17@ucl.ac.uk
Thank you for reading this information sheet and for considering to take part in this research study.

Appendix C

Participant Consent Form

BZD in MMT 2019

Study: Clinicians' experiences of working with BZD and opioids co-dependant service users

Please complete this form after you have read the Information Sheet and/or listened to an explanation about the research.

Researchers:
Efrat Chudin e.chudin.17@ucl.ac
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Department: Clinical, Educational and Health Psychology
UCL Data Protection Officer: Lee Shailer data-protection@ucl.ac.uk
This study has been approved by the UCL Research Ethics Committee (Project ID Number: XXXX)

Thank you for considering taking part in this research. The person organising the research must explain the project to you before you agree to take part. If you have any questions arising from the Information Sheet or explanation already given to you, please ask the researcher before you decide whether to join in. You will be given a copy of this Consent Form to keep and refer to at any time.

I confirm that I understand that by ticking/initialling each box below I am consenting to this element of the study. I understand that it will be assumed that unticked/initialled boxes means that I DO NOT consent to that part of the study. I understand that by not giving consent for any one element that I may be deemed ineligible for the study

		Tick Box
1.	*I confirm that I have read and understood the Information Sheet for the above study. I have had an opportunity to consider the information and what will be expected of me. I have also had the opportunity to ask questions which have been answered to my satisfaction	
2.	*I consent to participate in the study. I understand that my personal information *(name, contact details, gender, ethnicity)* will be used for the purposes explained to me. I understand that according to data protection legislation, 'public task' will be the lawful basis for processing.	
3.	**Use of the information for this project only** *I understand that all personal information will remain confidential and that all efforts will be made to ensure I cannot be identified. I understand that confidentiality will be maintained as far as possible, unless during our conversation I say anything which makes the interviewer worried that	

	someone might be in danger of harm, in which case they might have to inform relevant agencies of this. I understand that my data gathered in this study will be stored anonymously and securely. It will not be possible to identify me in any publications.	
4.	*I understand that my information may be subject to review by responsible individuals from the University for monitoring and audit purposes.	
5.	I understand the potential risks of participating and the support that will be available to me should I become distressed during the course of the research.	
6.	I understand the direct/indirect benefits of participating.	
7.	I understand that the data will not be made available to any commercial organisations but is solely the responsibility of the researcher(s) undertaking this study.	
8.	I understand that I will not benefit financially from this study or from any possible outcome it may result in in the future.	
9.	I understand that I will be compensated for the portion of time spent in the study (if applicable) or fully compensated if I choose to withdraw.	
10.	I agree that my pseudo-anonymised research data may be used by others for future research. [No one will be able to identify you when this data is shared.]	
11.	I understand that the information I have submitted will be published as a report and I wish to receive a copy of it. Yes/No	
12.	I hereby confirm that I understand the inclusion criteria as detailed in the Information Sheet and explained to me by the researcher.	
13.	I hereby confirm that I understand the inclusion criteria as detailed in the Information Sheet and explained to me by the researcher; and I fall under the inclusion criteria.	
14.	I have informed the researcher of any other research in which I am currently involved or have been involved in during the past 12 months.	
15.	I am aware of who I should contact if I wish to lodge a complaint.	
16.	Use of information for this project and beyond: I understand that my personal data will be processed so long as it is required for the research project. Once names and contact details are no longer required, these will be deleted, and all data will then become fully anonymised I agree that my anonymised research data may be used by others and shared beyond the department for future research. These researchers will not be given my name or contact details, and so they will not be able to identify you when this data is shared. I understand that other authenticated researchers will have access to my anonymised data. I would be happy for my anonymised data the data I provide to be archived within UCL stores.	

If you would like your contact details to be retained so that you can be contacted in the future by UCL researchers who would like to invite you to participate in follow up studies to this project, or in future studies of a similar nature, please tick the appropriate box below.

	Yes, I would be happy to be contacted in this way	
	No, I would not like to be contacted	

Name of participant	Date	Signature
Researcher	Date	Signature

Appendix D

Interview schedule

RESEARCH DEPARTMENT OF CLINICAL, EDUCATIONAL AND HEALTH PSYCHOLOGY

Clinicians' experiences of working with Benzodiazepines and Opioids co-dependant service users

Introduction

The following points will be discussed with participants:

- Informed Consent and right to withdraw at any point
- The structure and length of the interview
- Use of recording device
- Confidentiality and data storage
- Clarification- discussing with participants the population of interest to make sure they have had over a year of working in substance misuse services and direct experience with the population of interest (opioids and benzodiazepines co-dependant service users). They will also be asked to deciare their job title.

Interview questions:

1. Can you please tell me about your experience of working with the subpopulations of service users who are co-dependant on Opioids and Benzodiazepines?
2. Can you please tell me about your experiences with them around detox?
3. Can you please tell me about the thought process around treatment plan with these service users? What would be considered?
4. Can you please tell me about your experiences and thoughts around risk with these patients?
5. What would be helpful for you as a clinician working with this population?
6. Anything else before we finish? Any thoughts, ideas, questions? Anything you want to bring up?

Prompts

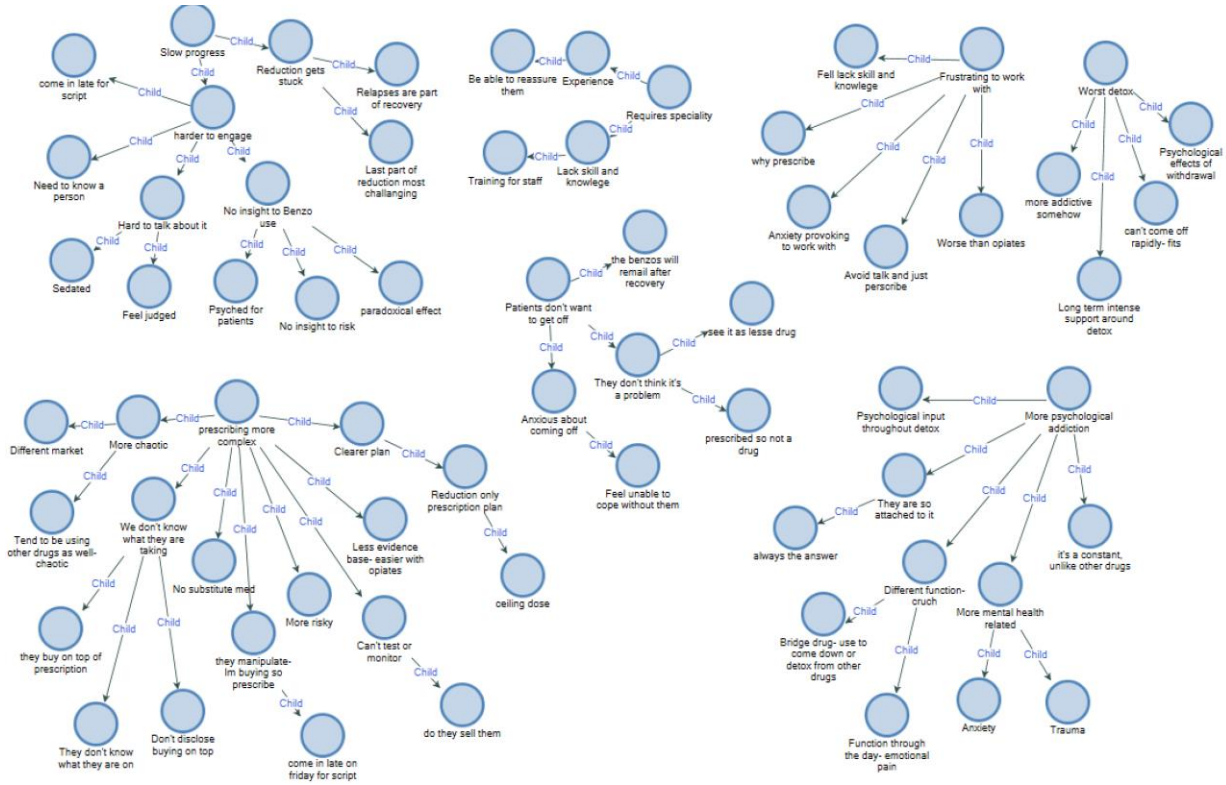
Following each question and depending on the content of their answers they were asked to follow up questions about the topics they came up with, such as:

- *In what way would you say?*
- *Can you please say a bit more about X?*
- *You mentioned X, can I please ask you to say more about you experience in this regard*
- *And how did you find this?*
- *Can you say more about how you felt about...?*
- *Can you say a bit about how that is being considered/affects the way you work?*
- *Can I ask what your thoughts are about this?*
- *Can you describe this please?*
- *What would be the thought process around this?*
- *Do you have any thoughts of your own about this that you are happy to share?*
- *Can you tell me about what that would look like?*
- *Can you say something about you experience of this/x?*

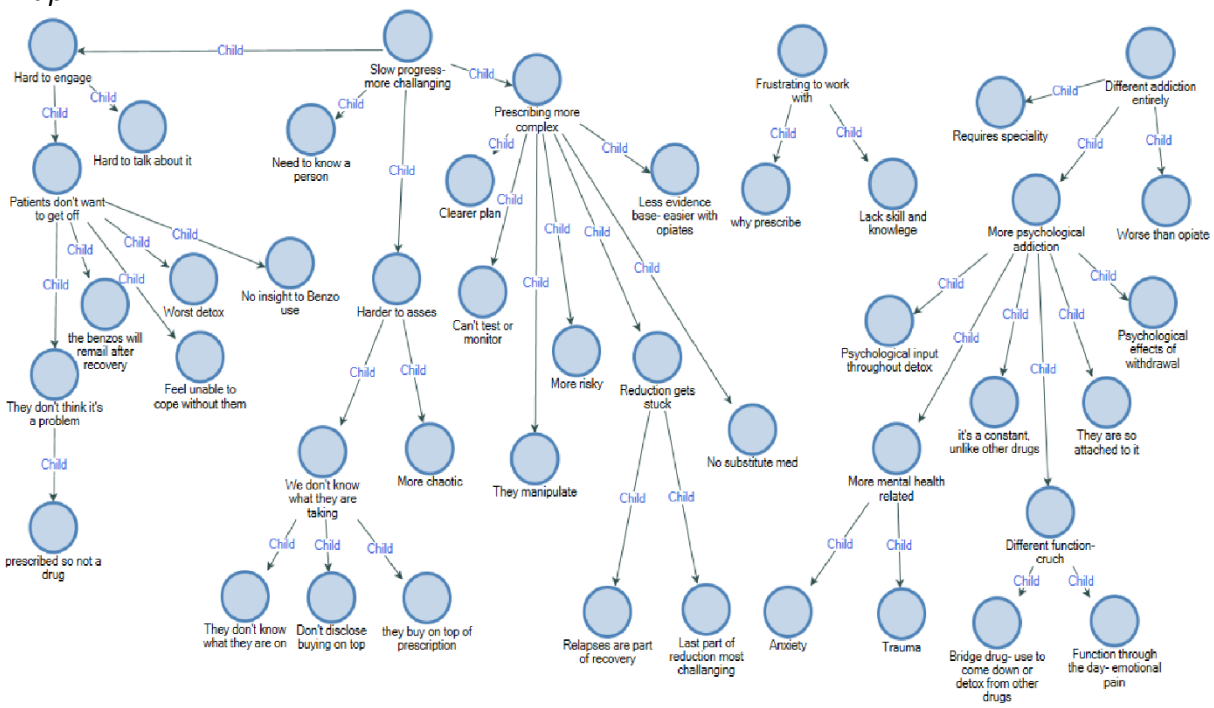
Appendix E

Evolution of themes map

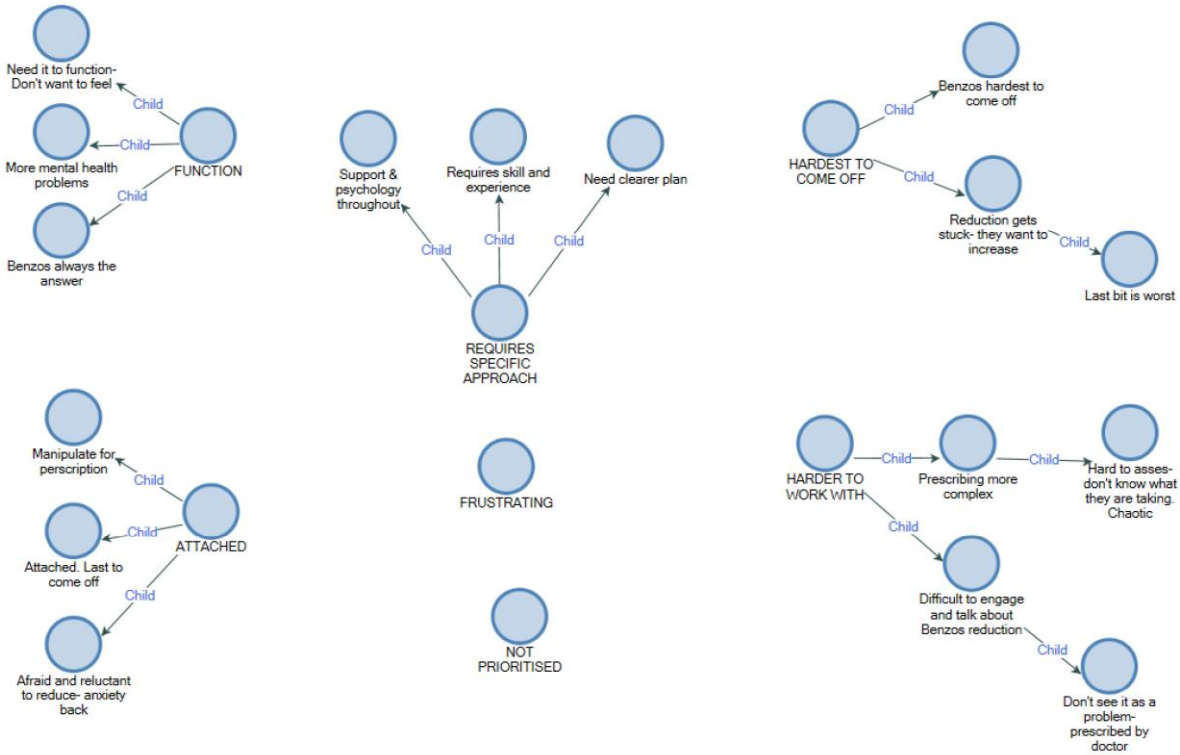
Map 1



Map 2



Map 3



Map 4- final