

Exploring mental health nursing student competence
and confidence in treating novel psychoactive
substance related health issues in the UK



A thesis submitted for the degree of Masters by Research
(MbR)

by

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Declaration

Candidate's declarations:

I, Iain Alasdair Lindsay, hereby certify that this thesis submitted in partial fulfilment of the requirements for the award of Masters by Research (MbR), Abertay University, is wholly my own work unless otherwise referenced or acknowledged. This work has not been submitted for any other qualification at any other academic institution.

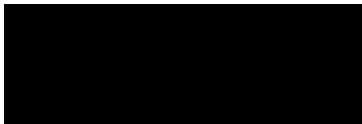
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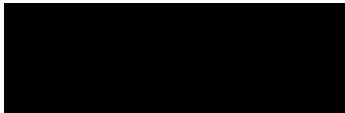


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Certificate of Approval

I certify that this is a true and accurate version of the thesis approved by the examiners, and that all relevant ordinance regulations have been fulfilled.

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Dedication

This work is dedicated to my partner Jess, to whom I will always be thankful to for everything.

Abstract

Context and aims

Novel psychoactive substances (NPS) present a significant challenge to healthcare professionals working in the UK, with them being involved in a substantial proportion of drug-related deaths and hospitalisations in recent years. Healthcare professionals report feeling ill-prepared to respond to the issue, and cite lack of education, knowledge and feelings of under-confidence in relation to NPS as being of particular concern.

One area that has not been researched thus far is student nurses' feelings of competence and confidence in relation to NPS. The author proposes that this area requires urgent investigation, given that many within this population will soon be primary caregivers to individuals who consume NPS.

This study aimed to provide nascent data on the subject described above and utilised a mixed-method approach.

Methodology

The initial phase of this was a series of overview of reviews from which an evidence-based presentation was produced. Five participants were recruited from Abertay University's undergraduate nursing programme through email invite in April 2023. They completed two identical quantitative questionnaires where basic demographic data and information regarding their perceived levels of knowledge and confidence surrounding NPS were assessed - one before and one after watching the presentation. An online focus group followed via Microsoft

Teams, where the same five participants were asked how they felt their knowledge and confidence in the topic related to feelings of competence. Upon completion of this, gathered quantitative and qualitative data was triangulated. Quantitative data was analysed using Microsoft Excel, whilst qualitative data was performed manually using a thematic analysis process. Triangulation of data was also performed manually.

Results

Findings suggested that participants greatly valued knowledge on *clinical vigilance/awareness* about NPS and utilised this as a vehicle through which to interpret NPS-related issues experienced during practice placements. Educational gaps that remained were the lived experience of service users, and the use of psychosocial interventions in managing NPS-related harms. Competence was perceived as being associated with experiential learning and working with more established professionals. Qualitative data suggests that a relationship may exist between qualities of previous healthcare experience and confidence and competence in treating NPS, though quantitative data proved too under-powered to support this during the triangulation process.

Discussion

The results were considered in the light of research regarding the theory practice gap, which was used as a model by which to account for the value placed on clinical vigilance/awareness over other themes by participants, where it was suggested that the relative absence of associated skills seen in this theme may explain why it was more readily internally accepted as an area of confidence. Discussion also touched on participants' suggestion that input in the form of lived experience was felt as valuable to their continued education, and evidence was found that supported this claim. It then turned to the issue of continuous professional development (CPD) in the context of substance misuse more generally, where it was found that this is an often-neglected area, despite the fact

that well produced CPD can address identified educational needs in healthcare professionals.

Conclusion

The thesis concludes by recounting the study, as well as its principal findings. Firstly, that clinical vigilance and awareness was a highly valued theme amongst participants, seemingly due in large part to its ability to act as a lens by which to understand NPS-related phenomena observed in practice. Secondly, that lived experience content from relevant service-user populations is considered as a highly valuable addition to any educational resource concerning psychosocial interventions - one that was seemingly viewed by participants as necessary to increase feelings of confidence in this theme.

The conclusion suggests that the study is subject to limitations, largely on the basis of its small sample size, though if considered – as intended – to be a small scale exploratory/pilot study in a relatively data-poor field of research using a mixed method design, then it can be seen as relatively robust.

It then ends by discussing the anomaly that although health professionals in the field of substance misuse have expressed a need for greater support in education/CPD, this is not addressed by Scottish or local-level government strategies, despite the current public health crisis caused by record levels of drug-related-deaths that the country has been experiencing in recent years.

Abstract word count: 693

Key words: Novel psychoactive substances; nurse education; nurse undergraduate education; substance misuse nursing; continuous professional development; mixed methodology research

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Table of abbreviations

ADHD - Attention deficit hyperactivity disorder

ACMD - Advisory Council for the Misuse of Drugs

CBC - Complete Blood Count

CNS - Central Nervous System

EMCDDA - European Monitoring Centre for Drugs and Drug Addiction

IM - Intra-muscular (usually in the context of sites for injection)

IV - Intra-venous (usually in the context of sites for injection)

MB - Myocardial Band test
 MOR - Mu Opioid Receptors
 MWHSWM - Men Who Have Sex with Men
 NBOMe - N-(2-methoxybenzyl)-2,5-dimethoxy-4-substituted phenethylamines
 NECPAA - Network of Early Career Professionals in Addiction Medicine
 NEPTUNE - Novel Psychoactive Treatment UK Network
 NMC - Nursing and Midwifery Council
 NPS - Novel Psychoactive Substances
 NSO - Novel Synthetic Opioid
 OAT - Opioid Agonist Therapy
 OAT CPD - Opioid Agonist Therapy Continuous Professional Development
 OUD - Opioid Use Disorder
 SCM – Supply Control Measures
 SCRA - Synthetic Cannabinoid Receptor Agonist
 SMI - Severe Mental Illness
 UNODC – United Nations Office on Drugs and Crime

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Introduction

“It’s very much... these are new drugs. These are new things that we maybe don’t have in our frame of reference ... as much as we might with other drugs”

(Participant 4)

1.1 Context

Novel psychoactive substances (NPS) are classified by the United Nations Office on Drugs and Crime (UNODC) as any “substance of abuse” that does not come under legal control under either the 1961 Single Convention on Narcotic Drugs or 1971 Convention on Psychotropic Substances, and has the potential to cause harm to public health (UNODC, 2022a). At national level, definitions often vary in their minutiae from this interpretation. For example, the UK’s Crown Prosecution Service define NPS as substances that are designed to emulate the effect of illegal substances controlled under the Misuse of Drugs Act 1971 (Crown Prosecution Service, 2021). This variance in definition may even be displayed at regional/local government level, with a definition proffered by the National Records of Scotland stating simply that NPS are “the kinds of substances that people have, in recent years, begun to use for intoxicating purposes” (National Records of Scotland, 2021).

Regardless of definition employed, the use of NPS by recreational drug users in Scotland and across the UK more generally is a subject that has garnered much attention in the last decade (Scottish Government, 2016). Whilst the reasons for the emergence of this new drug market are complex and manifold (EMCDDA, 2017) what is certain is that the physical and psychological harms stemming from their use have been noted in academic literature as being both potentially severe and differing somewhat in nature to those incurred by use of the more established drugs (Tracy, Wood and Baumeister, 2017).

NPS use may be considered of particular concern in mental health settings. In one Italian study examining relative rates of NPS use between young people in the general population and those with psychiatric comorbidities found that those in the latter group were significantly more likely to have used NPS (Martinotti et al., 2014). To give a more local context, a review of patients discharged from general psychiatric wards at the Royal Edinburgh Hospital between 1 October 2015 and 31 March 2016 found that 6.6% of patients were NPS users, who were more likely to have presented at admission with symptoms consistent with drug-induced psychosis than non-NPS users (Bennett et al., 2017).

In the Scottish context, early evidence seemed to suggest that the introduction of government legislation that allowed for innovative legal measures - such as Temporary Class Drug Orders - were hindering the importation and distribution of certain NPS and reducing the number of patients presenting with acute toxicity due to their use (Pettie *et al.*, 2018). However, figures published by the National Records of Scotland indicate that in the 1,330 drug-related deaths recorded in Scotland in 2021, NPS were implicated in or contributed to fatalities in 825 cases, or 64% of the overall total (National Records of Scotland, 2022a) thereby implying that legislation had not been as impactful in reducing harms stemming from NPS use as was initially hoped.

Rates of NPS usage in the general population in the UK in recent years are relatively low, with figures suggesting that 0.4% of 16-59 year olds in England Wales had used consumed them in the period from March 2020 to June 2022 (Office for National Statistics, 2022), whilst lifetime use of NPS has been estimated at 2.6% of 16-59 year olds in Scotland (Scottish Government, 2021a). However, the impact of the NPS phenomenon on certain vulnerable sub-populations has increased in recent years. For example, NPS are estimated to be used by between 20 and 87% of the UK's homeless population (Coombs *et al.*, 2023). NPS use is also a significant issue in the UK's prison population, with NPS being identified in 9,114 of 20,295 of drug finds in English and Welsh prisons in the 12-month period prior to March 2021 (Ministry of Justice, 2022). In regard to this latter population, research by Duke *et al.* (2023) suggests that in all drug

related deaths within the English and Welsh prison system over the period of 2015-2020, NPS were the sole substance implicated, with their prominence in this context increasing over the time period.

For clinicians, service users presenting with NPS associated harms pose a unique array of challenges. Schifano *et al.* (2019) note that the pharmacokinetics and pharmacodynamics of the majority of even recognised NPS remain, as of yet, unexplored. This makes the creation of viable treatment pathways for adverse effects encountered after their use difficult. One strategy postulated by Wood, Ceronie and Dargan (2016) involves the identification of what established drug or drug family the NPS in question is designed as an analogue for by monitoring patient symptoms and then utilising pre-existing treatment strategies for these accordingly. However, Wood, Ceronie and Dargan (2016) themselves stipulate that NPS often present with additional toxicities that may not be found in the drugs they are intended to mimic that carry increased risks for treatment. The synthetic cannabinoid receptor agonist (SCRA) class of NPS is a salient example of this.

First generation SRCAs were designed to mimic the actions of cannabis by sharing affinity for the CB1 and CB2 cannabinoid receptors in the brain though, unlike cannabis, they are often full rather than partial agonists of these (Tai and Fantegrossi, 2016). This in turn means that users of SRCAs frequently present with far more acute toxicities than those who use traditional cannabis, which manifest in symptoms ranging from psychosis and aggression to depressed breathing, unresponsiveness and tachycardia (Fattore, 2016). Treatment of aggression after consumption of SRCAs is particularly challenging. In one study that examined harms associated with NPS-using individuals admitted to an acute psychiatric facility in London, SRCAs were by far the most commonly used class of NPS at 91% of their sample (Shafi *et al.*, 2017) and use of NPS more generally was found to be significantly associated with concurrent violence and aggression either during preadmission or admission and the utilisation of rapid tranquilisation by clinicians. Use of rapid tranquilisation in these cases may give some cause for concern, given that many drug formulations used in rapid tranquilisation can

exacerbate the potential physical side-effects of SCRAAs identified above, with lorazepam and haloperidol – often used in conjunction during rapid tranquilisation – being associated with subsequent respiratory depression and tachycardia respectively (Paton *et al.*, 2019).

Further evidence pertaining to the UK as a whole implies that relevant legislative measures such as the Psychoactive Substances Act (2016) have failed to impact rates of NPS usage, with a study by (Deligianni *et al.*, 2020) suggesting that usage had increased amongst young people after implementation of the aforementioned Act, whilst awareness regarding the health risks inherent in their consumption. In the Home Office's own evaluation of the Psychoactive Substances Act, it is noted that although NPS usage had fallen in the general population - as discussed in more depth above – rates of NPS use in vulnerable groups such as prisoners and the homeless had remained largely the same or increased. Further, the same evaluation comments that although NPS-related deaths had reduced in England and Wales, they had increased by a significant amount in Scotland (Home Office, 2018).

The above gives some insight as to the potential complexity and diversity of harms that NPS use can initiate, as well the further complexities that treatment of symptoms presents. It is, perhaps, unsurprising that clinicians often express anxiety and concern regarding their knowledge about NPS and treatment of service users presenting with complications from their use (Wood, Ceronie and Dargan, 2016).

1.2 Clinician knowledge and confidence regarding NPS

Studies concerning UK-based clinicians' perceived confidence, competence and level of knowledge regarding NPS are limited, though the extant body of work suggests that healthcare professionals feel under-confident and under-prepared to facilitate treatment of health issues arising from their use.

A study by Guirguis *et al.* (2015) of London-based pharmacists' knowledge of NPS found that of 54 pharmacists surveyed, 40 (74%) considered themselves as having only poor to basic knowledge of NPS, and 50 (93%) felt that their level of knowledge was inadequate. Further, 16 (30%) respondents were unaware of any substances misused in an NPS context of 36 listed.

In a study of UK-based psychiatrists by Owie *et al.* (2017), of 108 survey respondents only 8 (7.4%) felt they had adequate knowledge of NPS, whilst 70 (64.8%) felt they did not, whilst 30 participants did not answer the question. Sixty-eight (63%) of respondents agreed that they required more training regarding NPS, 10 (9.3%) did not, and again 30 did not answer that specific question.

A survey of London-based emergency medical physicians and nurses by Wood, Ceronie and Dargan (2016) sought to ascertain their perceived levels of knowledge and confidence in relation to treatment of NPS toxicity in comparison to more established substances of misuse by use of a five-point Likert scale. Survey results of 188 respondents (consisting of 106 nurses and 82 physicians) found that both physicians and nurses were significantly less confident regarding treatment of NPS than orthodox drugs, with physicians' mean average score – inclusive of standard deviation - for confidence in treating classical substances being 3.0 ± 0.9 and 2.1 ± 1.1 for NPS, whilst nurses' scores for this were 3.0 ± 1.1 and 2.3 ± 1.1 for orthodox drugs and NPS respectively. A similar pattern emerged regarding perceived knowledge, with physicians' mean average rating of their perceived knowledge levels regarding management of acute toxicity arising from orthodox substance being 3.1 ± 0.8 and 2.1 ± 1.0 pertaining to NPS, and nurses' rating this as being 2.9 ± 1.0 for classical drugs and 2.1 ± 1.0 in relation to NPS.

One UK study examining healthcare professionals' self-ratings in terms of confidence and knowledge surrounding NPS issues found that whilst only 20% of nurses (inclusive of general, substance misuse and mental health) surveyed felt that their understanding of the subject was "Good/very good", 89.1% of the same population felt that "Knowledge on NPS/legal highs was fairly/very significant in work" and in health care professionals surveyed more generally

(nurses, pharmacists and doctors) 92.1% stated that they did not receive adequate learning material regarding NPS to care for their patients safely (Ramos *et al.*, 2020).

1.3 Rationale

An area that has not received much attention in the literature to date is awareness and confidence of nursing students in issues pertaining to NPS. As part of the preliminary research for this project the author performed scoping searches of PubMed, SCOPUS and Google Scholar to locate material regarding student nurses' awareness of NPS related issues, with no published material on the matter being found. The sole source of any data on this theme that could be found was from the aforementioned study by Ramos *et al.* (2020). Two percent of the 197 strong sample of healthcare workers surveyed in this study self-described as "students", with no clarification given as to the discipline these students were aligned to and no separate analysis of this sub-sample outwith the study's larger professional groupings provided.

The role of the student nurse in practice is not directly described by the Nursing and Midwifery Council (NMC) – the statutory body that regulates nursing practice in the UK. However, the organisation's *Standards for pre-registration nursing programmes* policy (Nursing and Midwifery Council, 2023a) states that educational institutions should – at a minimum – ensure that students' health and character are of an adequate standard to practice nursing in a safe and effective manner. Further, this guidance states that educational providers make certain that students at point of entry demonstrate values that align with *The Code* (Nursing and Midwifery Council, 2023b) – the code of conduct registered nurses have a statutory duty to abide by. To refer again to the aforementioned educational standards, these stipulate that students must also show ability to develop behaviours that accord with *The Code* (Nursing and Midwifery Council, 2023a). Amongst these behaviours, nurses (and therefore student nurses implicitly) must practice effectively in a manner that is evidence-based,

continuously maintaining and developing relevant skills and knowledge to do so (Nursing and Midwifery Council, 2023b).

Educational providers are asked by the NMC to ensure that students receive placement experiences (or – at a minimum – have learning opportunities to develop adequate skills to nurse relevant populations at point of registration) in the following areas: mental health, adult (or general), children’s (or paediatric) learning disability services (Nursing and Midwifery Council, 2023a).

Substance misuse is notable in its absence from this list of nursing specialities, despite it being recognised in the UK as a distinct role with its own set of specialist skills and accompanying knowledge-base (Public Health England, 2017a). Whilst literature regarding qualified/newly registrant nurses’ preparedness for accepting the role of substance misuse nurse in the UK is lacking, equivalent evidence from the United States of America suggests that - at least that in that country - nurses are ill-prepared at under-graduate (Lanzillotta-Rangeley *et al.*, 2020), registrant (Compton and Blacher, 2020) and even post-graduate/nurse practitioner level (Wright *et al.*, 2022). The researcher notes that the last three previously cited articles all explore this deficit in nursing knowledge in the context of the recent opioid deaths crisis in the USA, which bears parallels with the previously explored current drug deaths crisis in Scotland, not least in the fact that the rise of NPS use has proven to be significant factor in both (Pierce *et al.*, 2021). The researcher contests that if: qualified nurses and other practitioners in the UK feel under-prepared to be involved in NPS-related healthcare (as demonstrated in **Section 1.2**); substance misuse more generally is not prioritised as an essential area of practice for under-graduate students, and – in place of any definitive evidence to the contrary – are therefore under-prepared for this field at point of registration, then student nurses must reasonably be assumed to be under-prepared to provide adequate nursing to patients affected by NPS-related health issues.

Given the increasing relevancy of NPS to healthcare in Scotland in light of its dramatically increased rates of drug deaths, the author proposes that this is an

area that urgently requires research, as evaluation of deficits in knowledge of current students can allow educators to attune curricula to avoid future cohorts of nurses experiencing the anxieties that current registrants express.

1.4 Aims

This research had several aims, all of which centred on the necessity of this being an explorative, pilot study. The first was to assess subjective levels of knowledge, competence, and confidence in relation to the treatment of NPS-related health issues amongst undergraduate nursing students. The second was to assess the impact of a specifically designed educational resource on these feelings. A third aim was to identify improvements to future, similar educational resources, also in relation to the concepts of knowledge, competence, and confidence.

1.5 Objectives

1. Gather baseline quantitative data regarding a sample of undergraduate student nurses' feelings of knowledge, competence, and confidence in relation to treatment of NPS related health issues.
2. Investigate the effect of an evidence-based educational resource on the same sample's feelings on the above subjects, also in a quantitative manner.
3. Establish possible improvements to the educational resource, as well as proactively inform similar future educational resources aimed at undergraduate nurses more generally. This was to be achieved by the gathering of qualitative data from the same sample.

1.6 Methodology

This research project comprised two elements. The first of these was a series of four overviews of systematic reviews, designed to determine best practice for treatment of physical and psychological harms stemming from the use of NPS. The findings of these (in the form of identified and collated clinical recommendations organised thematically) was used to inform an evidence-based presentation on the topic. This was considered a necessary element, due to there being no current data – as attested to in **Section 1.3** - as to levels of knowledge regarding NPS related issues seen in undergraduate nursing populations of any year of study or discipline. To ensure that qualitative data gathered in a subsequent research element was meaningful and relevant, establishing a basic “standard” level of knowledge and familiarity with NPS-related health issues and their treatment was deemed prudent, given that recruited participants may be entirely naïve to pertinent issues, based on level of nursing-specific professional education attained, time worked in healthcare overall and life experience. The presentation was also considered a vehicle by which to gather rudimentary early data concerning the efficacy of educational content on NPS for nursing student populations.

The second part consisted of a focus group where undergraduate nursing students’ feelings of competence and confidence surrounding treatment of NPS-related health issues was assessed at baseline using a designed pre-test questionnaire (please see **Section 1.28** and **Appendix 8**). A recorded version of the presentation was then made available to participants that they watched prior to a focus group, during which a series of semi-structured open questions were asked of them to establish efficacy of the presentation, ascertain their perceived levels of competence and confidence and remaining educational needs in relation to NPS in a qualitative manner. Finally, a post-test questionnaire – identical to the pre-test version – was issued to participants to measure any changes from baseline quantitatively.

1.6.1 Considerations during research design

Alternative methodologies that may have been employed to achieve the aims of the study would have included the use of either an entirely quantitative or entirely qualitative design.

A quantitative approach, such as the use of a survey, would have allowed for the use of a larger – and hence more representative (Queirós, Faria and Almeida, 2017) – sample, resulting in potentially more reliable results (Choy, 2014). However, such an approach also has a distinct disadvantage. Quantitative methods - including surveys – present the danger of gathering data that does not elucidate the social context behind why participants have answered in a given way (Sutton, 2022). Therefore, use of a purely quantitative design risked underlying meanings and relationships observed in gathered data being inadequately interpreted (Rahman, 2016).

A purely qualitative design would have had a number of advantages. Firstly, an entirely qualitative methodology would have allowed for a deeper interrogation of relationships between phenomena seen in results (Moriarty, 2011) in a way that a quantitative design could not. Secondly, qualitative methods that feature researcher-participant interaction (such as focus groups or interviews) allow for richer data at the point of collection in terms of enabling lines of enquiry to be adapted to individual context (Rahman, 2016). As with quantitative designs, though, a strictly qualitative approach would present several issues. Purely qualitative research relies largely on the interpretation of data by the researcher (Jain, 2021). Related to this first disadvantage is that the content shared by the participant in qualitative research is selective, meaning that there is the possibility that key issues could remain unidentified (Choy, 2014).

The approach that was ultimately selected – a mixed method approach consisting of both quantitative and qualitative elements – was felt to be the most appropriate method to satisfy the aims of the current research. Whilst a full

justification for this choice can be found in **Section 1.27** a brief overview of why this approach was ultimately utilised is presented below.

Well-designed mixed method research can allow for deficits in qualitative and quantitative approaches – such as the ones identified above – to be ameliorated or eliminated (Malina, Nørreklit and Selto, 2011). A significant component of this advantage is mixed methodology's ability to generate both exploratory and confirmatory knowledge within a single research project (Ivankova and Wingo, 2018). In expansion of this point, a mixed methods approach grants the researcher the potential to explore complicated elements of a phenomenon in a symbiotically systemic (i.e., using an expansive consideration of manifold, ill-controlled variables) and analytical (assessing fewer, more tightly controlled variables in depth) manner (Malina, Nørreklit and Selto, 2011). Proponents of mixed-methods research note its suitability in both health science (Coyle *et al.*, 2018) and educational research (Bagur *et al.*, 2021) due to its inherent suitability for interrogating complicated phenomena in the manner just described. Given the exploratory nature of the current project and its combination of health science and educational concerns, a mixed methodology was considered as a highly appropriate vehicle of study.

However, this is not to say that mixed method approaches do not have disadvantages. These will be presented below, with design features of the research protocol that was used to combat them also presented.

Mixed method research is noted for being intensive in both resources and time (Mackey and Bryfonski, 2018) and intimidating in its potential complexity for the novice researcher (Giddings and Grant, 2006). So as to address both problems simultaneously, it was agreed by the research team to utilise a small, manageable number of participants to form the study's sample, which is considered a viable option in exploratory research where flexibility of design must be considered (Haile, 2023).

A common criticism of mixed-methodology levelled by quantitative-focused researchers is that collinearity – predictors being falsely correlated with one another in a statistical model (Vanhove, 2021) – is highly prevalent in mixed-methodological research where textual data is quantitatively analysed, particularly in projects where small sample sizes are used (Driscoll *et al.*, 2007). Following recommendations from the literature, text transformation was actively avoided (Driscoll *et al.*, 2007), and instead quantitative data was only utilised in a manual concurrent triangulation process alongside qualitative data more fully described in **Section 1.35**.

A third difficulty in mixed methods research is the inherent challenge in combining qualitative and quantitative data sets in a meaningful and accurate manner. One suggested strategy to overcome this issue is careful consideration of the relative weighting given to the value of qualitative and quantitative strands in a study during its design phase (Dawadi, Shrestha and Giri, 2021).

Although this study ultimately employed a concurrent triangulation process in its data analysis, priority was given to qualitative data overall. The quantitative strand was largely used to measure relative efficacy of aspects of the designed educational presentation on NPS in absolute terms – hence its use of pre and post-test elements.

The qualitative strand was used to not only inform interpretation of this, but to a far greater extent provide a more nuanced and expansive understanding of what participants' feelings of competence and confidence in relation to treatment of NPS-related health issues were. This was considered as highly necessary at the inception of the study, seeing as its primary purpose was to begin to establish a modest data-set in this field of study by which to direct later research efforts. Quantitative data also informed interpretation of the exploratory qualitative data to a degree, acting as a partial - this by no means definitive – confirmatory adjunct to this part major part of the research data.

Given that the qualitative data was given primacy, especial exploration of possible challenges and how they were addressed for this part of the research process must be presented.

The researcher is from a nursing background and is a member of teaching staff at the university that the students who were recruited as participants attended and acknowledges that this undoubtedly contributes to issues of insider perspective and positionality in the research.

Insider perspective can be thought of as the researcher belonging to some of the same cultural or social groupings as the subjects of research (Ross, 2017). Traditionally, qualitative research has emphasised a sharp distinction between this insider status and that of outsiders to an examined community, with each position entailing their own sets of benefits and deficits to the researcher process (Kee *et al.*, 2001). However, contemporary post-structuralist/modernist understandings of qualitative research suggest that a true, objective and entirely “outsider” researcher perspective is impossible to attain, due to any researcher having an innate set of identities that inform their position and therefore biases (Chavez, 2008). Therefore, many modern perspectives encourage researchers to not attempt to reduce consideration of their role to this binary. Instead, they are to acknowledge that theirs is a fluid position, ever-shifting in its varying facets to and from relatively insider-aligned and more outsider-aligned positions, and that this *positionality* is to be constantly scrutinised, reflected on and ultimately expressed in relevant research outputs (Soedirgo and Glas, 2020). This process of conscious consideration of one’s positionality can be summarised as the practice of reflexivity (Råheim *et al.*, 2016). Further, reflexivity in the context of positionality also involves the researcher’s interrogation of the impact of personal and professional point-of-view on a multitude of decisions made during the research process, including selection of topic of investigation, methodology used and results (Yip, 2023).

Whilst differentials in relative power may be considered as satisfactorily addressed through use of deliberate and methodological reflective practice in the

context of nurse-researcher/nurse-participant qualitative research (Aburn, Gott and Hoare, 2021), such dynamics in educator-researcher/student participant projects could be assumed as inherently more problematic and intractable (LeCompte, 2015). However, there is a strong tradition of action research in educational practice (Cohen, Manion and Morrison, 2017).

The current study cannot properly be considered as action research, as it did not seek to address a specific, practical educational problem (Clark *et al.*, 2020) and instead looks to generate novel data by which such problems may later be identified. However, the field of action research was considered as a valuable avenue for finding solutions to problems related to positionality and reflexivity, given that it very often concerns educators utilising students as participants in their studies (Gibbs *et al.*, 2017).

Participation in the current research was entirely voluntary, with participants having the right to withdraw from the study at any point prior to anonymisation of their data. This was clearly mentioned on distributed consent to participate forms and was reiterated to participants at the start of the focus group. The provision of such information is considered a key element of action research (Cohen, Manion and Morrison, 2017).

Ethical action research must make a conscientious effort to not be coercive in nature (Banegas and Villacañas de Castro, 2015). In the current project, the same consent to participate form made it clear that there was no tangible reward for participating, Participation did not result in any preferable treatment from the researcher in their role as a teaching fellow in terms of grading or similar actions/interactions.

However – in the interest of reflexivity – the researcher discloses that they have sent links to journal articles on NPS-related issues to one of the participants and advised two other participants on possible substance misuse adjacent practice placements as part of their elective placement applications via email correspondence. The researcher would like to clarify that such correspondence

was instigated spontaneously by each participant in question after their involvement in the research was completed, and help provided was in no way contingent on individuals' involvement. Further, the author contests that such measures can be considered as – loosely – aligned to the concept of participatory action research. This model of action research emphasises empowerment and democratisation of research processes (Cohen, Manion and Morrison, 2017), with empowerment of participants' being expressively linked to allowing them to engage in and maximise their own independent research potential in a given context (LeCompte, 2015).

Although the participants could not fully be considered as peer researchers in the current project, they can to a degree be seen as having been peer researchers in as much as they can be somewhat viewed as fulfilling the advisory, or most nascent form of peer research (Roche, Guta and Flicker, 2010). There is a debate in the literature on whether participatory action research should be considered as a subset of action research or a separate research clade in its own right (Cohen, Manion and Morrison, 2017), though in either case participatory action research often utilises a strong peer-researcher element (Chen *et al.*, 2023). Under the advisory model of peer research, peer-researchers are to advise and steer elements of research during its early phases (Roche, Guta and Flicker, 2010).

Whilst the participants in the current study were not advising on the research's own design in any way, an overriding aim of the project was to inform later educational resources on NPS for undergraduate nurses, and a question utilised in the focus group - *What gaps in your knowledge about NPS remain after watching the presentation, and what particular topics related to NPS do you think would be valuable for you to learn more about as a nurse?* – was designed with the specific intention of addressing this in a participant-focused/led manner, in inviting the participants to help develop later educational resources, with this intention also clearly being stated to the participants in the rewards section of consent to participate form, which has already been discussed. The researcher

posits that this measure aligns well with the advisory model of peer/participatory research (Roche, Guta and Flicker, 2010).

Moreover, the literature pertaining to positionality/reflexivity advises that qualitative research should be considered as an innate attempt to reduce as far as possible existing separation between the researcher/researched, part of which should be an inherent assumption that no knowledge generated within well designed qualitative research should be assumed as being entirely researcher-led, with participants often holding a high degree of ownership of eventual outputs. This proved to be the case for much of the participant discourse during the focus group, especially during their answers for the aforementioned question. An example here is participants' statements and discussion on the relative value of lived-experience content in any future educational resource, which was spontaneous and non-moderator directed. The researcher proposes that this is some evidence that – in feeling able to express educational needs freely and make spontaneous recommendations – participants felt at least some degree of ownership of the data that was generated, and therefore had felt to an extent autonomous in this process.

The researcher acknowledges that reflexivity and awareness of one's own positionality extends to all elements of any research design (Gary and Holmes, 2020), and invites the reader to consider relevant sections discussing how research decisions were reached as being at least in part related to this.

In terms of sections on thematic analyses processes (i.e., thematic analysis of collected clinical recommendations and thematic analysis of qualitative data from the focus group), both of these were collaborative processes between the researcher and their supervisors, who all share fairly similar professional backgrounds (principal researcher and one supervisor from a mental health nursing background, other supervisor from a counselling background). The reader will note that the relevant section describing how consensus was developed is more in-depth for the former thematic analysis process. The researcher proposes that in relation to this first instance - although the research

team all came from similar professional backgrounds – one (the principal researcher) was relatively more highly informed about NPS at the outset, and debate on meaning and its application to a nursing and general clinically was more intensive here due to this difference. During the latter thematic analysis of focus group data, all on the research team were approaching this data from a more aligned position from the offset, not only in terms of shared similar professional background but also in terms of understanding of NPS-related issues and how themes that emerged from the former thematic analysis process were to be related to this context, with this being a major factor in why consensus was more readily reached and therefore less worthy of comment. In retrospective consideration, the researcher feels that both stages of thematic analysis could have been made more robust if professionals from other clinical backgrounds who were more informed on NPS issues prior to their involvement (i.e., knowledge on the subject had been developed previously and independently of their interactions with principal researcher and had not been informed primarily through said contact).

This may have allowed for a more in-depth form of member-checking in the context of positionality/reflexivity (Finefter-Rosenbluh, 2017), with possibly more robust and valuable interpretation of results in turn. This issue of member-checking and other elements germane to positionality/reflexivity and other aspects of qualitative research more generally – such as use of participant debriefing and the addressing of social desirability and self-selection bias issues – will be explored in the limitations section.

1.6.2 Overviews of systematic reviews

The review of literature consists of four overviews of systematic reviews. This research protocol was selected for several reasons. Due to the timescale available to the researcher, the limitation that they would be working individually and the amount of published material regarding interventions for NPS available, a rapid yet effective methodology for synthesising evidence was required. Smith

et al. (2011) discuss the growing problem of an ever-expanding and overwhelming volume of academic material – both in the form of individual studies and systematic reviews - available to those aiming to develop clinical guidelines. They further note the growing need within this same group for more expeditious methods of synthesising material, though mention the paucity of evidence to support the use of so-called ‘rapid reviews’ and instead recommend ‘systematic reviews of reviews’ – a synonym for ‘overview of systematic reviews’ (Hunt *et al.*, 2018; Aromataris, *et al.*, 2015) for these objectives. The primary aim of the literature review was to inform the content of an educational presentation for undergraduate nurses, and this purpose can be considered as akin to formulation of clinical guidance, justifying the use of overviews. A further salient feature of overviews is their aptitude for synthesising data regarding the efficacy of multiple interventions for the same condition (Aromataris *et al.*, 2015; Lunny *et al.*, 2017) making it ideal for the purposes of this research project. Finally, the Joanna Briggs Institute emphasise overviews’ facility in addressing a wide range of issues relating to a considered topic (Aromataris *et al.*, 2020) which – given the breadth of categories of substances that potentially fall within the term NPS and the multitude of harms that they can cause – again, validates the use of this research strategy. Further, the majority of design features seen in overviews of reviews will be familiar to researchers who have previously enacted standard systematic reviews (Aromataris *et al.*, 2015). Given that the researcher has prior experience of the latter methodology, the decision to pursue use of the former seemed reasonable.

It is worth noting that a number of sub-categories of overviews of reviews exist, including what are described as scoping overviews of reviews. These are characterised as facilitating synthesis from a multitude of different types or standards of reviews to produce an overall evidence-base (Bougioukas *et al.*, 2023). A further salient feature of this sub-category is its potential flexibility in design, which allows for an iterative element to the process followed (Schultz *et al.*, 2018). Given the exploratory nature of the research (from the perspective of the researcher’s relatively nascent knowledge level of the subject) this was considered of benefit by the researcher, as it would allow for adaptations to be

made to the process based on emergent knowledge, provided that transparency of the finalised procedure was maintained (Schultz *et al.*, 2018). Therefore, the design of the overviews of reviews used in this study can be considered as scoping in nature, as they were not overly prescriptive as to the definition of systematic review used. However, although employment of critical appraisal methodology is not considered an essential feature of scoping overviews (Bougioukas *et al.* 2023), this and other aspects common to overviews of reviews overall were retained, though adapted to the needs of the research.

1.6.3 Design of research questions

This first part of the research consisted of designing a series of research questions to ascertain best practice in treatment for NPS-related health issues. This was achieved by the formulation of research questions using the Population, Intervention, Comparator and Outcome – or PICO – formulation, which is widely considered a reliable and effective framework for designing research questions for healthcare research (Aveyard, 2007). For each research question, population was considered to be people requiring treatment for adverse physical and mental health harms – including dependence or addiction - after consumption of NPS intervention was considered as treatment given, comparator was omitted, and outcome was efficacy of treatment.

These research questions were in turn adapted for each of four broad classes of NPS as described by Tracy, Wood and Baumeister (2017): stimulants; synthetic cannabinoids; hallucinogens and depressants. This system of categorisation was chosen over others available for several reasons, with justification for the rejection of other systems being presented below.

Several organisations at UK national and international level offer categorisation schemas for NPS.

The UNODC's categorisation system is useful in as much as it is generally comprehensive. For example, it categorises most major stimulant drug groups

(aminoindanes, synthetic cathinones and piperazines) as well as stimulants with hallucinogenic properties (phencyclidine-analogues, phenethylamines and tryptamines) relevant to the NPS context (UNODC, 2022a). However, their system includes a total of eight categories in total, which was considered an unmanageable number of systematic reviews to be conducted under the research strategy pursued. Further, the UNODC system includes the category *plant-based substances* (UNODC, 2022a), which was deemed as unsuitable for devising later relevant clinical recommendations. Finally, the UNODC system, both in terms of the *Categories of NPS sold in the market* and *Synthetic new psychoactive substances by effect group* includes the category of “other substances” (UNODC, 2022a), which was considered as vague and inadequate.

The EMCDDA’s categorisation method was considered in a very similar manner. As with the UNODC’s system, the EMCDDA’s is in one sense highly comprehensive, in having a total of fourteen distinct categories (EMCDDA, 2023). However, it also includes within these categories the terms “other” and plants and extracts (EMCDDA, 2023). Due to these elements, the EMCDDA’s system was also rejected.

In regards to relevant UK organisations’ categorisation systems, NEPTUNE’s (Novel Psychoactive Treatment UK Network) - in which NPS are divided into the groupings of: predominantly depressant drugs; predominantly stimulant drugs; hallucinogens drugs, and synthetic cannabinoids (Abdulrahim and Bowden-Jones, 2022) bears remarkable similarities to the one employed by Tracy, Wood and Baumeister (2017) that was ultimately utilised. The reader may reasonably consider these two categorisation methods as being effectively interchangeable, with the only reason that the latter has been described in the first instance being that it was the first of the pair to be encountered by the researcher.

The UK’s ACMD offered a relatively early taxonomy for NPS (ACMD, 2011). However, this was considered as being highly unsuitable for the purposes of the current research. This was due to the four categories offered being based not on substances’ primary subjective or physiological effects, nor the pharmacological

to the belong to. Instead the AMCD's system grouped NPS into categories based either on their relative similarities to established substances of misuse or medications, origin of substance on the phylogenetic tree (i.e., originating from plant or fungus), or using the confusing terminology of "[p]roducts with names which give no indication of what they contain" (ACMD, 2011).

Competing categorisation systems offered in the academic literature – such as those proposed by Schifano *et al.* (2019) (synthetic cannabinoids/cannabimimetics; new synthetic opioids; novel stimulants and novel psychedelics; prescription and over the counter drugs) or Newcombe and Measham (2016) (depressant; stimulant; hallucinogen) were felt by the author to lack taxonomic categories that were essential to the aims of the research project. Schifano *et al.* (2019)'s system groups benzodiazepines and z drugs – drugs such as zolpidem or zopiclone, which share similar subjective and physiological effects as well as mode of action benzodiazepines but which are pharmacologically distinct (Kapil *et al.*, 2014) - into prescription and over the counter (OTC) drugs. Benzodiazepines are a major contributor to drug deaths in the Scottish context, with their involvement being implicated in 73% of drug-related deaths in Scotland in 2020 (National Records of Scotland, 2021). Several of the benzodiazepines that are most strongly linked to drug deaths in Scotland – such as etizolam (McPhee, Sheridan and O'Rawe, 2019) – are illegal in the UK, with etizolam becoming formally controlled under the Misuse of Drugs Act 1971 in May 2017 and not being licenced for medical use (Home Office, 2017). In regard to Newcombe and Measham's (2016) system - this was considered too narrow in not including SCRAs as a separate category from hallucinogens, which would potentially result in appropriate papers salient to this family of drugs being undetected during the systematic search phase of the research. Therefore, a system of categorisation that included benzodiazepines regardless of legal status within the UK within its classification of depressants/sedatives generally whilst also including SCRAs in a discrete category was deemed to be the most fitting by the author, with Tracy, Woods and Baumeister's (2017) ultimately utilised.

1.6.4 Search strategy

For each of these independent questions search terms for the population element were tailored to increase efficacy of database searches, where population was considered to be people who had experienced adverse health effects after consumption of the specific family of drugs concerned for each search. For example, the terms 'novel tryptamines' or 'piperazines' were employed in the population criteria for the question concerning novel stimulants. A full list of search terms used for the population element of each systematic search can be found in **Section 1.6.4**.

The comparator element of the PICO question (Aveyard, 2007) was omitted so as to not preclude papers that did not compare treatment of NPS to more orthodox substances and instead focused on the former exclusively.

The search element for outcome/intervention remained the same across all four systematic searches, given that treatment aims and categorisation of possible outcomes from use of NPS (*addiction, overdose* or *withdrawal* as examples) were considered as largely applicable to all four classes identified. Search terms used in this element were: *adverse harm**; *acute harm**; *addiction*; *adverse effect**; *clinical feature**; *clinical guideline**; *clinical implication**; *clinical management*; *clinical practice*; *detox**; *drug management*; *health condition**; *intoxication*; *mental health*; *overdose*; *physical harm**; *psychological*; *toxicit**; *withdrawal*; *misuse*, and *abuse*.

Additionally, a further search element was used in each systematic search that was common to all four. This was labelled as study design and consisted of the search terms *systematic review* and *meta-analysis* and was included to limit results to papers that used a systematic review or similar methodology and, therefore, ensure their fit for the overview of systematic review protocol employed in this phase of the research.

Systematic searches in the manner described above were run on the following dates: SCRA on 21/1/21; sedatives and depressants on 28/1/21; stimulants 28/1/21, and hallucinogens on 5/2/21.

After designing appropriate research questions, searches were run on a series of academic/healthcare databases, namely CINAHL, SCOPUS, Web of Science, and PubMed, by entering chosen search terms in a systematic manner, with each search string being entered into each relevant database in the order of *population/problem* search, *outcome/intervention* search, and then finally *study design*, with searches then being combined.

The aforementioned databases were chosen due to the researcher's familiarity with them and due to their accessibility through the university that they are enrolled with. Further, according to research by Gusenbauer and Haddaway (2020), CINAHL, SCOPUS, Web of Science and PubMed are all considered as being robust enough databases to act as principal evidence sources, with other popular academic search systems such as Google Scholar being found in their research as only suitable as supplementary databases. Given that – essentially – four concurrent systematic reviews were to be performed by a lone researcher, the decision was made to limit the databases used to the aforementioned four. However, the researcher acknowledges that there are some disadvantages to this choice, and these will be explored in the limitations section of this thesis.

1.6.5 Abstract review and critical appraisal process

Once material had been gathered, abstracts were examined for suitability. During this process, abstracts - as well as full papers when required - were initially evaluated through use of inclusion/exclusion criteria devised to establish fitness of papers, including: type of evidence (i.e., confirmation that papers were systematic reviews) contemporaneity of material (were papers published within the last ten years) and specificity of material to the research question. A number of papers were ultimately excluded due to accessibility issues, with normal

requests for access through the university's library being limited or delayed at the time of the abstract review process due to COVID restrictions present at the time.

Papers that were accessible to the researcher and deemed as possibly suitable after abstract screening were then critically appraised. A quality assessment tool was designed by the author that was informed by Critical Appraisal Skills Programme (CASP) Checklist for Systematic Reviews (CASP, 2018) to ensure further robustness of included material to answer the research questions set, and due to the researcher and their supervisory team's familiarity with it. From the CASP checklist, seven questions were included in the final tool, namely: *Did the review address a clearly focussed question?*; *Did the authors look for the right type of papers?*; *Did the review's authors do enough to assess quality of the included studies?* (i.e., is there evidence in the review that its authors considered the rigour/reliability of data presented in its gathered studies); *If the results of the review have been combined, was it reasonable to do so?*; *Can the results be applied to the local population?* and *Were all important outcomes considered?* (questions 1 through 5, 8 and 9 respectively), whilst the questions *What are the results of the review?*, *How precise are the results?* and *Are the benefits worth the harms and costs?* (questions 6, 7 and 10 respectively) were omitted from the final appraisal tool that was developed. These questions were excluded from the developed tool due to the overview of systematic review design of this part of the study, as they were not deemed to impact on the quality of clinical recommendations offered within papers. To be considered suitable for final inclusion, papers had to score four or more (i.e., $\geq 50\%$) when appraised using the developed tool. In addition, the author added the conditions that papers had to be peer-reviewed and had to offer clinical recommendations suitable for nursing in order to be included.

After this process, a combined literature review – consisting of the four separate overviews of reviews written by the author - was written by the author which summarises best practice for treatment of health problems commonly seen in for each of the four classes of NPS. This document was then used as a basis from

which the researcher planned an evidence-based presentation regarding treatment of NPS (please see **Section 1.24**).

1.6.6 Thematic analysis of clinical recommendations

Once the inclusion/exclusion and critical appraisal processes were completed, the clinical recommendations of selected papers were thematically analysed to establish commonalities. This was performed by manually reviewing the papers. Clinical recommendations were paraphrased into the researcher's own words and entered into a spreadsheet (please see **Appendices 2, 3 and 4**) wherein said recommendations were clearly aligned to the paper that they were extracted from.

As per a suggestion regarding the formatting of results of overviews of reviews by Aromataris *et al.* (2015), relevant clinical recommendations were colour-coded by themes to facilitate synthesis and presentation of findings. Again, this process was manual, and no specialised software was utilised. Themes were initially ascribed by the principal researcher and then discussed with their project supervisors. During these discussions initial themes were reduced to four dominant themes overall: clinical vigilance/awareness; management of psychiatric symptoms; management of physical symptoms, and psychosocial interventions. A description of the process of how recommendations were aligned to sub-themes and then these aforementioned dominant themes is presented below.

1.6.6.1 Clinical vigilance and awareness

Recommendations were considered as belonging thematically to Clinical vigilance and awareness if they fulfilled any one of a set of criteria, with these being presented below in **Table 1**. The overriding factor for whether a clinical recommendation was to be considered as belonging to the theme of clinical vigilance/awareness was that it had the potential to usefully inform the nurse decision-making processes in relation to health-related issues originating from

service-users' use of NPS, though not in a manner specific to either psycho-social interventions or the management of physical or psychiatric symptoms. In other words, these recommendations were considered as holding value in making clinicians more aware or vigilant of the possibility of NPS usage (as well as probable qualities of such use) in their patients, though did not suggest direct patient treatment options available to the nurse stemming from this.

Table 1: Clinical recommendation sub-themes included within Clinical vigilance/awareness

Clinical recommendation sub-themes included within Clinical vigilance/awareness		
Sub-theme	General example	Specific example
Advice on identification of NPS use in service-users	Possible issues of identification of NPS use through routine drug screenings	Use of SCRAAs should be determined via clinical manifestations and history patient in lieu of toxicological testing (Akram, Mokrysz and Curran, 2019)
Knowledge of service-user populations where higher rates of NPS use is more likely, and/or population-specific information useful to the clinician in working with populations where NPS may be more prevalent	Commented on service-user populations where specific NPS substances/categories of substance use is more likely	Populations who are especially vulnerable to misuse novel synthetic opioids (NSOs) include: homeless people; those with a MH diagnosis/undiagnosed MH problem; substance misusers outwith treatment programmes; MWHSSWM (Lovrecic <i>et al.</i> , 2019)
Common norms of either consumption or circumstances when consumers may preferably use of specific NPS/classes of NPS though do not explore this in the context of harm-reduction strategies (latter considered instead under theme of psychosocial interventions)	<ol style="list-style-type: none"> 1) Commented on common modes of consumption of a specific NPS 2) Commented on circumstances when service-users may seek NPS substances 	<ol style="list-style-type: none"> 1) U-47700 is most commonly ingested via insufflation and IV injection (Rambaran <i>et al.</i> 2017) 2) Pregabalin may be used by patients to ameliorate withdrawal from other substances or to act as a "bridge" between periods when preferred substances are available to users (Freyenhagen <i>et al.</i> 2016)
Advice on pharmacological aspects of treatment of NPS-related health issues that did not comment directly on physical or mental health outcomes	Unspecified interactions between NPS and prescribed medications	Clinicians should be aware that NPS may have unknown drug/drug interactions that may result in severe adverse effects (Gray <i>et al.</i> , 2016)
Advice on medication-related issues outside of their direct administration	Commentary on preferable preparations of medications in an NPS context	Opioid drugs should always be prescribed in their least abusable preparation available for prison

		populations (Bi-Mohammed <i>et al.</i> 2017)
Advice on physical management and handling of NPS substances	Commentary on the safe-handling of NPS substances by clinicians	Clinicians should avoid direct contact with substances suspected of being NBOMe drugs, should use gloves when handling, avoid touching mouth area after decontamination. Special care should be taken to avoid making substances airborne (Suzuki <i>et al.</i> , 2015)
Preferable values and qualities of clinicians in regard to treatment of NPS-related health issues not directly related to manner of engaging with service-users (latter considered as pertaining to psychosocial interventions)	Willingness of clinicians to engage and be proactive in research regarding NPS	Clinicians should be involved in research into SCRA's, in terms of providing information and access to SCRA users (Akram, Mokrysz and Curran, 2019)
Similarities or differences in treatment of NPS in comparison to more "traditional" or "orthodox" substances of misuse that bear similarities in clinical effects or pharmacological properties, generally, though did not specify this in terms directly applicable to either psychosocial interventions, management of physical symptoms or management of psychiatric symptoms	Noted similarities in clinical presentation between an NPS and other more established substances of misuse	In the event that a patient presents with symptoms similar to overdose with orthodox stimulants though drug screening returns negative results, clinicians should consider NPS use and use appropriate services available to them such as toxicology laboratories (Hohmann, Mikus and Czock, 2014)

1.6.6.2 Psychosocial interventions

Recommendations were considered as belonging thematically to the category of psychosocial interventions when they corresponded to one of two definitions offered by the Committee on Developing Evidence-Based Standards for Psychosocial Interventions for Mental Disorders (2015). The initial one of these relates to the "non-specific" manners of clinician/service-user interactions that are nonetheless important to maintaining or building the therapeutic alliance or increasing service-user engagement in treatment, whilst the second pertains to "specific" strategies that can be aligned more concretely to psychological models of treatment.

Recommendations concerning referrals to or integration with other services/patient transfers were also ultimately considered under the broader theme of psychosocial interventions. The primary reason for this was the relative weighting of such recommendations, with: three specifically recommending consideration of referral to mental health services (Evoy *et al.*, 2021; Marsden *et al.*, 2019; Orsolini *et al.*, 2019); two to psychological services (Guirguis *et al.*, 2017; Marsden *et al.*, 2019); two to substance misuse/addictions services (Brewer and Collins, 2014; Evoy *et al.*, 2021); two to pain management services (Bi-Mohammed *et al.*, 2017; Marsden *et al.*, 2019); one to inpatient/residential services (unspecified) (Rinaldi *et al.*, 2020; Schifano *et al.*, 2016); one to emergency room/accident and emergency departments (Tait *et al.*, 2015), and one recommendation concerning increasing integration with community pharmacies (Schifano *et al.*, 2018).

Of these twelve recommendations, nine were considered as being readily justified as involving a substantial psychosocial component in the Scottish context, specifically those concerning mental health, psychological and substance misuse services. NHS Education for Scotland view psychosocial interventions (of the “specific” type described immediately above) as being a key component of any mental health or psychological treatment strategy (NHS Education for Scotland, 2023). Psychosocial interventions have been an integral feature of the Scottish Government’s substance misuse treatment strategy for some time (Scottish Government, 2018), with this being reinforced in their recent Medication Assisted Treatment standards policy (Scottish Government, 2021a).

The one recommendation concerning referral pathways/service integration for inpatient/residential services (unspecified) was considered in discussion between the researcher and their supervisors as lacking enough clarity to fully align it to psychosocial interventions as a dominant theme, though it was noted that in the Scottish context “residential” is normally understood as pertaining to inpatient mental health or substance misuse rehabilitation services in relation to substance misuse issues more generally (Cockburn *et al.*, 2022).

In regards to pain management, modern interpretations emphasise the centrality of psychosocial interventions to this field of healthcare (Driscoll *et al.*, 2021), and a recent Scottish Government directive on the matter reflects this concern, insofar as it relates to the “specific” formalised and psychology theoretically-informed category of psychosocial interventions described above (Scottish Government, 2022b).

The two remaining clinical recommendations regarded referral pathways/service integration concerned service links to emergency room/accident and emergency departments and community pharmacies respectively. Whilst inclusion of these cannot *directly* be justified as belonging to the dominant theme of psychosocial interventions, these were included within the broader umbrella of psychosocial interventions given that the vast majority of other recommendations concerning referral/service integration pathways. This was done largely to aid in clarity and also due to the Committee on Developing Evidence-Based Standards for Psychosocial Interventions for Mental Disorders (2015)’s mentioning in their definition that psychosocial interventions are broad enough to entail informational strategies pertaining to biological aspects of health, amongst others.

In the case of the recommendation that advised improving links with community pharmacies, this was phrased as a specific example amongst a more general suggestion to improve integration and inter-professional practice across relevant services more generally, which – if interpreted as inclusive of such services as mental health, pain management and substance misuse that have already been explored in the above paragraphs - was felt to align well with modern understandings of biopsychosocial healthcare practices in the multidisciplinary context suggested (Kusnanto, Agustian and Hilmanto, 2018). For clarification, biopsychosocial healthcare approaches are those that recognise the need to address physical/biological, psychological and interpersonal aspects of health in an inter-related, concurrent manner (Lehman, David and Gruber, 2017) with the biopsychosocial model in turn being acknowledged as central to the practice of psychosocial interventions generally (Jensen, 2011).

Psychoeducation and harm reduction were ultimately considered as sub-themes appropriate for inclusion within the dominant theme of psychosocial interventions. Psychoeducation can be defined as the structured and systematic transfer of knowledge from clinician to service-user that is intended to improve health outcomes for a given health condition, often in the context of substance misuse or mental health care (Ekhtiari *et al.*, 2017). Harm reduction is often typified as any strategy intended to reduce possible negative health effects of an activity though which may not inherently seek to dissuade the patient from refraining from said activity entirely, again commonly associated with substance misuse healthcare (Hawk *et al.*, 2017). Within literature regarding substance misuse treatment strategies, psychoeducation is often considered as a key component of harm reduction efforts overall (Meffert *et al.*, 2019), which is in itself commonly aligned with the concept of psychosocial intervention, both in terms of the “non-specific” (Jakubowski and Fox, 2020) and “specific”, theoretically grounded types previously described (Stockings *et al.*, 2016).

The in-depth recommendations regarding the design of withdrawal protocols from synthetic cannabinoids offered by Grigg *et al.* (2019), although featuring elements applicable to management of physical symptoms and management of psychiatric symptoms, was ultimately considered as thematically belonging to psychosocial interventions overall, given their emphasis on “non-specific” psychosocial norms, multidisciplinary team-working, psychoeducation and harm reduction.

Recommendations concerning provision of naloxone to service users were also ultimately considered as pertaining to psychosocial interventions, given that such provision is strongly aligned to harm reduction strategies within the UK (Advisory Council on the Misuse of Drugs, 2023).

Table 2: Clinical recommendation sub-themes included within Psychosocial interventions

Clinical recommendation sub-themes included within Psychosocial interventions		
Sub-theme	General example	Specific example
Manner of clinician interaction with service-users aligned with “non-specific” psychosocial interventions	Recommendation emphasises adopting a non-judgemental approach	For women who are pregnant or are planning pregnancy and use SCRAAs, clinicians should...be non-judgemental (Orsolini <i>et al.</i> , 2017)
Recommendation that clinician employs “specific”, psychological theoretically informed psychosocial interventions	Recommendation that clinician utilise cognitive behavioural therapy (CBT)	Evidence suggests that CBT with a tapered withdrawal protocol may be an efficacious intervention (Darker <i>et al.</i> , 2015)
Recommendation regarding appropriate referral pathways/service integration	Recommendation that referrals to mental health services are considered	HCPs should consider that patients may need better access to dependence and withdrawal focused services and support, including: ... mental health teams (Marsden <i>et al.</i> , 2019)
Consideration of clinician use of psychoeducation strategies	Recommendation regarding appropriate use and dangers of substances that may be misused in an NPS context	All health care professionals should be prepared to provide high quality and well communicated education re. the proper use of fentanyl and the potential dangers of its diversion, misuse or overuse (Cheema <i>et al.</i> , 2020)
Harm reduction strategies	Harm reduction advice regarding mode of or setting of NPS administration	Harm reduction strategies: avoid insufflation or injecting; use a “trip-sitter”; do not “eye-ball” doses (Suzuki <i>et al.</i> 2015)
Provision of naloxone to service users in an NPS context	Provision of naloxone to relevant sub-populations	Naloxone provision to groups vulnerable to opioid misuse or who have high rates of dual diagnoses (such as homeless people) should be a priority (Cheema <i>et al.</i> , 2020)
Withdrawal protocols emphasising “specific” and “non-specific” psychosocial intervention norms, psychoeducation, multidisciplinary team-working and linkage to relevant allied services	Suggested withdrawal protocols emphasising the role of psychoeducation/harm reduction strategies	Clinicians should provide psychoeducation aimed at harm reduction. This psychoeducation should seek to increase patients’ awareness around relevant mental/physical health risks, link SCs usage to presenting MH issues, provision of reduction of use strategies or better harm reduction, and strategies to allow users to see the achievement of increased wellbeing as being linked to vocational and social activities as well as having a healthier lifestyle (Grigg <i>et al.</i> , 2019)

1.6.6.3 Management of physical symptoms

Clinical recommendations were considered as belonging to the dominant theme of management of physical symptoms if they advised directly on: use of medication to treat specified physical symptoms/disorders arising from NPS use; use of mechanical supports (bag and mask ventilation, for example) to treat specified physical symptoms/disorders arising from NPS use, or general consideration of supportive measures pertaining to treatment of specified physical symptoms/disorders arising from NPS use (airways, breathing, and circulation monitoring and support, for example).

Clinical recommendations focused on administration of naloxone as a treatment strategy for adverse physical symptoms/overdose were considered as definitively belonging to the dominant theme of management of physical symptoms if they fulfilled one or more of three conditions. The first of these was if they commented on administration of naloxone in quantities outside of licensed/recommended use. The second was if they concerned clinical adverse physical health events where clinicians may be unaware that naloxone administration is a viable treatment option, such as loperamide overdose (Eggleston *et al.*, 2020). The last was if the recommendation concerned intra-venous (IV) administration of naloxone. This last condition was agreed upon in light of current recommendations by the Advisory Council on the Misuse of Drugs (2023) that only intranasal or intra-muscular naloxone preparations of naloxone be used in take-home naloxone kits. Therefore, the research team felt such recommendations to only be applicable to possible treatment strategies available to the clinician and not service-user focused harm-reduction/psychoeducational strategies in the UK context.

Table 3: Clinical recommendation sub-themes included within Management of physical symptoms

Clinical recommendation sub-themes included within Management of physical symptoms		
Sub-theme	General example	Specific example
Use of medication to treat specified physical symptoms/disorders arising from NPS use	Use of medication to treat seizures after consumption of NPS stimulants	Midazolam or diazepam in the case of seizures (Guirguis <i>et al.</i> , 2017)
Use of mechanical supports to treat specified physical symptoms/disorders arising from NPS use	Use of bag and mask ventilation to maintain blood oxygen levels	Treatment would include... provision of bag and mask ventilation to increase blood oxygen levels [in response to opioid overdose] (Lovrecic <i>et al.</i> 2019)
General consideration of supportive measures pertaining to treatment of specified physical symptoms/disorders arising from NPS use	Consideration of ABC (airway, breathing, circulation support) in event of SCRA overdose	Treatment should be supportive, including ABC management (Piccioni <i>et al.</i> , 2020)
Commentary on administration of naloxone in quantities outside of licensed/recommended use	Commentary on use of higher than usual doses of naloxone in response to novel synthetic opioid overdose	The review could not determine whether or not higher doses of naloxone were more effective or safe for presumed ultra-potent opioid overdoses (Moe <i>et al.</i> , 2020)
Clinical adverse physical health events where clinicians may be unaware that naloxone administration is a viable treatment option	Use of naloxone in cases of loperamide overdose	Naloxone is recommended as a treatment option [for loperamide overdose], though there is little evidence to suggest that this may counter the drug's cardiotoxic effects (Schifano <i>et al.</i> , 2018)
Recommendation concerned intravenous (IV) administration of naloxone	Use of IV naloxone to reverse U-47700 overdose	IV naloxone is able to reverse symptoms of depressed mental state and bradypnea (Rambaran <i>et al.</i> 2017)

1.6.6.4 Management of psychiatric symptoms

Recommendations were categorised under the dominant theme of management of psychiatric symptoms if they: advised on the use of medication to treat specified mental health symptoms/disorders arising from NPS use or advised on the use of non-pharmaceutical interventions in response to specified mental health symptoms/disorders arising from NPS use. This was considered as inclusive of: movement of patient to a low stimulus environment, patient

observation, de-escalation techniques or physical management of violence and aggression (PMVA). In regard to this latter sub-theme, it was originally considered that recommendations concerning de-escalation techniques may belong under the psychosocial interventions dominant themes. However, consensus was eventually reached that such recommendations were more germane to management of psychiatric symptoms, given that the primary purpose of such interventions is preservation of the immediate safety of the relevant service user, clinicians and other patients rather than long-term health outcomes (Accinni, Papadogiannis and Orso, 2021).

Table 4: Clinical recommendation sub-themes included within Management of psychiatric symptoms

Clinical recommendation sub-themes included within Management of psychiatric symptoms		
Sub-theme	General example	Specific example
Advice on the use of medication to treat specified mental health symptoms/disorders arising from NPS use	Use of medication to control hallucinations or psychosis after SCRA consumption	Antipsychotics for hallucinations/psychosis (Kersten and McLaughlin, 2015)
Advice on the use of non-pharmaceutical interventions in response to specified mental health symptoms/disorders arising from NPS use	Use of de-escalation techniques to counter aggression/agitation after novel stimulant consumption	De-escalation (including verbal) should be the primary initial focus in the case of patients presenting with aggression/agitation as the result of NPS ingestion (Schifano et al., 2016)

The researcher acknowledges that the above form of thematic analysis used – i.e., attribution of recognised sub-themes to dominant themes through research team discussion and consensus – may have some disadvantages in light of the professional backgrounds of members of the research team. Specifically, two members of the research team (the primary researcher and one supervisor) have a professional background in mental health nursing, whilst the second supervisor has a counselling background. The researcher posits that having a more diverse research team in terms of professional background may have had been advantageous in number ways. However, this will be explored more fully in the limitations section of the thesis, along with a justification for the strategy that was ultimately pursued.

Sedatives and depressants Overview of Systematic Reviews

1.7 Benzodiazepines and z-drugs – clinical context

Benzodiazepines are a family of substances united by their shared mechanism of action upon the gamma-aminobutyric acid receptor type A (GABA_A) receptor (Maskell and Wilson, 2019). First introduced for legitimate medical practice in the early 1960's (Zawilska and Wojcieszak, 2019), benzodiazepines rapidly saw widespread adoption for treatment of a diverse range of health conditions, most notably as a less hazardous alternative to the anxiolytic barbiturates commonly in use at the time (Wilde, Auwärter and Moosmann, 2021). Benzodiazepines are often organised into the categories of short, medium or long-acting, with individual drugs' elimination half-life and duration of action being the primary factors in deciding where on this spectrum they are placed (Wolfe, 2022). Further, this placement plays a part in determining indications of use for individual benzodiazepines. The legitimate medical uses of benzodiazepines are manifold, including - though not limited to - as sedatives, anxiolytics or anti-seizure medication (Nielsen, Suzanne, 2017), and elimination half-life and duration of action play a part in determining what conditions an individual benzodiazepine is indicated as treatment in medical guidelines. For example, short acting benzodiazepines that feature rapid onset of effects such as midazolam may be utilised as an anti-seizure medication or to provide anaesthesia during short duration surgical procedures (Nikfarjam *et al.*, 2022).

Whilst - from a technical perspective - "true" benzodiazepines share the structural properties of a bicyclic core featuring fused diazepine and benzene rings, in common medical parlance a number of chemically similar substances which share comparable subjective and objective effects to true benzodiazepines are often included in the category of benzodiazepines (Wilde, Auwärter and Moosmann, 2021), and are often characterised as benzodiazepine-type drugs, designer benzodiazepines or novel benzodiazepines within literature concerning NPS (Marland *et al.*, 2023).

A pertinent example of benzodiazepine-analogues which possess different chemical structure from “true” benzodiazepines but are often aligned with them include the thienotriazolodiazepines. The latter class of substances differ in having a diazepine fused to a thiophene as opposed to benzene ring (Orsolini *et al.*, 2020) though share broad similarities in their action upon the GABA_A receptor (Tamama and Lynch, 2020). Amongst the thienotriazolodiazepines one - etizolam - has come to hold particular prominence and notoriety in the landscape of illicit substances in Scotland in recent years.

Etizolam was reported as a possible contributory substance in 772 (National Records of Scotland, 2022b) of the 1,330 drug-related deaths recorded in Scotland in 2021 (National Records of Scotland, 2022a). The emergence of etizolam and other novel benzodiazepines in Scotland has been linked to a number of factors, including lowered prescription rates of “legitimate” benzodiazepines that were often diverted to the black-market creating a gap in the same that was ultimately fulfilled by etizolam and other novel benzodiazepines, which in turn was facilitated by the increased accessibility of these alternative substances offered by the internet (Nielsen and McAuley, 2020). As the popularity of novel benzodiazepines increased so did the sophistication of drug production and distribution infrastructure utilised by Scotland-based suppliers, including the use of industrial pill-presses (Scottish Government, 2022a), often used with the intent of producing pills designed to mimic the appearance of “legitimate” benzodiazepines such as diazepam to the eyes of end-users but which in fact contain novel benzodiazepines such as etizolam (EMCDDA, 2021). At this juncture it is germane to mention that some substances commonly used in the production of these ersatz tablets may be significantly more powerful than the substance they are intended to emulate, with etizolam being considered ten times stronger than diazepam (Johnson, Barnsdale and McAuley, 2016) Variance in the type of novel benzodiazepine used and dosage per unit of these so-called “street” benzodiazepines has resulted in a phenomenon colloquially referred to as “consumption roulette” wherein users may be unaware of the relative strength of given pill and consume a far greater dose than intended, further contributing to drug-related death rates in Scotland

(Asplin, 2023). Whilst etizolam remains perhaps the most notorious example, other novel benzodiazepines such as alprazolam (Corkery *et al.*, 2022) and phenazepam (McAuley, Matheson and Robertson, 2022) have also played significant roles in the “street” benzodiazepine phenomenon at various times.

Several substances, including zopiclone and zolpidem, are collectively known as “z-drugs” (Kapil *et al.*, 2014). These substances have very similar effect to benzodiazepines, are licensed for use in the UK for treatment of insomnia (Joint Formulary Committee, 2023) and can have the potential to be misused in an NPS context (Kapil *et al.*, 2014).

1.8 Gabapentinoids – clinical context

Gabapentinoids – the two prototypical examples of which are gabapentin and pregabalin (Manville and Abbott, 2018) - are drugs originally developed to act as analogues of the gamma-aminobutyric acid (GABA) neurotransmitter in the brain (Patel and Dickenson, 2016). Although their full mechanism of action is not entirely understood, it is believed to be primarily related to their inhibitory effect on $\alpha 2\delta$ subunit-containing calcium channels in the central nervous system (Manville and Abbott, 2018). This effect is thought to be the primary means by which these substances achieve an analgesic influence, though other actions - such as their inhibition of the noradrenergic system – are theorised to also play a possible role in this (Chincholkar, 2018).

Gabapentin and pregabalin are licensed for use in the treatment of neuropathic pain – where the former is considered a first-line treatment (Russo, Graham and Santarelli, 2023) - and epilepsy in the UK, with the latter also being approved for treatment of generalised anxiety disorder (Chincholkar and Mahindra, 2020). Off-label use of both had been common in the UK until recently, accounting for more than half of prescriptions in the UK, where the drugs may be used in treatment of conditions as diverse as chronic back pain, alcohol withdrawal, attention deficit disorders or bipolar disorder (Chincholkar and Mahindra, 2020).

However, a rapid increase in the volume of prescriptions of both aforementioned gabapentinoids in the UK – wherein relative rates of prescriptions nearly tripled for both substances in the period from 2007-2017 (Evoy *et al.*, 2021) – began to be a cause of concern amongst medical professionals. This, along with contemporaneous emerging evidence regarding the abuse potential of gabapentinoids (Schifano, 2014) was a factor in the ACMD’s recommendation to the UK government to have both gabapentin and pregabalin to be reclassified as controlled substances (Iacobucci, 2017) This was ultimately enacted in 2019 when they were rescheduled as schedule 3 controlled/class C drugs (Health and Care Professions Council, 2019).

In relation to the theme of NPS use, illicit gabapentinoid use appears to largely take place in the context of poly-drug use, where they are co-consumed with other substances to create/enhance a euphoric effect, and/or ameliorate symptoms of withdrawal (Evoy *et al.*, 2021). Evidence from Scotland suggests that this form of poly-drug use involving gabapentinoids most commonly sees benzodiazepines and opioids being preferred co-consumed substances, with this being a factor in recent increases in drug-related deaths in the country (Torrance *et al.*, 2020). Evidence suggests that gabapentinoids continue to play a substantial role in Scotland’s high rates of drug-related deaths, with the latest figures at time of writing suggesting that they can be implicated in 35% of overall drug deaths (National Records of Scotland, 2023).

1.9 Opioids – clinical context

Opioid drugs can be split into two inter-related categories. Opiates would include a number of substances used in a medical context derived from the opium poppy, such as opium or morphine, whereas the term “opioid” itself can be expanded to include not only these naturally occurring substances, but semi-synthetic or synthetic substances that have a similar pharmacological effect (Centers for

Disease Control and Prevention, 2021). In the context of NPS, fully synthetic opioids are the most significant sub-category (Frisoni *et al.*, 2018).

Mu, kappa and delta are opioid sub-receptors found at various sites throughout the brain and peripheral nervous system that opioids bind to (Wang, 2019). Fentanyl, codeine and morphine are examples of full mu agonist opioid receptors, and this action on the mu opioid receptor (MOR) is the primary mechanism (although action on the kappa and delta receptors also play a more minor role) by which such opioids achieve their desired analgesic effect in legitimate medical uses (Ghelardini, Di Cesare Mannelli and Bianchi, 2015), with all three of these substances being licensed for use within the UK for this purpose (Joint Formulary Committee, 2023). However, whilst being the principal actor in this beneficial effect on the management of pain, the MOR is also the primary instigator by which opioids have their more problematic effects of euphoria and respiratory depression (McDonald and Lambert, 2014). MOR activation by way of opioid administration creates euphoria – as well as contributing considerably to opioids' addicting qualities – by a complex interaction resulting in a net increase of dopamine in the brain's nucleus accumbens (Frisoni *et al.*, 2018). MORs are also distributed widely throughout brain regions involved in the control of respiration, such as the ventrolateral medulla, where their activation results in subsequent disruption of inspiratory rhythm and – ultimately – respiratory depression (Baldo and Rose, 2022).

In recent years, novel synthetic opioids (NSOs) such as fentanyl and its derivatives/analogues have emerged as a significant public health issue in many areas of the globe (Abbate, Moreno and Wiegand, 2022). In the United States, fentanyl and derivatives such as acetylfentanyl and carfentanil as well as analogues such as U-47000 have come to be the subset of opioids most implicated in drug-deaths. Adulteration of black-market heroin with fentanyl-based opioids has grown to become a very common feature of drug markets in North America generally, with one study reporting the results of a drug-testing scheme in Vancouver, Canada found that 90.6% of samples purported to be heroin were in fact instead identified as fentanyl (Tupper *et al.*, 2018).

Illicit NSO use involving fentanyl or fentanyl-like substances is not considered – as of yet – to be of major concern in the UK or Scottish milieu (Pierce *et al.*, 2021). However, opioid use more generally is still an important factor to consider in the NPS context of Scotland, given that poly-drug use of NPS benzodiazepines such as etizolam and/or gabapentinoids alongside opioids more traditionally associated with abuse is a major factor in the country’s current high rates of drug-related deaths (van Amsterdam, van den Brink and Pierce, 2021).

1.10 Methodology

As described in **Section 1.6.3.**, only one search element (population/problem) was adapted for suitability for each independent review. For a full description of the search strategy employed outside of the population section, please see the aforementioned section. In the case of sedatives and depressants, search terms used for population/problem were: *synthetic opioid**; *synthetic opiate**; *designer opioid**; *designer opiate**; *novel opioid**; *novel opiate**; *fentanyl analo**; *synthetic heroin**; *fentanyl derivative**; *oxycodone*; *dihydrocodeine*; *fentanyl*; *novel benzodiazepine**; *new benzodiazepine**; *“street” benzo**; *illicit benzodiazepine**; *“street” diazepam*; *“street” Valium*; *novel hypnotic**; *novel sedative**; *benzodiazepine analo**; *gabapentin*; *pregabalin*; *alprazolam*; *diclazepam*; *etizolam*; *flualprazolam*; *phenazepam*; *opioid analo**, and *nontraditional opioid*, with these search terms being derived from nomenclature identified during the researcher’s initial investigations.

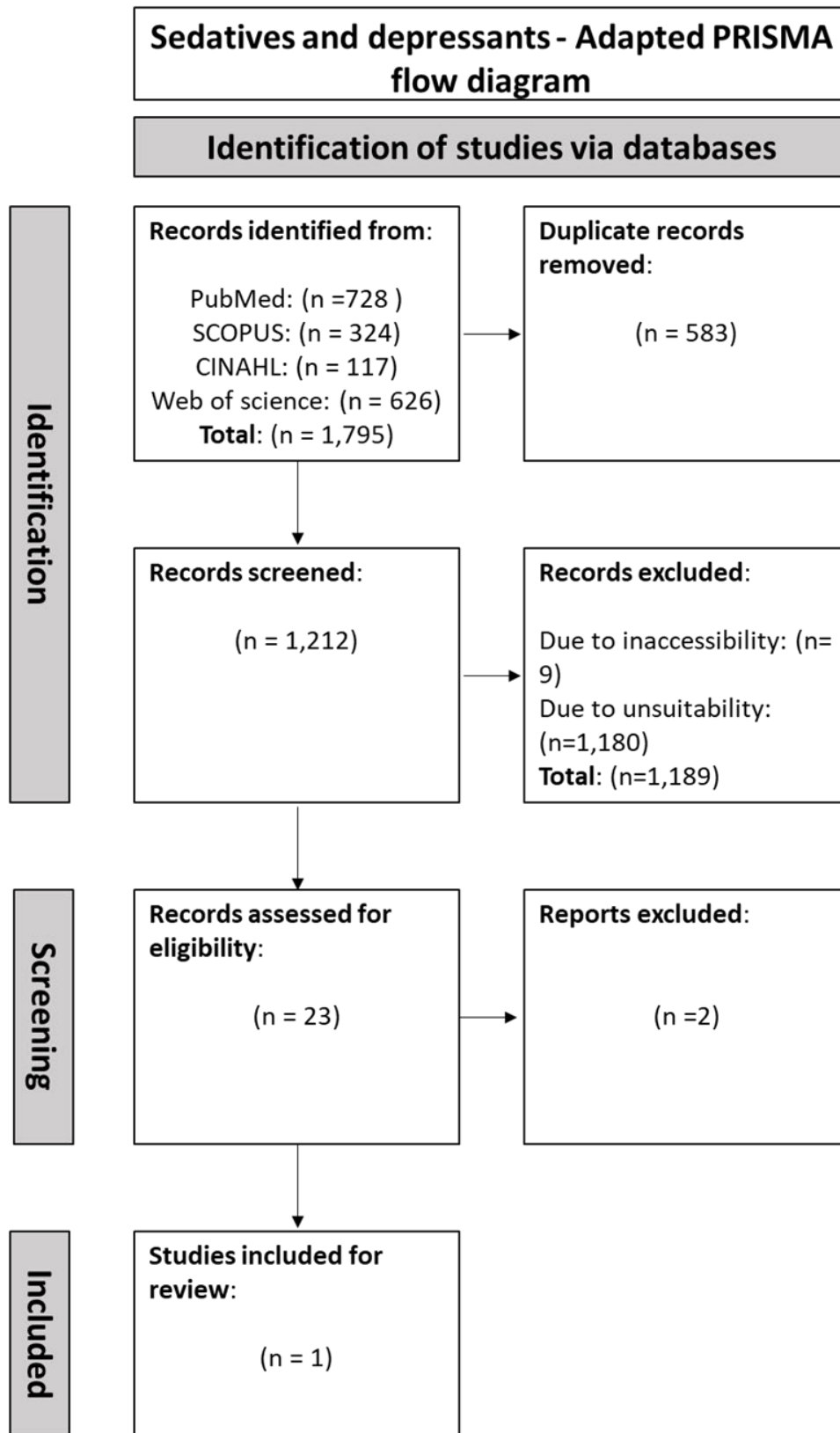
For more details of the search strategy employed, please see **Figures 2** and **3** below, as well as **Appendix 2** (search strategy, PRISMA diagram and critical appraisal tool respectively).

Search #2 (to align with population/problem)					
Search Terms employed (all combined with OR boolean operator)					
synthetic opioid*; synthetic opiate*; designer opioid*; designer opiate*; novel opioid*; novel opiate*; fentanyl analo*; synthetic heroin*; fentanyl derivative*; oxycodone; dihydrocodeine; fentanyl; novel benzodiazepine*; new benzodiazepine*; "street" benzo*; illicit benzodiazepine*; "street" diazepam; "street" Valium; novel hypnotic*; novel sedative*; benzodiazepine analo*; gabapentin; pregabalin; alprazolam; diclazepam; etizolam; flualprazolam; phenazepam; opioid analo*; nontraditional opioid					
	Database				
	Pubmed	SCOPUS	CINAHL	WOS	
Date Searched	28/1/21	28/1/21	28/1/21	28/1/21	28/1/21
No. of results	8,677	55,365	467,078	1,012	3,165,826
Date Searched	28/1/21	28/1/21	28/1/21	28/1/21	28/1/21
No. of results	1,664,328	3,350,007	467,078	1,012	3,165,826

Search #3 (to align with study design)					
	Database				
	Pubmed	SCOPUS	CINAHL	WOS	
Date Searched	28/1/21	28/1/21	28/1/21	28/1/21	28/1/21
Terms (combined with OR boolean operator)	systematic review; meta-analysis				
	Not used due to appropriate filter as search option				
No. of results	N/A	332,244	97,230	1,012	2,845,488

Database	Pubmed	SCOPUS	CINAHL	WOS	Exported to RefWorks	After duplicates removed
Combined search – no. of results	8,677	665	141	1,012		
Filters used	Limit to reviews, systematic reviews and Meta-analysis; Published after 2010; human subjects; English language	Limit to review; published after 2010; English language	Published after 2010, English language; peer reviewed	Published after 2010, Limit to review		
After filters	728	324	117	626	1,795	1,212

Figure 1: Unique search terms and returns in sedatives and depressants search strategy



Design adapted from Page *et al.* (2021)

Figure 2: PRISMA flow diagram for sedatives and depressants search strategy

1.11 Results

All relevant searches were run on 28/1/21. After the search strategy was completed, 1,212 candidate papers were identified. After abstract review, this was reduced to 23 papers deemed suitable for critical appraisal. Following the critical appraisal process, 21 papers were ultimately included in the final review due to them scoring greater than 50% using the scoring system on the devised tool. The CASP score ranges on included in the included paper were: 14 papers scoring 7/7; 7 papers scoring 6/7, and one paper scoring 5/7.

Both papers that were excluded – Van Hout (2014) and Shorter, Hsieh and Kosten, 2015 – were done so on the basis that they scored <4 (i.e., less than 50% score) using the developed tool.

Although two papers – Schifano *et al.* (2018) and Piccioni *et al.* (2020) - included clinical advice for multiple classes of NPS (stimulants, hallucinogens and/or SCRAAs as well as sedatives/depressants), the recommendations pertaining to sedatives/depressants was clearly differentiated from advice concerning these other NPS categories, and therefore their recommendations were deemed viable for this review. Therefore, no measure to consider the relevant guidance in discrete sections relevant to classes of NPS outwith and inclusive of sedatives/depressants was deemed necessary by the author in this instance. However, some recommendations specific to groups of drugs within the broader category of sedatives/depressants were found and are presented in sub-sections immediately below as appropriate to aid in clarity.

1.12 Clinical recommendations from included papers

1.12.1 Vigilance/Awareness on the part of the clinician

Fifteen of the 21 papers made recommendations regarding clinician vigilance and awareness, with these being presented in discrete sub-sections below.

1.12.1.1 Benzodiazepines and non-opioid, non-gabapentinoid central nervous system depressants generally

Anderson, Flynn and Pilgrim (2017) note that most cases of drug-assisted sexual assaults (DFSAs) are related to alcohol intoxication, with benzodiazepines being the next most common category of substance used for this purpose by perpetrators. Further, they suggest that due to the rapid metabolisation of many substances utilised by perpetrators of DFSAs (often within 12 to 24 hrs), victims of DFSAs should be encouraged to submit to urine and blood screening at the earliest juncture. Marsden et al. (2019) found that patients feel that clinicians tend to misunderstand withdrawal symptoms (such as somatic symptoms, anxiety, subdued mood or agitation) from antidepressants, benzodiazepines, opioids, gabapentinoids and z-drugs, misinterpret these as being related to other health conditions, and, therefore, suggest that improved training for healthcare workers in this regard is necessary. In reference to the same drug categories, Marsden *et al.* (2019) state that prescribing should not be curtailed if patients have an acute or long-term need for them stemming from a health condition. Marsden *et al.* (2019) add that weighing up the potential negative consequences for the patient should be made in any decision concerning their prescription, given that cessation of the above medication classes without the proper consideration process can not only stop patients from receiving clinical benefit. The same authors also note that cessation in the manner described can lead to service-users taking suicidal action or seeking previously prescribed substances (or even orthodox illicit substances) from black market sources.

In reference to the benzodiazepine phenazepam specifically, Corkery, Schifano and Ghodse (2012) note that co-ingestion of the substance with other psychoactives such as opiates can increase chances of mortality. In a review that focuses on diversion of sedative-type substances in prison populations, Bi-Mohammed *et al.* (2017) found that there is some evidence to suggest that sedative antidepressants and psychotropics are being misused/diverted within prison settings, with service users seeking euphoric or sedative effects from these drugs, including self-medicating for insomnia – presumably in the absence of

preferred substances. Schifano *et al.* (2018) note that loperamide can be misused in large quantities by service users for a euphoric effect, with resultant CNS depression.

1.12.1.2 Gabapentinoids

In reference to gabapentin misuse, Mersfelder and Nichols (2016) state that gabapentin is often consumed alongside opioids in the belief that it will enhance the effects of these latter substances, a finding supported by Freynhagen *et al.* (2016), who note that some users consume the gabapentinoid pregabalin in the belief that it acts as a potentiator for other psychoactives. Further, Mersfelder and Nichols (2016) suggest that gabapentin may be misused – often alongside quetiapine – as a perceived substitute for cocaine or to ameliorate withdrawal symptoms of the latter. Again, this is mirrored in the recommendations of Freynhagen *et al.* (2016) regarding pregabalin, who note that this may be used by patients to ameliorate withdrawal from other substances or to act as a “bridge” between periods when preferred substances are not available to users.

Smith, Havens and Walsh (2016) review found that gabapentin is most commonly misused alongside other drugs of abuse, with co-consumption of opioids, benzodiazepines and alcohol being most frequency, which Smith, Havens and Walsh (2016) note is of particular importance given that gabapentin is often co-prescribed with benzodiazepines (for anxiety or sleep issues) and/or opioids. Evoy, Morrison and Saklad (2017) recommend that clinicians should be aware of the abuse potentials and inherent dangers of gabapentinoids in abuse contexts – such as tachycardia or hypotension - and perform patient risk assessments before prescribing, specifically those related to opioid-related overdose, with this suggestion being supported by a recommendation from Bonnet and Scherbaum (2017), who state that - if unavoidable – prescription of gabapentinoids should have accompanying abuse monitoring plans for both therapeutic and prescription types. In relation to pregabalin specifically, Schjerning *et al.* (2016) – in the specific context of pregabalin misuse – recommend that clinicians should monitor for patients experiencing euphoria as a side-effect of administration of pregabalin,

as this is implicated in later likelihood of abuse. Evoy *et al.* (2021) note that clinicians should seek to include multi-modal pain management in their practice to mitigate abuse potential of gabapentinoids, and caution that clinicians should be aware that many misusers consume gabapentinoids to self-medicate against anxiety, pain or withdrawal from other substances. In discussing drug-seeking behaviours seen in patients who misuse gabapentin, Mersfelder and Nichols (2016) suggest that clinicians should consider requests for earlier than anticipated repeat prescriptions or physical signs of withdrawal as being indicative of dependence or misuse, whilst Evoy *et al.* (2017) caution that misuse of gabapentinoids may be suggested by patients asking for them specifically or greater doses of them. Further, Evoy *et al.* (2017) recommend that clinicians should be aware that gabapentinoids are mostly used to treat ailments where their efficacy is quantified using subjective measures – such as in the treatment of neuropathic pain - meaning there is potential for patients to invent or exaggerate severity of symptoms in order to secure re-prescription or higher titration. At an organisational level, Evoy *et al.* (2021) suggest that health services ensure that appropriate abuse/misuse monitoring protocols are in place, and that supply control measures (SCM) should be optimised, though caution that overly strict SCMs may have a detrimental effect on patient outcomes.

In regard to at-risk populations for misuse of gabapentinoids, Smith, Havens and Walsh (2016) state that in their review that determination of risk factors for gabapentin misuse proved difficult. However, the findings of the papers in the study suggest that a history of substance misuse or current substance misuse (particularly opioids) can be considered likely to be a risk factor, whilst Mersfelder and Nichols (2016) expand on this in specifying a history of alcohol misuse as being a risk factor for developing gabapentin dependency. Freynhagen *et al.* (2016) concur with this advice in the context of pregabalin. Bonnet and Scherbaum (2017) offer a similar recommendation for gabapentinoids more generally, stating that whilst for those without a history of substance misuse the risk factor for developing dependency from administration of gabapentinoids appears low, in individuals with a history of substance misuse the risk of addiction is far greater, and prescription should be avoided where possible. Evoy *et al.*

(2017) also comment on risk factors for developing dependency on gabapentinoids, though they recommend that a history of mental illness be included in as a risk factor as well as a history of substance misuse and suggest that close monitoring of possible abuse of gabapentinoids in patients is advisable rather than avoiding prescription entirely. Finally, Schjerning et al. (2016) report that although it is theorised that pregabalin may potentially have utility in the treatment of benzodiazepine or alcohol addiction the mechanism for this is not yet established – although it is proposed that the drug’s action in lessening the release of the neurotransmitters glutamate and norepinephrine plays a part Freynhagen *et al.* (2016) - and clinicians should bear in mind that a history of substance misuse is a risk factor for potential pregabalin misuse.

1.12.1.3 Opioids

Lovrecic *et al.* (2019) suggest that the primary focus of clinician efforts should be on avoidance of overdose in people who misuse novel synthetic opioids. Giorgetti, Centola and Giorgetti (2017)’s findings suggest fentanyl novel derivative-based transdermal patches present a high risk of overdose, though they note that fatalities may ensue from non-recreational intended use, through patients forgetting to remove a patch or its application to bruised skin, which should not be considered in the context of misuse/abuse by clinicians. In the context of the novel opioid U-47700, Rambaran *et al.* (2017) note that the most common methods of use are insufflation and intra-venous (IV) injection. In reference to prison populations, Bi-Mohammed *et al.* (2017) recommend that opioid drugs should always be prescribed in the least abusable preparation available, and that clinicians be vigilant to avoid not only under-dosing patients but also over-prescribing.

1.12.1.4 Specific populations

Several reviews made commentary on populations most at risk of misuse/dependence on novel opioids. Lovrecic *et al.* (2019) suggest that these include: homeless people; those with a mental health (MH) diagnosis/undiagnosed MH problem; substance misusers outwith treatment programmes, and men who have sex with men (MWHWSM). Further, Lovrecic *et al.* (2019) note that older age places people who use opioids at a higher risk of overdose (OD), particularly for those outside treatment. Huhn, Berry and Dunn, (2019) suggest that women are more likely to present to opioid use disorder treatment services with mental health comorbidities, especially depression, whilst Bi-Mohammed *et al.* (2017) note that, when treating prison populations, health care staff should be aware that certain demographics (those of younger/older age, those with mental health problems) can be subject to intimidation by other inmates to be involved in diversion of medications.

1.12.1.5 Diversion/drug-seeking behaviours

Two reviews commented extensively on the topic of diversion/drug-seeking of medication in the context of novel opioids. In their review on the misuse of sedatives in the prison population, Bi-Mohammed *et al.* (2017) found that although opioids often enter prison settings by means other than diversion, this remains a common method, and that substance users appear to have formulated sophisticated strategies to circumvent supervised medication consumption. Generally, Bi-Mohammed *et al.* (2017) recommend that liquid preparations - where available and licensed for use - are preferred over tablet preparations to help prevent diversion. In reference to specific substances, Bi-Mohammed *et al.* (2017) state that sublingual buprenorphine may be diverted for intranasal use by prison populations, though buprenorphine/naloxone preparations appear less viable for diversion than mono-buprenorphine preparations – presumably due to the latter causing less subjective and physiological effects associated with pleasure and addiction in misuse contexts (Middleton *et al.*, 2011) and that buprenorphine is more likely to be diverted than methadone. Finally, Bi-Mohammed *et al.* (2017) suggest that a typical presentation for those seeking to

misuse or divert prescribed opioids would be individuals with a prior history of substance misuse citing musculoskeletal pain, though caution that ascertaining whether the above type of complaint is genuine or an attempt to gain medications for misuse/diversion is challenging. In their review concerning overdose deaths related to fentanyl-derivatives, Giorgetti, Centola and Giorgetti (2017) recommend that clinicians be cognisant that fentanyl derivative patches may be misused through several methods, such as: multiple applications; application to an atypical site; licking/chewing; volatilisation, smoking or swallowing. Furthermore, Giorgetti, Centola and Giorgetti (2017) state that users may chew patches to achieve faster absorption rates, which has the potential to increase dosage tenfold. Swallowing of patches/tablets also alters dosage, which has proven to be extremely variable in in vivo/post-mortem examination, and the same issue is also present when liquid has been clandestinely recovered from patches using a syringe for later injection (Lilleng *et al.*, 2004) as a mode of misuse.

1.12.2 Patient Education, shared decision-making and harm reduction strategies

In making clinical recommendations regarding the misuse of prescribed CNS-depressant medications generally (i.e., inclusive of benzodiazepines, Z-drugs, gabapentinoids and antidepressants), Marsden *et al.* (2019) state that healthcare professionals should work closely and in alignment with patients in shared decision-making processes to protect them against the risk of dependence and/or withdrawal, and that informed choice and regular clinical reviews are also key to preventing risk to service-user health. In reference to treatment of individuals who are victims of drug-facilitated sexual assaults, Anderson, Flynn and Pilgrim (2017) emphasise the importance of encouraging people who report DFSAs to discuss their own personal drug use in a non-judgemental, candid manner to maximise patient engagement and optimise outcomes. In the context of gabapentinoids, Evoy *et al.* (2021) state that service users are to be provided with sufficient counselling regarding potential risks with their use, and - in cases of polydrug use – clinicians should explore with patients their reasons for combining substances

and discuss risks involved in this, as well as their use of gabapentinoids generally. Cheema *et al.* (2020) in their review of fentanyl-related deaths, advise that all health care professionals should be prepared to provide high quality and well-communicated education regarding the proper use of fentanyl and the potential dangers of its diversion, misuse or overuse in prescribing or administering the substance. Further, they recommend that patients who have a history of substance misuse and who are prescribed fentanyl need to be given education regarding the signs and symptoms of respiratory depression as well as chest wall rigidity. Nielsen *et al.* (2016) in discussing misuse of pharmaceutical opioid misuse and selection of opioid agonist medication for addiction treatment, state that this decision should be dependent on the preference of the patient, safety and availability.

Three of the reviews mentioned harm-reduction within their clinical recommendations. Evoy *et al.* (2021) mention harm reduction in the context of gabapentinoids, stating that this should be used in conjunction with supply reduction strategies, though do not expand further on the issue. Similarly, Lovrecic *et al.* (2019) – in discussing misuse of novel opioids – mention harm reduction as playing a role in treatment, though they do not comment on it other than to contrast the methodology to agonist opioid maintenance therapy, and then by stating that in the former there is higher degree of patient decision-making in down-titrating dosing regimens. In reference to the benzodiazepine phenazepam, Corkery, Schifano and Ghodse (2012) proffer the following harm reduction information: users should be advised not to “eyeball” powder doses of the substance; the substance’s long half-life means that users are liable to re-dose before peak effects are felt (2-3 hours), precipitating overdose; users are liable to consume phenazepam in the mistaken belief that it is a more established substance such as diazepam, leading to hazardous consumption due to the former’s relative potency; injection of crushed tablets of phenazepam with heroin can lead to risks other than OD, including vascular damage, granulomatosis, limb ischemia, infection and foreign body pulmonary micro-embolism.

1.12.3 Pharmaceutical treatment, physical management of symptoms and psychosocial interventions

Six reviews discussed the use of naloxone in the context of treatment of overdose in novel opioid-based substances. Schifano *et al.* (2018) advises its use in loperamide overdose, though note that there is no evidence to suggest that this treatment will reverse the drug's cardiotoxic effects. Cheema *et al.* (2020), recommend that health care providers should consider the provision of naloxone to those who use fentanyl, and that naloxone provision to groups vulnerable to opioid misuse or who have high rates of dual diagnoses – i.e., having diagnoses of both mental illnesses and substance misuse disorders (Dixon, Holoshitz and Nossel, 2016) - (such as the homeless population) should be a priority. In their review of naloxone provision in treatment of high-potency opioids overdoses,

Moe *et al.*, (2020) could not determine whether higher doses (considered as both higher than maximum licensed initial doses or cumulative volume doses overall) of naloxone were more effective or safer than standard doses and recommend that clinical guidelines remain in place until further evidence can be gathered. However, in cases where users are provided with naloxone kits and ultra-potent opioid overdoses are detected, provisions in such kits should be reviewed at jurisdictional (local authority) level. This is to ensure that the potential benefit of bystander intervention is maximised (through the provision of naloxone dosing and patient ventilation guidelines in kits) is maximised in the context of preventing deaths (Moe *et al.*, 2020). Also, in the context of high potency opioid overdose, Lovrecic *et al.* (2019) recommend the administration of IV naloxone (though do not comment on doses) in cases where patients present with a respiratory rate of <12 and/or SP02 saturation levels lower than 90%, with supplementary treatment consisting of protection of airways and the provision of bag and mask ventilation to increase blood oxygen levels. Piccioni *et al.* (2020) state that naloxone is recommended as a safe and effective treatment in treatment of synthetic opioid overdoses, though practitioners often overestimate required doses, which can result in acute opiate withdrawal, with the authors recommending that low dose naloxone (0.04mg) is used and titrated appropriately for the desired effect of

ventilation depression reversal. In reference to the treatment of overdose of the synthetic opioid U-47700, Rambaran *et al.* (2017) suggest that administration of IV naloxone is able to reverse symptoms of depressed mental state, respiratory depression and bradypnea. Although naloxone doses for this purpose in their collected literature ranged from 0.4–4 mg, Rambaran *et al.* (2017) do not provide a recommended dose overall or dosing frequency.

In discussing broader treatment strategies for misused prescription drugs, Schifano *et al.* (2018) recommend that clinicians consider strategies to improve referral protocols and clinical pathways involving multiple services/agencies, particularly those involving community pharmacies, these being the professionals best placed to recognise a repeat supply issue, whilst Marsden *et al.* (2019) state that healthcare professionals should consider that patients may need better access to dependence and withdrawal focused services and support, including: social prescribing; support groups; psychological therapies; mental health teams; pain clinics and appropriate medical services.

Discussing the use of prescribed and/or diverted medications in prison settings, Bi-Mohammed *et al.* (2017) suggest that healthcare services within prisons seek to improve links with addiction and pain management services. In reference to gabapentinoids specifically, Evoy *et al.* (2021) state that exploring reasons for use may lead to patients being referred to appropriate treatment services. In the context of synthetic opioids, Cheema *et al.* (2020) advise that greater accessibility to substance misuse services is required to service affected populations generally, whilst Lovrecic *et al.* (2019) suggest that the major focus of any treatment package should be to reduce risk of overdose in service users through managing dependence, either through harm reduction interventions or agonist opioid maintenance treatment. In reference to the latter strategy, Nielsen *et al.* (2016) advise that there is little evidence to suggest that methadone or buprenorphine should be preferred over one another, and that other factors should decide their employment. Darker *et al.* (2015) in their exploration of psychosocial interventions for benzodiazepine misuse, found evidence to suggest that cognitive behavioural therapy (CBT) with a tapered withdrawal

protocol may be an efficacious intervention, that there is little evidence to support the use of intra-muscular (IM) for treatment of benzodiazepine abuse/dependence, though state that there is some emerging evidence that certain interventions such as structured consultations combined with individually tailored general practitioner letters may have some therapeutic benefit.

Stimulants and Hallucinogens Overview of Systematic Reviews

1.13 Stimulants and hallucinogens – clinical context

Psychomotor stimulant drugs can be categorised into two broad groupings – sympathomimetic (including direct and indirect) and non-sympathomimetics, wherein use of either sub-category results in increased motor activity, arousal and alertness in subjects, with this achieved in the case of sympathomimetics through emulation of the effects of norepinephrine in the autonomic nervous system and - either directly or indirectly – actuation of monoamine receptors, and through other methods in the case of non-sympathomimetics (Koob *et al.*, 2020). Among common NPS categories listed by the UNODC, aminoindanes, synthetic cathinones, phenethylamines, piperazines and tryptamines (UNODC, 2022c) may reasonably be described as novel psychoactive stimulants, with the proviso that – as the UNODC itself comments - concrete classification of many NPS of primarily stimulant action is complicated by many individual substances having additional hallucinogenic and even analgesic action (UNODC, 2019). Given how highly diverse the pharmacology of these various “families” of stimulant NPS are, in-depth exploration of individual categories will not be given. Instead, this section will begin with a brief argument as to why certain NPS hallucinogens of particular clinical concern may be better considered alongside more definitively stimulant-type NPS when discussing, largely due to shared features of their respective toxidromes. A consideration of recent trends and developments of stimulant NPS in the UK will then be given.

As previously attested to, it is notable that many stimulant-type NPS are categorised as having hallucinogenic properties, such as phenylisopropylamines often being referred to as “psychedelic amphetamines” (Poulie *et al.*, 2020). This “blurring of lines” over whether certain novel psychoactive substances are to be considered as hallucinogens or stimulants is exacerbated by the varying subjective and physiological effect of substances belonging to the same family. For example, whilst tryptamines can be considered as primarily hallucinogenic substances (Malaca *et al.*, 2020), tryptamines that feature an alpha carbon methyl group as part of their structure tend to produce comparatively higher levels of stimulant effects upon consumption (Greene, 2022). Similarly, both 2,5-dimethoxyphenylethylamines (2C) and N-(2-methoxybenzyl)-2,5-dimethoxy-4-substituted phenethylamines (NBOMes) are both considered phenethylamines (Poulie *et al.*, 2020) where the former family of molecules can be considered a “parent” to the latter (Herian and Świt, 2023). However, NBOMes are noted for not only the strong psychedelic/hallucinogenic effects they share with 2C drugs and other typical phenethylamines - stemming from their interactions with the serotonergic system (Poulie *et al.*, 2020) - but their pronounced actions on the adrenergic and dopaminergic systems (Kamińska, Świt and Malek, 2020), which may account for their stimulant-like toxic effects, inclusive of symptoms such as hyper-tension and tachycardia (Potts, Thomas and Hill, 2022). Even outwith the NBOME sub-family, some 2C phenethylamines derivatives such as 2C-B and 2C-I are also significant for their stimulant subjective effects and stimulant-like toxidrome in overdose (Locatelli, Lonati and Petrolini, 2020).

In the context of the UK, the most prominent NPS stimulant to date is the synthetic cathinone mephedrone. Widespread use of mephedrone began in the UK in 2008, with it being postulated that a scarcity of MDMA in the country was a factor in the former’s sudden increase in popularity (Mounteney *et al.*, 2018). However, widespread contemporary media coverage of the drug’s use – in which its legal status at the time, and accessibility via internet markets were emphasised - is thought to have further increased interest and subsequent acquisition of mephedrone by the wider public (Forsyth, 2012), to the extent that by 2011 Home Office records show that 1.4% of people aged between 16 and 59 in England and

Wales had tried the drug on at least one occasion (Home Office, 2011). Further, a survey of 1,006 students in the Tayside area of Scotland conducted in 2010 suggests that 20.3% of the sample had used mephedrone at least once (Dargan, Albert and Wood, 2010). Whilst rates of use have dropped since the UK government's banning of mephedrone and other synthetic cathinones in 2010 (Mead and Parrott, 2020) the drug has seen continued popularity in the chemsex – drug-facilitated sexual activity, usually in the context of men who have sex with men (MSM communities (Whitlock *et al.*, 2021) – scene (Kohli *et al.*, 2019). Whilst mephedrone use is not directly associated with greater risks to health in comparison to more traditional stimulants such as cocaine or amphetamines (Nutt, 2020), it is – along with other drugs commonly used in chemsex contexts – associated with increased likelihood of engaging in high risk sexual behaviours such unprotected anal sex and having multi-partner encounters (Kohli *et al.*, 2019). Further, it is notable that – in the general population – users of mephedrone who inject the substance may be up to twice as likely to pool injecting works as users who consume other substances (Public Health England, 2017b), with injection being a common method of delivery of mephedrone in the chemsex context (Howarth *et al.*, 2021).

Outside of mephedrone, other novel stimulants have been directly implicated in drug deaths in the UK. The novel amphetamines PMA (paramethoxyamphetamine) and PMMA (paramethoxymethamphetamine) frequently began to be sold as MDMA/ecstasy in the 2010s (again in response to scarcity of the preferred latter substance), with the comparatively greater toxicity of PMA and PMMA (Nutt, 2020) theorised to be a factor in the two substances accounting for 73 of 368 drug-related deaths where amphetamines were involved in England and Wales in the period of 2012 to 2014 (Office for National Statistics, 2015). Novel hallucinogens, such as the aforementioned NBOMe family of drugs, have also seen sporadic periods of increased usage in the UK, with one case series reporting clinically confirmed use of 25I-NBOMe resulting in adverse events and hospitalisation in seven users in North-East England in January 2013 (Hill *et al.*, 2013).

Several stimulant drugs, including methylphenidate, dexamfetamine and lisdexamfetamine are licensed for treatment in attention deficit hyperactivity disorder (ADHD) (Joint Formulary Commission, 2023), and are also liable for misuse in an NPS context (Weyandt *et al.*, 2016).

1.14 Methodology

As previously discussed in **Section 1.6.4** only one element of the search strategy – population/problem - was modified to suit each independent search strategy. For full details of the overall methodology, please see the aforementioned section. Search terms utilised for the population/problem element for hallucinogen the search were: *novel hallucinogen**; *designer hallucinogen**; *novel dissociative**; *designer dissociative**; *novel tryptamine**; *designer tryptamine**; *novel ergoline**; *designer ergoline**; *novel phenethylamine**; *designer phenethylamine**; *LSD analo**; *lysergic acid diethylamide analo**; *psilocybin analo** and *psilocin analo**, whilst for the equivalent search in relation to stimulants the following terms were used: *novel amphetamine**; *designer amphetamine**; *novel cathinone**; *designer cathinone**; *novel stimulant**; *designer stimulant**; *cathinone derivative**; *cathinone analo**; *amphetamine analo**; *cocaine analo**; and *methamphetamine analo**. In both instances, search terms were derived from relevant literature the author had conducted during initial research for the project.

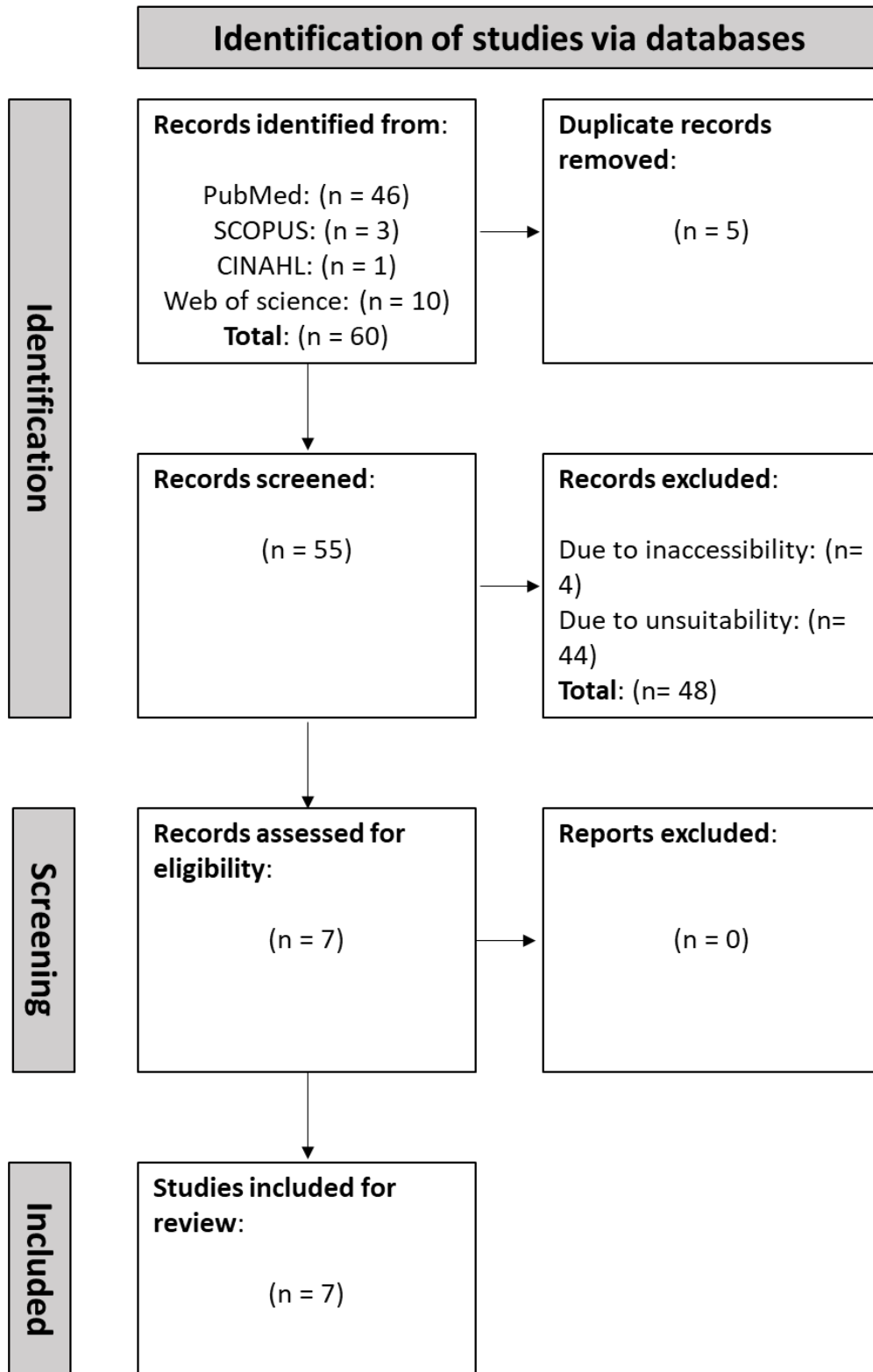
For more details of the search strategy employed, please see **Sections 3** through **6** immediately below, as well **Appendix 3** (search strategies, PRISMA diagrams and critical appraisal tool respectively).

Search #2 (to align with problem)					
Search terms employed					
novel hallucinogen*; designer hallucinogen*; novel dissociative*; designer dissociative*; novel tryptamine*; designer tryptamine*; novel ergoline*; designer ergoline*; novel phenethylamine*; designer phenethylamine*; LSD analo*; lysergic acid diethylamide analo*; psilocybin analo*; psilocin analo*					
	Database				
	Pubmed	SCOPUS	CINAHL	WOS	
Date Searched	5/2/21	5/2/21	5/2/21	5/2/21	5/2/21
No. of results	1,488	1,734	3,357,077	468,371	3,971,412

Search #3 (to align with study design)				
	Database			
	Pubmed	SCOPUS	CINAHL	WOS
Date Searched		5/2/1	5/2/21	5/2/21
Term	systematic review; meta-analysis			
	Not used due to appropriate filter as search option			
No. of results	N/A	333,549	97,607	393,808

Database	Pubmed	SCOPUS	CINAHL	WOS	Exported to Refworks	After duplicates removed
Combined search – no. of results	369	3	1	10		
Filters used	Limit to reviews, systematic reviews and Meta-analysis; Published after 2010; human subjects; English language	Limit to review; published after 2010; English language	Published after 2010, English language; peer reviewed	Published after 2010, Limit to review		
After filters	46	3	1	10	60	55

Figure 3: Unique search terms and returns in hallucinogens search



Design adapted from Page *et al.* (2021)

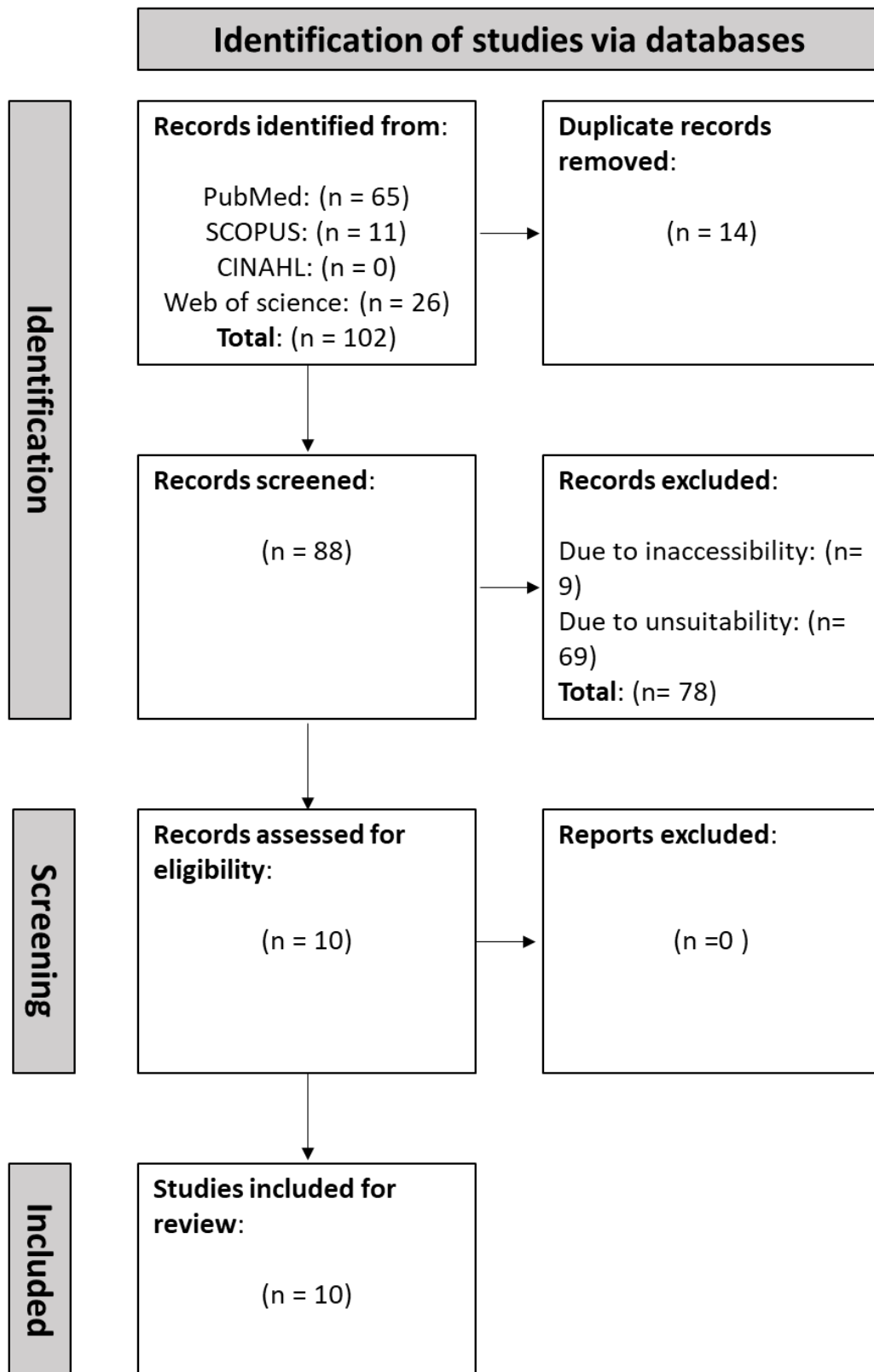
Figure 4: PRISMA flow diagram for hallucinogens search

Search #2 (to align with problem)				
Search terms employed				
novel amphetamine*; designer amphetamine*; novel cathinone*; designer cathinone*; novel stimulant*; designer stimulant*; cathinone derivative*; cathinone analo*; amphetamine analo*; cocaine analo*; methamphetamine analo*				
	Database			
	Pubmed	SCOPUS	CINAHL	WOS
Date Searched	28/1/21	28/1/21	28/1/21	28/1/21
No. of results	1,077	5,765	183	7,780

Search #3 (to align with study design)				
	Database			
	Pubmed	SCOPUS	CINAHL	WOS
Date Searched	28/1/21	28/1/21	28/1/21	28/1/21
Term	systematic review; meta-analysis			
	Not used due to appropriate filter as search option			
No. of results	N/A	332,244	97,230	2,845,488

Database	Pubmed	SCOPUS	CINAHL	WOS	Exported to Refworks	After duplicates removed
Combined search – no. of results	411	17	0	37		
Filters used	Limit to reviews, systematic reviews and Meta-analysis; Published after 2010; human subjects; English language	Limit to review; published after 2010; English language	Published after 2010, English language, Peer reviewed	Published after 2010, Limit to review		
After filters	65	11	0	26	102	88

Figure 5: Unique search terms and returns in stimulants search



Design adapted from Page *et al.* (2021)

Figure 6: PRISMA flow diagram for stimulants search

1.15 Results

Relevant searches pertaining to NPS hallucinogens were made on 5/2/21. In the hallucinogens search, 55 papers were identified from relevant searches after removal of duplicates. After the initial abstract review, seven remained for critical approval, with all 7 remaining after this process. However, of the seven papers included, 3 made clinical recommendations for treatment in the stimulant, hallucinogen and SCRA families of NPS more generally, whilst a further 3 commented exclusively on the NBOMe family of hallucinogens. Given that NBOMe drugs have both stimulant and hallucinogenic properties (Gee *et al.*, 2016) and that there are notable similarities in the clinical manifestations of NBOMe drugs and stimulants such as amphetamines and cathinones (Rose, Poklis and Poklis, 2013), with resultant treatment strategies proving to be similar during the course of the current analysis, ultimately clinical recommendations for hallucinogens were considered alongside those of stimulants.

Searches regarding stimulant NPS were ran on 28/1/21. For the stimulant search, 88 papers candidate papers were identified from the relevant search after duplicates were removed. After the abstract review process, 10 remained for critical appraisal, with all papers being ultimately included. Once included hallucinogen papers from that search strategy were included within this totality, there were fifteen papers overall, of which 7 discussed treatment of stimulants, hallucinogen and SCRAs harms generally, 4 explored treatment of hallucinogens, and 3 focused exclusively on stimulants.

1.16 Clinical Recommendations

Nine of the fifteen identified papers discussed stimulant/hallucinogenic-type substances solely, with the remaining seven discussing stimulants/hallucinogens as part of a wider focus that also encompassed SCRAs. Of papers discussing multiple classes of substances, only Kersten and McLaughlin, 2015) and Schifano *et al.* 2018) included discrete clinical advice for treatment of different

families of compounds. To aid clarity, the seven reviews that provided clinical recommendations for stimulants/hallucinogens will be considered immediately below, as will the relevant clinical recommendations of Kersten and McLaughlin (2015) and Schifano *et al.* (2018). After this, papers that proffered clinical advice common to both stimulants/hallucinogens and SCRAAs will be considered as a whole in **Sections 1.20** through **1.23**.

1.16.1 Vigilance/awareness on the part of the clinician

Three of the seven stimulant/hallucinogen-exclusive papers commented on vigilance/awareness on the part of clinicians. In their discussion of cathinone misuse, Guirguis *et al.* (2017) state that determination of the type and quantity of NPS consumed by service-users experiencing adverse effects is of importance, though if this cannot be established symptomatic treatment should be initiated. Guirguis *et al.* (2017) further comment that raising healthcare professional awareness about NPS generally and their treatment is considered important by the authors. In reference to the NBOMe group of hallucinogens, Bersani *et al.* (2014) suggest that medical staff should be prepared to treat patients who have consumed drugs within the NBOMe family in the mistaken belief that it was LSD, with treatment for the latter requiring more aggressive management strategies. Also, in reference to NBOMes Suzuki *et al.* (2015) state that clinicians should consider possible accidental or purposeful consumption of NBOMes in cases where use of hallucinogens is suspected or suspicion is warranted and - when possible - analytic confirmation of consumption should be sought. Furthermore, Suzuki *et al.* (2015) caution that healthcare professionals should avoid direct contact with substances suspected of being NBOMe drugs, should use gloves when handling, avoid touching mouth area after decontamination – assumedly on the basis of this category of drugs high potency in powder form (Dye, 2013) and that care should be taken to avoid making substances airborne.

Schifano *et al.* (2018) discuss misuse of prescription medication in the context of NPS. They state that bupropion can be consumed in large doses – reportedly up to 4050mg per day, or approximately 14 times the maximum therapeutic dose –

to produce a stimulant-like effect, with it being a cathinone-derivative being postulated as explaining its abuse potential. It is usually consumed intranasally or orally in misuse, though IV injection has also been reported as mode of delivery. Adverse effects from recreational use include cardio-toxicity, seizures, tremor, hallucinations and nasal pain/irritability. Further, Schifano *et al.* (2018) report that venlafaxine has been misused as a dissociative. Sudden discontinuation from both substances is associated with anxiety, disorientation, depression, suicidality, psychotic symptoms, nausea, stomach cramps and sexual dysfunction, and, therefore, Schifano *et al.* (2018) caution that health professionals should consider an individual's background/circumstances when prescribing certain prescription medications to them.

1.16.2 Management of symptoms

All seven stimulant/hallucinogen-specific reviews made recommendations regarding the management of adverse effects from stimulant/hallucinogen NPS use, as did Kersten and McLaughlin (2015). Hill and Thomas (2011) recommend that treatment strategies for patients suffering adverse effects from consumption of stimulant-type NPS should be symptomatic/pragmatic in nature, and mirror those utilised for corresponding classes of orthodox drugs, with this second suggestion being shared by Guirguis *et al.*, (2017) in relation to cathinones.

1.16.2.1 Management of psychiatric symptoms

Six reviews commented on the management of psychiatric symptoms using pharmaceuticals, with Guirguis *et al.* (2017) suggesting the administration of benzodiazepines or haloperidol to manage agitation or aggression in cases of cathinone use, whilst antipsychotics including: quetiapine; risperidone; olanzapine; aripiprazole droperidol and haloperidol can be considered in cases of cathinone drug-induced psychosis. Kersten and McLaughlin (2015) also comment on the use of pharmaceuticals to address agitation and aggression in cathinone intoxication, further specifying benzodiazepines as an option that may have the added benefit of ameliorating symptoms of hypertension and/or

hyperthermia. However, Kersten and McLaughlin (2015) note that frequent redosing (thereby leading to a higher overall dose than normally recommended) of benzodiazepines may be necessary to achieve adequate sedation. Kersten and McLaughlin (2015) further state that - rarely - antipsychotics, propofol or barbiturates may be considered should treatment with benzodiazepines be ineffective in treating cathinone toxicity, though caution that clinicians should be cognisant that toxic effects may be due to substances other than cathinones, potentially precluding their use.

Bersani et al (2014) also recommend use of benzodiazepines in cases of NBOME induced agitation and aggression and hallucinations, as do Marchi *et al.* (2019) and Suzuki *et al.* (2015). In their review of amphetamine-like substances, derivatives, and analogues, Richards *et al.*, (2015) note that agitation and psychosis may be treated using butyrophenones and second-generation antipsychotics, with agitation also being managed well with benzodiazepine administration, particularly in the case of methylphenidate intoxication resulting from recreational, non-prescribed use, though they also caution that benzodiazepine administration may result in under-sedation in treating agitation arising from misuse of stimulant-type NPS. In their commentary related to piperazine toxicity and resultant agitation, Kersten and McLaughlin (2015) recommend administration of IM/IV (i.e., intra-muscular or intra-venous delivery) benzodiazepines, though noting that antipsychotics are to be avoided as an option, as these can affect the patient's ability to thermoregulate, as well as cause extrapyramidal side-effects and/or hypotension, arrhythmias or tachycardia. Orsolini *et al.*, (2017), in their review of hallucinogen-persisting perception disorder (HPPD) state that risperidone is not recommended in treatment of the condition as the majority of included studies suggest that it worsens symptoms, with these returning to baseline after risperidone is discontinued. However, HPPD symptoms may be improved when risperidone is used in conjunction with sertraline, though the authors ultimately reported a low evidence-base for this. The same review reports that high potency benzodiazepines such as clonazepam may be of superior benefit.

Outwith pharmaceutical treatment of psychiatric symptoms, Guirguis *et al.* (2017) comment on psychosocial interventions for treatment of cathinone use, suggesting that behaviour modification and abstinence should be offered as part of a holistic package of care, that psychological interventions to address concurrent mental health issues should also be considered, and that psychosocial interventions should be considered a standard treatment generally. In reference to the NBOMe family of drugs, Suzuki *et al.* (2015) offer clinical recommendations pertaining to harm-reduction strategies that may be suggested to users, namely that they avoid insufflation or injecting, use a “trip-sitter” (a non-intoxicated observer who remains nearby during the individual’s use of the substance) and do not “eye-ball” (visually estimate) doses.

1.16.2.2 Management of physical symptoms

Management of physical symptoms proved to be a further sub-theme. In discussing NBOMe intoxication, Bersani *et al.* (2014) urge that patients suspected of consuming NBOMes be monitored for heart disorders, hypertension, hyperthermia, seizure, lung and/or kidney failure, metabolic acidosis and symptoms of serotonin toxidrome, with treatment strategies including administration of fluid – a recommendation also proffered by Suzuki *et al.* (2015), who suggest utilisation of cooling strategies and pharmacological treatments (though this latter recommendation is not expanded upon further). In their clinical recommendations for amphetamine-type (inclusive of cathinones) substance overdose management, Richards *et al.* (2015) suggest that beta-blockers are an appropriate choice for the treatment of hyperadrenergic state. In the case of unopposed alpha-stimulation – in essence, continued increase in blood pressure and/or coronary artery vasoconstriction that remains unchallenged after beta-blocker therapy (Richards *et al.*, 2017) - combination therapy with alpha and beta blockers is considered reasonable, though the phenomenon does not often appear to occur (Richards *et al.*, 2015). Richards *et al.*, (2015) further note that calcium channel blockers can also be used to treat

hypertension, though not tachycardia, and that nitroglycerin may be administered for chest pain, though caution that this may result in reflex tachycardia.

Kersten and McLaughlin (2015) discuss treatment of piperazine overdoses, stating that care should include general supportive measures similar to those used to treat SCRA overdose (see **Section 1.19.3.2**), as well as initiation of electrocardiogram and electrolyte monitoring. Commonly seen cardiovascular symptoms – such as tachycardia and hypertension – may respond to placing the patient in a calm environment. Further, Kersten and McLaughlin (2015) suggest that severe hypertension may be treated through IV antihypertensives and clonidine, that selective betablockers are not recommended for severe hypertension as they can serve to worsen the effects in the case of piperazine toxicity, and that for refractory hypertension, labetalol is a preferred treatment option.

In relation to cathinone toxicity, intravenous delivery of fluid is recommended by Guirguis *et al.* (2017) to alleviate hyperthermia or rhabdomyolysis – clinical advice shared by Kersten and McLaughlin (2015), which they expand to include treatment of dehydration - with haemodiafiltration further suggested by Guirguis *et al.* (2017) as a treatment for rhabdomyolysis. Kersten and McLaughlin (2015) state that should a patient present with sympathomimetic toxicity or hyperthermia/hypertension unaffected by benzodiazepine administration, cooling and antihypertensives are recommended. Guirguis *et al.* (2017) comment on management of other physical conditions arising from cathinone use, with midazolam or diazepam specified to treat seizures, sodium bicarbonate to alleviate metabolic acidosis, nitrates/calcium channel blockers to address hypertension and vasopressors/inotropes in presentations of hypotension, and that vitamins/nutritional supplements be considered generally. Finally, Kersten and McLaughlin (2015) suggest that serotonin syndrome may be treated using benzodiazepines or cyproheptadine.

SCRAs Overview of Systematic Reviews

1.17 SCRAs – clinical context

Synthetic cannabinoid receptor agonists (SCRAs) were first synthesised in the late 1960's in an effort to develop drugs that would mimic delta-9-tetrahydrocannabinol's (THC) - the primary psychoactive phyto-cannabinoid found in herbal cannabis - analgesic and anti-inflammatory effects but which did not share THC's psycho-activity (Chung *et al.*, 2021). From this period on, a number of research groups continued to formulate and publish novel SCRAs molecules for potential legitimate medical use, including - perhaps most notably - the Huffman laboratory at Clemson university (Howlett, Thomas and Huffman, 2021). Many of the SCRAs developed as part of these projects were ultimately found to have little therapeutic benefit, with many continuing to display pronounced psychoactive effects. In 2008, an SCRA developed in the Huffman laboratory - JWH-018 - was detected in "smokable herbal mixtures" marketed in both Austria and Germany (EMCDDA, 2009). By July 2022, a total of 237 SCRAs were being actively monitored by the EMCDDA (Andrews *et al.*, 2023), which demonstrates the rapid proliferation of this family of substances.

The endocannabinoid system (ECS) is a highly complex structure, comprising a network of cannabinoid/receptor interactions in organs throughout the body so labyrinthine that some researchers posit that the term "endocannabinoidome" is a more appropriate description, given its regulatory role in the vast majority of biological systems (Davis, 2022). At a physiological level the ECS is - at a minimum - involved in the generation and control of glycerol and fatty acids, homeostasis of energy systems - including glucose metabolism specifically - within the body (Chanda, Neumann and Glatz, 2019). Psychologically, the ECS has been demonstrated to be involved in the regulation of anxiety, fear and stress response in organisms (Maldonado, Cabañero and Martín-García, 2020), with interactions between elements of the ECS and a plethora of neurotransmitter-systems - inclusive of the GABAergic, serotonergic, cholinergic and

noradrenergic systems - being hypothesised as playing a key role in regulation of behaviours relating to the aforementioned responses to environmental stimuli (Lutz *et al.*, 2015). The two principal receptors involved in this vast array of regulatory processes are the cannabinoid receptor 1 (CB1) and cannabinoid receptor 2 (CB2) (Reekie and Kassiou,2023), with CB1 receptors primarily being located within the central nervous system whilst CB2 receptors are more common in peripheral and immune cells (Battista *et al.*, 2012).

Whilst the phytocannabinoid THC acts as a partial agonist of the CB1 and CB2 receptors (Chung *et al.*, 2021) SCRA tend to act as full or high agonists of CB1 (Darke *et al.*, 2021) with variable (though in some instances high or full) CB2 affinity (Wiley, Marusich and Thomas,2017). The resultant binding affinity for CB1 may be up to 100 times more pronounced in some SCRA than that observable for THC (Darke *et al.*, 2021). This affinity for CB1 in particular is theorised as being a major contributory factor to the relatively severe (compared to THC) adverse physical (Sachdev *et al.*, 2019) and mental health (Hobbs *et al.*, 2018) symptoms associated with SCRA consumption. The pronounced effect on CB1 of some SCRA creates a further, indirect effect upon the dopaminergic system, in that SCRA's action on the receptor inhibits GABA, in turn increasing dopamine activity within the pre-frontal cortex and raising likelihood of psychotic symptoms (Hobbs *et al.*, 2018). The increased volume of extracellular dopamine within the nucleus accumbens this indirect effect creates is also thought to contribute to the increased abuse liability of SCRA in comparison to THC/natural cannabis, and this may factor into the more problematic and protracted withdrawal process often seen in the former (Darke *et al.*, 2021).

A major obstacle in attempts to control SCRA at legislative level has been the sheer diversity of substances that can be included within the category. One classification system suggests that SCRA may be divided into one of thirteen distinct categories according to structural properties (Chung *et al.*, 2021). To promote consistency in naming protocols the EMCDDA recommend that newly detected SCRA be classified according to a more flexible model, in which four constituent molecular features: core; linker; linked group and tail (Pulver *et al.*,

2023) are considered. However, even this supposedly comprehensive methodology has proven inadequate as a protocol in classifying 15 currently monitored substances, due to their divergence from the afore-mentioned molecular model (Andrews *et al.*, 2023). This again attests to the vast pharmacological divergence inherent in this class of NPS, with perhaps their sole unifying factor being the profound effects they exhibit upon the CB1 and/or CB2 endocannabinoid receptors of the central nervous system (Wiley, Marusich and Thomas, 2017). Researchers and legislators typically divide illicit SCRA into a number of distinct 'generations', wherein the first generation are considered as the afore-mentioned SCRA designed from the 1970s to the 1990s by legitimate laboratories such as the Huffman laboratory, co-opted by clandestine producers in efforts to produce - at the time - legal alternatives to herbal cannabis (EMCDDA, 2009). The SCRA produced within their second and third generations are largely regarded as being conscious attempts by illicit producers to circumvent legislation put in place to control preceding generations (Waugh *et al.*, 2016).

For each generation of SCRA changes to molecular structure from "parent" molecules (i.e., the molecule belongs to a prior generation which acts as a template from which to design a new SCRA) are observed. For example, many third generation SCRA are typified as having substituted the indole ring commonly seen in first generation SCRA such as the afore-mentioned JWH-018 (Wiley *et al.*, 2016) for an indazole or benzimidazole structure (Hobbs *et al.*, 2018). Now in their fourth generation, researchers note that a paucity of data regarding the pharmacodynamics of these very recently designed substances - combined with the lack of drug screening infrastructure to help monitor prevalence and understand issues of mortality/morbidity - inhibits the development of appropriate clinical guidance and public health measures (Malaca, Tini and Umani Ronchi, 2022). Aside from the previously explored issue of relative CB1/CB2 affinity in SCRA and their impacts on health outcomes, this landscape of evermore divergent molecules presents further complications that may not be considered by either users of SCRA or researchers. For example, Howlett, Thomas and Huffman (2021) note that even comparatively limited

alteration of a molecular structure can greatly affect its volatility/thermal stability, which in turn may impact absorption, metabolism and the pharmacodynamic effects of substances when consumed, particularly in context of smoked or vapourised products.

Typically, SCRAs are made available to end users in the form of the aforementioned “smokable herbal mixtures”, which consist of one or more inert dried plant material sprayed with an SCRA as the psychoactive ingredient (Chung *et al.*, 2021). These are generally smoked, are often collectively known as “spice” in grey and black markets (Howlett, Thomas and Huffman, 2021). However, other preparations are observed, with vapouriser liquids, powders and edible preparations such as sweets or baked goods all being recorded as vehicles for SCRAs (Darke *et al.*, 2021). In the context of the UK, use of SCRA-infused blotter papers – often in the form of SCRA-impregnated letters mailed to inmates - is common in prison populations, as this form of preparation lowers likelihood of detection before consumption (Norman *et al.*, 2021). SCRA use in the prison or other forensic settings is relatively common for the described reason, as well as due to lowered chance of detection during routine screenings (Rogers *et al.*, 2022). SCRA usage is also high in the homeless population in the UK (Coombs *et al.*, 2023), with their availability, low cost, potency and subjective effect being motivating factors for their use amongst this demographic (Gray, Ralph and Williams, 2021).

To the researcher’s best knowledge, only one SCRA – nabilone – is currently licensed for use in the UK, where it is indicated for use as an antiemetic in the context of chemotherapy (Joint Formulary Commission, 2023).

1.18 Methodology

As described in **Section 1.6.4**, only the population element of each search was modified for their specific context, with all other elements remaining identical

across the overviews of reviews. In the SCRA overview, search terms employed in the population element were: *synthetic marijuana*; *synthetic cannabi**; *SCRA**; *spice*, with these terms being ascertained as suitable during the researcher's initial research as part of the project overall.

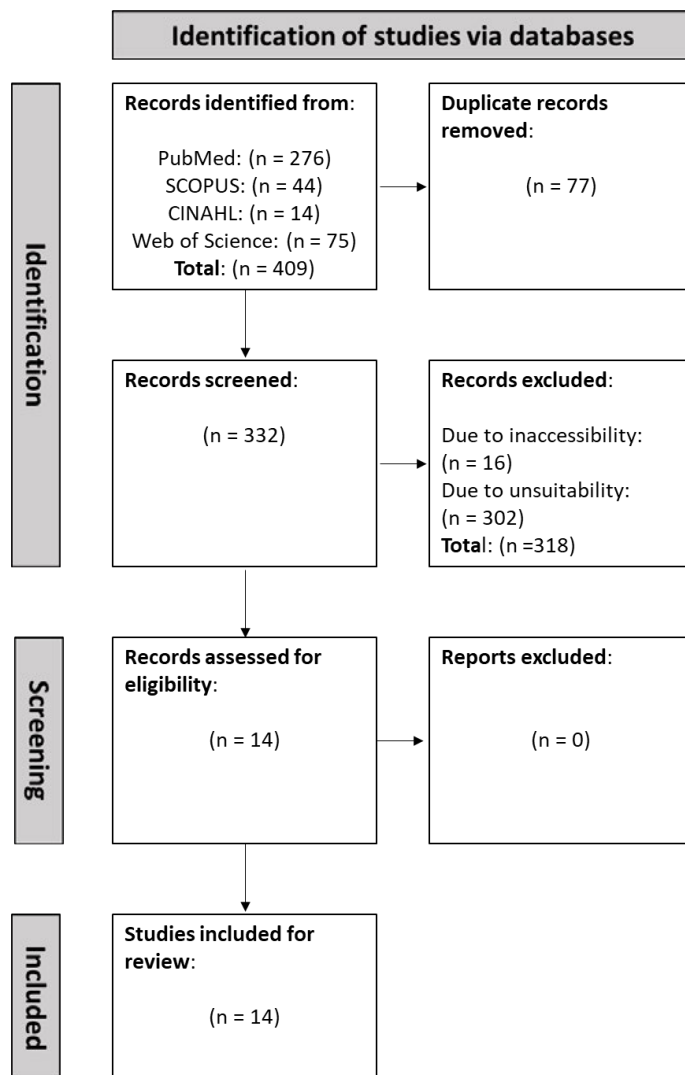
For more details of the search strategy employed, please see **Figures 7** and **8** immediately below, as well as **Appendix 4** (search strategy, PRISMA diagram and critical appraisal tool respectively).

Search #2 (to align with problem/population)				
Search Terms employed				
synthetic marijuana; synthetic cannabi*; SCRA*; spice				
	Database			
	Pubmed	SCOPUS	CINAHL	WOS
Date Searched	28/1/21	28/1/21	28/1/21	28/1/21
No. of results	45,907	153,642	5,068	127,456

Search #3 (to align with study design)				
	Database			
	Pubmed	SCOPUS	CINAHL	WOS
Date Searched	28/1/21	28/1/21	28/1/21	28/1/21
Term	systematic review; meta-analysis			
	Not used due to appropriate filter as search option			
No. of results	N/A	332,244	97,230	2,845,488

Database	Pubmed	SCOPUS	CINAHL	WOS	Exported to Refworks	After duplicates removed
Combined search – no. of results	2,985	86	20	122		
Filters used	Limit to reviews, systematic reviews and Meta-analysis; Published after 2010; human subjects; English language	Limit to review; published after 2010; English language	Published after 2010, English language; peer reviewed	Published after 2010, Limit to review		
After filters	276	44	14	75	409	332

Figure 7: Unique search terms and returns in SCRA's search



Design adapted from Page *et al.* (2021)

Figure 8: PRISMA flow diagram for SCRA search

1.19 Results

Searches were conducted on 21/1/21. After removal of duplicates, 332 papers remained for abstract screening. After this process, 14 papers remained for critical appraisal, with 14 papers ultimately being included. As noted in **Section 1.15**, 7 included papers discussed treatment of stimulants, hallucinogen and SCRA harms generally, whilst 7 discussed these in relation to SCRA exclusively. For a discussion of how papers that discussed SCRA, stimulant and hallucinogen treatment generally were considered please see **Section 1.16**, and

for clinical recommendations derived from the same papers see **Sections 1.20** through **1.23**.

1.19.1 Awareness/vigilance on the part of the clinician

Six of the 7 papers discussed recommendations regarding awareness/vigilance on the part of the clinician. Tait *et al.* (2015) note that – in the event of SCRA overdose - there are no antidotes similar to naloxone as used in cases of opioid overdose, making management of these more problematic. Further, they caution that SCRA overdose lacks a distinct toxidrome as may be observed in use of other recreational drugs, and that clinicians should eliminate a range of other health conditions before diagnosing SCRA overdose, including: hypoglycaemia; CNS infection; hyperactivity of thyroid; head trauma or mental health disorder. Since drug testing will generally produce negative results in SCRA intoxication cases, Brewer and Collins (2014) recommend that use of these substances be determined via clinical manifestations and patient history. Courts *et al.* (2016) state that the symptomology of SCRA toxicity can vary considerably, though in cases of young adult male patients presenting to services with agitation and/or cardiovascular issues without clear cause SCRA intoxication should be considered. Grigg *et al.* (2019) note that clinicians should be aware of drug interactions between SCRA and prescribed drugs such as valproic acid, sertraline and fluvoxamine – which may impact their relative metabolism and half-lives, posing serious health risks (Tai and Fantegrossi, 2017) - as well as consider ones that may not yet be established when planning treatment.

In their review of cognitive issues manifesting in service users after SCRA usage, Cohen and Weinstein (2018) recommend that healthcare professionals be aware of cognitive impairments caused through use of SCRA, should assess for these when appropriate, and that such impairments may be especially pronounced in patients who have used SCRA in large, regular quantities over extended periods or in young people who have used SCRA early in life for prolonged periods. Akram, Mokrysz and Curran (2019) suggest that clinicians specialising in medical treatment of high risk populations for use of SCRA via administration by smoking

or other means (such as in homeless people or prison settings) should strive to have good working knowledge of this drug category in terms of their use and consequences, so as to provide optimum support to users, and that clinicians should consider ways that they can facilitate in research into SCRA, including provision of clinical information as well as access to SCRA users as potential participants for studies.

1.19.2 Design of withdrawal assessment and protocols

Grigg *et al.* (2019) comment extensively regarding clinician awareness as to how SCRA withdrawal assessment should be formulated, suggesting that this should consist of several dimensions. These include identification of SCRA, concurrent cannabis and other drug usage in the patient and comorbid mental health issues in a non-judgemental and supportive manner; explanation of confidentiality and its exceptions, and use of a screening tool such the Cannabis Withdrawal Assessment Scale (Allsop *et al.*, 2011). Consideration of other factors adjunct to the patient's immediate SCRA dependence, such as quantity and frequency of use, natal status if relevant, the patients' prior attempts at withdrawal and potential supports if relevant, as well as identification of risks and complex needs; assessment of psychiatric adverse effects, should also be given (Grigg *et al.*, 2019). Grigg *et al.* (2019) state that measurement of psychological symptoms and distress should be included, addressing: anxiety; agitation; irritableness; insomnia; somatic sensation of pain; psychosis, and suicidality. Physical symptoms that require consideration include: craving, feeling cold; excess sweating; tremor; headache; diarrhoea, nausea/vomiting; pains in chest; palpitations; tachycardia; hypertension; muscle pain; hyperventilation and seizures (Grigg *et al.*, 2019).

Programming of the withdrawal plan should be conducted in a collaborative manner with the patient, with information gathered in such a way informing planning for potential severity of withdrawal, setting for withdrawal, contingency for risk and identified complex needs (Grigg *et al.*, 2019). Finally, Grigg *et al.* (2019) state that plans for the post-withdrawal period should be made in full

conjunction with the patient and should include relapse prevention as well as provision of supports/services to address psychosocial needs. In their review focused on cannabis and SCRA misuse amongst pregnant women, Orsolini *et al.*, (2017) emphasise the importance of clinicians' engagement with the relevant population being non-judgemental in approach and stipulate that consultations should focus on the collection of relevant patient history and assessment.

1.19.3 Management of symptoms

1.19.3.1 Management of psychiatric symptoms

Three reviews made recommendations concerning management of psychiatric symptoms. Both Brewer and Collins (2014) and Tait *et al.* (2016) discuss use of benzodiazepines, with the former authors suggesting their use in cases of extreme anxiety whilst the latter recommend their use in management of agitation. Kersten and McLaughlin (2017) also recommend benzodiazepine administration for both anxiety and agitation and expand this to include catatonia as a symptom that may respond well to this treatment strategy. Kersten and McLaughlin (2017) advise that antipsychotics be considered to treat hallucinations or psychosis, though Tait *et al.* (2014) caution that although haloperidol is also an option, it is not recommended in the case of undifferentiated diagnoses.

1.19.3.2 Management of physical symptoms

Management of physical symptoms was a further major themes in the papers, with it being discussed in four of the 7. Brewer and Collins *et al.* (2014) recommend intravenous fluid administration in cases of copious vomiting, and that this – along with cooling measures - can be initiated to counter hyperthermia, as well as acting as a prophylactic against rhabdomyolysis. Tait *et al.* (2016) state that the main foci of treatment in SCRA overdose should consist of: giving of IV fluids to combat dehydration; preservation of airway; circumventing

rhabdomyolysis; being vigilant for cerebral/cardiac ischemia, though noting that for mild intoxications admission to accident and emergency wards for treatment may not be unwarranted, and symptomatic treatment preferred. Further, Tait *et al.* (2016) suggest that if benzodiazepine treatment for agitation fails, direct methods of ensuring patient airways are maintained should be considered. Brewer and Collins (2014) recommend that treatment should largely be supportive, include vital signs monitoring and placement of patients in low stimulus, quiet environments, and caution that use of activated charcoal for gastrointestinal decontamination should only be considered in the case of consumption of large volumes of SCRA, whilst Kersten and McLaughlin (2017) advise the use of antiemetics where presentations include nausea or vomiting. Kersten and McLaughlin (2017) also emphasise the importance of standard measurement of vital signs and protection of airways in cases of SCRA overdose and concur that treatment should largely be symptomatic and supportive in nature, with IV fluid administration also advised by the authors. Kersten and McLaughlin (2017) also advise that the introduction of telemetric monitoring should be a first priority, and that laboratory testing may be indicated depending on symptoms displayed and may include: complete blood count (CBC); basic metabolic panel; troponin; creatine kinase myo-cardial band (MB) test; creatine phosphokinase and blood gas, with the intention of aiding health professionals in determining what substances the patient may have consumed alongside SCRA.

In their discussion of elements integral for assessment of use and withdrawal protocols for SCRA, Grigg *et al.* (2019) suggest that physical consequences of use assessment should contain examination of: medical history, history of substance abuse, physical examination; consideration of cardiac functioning including electrocardiogram to measure tachycardia, bradycardia and/or arrhythmia, as well as testing of serum electrolytes, renal and hepatic function. More generally, Griggs *et al.* (2019) note that in planning withdrawal from SCRA, physical effects of withdrawal such as psycho-motor agitation and seizures should be planned for, managed or circumvented, with short-term benzodiazepines prescription recommended for withdrawal symptoms, as well as other targeted approaches for other adverse symptoms. Finally, Kersten and

McLaughlin (2017) state that inpatient observations, ventilatory support and/or intubation are – on occasion – required in the event of SCRA overdose.

1.19.3.3 Psychosocial interventions/referrals to other services and harm reduction

Four included reviews included recommendations regarding psychosocial interventions – including harm reduction - or the referral of patients to other services. Cohen and Weinstein (2018) suggest that in the case of cognitive impairment detected after use of SCRA health professionals should consider behavioural therapy or cognitive rehabilitation strategies as treatments. Grigg *et al.* (2019) recommend that clinicians should provide a link to psychosocial supports as part of SCRA withdrawal strategies and should provide psychoeducation aimed at harm reduction. This psychoeducation should seek to increase patients' awareness around relevant mental/physical health risks, link SCRA usage to presenting mental health issues, provision of reduction of use strategies, and strategies to allow users to see the achievement of increased wellbeing as being linked to vocational and social activities, as well as having a healthier lifestyle. Brewer and Collins (2014) note that after recovery from SCRA overdose referral to substance misuse focussed social services may be warranted. Finally, Orsolini *et al.* (2017) state that healthcare workers should provide honest information on the risks of persisting in use of SCRA whilst pregnant when engaging with relevant populations.

Clinical recommendations common to stimulants/hallucinogens and SCRA

Seven papers identified during the initial systematic searches discussed treatment for both stimulants/hallucinogens and SCRA generally, where clinical recommendations were applicable for all categories of substances mentioned.

Recommendations included in these papers were analysed thematically, with results presented below.

1.20 Vigilance/awareness on the part of the clinician

Recommendations regarding vigilance/awareness on the part of the clinician were provided in five of the 7 papers. In their review of the effects of NPS intoxication on people with severe mental health disorders, Gray *et al.* (2016) note that use of NPS by people with severe mental illness (SMI) may lead to significant change to their behaviour, that use of NPS by people with SMI is under-reported and is only recorded when individuals display extreme behaviours, such as agitation and aggression. Furthermore, Gray *et al.* (2016) suggest that it is likely that many individuals with SMI may not understand that NPS are psychoactive substances in the same way that illegal substances are, seeing them as “more natural”, “less harmful” and not see the need to report their use. Gray *et al.* (2016) therefore contest that - considered with their finding that NPS are rarely detected in routine drug screenings – clinicians should ask about NPS specifically in assessments to gain a full understanding of contributing factors to presentation of SMI. Orsolini *et al.*, (2019) also recommend health professionals should be aware of the associations between NPS usage and mental health issues and respond appropriately, whilst Schifano *et al.* (2016) note that routine drug screening is likely to provide negative results in the case of NPS toxicity, and Hohmann, Mikus and Czock (2014) specify that in the event that a patient presents with symptoms similar to overdose with orthodox stimulants though drug screening returns negative results, clinicians should consider NPS use and utilise appropriate services available to them, such as toxicology laboratories to identify specific substances that have led to this presentation.

Orsolini *et al.* (2019) advise that clinicians be aware of possible interactions between prescribed medications and NPS, which may result in: reduced efficacy of prescribed drugs; worsening of symptoms, and reduction of adherence to

treatment plans by patients, with this suggestion also being included in Gray *et al.*'s (2016) recommendations for practice.

1.21 Management of psychiatric symptoms

Management of psychiatric symptoms, especially agitation, aggression and hallucinations, was a notable theme, with it being addressed in three of the 7 papers. Piccioni *et al.* (2020) state that health professionals should be prepared to manage agitation in cases of NPS intoxication, whilst Gray *et al.* (2016) note that in the 14 articles included in their review, agitation necessitating restraint was mentioned in one third of these, with one-fifth making mention of violence and aggression as a feature. Schifano *et al.* (2016) urge that de-escalation (including verbal) should be the primary initial focus in the case of patients presenting with aggression/agitation as the result of NPS use. The same authors recommend midazolam delivered IM 5-10mg or IV/intranasal 2.5-5mg or lorazepam, 4-8mg IM or 2-4mg IV as preferred first line treatment in cases where de-escalation has failed, though note that benzodiazepines often require re-dosing or high dosing to achieve efficacy and this should be taken into account if there is evidence that the patient has co-consumed alcohol. In a similar vein, Richards *et al.* (2015) relate that in three of the papers they reviewed benzodiazepines proved to be inadequate in providing sedation. Schifano *et al.* (2016) also note that if administration of benzodiazepines proves ineffective, antipsychotics may be considered though caution is advised as their administration may contribute to toxicity. Of these, haloperidol/droperidol are preferred (5-10mg IM/IV). Risperidone, olanzapine, aripiprazole and quetiapine may be considered, though there is paucity of evidence regarding their efficacy (Schifano *et al.*, 2016).

1.22 Management of physical symptoms

Two papers commented on management of physical symptoms. Piccioni *et al.* (2020) state that NPS treatment generally should be similar to corresponding classes of "traditional" drugs (such as MDMA, cocaine or cannabis), focus on

maintaining the safety of the patient, and that treatment should be supportive, include ABC management and maintenance of normal body temperature. Piccioni *et al.* (2020) also recommend that clinicians monitor for and counter dehydration and rhabdomyolysis. Schifano *et al.* (2016) urge that treatment of hyperthermia should be considered, including utilisation of cooling strategies and the provision of IV fluid to ameliorate rhabdomyolysis. Schifano *et al.* (2016) also mention that serotonin syndrome can be treated with benzodiazepines or cyproheptadine.

1.23 Psychosocial interventions and referral to other services

Two papers commented on this. Rinaldi *et al.* (2020) recommend that, in cases of addiction arising from use of NPS compounds, treatment should mirror that used for addiction treatment for corresponding orthodox drugs of misuse, and include a 'gradual care' approach, combined with low intensity psychosocial interventions. Withdrawal management, including the possibility of inpatient/residential treatment, can also be considered. Schifano *et al.* (2016) also suggest that appropriate referral to inpatient facilities should be considered, whilst Orsolini *et al.* (2019) state that in reference to NPS and comorbid mental health issues, health professionals should seek to develop tailored treatment strategies, therapeutic pathways and deepen integration between relevant services.

Synthesis of clinical recommendations and design of presentation

1.24 Formatting of clinical recommendations

The main body of the presentation contains most clinical recommendations included above. Certain minor recommendations, such as the use of naloxone to treat loperamide overdose (Schifano *et al.*, 2018) were omitted if: they were considered by the researcher to bear little relevance to the overall focus of the

presentation; were only mentioned by a single source paper and affected the clarity and flow of the narrative. Methodology of gathering evidence (i.e., the literature reviews), as well as sources of information were omitted (i.e., in-text citations and a reference list) were not included in the presentation, as delivery of clinical recommendations was prioritised. In the one instance found where clinical recommendations partially disagreed – where second generation antipsychotics were recommended for treatment of agitation and other psychiatric symptoms during stimulant toxicity by Richards et al., (2015) and Guirguis *et al.* (2017), though Schifano *et al.* (2018) advised that they could be considered though evidence was uncertain – it was expressed that specific second generation antipsychotics are considered safe in treating cathinone toxicity (Guirguis, *et al.*, 2017), though for stimulants and hallucinogens generally there is a lack of consensus concerning efficacy of second generation antipsychotics (Schifano *et al.*, 2018).

Formatting generally followed the organisation of themes presented in the discussions of identified papers' clinical presentations section of this thesis. However, some minor alterations in terms of order or thematic groupings were made to assist in clarity. The section on NPS sedatives/depressants was simplified, with clinical recommendations on topics such as specific populations of concern being included within clinical vigilance, and recommendations regarding specific classes of substances (opioids, gabapentinoids, benzodiazepines) being presented as a whole. Due to the high number of clinical recommendations that were applicable to both NPS stimulants/hallucinogens and SCRA, these were presented together where applicable, before more specific recommendations were shown.

Slide headings used in the presentation's main body were: *Treatment of NPS sedatives/depressants; NPS sedatives/depressants – clinical vigilance; NPS sedatives/depressants – patient education, shared decision-making and harm reduction strategies; NPS sedatives/depressants – Use of naloxone in treating high potency opioids; NPS sedatives/depressants – psychosocial interventions and access to services; Treatment of NPS Stimulants and hallucinogens;*

Treatment of SCRA; NPS Stimulants and hallucinogens and SCRA; NPS Stimulants, hallucinogens and SCRA – clinical vigilance; NPS Stimulants and hallucinogens – clinical vigilance; SCRA – clinical vigilance; NPS Stimulants, hallucinogens and SCRA – management of psychiatric symptoms; NPS Stimulants and hallucinogens – management of psychiatric symptoms; NPS Stimulants and hallucinogens and SCRA – management of physical symptoms; SCRA – management of physical symptoms; NPS Stimulants and hallucinogens – treatment of hypertension and use of beta-blockers; NPS Stimulants, hallucinogens and SCRA – psychosocial interventions; NPS Stimulants and hallucinogens – psychosocial interventions and harm reduction; SCRA – psychosocial interventions and harm reduction, and SCRA – withdrawal protocols and assessment.

1.25 Introduction and conclusion of presentation

The designed presentation began with a brief overview of NPS generally, which included a broad definition of NPS, as well as a justification as to why treatment of these may be considered a clinical challenge.

The definition of NPS used was that proffered by the National Records of Scotland, who state: “The term ‘New Psychoactive Substances’ (NPSs) is meant to cover the kinds of substances that people have, in recent years, begun to use for intoxicating purposes” (National Records of Scotland, 2021), with it being explained in the presentation that this characterisation is preferred by the author due to: it not defining NPS according to legal status of substances; its recognition that the primary motivation for service-user use of NPS is to achieve a psychoactive effect, and its acknowledgement that NPS use is relatively recent phenomenon.

The proposal that NPS constitute a clinical challenge consisted of three supporting arguments. Firstly, the volume of newly recognised NPS that are reported on an annual basis (EMCDDA, 2022), and that the physiological and psychological effects of even relatively established NPS being under-researched

and under-reported (Schifano *et al.*, 2019) was presented as a contributory factor to NPS being clinically challenging. As described in the introduction to this thesis, the relative lack of perceived knowledge and competence in treatment of NPS displayed by even experienced health professionals (Ramos *et al.* 2020) was mentioned in the introduction, as was the high contributory rate of NPS to drug related deaths in Scotland in recent years (National Records of Scotland, 2022).

The presentation's conclusionary slide emphasised key "take home" messages identified by the researcher, derived from the evidence-base gathered from the initial overviews of reviews. These were: that treatment of an NPS substance should primarily mirror established protocols for the family of drugs that the substance belongs to (Guirguis *et al.*, 2017; Piccioni *et al.*, 2020; Rinaldi *et al.*, 2020); that consideration of basic nursing skills, such as ABC management (Kersten and McLaughlin, 2015; Tait *et al.*, 2015; Lovrecic *et al.*, 2019; Piccioni *et al.*, 2020), and maintenance of normal body temperature and attendance to hydration in relation to stimulants/hallucinogens and SCRAAs (Bersani *et al.* 2014; Kersten and McLaughlin, 2015; Suzuki *et al.*, 2015; Schifano *et al.*, 2016; Guirguis *et al.*, 2017) are paramount in emergency situations; that treatment should be symptomatic and supportive in nature (Hill and Thomas, 2011; Brewer and Collins, 2014; Tait *et al.*, 2015; Kersten and McLaughlin, 2015; Guirguis *et al.*, 2017); that treatment of psychosocial elements of NPS misuse should not be neglected (Darker *et al.*, 2015; Guirguis *et al.* 2017; Marsden *et al.*, 2019; Rinaldi *et al.*, 2020), and that withdrawal/dependence treatment for NPS share commonalities with those used for traditional substances of misuse (Darker *et al.*, 2015; Grigg *et al.*, 2019; Rinaldi *et al.*, 2020).

1.26 Delivery of presentation to participants

Once completed, the recorded presentation was uploaded to the researcher's Abertay staff Microsoft OneDrive volume. Upon completion of the pre-test quantitative questionnaire by all participants (please see **Section 1.28** and **Appendix 8**) the recorded presentation was made available to the same by email invitation link to the file.

Use of mixed methodology

1.27 Mixed method approach

Since the central theme explored in the current research – levels of competence and confidence in treatment of NPS related-health issues amongst nursing students – is currently under-researched and understood, it may be understood as exploratory in nature, in that that relevant issues pertaining to it are largely unknown (Watkins and Gioia, 2015). For under-researched topics, mixed-methodological approaches are considered advantageous in that they allow researchers to probe relatively unknown subjects and produce comparatively valid results, compared to those that may be produced if entirely qualitative or quantitative methods are followed (Mackey and Bryfonski, 2018).

Whilst the literature cautions that it is not always necessary (or indeed, possible) to describe a mixed-methodology employed in discrete, established categorisations (Teddlie and Tashakkori, 2006), the experimental portion of the current study can be described as generally following a concurrent triangulation design, in that the data collection and analysis of both qualitative and quantitative elements take place simultaneously, with interpretation of the results of both being considered as a whole (Creswell *et al.*, 2003). Concurrent triangulation specifically is advantageous given the paucity of research on the topic driving the current study, in that the qualitative and quantitative data generated can be integrated during the interpretative phase, and convergence or divergence of the data gathered are both anticipated outcomes (Burns, 2009).

1.28 Design of questionnaire

The questionnaire element consisted of two sections. Given that this was an exploratory research project, the use of this questionnaire can be considered a pilot for its employment in later research stemming from the current study. Both questionnaires have been included as appendices, with **Appendix 6** containing the pre-test questionnaire and **Appendix 7** the post-test.

The initial section queried participants about their demographic information relating to years of life experience and level of professional experience in nursing and healthcare working as a whole, and was influenced by a number of previous, relevant studies.

One study conducted by Guirguis *et al.* (2015), queried London-based pharmacists about their level of knowledge regarding NPS by use of a questionnaire. As part of their findings, Guirguis *et al.* (2015) found that there was a negative correlation between age and knowledge level of NPS, with this finding being supported by a subsequent study by Ramos *et al.* (2020) for healthcare professionals more generally. Therefore, enquiring as to participant age in the current study seemed relevant, to help establish whether this phenomenon is replicated amongst nursing students.

Of the two afore-mentioned studies, Guirguis *et al.* (2015) also enquired as to level of experience of participants - expressed as number of years qualified – although no correlation between this and level of knowledge/confidence was mentioned in their results. However, in their study of psychiatrists' levels of knowledge and experience of NPS related issues, Owie *et al.* (2017) found that level of experience – conceptualised in terms of level of qualification held, number of year in current position and amount of contact with patients who had used NPS – had a correlation with knowledge of NPS in terms of number of NPS substances they were able to name. Level of experience was also included in the questionnaire used in the current study and expressed as year of study and number of years worked in healthcare, to help ascertain whether this had any association with perceived competence pre- and post-test.

Of the three demographic questions asked of participants, possible answers for year of study were presented in absolute terms (1,2 or 3), whilst those for age and number of years of working in healthcare were expressed in ranges (18-22, 23-27, etc. in the former, *no experience*, *1 year or less*, etc. in the latter) to help preserve anonymity of the relatively small sample size used.

The design of the questionnaire's second element was partially modelled on a format utilised in Wood, Ceronie and Dargan's (2015) study of physician and nurses' perceived confidence in treating NPS, where clinicians were asked to rate their perceived level of knowledge and perceived confidence in treating NPS acute intoxication compared to orthodox drugs. As in Wood, Ceronie and Dargan's (2015), Likert scale questions were used to rate participant's level of perceived knowledge and confidence in treatment of NPS, with a score of 1 on the Likert scale used equating to "No knowledge at all/very poor knowledge", and 5 equating to "Extremely knowledgeable" in questions ascertaining knowledge, and 1 equating to "No confidence at all/very little confidence" and 5 equating to "Extremely confident" in questions pertaining to self-rated confidence in the current study. Unlike Wood, Ceronie and Dargan's (2015) study, no attempt was made to gauge participants' professional familiarity with orthodox drugs of misuse. A further divergence of the current study is that questions were formulated from themes that emerged during the literature reviews. These were: *vigilance/awareness on the part of the clinician; use of psychosocial interventions; management of psychiatric symptoms, and management of physical symptoms*, with both perceived knowledge and confidence assessed for each theme with separate questions.

Whilst one the overriding aims of the current study was to explore nursing students' level of perceived competence in relation to NPS, for the quantitative questions included in the questionnaire relating directly to the issue the term *knowledge* was instead chosen. This was due to the relatively ambiguous and nebulous nature of the term *competence* in relation to nursing (Garside and Nhemachena, 2013). However, given that nursing competence is recognised - at a minimum - to include elements of skill, attitude and knowledge (Cowan,

Norman and Coopamah, 2005; Zasadny and Bull, 2015), using the less esoteric term *knowledge* seemed more appropriate for the quantitative element of the experiment, with competence – and its meaning for students in relation to NPS – being explored in the later qualitative element.

The questionnaire was designed on Microsoft Forms, and pre- and post-test versions (which were identical in every regard other than their title) were distributed to participants via email invitations. The pre-test version was released to participants after completion of the recruitment process, and the post-test version was released after completion of the focus group. Data from the questionnaires were tabulated on and analysed using a Microsoft Excel file. Completion of the questionnaires was ascertained by the number of responses recorded on Forms, as the questionnaires were formatted to only allow one completion per form per participant.

1.29 Design of focus group and open-ended questions

For the qualitative element of the experimental stage of the study, the use of a focus group design was chosen for several reasons. Firstly, focus groups are recognised as facilitating the discovery of population values, norms and attitudes relating to a given subject that may otherwise be difficult to establish using quantitative methods, with their relatively informal nature, high degree of participant interaction and low level of moderator direction being integral to this (Parker and Tritter, 2006). The type of participant interaction typical of focus groups is characterised as forming an integration of individual perspectives through the promotion of group members' reasoning, rationalising and expansion of one another's narratives to create "collective narratives" that can provide more nuanced and granular understandings of a topic than individual narratives alone (Hennink, 2014b). Further to this point, Caillaud and Flick (2017) note that focus groups are an ideal qualitative component of mixed-methodological approaches where triangulation of data is required, as they allow for deeper, more systemic understanding of a topic when used in conjunction with other methods than

quantitative data alone or quantitative data combined with other methodologies may allow for. Finally, focus groups are also considered a salient research methodology to assess implementation (Hamilton and Finley, 2019). Given that part of this study sought to assess the implementation of an educational strategy (the evidence-based presentation shown to participants prior to the focus group) the methodology is a valid approach to use. Ultimately, due to the field of study in question being relatively unknown, a focus group design seemed to be justified and appropriate for the research's qualitative dimension, given the methodology's intrinsically explorative nature (Henrik, 2014b).

In terms of design, two major factors needed to be addressed. Firstly, due to the participants consisting of undergraduate nursing students, consideration had to be made as to their availability whilst on practice placement. To ameliorate this potential issue, a synchronous online design was chosen. Lobe (2017) suggests that for this form of focus group to be effective, though thought must be given to the number of participants recruited and their familiarity with technology used. Lobe (2017) recommends 4-6 as being a manageable number of participants for synchronous online focus groups, whilst Hennink (2014b) propose 5 to 10 for focus groups more generally, dependant on study design and purpose. Therefore, a minimum of 5 participants were sought, with 5 ultimately recruited. In term of technological consideration, the focus group was hosted on Microsoft Teams due to the participants' – and researcher's - experience in using this as part of enrolment at Abertay, where the programme is used extensively throughout the mental health nursing course for teaching activities.

Secondly, consideration had to be given to group composition. Hennink, (2014a) states that factors pertaining to this element of focus design that require address include participant level of acquaintance and homogeneity. A high degree of homogeneity amongst group members is valued in focus group methodology, as it is perceived as minimising power imbalances within group dynamics, thus encouraging a greater degree of participant interaction (Sim and Waterfield, 2019). Relative level of acquaintance must be considered in the context of the research topic being studied, as a high level of acquaintance can influence

participant willingness to disclose information should sensitive topics be discussed (Krueger and Casey, 2014). For the current project, a level of participant homogeneity was desired, given the narrow focus of topic under investigation. To expand on this point, it is reasonable to assume that nursing students from a given cohort will have similar levels of expertise, knowledge and experience in terms of nursing and healthcare related issues in a general sense, with these factors being appropriate for the focus of the current study, as well as focus group methodology more generally (Busetto, Wick and Gumbinger, 2020) Level of acquaintance was considered by the researcher to require less attention, as discussion of educational needs is unlikely to be a sensitive topic of discussion for most individuals. Ultimately, recruitment strategy for the focus group (and therefore quantitative questionnaire surveys also) considered all undergraduate mental health students at Abertay university as potential participants, as this would ensure high homogeneity (all participants would be undergraduate nursing students), and a relatively uncontrolled participant level of acquaintance, given that recruitment was open to all year groups. For full details of the recruitment process, please see **Section 1.30**.

In terms of questions that questions were asked of participants during the focus group, these were kept broad and open-ended, in line with recommendations for focus group methodology (Mitchell and Branigan, 2000), Four questions were developed for an hour-long session, which is considered a manageable, appropriate number for this timeframe (Morgan, 1995; Fagerheim and Weingart, 2005). Developed questions were designed to instigate conversation based on participant responses to the recorded presentation in the first instance, before exploring their feelings of competency in relation to NPS-related issues, and finally their remaining educational needs surrounding their topic more generally. This sequencing can be seen to follow a suggestion offered by Krueger, (2012), in that introductory questions concerned a narrower issue that participants had familiarity with (the content of the recorded presentation), before moving to key questions, which were designed to prompt data salient to answering research questions.

In relation to the issues of competence and confidence, as previously discussed, competence is widely considered in relation to nursing to be a somewhat confusing term with a number of differing interpretations (O'Connell, Gardner and Coyer, 2014). However, most definitions agree that elements of knowledge and skill are central to the concept (Weeks and Pontin, 2020). Confidence is regarded as being important in direct relation to competence, both in terms of the development and demonstration of the latter (Zieber and Sedgewick, 2018). Therefore, the sequencing of questions was formatted to stimulate consideration of key elements of competence (knowledge level, feelings of confidence), before introducing the topic of competence itself (as well as its further constituent of skill-level) in direct relation to these. Formulated questions ultimately utilised in the focus group were delivered in the order presented below:

1. *In what ways do you feel that your level of knowledge and understanding of NPS has changed after watching the presentation?*
2. *In what ways has your level of confidence in treating NPS related health issues changed?*
3. *Based on your level of knowledge and confidence concerning NPS and your current level of nursing skill, how competent do you feel in treating NPS-related health issues?*
4. *What gaps in your knowledge about NPS remain after watching the presentation, and what particular topics related to NPS do you think would be valuable for you to learn more about as a nurse?*

Two additional, unplanned questions were asked by the researcher to clarify discourse, with these being:

What's your understanding of the term competency in relation to nursing? (asked after question 3).

Do you feel that your attitudes towards people who use NPS has changed at all in response to the presentation? (asked after question 4).

Recruitment and procedure

1.30 Recruitment and ethics

Participants were recruited by issuing a cohort-wide, blind-carbon-copy email (included as **Appendix 5**) to all undergraduate students currently enrolled on Abertay University's mental health nursing programme. Within the email, details regarding the nature and process of the study were explained, and a consent to participate form that had been approved by the university's Research Ethics Committee attached (please see **Appendix 1**). The email stated that that consideration for inclusion on the study was dependant on return of a completed consent to participate form. The only inclusion criteria considered was that participants had to be active students on the aforementioned programme. Once five completed forms were returned, identified participants were then contacted and advised that they had been recruited for the study.

1.31 Procedure

1. Initial contacting of potential participants (please see **Section 1.30**)
7/4/2023
2. Identification and contacting of recruited participants (please see **Section 1.30**) 10/4/2023
3. Pre-test questionnaire made available to participants by email invitation (please see **Section 1.28**) 13/4/2023
4. Results of pre-test questionnaire gathered and tabulated (please see **Section 1.28**)
5. Recorded presentation made available to participants via Microsoft OneDrive for Office (please see **Section 1.26**) 20/4/23

6. Time and date of focus group organised by individual consultation with participants 20/4/2023
7. Delivery of focus group (please see **Section 1.29**) 23/4/23
8. Post-test questionnaire made available to participants (please see **Section 1.28**) 23/4/23
9. Analysis and interpretation of qualitative and quantitative data

Data analysis

1.32 Analysis of quantitative data

Analysis of data was performed on Microsoft Excel. Due to the extremely small sample size (n=5) no statistical analyses techniques beyond calculation of mean averages of scores and standard deviation (where appropriate) were employed.

From the demographic data, a number of sub-groups emerged, with these being: 2nd year students (n=4) and 3rd year students (n=1) in terms of year of study; those aged 23-32 years old (consisting of n=1 23-27 year-old and n=2 28-32 year-old, totalling n=3, with this group labelled as 23-32YO) and those aged 38-47 (consisting of n=1 38-42 year-old and n=1 43-47, totalling n=2, with this group labelled as 38-47YO) in terms of age.

In demographic information pertaining to number of years of experience working in healthcare, an anomaly emerged in comparing the pre-test and post-test questionnaires. Specifically, in the pre-test questionnaire two individuals described themselves as having had 7-9 years of experience working in healthcare, whereas in the post-test questionnaire 1 individual answered that they had 4-6 years, whilst another answered 7-9 years, with all other answers to this question being identical for other participants across the pre- and post-test phases. The participant who had answered that they had 4-6 years of healthcare experience presented no other discrepancies in regards to their answers related to demographic information pre- and post-test (and could be identified due to this), and assumedly this variance is due to their estimating the time period worked slightly differently when answering the relevant question in the pre- and

post-test surveys those - i.e., they had worked in healthcare for almost exactly 7 years, estimating slightly more than this in the pre-test survey and slightly less in the post-test. Regardless of this, two sub-groups emerged from the data in relation to number of years' experience of working in healthcare. These were: those with 3 years or less of working in healthcare (consisting of n=1 with 1 year or less healthcare experience, n=2 with 1-3 years' experience, totalling n=3, with this group labelled as YHCE \leq 3) and those with 4 to 9 years' experience (consisting of n=2 who had worked 7-9 years in pre-test, and – factoring in the anomalous answer – n=1 with 4-6 years' experience and n=1 with 7-9 years' experience post-test, totalling n=2, with this group labelled as YHCE \geq 4).

Mean averages and standard deviations for the entire sample as well as within and across the aforementioned sub-groups were analysed for pre-test and post-test scores, as well as comparing changes across these phases. Ultimately, analyses by demographic sub-groups proved under-powered and lacking in corresponding qualitative data to generate convincing arguments during triangulation. Therefore, only quantitative trends present in the sample as a whole are presented, as in this instance supportive qualitative data - when compared during the triangulation process - allowed for some working hypotheses to direct future research to emerge.

Data-sets are included as appendices to this thesis, with pre-test results being displayed in **Appendix 8**, post-test in **Appendix 9** and comparison between pre and post-test results in **Appendix 10**.

1.32.1 Pre-test

For the entire sample (n=5), the mean average overall score for non-demographic questions (labelled as NPS-OA) at pre-test was 2.3 ± 0.6 . Overall scores regarding confidence (C-OA) were marginally lower - 2.3 ± 0.7 - than those for overall knowledge (K-OA) at 2.4 ± 0.4 , with SD standard deviation being notably higher for the former.

The highest mean average score was for an individual question was for *What is your level of knowledge regarding psychosocial interventions for treatment of health issues arising from patient use of NPS?* (hereafter labelled as K-PSI), with an average of 2.6 ± 0.5 for this. The score for questions relating to psychosocial interventions combined (i.e., mean average of knowledge and confidence, hereafter KC-PSI) was 2.4 ± 0.7 , with this also being the combined mean average for questions concerning knowledge and confidence relating to management of psychiatric symptoms (KC-PSYCH), making these the joint highest combined scores pre-test.

The highest mean average score for questions relating confidence to individual themes was in *What is your level of confidence regarding vigilance/awareness on the part of the clinician regarding patient use of NPS?* (C-VIG), with a score of 2.4 ± 0.5 , closely followed by the mean average score for *What is your level of confidence regarding the management of psychiatric symptoms in the treatment of health issues arising patient use of NPS?* (C-PSYCH), which was 2.4 ± 0.9 . Corresponding scores for these themes in relation to knowledge were 2.4 ± 0.5 for clinical vigilance (K-VIG) and 2.4 ± 0.5 for management of psychiatric symptoms (K-PSYCH), with it being notable that scores for knowledge and confidence in relation to clinical vigilance/awareness were identical (and thus their combined mean average score – KC-VIG - was also 2.4 ± 0.5), and that the combined mean average score for questions relating to management of psychiatric symptoms (KC-PSYCH) was slightly higher when variance was accounted for at 2.4 ± 0.7 .

The lowest scores for knowledge and confidence by theme were for *What is your level of knowledge regarding the management of physical symptoms in the treatment of health issues arising patient use of NPS?* (K-PHYS) at 2.0 ± 0.0 and *What is your level of confidence regarding the management of physical symptoms in the treatment of health issues arising patient use of NPS?* (C-PHYS), at 2.0 ± 0.7 , respectively with a far higher variance (considered as standard deviation) in the latter. Further, the lowest combined mean average score was also found to be in relation to management of physical symptoms (K-PHYS), at 2.0 ± 0.4 .

1.32.2 Post-test and comparison

Scores increased for all measures in the entire sample. The mean average total post-test for NPS-OA 3.1 ± 0.5 (a mean average increase of 0.8), with the mean average post-test for K-OA being 3.3 ± 0.4 (mean average increase of 0.9) and the mean average post-test score for C-OA being 3.0 ± 0.7 (mean average increase of 0.75), indicating that perceived level of knowledge overall had increased more substantially and with less variance than it had for confidence.

By themes overall, the greatest increases were seen in KC-VIG (mean average of 3.3 ± 0.5 post-test) and KC-PHYS (mean average score of 2.9 ± 0.4), both of which had mean average increases of 0.9. This is of particular interest, given that KC-VIG and KC-PHYS had the highest and lowest mean average scores at baseline. When data concerning confidence and knowledge in relation to these themes is interrogated separately, a similar pattern emerges, with K-VIG and K-PHYS both increasing by a mean average score of 1.0, and C-VIG and C-PHYS also both having mean average increases of 0.8 from baseline.

The least pronounced increase was in KC-PSI, with the post-test mean average score being 3.1 ± 0.6 , representing a mean average increase of 0.7. When knowledge and confidence for this theme were considered separately, K-PSI post-test was 3.2 ± 0.4 - an increase of 0.6 from baseline. This was the lowest increase amongst knowledge related questions by theme, with all other themes recording an increase of 1.0 for knowledge – whilst C-PSI mean average score was 3.0 ± 0.7 , a mean average increase of 0.8, which – as noted above – it had in common with C-VIG and C-PHYS. The lowest increase for confidence by theme was in C-PSYCH which – at a mean average 3.0 ± 0.7 – represents an increase of 0.6 from its baseline.

1.33 Thematic analysis approach of qualitative data

A thematic analysis approach was adopted to interrogate qualitative data from the focus group for several reasons. Firstly, thematic analysis is considered a

highly flexible approach that supports interpretation of differing types of datasets, whether these are considered by relative sample-size, homogeneity of participants (Clarke and Braun, 2017). Claims to thematic analysis's wide-ranging utility are also supported by the observation that it can be applied to both inductive and deductive theoretical approaches, as well semantic or latent data exploration (Braun and Clarke, 2021). Given the fact that an inductive approach was primarily preferred - though a secondary, deductive element (in relation to understanding participant attitudes towards the relationship between knowledge, confidence and competency as it pertains to NPS, in comparison to understandings of this relationship more generally) was postulated as potentially necessary – a thematic analysis method was considered attractive. Another salient feature of thematic analysis is that - in using the method – one is able to identify not only themes emerging from the research question, but ones that arise that are suitable to inform future research relevant to a topic (Clarke and Braun, 2017), thus making it appropriate for this research. Further, thematic analysis is noted as being a readily understood and applied method for nascent qualitative researchers (Lester, Cho and Lochmiller, 2020), therefore making it suitable in respect to the novice status of the researcher.

As suggested by Braun and Clarke (2006), a process that consisted of: data familiarisation; initial code generation; searching, reviewing and defining themes, before findings were presented herein was followed, with these stages being actioned independently, reviewed and discussed by both the researcher and their supervisors.

The focus group was conducted on Microsoft Teams and was recorded using Kaltura. From the latter software, an initial transcript was produced, that was then amended by the primary researcher to ensure that it represented a true and accurate record (i.e., to account for any errors that Kaltura's automatic transcription had produced). The focus group recording, original and amended versions of the transcripts were made available to the primary researcher's supervisors, who ensured that the final, amended version represented a true and accurate record. This process took approximately four days.

Identified dominant and sub-themes are displayed in **Figure 9**, and then discussed immediately below.

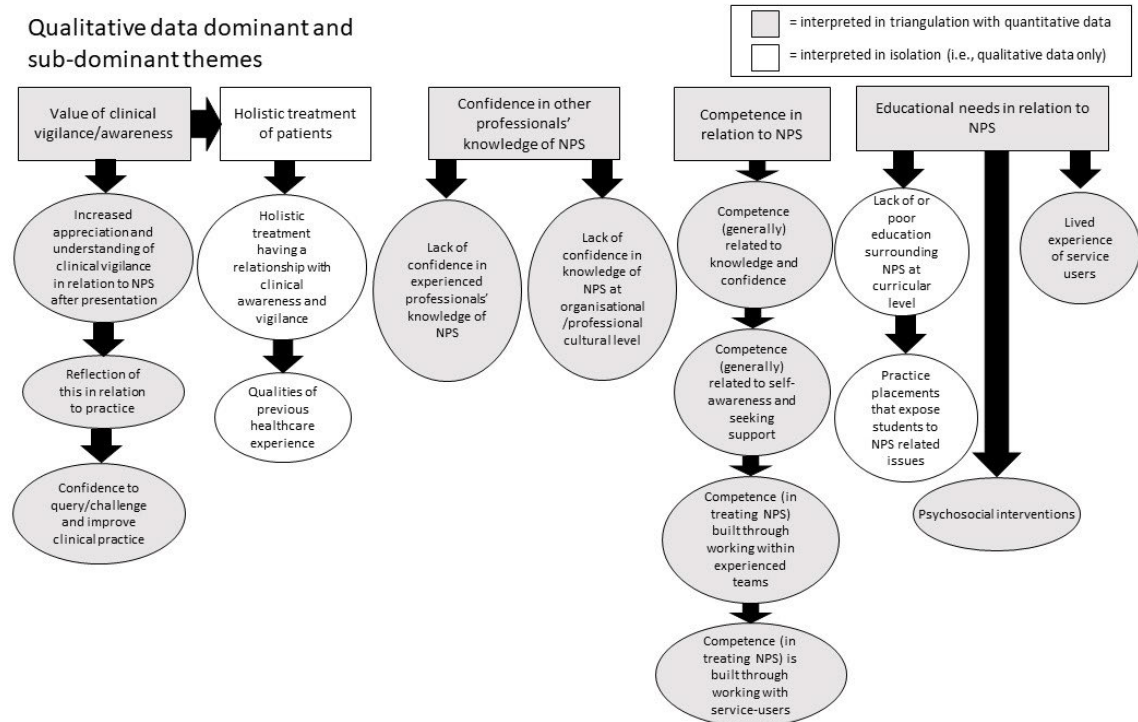


Figure 9: Dominant and sub-dominants themes identified during thematic analysis of qualitative data

1.34 Qualitative themes

1.34.1 Value of clinical vigilance/awareness in relation to NPS

Clinical vigilance/awareness proved to be a theme that was highly valued by participants:

What we should be looking at – and what I found really useful - was the clinical vigilance. Just asking about assessments and making time to ask the question about whether they're using any of these substances.
 (Participant 4)

The clinical vigilance is something that I think was really... that was probably the most important part to me, and something that I think that everyone would gain something from learning. (Participant 1)

1.34.1.1 Appreciation of clinical vigilance/awareness after presentation

Participants expressed that their clinical vigilance regarding NPS had expanded – at least in part – due to the presentation. More specifically, it served to increase their understanding that – in relation to NPS – clinical vigilance/awareness necessitates a broader conceptual understanding than may typically be seen in other health-related subjects. This was related specifically to understandings of how NPS can be defined:

I wasn't aware that it was also things like fentanyl and things that we actually are administering. And I was thinking of it more as- yeah - things that are being created and sold on the internet or these kinds of things. (Participant 2)

as well as the populations that may be affected by NPS:

I think I didn't realise the groups of people so much who it could affect and what the effect could be on a person as much. I think I had the belief that it's like "it's a legal high, it's not that important. It's not that disruptive." But I've definitely changed my view on that. (Participant 3)

1.34.1.2 Reflection on placement experiences in light of clinical vigilance/awareness

Further, participants often reflected on the importance of clinical vigilance and awareness in relation to their own previous experiences on placement. This was related to both the need to treat holistically:

[O]n placement, I found that quite often, maybe in community, we've got the community team that know the psych drugs and they know the psych history, but they don't necessarily know the physical history. (Participant 4)

as well as to how definitions of NPS are utilised in professional practice, where participants implied they were poorly defined:

I think even last placement in forensics, I remember somebody's history. It was said that they took drugs that we're more used to hearing or seeing about and novel psychoactive substances. And then, after watching that presentation, it's like we really need to actually define what those are, because actually they're all going to have really different effects. (Participant 2)

1.34.1.3 The relationship between clinical vigilance/awareness and confidence to query observed practice

Generally, content regarding clinical vigilance was applied by participants to their feelings of confidence to query current practice that they had observed, as well as in anticipation of becoming registrants:

The thing about having more confidence is to make sure those questions are asked, those questions to really explore more in depth. The [patient] history is really important. (Participant 4)

Some participants felt that they had gained confidence to challenge – or at least seek clarity and expansion upon - protocols concerning NPS seen in practice. This was especially pronounced in relation to operational definitions of NPS:

I think I would feel more confident in actually questioning... well, everyone now. Like let's say... whether it was like nursing staff, I would feel like way

more confident in being like “Okay, you're saying they're NPS, but like what is it? Like, do we need to do a further assessment?” (Participant 1)

Realistically, if I see that phrase [NPS] coming up, if I'm on placement, you know, be like “Do we know what the substances are?” Kinda, “What's going on with that?” (Participant 2)

For other participants, knowledge gained regarding NPS had increased their confidence, though not to the extent that they felt they could challenge current practice now or in the near future:

At this stage in my nursing career, I would feel a bit anxious about being this newly qualified that comes in and just goes, “well, what about this? What about that?” But I suppose that's our role to really shake it up a little bit. (Participant 4)

1.34.2 Importance of holistic treatment

A further dominant theme to emerge was participants' realisation of the need to treat patients with NPS-related health issues in a holistic manner. This was considered in direct relation to another dominant theme – clinical vigilance and awareness – as well as in relation to qualities of previous healthcare experience that participants had.

1.34.2.1 Holistic treatment and its relationship with confidence and clinical vigilance

Often, this was again related to feelings of confidence, as well as the theme of clinical vigilance:

I think I'd feel more confident to monitor physical health as well. Because I think sometimes you forget like all the links between that. You just think, "Oh, they're using drugs" and you just think because - I don't know if it's because it's mental health nursing - but you just automatically think of mental health and, like, delirium or psychosis, and I think I do forget about the physical side of it sometimes. So yeah, I'd definitely be more confident in doing the kind of assessment and following up on it. (Participant 1)

I suppose, with any substances as well... You really are thinking about both physical and mental health aspects. Like, yeah, as nurses, it becomes really important to be alert to both of those sides because yeah... because of the things that can happen to your body and the risks. And the risk of - what you said - like diagnostic overshadowing. Like thinking - "Okay, this person could actually just be in withdrawal" - you're seeing as their mental health issues or yeah. I don't know. I think actually it makes me realize, again, being attuned to both aspects is very important. (Participant 2).

1.34.2.2 Holistic treatment and qualities of prior healthcare experience

A further sub-theme related to the value of holistic treatment that arose was the effect that the *qualities* of prior healthcare experience that participants had gained upon consideration for this:

I don't know if it's because I've done so many general bank shifts as a health care that I'm more in tune to physical health becoming problematic in mental health. I correlate it quite a lot. I've had them say to me quite a few times on placement that I look at the physical and then the mental. Again, I just don't know if that's because of my work and background that I question. (Participant 3)

Yeah, that's really interesting [PARTICIPANT 3], because that kinda goes back to the environment thing. Like, because I've only really worked in mental health wards, I feel like that's probably where I get that first line of thinking about the mental health side of things. And you've done the general side of it. So that does again kind of reinforce it - whatever environment you're in, that's where you're doing that learning about it. (Participant 1)

I was quite like [PARTICIPANT 3] - she's had an awful lot more experience in general than me - but in the last placement I had, the ICU placement - really made a difference to seeing how much somebody's physical health can be affected by drug use. And I was surprised. I thought the ICU would be very much everyone who'd been in a car crash or something like this. And so many people who were going through this process of being there, it was down to - in part - to drug use and substance misuse, unfortunately. That was a real surprise to me. (Participant 4)

1.34.3 Confidence in relation to other health professionals' competence and organisational culture

As previously touched upon, participants implied that health professionals often lacked sufficient understanding of what is meant by the term NPS, which participants perceived as having a negative effect on their subsequent clinical vigilance and awareness. Concern regarding the knowledge levels of established professionals was also expressed in other ways. Namely, in relation to established professionals themselves, as well as in relation to organisational and professional culture.

1.34.3.1 Confidence in relation to other healthcare professionals' level of knowledge regarding NPS

Participant 4 expressed concerns regarding post-registrant levels of knowledge and competence in relation to NPS generally:

I would be worried that maybe staff that haven't had this sort of training or perhaps staff that are coming towards more, the end of their career and they're not as interested in gaining new skills because they're quite happy with the skills they've got already. I would lack confidence in them actually being able to identify and make these inquiries about the patients.

and also provided a specific example:

Although - I did mention the fentanyl patches, that they can be burnt or chewed - here in placement. And they said, "Yes, but the patches have got a really low therapeutic dose." (Participant 4)

1.34.3.2 Confidence in relation to organisational and professional culture

Whilst the above sentiment was not explicitly echoed by other participants, parts of their discourse suggested that they felt that lack of awareness regarding NPS – considered at organisational/cultural level – may result in poor or insufficient working practices in relation to NPS within healthcare environments. At times this was somewhat speculative:

Coming back to what [PARTICIPANT 1] just said, I would be interested in... in the prison settings aspect of it, because the Mental Health Act really isn't used fully within prison settings. So I would be quite interested to see what they would do - because I know spice is a big problem in prison settings - what they do with people who are obviously going through really bad mental health rather than carting them off into segregation. I'd like to see how they dealt with that. (Participant 3)

Though in other examples was founded in more concrete experience:

[O]bviously, if someone's coming in at that crisis point - until you can get them down to a level where you can fully assess them - It's kinda keeping them safe and that in the meantime. And I think I've definitely seen some bad practice surrounding that on placements and wards that I've been in before. And I don't think that's based on the staff themselves. I think it's based on not being educated in what the best practice actually is.
(Participant 1)

I've just got a post in addictions. And I'm, like... so it's definitely good to have this as a starting point and to be able to find out more about it. Because a lot of the time, it's kinda more generalised in drug and alcohol.
(Participant 1)

Others saw their position as student nurses/imminent registrants as presenting an opportunity to instigate reflection in established professionals on their working practices and levels of knowledge regarding NPS:

I think sometimes it can be good to be a student or be newly qualified and just ask questions and almost sound - like - slightly naïve. Like, as if... you don't have an agenda, but actually you are kind of saying "No, but why are we doing this?" But you can make it sound a little bit like, "Oh, but why do we not know what substances a person's taken?" I don't know. Sometimes there can be – like - you can have a bit of strength in just seeming like you're not that knowledgeable yet. Because actually then people think "Well, I don't actually know the answer to that question", and then it makes them think about it. (Participant 2)

1.34.4 Conceptual understandings of competence

Participants discussed their understanding of competence as a general concept, as well as applied to treatment of NPS-related health issues more specifically.

Although there were clear similarities between the two conceptualisations, one element – working with service-users – was related exclusively to building competence in relation to NPS.

1.34.4.1 Understanding of competence generally in relation to knowledge and confidence

The participants proved to have a nuanced understanding of the term competence. Some in the group related it to confidence and the ability to work independently:

[Competence is] to be able to do something with great confidence with minimal assistance and actually feel that you definitely know what you're doing. That's what it would mean to me. I would want that to feel at that level. (Participant 5)

Others emphasised the importance of working from an established evidence-base - as well as having the willingness to continually build upon and develop one's own professional knowledge – as being a key aspect of competence:

I think to the best of your ability, [competence is] just trying to be aware of what is the latest evidence. Like, just to know that what you're doing is coming from a background of knowledge and experience and research, and all of these different things. (Participant 2)

I feel competent nurses are willing to learn as well, always expanding your knowledge. Otherwise, I think people become quite stagnant in their roles. (Participant 3)

1.34.4.2 Understanding of competence generally in relation to self-awareness and professional responsibility

The participants also felt general nursing competence to be related to self-awareness, professional responsibility and attitudes pertaining to their level of ability and its limitations. Additionally, this was related to willingness to seek advice or support:

I agree with what [PARTICIPANT 5] said, but also the aspect that if something did go wrong, that I would have the knowledge and the insight and awareness of my own level of responsibilities to actually be able to say, “Hang on, something's going wrong here” or “something has gone wrong” and then know where to report to and where to seek assistance (Participant 4)

I think something about competence is also about boundaries. It's kinda like knowing “this is what I'm operating within”. Like [PARTICIPANT 4] was saying - like knowing when to escalate, or knowing when to... like, it's about working with other people as well. (Participant 2)

1.34.4.3 Competence in relation to NPS built through working within experienced teams

The concept of competence – in relation to NPS – was related by the participants primarily to gaining working experience in appropriate settings, and – as with competence generally – in working alongside experienced and skilled team-members:

I think I would just need that real life practice and real-life observation and to be part of a team, and to be part of discussions and to meet. (Participant 2)

I also think having practical experience of it and speaking to nurses who have experience or medics as well is highly important – pharmacists, etc. - just to build on this knowledge as well. (Participant 3)

So I think working on an MDT would be the way forward to build up your confidence on both sides for mental health disorders and also for any addictions, drug service. I think we all have to build up our confidence and our skills before we could be fully competent or confident around it [the issue of NPS]. (Participant 4)

1.34.4.4 Competence in relation to NPS built through working with service-users

However, another element the participants considered important in building competence in treating NPS-related health issues was working directly with service-users. This was notable as it had not been expressed in relation to competence as a general concept. The sub-theme was considered by participants as being of comparative importance as working with experienced professionals, and was related by the participants' to improved health outcomes and increased professional confidence:

Having that team perspective is going to give you a better outcome for that person as well - and involving them in it [their NPS related care-planning] - as well. (Participant 1)

I would just echo what everybody else has been saying in relation to that [competence]. I think it would take a lot of experience dealing with patients to slowly build your confidence up. Or perhaps in a certain area, where you see the same thing happen time and time again. (Participant 5)

1.34.5 Educational needs in relation to NPS

Remaining educational needs that were identified by participants were related to a perceived deficit or poor standard of content in currently available resources generally, which was contrasted with the relevance of the issue of NPS locally and nationally. Specifically, the need for content concerning the lived experience of service-users and the use of psychosocial interventions in treating NPS emerged as further sub-themes.

1.34.5.1 Lack of education on NPS at curricular level and from other sources

Participants stressed that they felt that education surrounding NPS – as well as substance misuse more generally – was lacking in university curricula, and that learning about NPS came primarily from placement experience.

I haven't really learned that much about it through uni or through, like, other education, as much as just being in that environment and actually seeing it, if that makes sense. (Participant 1)

This was often also discussed in the context of how pertinent the issue was to the local area:

Yeah, considering that we're based in Dundee, it's quite interesting that we don't get a lot on NPS or as much substance misuse as I thought we would at uni. Considering the levels of it actually in Dundee. So that PowerPoint is quite interesting in the fact that it's definitely furthered my education of them, which I'm quite surprised the uni doesn't do? (Participant 3)

I think one of the statistics at the start really stuck out that they're [NPS] involved in 64% of drug deaths [in Scotland] and just made me realise this isn't - this shouldn't be like a sidelined additional note to talking about drugs, alcohol. That's going to be a part of it now. (Participant 2)

Current educational resources about NPS at university level and from other sources was felt to be lacking, and antiquated in their terms of reference:

My learning on the subject mostly comes from other courses or just general knowledge gained from the media. So I don't think it's something that's really, as we say... we talk about people having addictions and I think we have this image. And unfortunately, I would actually say that some of the slides and presentations that we get, maybe we use the typical stereotypical sort of "needle and spoon". All these sorts of pictures. That is, we have this idea of addictions just being like the typical, stereotypical images. (Participant 4)

1.34.5.2 The need for practice placements that involve management of NPS-related health issues

Practice placements that would help participants gain experience of managing NPS-related health issues were considered as valuable by the participants:

I think just having experience with NPS as well – overall - within placements, because some of the placements we've had... really this is probably my first time in placement experience in somebody that does have an issue but NPS. Whereas any other ones, I've never had an experience of it. (Participant 3)

Interestingly, some participants reflected that – in considering placement experience in light of new information gained from the presentation – previous or current placements had involved management of NPS in terms of clinical vigilance/awareness:

[L]iterally on the placement I'm on at the moment... this week we've had a change from pharmacy, which – this is [name of placement] - where certain medications such as pregabalin are now treated as locked cupboard. I

mean, obviously the supply - the storage - is always locked, but they are now classed as “attractive medications”, and... because they have been subject to going missing from the hospital environment. So they're not controlled drugs. However, they are subject to new controls within the practice environment. So that ties in effectively to what we've been looking at with this presentation.

This form of reflection also prompted participants to consider events that had occurred on placement in terms of treatment they had seen of placement, in light of newly gained knowledge of NPS:

But it's something I did think about before in a placement where somebody was admitted and it was kinda that thing of – like - nobody really knew what drugs they were taking, or how much it was impacting their presentation, and what was safe to give to them and what could really be hoped for expected in terms of returning to some kind of baseline.
(Participant 2)

1.34.5.3 The need for lived-experience-based content within education on NPS

Something that was widely agreed upon by participants was the need for educational content in nursing curricula regarding the lived experience of people who had used NPS:

[W]hat would be nice is to get some lived experience voices in there, because that's obviously - this [the presentation] is very much a knowledge... almost like a knowledge dump. But there's no real comment on how it would be to go through that recovery process. Or perhaps even not necessarily somebody who's experienced it themselves, but perhaps families who are looking at what has gone wrong for their loved one and how that can impact on them. So I think that would be interesting point to bring in. (Participant 4)

I think definitely what [PARTICIPANT 4] was saying, the lived experience or service user's experience could be an interesting thing to bring in – just, yeah - because if you're reading about a drug and its impacts, it's all very abstract unless you've actually experienced it. (Participant 2)

Others agreed, though saw inclusion of lived-experience content as presenting potential challenges:

I think that lived experience is something that is quite important for myself to hear as well. But I do understand the barriers, and a lot of people may be resistant to actually talking about it, chatting about it, because of stigma, etc. That could be quite a difficult one to conquer. Or they might downplay what's going on because they don't want to see it as a problem. So again, I see that as an issue, but I do feel life experience is one of the most valuable feedback forms you can have. (Participant 5)

1.34.5.4 The need for education on psychosocial interventions

Participants expressed a need for more educational content on psychosocial interventions:

I think something I would also be interested in is just talking about some of the challenges of developing therapeutic relationships surrounding NPS. Like - maybe how difficult that could be - dependent on what point somebody is with the recovery if they are in that recovery process. Or, if they're actually taking something, or if they're taking something recently or - I don't know - just a bit about how that can impact maybe more – like - psychosocial interventions. (Participant 2)

Further, this need was mentioned explicitly in relation to feelings of competence:

I wouldn't feel competent in delivering anything at the moment bar working in a team to assess. I would want to go and do CBT training well before I offer anything like that to a person. (Participant 3)

Finally, it was noted by one participant that knowledge of people's motivations surrounding qualities of their NPS use would inform clinician strategies for building therapeutic relationships:

There's gonna be different reasons why you'd want to take one [NPS] versus another. Then it also would inform how you would approach that person (Participant 2)

1.35 Triangulation and interpretation of both data-sets

1.35.1 General strategy and overview of emergent themes

Findings of the qualitative and quantitative data were considered in tandem. Where discourse from the focus group could not add context to phenomena recognised in the quantitative data – such as trends seen in the pre- and post-test self-ratings of the sample considered as separate age groups - these were not pursued. The reason for this being that the extremely small sample size meant that the quantitative data alone was considered as too low-powered by the researcher - unless supported by the relatively richer data-set gathered in the qualitative phase of the project – to have enough value for identification of avenues for further research. In summary, data triangulation only proved satisfactory when the sample as a whole was considered.

Ultimately, two themes emerged when quantitative and qualitative data were triangulated. The first of these was: *Understanding of clinical vigilance/awareness in relation to NPS*, with the second being: *Knowledge, confidence and feelings of competence in relation to psychosocial interventions*.

1.35.1.1 Understanding of clinical vigilance/awareness in relation to NPS

As noted in **Section 1.32.1.**, the highest scored theme – if degree of standard deviation is considered - by the entire sample was clinical vigilance/awareness, with the mean average score for this being 2.4 ± 0.5 . From this data alone, one may surmise that clinical vigilance/awareness was the area in which participants felt the most competent in and would perhaps assume that this measure would see the lowest increase in score in the post-test phase. However, this was not the case, with the mean average post-test increase for this measure being 0.9, the joint highest alongside management of physical symptoms, which had the lowest mean average score at pre-test (see **Section 1.32.2.**).

Much discussion during the focus group concerned the value and importance of clinical vigilance/awareness. This was expressed by participants in terms of: having a greater understanding of and appreciation for how clinical vigilance/awareness is considered in relation to NPS after viewing the presentation (see **Section 1.34.1.1**); applying newly gained knowledge of NPS-related clinical vigilance/awareness to reflection on previous placement experience (see **Sections 1.34.1.2.** and **1.34.5.2.**); confidence to query observed practice (see **Section 1.34.1.3.**) and in relation to newly gained confidence to treat patients holistically (see **Section 1.34.2.1**).

When the quantitative and qualitative are interpreted together, evidence - albeit tentative - emerges to suggest that participants may have over-estimated their initial perceived knowledge and confidence in regard to clinical vigilance and awareness. This hypothesis explains both the relatively high initial scoring given to this theme and subsequent high increase post-test. Further, it helps drive interpretation of how participants consider clinical vigilance/awareness in relation to their ongoing development as nurses.

Within the qualitative discourse, participants greatly valued clinical vigilance/awareness as being a tool by which they could interrogate both prior

and anticipated experiences of healthcare working. In a phenomenon that at first appears paradoxical, participants expressed uncertainty regarding established healthcare professionals' levels of knowledge and their subsequent competence surrounding NPS, whether this was viewed as being in relation to such individuals as discrete entities (see **Section 1.34.3.1**) or more as a result of them belonging to organisational/professional cultures that did not give due consideration for NPS-related issues (see **Section 1.34.3.2**), though competence – both generally (see **Section 1.34.4.1**) and in specific relation to NPS (see **Section 1.34.4.3**) and its development in student or registrant nurses was directly related by participants to working within experienced healthcare teams.

This paradox may be resolved in light of the idea that participants viewed a robust level of clinical vigilance/awareness as being a framework from which to evaluate observed practice. Competence in relation clinical vigilance/awareness is possibly viewed by participants as being comparatively more knowledge than experientially driven than it is in the other themes discussed in the presentation. For these other themes, competence is not built from strong theoretical knowledge alone, but through practicing skills that are applicable to both NPS-related issues as well as substance misuse more generally in close conjunction with professionals who have high experiential levels of their delivery. Using this theoretical model, working with established professionals is still considered invaluable in building competence in many aspects of NPS related treatment, regardless of said professionals' relative levels of knowledge regarding clinical vigilance/awareness in NPS, as it is their proficiency in these more generalisable (in the sense that they have utility within and beyond NPS-related treatment) healthcare skills that is prized by student nurses.

Other quantitative data gives further – if again, tentative – support for this working model. Although confidence considered independently for each theme had increased by the same mean average amount - 0.8 - for the three joint highest rated themes considered by this measure - clinical vigilance/awareness, psychosocial interventions and physical management - clinical vigilance/awareness had the lowest standard deviation for this score, at 0.4

compared to 0.7 for the other two themes, which was also the lowest standard deviation observed for any independent measure of theme, aside from the SD score of 0.0 observed in knowledge of physical management of symptoms. Obviously, this suggests that participants had greater uniformity in their perceived increase in confidence for the theme of clinical vigilance/awareness compared to other themes.

The greater variance seen in these other themes may be explained if one works from a particular viewpoint. Specifically, that – due to combination of participant-to-participant differences in established skill-sets, life and work experience, as well as innate ability, preference and professional interest – participants will naturally display more uneven levels of confidence, due to them associating confidence pertaining to themes - outside of clinical vigilance/awareness - more definitively to practical skillsets allied to these themes, as well as level of experience in delivering such skills. Participants may equate confidence in relation to clinical vigilance/awareness more directly to knowledge than to skillset/level of experience, and subsequently feel relatively competent in this regard, given that they primarily perceive this domain of NPS in the context of the querying of and reflection upon observed practice.

Some credence is – again, partially - given to this theory when further quantitative data is examined. Whilst variance considered as standard deviation is considered for knowledge scores independently by theme post-test, these prove lower than those observed for corresponding confidence scores. This may suggest that although acquisition of knowledge is perceived as relatively attainable and incorporable from sources such as the presentation and similar resources, its translation into competence – considered as being partially expressed through confidence – is less readily so, as this also requires attainment of skills and supervised, hands-on experience of their delivery. As demonstrated above, the sole exception to this phenomenon is observed in clinical vigilance/awareness.

1.35.1.2 Knowledge, confidence and feelings of competence in relation to psychosocial interventions

Further to the above, an observable phenomenon that emerged from quantitative data was a relative disparity between mean average score increases from pre-test to post-test in confidence and knowledge in relation to psychosocial interventions. The theme of psychosocial interventions considered as inclusive of both knowledge and confidence received the least pronounced increase of any theme at 0.7. When expressed independently, knowledge pertaining to psychosocial interventions received the lowest increase of any independent knowledge score at 0.6. Perceived increase in confidence was more comparable to other themes, with increase in confidence in relation to psychosocial interventions receiving a mean average score of 3.0 ± 0.7 , representative of an increase of 0.8, which it had in common with both confidence in relation to clinical vigilance and with management of physical symptoms. This relationship (mean average knowledge increase being higher than confidence increase) was unique to psychosocial interventions, with the inverse being true for all other themes.

A possible explanatory model for this disparity emerges when qualitative data related to participant's perceptions of psychosocial interventions is explored. Not only were psychosocial interventions – uniquely amongst the four themes - specifically highlighted as being an extant gap in their knowledge by participants (please see **Section 1.34.5.4**), but the need for material on the lived-experience of relevant service-user populations was also felt as being an educational necessity meriting address (see **Section 1.34.5.3**). Further, participants associated achievement of competence in relation to NPS with close working with client groups (see **Section 1.34.4.4**), something they did not express in relation to competence more generally.

As explored in the previous sub-theme, there is some tentative evidence to suggest that participants felt that they could rely on building competence and confidence in the majority of themes through experiential learning whilst working alongside more established professionals, and that this could not solely be built

through increasing theoretical knowledge, with the exception of clinical vigilance/awareness. If participants felt that increasing knowledge for most themes pertaining to NPS was reasonably well served by the designed presentation, an exception to this expressed in the qualitative data was its lack of lived experience of service-users. Though speculative, the author proposes that this *may* have been reflected in the relatively low post-test quantitative score for knowledge in relation to psychosocial interventions.

Whilst confidence in relation to psychosocial interventions increased relatively well – perhaps in response to the realisation from the presentation that many psychosocial interventions already known to them were applicable to NPS treatment – knowledge did not. As attested to by quotations included in the aforementioned sections, participants felt that there were gaps in their knowledge that they felt could be best ameliorated through content concerning service-users' lived experience, with motivations for use being mentioned amongst these. This raises the possibility that whilst confidence in relation to psychosocial interventions may be improved relatively well by an educational strategy such as that employed in the current research, knowledge surrounding these - which the participants seemed to imply must include information on service user motivations, preferences and life experience from that same population's perspective in order to be considered authentic and fit for purpose – is comparatively less well served by this mode of dissemination.

1.36 Interpretation of qualitative data

Whilst the themes explored in **Section 1.35** could be pursued using a triangulation method, several others that emerged from the focus group alone proved to have no supportive data that was considered interpretable in the corresponding quantitative data-set. However, given that that a sample of n=5 is considered relatively data-rich in relation to qualitative research (Braun and Clarke, 2006; Hennink, 2014b; Lobe, 2017), interpretation of non-triangulated data from the qualitative analysis was felt by the researcher to be merited.

Two themes emerged from the non-triangulated qualitative data, with these being: *Qualities of previous healthcare experience and consideration of holistic treatment*, and *Educational need for NPS-specific practice placements in light of increased clinical vigilance/awareness*

1.36.1 Qualities of previous healthcare experience and consideration of holistic treatment

At this juncture, it is important to acknowledge certain demographic traits of two individual participants involved in the study. The participant labelled as Participant 1 within qualitative data belonged to the 23–32-year-old age group, was the only third year participant, and was also one of the two participants who had 4-9 years of health care experience. The participant labelled as Participant 3 was in the 38-47-year-old age group, and was the other of the two participants who had 4-9 years of healthcare experience.

As related in **Section 1.34.2.2**, Participant 3 disclosed that the majority of their healthcare experience had been in general settings, as opposed to Participant 1, the majority of whose healthcare experience had been specifically in mental health settings. Participant 3 also mentioned that they had been told by established healthcare staff during placements that they were conscientious about considering patient care in a holistic manner. This may be related to their having a professional background as a healthcare assistant working mostly within general settings, whilst simultaneously being enrolled in a nursing course that emphasises mental health care.

The researcher notes that in many broader themes discussed within the presentation, management of physical symptoms proved to be an ancillary sub-theme within these. For example, within the context of management of psychiatric symptoms, mention was made that in treating piperazine toxicity, administration of anti-psychotics may result in tachycardia, hypotension or arrhythmia in the patient. The author postulates that for Participant 3 – perhaps due to them having a relatively long professional background in general nursing combined with a current enrolment in a mental health focused programme – a need for such a holistic approach may have been anticipated by them at pre-test and confirmed

at post-test, with some supporting evidence for this hypothesis being found in the qualitative data. In the case of Participant 1, qualitative data provided by them suggests that their focus – arising from their relatively long professional background in psychiatric healthcare – was more exclusively related to psychiatric management of NPS related health issues.

Although – as previously discussed – *in-depth* data triangulation by sub-groups according to demographic traits proved unproductive, two points salient to this argument do emerge from the quantitative data. Firstly, it is notable that in the one demographic sub-group to which Participants 1 and 3 both belonged (those with 4-9 years of healthcare experience) variance as standard deviation tended to be higher than in the corresponding group (i.e., those with less than 3 years healthcare experience), with this being particularly pronounced in post-test. Secondly, the described variance is attributable largely to the more variable manner in which Participant 1 answered survey questions at both pre and post-test phases compared to Participant 3, whose answers were more uniform at both phases.

This may suggest that Participant 3 – influenced by their professional and educational background - approached answering the pre-test questionnaire from a more holistic standpoint, with their assuming that the various themes were more interrelated than other participants may have. Upon viewing the presentation, Participant 4 may have found these assumptions to have been supported by and large, accounting for their more uniform answers in the post-test questionnaire. In essence, due to their more intrinsically holistic, integrated understanding of health issues at baseline, Participant 3 found information presented in the presentation to be more immediately applicable to both their confidence and knowledge levels for the majority of themes post-test.

The researcher once again acknowledges that the above contention is extremely speculative. However, given the amount of discourse that was devoted by participants to holistic treatment during the focus group, this appeared as a key

qualitative theme, necessitating the devising of some form of nascent explanatory model with which to direct formulation of future research.

1.36.2 Educational need for NPS-specific practice placements in light of increased clinical vigilance/awareness

An inconsistency emerged during the qualitative analysis that merits interpretation. Specifically, participants expressed that - on the one hand - educational resources on NPS – whether from university or other sources – were antiquated and utilised out-dated frames of reference (see **Section 1.34.5.1**) and instead placement experiences that would allow students the opportunity to work with NPS affected service-user populations were preferred (see **Section 1.34.5.2**). However, on the other hand, post-registrant staffs' deficits in knowledge and awareness of NPS related issues (as perceived by the participants) somewhat inhibited the utility of placements that the participants had experienced where NPS proved to be an issue.

The paradox is somewhat resolved if one returns to the hypotheses discussed in **Section 1.35.1.1**. Namely, that increased levels of knowledge and confidence in relation to clinical vigilance/awareness serves as a vehicle through which students can interrogate prior and future healthcare experiences in the context of NPS. Whilst this is explored in the aforementioned section and does not merit a great deal of further expansion, it is worthwhile deliberating upon it briefly in light of the identified phenomenon.

Whilst participants expressed a need for more NPS relevant placements, the researcher contests that this is not the case. As attested to in discourse presented in numerous sub-sections within **Section 1.34**, as a whole, participants became better able to evaluate the relevancy of NPS to clinical environments after internalising the presentation's content on clinical vigilance/awareness. Perhaps the most emblematic example of this is found in discourse presented in **Section 1.34.5.2**, wherein Participant 4 recounts their realisation as to why pregabalin had recently being labelled as an "attractive medication" on their current

placement after viewing the presentation. Therefore, the educational need expressed by participants is not so much *a greater number* of practice placements related to NPS, but the provision of an internalised taxonomy and conceptual understanding of NPS related issues – achieved primarily through education on clinical vigilance/awareness - that equips students with a nascent framework by which to understand the ways in which *any* practice placement is potentially related to NPS.

Discussion

A proposed explanatory theory as to how the theme of clinical vigilance/awareness was internalised and utilised by participants proved a key component of discourse throughout the interpretation of findings. To recount in brief, the researcher contends that clinical vigilance/awareness – perhaps due to its relatively large theoretical and correspondingly small practical components – was more readily internalised as being sufficient in and of itself to achieve competence compared to other themes, which are perceived as being more reliant on experiential, supervised practice of relevant skills to achieve competence. Perceived increases in knowledge and confidence were greater, more even and less variable in clinical vigilance/awareness than in other themes because confidence pertaining to the former is directed more towards participants' self-confidence to detect, interpret and query NPS-related phenomenon experienced during professional practice. Whilst there is little in the literature to support or disprove this model in specific relation to NPS or substance misuse more generally, when considered within the context of the so-called theory-practice gap, some evidence emerges to support the hypothesis.

It is widely promulgated that the exact nature of the theory-practice gap is difficult to ascertain (Scully, 2011), and debate exists as to whether it is in any way a useful theory (Ousey and Gallagher, 2007). However, Greenway, Butt and Walthall (2019) offer that the phenomenon consists of three interrelated concepts as experienced by student or newly registrant nurses: failure of practice and

university-based learning to correlate; theory failing to be reflected in observed practice, and theory being considered as irrelevant to practice. All three of these concepts largely fail to be applicable to the theme of clinical vigilance/awareness for the reasons presented immediately below.

It was suggested by participants in the focus group that education on NPS was felt to be outmoded or almost entirely lacking at university level. It has long been held that as well as modelling good clinical practice, a primary task of mentors of undergraduate nurses is to assist their consolidation of theoretical knowledge into practical knowledge (Perry, 2009). Within placement, learning regarding NPS was also found to be deficient by participants, largely due to many established clinicians failing to have more than a rudimentary understanding of the concept of NPS – they could neither transmit nor consolidate knowledge on this topic as they held little knowledge of the subject themselves. If there is no rivalling counterpart to theoretical knowledge on a subject offered in practice environments in the form of knowledge as practiced, a theory-practice gap cannot exist.

However, it is perhaps more useful to consider the position of theoretical knowledge on NPS clinical vigilance/awareness within the theory-practice gap if one examines it using a model proposed by Hatlevik (2012). In this model, coherence (the internal harmonisation of theory and practice) is achieved through the student's reflection on theoretical knowledge, within reflection on practice being ancillary to this. As explored earlier in this thesis, clinical vigilance/awareness may act as a lens through which students can reflect on observed practice within placement settings. Other themes covered within the presentation *are* however still subject to the theory-practice gap, as they necessitate a far greater degree of practical nursing skill – they trend closer to the practice end of the theory-practice continuum. Therefore, the feelings of incompetence and uncertainty inherently generated within student nurses as part of the theory-practice gap's effect (Scully, 2011; Greenway, Butt and Walthall, 2019) were felt by participants to a higher degree in these other themes, with this being expressed through the comparatively lower scores awarded by the

participants for their perceived confidence in relation to these themes (as well as their comparatively higher standard deviation) in the post-test questionnaire.

The awareness of treating NPS-related health issues in a holistic manner proved to be a major theme within the qualitative data. This, in turn, was related by participants to qualities of previous healthcare working experiences. The literature concerning the impact of prior experience of working in healthcare upon qualities of nursing students is limited (Field-Richards *et al.*, 2023). However, existing research suggests that experience of working as a healthcare assistant prior to commencing nursing studies can have both positive and negatives upon the individual, in that they may have increased confidence and a more rapid socialisation into their new role, though also experience a degree of “culture shock” stemming from increased levels of accountability (Brennan and McSherry, 2007). Successful role transitions are associated with positive experiences of the healthcare assistant position (Houghton, 2014), and experience of being a healthcare assistant is also associated with enhanced skill acquisition (Houghton *et al.*, 2013). Perhaps most significantly for the current research – evidence suggests that paid clinical work either before and/or during the course of nurse study improves perceived competence and creates a more nuanced perspective of the role of the nurse in healthcare (Manoochehri *et al.*, 2015). Whilst two participants expressed possessing a relatively long career of prior healthcare-working experience both in the questionnaire and during the focus group, the qualities of these careers seemed qualitatively different, in that one appeared primarily based in general settings whilst the other primarily in mental health care. Further, the two participants’ levels of appreciation of the need for holistic care in treatment of NPS-related health differed, with the one who had worked more extensively in general settings postulating that this was more innate to their thinking, due to this background. Although data triangulation failed to produce any meaningful results by which to explore this issue in greater depth, it remains an intriguing avenue for future research.

Participants felt that lived experience of service users was a vital and - at present - largely absent feature of NPS educational resources, the possession of which

they felt would improve their ability to communicate with and deliver psychosocial interventions to NPS-affected service-user populations. Further, they explicitly mentioned population-specific psychosocial interventions as being an extant gap in their education. Research concerning the lived experience of NPS users is supportive of both assumptions. Gittins *et al.* (2018) note that motivations for use of NPS is extremely variable from individual-to-individual, and that, therefore, psychological and psychosocial interventions must be bespoke to discrete patient needs. Ralphs and Gray (2018), in exploring the needs of NPS-using service-users in Manchester, argue not only that services adapted to the needs of relevant populations are required at the more general level, but offer the specific example of the requirement for concurrent psychosexual and psychosocial interventions to address the health needs of MWHSWM who use NPS within chemsex – the recreational use of psychoactive substances to enhance sexual performance or pleasure (Giorgetti *et al.*, 2017) - contexts. Further, in their mixed methodological report on NPS as a public health issue Higgins *et al.* (2019) state that research into psychological and psychosocial treatment specific to NPS should be considered an urgent matter.

More generally, the findings of the present study suggest that knowledge and confidence regarding treatment of NPS-related health conditions at the level of undergraduate nurse level is relatively low at baseline, which is consistent with findings from other studies concerning registrants' subjective feelings in the area explored at the outset of this thesis (Guirguis, 2015; Owie *et al.*, 2017; Wood, Ceronie and Dargan, 2016; Ramos *et al.*, 2020). Qualitative/mixed methods studies in this field of study were relatively lacking at the current project's initiation. However, the researcher has identified two that have emerged recently, and these will be considered in relation to the current study's findings.

One Australian mixed-methods study examined the confidence of junior doctors in relation to treatment of acute drug intoxication (Smith *et al.*, 2022). Qualitative evidence from the survey used indicated that participants felt strongly that formal and ongoing education in relation to risk assessment/management strategies in the event of unknown/identified drug consumption (as is often relevant to NPS

contexts) by patients is required, with this being a recurrent theme across participant responses.

A qualitative study of UK healthcare professionals - including nurses - who interact with service users who use NPS had findings relevant to the current discussion (Solomon *et al.*, 2023). Professionals who were interviewed reported a lack of training on NPS, specifying that education on relevant interventions, policy pathways, information regarding sub-types/classes of NPS and psychosocial interventions as being educational needs of particular urgency to their work that currently remained un-addressed. Further, they reported on a lack of suitable assessment tools tailored to an NPS context (Solomon *et al.*, 2023). Both sets of findings in the two previously mentioned studies draw parallels with the findings of the current research. Participants in the current research mentioned that current educational resources were outdated or lacking entirely in curricula, with this somewhat matching the experiences of junior doctors (Smith *et al.*, 2022). Healthcare professionals (Solomon *et al.*, 2023) in the two studies currently under consideration. In particular regards to the study by Solomon *et al.* (2023) it is of interest that psychosocial interventions was mentioned as an area in which extra support/education was needed, given that this was highlighted as a point of interest by participants in the current study also. What is striking about this similarity is that it suggests that support identified by a population who are relatively inexperienced/entirely inexperienced in working with NPS-affected service-users (undergraduate mental health nurses) anticipate this as being an area in which they will need help to further their professional education, and this is in fact borne out when compared to the self-identified needs of a population of working healthcare professionals who are experienced or very experienced in working with the same service-user group (Solomon *et al.*, 2023).

The participants in the current study emphasised the need for lived-experience content in their education on NPS. The researcher agrees entirely that this is a valuable aspect of any future educational package, that should be given high prominence given that undergraduate health professionals may not have the opportunity to work with relevant service-user populations. However, the

evidence provided by Solomon *et al.* (2023) is strongly suggestive that exposure to lived experience alone – such is likely in the sample interviewed in their study – is not a sufficient measure in and of itself to address self-perceived deficits in confidence, knowledge or competence at post-registrant level, with this also borne out (to a lesser degree) by Smith *et al.*'s study (2022) also. Therefore, a brief consideration of continuous professional development (CPD) in the context of NPS follows.

Although evidence on the effectiveness of CPD in relation to NPS specifically is almost entirely absent, there is some literature on CPD in the context of substance misuse health and social care more generally, though this in itself is a relatively unexplored area. One systematic review of online educational packages for substance misuse workers comments on the absence of studies in this area, with the review ultimately finding that available studies were too dissimilar and low in validity/reliability to make effective conclusions other than quality and content of such packages was highly variable (Calder *et al.*, 2017). However, some relevant evidence on the subject has been produced since the review in questions' publication.

One Australian study used a quantitative survey design to ascertain self-identified professional training needs of alcohol and drug workers (Roche, Skinner and McEntee, 2022). The most cited CPD needs across the entire sample was training on specific therapies, working with people with complex needs and advanced clinical skills. When early career workers (those with three or less years of working experience) were considered separately, they were significantly more likely to cite training on building partnerships, working with clients with dual diagnosis/comorbid mental health issues, multidisciplinary team-working and trauma-informed care as urgent CPD needs compared to mid/late career stage workers (Roche, Skinner and McEntee, 2022). Whilst some findings in the study were unclear (for example, it did not allude to what was meant by the term "specific therapies"), what is tangible is that many of the CPD areas accentuated by alcohol and drug workers – especially those in the early stage of their career

- in the study align to what has thematically been considered as belonging to psychosocial interventions in the current project.

A further study from Australia measured the efficacy of an evidence-based e-learning package on co-morbid mental health issues relating to a substance misuse context delivered to alcohol and drug workers (Marel *et al.*, 2023). It found that delivery of the package was effective in improving self-perceived feelings of confidence and knowledge in the sample, and that 89% stated that they had utilised skills gained from the CPD package in their practice. This is suggestive that at least one of the highlighted areas of CPD identified in the study by Roche, Skinner and McEntee (2021) - working with clients with dual diagnosis/comorbid mental health issues – can be effectively addressed using an appropriately designed educational package in a culturally and socially similar group of healthcare workers.

One systematic review and realist synthesis focused on opioid agonist therapy CPD (OAT CPD), drawing on studies from five nations (including four from the UK) (Sachidanandan *et al.*, 2022). The review ultimately identified five possible configurations of OAT CPD, two of which are particularly relevant to the current study.

The first of these was the configuration of *OAT CPD as drug policy* (Sachidanandan *et al.*, 2022), in which the researchers noted the lack of assessment of OAT CPD practices against stated aims at policy level such as contextual overdose crises in the various countries the included studies were collected from. Some sub-configurations identified in the review – such as motivation transformation or communities of practice expansion – were more innately tied to large scale policy at organisational or national level in studies, whilst others – such as expert influence or confidence development – appear more relevant and successful in the milieu of knowledge and confidence bolstering at individual practitioner level.

The second configuration of particular note was that of *OAT CPD as a facilitator and barrier to OUD [opiate use disorder] care* (Sachidanandan *et al.*, 2022). This configuration formulates that OAT CPD measures can be a barrier or facilitator to improved care according to the specific context of intended consumers and how they are presented accordingly. Measures can be a barrier if they are presented in relation to statutory or career-advancement necessity (with the review using the example of relevant prescribing qualifications for this), especially if offered to relatively amotivated and/or contextually unaware professionals. However, identical or highly similar measures can be perceived as facilitators to improved practice if offered to contextually aware and motivated practitioners and in a manner that does not focus on regulatory/statutory necessity. This dichotomy is emphasised in the review as being a key consideration for developers of relevant CPD packages and policy-makers generally (Sachidanandan *et al.*, 2022).

Taken together, these two points of practice bear particular relevance in light of the findings of the current study.

Sachidanandan *et al.* (2022)'s finding that some thematic foci of OAT CPD packages are more effective in increasing practitioner knowledge and confidence is relevant when one considers the underlying meaning of successful elements of this. Sachidanandan *et al.* (2022) categorise expert influence as instructor-focused educational packages, low in two-way interaction with novice practitioner/consumers, which the researchers identify as preferable as they do not overly "pressurise" already resource and time-poor audiences. This relates well to the findings of the current study, in that whilst the participants commented on the lack of adequate educational resources pertaining to NPS generally their implied mode of delivery was not commented on negatively. Given that these were generally expressed as having a mode of delivery – along with the mode of delivery of the educational resource used in the study – that appears to align well with the expert influence form of intervention identified by Sachidanandan *et al.* (2022) - i.e., high expert and low learner involvement - this would seem to implicitly suggest that this is a desirable mode of transmission for undergraduate

nursing students. However, greater consideration for preferred mode of delivery and underlying reasons for these should be explored in more detail in subsequent, relevant research.

Confidence development was considered by Sachidanandan *et al.* (2022) as relating to interventions targeting relatively knowledge-rich practitioners who have correspondingly low levels of confidence in their delivery of practical skills, in which the primary strategy for addressment is supervised, deliberate practice. It is remarkable how this parallels with participant expressions of understanding of competence and confidence in relation to NPS and nursing practice generally and inter-relations, as well as the hypothesised unique relation between competence and confidence offered by the researcher, adding some further credence to the offered model.

As attested to earlier, both of the aforementioned CPD formats were theorised to help improve practitioner knowledge and confidence at the individual level, in opposition to other formats that emphasised higher level policy and statutory requirements Sachidanandan *et al.* (2022) and greater exploration of how these align to protocols for undergraduate nursing education on NPS should be a priority for the researcher and appropriate policy-makers more generally.

Further, Sachidanandan *et al.* (2022)'s finding that OAT CPD can be a barrier or facilitator according to context merits some attention in relations to this thesis's findings. Substance misuse CPD protocols appear to be a barrier to improved practice if they are directly related to statutory requirements presented to unaware/amotivated consumers. This raises points for further investigation as to the importance of contextually relevant information included in educational resources alluding to the relevance of NPS to practice, in terms of "scale of the problem", relevance to various service-user and practitioner populations, and how such information effects consumer motivation. As will be related in the limitations section of this thesis, self-selection bias of participants who already held an interest in NPS/general substance misuse-related issues generally is a

distinctly possible flaw in the current study, which again should be a consideration in the researchers subsequent research in this area.

The researcher will conclude the discussion section by drawing the reader's attention to what the researcher sees as a fundamental mismatch between a recognised need for further development in healthcare professional education in relation to NPS and substance misuse more generally.

In relation to NPS as an emergent phenomenon, researchers have urged policy-makers to integrate education "in its widest and original sense" (i.e., inclusive of provision of it to practitioners) regarding NPS in a holistic manner incorporating both top-down and grassroots perspectives (Zamengo, Frison and Zwitter, 2019). More generally, a positional piece written by members Network of Early Career Professionals in Addiction Medicine (NECPAM) noted the lack of inconsistency and general inadequacy of CPD provision pertaining to substance misuse at international level and urged that there be an assessment of the training needs of substance-misuse professionals at a global level, along with the development of an internationally acceptable set of core competencies in the field (Arya *et al.*, 2020).

As has been demonstrated at the beginning of this thesis, Scotland – and the city of Dundee in particular - is experiencing a drug-related deaths crisis, in which NPS play a central role. The researcher has provided strong evidence to suggest that there is deficit in relevant and appropriate solutions to address a recognised lack of education at either pre-registration or post-registrant level. Given this background, what is both surprising and disappointing in recent strategic statements from both the Scottish Government (Scottish Government, 2022c) and Dundee Health and Social Care Partnership – inclusive of input from NHS Tayside the Dundee Drug Commission - (Dundee Health and Social Care Partnership, 2023) – is that no mention is made whatsoever in their recommendations of the need for improvement in education on illicit substances generally or on NPS specifically, either at undergraduate health professional curricular level, nor at post-registrant, CPD level.

Recommendations for future research

Several avenues for future research are presented from the findings of the current study.

As will be mentioned in the limitations section of this thesis, the researcher is cognisant that the extremely small sample size greatly limits the findings of their research. Whilst this was a conscious decision in response to the research's highly exploratory nature, larger-scale studies are needed to help to confirm or disprove hypotheses developed from the findings of the current study. In particular, larger scale quantitative studies are recommended to help generate more highly powered data in the field of study.

The impact of student knowledge surrounding the theme of clinical vigilance/awareness merits further investigation. Given that tentative evidence emerges from the current research that this may act as a vehicle by which students can reflect upon NPS-issues relate to practice placement experiences, the researcher recommends that prospective studies are performed to analyse how mental health nursing students utilise education on clinical vigilance/awareness (as well as other themes) to evaluate NPS-related issues experienced during placement in greater detail.

The author notes that all participants included in the current research were in the 2nd or 3rd year of their nursing studies and recommends that students in the first year of study are included as participants in future studies, to help increase understanding of how students at varying stages of their enrolment utilise education on NPS more generally. Similarly, the researcher observes that all participants were recruited from a single site for the study. Future research should seek to recruit participants from multiple academic institutions, as this may add richer data.

Findings tentatively suggest that qualities of prior healthcare experience may impact perceived levels of knowledge and confidence in relation to NPS. Future

quantitative studies need to interrogate the nature of prior healthcare experience in more granular detail to further investigate this matter, and this should be presented as a further theme to be explored in future qualitative/mixed-method research.

Finally, participants in the current study expressed that the lived-experience of relevant service-users was a key remaining gap in their knowledge, as were psychosocial interventions to address the health needs of NPS-affected populations. Methods to incorporate these into educational resources and evaluation of their efficacy should be an aim for future pedagogical research.

Limitations

The author contests that the current study is subject to several severe limitations.

Lack of grey literature

Grey literature was initially considered as being a resource with which to enrich the clinical guidance gathered during the review process. This form of literature has distinct advantages, in that it can help overcome publication bias in synthesised evidence or may help broaden the contextual information used in a review such as details of relevant populations in relation to an intervention (Adams *et al.*, 2016). Further, grey literature can help steer reviews towards more meaningful, concrete conclusions regarding the suitability of the interventions that are explored (Benzies *et al.*, 2006). However, utilising grey literature was ultimately rejected for several, inter-related reasons.

There exist definitional problems as to what actually constitutes grey literature, with several, competing interpretations as to what may be considered as including within the term available (Mahood, Eerd and Irvin, 2014), and searching for and successfully integrating grey literature systematic reviews can prove challenging even for the highly experienced researcher. Benzies *et al.* (2006) suggest that

these issues may be ameliorated by seeking advice from what they term expert advisors – people in the field of study who possess a knowledge level sophisticated enough to guide the novice researcher as to what is to be considered as suitable grey literature, and where such material can be collected from.

The current study was initiated during the COVID pandemic, with design of the literature review element being undertaken and completed prior to January 2021. During this time period, the author contacted several experts on NPS to ask if they would be able to help consult on the current project. Understandably given the circumstances, some did not respond to email requests, and others replied offering support though not to the extent of acting as full advisors/consultants on the project, citing other pressing matters related to the pandemic, as well as travel restrictions in place at the time that limited potential collaboration (BBC, 2021).

Due to the lack of available expertise, the research team felt that it was unwise to attempt to incorporate grey literature into the review process, and utilise only peer-reviewed, published material. The researcher acknowledges that this opens the information gathered in the review process to allegations of publication bias, amongst other deficits. However, they note that unlike the majority of material published academic journals, grey literature often does not undergo any rigorous peer-review process (Yasin *et al.*, 2020), and using only the former source of information ensured at a minimum that all gathered and synthesised data was verifiable as accurate and generally reflective of the current “state of the evidence” from a novice researcher perspective.

Still, the researcher recognises the lack of grey literature in their review process as a valid and legitimate criticism of the current research overall. They will seek to improve their capacity to utilise it effectively in subsequent relevant research to add to its robustness though liaising with more experienced researchers in the field of NPS in healthcare contexts, and by being involved in other, unrelated research projects generally.

1.37 Number of databases used in the review process

Whilst a limited justification as to why only Web of Science, Scopus, CINAHL and PubMed were used as databases in the overview of review process has already been presented in **Section 1.6.4**, the researcher concedes that a further expansion – not only in terms of justification for the decision, but discussion of it as a limitation – on the matter is merited.

As already attested to, research by Gusenbauer and Haddaway (2020) found that the aforementioned databases hold a high enough level of robustness to act as the principal databases from which to inform an accurate and systematic literature review, with Google Scholar being found as generally only suitable to act as an adjunct to these.

It is undeniable that Google Scholar is a research tool unparalleled in its power by some measures. For example, one study examining the relative strengths of Google Scholar and five other similar databases' citation coverage found Google Scholar to be unmatched in this regard, with it locating 88% of the 3,073,351 citations used in the study, with Microsoft Academic being the next highest scoring database at 60% coverage (Martín-Martín *et al.*, 2021). However, whilst Google Scholar has by far the largest coverage, it is notable that approximately fifty percent of this coverage includes non-journal sources, that between 19 and 38% of material is not in English, and that citations unique to Google Scholar have a far lower rate of scientific impact when compared to Scopus or Web of Science (Martín-Martín *et al.*, 2018). Traditionally, Google Scholar is considered as a highly suitable source by which to find non-peer reviewed material, such as in the context of grey literature (Haddaway *et al.*, 2015) with this advice being applicable to the time at which the review processes was initiated (Yasin *et al.*, 2020). Therefore, use of Google Scholar was ultimately rejected for reasons similar to those given for employing grey literature overall.

The project lacked input from researchers experienced in the study of NPS, and therefore the suitability of material gathered from Google Scholar could not be

fully ascertained in the absence of clearly discernible information on peer-review processes followed. Google Scholar does not allow its results to be filtered to peer-reviewed items only (University of Wisconsin Whitewater, 2023). Manually checking the peer-review status of the potentially vast amount of literature that would have been made available through its use was decided by the research team as adding a layer of complexity to what was already a highly-compound project, consisting as it did of four parallel systematic reviews and a mixed-method experimental element.

Again, the researcher acknowledges this as a relative weakness of the current project overall, and endeavours to include the use of Google Scholar (among other suitable sources) as part of the process involving grey literature in research developed from the current study described in the previous sub-section.

1.38 Sample Size

The author once again acknowledges that the small scale of the study severely limits the utility and generalisability of its findings and resultant hypotheses, especially in relation to its quantitative results, with this mostly relating to sample size.

It barely requires comment that a sample size of five would be highly unlikely to be considered adequate in a purely quantitative research design, in terms of reliability, reproducibility (Gumpili and Das, 2022), or the statistical significance of any findings (Andrade, 2020), and the reader will note that no assessment of or claims to these aspects have been pursued. However, the researcher suggests that such a sample size may be justified within the larger context of the mixed method protocol that was utilised, with an argument for this presented below.

Researchers note that “quality” in mixed-method research is often subjective and context specific, that quality is often incorrectly conflated with rigour and that in fact only the latter can be objectively demonstrated in the modality (Harrison,

Reilly and Creswell, 2020). The researcher contends that the work presented in this thesis abides by assessment tools that arguably misinterpret quality as being equivalent to rigor, such as the Good Reporting of a Mixed Methods Study (GRAMMS) system (Harrison, Reilly and Creswell, 2020).

The GRAMMS, originally developed to assess “quality” in mixed methods health research (O’Cathain, Murphy and Nicholl, 2008), and asks the researcher to: *Describe the justification for using a mixed methods approach to the research question; Describe each method in terms of sampling, data collection and analysis; Describe where integration has occurred, how it has occurred and who has participated in it; Describe any limitation of one method associated with the present of the other method; Describe any insights gained from mixing or integrating methods* (O’Cathain, Murphy and Nicholl, 2008), which the researcher contends they have – with the exception of the second last directive – fulfilled throughout the content of the thesis taken in its entirety.

Further, the researcher notes that their work also aligns relatively well with alternative tools designed to solely scrutinise rigour, such as the rigorous mixed methods framework developed by Harrison, Reilly and Creswell (2020), In using this tool to self-assess this thesis, the researcher suggests that the project would be calculated as scoring “medium-high” in the scoring system proffered by Harrison, Reilly and Creswell (2020), as shown in **Table 5** immediately below.

Table 5: Study as assessed using the Rigorous Mixed Methods assessment tool

Rigorous Mixed Methods Coding Scheme – adapted from Harrison, Reilly and Creswell (2020)				
Coding	High levels of rigor	Medium levels of rigor	Low levels of rigor	Researcher's self-scoring and notes
Green highlighting indicates researcher's self-assessment of which score each element aligns to				
Aims and purpose	Includes a rationale for using mixed methods. Includes a mixed methods research question.	Includes a rationale for using mixed methods. May include a mixed methods research question. May include a discussion of the value of mixed methods.	Includes no discussion of a rationale for using mixed methods, a mixed methods research question, or a discussion of the value of mixed methods.	M
Data collection	Includes the reporting of specific data collection procedures for both qualitative and quantitative data strands (e.g., sampling procedures, types of data to be collected, and instruments used in data collection).	Includes the collection of both qualitative and quantitative data strands, but limits the discussion of collection procedures for both data types.	Includes the collection of both qualitative and quantitative data strands, but does not discuss data collection procedures.	H
Data analysis	Includes the reporting of analysis procedures for both qualitative and quantitative data strands that range from basic to more sophisticated approaches, from descriptive to inferential quantitative analysis, to coding and thematic development qualitative analysis.	Includes qualitative and quantitative analyses, but at least one is not well reported. It is unclear how mixed methods are used to support the overall analysis. strand.	Includes the reporting of analysis procedures for only one, primary data.	H
Data integration	Includes the linking of both data strands. Depending on the design type, both data strands are either merged or one data strand is used to explain, or build from, the other. Joint displays and/or data comparisons are utilized.	Includes the linking of both data strands, but researchers do not describe a clear plan or reason for doing so. Some discussion of how integration affects the overall study.	Includes little to no integration of both data strands. Little to no discussion of how integration affects the study.	M
Mixed methods design type	Includes a mixed methods design type (e.g., sequential explanatory). Uses a diagram to show the design type.	Includes no discussion of a mixed methods design type. Includes a discussion of qualitative and Quantitative components individually.	Includes no discussion of a mixed methods design type. Either the qualitative or quantitative component is missing or significantly lacking.	H Note: research does not use a diagram to illustrate design type. However, cannot reasonable be said to align to a score of M either
Elements of writing	Includes references to mixed methods literature. Identifies the study as mixed methods in the title, abstract, and/or paper.	Includes a discussion of mixed methods, but fails to cite any mixed methods literature. Does not identify the study as mixed methods.	Includes no discussion of mixed methods or references to mixed methods literature.	H

With these factors considered together, the researcher feels that the use of a such a small sample for the quantitative element is justifiable, given that it was an element used entirely in conjunction with – and to add support to - the other qualitative aspect. The latter element can be considered as the “dominant” in the research, and this is generally not considered as unusual or problematic if

rationale for such as choice is presented (Walker and Baxter, 2019). Furthermore, the researcher notes that estimating sample size is notoriously difficult in mixed method research (Onwuegbuzie and Collins, 2007), and that reducing sample size overall to facilitate the qualitative aspect and avoid the creation of inaccurate integrated data is a relatively common and recommended practice (Venkatesh, Brown and Sullivan, 2016). Whilst it is certainly a relevant argument that the small sample remains inadequate even for the dominant, qualitative element, the researcher notes that it is considered that in the context of thematic analysis (as was employed in the current study), a relatively small sample size can be justified in scenarios where data saturation – i.e., the relative prevalence of themes – is not considered a desirable or necessary aspect (Fugard and Potts, 2015). A purpose of this research was to gather data on a subject that has hitherto had an almost complete absence of relevant datasets. As stated in the projects aims and objectives – one primary purpose was to gather useful insights by which to direct later studies. Therefore, collection of a set of initial themes by which to direct this latter aspect, with establishing a base of these being given primacy in the first instance being given primacy over assessment of their prevalence.

The researcher reiterates that this is a vastly under-researched field of knowledge, and a small-scale, mixed-methods approach that would allow for unproblematic triangulation of data was deemed as the most appropriate method by which to establish nascent concepts and themes by the research team. Whilst the above exploration attests that it is often difficult to systematically gauge the overall quality of mixed methods research (due to the contextuality and subjectivity of this), the overall rigour of the current project has been interrogated and found to be fairly satisfactory in this regard.

The author again urges the reader not to interpret this study as being generative of definitive data, but as a pilot study by which the researcher seeks to direct their own future study into this unknown field. They acknowledge that larger scale studies are needed to verify any knowledge claims, with this being mentioned explicitly in their recommendations for future research.

1.39 Qualitative limitations

The researcher acknowledges that the current study has several limitations in relation to its qualitative component.

Firstly, the researcher recognises that no participant debrief process was followed. This can be described as the process of having participants involved in a study review gathered data and its interpretation (Megheirkouni and Moir, 2023). It is important at this juncture to emphasise that the term “member-checking” is open to multiple interpretations. The traditional meaning is understood as being akin to the aforementioned debrief process (Motulsky, 2021) though can also be applied to a process by which experts in a field of study review a research methodology that was followed in a study as well as interpretation of results data stemming directly from it (Megheirkouni and Moir, 2023). The researcher has selected to use the second interpretation of the term for this study, and giving clarity surrounding its use is essential as it will be employed in a later section of the limitations section.

Whilst participant debriefing is considered an important element of verifying the credibility of data in many forms of qualitative research (Kornbluh, 2015), some authors note that the value of such debriefing processes is often taken as an un-interrogated assumption that does not necessitate any form of justification (Thomas, 2017). Others offer that there is critical lack of consensus on what particular elements of participant debriefing methods are essential for them to be considered reliable (Chase, 2017). Motulsky (2021) notes that interviewee debriefing is fraught with many inherent difficulties, such as interpretative authority, or how to successfully manage participant disagreement with interpretation. Due to the lack of evidence regarding how debriefing is to be conducted in a meaningful valid manner and its highly complex nature – combined with limited time and resources available to the research team – participant debriefing was ultimately not pursued.

Secondly, the author recognises that the self-selection of participants is a relevant issue of their study's design. Self-selection bias is the phenomenon of those who choose to participate in a research study are unlikely to be truly representative of any theoretical sample overall – i.e., they are likely to have characteristics dissimilar to the population under consideration generally (Alarie and Lupien, 2021). It is highly likely that recruited participants had especial interest in the fields of NPS or substance misuse more generally, and it is also likely that participants included in the study are not representative of the entire population considered. However, it is noted in the literature that - due to the importance of ethical practice – the vast majority of participation in research must be voluntary in nature, and therefore some degree of selection bias in any given qualitative study is in essence unavoidable (Robinson, 2014). Due to this, selection bias is considered as a limitation though not a serious one, given that the having enthusiastic participants interested in the topic area – and who were therefore likely to share relevant insights - was considered as valuable to the study, given its aims.

Finally, social desirability may have been influential in the way that participants answered questions in the focus group. Social desirability can be defined as the tendency of participants in a research study to omit or lessen the inclusion of socially undesirable attitudes in their contributions, and instead present ones that are not innately held by them but are likely to be perceived as less problematic (Latkin *et al.*, 2017). However, the researcher notes that social desirability is normally associated with ethically sensitive research (Tan *et al.*, 2021), and holds that only one question - *Do you feel that your attitudes towards people who use NPS has changed at all in response to the presentation?* – is likely to have been interpreted as being ethically sensitive and subject to possible high levels of social desirability bias in the way that participants answered. This question was supplementary in nature, and was not impactful in the majority of data analysis, interpretation or triangulation. Furthermore, it is held that the use of concurrent self-administered questionnaires can be considered a viable method of addressing the issue of social desirability to some extent (Bergen and Labonté, 2020), and this was a feature of the current study.

1.40 Member-checking

Perhaps the most serious limitation of the current research is the absence of member-checking throughout the entirety of the study. To re-emphasise, the researcher uses the definition offered by Megheirkouni and Moir (2023), which is applied to the use of expert advisors within the research team to provide feedback on methodology and data interpretation, as opposed to participants.

Megheirkouni and Moir (2023) recommend the use of a minimum of one internal (i.e., attached to the educational institute that the primary researcher attends) and one external member of the research team for this, wherein one is an expert on the field of study under examination and the other an expert on the methodology employed.

As previously explored in the methodology and thematic analysis of clinical recommendations sections of this thesis, whilst such a process was carried out for the thematic analyses in relation to both the review of literature and qualitative results, it utilised only two *internal* supervisors, rather than any input from an external expert of topic. The researcher contests that this limitation is more serious when considered in relation to the first thematic analysis, as an external expert would have allowed for far more robust interpretation of clinical recommendations, their relevance, and how they may be applied to the nursing context and other clinical roles. This impact is considered lesser in the second instance, due to one member of the supervisory team being highly experienced in the delivery of qualitative research (Arnot and Thurston, 2017) and the other being an expert in mental health nursing (Caie, 2012) and nurse education (Kelly *et al.*, 2020). The researcher contests that this is a less important factor here due to – at this stage of the research – the focus being primarily on the views of student nurses in terms of their education, rather than NPS per se.

However, the researcher feels that an absence of member-checking in the manner described can be considered as major limitation of the work at a systematic level. As just one example of this, a suggested improvement proposed by external examiners (who are pharmacologists with a strong knowledge of NPS) during the viva process was the inclusion of the search terms *toxic**, *fatal**, *poison**, *death** and *disability** in the intervention/outcome portions of the search strategies. Such insights on the methodology used (as well as other elements) would have been invaluable during the project, and the researcher therefore suggests that the lack of external expert in field of topic member checking is the most notable limitation of the research.

The researcher considers this a key point of reflection from the project, and intends to ensure that future, related research is enhanced through collaboration with relevant experts in the field at every stage.

Conclusions

Novel psychoactive substances have been a public health concern in the UK for some time. In the last decade, the increasing use of certain classes of NPS – such as novel benzodiazepines, with etizolam being one such drug of particular note – has contributed significantly to an increased number of drug related deaths, with this being especially applicable in Scotland.

Evidence suggests that clinicians feel under-confident and lacking in knowledge in relation to treatment of NPS-related health harms, though no previous studies have examined feelings of confidence and knowledge in this area in the context of undergraduate nurses. The researcher holds that this an area worthy of investigation, given the increased rates of drugs related deaths, the lack of focus on substance misuse as an area of nursing in practice placement education generally, demonstrable lack of registrant confidence and competence in relation to NPS and the current drug-related deaths crisis in Scotland/the UK.

The aims of this study were to: determine self-perceived feelings of knowledge, competence and confidence regarding treatment of NPS-related health problems in undergraduate nursing students; determine the extent an evidence-based educational presentation would impact these feelings, and identify potential enhancements to subsequent, similar resources of a similar nature.

Owing to the fact that this is a vastly under-researched field of study, the decision was made to limit the number of participants to five. This was to allow for richer triangulation of qualitative and quantitative data on a manageable scale. The current study should be viewed as an exploratory, pilot project, conducted primarily to gather initial data by which to inform later, more expansive studies – as implied by its third aim in particular.

Due to the varying aims of the project, a mixed method approach was utilised. In this approach, the first two aims were primarily addressed by use of two identical quantitative questionnaires distributed to participants before and after delivery of the presentation. The initial, pre-test questionnaire assessed feelings of knowledge and confidence on the topic at baseline in the participants, whilst the second, post-test one assessed how the presentation impacted these. The third aim was primarily addressed by means of the focus group, though this element also addressed participants' understanding of the concept of competence in relation to NPS-related healthcare, as well as other issues that arose from the focus group itself contextually. The same five participants were utilised for each of these elements.

Data for the evidence-based presentation was gathered through the use of four systematic overviews of reviews, with each of the reviews corresponding to the one of the following four sub-categories of NPS: sedatives and depressants; stimulants; hallucinogens, and SCRA. These reviews were gathered to collate a set of clinical recommendations relating to management of NPS-related health issues. Once data was gathered, the decision was made to amalgamate the clinical recommendations regarding stimulants and hallucinogens, given that the

dominant focus of the vast majority of recommendations pertaining to the latter class of substances concerned adverse events arising from stimulant-like effects. Thematic analysis of clinical recommendations was conducted by the entire research team, and four dominant themes emerged from discussion: clinical vigilance and awareness; psychosocial interventions; management of physical symptoms and management of psychiatric symptoms. These were used to inform variables measured in the quantitative questionnaires – i.e., self-perceived feelings of confidence and competence were measured each of these themes pre-and-post-test – and also influenced the formatting of clinical recommendations as they were presented in the educational resource. The two questionnaires, educational presentation and focus group were administered to the same five participants, and all elements involving their active participation were completed by 23rd April, 2023.

Qualitative data from the focus group was analysed using a thematic analysis method, in which the research team arrived at an agreed model of dominant and sub-dominant themes. Dominant themes identified were: value of clinical vigilance and awareness; holistic treatment of patients; confidence in other professionals' knowledge of NPS; competence in relation to NPS, and educational needs in relation to NPS.

Quantitative data from the questionnaires was analysed on Microsoft Excel. Due to the small sample size, significance was not analysed for, and only mean averages and standard deviations were calculated, with pre-test and post-test calculated for. The questionnaires used a five-point Likert-scale system, and the average mean average score for all measures was 2.3 ± 0.6 , with mean average for all confidence scores combined being 2.3 ± 0.7 and knowledge scores combined being 2.4 ± 0.7 . The highest rated individual score overall was in self-perceived knowledge of psychosocial interventions at 2.6 ± 0.5 , and the highest rated individual score for confidence was seen in relation to clinical vigilance/awareness at 2.4 ± 0.5 . The lowest scores were seen in relation to management of physical symptoms, with the knowledge score for this theme being 2.0 ± 0.0 and confidence score being 2.0 ± 0.7 .

In comparing scores from post and pre-test, the mean average increase across all questions was 0.8. For all themes considered by the measure of knowledge, the mean average increase was 0.9, and the mean average score for confidence overall was 0.75. When considered by individual themes, clinical vigilance/awareness and physical symptoms had the highest increase, with both being 0.9. When these two themes were interrogated by separate measure, mean average knowledge increase was 1.0 and mean average confidence increase was 0.8 for both. The most modest increase by theme overall was in psychosocial interventions. The lowest increase in knowledge score by individual theme was also in psychosocial interventions at 0.6, with the lowest increase in confidence by theme being observed in psychiatric symptoms, also at 0.6.

Data from the qualitative and quantitative strands of the research were triangulated. In the triangulation process the qualitative data was considered as dominant, with quantitative used to guide interpretation of the former's themes. Ultimately, two major themes emerged from this process: *understanding of clinical vigilance/awareness in relation to NPS and knowledge*, and *confidence and feelings of competence in relation to psychosocial interventions*.

In the first of these two themes, it was observed in the quantitative data that the theme of clinical vigilance and awareness was the highest scoring theme in the pre-test phase, though also saw the most significant improvements at post-test. The researcher proposes that this is not simply a matter of participants over-estimating their feeling of knowledge and confidence in this area at pre-test, but that the value of increased clinical vigilance and awareness lies in its aptitude for acting as a framework by which they are able to interrogate and orientate experiences in practice that may be applicable to NPS contexts, with this being borne out by discourse within the qualitative data. Further, the researcher suggests that confidence in relation to clinical vigilance and awareness is more readily attained, with it being theorised that this is due to it having a relatively low level of practical skill associated with it when compared to the other themes, and that in these other areas confidence is built through working alongside experienced professionals. This is somewhat supported by the quantitative data,

in that not only did confidence in relation to clinical vigilance and awareness increase more than in other themes, but far more uniformly in having far lower standard deviation.

In considering the second theme, it was noted in the quantitative data that the theme of psychosocial interventions received the least pronounced increase at post-test. When divided by separate measure, the score increase for confidence was fairly similar to increases for this measure seen in other themes, whilst its score increase for knowledge was weaker in comparison. In fact, psychosocial interventions displayed a unique pattern, in that it was the only theme in which knowledge score increase was greater than confidence score increase. Much discussion in the qualitative data was devoted to the value of lived experience to participants' understanding of the social contexts that service-users lived within. It is proposed by the researcher that the inclusion of authentic voices of this type are needed for educational content on psychosocial interventions in relation to NPS for them to be felt as having true value in increasing their confidence in this area.

Two other themes from the analysis of qualitative data emerged that proved difficult to explore in the triangulation process but were still worthy of greater discussion, with these being *qualities of previous healthcare experience and consideration of holistic treatment*, and *educational need for NPS-specific practice placements in light of increased clinical vigilance and awareness*.

In regards to the former theme, the researcher notes that one participant expressed during their discourse that they had had much working experience in general settings, and appeared to answer more uniformly in regards to their confidence and competence in relation to the quantitative themes than did the other participants. The researcher suggests that this may be due to their having coming from a more holistic perspective than other participants - perhaps in relation to their working background – and that the educational resource may have confirmed the participant's anticipation at baseline that the themes would be relatively inter-related (i.e., management of psychiatric symptoms would entail

a certain degree of management of physical symptoms, as one example. However, the researcher emphasises that this is extremely speculative, and this finding is only offered as an area of possible future research.

The final theme that will be discussed here arose from participant discourse relating to the need for more NPS-relevant practice placement experiences. However, the researcher contests this viewpoint, again noting that increased knowledge on clinical vigilance and awareness gained from the presentation seemed to act as a lens by which to interpret placement experiences more generally from a newly NPS-informed viewpoint. As the qualitative data itself suggests, the relevance of NPS to many practice placements was revealed through this increased knowledge, and therefore it is more that this knowledge is needed to see how a placement *can* be related to NPS, than it is the case that more intrinsically NPS-related placements are needed in undergraduate education, *per se*.

The discussion section of this thesis centred on the concept of the theory-practice gap in the first instance. Using Hatlevik's (2012) idea of coherence – in which harmonisation between theoretical knowledge and practical knowledge is achieved primarily through reflection on the former, though some reflection on the latter is also needed – it was posited that coherence is more readily achieved in relation to clinical vigilance and awareness than in other themes due to it having a higher degree of theoretical basis than practical. Due to this, coherence is more readily achieved in this area, whilst coherence for other themes necessitates more clinical practice, in which skills can be reinforced by working alongside experienced professionals, regardless of those professional's understanding of the NPS phenomenon.

Discussion also touched on the relevance of prior healthcare working experience. Whilst not much literature was located to fuel this discussion, evidence was found that having held prior healthcare assistant positions is associated with increased self-perceived competence and a more nuanced appreciation of the role of the nurse, which may be applicable to the finding regarding the holding of such a

position in a general setting from the current study. Again, the researcher asserts to the reader that this is in relation to what may be the study's most tentative finding.

The discussion also found that participants' position that lived-experience is an important element of educational resources/programmes related to NPS is of great importance to be well supported by evidence. It was found that understanding of service-user motivation for NPS use was of great value in the design of later psychosocial interventions, and that service design in this aspect should not just adopt a generalist approach but should be tailored to the needs of the specific populations that are served.

Discussion also related that early career health professionals also expressed anxieties surrounding treatment of substance misuse generally. Not only this, but even relatively experienced workers in the field of NPS felt that their educational needs in relation to psychosocial interventions are not well supported, suggesting that although lived experience may remain an important aspect in this area, more formalised, clinician-focused education is also of valuable.

Continuous professional development in relation to substance misuse generally was explored, and it was found that targeted educational resources – in the area of psychosocial interventions at least – aimed at specific populations of healthcare workers can serve to alleviate recognised areas where there are deficits in knowledge and confidence.

Future research directions suggested include larger scale studies, in which the role of clinical vigilance and awareness, the effect of previous healthcare working experience and/or the role of lived experience input on psychosocial interventions be conducted on students across all stages of their undergraduate careers.

Limitations focused largely on the implications of the small scale of the study in terms of the sample size. This was ultimately found to be supportable in the context of the study being a mixed-method research project. Under this lens, the

study can be seen as relatively robust and appropriate for a preliminary exercise for gathering an initial data set and directing larger, more expansive study. However, the researcher posited that the greatest limitation overall was the lack of member-checking of the form in which a more diverse, field-of-study experienced research team is needed. Here, the researcher emphasised that their being more vigilant in this respect would be of huge benefit in influencing the design of later studies and greater validity of results.

The researcher ends by again drawing attention to the one facet of the thesis's discussion section that has not been explored in this section until now. Healthcare workers involved in the field of substance misuse have made it clear – in the limited instances where their views have been researched - that they feel under-supported in their roles by current continuous professional development materials. Despite current policy at Scottish Government and local government level devoting much to entirely reasonable measures to combat Scotland's unacceptably high drug-related death rates, improvement in clinical education – in the context of NPS or otherwise – is not well addressed in current strategies. The researcher contests that this is a glaring omission, and that being more conscientious in this area – in regard to both undergraduate and registrant levels – can only help in ensuring that a more knowledgeable, confident and competent workforce is created. This must surely be seen as a vital factor in combatting not only the current public health crises, but any future ones that emerge in which the ever-evolving phenomenon of NPS plays an integral part.

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Appendices

Appendix 1: Approved ethics application

Appendix 2: Sedatives critical appraisal

Appendix 3: Stimulants and hallucinogens critical appraisal

Appendix 4: SCRA critical appraisal

Appendix 5: Participant recruitment email

Appendix 6: Pre-test questionnaire


Appendix 7: Post-test questionnaire

Appendix 8: Quantitative questionnaire pre-test results

Appendix 9: Quantitative questionnaire post-test results

Appendix 10: Quantitative questionnaire pre and post-test results comparison

1.41 Appendix 1: Approved ethics application



Name: IAIN LINDSAY

Project Title: What are the educational needs of student mental health nurses to prepare them for the treatment of service users presenting with complications arising from novel psychoactive substance use in inpatient settings?

Reference: EMS7178

Status: Submitted to School Research Ethics Committee

Approval Date: 04.04.23

The Standard Conditions below apply to all approved student Research Ethics applications:

- i. If any substantive changes to the proposed project are made, a new ethical approval application must be submitted to the Committee.
- ii. The Proposer must remain in regular contact with the project supervisor.
- iii. The Supervisor must see a copy of all materials and procedures prior to commencing data collection.
- iv. Any changes to the agreed procedures must be negotiated with the project supervisor.

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1.42 Appendix 2: Sedatives and depressants critical appraisal

Key to colour-coding system	Authors	Title	Peer-reviewed?	CASP 1 Did the review address a clearly focussed question?	CASP 2 Did the authors look for the right type of papers?	CASP 3 Do you think all the important, relevant papers were included?	CASP 4 Did the review's authors do enough to assess quality of the included studies?	CASP 5 If the results of the review have been combined, was it reasonable to do so?	CASP 8 Can the results be applied to the local population?	CASP 9 Were all important outcomes considered?	Score	Clinical Reccs.
<p><u>Columns Authors to Score</u></p> <p>Green = included in study</p> <p>Yellow = included in current systematic review and also other systematic reviews in same project (i.e., stimulants and hallucinogens or SCRAS), relevant clinical recommendations separated and presented in clinical recommendations accordingly</p> <p>Red = not included in study Clinical recommendations</p>	Anderson, Flynn and Pilgrim (2017)	A global epidemiological perspective on the toxicology of drug-facilitated sexual assault: A systematic review	YES	YES	YES	YES	YES	YES	YES	YES	6	<p>Most DFSAs are related to alcohol intoxication, with benzodiazepines being the next most common</p> <ul style="list-style-type: none"> Due to the rapid metabolization of many substances utilised by perpetrators of DFSAs (often within 12 to 24 hrs), victims of DFSAs should be encouraged to submit to urine and blood screening at the earliest juncture People who report DFSA should be encouraged to discuss their own personal drug use in a non-judgemental, candid manner

Key to colour-coding system	Authors	Title	Peer-reviewed?	CASP 1 Did the review address a clearly focussed question?	CASP 2 Did the authors look for the right type of papers?	CASP 3 Do you think all the important, relevant papers were included?	CASP 4 Did the review's authors do enough to assess quality of the included studies?	CASP 5 If the results of the review have been combined, was it reasonable to do so?	CASP 8 Can the results be applied to the local population?	CASP 9 Were all important outcomes considered?	Score	Clinical Reccs.
<p>Blue highlighting = Clinical vigilance/awareness</p> <p>Green highlighting = Psychosocial interventions including harm reduction, psycho-education, withdrawal protocols, service integration and referral pathways</p> <p>Yellow highlighting = Management of psychiatric symptoms</p> <p>Red highlighting = Management of physical symptoms</p>	Evoy <i>et al.</i> (2017)	Abuse and Misuse of Pregabalin and Gabapentin	YES	YES	YES	YES	YES	YES	YES	YES	7	<ul style="list-style-type: none"> Clinicians should note that gabapentinoids are mostly used to treat ailments where its efficacy is quantified using subjective measures, meaning there is potential for patients to invent or exaggerate severity of symptoms in order to secure re-prescription or higher titration. Clinicians should be especially mindful of the above in populations where there is higher potential for abuse, such as people with a history of substance misuse or mental health illness and monitor as appropriate. Misuse of these drugs may be suggested by patients asking for them specifically or greater doses of them.

Key to colour-coding system	Authors	Title	Peer-reviewed?	CASP 1 Did the review address a clearly focussed question?	CASP 2 Did the authors look for the right type of papers?	CASP 3 Do you think all the important, relevant papers were included?	CASP 4 Did the review's authors do enough to assess quality of the included studies?	CASP 5 If the results of the review have been combined, was it reasonable to do so?	CASP 8 Can the results be applied to the local population?	CASP 9 Were all important outcomes considered?	Score	Clinical Reccs.
<p><u>Columns Authors to Score</u></p> <p>Green = included in study</p> <p>Yellow = included in current systematic review and also other systematic reviews in same project (i.e., stimulants and hallucinogens or SCRA), relevant clinical recommendations separated and presented in clinical recommendations accordingly</p> <p>Red = not included in study Clinical recommendations Blue highlighting = Clinical vigilance/awareness Green highlighting = Psychosocial interventions including harm reduction, psycho-education, withdrawal protocols, service integration and referral pathways Yellow highlighting = Management of psychiatric symptoms Red highlighting = Management of physical symptoms</p>	Evoy et al. (2021)	Abuse and Misuse of Pregabalin and Gabapentin: A Systematic Review Update	YES	YES	YES	YES	YES	YES	YES	YES	7	<ul style="list-style-type: none"> Clinicians should be wary of the abuse potentials and inherent dangers of gabas and Perform patient risk assessments before prescription (specifically ORO RA) Provide sufficient counselling to patients re. potential risks with gaba use Ensure appropriate abuse/misuse monitoring protocols are in place In institutional settings (prisons, rehab services) clinicians should seek to: <ul style="list-style-type: none"> Explore with patients their reasons for combining substances and discuss risks involved in this as well as use of gabas generally Increase supply control measures, with the caveat that strict SCMs may have a detrimental effect on patient outcomes Harm reduction strategies are vital to improving patient outcomes Clinicians should be aware that many "abusers" consume gabas to self-medicate against anxiety, pain or withdrawal from other substances exploring reasons for use may lead to patients being referred to appropriate treatment services (MH, SUD, etc) Clinicians should seek to include multi-modal pain management in their practices

Key to colour-coding system	Authors	Title	Peer-reviewed?	CASP 1 Did the review address a clearly focussed question?	CASP 2 Did the authors look for the right type of papers?	CASP 3 Do you think all the important, relevant papers were included?	CASP 4 Did the review's authors do enough to assess quality of the included studies?	CASP 5 If the results of the review have been combined, was it reasonable to do so?	CASP 8 Can the results be applied to the local population?	CASP 9 Were all important outcomes considered?	Score	Clinical Reccs.
<p><u>Columns Authors to Score</u></p> <p>Green = included in study</p> <p>Yellow = included in current systematic review and also other systematic reviews in same project (i.e., stimulants and hallucinogens or SCRA), relevant clinical recommendations separated and presented in clinical recommendations accordingly</p> <p>Red = not included in study Clinical recommendations Blue highlighting = Clinical vigilance/awareness Green highlighting = Psychosocial interventions including harm reduction, psycho-education, withdrawal protocols, service integration and referral pathways Yellow highlighting = Management of psychiatric symptoms Red highlighting = Management of physical symptoms</p>	Schifano <i>et al.</i> (2018)	Abuse of Prescription Drugs in the Context of Novel Psychoactive Substances (NPS): A Systematic Review	YES	YES	YES	YES	YES	YES	YES	YES	7	<p>Loperamide</p> <ul style="list-style-type: none"> Loperamide can be used in large quantities to achieve CNS depression and euphoria Naloxone is recommended as a treatment option, though there is little evidence to suggest that this may counter the drug's cardiotoxic effects <p>General</p> <ul style="list-style-type: none"> Clinicians should consider strategies to improve referral protocols and clinical pathways involving multiple services/agencies, particularly those involving community pharmacies, these being the professionals best placed to recognise a repeat supply issue
	Schjerning <i>et al.</i> (2016)	Abuse Potential of Pregabalin: A Systematic Review	YES	YES	Cannot determine	YES	Cannot determine	YES	YES	YES	5	<ul style="list-style-type: none"> Clinicians should be vigilant, and should monitor for patients experiencing euphoria as a side effect of administration of pregabalin Although it is theorised that pregabalin may potentially play a role in the treatment of benzo or alcohol addiction, the mechanism for this is not as yet established, and clinicians should bear in mind that history of substance misuse is a risk factor for potential pregabalin misuse

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	Mersfelder and Nichols (2016)	Gabapentin: Abuse, Dependence, and Withdrawal	YES	YES	YES	YES	Cannot determine	YES	YES	YES	6	<ul style="list-style-type: none"> When assessing patients for risk of gabapentin misuse, possessing a history of alcohol or illicit substance abuse is a key factor. Gabapentin is often used alongside opioids to enhance the effects of the latter. Gabapentin can be misused – often alongside quetiapine – as a substitute for cocaine or to ameliorate withdrawal symptoms of the latter. Clinicians should be vigilant in monitoring gabapentin patients for signs of misuse/abuse, such as drug seeking or early refills, dependence or withdrawal.

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	Van Hout (2014)	Kitchen chemistry: A scoping review of the diversionary use of pharmaceuticals for non-medical use and home production of drug solutions	YES	YES	Cannot determine	Cannot determine	Cannot determine	YES	YES	Cannot determine	3	N/A

<p><u>Columns Authors to Score</u></p> <p>Green = included in study</p> <p>Yellow = included in current systematic review and also other systematic reviews in same project (i.e., stimulants and hallucinogens or SCRA), relevant clinical recommendations separated and presented in clinical recommendations accordingly</p> <p>Red = not included in study</p> <p>Clinical recommendations</p> <p>Blue highlighting = Clinical vigilance/awareness</p> <p>Green highlighting = Psychosocial interventions including harm reduction, psycho-education, withdrawal protocols, service integration and referral pathways</p> <p>Yellow highlighting = Management of psychiatric symptoms</p> <p>Red highlighting = Management of physical symptoms</p>	Marsden et al. (2019)	Medicines associated with dependence or withdrawal: a mixed-methods public health review and national database study in England	YES	YES	YES	YES	YES	YES	YES	YES	YES	7	<ul style="list-style-type: none"> • Patients state that clinicians tend to misunderstand withdrawal symptoms from antidepressants, benzos, opioids, gabas and z-drugs, and misinterpret these as being related to a health condition • Improved training for healthcare workers in this regard is therefore necessary • Prescribing should not be curtailed for these classes of medications if patients have an acute or long-term need for them stemming from a health condition, and weighing up the potential negative consequences for the patient should be made in any decision concerning their prescription • The ceasing of the above medication classes without the proper consideration process can not only stop patients from receiving clinical benefit, but can lead to suicidal action or the seeking of such substances (or even classical illicit substances) from blackmarket sources • HCPs should work closely and in alignment with patients in shared decision making processes to protect them against the risk of dependence and/or withdrawal • Informed choice and regular clinical reviews are also key to preventing the above risks • HCPs should consider that patients may need better access to dependence and withdrawal focused services and support, including: social prescribing; support groups; psychological therapies; mental health teams; pain clinics and
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												appropriate medical services
See above page for key	Moe <i>et al.</i> (2020)	Naloxone dosing in the era of ultra-potent opioid overdoses: a systematic review	YES	YES	YES	YES	YES	YES	YES	YES	7	<ul style="list-style-type: none"> The review could not determine whether or not higher doses of naloxone were more effective or safe for presumed ultra-potent opioid overdoses Therefore, the authors recommended that clinical guidelines remain in place However, in the case where users are provided with naloxone kits and ultra-potent opioid ODs are detected provisions in such kits should be reviewed at jurisdictional (local authority) level

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	Nielsen <i>et al.</i> (2016)	Opioid agonist treatment for pharmaceutical opioid dependent people	YES	YES	YES	YES	YES	YES	YES	YES	7	<ul style="list-style-type: none"> There was little evidence to suggest that methadone or buprenorphine should be preferred over one another Rather, the decision over when medication over another should be based on: preference of patient, safety and availability
<p><u>Columns Authors to Score</u></p> <p>Green = included in study</p> <p>Yellow = included in current systematic review and also other systematic reviews in same project (i.e., stimulants and hallucinogens or SCRA), relevant clinical recommendations separated and presented in clinical recommendations accordingly</p> <p>Red = not included in study</p> <p>Clinical recommendations</p> <p>Blue highlighting = Clinical vigilance/awareness</p> <p>Green highlighting = Psychosocial interventions including harm reduction, psycho-education, withdrawal protocols, service integration and referral pathways</p> <p>Yellow highlighting = Management of psychiatric symptoms</p> <p>Red highlighting = Management of physical symptoms</p>	Shorter, Hsieh and Kosten (2015)	Pharmacologic management of comorbid post-traumatic stress disorder and addictions	Y	Y	Cannot determine	Cannot determine	Cannot determine	Cannot determine	Cannot determine	Cannot determine	3	N/A
	Corkery, Schifano and Ghodse (2012)	Phenazepam abuse in the UK: an emerging problem causing serious adverse health problems, including death	YES	YES	YES	YES	Cannot determine	YES	YES	YES	6	<ul style="list-style-type: none"> Co-ingestion of phenazepam with other psychoactives (especially opiates) can increase chances of mortality Harm reduction advice would include: not to "eyeball" powder doses of the substances; the substance's long half-life means that users are liable to re-dose before peak effects are felt (2-3 hours), precipitating overdose; users are liable to consume phenazepam in the mistaken belief that it is a more established substance such as diazepam, leading to hazardous consumption due to the former's relative potency; injection of crushed tablets of phenazepam with heroin can lead to risks other than OD, including vascular damage, granulomatosis, limb ischemia, infection and foreign body pulmonary microembolism

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Columns Authors to Score	Bi-Mohammed <i>et al.</i> (2017)	Prescription opioid abuse in prison settings: A systematic review of prevalence, practice and treatment responses	YES	YES	YES	YES	YES	YES	YES	YES	7	<ul style="list-style-type: none"> • Sublingual buprenorphine may be diverted for intranasal use by prison populations • Opiates enter the prison system through means other than diversion, though this is a common means • Buprenorphine/naloxone preparations appear less viable for diversion than mono-buprenorphine preparations • Substance users appear to have formulated sophisticated strategies to circumvent supervised medication consumption • Liquid preparations are preferred over tablet preparations to help prevent diversion • The review suggests that buprenorphine is more likely to be diverted than methadone • It has been highlighted that that non-opioids, including tramadol, pregabalin and gabapentin have potential for misuse or diversion • A typical presentation for those seeking to misuse or divert the above would be individuals with a prior history of substance misuse citing musculoskeletal pain • Ascertaining whether the above type of complaint is genuine or an attempt to gain medications for misuse/diversion is challenging. The authors suggest that healthcare services within prisons seek to improve links with addiction and pain management services • There is some evidence to suggest that sedative antidepressants and psychotropics are being misused/diverted within prison settings, the reason
<p>Green = included in study</p> <p>Yellow = included in current systematic review and also other systematic reviews in same project (i.e., stimulants and hallucinogens or SCRA), relevant clinical recommendations separated and presented in clinical recommendations accordingly</p> <p>Red = not included in study</p> <p>Clinical recommendations</p> <p>Blue highlighting = Clinical vigilance/awareness</p> <p>Green highlighting = Psychosocial interventions including harm reduction, psycho-education, withdrawal protocols, service integration and referral pathways</p> <p>Yellow highlighting = Management of psychiatric symptoms</p> <p>Red highlighting = Management of physical symptoms</p>												

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												<ul style="list-style-type: none"> for which is users seeking euphoric or sedative effects, including to self-medicate for insomnia. Clinicians feel that diversion of such medications are a threat to the wellbeing of what is already a vulnerable patient group and may negatively effect care planning and treatment outcomes for this population. Opioid drugs should always be prescribed in their least abusable preparation available for prison populations. Clinicians need to be vigilant to avoid not only under-dosing patients but also over-prescribing. Health care staff should be aware that certain demographics (those of younger/older age, those with mental health problems) can be subject to intimidation by other inmates to be involved in diversion of medications.
For key please see page above	Darker <i>et al.</i> (2015)	Psychosocial interventions for benzodiazepine harmful use, abuse or dependence	YES	YES	YES	YES	YES	YES	YES	YES	7	<ul style="list-style-type: none"> Evidence suggests that CBT with a tapered withdrawal protocol may be an efficacious intervention. There is little evidence to support the use of MI for treatment of benzo abuse/dependence. There is some emerging evidence that certain interventions such as individually tailored GP letters and structured consultations may have some therapeutic benefit.

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	Huhn, Berry and Dunn (2019)	Review: Sex-Based Differences in Treatment Outcomes for Persons With Opioid Use Disorder	YES	YES	YES	YES	Cannot determine	YES	YES	YES	6	<ul style="list-style-type: none"> Women are more likely to present to OUD treatment services with mental health comorbidities, especially depression
<p><u>Columns Authors to Score</u></p> <p>Green = included in study</p> <p>Yellow = included in current systematic review and also other systematic reviews in same project (i.e., stimulants and hallucinogens or SCRAS), relevant clinical recommendations separated and presented in clinical recommendations accordingly</p> <p>Red = not included in study Clinical recommendations</p> <p>Blue highlighting = Clinical vigilance/awareness</p> <p>Green highlighting = Psychosocial interventions including harm reduction, psycho-education, withdrawal protocols, service integration and referral pathways</p> <p>Yellow highlighting = Management of psychiatric symptoms</p> <p>Red highlighting = Management of physical symptoms</p>	Piccioni et al. (2020)	Risk management in first aid for acute drug intoxication	YES	YES	YES	YES	YES	YES	YES	YES	7	<ul style="list-style-type: none"> Naloxone is recommended as a safe and effective treatment, though practitioners often overestimate required doses, which can result in acute opiate withdrawal. The authors recommend that doses start at 0.04mg before titrating up for the desired effect of ventilation depression reversal
	Rambaran et al. (2017)	U-47700: A Clinical Review of the Literature	YES	YES	YES	YES	Cannot determine	YES	YES	YES	6	<ul style="list-style-type: none"> U-47700 is most commonly ingested via insufflation and IV injection IV naloxone is able to reverse symptoms of depressed mental state and bradypnea

1.43 Appendix 3: Stimulants and hallucinogens critical appraisal

Key to colour-coding system	Authors	Title Primary	Peer-reviewed?	CASP 1 Did the review address a clearly focussed question?	CASP 2 Did the authors look for the right type of papers?	CASP 3 Do you think all the important, relevant papers were included?	CASP 4 Did the review's authors do enough to assess quality of the included studies?	CASP 5 If the results of the review have been combined, was it reasonable to do so?	CASP 8 Can the results be applied to the local population?	CASP 9 Were all important outcomes considered?	Score	Clinical Reccs.
<p>Columns Authors to Score</p> <p>Green = included in study</p> <p>Blue = originally included in separate systematic search for hallucinogens, added to results for stimulants and hallucinogens overall</p> <p>Yellow = included in current systematic review and also other systematic reviews in same project (i.e., sedatives and depressants or SCRA), relevant clinical recommendations separated and presented in clinical recommendations accordingly</p> <p>Clinical recommendations</p> <p>Blue highlighting = Clinical vigilance and awareness</p> <p>Green highlighting = Psychosocial interventions including harm reduction, psycho-education, withdrawal protocols, service integration and referral pathways</p> <p>Yellow highlighting = Management of psychiatric symptoms</p> <p>Red highlighting = Management of physical symptoms</p>	Bersani <i>et al.</i> (2014)	25C-NBOMe: Preliminary Data on Pharmacology, Psychoactive Effects, and Toxicity of a New Potent and Dangerous Hallucinogenic Drug	YES	YES	YES	YES	Cannot determine	YES	YES	YES	6	<ul style="list-style-type: none"> Medical staff should be prepared to treat patients who have consumed drugs within the NBOMe family of drugs in the mistaken belief that it was LSD, treatment for the latter requiring more aggressive management strategies NBOMe class drugs may cause psychiatric symptoms including hallucinations, aggression and/or agitation, necessitating administration of benzodiazepines Patients suspected of ingesting NBOMes should be monitored for: heart disorders; hypertension; hyperthermia; seizure; lung and/or kidney failure; metabolic acidosis and symptoms of serotonin toxidrome Treatment for the above may consist of: administration fluid; utilisation of cooling strategies; pharmacological treatments
	Gray <i>et al.</i> (2016)	A systematic review of the effects of novel psychoactive substances 'legal highs' on people with severe mental illness	YES	YES	YES	YES	YES	YES	YES	YES	7	<ul style="list-style-type: none"> Use of NPS by people with severe mental illness (SMI) may lead to significant change to their behaviour Agitation necessitating restraint appears to be a common feature (1/3 of papers included in review), as is violence/aggression (1/5) Authors postulate that use of NPS by people with SMI is under-reported and that it is only recorded when individuals display the extreme behaviours described above Authors suggest that it is likely that individuals with SMI may not understand that NPS are psychoactive substances in the same way that illegal substances are (seeing them as "more natural", "less harmful") and do not see need to report their use The above – considered with the fact that NPS are rarely detected in routine drug screenings – suggests that clinicians should ask about NPS specifically in assessments to gain a full understanding of contributing factors to presentation of SMI Clinicians should be aware that NPS may have unknown drug/drug interactions that may result in severe adverse effects

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<p>Columns Authors to Score</p> <p>Green = included in study</p> <p>Blue = originally included in separate systematic search for hallucinogens, added to results for stimulants and hallucinogens overall</p> <p>Yellow = included in current systematic review and also other systematic reviews in same project (i.e., sedatives and depressants or SCRA), relevant clinical recommendations separated and presented in clinical recommendations accordingly</p> <p>Clinical recommendations</p> <p>Blue highlighting = Clinical vigilance and awareness</p> <p>Green highlighting = Psychosocial interventions including harm reduction, psycho-education, withdrawal protocols, service integration and referral pathways</p> <p>Yellow highlighting = Management of psychiatric symptoms</p> <p>Red highlighting = Management of physical symptoms</p>	Guirguis <i>et al.</i> (2017)	Intended and unintended use of cathinone mixtures	YES	YES	YES	YES	YES	YES	YES	7	<ul style="list-style-type: none"> Determination of the type of NPS and quantity of it ingested are of great importance in treatment In the case that the type of substance cannot be identified, treatment is normally symptomatic Psychosocial interventions such as behaviour modification and abstinence should be offered as part of a holistic package of care Psychological interventions to address concurrent mental health issues should also be considered According to NEPTUNE, treatment should be based on class of NPS that the substance belongs to Pharmaceutical treatment may include: antidepressants; hypnotic-sedatives; vitamins/nutritional supplements Toxbase suggests use of: diazepam or haloperidol in the case of delirium or agitation; midazolam or diazepam in the case of seizures; sodium bicarbonate to treat metabolic acidosis; nitrates/calcium channel blockers for hypertension; vasopressors/inotropes in the case of hypotension, haemodiafiltration to treat rhabdomyolysis Antipsychotics including: quetiapine; risperidone; olanzapine; aripiprazole droperidol and haloperidol can be considered in the case of drug-induced psychosis Intravenous delivery of fluid is recommended by the authors to alleviate hyperthermia or rhabdomyolysis Overall, psychosocial intervention are considered a standard for treatment, with benzodiazepines being effective in managing aggression/agitation Raising HCP awareness about NPS and their treatment is considered important by the authors 	

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	Hill and Thomas (2011)	Clinical toxicology of newer recreational drugs	YES	YES	YES	YES	Cannot determine	YES	YES	Cannot determine	5	<ul style="list-style-type: none"> • Treatment of patients suffering adverse effects from ingestion of stimulant/hallucinogenic-type NPS should be symptomatic/pragmatic • Treatment strategies should follow best practice for those used for established drugs
	Hohmann, Mikus and Czock (2014)	Effects and risks associated with novel psychoactive substances: mislabeling and sale as bath salts, spice, and research chemicals	YES	YES	YES	YES	Cannot determine	YES	YES	Cannot determine	5	<ul style="list-style-type: none"> • In the event that a patient presents with symptoms similar to overdose with orthodox stimulants though drug screening returns negative results clinicians should consider NPS use and use appropriate services available to them such as toxicology laboratories

Columns	Authors	Score										
<p><u>Green = included in study</u></p> <p>Blue = originally included in separate systematic search for hallucinogens, added to results for stimulants and hallucinogens overall</p> <p>Yellow = included in current systematic review and also other systematic reviews in same project (i.e., sedatives and depressants or SCRA), relevant clinical recommendations separated and presented in clinical recommendations accordingly</p> <p><u>Clinical recommendations</u></p> <p>Blue highlighting = Clinical vigilance and awareness</p> <p>Green highlighting = Psychosocial interventions including harm reduction, psycho-education, withdrawal protocols, service integration and referral pathways</p> <p>Yellow highlighting = Management of psychiatric symptoms</p> <p>Red highlighting = Management of physical symptoms</p>	Kersten and McLaughlin (2015)	Toxicology and management of novel psychoactive drugs	YES	YES	YES	YES	Cannot determine	YES	YES	YES	5	<p>Synthetic cathinones</p> <ul style="list-style-type: none"> Use of benzos to target agitation/aggression may serve to ameliorate symptoms of hypertension and/or hyperthermia Frequent redosing (thereby leading to a higher overall dose than normally recommended) of benzos may be necessary to achieve adequate sedation Rarely, antipsychotics, propofol or barbiturates may be considered should treatment with benzos be ineffective, though clinicians should be cognisant that toxic effects may be due to substances other than the cathinone Should a patient present with sympathomimetic toxicity or hyperthermia/hypertension unaffected by benzo administration, cooling and antihypertensives are recommended Serotonin syndrome can be treated using benzos or cyproheptadine In the case of dehydration and/or rhabdomyolysis, IV fluids should be given Inpatient observations may be needed <p>Piperazines</p> <ul style="list-style-type: none"> As well as general support, electrocardiogram and electrolyte monitoring should be started Seizures, agitation are to be treated with IV/IM benzos Antipsychotics should not be used to treat severe agitation as these can effect the patient's ability to thermoregulate, as well as cause extrapyramidal side effects and/or hypotension, arrhythmias tachycardia, hypertension may be ameliorated by transiting the patient to a calmer locale Severe hypertension may be treated through IV antihypertensives and clonidine Selective betablockers are not suggested for severe hypertension as they can serve to worsen the effects in the case of piperazine toxicity For refractory hypertension, labetalol is suggested
	Marchi et al. (2019)	Clinical and Toxicological Profile of NBOMes: A Systematic Review	YES	YES	YES	YES	YES	YES	YES	YES	7	<ul style="list-style-type: none"> Management of psychiatric symptoms using benzos

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	Orsolini et al. (2019)	The use of new psychoactive substances (NPS) in young people and their role in mental health care: a systematic review	YES	YES	YES	YES	YES	YES	YES	YES	7	<ul style="list-style-type: none"> Clinicians should be aware of possible interactions between prescribed medications and NPS, which may result in: reduced efficacy of prescribed drugs; worsening of symptoms; reduction of adherence to treatment plans by patients Mental health professionals should be aware of the associations between NPS usage and mental health issues and respond by developing tailored treatment strategies, therapeutic pathways and deepening integration between relevant services

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<p>Yellow highlighting = Management of psychiatric symptoms</p> <p>Red highlighting = Management of physical symptoms</p>	Piccioni <i>et al.</i> (2020)	Risk management in first aid for acute drug intoxication	YES	YES	YES	YES	YES	YES	YES	YES	7	<ul style="list-style-type: none"> • NPS treatment generally should be similar to corresponding classes of "traditional" NPS • Treatment should be supportive, including ABC management • Maintain normal body temperature • Manage agitation • Monitor and counter dehydration and rhabdomyolysis • Maintain safety of patient
<p><u>Columns Authors to Score</u></p> <p>Green = included in study</p> <p>Blue = originally included in separate systematic search for hallucinogens, added to results for stimulants and hallucinogens overall</p> <p>Yellow = included in current systematic review and also other systematic reviews in same project (i.e., sedatives and depressants or SCRA), relevant clinical recommendations separated and presented in clinical recommendations accordingly</p> <p><u>Clinical recommendations</u></p> <p>Blue highlighting = Clinical vigilance and awareness</p>	Richards <i>et al.</i> (2015)	Treatment of toxicity from amphetamines, related derivatives, and analogues: A systematic clinical review	YES	YES	YES	YES	YES	YES	YES	YES	7	<p>Overall, the authors found that:</p> <ul style="list-style-type: none"> • Agitation and psychosis may be treated using butyrophenones and second gen antipsychotics • Agitation also responds well to benzo administration, particularly in the case of methylphenidate intoxication • Benzo treatment may result in under-sedation • Beta-blockers are an appropriate choice for the treatment of hyperadrenergic state. • In the case of "unopposed alpha-stimulation", combination therapy with alpha and beta blockers is considered reasonable, though the phenomenon does not often appear to occur • Calcium channel blockers can be used to treated hypertension, though not tachycardia • Nitroglycerin may be administered for chest pain though the fact it may result in reflex tachycardia must be considered

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<p>Green highlighting = Psychosocial interventions including harm reduction, psycho-education, withdrawal protocols, service integration and referral pathways</p> <p>Yellow highlighting = Management of psychiatric symptoms</p> <p>Red highlighting = Management of physical symptoms</p>	Rinaldi <i>et al.</i> (2020)	The rise of new psychoactive substances and psychiatric implications: A wide-ranging, multifaceted challenge that needs far-reaching common legislative strategies	YES	YES	YES	Cannot determine	Cannot determine	YES	YES	Cannot determine	4	<ul style="list-style-type: none"> In the case of addiction from use of NPS compounds, the authors suggest that treatment should mirror that used for addiction treatment for orthodox drugs of misuse. This includes a 'gradual care' approach, combined with low intensity psychosocial interventions. Withdrawal management, including the possibility of inpatient/residential treatment, can be considered
	Schifano <i>et al.</i> (2016)	Novel psychoactive substances: the pharmacology of stimulants and hallucinogens	YES	YES	YES	YES	YES	YES	YES	YES	7	<ul style="list-style-type: none"> Drug screening is likely to provide negative results in the case of NPS toxicity De-escalation (including verbal) should be the primary initial focus in the case of patients presenting with aggression/agitation as the result of NPS ingestion Benzos often require re-dosing or high dosing to achieve efficacy and this should be taken into account if there is evidence that the patient has co-ingested alcohol If benzos prove ineffective antipsychotics may be considered though caution is advised as their administration may contribute to toxicity. Haloperidol/droperidol are preferred (5-10mg IM/IV). Risperidone, olanzapine, aripiprazole and quetiapine may be considered, though there is paucity of evidence regarding their efficacy Treatment of hyperthermia should be considered and should include cooling strategies and provide IV fluid to counter rhabdomyolysis Serotonin symptom can be treated with benzos cyproheptadine Appropriate referral to inpatient facilities should be considered

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<p>Columns Authors to Score</p> <p>Green = included in study</p> <p>Blue = originally included in separate systematic search for hallucinogens, added to results for stimulants and hallucinogens overall</p> <p>Yellow = included in current systematic review and also other systematic reviews in same project (i.e., sedatives and depressants or SCRA), relevant clinical recommendations separated and presented in clinical recommendations accordingly</p> <p>Clinical recommendations</p> <p>Blue highlighting = Clinical vigilance and awareness</p> <p>Green highlighting = Psychosocial interventions including harm reduction, psycho-education, withdrawal protocols, service integration and referral pathways</p> <p>Yellow highlighting = Management of psychiatric symptoms</p> <p>Red highlighting = Management of physical symptoms</p>	Schifano <i>et al.</i> (2018)	Abuse of Prescription Drugs in the Context of Novel Psychoactive Substances (NPS): A Systematic Review	YES	YES	YES	YES	YES	YES	YES	YES	7	<ul style="list-style-type: none"> Bupropion can be consumed in large doses – reportedly up to 4050mg per day, or approximately 14 times the maximum therapeutic dose – to produce a stimulant-like effect, with it being a cathinone-derivative being postulated as explaining its abuse potential. It is usually ingested intranasally or orally in misuse, though IV injection has also been reported as mode of delivery. Adverse effects from recreational use include cardio-toxicity, seizures, tremor, hallucinations and nasal pain/irritability# Venlafaxine has been reportedly misused as a dissociative. Sudden discontinuation from both of these substances is associated with anxiety, disorientation, depression, suicidality, psychotic symptoms, nausea, stomach cramps and sexual dysfunction Health professionals should consider an individual's background/circumstances when prescribing certain prescription medications to them. If individuals found to be seeking/misusing prescribed drugs in this manner, appropriate treatment services should be contacted
	Suzuki <i>et al.</i> (2015)	Toxicities associated with NBOMe ingestion-a novel class of potent hallucinogens: a review of the literature	y	y	y	Cannot determine	y	y	y	y	6	<p>Clinicians should consider possible accidental or purposeful ingestion of NBOMes in cases where use of hallucinogens is suspected or suspicion is warranted.</p> <ul style="list-style-type: none"> When possible, analytic confirmation of ingestion should be sought Treatment for NBOMe ingestion may include administration of benzos and/or aggressive giving of fluids Harm reduction strategies: avoid insufflation or injecting; use a "trip-sitter; do not "eye-ball" doses <p>Clinicians should avoid direct contact with substances suspected of being NBOMe drugs, should use gloves when handling, avoid touching mouth area after decontamination. Special care should be taken to avoid making substances airborne</p>

1.44 Appendix 4: SCRA critical appraisal

Key to colour-coding system	Authors	Title Primary	Peer Reviewed?	CASP 1 Did the review address a clearly focussed question?	CASP 2 Did the authors look for the right type of papers?	CASP 3 Do you think all the important, relevant papers were included?	CASP 4 Did the review's authors do enough to assess quality of the included studies?	CASP 5 If the results of the review have been combined, was it reasonable to do so?	CASP 8 Can the results be applied to the local population?	CASP 9 Were all important outcomes considered?	Score	Clinical Recommendations
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	Brewer and Collins (2014)	A review of clinical manifestations in adolescent and young adults after use of synthetic cannabinoids	YES	YES	YES	YES	YES	YES	YES	YES	YES	7

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<p>Yellow highlighting = Management of psychiatric symptoms</p> <p>Red highlighting = Management of physical symptoms</p>	Cohen and Weinstein (2018)	The Effects of Cannabinoids on Executive Functions: Evidence from Cannabis and Synthetic Cannabinoids-A Systematic Review	YES	YES	YES	YES	YES	YES	YES	YES	7	<ul style="list-style-type: none"> Clinicians should be more aware of cognitive impairments caused through use of SCs and should assess for these when appropriate In the case of cognitive impairment detected after use of SCs clinicians should consider use of behavioural therapy or cognitive rehabilitation strategies as treatments Clinicians should be especially aware of cognitive impairments in patients who have used SCs in large, regular quantities over extended periods or in young people who have used SCs early in life for prolonged periods
<p><u>Columns Authors to Score</u></p> <p>Green = included in study</p> <p>Yellow = included in current systematic review and also other systematic reviews in same project (i.e., sedatives and depressants or stimulants and hallucinogens), relevant clinical recommendations separated and presented in clinical recommendations accordingly</p> <p><u>Clinical recommendations</u></p> <p>Blue highlighting = Clinical vigilance and awareness</p> <p>Green highlighting = Psychosocial interventions including harm reduction, psycho-education, withdrawal protocols, service integration and referral pathways</p> <p>Yellow highlighting = Management of psychiatric symptoms</p>	Courts <i>et al.</i> (2016)	Signs and symptoms associated with synthetic cannabinoid toxicity: systematic review	YES	YES	YES	NO	YES	YES	YES	YES	6	<ul style="list-style-type: none"> Symptomology of SCRA toxicity can vary considerably. In the case of young male adult patients presenting to services with agitation and/or cardiovascular issues without clear cause SCRA intoxication should be considered
	Grey <i>et al.</i> (2016)	A systematic review of the effects of novel psychoactive substances 'legal highs' on people with severe mental illness	YES	YES	YES	YES	YES	YES	YES	YES	7	<ul style="list-style-type: none"> Use of NPS by people with severe mental illness (SMI) may lead to significant change to their behaviour Agitation necessitating restraint appears to be a common feature (1/3 of papers included in review), as is violence/aggression (1/5) Authors postulate that use of NPS by people with SMI is under-reported and that it is only recorded when individuals display the extreme behaviours described above Authors suggest that it is likely that individuals with SMI may not understand that NPS are psychoactive substances in the same way that illegal substances are (seeing them as "more natural", "less harmful") and do not see need to report their use

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Red highlighting = Management of physical symptoms												<ul style="list-style-type: none"> The above – considered with the fact that NPS are rarely detected in routine drug screenings – suggests that clinicians should ask about NPS specifically in assessments to gain a full understanding of contributing factors to presentation of SM Clinicians should be aware that NPS may have unknown drug/drug interactions that may result in severe adverse effects
<p><u>Columns Authors to Score</u></p> <p>Green = included in study</p> <p>Yellow = included in current systematic review and also other systematic reviews in same project (i.e., sedatives and depressants or stimulants and hallucinogens), relevant clinical recommendations separated and presented in clinical recommendations accordingly</p> <p><u>Clinical recommendations</u></p> <p>Blue highlighting = Clinical vigilance and awareness</p> <p>Green highlighting = Psychosocial interventions including harm reduction, psycho-education, withdrawal protocols, service integration and referral pathways</p> <p>Yellow highlighting = Management of psychiatric symptoms</p>	Grigg et al. (2019)	Synthetic cannabinoid use disorder: an update for general psychiatrists	YES	YES	YES	Cannot determine	Cannot determine	YES	YES	Cannot determine	4	<ul style="list-style-type: none"> Patients who present with chronic SCRA use should be assessed across three measures: physical consequence of use; features of withdrawal; withdrawal assessment Physical consequences of use assessment should contain examination of: medical history, history of substance abuse, physical exam; consideration of cardiac functioning including electrocardiogram to measure tachycardia, bradycardia and/or arrhythmia; testing of serum electrolytes, renal and hepatic function Assessment of features of withdrawal should measure physical symptoms including: craving, feeling cold; excess sweating; tremor; headache; diarrhoea; nausea/vomiting; pains in chest; palpitations; tachycardia; hypertension; muscle pain; hyperventilation and seizing. Psychological symptoms should also be assessed, including: anxiety; agitation; irritability; insomnia; somatic sensation of pain; psychosis; suicidality Withdrawal assessment should feature seven steps. These are: 1) Identification of SC usage in the patient and comorbid mental health issues in a non-judgemental and supportive manner 2) Explanation of confidentiality and its exceptions 3) Use of a screening tool such as the Cannabis Withdrawal Assessment Scale should be considered 4) Along with the patient SC dependence, quantity and frequency of use, natal status if relevant, prior attempts at withdrawal and potential supports should be explored as well as identification of risks and complex needs 5) Assessment of psychiatric adverse effects as well as comorbid mental health problems should be made 6) The withdrawal plan should be made in collaboration with the patient and should be based on info gathered during the assessment. This info should inform planning for potential severity of withdrawal, setting for withdrawal, contingency for risk and identified complex needs 7) Plans for the post-withdrawal period should be made in full conjunction with the patient and should include

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Red highlighting = Management of physical symptoms												<p>relapse prevention as well as provision of supports/services to address psychosocial needs</p> <ul style="list-style-type: none"> Management of withdrawal should have the following features: 1) Severe adverse psychiatric and physical effects of withdrawal (agitation, seizures and so on) should be planned for, managed or circumvented 2) Psychological and physical distress 3) Benzodiazepines prescription should be considered in the short term for withdrawal symptoms as well as other targeted approaches for other adverse symptoms 4) Clinicians should facilitate links to appropriate services for ongoing treatment as needed 5) In the same vein clinicians should provide a link to psychosocial supports 6) Clinicians should provide psychoeducation aimed at harm reduction. This psychoeducation should seek to increase patients' awareness around relevant mental/physical health risks, link SCs usage to presenting MH issues, provision of reduction of use strategies or better harm reduction, and strategies to allow users to see the achievement of increased wellbeing as being linked to vocational and social activities as well as having a healthier lifestyle Clinicians should be aware of drug interactions between SCs and prescribed drugs such as valproic acid, sertraline, fluvoxamine as well as consider ones that may not yet be established when planning treatment
For key please see previous page	Hohmann, Mikus and Czock (2014)	Effects and risks associated with novel psychoactive substances: mislabeling and sale as bath salts, spice, and research chemicals	YES	YES	YES	YES	Cannot determine	YES	YES	Cannot determine	5	<ul style="list-style-type: none"> In the event that a patient presents with symptoms similar to overdose with orthodox stimulants though drug screening returns negative results, clinicians should consider NPS use and use appropriate services available to them such as toxicology laboratories
	Kersten and McLaughlin (2015)	Toxicology and management of novel psychoactive drugs	YES	YES	YES	Cannot determine	Cannot determine	YES	YES	YES	6	<p>Synthetic cannabinoids</p> <ul style="list-style-type: none"> If ingestion of synthetic cannabinoids is suspected, standard measurement of vital signs, protection of airways and introduction of telemetric monitoring should be a first priority Laboratory testing may be advisable depending on symptoms displayed, and may include: CBC, basic metabolic panel, troponin, creatine kinase MB, creatine phosphokinase, blood gas.

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												<p>These may help health professionals determine what the patient may have ingested alongside the SCRA</p> <ul style="list-style-type: none"> • Treatment should be symptomatic and supportive • IV fluid administration may be advisable • Anxiety, agitation or catatonia may be treatable through use of benzos • Antiemetics should be considered for nausea or vomiting • Antipsychotics for hallucinations/psychosis • Inpatient observations, ventilatory support and/or intubation are – on occasion – required
<p>Columns Authors to Score</p> <p>Green = included in study</p> <p>Yellow = included in current systematic review and also other systematic reviews in same project (i.e., sedatives and depressants or stimulants and hallucinogens), relevant clinical recommendations separated and presented in clinical recommendations accordingly</p> <p>Clinical recommendations</p> <p>Blue highlighting = Clinical vigilance and awareness</p> <p>Green highlighting = Psychosocial interventions including harm reduction, psycho-education, withdrawal protocols, service integration and referral pathways</p> <p>Yellow highlighting = Management of psychiatric symptoms</p> <p>Red highlighting = Management of physical symptoms</p>	Orsolini <i>et al.</i> (2017)	Is there a Teratogenicity Risk Associated with Cannabis and Synthetic Cannabinimimetics' ('Spice') Intake?	YES	YES	YES	YES	YES	YES	YES	YES	7	<ul style="list-style-type: none"> • For women who are pregnant or are planning pregnancy and use SCRA, clinicians should: <ul style="list-style-type: none"> • Assess • Be non-judgemental • Collect history • Provide honest information on risks of persisting in use of SCRA whilst pregnant
	Orsolini <i>et al.</i> (2019)	The use of new psychoactive substances (NPS) in young people and their role in mental health care: a systematic review	Yes	YES	YES	YES	YES	YES	YES	YES	7	<ul style="list-style-type: none"> • Clinicians should be aware of possible interactions between prescribed medications and NPS, which may result in: reduced efficacy of prescribed drugs; worsening of symptoms; reduction of adherence to treatment plans by patients • Mental health professionals should be aware of the associations between NPS usage and mental health issues and respond by developing tailored treatment strategies, therapeutic pathways and deepening integration between relevant services
	Piccioni <i>et al.</i> (2020)	Risk management in first aid for acute drug intoxication	YES	YES	YES	YES	YES	YES	YES	YES	7	<ul style="list-style-type: none"> • NPS treatment generally should be similar to corresponding classes of "traditional" NPS • Treatment should be supportive, including ABC management • Maintain normal body temperature • Manage agitation

Key to colour-coding system	Authors	Title Primary	Peer Reviewed?	CASP 1 Did the review address a clearly focussed question?	CASP 2 Did the authors look for the right type of papers?	CASP 3 Do you think all the important, relevant papers were included?	CASP 4 Did the review's authors do enough to assess quality of the included studies?	CASP 5 If the results of the review have been combined, was it reasonable to do so?	CASP 8 Can the results be applied to the local population?	CASP 9 Were all important outcomes considered?	Score	Clinical Recommendations
												<ul style="list-style-type: none"> Monitor and counter dehydration and rhabdomyolysis Maintain safety of patient
<p><u>Columns Authors to Score</u></p> <p>Green = included in study</p> <p>Blue = originally included in separate systematic search for hallucinogens, added to results for stimulants and hallucinogens overall</p> <p>Yellow = included in current systematic review and also other systematic reviews in same project (i.e., sedatives and depressants or stimulants and hallucinogens), relevant clinical recommendations separated and presented in clinical recommendations accordingly</p>	Rinaldi et al. (2020)	The rise of new psychoactive substances and psychiatric implications: A wide-ranging, multifaceted challenge that needs far-reaching common legislative strategies	YES	YES	YES	Cannot determine	Cannot determine	YES	YES	Cannot determine	4	<ul style="list-style-type: none"> In the case of addiction from use of NPS compounds, the authors suggest that treatment should mirror that used for addiction treatment for orthodox drugs of misuse. This includes a 'gradual care' approach, combined with low intensity psychosocial interventions. <p>Withdrawal management, including the possibility of inpatient/residential treatment, can be considered</p>
<p><u>Clinical recommendations</u></p> <p>Blue highlighting = Clinical vigilance and awareness</p> <p>Green highlighting = Psychosocial interventions including harm reduction, psycho-education, withdrawal protocols, service integration and referral pathways</p>	Schiano et al. (2016)	Novel psychoactive substances: the pharmacology of stimulants and hallucinogens	YES	YES	YES	YES	YES	YES	YES	YES	7	<ul style="list-style-type: none"> Drug screening is likely to provide negative results in the case of NPS toxicity De-escalation (including verbal) should be the primary initial focus in the case of patients presenting with aggression/agitation as the result of NPS ingestion Benzos often require re-dosing or high dosing to achieve efficacy and this should be taken into account if there is evidence that the patient has co-ingested alcohol

Key to colour-coding system	Authors	Title Primary	Peer Reviewed?	CASP 1 Did the review address a clearly focussed question?	CASP 2 Did the authors look for the right type of papers?	CASP 3 Do you think all the important, relevant papers were included?	CASP 4 Did the review's authors do enough to assess quality of the included studies?	CASP 5 If the results of the review have been combined, was it reasonable to do so?	CASP 8 Can the results be applied to the local population?	CASP 9 Were all important outcomes considered?	Score	Clinical Recommendations
<p>Yellow highlighting = Management of psychiatric symptoms</p> <p>Red highlighting = Management of physical symptoms</p>												<ul style="list-style-type: none"> If benzos prove ineffective antipsychotics may be considered though caution is advised as their administration may contribute to toxicity. Haloperidol/droperidol are preferred (5-10mg IM/IV). Risperidone, olanzapine, aripiprazole and quetiapine may be considered, though there is paucity of evidence regarding their efficacy Treatment of hyperthermia should be considered and should include cooling strategies and provide IV fluid to counter rhabdomyolysis Serotonin symptom can be treated with benzos cyproheptadine Appropriate referral to inpatient facilities should be considered
<p><u>Columns Authors to Score</u></p> <p>Green = included in study</p> <p>Blue = originally included in separate systematic search for hallucinogens, added to results for stimulants and hallucinogens overall</p> <p>Yellow = included in current systematic review and also other systematic reviews in same project (i.e., sedatives and depressants or stimulants and hallucinogens), relevant clinical recommendations separated and presented in clinical recommendations accordingly</p> <p><u>Clinical recommendations</u></p> <p>Blue highlighting = Clinical vigilance and awareness</p>	Tait et al. (2015)	A systematic review of adverse events arising from the use of synthetic cannabinoids and their associated treatment	YES	YES	YES	YES	YES	YES	YES	YES	7	<ul style="list-style-type: none"> For mild intoxications admission to ER for treatment may not be needed and symptomatic treatment preferred There is no antidote similar to that seen for opioid overdose (naloxone?) for SCRAS, making management of OD in the latter more problematic SC overdose lacks a distinct toxidrome that may be seen in other recreational drugs Clinicians should eliminate a range of other health conditions before diagnosing SC overdose including: hypoglycaemia, CNS infection, hyperactivity of thyroid, head trauma or MH Benzos are considered adequate to manage agitation Haloperidol is also an option, though is not recommended in the case of undifferentiated diagnosis In cases of benzos failing to manage symptoms – direct, manual methods of ensuring patient airways are maintained should be considered The main foci of treatment should consist of: giving of IV fluids to combat dehydration; preservation of airway; circumventing rhabdomyolysis; be vigilant for cerebral/cardiac ischemia

Key to colour-coding system	Authors	Title Primary	Peer Reviewed?	CASP 1 Did the review address a clearly focussed question?	CASP 2 Did the authors look for the right type of papers?	CASP 3 Do you think all the important, relevant papers were included?	CASP 4 Did the review's authors do enough to assess quality of the included studies?	CASP 5 If the results of the review have been combined, was it reasonable to do so?	CASP 8 Can the results be applied to the local population?	CASP 9 Were all important outcomes considered?	Score	Clinical Recommendations
<p>Green highlighting = Psychosocial interventions including harm reduction, psycho-education, withdrawal protocols, service integration and referral pathways</p> <p>Yellow highlighting = Management of psychiatric symptoms</p> <p>Red highlighting = Management of physical symptoms</p>												

1.45 Appendix 5: Participant recruitment email

23/11/2023, 12:08

Mail - Iain Lindsay - Outlook

Seeking participants for study regarding Novel Psychoactive Substances

Iain Lindsay

Fri 4/7/2023 5:40 PM

To: MHN111-S1S2S3-A <MHN111-S1S2S3-A@abertay.ac.uk>; MHN221-S1S2-A <MHN221-S1S2-A@abertay.ac.uk>;
MHN341-S2S3-A <MHN341-S2S3-A@abertay.ac.uk>
Cc: Judith Kelly; Mhairi Thurston

1 attachments (37 KB)

EMS7178 Consent to participate form.docx

Hi all,

I'm currently recruiting participants for a study into the educational needs of nursing students regarding patient use of Novel Psychoactive Substances (NPS).

For the study, you would have to answer a short online questionnaire regarding your level of confidence and knowledge regarding NPS and treatment of health conditions arising from their use by patients. You would then have to attend a focus group, during which you would watch a pre-recorded presentation about treatment of NPS related health issues, and after which you would discuss the presentation. Finally, you would have to repeat the same questionnaire to see if your levels of knowledge and confidence have changed after watching the presentation.

In terms of time lengths involved, the questionnaires should take no more than 10 minutes each to complete. The focus group may take up to two hours of time, though may take less than this. The time and date for the focus group would be decided through negotiation, though are likely to take place at some time during the week beginning the 17th of April.

If you would be interested in participating, please complete and return the attached consent to participate form. Please note that only the first five participants who return a completed consent to participate will be included in the study.

Many thanks,

Iain Lindsay
Teaching Fellow
Division of Health Sciences
Abertay University
1 Bell Street
Dundee
DD1 1HG

1.46 Appendix 6: Pre-test questionnaire

16/11/2023, 09:53

NPS Questionnaire - Pre-presentation (2)

NPS Questionnaire - Pre-presentation (2)

Hi! Would you mind taking 2 minutes to complete this form? It would be great if you can submit your response by 29 Sept 2023. Thank you!

Demographic information

1. What age are you?

- 18-22
- 23-27
- 28-32
- 33-37
- 38-42
- 43-47
- 48-52
- 53 or older

2. What year of study are you in?

- 1st Year
- 2nd Year
- 3rd Year

3. How many years of experience have you had of working in healthcare?

- No experience
- 1 year or less
- 1-3 years
- 4-6 years
- 7-9 years
- 10 years or more

Knowledge and confidence about NPS-related issues

NPS stands for Novel Psychoactive Substances. This means any substance that – in recent decades – has come to be used for a psychoactive effect (in other words: used as a recreational drug; used to achieve a "high"), and is not a drug that has been traditionally used for this purpose, such as alcohol, cannabis, heroin or cocaine. Often referred to as "legal highs" in the media until recently, NPS can in fact include any drug, regardless of legal status, that has started to be used for its psychoactive effect in recent years. Examples you may have heard of include "spice" (synthetic cannabis), mephedrone and etizolam. However, it can also include drugs that are commonly prescribed to people legally, and which have recently begun to be misused in recreational contexts, such as fentanyl.

In questions below that ask about your **level of knowledge**, please rate this from 1 to 5, with 1 meaning "no knowledge at all/very poor knowledge", and 5 meaning "extremely knowledgeable".

For questions that ask about **level of confidence**, please rate this from 1 to 5, with 1 meaning "no confidence at all/very little confidence" and 5 meaning "extremely confident".

4. What is your level of knowledge regarding vigilance/awareness on the part of the clinician regarding patient use of NPS?

- 1 - No knowledge at all/very poor knowledge
- 2
- 3
- 4
- 5 - Extremely knowledgeable

5. What is your level of confidence regarding vigilance/awareness on the part of the clinician regarding patient use of NPS?

- 1 - No confidence at all/very little confidence
- 2
- 3
- 4
- 5 - Extremely confident

6. What is your level of knowledge regarding psychosocial interventions for treatment of health issues arising from patient use of NPS?

- 1 - No knowledge at all/very poor knowledge
- 2
- 3
- 4
- 5 - Extremely knowledgeable

7. What is your level of confidence regarding the use of psychosocial interventions for treatment of health issues arising from patient use of NPS?

- 1 - No confidence at all/very little confidence
- 2
- 3
- 4
- 5 - Extremely confident

8. What is your level of knowledge regarding the management of psychiatric symptoms in the treatment of health issues arising patient use of NPS?

- 1 - No knowledge at all/very poor knowledge
- 2
- 3
- 4
- 5 - Extremely knowledgeable

9. What is your level of confidence regarding the management of psychiatric symptoms in the treatment of health issues arising patient use of NPS?

- 1 - No confidence at all/very little confidence
- 2
- 3
- 4
- 5 - Extremely confident

10. What is your level of knowledge regarding the management of physical symptoms in the treatment of health issues arising patient use of NPS?

- 1 - No knowledge at all/very poor knowledge
- 2
- 3
- 4
- 5 - Extremely knowledgeable

11. What is your level of confidence regarding the management of physical symptoms in the treatment of health issues arising patient use of NPS?

- 1 - No confidence at all/very little confidence
- 2
- 3
- 4
- 5 - Extremely confident

This content is neither created nor endorsed by Microsoft. The data you submit will be sent to the form owner.



1.47 Appendix 7: Post-test Questionnaire

16/11/2023, 09:56

Novel Psychoactive Substances Questionnaire - Post-presentation (2)

Novel Psychoactive Substances Questionnaire - Post-presentation

Demographic information

1. What age are you?

- 18-22
- 23-27
- 28-32
- 33-37
- 38-42
- 43-47
- 48-52
- 53 or older

2. What year of study are you in?

- 1st Year
- 2nd Year
- 3rd Year

3. How many years of experience have you had of working in healthcare?

- No experience
- 1 year or less
- 1-3 years
- 4-6 years
- 7-9 years
- 10 years or more

Knowledge and confidence about NPS-related issues

NPS stands for Novel Psychoactive Substances. This means any substance that – in recent decades – has come to be used for a psychoactive effect (in other words: used as a recreational drug; used to achieve a "high"), and is not a drug that has been traditionally used for this purpose, such as alcohol, cannabis, heroin or cocaine. Often referred to as "legal highs" in the media until recently, NPS can in fact include any drug, regardless of legal status, that has started to be used for its psychoactive effect in recent years. Examples you may have heard of include "spice" (synthetic cannabis), mephedrone and etizolam. However, it can also include drugs that are commonly prescribed to people legally, and which have recently begun to be misused in recreational contexts, such as fentanyl.

In questions below that ask about your **level of knowledge**, please rate this from 1 to 5, with 1 meaning "no knowledge at all/very poor knowledge", and 5 meaning "extremely knowledgeable".

For questions that ask about **level of confidence**, please rate this from 1 to 5, with 1 meaning "no confidence at all/very little confidence" and 5 meaning "extremely confident".

4. What is your level of knowledge regarding vigilance/awareness on the part of the clinician regarding patient use of NPS?

- 1 - No knowledge at all/very poor knowledge
- 2
- 3
- 4
- 5 - Extremely knowledgeable

5. What is your level of confidence regarding vigilance/awareness on the part of the clinician regarding patient use of NPS?

- 1 - No confidence at all/very little confidence
- 2
- 3
- 4
- 5 - Extremely confident

6. What is your level of knowledge regarding psychosocial interventions for treatment of health issues arising from patient use of NPS?

- 1 - No knowledge at all/very poor knowledge
- 2
- 3
- 4
- 5 - Extremely knowledgeable

7. What is your level of confidence regarding the use of psychosocial interventions for treatment of health issues arising from patient use of NPS?

- 1 - No confidence at all/very little confidence
- 2
- 3
- 4
- 5 - Extremely confident

8. What is your level of knowledge regarding the management of psychiatric symptoms in the treatment of health issues arising patient use of NPS?

- 1 - No knowledge at all/very poor knowledge
- 2
- 3
- 4
- 5 - Extremely knowledgeable

9. What is your level of confidence regarding the management of psychiatric symptoms in the treatment of health issues arising patient use of NPS?

- 1 - No confidence at all/very little confidence
- 2
- 3
- 4
- 5 - Extremely confident

10. What is your level of knowledge regarding the management of physical symptoms in the treatment of health issues arising patient use of NPS?

- 1 - No knowledge at all/very poor knowledge
- 2
- 3
- 4
- 5 - Extremely knowledgeable

11. What is your level of confidence regarding the management of physical symptoms in the treatment of health issues arising patient use of NPS?

- 1 - No confidence at all/very little confidence
- 2
- 3
- 4
- 5 - Extremely confident

This content is neither created nor endorsed by Microsoft. The data you submit will be sent to the form owner.



1.49 Appendix 9: Quantitative questionnaire post-test results

What age are you?	What year of study are you in?	How many years of experience have you had of being a nurse? health care?	What is your level of knowledge regarding the use of NPS2? (K-PNS)	What is your level of confidence regarding the use of NPS2? (C-PNS)	What is your level of knowledge regarding psychosocial interventions for treatment of health issues arising from patient use of NPS2? (K-PSI)	What is your level of confidence regarding the use of NPS2? (C-PSI)	What is your level of knowledge regarding the presentation of symptoms in the treatment of health issues arising from patient use of NPS2? (K-PSYCH)	What is your level of confidence regarding the presentation of symptoms in the treatment of health issues arising from patient use of NPS2? (C-PSYCH)	What is your level of knowledge regarding the management of physical symptoms in the treatment of health issues arising from patient use of NPS2? (K-PHS)	What is your level of confidence regarding the management of physical symptoms in the treatment of health issues arising from patient use of NPS2? (C-PHS)	Mean average scores of questions (MPS-QA)	Mean averages for knowledge for questions (K-QA)	Mean averages for confidence for questions (C-QA)	Mean averages for vignette awareness questions (KC-VIA)	Mean averages for psychosocial intervention-related questions (KC-PSI)	Mean averages for management of physical symptoms related questions (KC-PSYCH)	Mean averages for questions of management of symptoms related (KC-PHS)	
2	3	5	3	3	3	2	3	2	3	2								
3	3	3	3	3	3	2	3	2	3	2								
6	2	4	4	3	3	3	3	3	3	3								
2	2	4	4	4	4	4	4	4	4	4								
3	2	5	4	4	4	4	4	4	4	4								
			Mean average	3.4	3.2	3.2	3.4	3.0	3.0	2.8	3.1	3.3	3.0	3.3	3.1	3.2	2.9	
			SD	0.9	0.4	0.4	0.6	0.7	0.0	0.8	0.5	0.4	0.7	0.5	0.6	0.6	0.4	
			2nd year students	3.8	3.2	3.2	3.5	3.0	3.0	3.0	3.3	3.3	3.2	3.4	3.3	3.4	3.0	
			SD	0.8	0.2	0.2	0.6	0.0	0.0	0.8	0.5	0.4	0.6	0.5	0.5	0.5	0.4	
			3rd year student	3.0	3.0	3.0	3.0	2.0	3.0	2.0	2.6	3.0	2.3	3.0	2.5	2.5	2.5	
			Difference: 2nd to 3rd year mean averages	-0.6	-0.3	-0.3	-0.5	-1.0	-1.0	-1.0	-0.6	-0.3	-0.9	-0.4	-0.8	-0.9	-0.5	
			Mean averages - 23-29 year olds	3.0	3.0	3.0	3.2	3.0	3.0	2.8	2.9	3.1	2.8	3.0	2.8	2.8	2.7	
			SD	0.0	0.0	0.0	0.2	0.0	0.0	0.2	0.2	0.1	0.3	0.0	0.3	0.3	0.2	
			Mean averages - 38-47 year olds	4.0	3.6	3.6	3.6	3.0	3.0	3.5	3.5	3.5	3.5	3.8	3.5	3.5	3.3	
			SD	0.0	0.7	0.7	0.7	0.0	0.7	0.7	0.5	0.4	0.7	0.4	0.7	0.7	0.4	
			Difference: 23-29 year olds averages - Less than 1 year to 3 years of healthcare experience	1.0	0.6	0.6	0.2	0.0	0.0	1.2	0.6	0.4	0.8	0.8	0.7	0.3	0.6	
			Mean averages - 4-9 years of the healthcare experience	3.8	3.6	3.6	3.6	3.0	3.0	3.0	3.3	3.4	3.1	3.5	3.3	3.3	3.0	
			SD	0.7	0.7	0.7	0.7	0.0	0.0	1.4	0.9	0.9	1.2	0.7	1.1	1.1	0.7	
			Difference: 1st year and 7-9 years healthcare	0.2	0.6	0.6	0.2	0.0	0.0	0.3	0.2	0.2	0.3	0.3	0.3	0.1	0.2	

1.50 Appendix 10: Quantitative questionnaire pre and post-test results comparison

Demographic Group	What is your level of knowledge regarding vigilance/awareness on the part of the clinician regarding patient use of MP-S? (K-VIG)	What is your level of confidence regarding vigilance/awareness on the part of the clinician regarding patient use of MP-S? (C-VIG)	What is your level of knowledge regarding psychosocial interventions for treatment of health issues arising from patient use of MP-S? (K-FSI)	What is your level of confidence regarding the use of psychosocial interventions for treatment of health issues arising from patient use of MP-S? (C-FSI)	What is your level of knowledge regarding the management of psychiatric symptoms in the treatment of health issues arising from patient use of MP-S? (K-PSYCH)	What is your level of confidence regarding the management of psychiatric symptoms in the treatment of health issues arising from patient use of MP-S? (C-PSYCH)	What is your level of knowledge regarding the management of physical symptoms in the treatment of health issues arising from patient use of MP-S? (K-PHYS)	What is your level of confidence regarding the management of physical symptoms in the treatment of health issues arising from patient use of MP-S? (C-PHYS)	Mean average scores all questions comparison between pre and post test (MP-S-DA)	Average differences between pre and post-test totals - knowledge only (K-DA)	Average differences between pre and post-test totals - confidence only (C-DA)	Mean averages for vigilance/awareness questions (K-C-VIG)	Mean averages for psychosocial intervention-related questions (K-FSI)	Mean averages for management of psychiatric symptoms-related questions (K-C-PSYCH)	Mean averages for management of physical symptoms-related questions (K-C-PHYS)
Difference between pre and post-totals - Zulu/real students	1.0	0.8	0.5	0.8	1.0	0.8	1.0	1.0	0.8	0.9	0.8	0.9	0.7	0.8	0.9
Differences between pre and post-west-totals - 3/0 year student	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	0.8	1.0	0.8	1.0	1.0	1.0	0.5
Differences between pre and post-west-totals - 2/0 to 3/0 year students	0.0	0.3	0.5	0.3	0.0	0.5	0.0	-1.0	0.1	0.1	0.0	0.1	0.4	0.3	-0.5
Differences between pre and post-totals - 2/0-2/2 year olds	0.7	0.7	0.7	0.7	1.0	0.7	1.0	0.0	0.7	0.8	0.5	0.7	0.7	0.8	0.5
Differences between pre and post-totals - 2/0-4/7 year olds	1.5	1.0	0.5	1.0	1.0	1.0	1.0	2.0	1.1	1.0	1.3	1.3	0.8	1.0	1.5
Differences between pre and post-totals - year olds to 3/0-4/7	0.8	0.3	-0.2	0.3	0.0	0.3	0.0	2.0	0.5	0.2	0.8	0.6	0.1	0.2	1.0
Differences between participants with Less than 1 year to 3 years of healthcare experience	1.0	0.7	0.3	0.7	1.0	0.3	1.0	0.7	0.7	0.8	0.6	0.8	0.5	0.7	0.8
Differences between pre and post-totals - participants with 4-9 years experience	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Differences between pre and post-totals - participants with less than a year to 3 years and participants with 7-9 years healthcare experience	0.0	0.3	0.7	0.3	0.0	0.7	0.0	0.3	0.3	0.2	0.4	0.2	0.5	0.3	0.2