PSYCHOSIS WITH COEXISTING SUBSTANCE MISUSE

Psychosis with coexisting substance misuse: assessment and management in adults and young people

National Clinical Guideline Number X

National Collaborating Centre for Mental Health
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GUIDELINE DEVELOPMENT GROUP MEMBERS

Professor Peter Tyrer (Chair, Guideline Development Group)
Professor of Community Psychiatry, Imperial College, London

Dr Tim Kendall (Facilitator, Guideline Development Group)
Director, National Collaborating Centre for Mental Health (NCCMH)
Medical Director, Sheffield Health and Social Care Trust
Consultant Adult Psychiatrist

Professor Mohammed T. Abou-Saleh
Professor of Psychiatry, St George's, University of London and Honorary Consultant in Addiction Psychiatry, South West London and St George's Mental Health NHS Trust, London

Professor Christine Barrowclough
Professor of Clinical Psychology, University of Manchester

Ms Tina Braithwaite
Representing Service User/Carer Interests.
Director of Service User Involvement, Revolving Doors Agency.

Dr Andy Cotgrove
Young people (CAMHS level 4), Pine Lodge Young People's Centre, Chester

Dr Mike Crawford
Reader in Mental Health Services Research, Imperial College London / Central and North West London Mental Health NHS Trust

Professor Ilana Crome
Professor of Addiction Psychiatry, Keele University Medical School
Honorary Consultant Addiction Psychiatrist, South Staffordshire and Shropshire NHS Foundation Trust

Mr Matthew Dyer
Health Economist, NCCMH

Mr Mike Firn
Clinical Service Development Lead, South West London & St George's Mental Health NHS Trust

Dr Frank Holloway
Consultant Psychiatrist and Clinical Director, Bethlem Royal Hospital

Dr Cheryl Kipping

Nurse Consultant, South London And Maudsley NHS Foundation Trust

Ms Katherine Leggett
Guideline Development Manager, NCCMH

Dr Kate McKinnell
Senior Medical Officer (Addictions), Sefton Integrated Recovery Team (CRI)

Dr Jonathan Mitchell
Consultant Psychiatrist, Early Intervention & Continuing Needs Services, Sheffield Health & Social Care Trust,

Dr David Ndegwa
Consultant Forensic Psychiatrist / Clinical Director, South London & Maudsley NHS Foundation Trust

Mr Peter Pratt
Chief Pharmacist, Sheffield Health & Social Care Trust / Rotherham Doncaster & South Humber NHS Trust

Ms Theresa Renwick
Social Care Lead for Mental Health, Royal Borough of Kensington and Chelsea

Ms Laura Shields
Research Assistant, NCCMH

Mr Leroy Simpson
Representing Service User/Carer Interests.
Board Member, Salvation Army Housing Association.

Ms Sarah Stockton
Senior Information Scientist, NCCMH

Dr Clare Taylor
Editor, NCCMH

Dr Craig Whittington
Senior Systematic Reviewer, NCCMH

Mrs Penelope Wigram
Representing Service User/Carer Interests
Psychoanalytic Psychotherapist, BPC.

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1 PREFACE

This guideline has been developed to advise on the assessment and management of adults and young people with psychosis and coexisting substance misuse. The guideline recommendations have been developed by a multidisciplinary team of healthcare professionals, a service user, a carer and guideline methodologists after careful consideration of the best available evidence. It is intended that the guideline will be useful to clinicians and service commissioners in providing and planning high-quality care for people with psychosis and coexisting substance misuse while also emphasising the importance of the experience of care for people with psychosis and coexisting substance misuse and their carers (see Appendix 1 for more details on the scope of the guideline).

Although the evidence base is rapidly expanding, there are a number of major gaps, and future revisions of this guideline will incorporate new scientific evidence as it develops. The guideline makes a number of research recommendations specifically to address gaps in the evidence base (see Appendix 12 for the recommendations that the GDG thought were of high priority). In the meantime, it is hoped that the guideline will assist clinicians, people with psychosis and coexisting substance misuse and their carers by identifying the merits of particular treatment approaches where the evidence from research and clinical experience exists.

1.1 NATIONAL GUIDELINE

1.1.1 What are clinical practice guidelines?

Clinical practice guidelines are 'systematically developed statements that assist clinicians and patients in making decisions about appropriate treatment for specific conditions' (Mann, 1996). They are derived from the best available research evidence, using predetermined and systematic methods to identify and evaluate the evidence relating to the specific condition in question. Where evidence is lacking, the guidelines incorporate statements and recommendations based upon the consensus statements developed by the Guideline Development Group (GDG).

Clinical guidelines are intended to improve the process and outcomes of healthcare in a number of different ways. They can:

- provide up-to-date evidence-based recommendations for the management of conditions and disorders by healthcare professionals

- be used as the basis to set standards to assess the practice of healthcare professionals
- form the basis for education and training of healthcare professionals
- assist patients and carers in making informed decisions about their treatment and care
- improve communication between healthcare professionals, patients and carers
- help identify priority areas for further research.

1.1.2 Uses and limitation of clinical guidelines

Guidelines are not a substitute for professional knowledge and clinical judgement. They can be limited in their usefulness and applicability by a number of different factors: the availability of high-quality research evidence, the quality of the methodology used in the development of the guideline, the generalisability of research findings and the uniqueness of individuals with psychosis and coexisting substance misuse.

Although the quality of research in this field is variable, the methodology used here reflects current international understanding on the appropriate practice for guideline development (AGREE: Appraisal of Guidelines for Research and Evaluation Instrument; www.agreecollaboration.org), ensuring the collection and selection of the best research evidence available and the systematic generation of treatment recommendations applicable to the majority of people with these disorders and situations. However, there will always be some people and situations for which clinical guideline recommendations are not readily applicable. This guideline does not, therefore, override the individual responsibility of healthcare professionals to make appropriate decisions in the circumstances of the individual, in consultation with the person with psychosis and coexisting substance misuse or carer.

In addition to the clinical evidence, cost-effectiveness information, where available, is taken into account in the generation of statements and recommendations of the clinical guidelines. While national guidelines are concerned with clinical and cost effectiveness, issues of affordability and implementation costs are to be determined by the National Health Service (NHS).

In using guidelines, it is important to remember that the absence of empirical evidence for the effectiveness of a particular intervention is not the same as evidence for ineffectiveness. In addition, of particular relevance in mental health, evidence-based treatments are often delivered within the context of an

overall treatment programme including a range of activities, the purpose of which may be to help engage the person and to provide an appropriate context for the delivery of specific interventions. It is important to maintain and enhance the service context in which these interventions are delivered; otherwise the specific benefits of effective interventions will be lost. Indeed, the importance of organising care in order to support and encourage a good therapeutic relationship is at times as important as the specific treatments offered.

1.1.3 Why develop national guidelines?

The National Institute for Health and Clinical Excellence (NICE) was established as a Special Health Authority for England and Wales in 1999, with a remit to provide a single source of authoritative and reliable guidance for patients, professionals and the public. NICE guidance aims to improve standards of care, to diminish unacceptable variations in the provision and quality of care across the NHS and to ensure that the health service is patient centred. All guidance is developed in a transparent and collaborative manner using the best available evidence and involving all relevant stakeholders.

NICE generates guidance in a number of different ways, three of which are relevant here. First, national guidance is produced by the Technology Appraisal Committee to give robust advice about a particular treatment, intervention, procedure or other health technology. Second, NICE commissions public health intervention guidance focused on types of activity (interventions) that help to reduce people's risk of developing a disease or condition or help to promote or maintain a healthy lifestyle. Third, NICE commissions the production of national clinical practice guidelines focused upon the overall treatment and management of a specific condition. To enable this latter development, NICE originally established seven National Collaborating Centres in conjunction with a range of professional organisations involved in healthcare.

1.1.4 The National Collaborating Centre for Mental Health

This guideline has been commissioned by NICE and developed within the National Collaborating Centre for Mental Health (NCCMH). The NCCMH is a collaboration of the professional organisations involved in the field of mental health, national patient and carer organisations, a number of academic institutions and NICE. The NCCMH is funded by NICE and is led by a partnership between the Royal College of Psychiatrists and the British Psychological Society's Centre for Outcomes Research and Effectiveness, based at Univeristy College London.

1.1.5 From national guidelines to local protocols

Once a national guideline has been published and disseminated, local healthcare groups will be expected to produce a plan and identify resources

for implementation, along with appropriate timetables. Subsequently, a multidisciplinary group involving commissioners of healthcare, primary care and specialist mental health professionals, patients and carers should undertake the translation of the implementation plan into local protocols taking into account both the recommendations set out in this guideline and the priorities set in the National Service Framework for Mental Health and related documentation. The nature and pace of the local plan will reflect local healthcare needs and the nature of existing services; full implementation may take a considerable time, especially where substantial training needs are identified.

1.1.6 Auditing the implementation of guidelines

This guideline identifies key areas of clinical practice and service delivery for local and national audit. Although the generation of audit standards is an important and necessary step in the implementation of this guidance, a more broadly based implementation strategy will be developed. Nevertheless, it should be noted that the Healthcare Commission will monitor the extent to which Primary Care Trusts, trusts responsible for mental health and social care and Health Authorities have implemented these guidelines.

1.2 THE PSYCHOSIS WITH COEXISTING SUBSTANCE MISUSE: ASSESSMENT AND MANAGEMENT IN ADULTS AND YOUNG PEOPLE GUIDELINE

1.2.1 Who has developed this guideline?

The GDG was convened by the NCCMH and supported by funding from NICE. The GDG included a service user and a carer, and professionals from psychiatry, clinical psychology, general practice, nursing, pharmacy and social care.

Staff from the NCCMH provided leadership and support throughout the process of guideline development, undertaking systematic searches, information retrieval, appraisal and systematic review of the evidence. Members of the GDG received training in the process of guideline development from NCCMH staff, and the service users and carer received training and support from the NICE Patient and Public Involvement Programme. The NICE Guidelines Technical Adviser provided advice and assistance regarding aspects of the guideline development process.

All GDG members made formal declarations of interest at the outset, which were updated at every GDG meeting. The GDG met a total of ten times throughout the process of guideline development. It met as a whole, but key topics were led by a national expert in the relevant topic. The GDG was

supported by the NCCMH technical team, with additional expert advice from special advisers where needed. The group oversaw the production and synthesis of research evidence before presentation. All statements and recommendations in this guideline have been generated and agreed by the whole GDG.

1.2.2 For whom is this guideline intended?

This guideline will be relevant for adults and young people with psychosis and coexisting substance misuse.

The guideline covers the care provided by primary, community, secondary, tertiary and other healthcare professionals who have direct contact with, and make decisions concerning the care of, adults and young people with psychosis and coexisting substance misuse.

The guideline will also be relevant to the work, but will not cover the practice, of those in:

- occupational health services
- social services
- the independent sector.

The experience of people with psychosis and coexisting substance misuse can affect the whole family and often the community. The guideline recognises the role of both in the treatment and support of people with psychosis and coexisting substance misuse.

1.2.3 Specific aims of this guideline

The guideline makes recommendations for the assessment and management of adults and young people with psychosis and coexisting substance misuse. It aims to:

- review the experience of care from the servicer user and their families/carers perspective
- evaluate service delivery models
- evaluate the role of psychological/ psychosocial interventions
- evaluate the role of pharmacological interventions
- integrate the above to provide best-practice advice on the assessment and care of individuals throughout the care pathway

- promote the implementation of best clinical practice through the development of recommendations tailored to the requirements of the NHS in England and Wales.

1.2.4 The structure of this guideline

The guideline is divided into chapters, each covering a set of related topics. The first three chapters provide a summary of the clinical practice and research recommendations, a general introduction to guidelines and the topic, and to the methods used to develop this guideline. Chapters 4 to 9 provide the evidence that underpins the recommendations.

Each evidence chapter begins with a general introduction to the topic that sets the recommendations in context. Depending on the nature of the evidence, narrative reviews or meta-analyses were conducted, and the structure of the chapters varies accordingly. Where appropriate, details about current practice are provided. Where meta-analyses were conducted, information is given about both the interventions included and the studies considered for review. Further sub-sections are used to present GRADE summary of findings tables, clinical summaries, and health economic evidence. A sub-section called 'from evidence to recommendations' is used explain how the GDG moved from the evidence to the recommendations. Finally, recommendations (clinical and research) related to each topic are presented at the end of each chapter. A list of research recommendations that the GDG thought were of high priority, with the rationale for this decision, can be found in Appendix 12. On the CD-ROM, further information about the evidence and the economic plan is provided in seven appendices (see Table 1 for details).

Table 1. Appendices on CD-ROM

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2 PSYCHOSIS WITH COEXISTING SUBSTANCE MISUSE

2.1 INTRODUCTION

Many people with mental health issues use substances, and for psychosis, problematic drinking and use of illicit drugs occur more frequently than in the general population (McCreadie *et al*., 2002; Regier *et al*., 1990). For example, the Epidemiological Catchment Area (ECA) study in the USA reported a 47% and 60% lifetime prevalence rate of substance misuse (drugs and alcohol) among people with schizophrenia and bipolar disorder, respectively; in the general population, the rate was 16% (Regier *et al*., 1990). . Although there is still debate as to whether there is a causal link between developing psychosis and illicit drug use, it is well established that the course of psychosis is adversely affected by substance misuse, resulting in a more prolonged and serious condition. Associated problems include nonadherence to prescribed medication, poor engagement with treatment programmes, increased risk of suicide, more inpatient stays, increased risk of violence and time spent in the criminal justice system, and poorer overall prognosis. However, many of these associations occur with substance misuse alone; the relationship between psychosis and substance misuse is complex.

Whilst an understanding of the linkage of psychosis and coexisting substance use would greatly facilitate the development of treatment approaches, knowledge to date is limited (Blanchard *et al.,* 2000). A consistency in the pattern of substance use in psychosis – alcohol being the most common substance, cannabis the most common drug, with poly substance use frequently occurring - has been established in the UK (Weaver *et al.,* 2003), the US (Blanchard *et al.,* 2000) and Australia (Kavanagh *et al.,* 2004). This pattern of substance use in psychosis seems to be largely unrelated to patients' symptomatology (Brunette *et al*., 1997) but rather, is associated with the same demographic correlates as for the general population (Teeson *et al*., 2000). This suggests that in a similar way to other substance users, it is the social context and availability of substances that most often dictates substance choices in psychosis (Kavanagh *et al*., 2004; Patkar *et al*., 1999). The small literature on reasons for substance use in psychosis also suggests that people with psychosis do not differ from other groups, with reasons including response to negative affective states, interpersonal conflict, and social pressures (Conrod & Stewart, 2005; Gregg *at al*., 2009).

Since these key dimensions of substance use are shared with the general population, the indications are that the psychological processes determining and maintaining use in people with psychosis may be similar to those found

for other substance users. Hence it would seem likely that the treatment approaches developed for non – psychosis individuals will be of benefit to people with psychosis although they may need to be adapted to take account of psychosis related issues. Patient reports indicate that situations and cues triggering use may be related if not directly to psychotic symptoms then to some of the negative consequences of the illness, particularly dysphoria and distress (Blanchard *et al.,* 2000). Some individuals with psychosis describe using substances to try and counteract the side effects of anti-psychotic medication; or as a preferred alternative to taking prescribed medications (Schneier & Siris, 1987). Coping motives (Mueser *et al.,* 1995), and poor problem solving abilities of this group (Carey & Carey, 1995) along with restrictive lifestyles and limitations for obtaining pleasure in other ways may then reinforce learned expectancies of the positive benefits of use.

These vulnerability factors present considerable challenges in developing treatment programmes, and the functional aspects of substance use in psychosis may in part explain why motivation for reduction of substance use in people with psychosis is usually low (Baker *et al*., 2006a; Barrowclough *et al.,* 2001; Martino *et al.,* 2002). Additionally, people with psychosis often suffer from low self esteem (Barrowclough *et al.,* 2003); thus, self efficacy may be low, which may further decrease motivation since people with psychosis may feel unable to implement changes. Moreover, psychosis is often associated with a range of complex problems and within this context the contributing role of substance use may not be salient to the service user. A related issue, and again in common with substance misusers who do not have a coexisting psychosis, is that the levels of substance use may not be excessive in terms of the person's peer group, making it less likely that the person will regard their substance use as problematic.

However, a number of psychosis-related issues increase treatment complexity. Engaging this group in treatment is often difficult and studies indicate that attrition rates are high, even for those agreeing to come into treatment (Drake *et al.,* 2004). Contributory factors may include a bias towards suspiciousness or paranoid interpretation of relationships arising from the psychotic symptoms and exacerbated by substance use; and a chaotic lifestyle along with concurrent problems making appointment scheduling and engaging in structured work more difficult. Finally, there are often medication issues that are not helpful to service user's mental state, either with patients not taking prescribed anti-psychotics (Martino *et al*., 2002) or the non-prescription substances rendering the prescribed medication less effective.

2.2 PSYCHOSIS AND COEXISTING SUBSTANCE MISUSE

2.2.1 Incidence and prevalence

Reviewing the literature on comorbidity between substance misuse and psychosis presents significant challenges not least because of issues surrounding the definition of the terms involved. Substance misuse is differently defined within the diagnostic classifications (DSM-III, DSM-III-R, DSM-IV and ICD-10) and operational definitions (generally scores above threshold in standardized measures of alcohol and drug misuse) employed in the contemporary literature. The literature also includes both studies relating to the comorbidity between schizophrenia (as variously defined) and substance misuse and a broader concept of psychosis that includes bipolar disorder. There is an important distinction between use of substances (which is almost ubiquitous for alcohol) on the one hand and abuse (or harmful use) and dependence on the other. In the literature by definition use of illicit substances is "abuse" and therefore problematic, although not necessarily representing harmful use or dependence on the substance. Epidemiological research in this area presents many challenges and the evidence it produces must be interpreted with a degree of caution.

Substance misuse is common in the general population: the ECA study, carried out in the USA, reported a life-time prevalence of substance misuse (including misuse of alcohol and drugs) of 16% (Regier *et al.*, 1990). In the ONS survey of psychiatric morbidity among adults living in private households in the UK, a quarter had a hazardous pattern of drinking during the year before interview, and overall, 13% of men and 8% of women aged 16–74 reported using illicit drugs in the preceeding 12 months (Singleton et al., 2000).

Schizophrenia has a wide range of comorbidities of which substance misuse is probably the commonest (Buckley *et al.*, 2009). The ECA study in the USA found high levels of comorbidity between schizophrenia and substance misuse (47% of people with schizophrenia had a lifetime substance misuse diagnosis: odds ratio 4.6) (Regier *et al.*, 1990). Analysis of a study from Sweden that focused on the relationship between schizophrenia and offending behaviour, which found that the relationship between violent crime and schizophrenia was almost completely attenuated by coexisting substance misuse, identified comorbidity in 24.5% of patients (Fazel *et al.*, 2009a).

Community studies of people with psychosis are challenging, but results from the US, the UK and Australia have been fairly consistent. In Australia Kavanagh and colleagues (2004) found lifetime rates of substance misuse or dependence of 39.8% (42.1% for people with schizophrenia), with alcohol misuse (27.6%) and cannabis misuse (22.8%) the commonest. US data from the

National Comorbidity Survey has provided odds ratios for coexisting substance misuse: non-affective psychosis and alcohol disorders 2.2; non-affective psychosis and drug disorders 2.7; bipolar 1 disorder and alcohol disorder 4.9; bipolar 1 and drug disorder 2.7 (Kessler *et al*., 1994). Earlier data showed that 47% of respondents with schizophrenia met diagnostic criteria for lifetime substance misuse (including alcohol) (OR 4.6) (Regier *et al*., 1990).

Studies of inpatients with mixed diagnoses identify high proportions of people being admitted to a psychiatric unit with current coexisting alcohol and substance misuse – from 30% in a US sample (Huntley *et al*., 1998) to 48% in a UK sample (Sinclair *et al*., 2008). Similar rates are to be found in studies of service users in contact with community mental health services. Weaver and colleagues (2003) found that 44% of service users of community mental health teams in inner urban areas, where 75% of service users had a diagnosis of psychosis, had comorbid problematical use of alcohol (25%) and/or drugs (31%). Alcohol and cannabis were the commonest substances to be abused and comorbidity was the norm. This was a multi-centre study and the authors noted higher levels of substance misuse in one centre (London) than the other centres (Nottingham and Sheffield). These are similar to findings from a study of the service users of a South London CMHT with "severe mental illness" where the one year prevalence of substance misuse was 36% (alcohol misuse 31.6%; drug misuse 15.8%) (Menezes *et al*., 1996).

Margoles and colleagues (2004) reported lower rates of current substance misuse amongst a cohort of service users with schizophrenia attending an outpatient programme in Canada (15%): however they provide a telling rank order of misused substances: alcohol (10.1%); cannabis (8.2%); cocaine (2.9%); benzodiazepines (1.5%); amphetamines, stimulants and heroin (0.5% each). Substance misuse was also less common in a community cohort of service users with schizophrenia from Scotland – with 16% of patients experiencing alcohol misuse and 7% substance misuse (McCreadie *et al*., 2002). The CATIE study, which looked at drug treatment for schizophrenia, identified 37% of participants as meeting diagnostic criteria for substance misuse (Swartz *et al*., 2006).

Studies of people with first-episode psychosis demonstrate marked differences in the prevalence of substance misuse between sites, which will plausibly reflect local patterns of substance misuse. In a German study, 23.7% of first-episode service users had a lifetime history of alcohol misuse and 14.2% substance misuse (Buhler *et al*., 2002). In contrast, 43% of a cohort of first-episode service users presenting to a service in Cambridge, UK, were diagnosed as suffering from DSM-IV alcohol misuse and 51% from cannabis misuse or dependence (Barnett *et al*., 2007). Although the percentages of individuals with coexisting disorders are markedly different, the odds ratios between patients and age-matched controls are not. Buhler and colleagues (2002) provided an odds ratio for substance misuse against age-matched

controls which for both alcohol and drugs was 2.0 – very similar to the data reported by Barnett and colleagues (2007) for all substance misuse in the previous month (OR 2.2); use of Class A drugs (OR 2.1) and use of amphetamines (OR 1.6). In addition, McCreadie *et al*. (2002) reported data that showed that people with schizophrenia compared to age and gender matched general population controls, reported in the past year significantly more alcohol dependence (OR 2.7) and problem use (OR 1.80), and drug dependence (OR 7.0) and problem use (OR 4.2).

Two recent meta-analytic studies have brought together the literature on the relationship between alcohol misuse and schizophrenia, and cannabis use and schizophrenia – cannabis being by far the commonest misused substance – based on all reliable sources (Koskinen, 2009a, 2009b). These provide estimates for prevalence of comorbidity and its correlating factors. The figures are somewhat lower in absolute terms than those identified above (current alcohol use disorder 9% (IQR 4.6–19.0) – lifetime 20.6%; current cannabis use disorder 16% (IQR 8.6–28.6) – lifetime 27.1%). Cannabis use was commoner amongst first-episode patients, younger people and males rather than females (Koskinen, 2009b). Nevertheless, the prevalence and pattern of substance misuse amongst people with a psychosis will vary between geographical locations in ways that are most likely to be explained by local patterns of substance misuse in the local population; and that will be influenced by local supply and availability.

2.2.2 Course and prognosis

In some cases, the course of coexisting substance use and psychosis may be determined by the way in which it has arisen. Four main routes can be identified; (1) a primary diagnosis of psychosis with subsequent development of substance misuse, (2) a primary diagnosis of substance misuse with the secondary development of psychosis as a manifestation of the substance misuse, (3) concurrent presence of substance misuse and psychosis, the former exacerbating the latter, and (4) psychotic disorder exacerbating or altering the course of substance misuse (Lehmann *et al.,* 1989). Only the second of these has a short course and good prognosis, at least in the short term, but it has been suggested that the third group, in which the substance misuse and psychosis co-occur, can be separated further into a better outcome group in which there is clearly no pre-existing psychosis, and a worse outcome group where psychosis clearly has been present in the longer term (Caton *et al.,* 2005, 2007). Several drugs of misuse can led to psychotic reactions that are unequivocally a direct consequence of the drug taken. In such cases the drug is usually taken in large or repeated doses and the psychotic reaction is manifest shortly afterwards, often after only a few hours.

Opiates do not precipitate psychosis, but LSD (lysergic acid diethylamide) has been known to do so for many years, and perhaps is the only drug that has

been incriminated in the development of long-term psychosis (Vardy & Kay, 1983). True cannabis psychosis, as opposed to schizophrenia-precipitated psychosis, is a toxic state with confusion and disorientation at times as well as clearly manifest delusions and hallucinations, but this only lasts for a few hours or days (Chopra & Smith, 1974; Ghodse, 1986). Cocaine can also lead to a psychotic state with persecutory delusions and hallucinations, including the tactile hallucinations of formication (the feeling of insects crawling beneath the skin) (cocaine bug)(Ghodse *et al.,* 1998). The tropical grass, khat, although normally just acting as a mild stimulant when chewed, may also lead to brief psychotic episodes after continuous use (Alem & Shibbe, 1997). All these psychotic episodes can be regarded as toxic effects of the relevant drug and, with the possible exception of LSD, resolve without any long-term consequences.

Unfortunately, the first and fourth of these pathways to psychosis and coexisting substance misuse tend to be associated with a long course and frequent relapse. There are a series of studies that demonstrate a significantly worse outcome in terms of hospital admission (Menezes *et al.,* 1996; Zammit *et al.,* 2008) and bed occupancy (Menezes *et al.,* 1996; Wade *et al.,* 2006), cost (McCrone *et al.,* 2000), ceasing antipsychotic drug treatment (Wade *et al.,* 2006; Zammit *et al.*, 2008), recurrence of depression and other disorders of mood (Turkington *et al.,* 2009), and the development of diabetes and early mortality (Jackson *et al.,* 2007).

2.2.3 Morbidity and mortality

People with a history of psychosis have substantially higher levels of morbidity and mortality than people without a history of psychosis. Poor physical health and premature mortality are also seen among people with drug and alcohol misuse problems. It would therefore be expected that people with psychosis plus coexisting substance misuse would have increased levels of morbidity and mortality and a large number of studies have found this to be the case.

People with severe mental illness and substance misuse are less likely to recover from a psychotic episode and more likely to experience relapse (Dixon, 1999). Most research has focussed on the role of cannabis which appears to increase the likelihood of psychotic relapse (Linszen *et al.,* 1994). Among those admitted to hospital, symptoms of psychosis are worse among people who use cannabis and the length of stay in hospital is greater (Isaac *et al*., 2005). Rates of relapse in psychosis are also higher among those who misuse other drugs, especially stimulants and cannabis.

The relationship between psychosis and coexisting substance misuse and social functioning is complex. There is evidence that, among people who develop psychosis, those with substance use have better social functioning

and greater numbers of social contacts. However coexisting substance misuse can lead to social problems including impaired relationships with family members and reduced self efficacy and these may be responsible for adverse social outcomes such as housing problems and homelessness (Salyers & Museser, 2001; Drake *et al*., 1991).

The relationship between psychosis and coexisting substance misuse and violence is more straightforward. Among people with psychosis those with coexisting substance misuse are more likely be involved in violent incidents (Cuffel *et al*., 1994). Results from a recent population-based study in Sweden suggest that the relationship between psychosis and violence may largely be the result of higher rates of substance misuse among people with severe mental illness (Fazel *et al*., 2009b). In this study people who had schizophrenia and substance misuse were over four times more likely to be convicted of a violent crime than members of the general public. In contrast, levels of violent crime in those with schizophrenia but no substance misuse were similar to those among the general public. This study, and findings from others, provides strong evidence that any increase in levels of violence among people with psychosis is largely the result of higher levels of substance misuse in this group.

People with psychosis and coexisting substance misuse often have poor physical health. In addition to higher rates of cardiovascular disease and other conditions that are found more frequently, those who use intravenous drugs are at far greater risk of hepatitis C, HIV and other blood borne viruses. Mortality rates are higher among people with psychosis, partly as a result of physical health problems, but also as a result of suicide. Among people with schizophrenia, coexisting substance misuse is an important risk factor for suicide with levels more than three times higher than would otherwise be expected (Hawton *et al*., 2005).

2.3 AETIOLOGY

There is no single explanation for the high level of association between psychosis and substance misuse. These two disorders are usually regarded as separate diagnostic entities and therefore satisfy the strict criteria for comorbid disorders (the presence of 'any distinct clinical entity that has existed or that may occur during the clinical course of a patient who has the index disease under study (Feinstein, 1970). Although neither substance misuse nor schizophrenia are uncommon, the frequency with which they present together is many times higher than would be expected by chance (see 2.2.1). It is far from clear why this is so, but several theories have been put forward for the association:

1. Substance misuse either precipitates the onset of, or is a direct cause of, psychosis.

2. Substance misuse is a common consequence of a psychotic disorder.

3. There is a common cause, or vulnerability, to both substance misuse and psychosis.

Substance misuse precipitates or causes psychosis

It has been known for over 40 years that substances like hallucinogens, stimulants and cannabis in high doses can be associated with or possibly cause psychotic states (Talbott & Teague, 1969). These drugs affect the dopaminergic and glutaminergic systems in the brain, which have both been associated with psychotic symptoms such as hallucinations and delusions. However, psychotic symptoms induced by substances generally tend to be short lived in comparison to psychosis in schizophrenia, and the presentation is slightly different, with predominating agitation and confusion in psychosis following drug use.

There is a growing body of evidence showing that some substances, particularly cannabis, alcohol to a lesser extent, but not opiates, can precipitate psychosis in vulnerable people, so that the onset appears to be earlier than in those who do not take cannabis (Barnes *et al.*, 2006). Based on findings from prospective cohorts, it has been suggested that cannabis is an independent risk factor for the development of psychosis (Andreasson *et al.*, 1987; Arsenault *et al.*, 2002; Van Os *et al.*, 2002), although the possibility that this association results from confounding factors or bias cannot be ruled out (Moore *et al.*, 2007). If cannabis caused schizophrenia in those who would not otherwise ever have the disease there should be an increasing prevalence of schizophrenia but this does not appear to be happening, and a very large number of cannabis consumers (1300–2700) would have to be prevented from taking cannabis to prevent just one case of schizophrenia (Hickman *et al.*, 2009). The evidence to date suggests that cannabis, and to a lesser extent alcohol misuse, brings forward the onset of a psychosis that would have been likely to develop anyway.

Psychosis causes substance misuse

The most common hypothesis underlying this explanation is that people with psychosis self-medicate with substances to alleviate distressing and dysphoric symptoms of their illness. Respondents in many studies report that they use substances in order to alleviate their symptoms or negative emotional states. At the same time, it is also well documented that many patients experience exacerbation of symptoms after substance use, and there is strong evidence that the presence of substance misuse provokes relapse and generally poorer outcomes than in those with psychosis alone (Wade *et al.*, 2006). Furthermore, if substances are used to alleviate symptoms, one would expect specific substances to be used to alleviate specific symptoms and substance misuse to increase with the severity of symptoms. Neither phenomenon has been demonstrated.

However, there is some evidence to suggest that substances may be used to alleviate a more general state of dysphoria. Individuals with psychosis are more vulnerable to experiencing low mood and anxiety, not only due to symptoms of their illness, but due to social factors surrounding their situation such as stigma, social exclusion, loss of functioning ability and financial difficulties. They are therefore more likely to use substances as short term relief from the consequent unpleasant feelings (Phillips & Johnson, 2001). There are further ways in which social factors may contribute to substance misuse in individuals with psychosis. This is a population in which educational and vocational failure, poverty, lack of social and recreational activity are common. Already at the margins of society, such people may feel more accepted and identify more with the drug-using population, and, because of their socio-economic position, may be housed in neighbourhoods where drug misuse is commonplace.

It is also possible that antipsychotic medication may itself lead to an increase in substance misuse. These medications work by blocking dopamine receptors in the brain, including dopaminergic reward systems in the brain. Individuals may attempt to counteract this effect by using substances.

A common cause for both disorders

It has been suggested that there may be a common genetic risk factor for both psychosis and substance misuse, particularly via the catechol-O-methyltransferase gene (COMT). This was initially suggested by Caspi and colleagues (2005), who postulated a gene-environment interaction as the cause of some episodes of psychosis. However, this has not been confirmed and on present evidence (Hosák, 2007; Zammit *et al*., 2007**)** the relationship is too non-specific to be causal. Several studies have shown that the presence of antisocial personality disorder independently increases the incidence of both psychosis and substance misuse. Furthermore, people with antisocial personality disorder also tend to develop both psychosis and substance misuse disorder at an earlier age. More evidence is required to establish the nature of this relationship and whether there is a causative element. Further research has proposed that abnormalities in the hippocampus and frontal lobes of the brain may cause symptoms of schizophrenia and these areas also provide positive reinforcement of drug reward and reduce inhibition of drug seeking behaviour.

A similar framework to the above three categories has been used to understand the specific group of individuals with psychosis and cannabis use. Hambrecht and Hafner (2000) describe a "vulnerability-stress-coping" model of schizophrenia and cannabis use which divides this group into three categories:

- The vulnerability group are those who use cannabis years before developing psychosis. The authors explain that cannabis may reduce their threshold of vulnerability to developing schizophrenia, either by a biological, psychological or social process, as well as reducing the clients coping resources.

- The stress group in whom the onset of cannabis misuse and psychosis occurs around the same time. This group comprises individuals already vulnerable to schizophrenia for genetic, pre- or perinatal influences and cannabis cause dopaminergic stress, precipitating the onset of disease.

- The coping group start using cannabis after the onset of psychosis and they self medicate with the drug. The theory is that they learn to counterbalance the unpleasant hypodopaminergic prefrontal state of schizophrenia with the dopaminergic effects of cannabis.

This model has also to accommodate the evidence of a dose-response relationship between cannabis and psychosis, as the data suggest that consumption of the strongest forms of cannabis, particularly 'skunk', are more prone to psychosis (Verdoux *et al.,* 2005; Murray *et al.,* 2007).

In summary, there is still some doubt as to whether cannabis precipitates the onset of psychosis in those who are vulnerable to the condition and the precise mechanism whereby such an association is generated still remains open to many explanations.

2.4 DIAGNOSIS

The term "dual diagnosis" is often used in both clinical practice and healthcare literature, and covers a wide spectrum of co-occurring psychiatric disorders and substance misuse with complex inter-relationships and interactions. The coexistence of psychosis with substance misuse is commonly referred to as 'dual diagnosis' when it is defined narrowly, but as this term is also used to describe other forms of comorbidity (for example, mental illness and intellectual disability), it is best avoided or, if used, the comorbidities described specifically.

People with psychosis and coexisting substance misuse may have multiple (rather than two as implied by 'dual' diagnoses both in relation to mental illness (for example, schizophrenia and anxiety, depression, personality disorder) and substance misuse (for example, alcohol dependence, and harmful use of another substance(s)).

In DSM-IV (American Psychiatric Association, 1994), a distinction is made between independent (primary psychiatric comorbidity) and substance-

induced (organic) psychiatric comorbidity and the category of expected symptoms of substance use or withdrawal (Abou-Saleh, 2004).

DSM-IV diagnostic criteria enable clinicians to distinguish 'primary', 'substance-induced' psychiatric disorders, and the 'expected effects' of intoxication and withdrawal (Samet *et al.*, 2004). A 'primary' disorder is diagnosed if 'the symptoms are not due to the direct physiological effects of a substance'. Before diagnosing a 'substance-induced'disorder, a primary classification must first be ruled out (see Table 2 and Table 3).

Table 2. Criteria for substance abuse (DSM-IV) and harmful use (ICD-10)

DSM-IV	ICD-10
1) A maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by one (or more) of the following occurring within a 12-month period	1) A pattern of psychoactive substance use that is causing damage to health; the damage may be to physical or mental health
2) Recurrent substance use resulting in a failure to fulfil major role obligations at work, school, or home	
3) Recurrent substance abuse in situations that are physically hazardous	
4) Recurrent substance-abuse-related legal problems	
5) Continued substance abuse despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance	
6) Has never met the criteria for substance dependence for this class of substance	
Note. DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th Edition ((American Psychiatric Association, 1994); ICD-10 = Tenth Revision of the International Classification of Diseases and Related Health Problems (World Health Organization, 1992).	

There are four conditions under which an episode that coexists with substance intoxication or withdrawal can be considered primary:

1. Symptoms 'are substantially in excess of what would be expected given the type or amount of the substance used or the duration of use'.
2. A history of non-substance-related episodes.
3. The onset of symptoms precedes the onset of the substance use.
4. The symptoms persist for a substantial period of time (i.e. at least a month) after the cessation of intoxication or acute withdrawal.

If neither 'primary' nor 'substance-induced' criteria are met, then the syndrome is considered to represent intoxication or withdrawal effects of alcohol or drugs

The ICD-10 Diagnostic Criteria for Research (WHO, 1992) provides specified criteria to differentiate primary disorders and disorders resulting from psychoactive substance use for psychotic disorders. As in DSM-IV, ICD-10 excludes psychotic episodes attributed to psychoactive substance use from a primary classification.

Table 3. Criteria for dependence syndrome in DSM-IV and ICD-10

DSM-IV	ICD-10
Diagnosis of dependence should be made if three (or more) of the following have been experienced or exhibited at any time in the same 12-month period	Diagnosis of dependence should be made if three or more of the following have been experienced or exhibited at some time during the last year
Tolerance defined by either need for markedly increased amount of substance to achieve intoxication or desired effect or markedly diminished effect with continued use of the same amount of the substance	A strong desire or sense of compulsion to take the substance
Withdrawal as evidenced by either of the following: the characteristic withdrawal syndrome for the substance **or** the same (or closely related) substance is taken to relieve or avoid withdrawal symptoms	Difficulties in controlling substance-taking behaviour in terms of its onset, termination, or levels of use
The substance is often taken in larger amounts over a longer period of time than was intended	Physiological withdrawal state when substance use has ceased or been reduced, as evidenced by either of the following: the characteristic withdrawal syndrome for the substance **or** use of the same (or closely related) substance with the intention of relieving or avoiding withdrawal symptoms
Persistent desire or repeated unsuccessful efforts to cut down or control substance use	Evidence of tolerance, such that increased doses of the psychoactive substance are required in order to achieve effects originally produced by lower doses
A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects	Progressive neglect of alternative pleasures or interests because of psychoactive substance use and increased amount of time necessary to obtain or take the substance or to recover from its effects
Important social, occupational, or recreational activities given up or reduced because of substance use	Persisting with substance use despite clear evidence of overly harmful consequences (physical or mental)
Continued substance use despite knowledge	

of having had a persistent or recurrent physical or psychological problem that was likely to have been caused or exacerbated by the substance	

Note. DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th Edition ((American Psychiatric Association, 1994); ICD-10 = Tenth Revision of the International Classification of Diseases and Related Health Problems (World Health Organization, 1992).

In ICD-10, psychotic disorders can be attributed to psychoactive substance use under three conditions:

1. The onset of symptoms must occur during or within 2-weeks of substance use.
2. The psychotic symptoms must persist for more than 48-hours.
3. The duration of the disorder must not exceed 6 months.

A psychotic disorder attributed to psychoactive substance use can be specified as predominantly depressive or predominantly manic. However, unlike DSM-IV, ICD-10 does not provide a separate psychoactive substance related category for any other type of psychiatric disorder. By definition, ICD-10 'organic mental disorder' excludes alcohol or other psychoactive substance-related disorders. ICD-10 organic mood disorder and organic delusional disorder cannot be used to diagnose episodes co-occurring with heavy psychoactive substance use. Thus, the DSM-IV concept of symptoms that are greater than the expected effects of intoxication and withdrawal is not included in ICD-10. The DSM-IV concept of 'primary' and 'substance-induced' syndromes, and the ICD-10 concept of 'psychotic disorders due to psychoactive substance use,' support the notion that a psychiatric disorder warranting clinical attention can co-occur with heavy substance use. However, these categories continue to present diagnostic challenges. Differential diagnosis of categories of depression, anxiety, and psychosis often hinges on interpretation of the term 'in excess' of the 'expected' effects of substance use, including service users with chronic substance use beginning at an early age. These expected effects are not clearly defined by either system and are thus left to clinical judgment (Samet *et al.*, 2004).

2.5 TREATMENT AND MANAGEMENT IN THE NHS

A major problem in the treatment and management of psychosis and coexisting substance misuse is that services fail to recognise and detect both problems, hence the need for a comprehensive assessment and package of care.

2.5.1 Pharmacological treatments

Treatments for psychosis

As part of a comprehensive package of care, a range of treatments can be offered for people with psychosis and coexisting substance misuse. Most commonly, antipsychotic drugs are used to manage the symptoms of psychosis. The updated NICE guidelines for the management of schizophrenia provide a helpful framework to guide the use of these drugs (NICE, 2009a). The range of treatments offered for people with psychosis and coexisting substance misuse may not be in line with treatments offered in other NICE guidelines however, as there is significant local variation in treatments offered for this population.

With the exception of clozapine, all available antipsychotic drugs appear to be equally effective in controlling symptoms; therefore the decision to use a particular agent may be determined by the need to avoid particular side effects or other complications of treatment such as drug interactions.

Where possible, the choice of which antipsychotic to use can be guided by the informed view of the service user. Outcomes from previous treatments may help refine the choice. Oral formulations are generally preferable, but where covert non-adherence is problematic, a long acting depot formulation may be advantageous.

Previous guidance has stated that high doses or combinations of antipsychotics are problematic (NICE, 2002; NICE, 2009a; Royal College of Psychiatrists, 2006), as for the majority of service users, there have been few advantages found over the licensed dose of the individual drugs. If treatment response is inadequate, despite the use of licensed doses of at least two antipsychotics over a fixed duration of time, one option which can be considered for further treatment is clozapine.

Treatments for addiction

Engagement with the service user is vital so that active treatment can then commence. There are a wide range of pharmacological treatments for substance problems which are almost invariably prescribed if service users are dependent on one or more substances. These are typically always delivered within the context of psychosocial interventions, and the overall framework of a primary care setting and/or the specialist multidisciplinary team. Medications are available for the treatment of withdrawal, for stabilization, for substitution and maintenance regimes, and for relapse prevention. For alcohol, medications include chlordiazepoxide and diazepam for withdrawal while for opiates, methadone and buprenorphine are prescribed. Relapse prevention is achieved by the use of naltrexone and acamprosate for alcohol dependence, and naltrexone for opiate dependence.

Additional treatment for vitamin deficiency syndromes, or physical illness, such as diabetes or hypertension may be required as many people with psychosis and coexisting substance misuse will have physical illnesses (associated with, or independent of, their psychosis and substance misuse) that will require the appropriate pharmacological interventions. Careful consideration of potential interactions between prescribed medication taken compliantly and non-compliantly, and illicit drugs and alcohol is needed. There are a range of NICE guidelines and health technology assessments which are related to the treatment of addiction and mental illness (see NICE website: www.nice.org).

2.5.2 Psychological treatments

Similarly, there are a range of psychological interventions that are beneficial in the treatment of psychosis and coexisting substance misuse. In general, a non-judgmental style of engagement is considered appropriate as a prelude to enhancing engagement. In the course of such a motivational approach, the individual's appreciation and attitude to their illness can be elicited and further, more intensive psychosocial interventions commenced. These may include supportive counselling, behavioural and cognitive techniques with an individual, group or family, as well as contingency management and skills training. There are a wealth of self-help mutual aid groups which provide sustained support.

Psychological treatment approaches

In both the UK and the US consensus agreements have been reached on key elements of treatment approaches for assisting clients with coexisting substance use and psychosis (Department of Health, 2002; Ziedonis *et al.*, 2005). It is proposed that effective treatment for people with coexisting substance use and psychosis usually requires an integrated treatment approach. Such "integrated care" combines elements of mental health and substance use approaches in one delivery system, was pioneered in New Hampshire, US, in the 80's, and has been well documented (Mueser & Drake, 2003). The advantages of an integrated approach include ensuring that both elements of the dual problems are given attention and that interaction between mental health and substance use problems described above can be formulated and addressed. There is further consensus agreement that interventions need to take account of clients' motivation to address or reduce their substance use and there has been particular emphasis on applying motivational interventions, and in particular motivational interviewing (MI) (Miller & Rollnick, 2002). Miller & Rollnick define MI as "a client-centred, directive method for enhancing intrinsic motivation to change by exploring and resolving ambivalence". Building intrinsic motivation for change involves the therapist selectively eliciting and reinforcing `Change Talk`, that is the client's own arguments and motivations for change. Essentially this

involves engaging the client, offering information and feedback from assessments where appropriate and exploring and resolving ambivalence in an affirming and non judgemental way.

The additional element that has been used most commonly in recent treatment approaches for psychosis and coexisting substance misuse is cognitive behaviour therapy (CBT). CBT is one of the most commonly used therapeutic orientations in the field of substance disorders (Stewart & Conrod, 2005). Moreover, in recent years CBT has been recognised to be effective in reducing the symptoms of psychosis (Pilling *et al.,* 2002). The CBT approach for individuals with psychosis and coexisting substance use problems is guided by individual formulations and by Marlatt and Gordon's (1985) model of relapse prevention. Components may include: identifying and increasing awareness of high risk situations/warning signs; developing new coping skills for handling such high risk situations/warning signs, with particular attention to psychosis symptom and mental health related problems highlighted in the formulation (for example, strategies for dealing with distressing voices or with depressed mood); coping with cravings and urges; making lifestyle changes so as to decrease need/urges for drugs and/or alcohol or to increase healthy activities/alternative options to substance use; normalising lapses in substance use and developing strategies and plans for acting in the event of lapse/relapse so that adverse consequences may be minimized; cognitive restructuring around alcohol and drug expectancies.

Environmental factors also play an important part in the maintenance and persistence of drug misuse in psychosis. Many individuals in this group have life styles in which drug use is part of the daily fabric of existence and they cannot contemplate changes that are associated with cessation of substances that are regarded as essential requirements. Major environmental change is often regarded as desirable but very difficult to achieve. Exhortations to stop or reduce drug intake usually fail but concentration on changing the social and personal environment may be of value (Tyrer *et al.,* in press).

2.5.3 Service level and other interventions

Three models of service provision have been identified for the care and treatment of people with psychosis and coexisting substance misuse: serial, parallel and integrated. In the serial model psychosis and substance misuse disorders are treated consecutively by different services. In the parallel both are treated at the same time but by different services (mental health address the psychosis, substance misuse the drug and/or alcohol issues). In the integrated model, psychosis and substance issues are addressed at the same time, in one setting, by one team. This is the model that was advocated by the Department of Health (2002) building on work conducted in New Hampshire (US) (for example, Mueser & Drake, 2003).

In the UK service configurations, treatment philosophies and funding streams militate against integrated provision. Mental health and substance misuse services are separate. They are often provided by different organisations and even when both are provided by the same NHS Trust they usually have different organisational and managerial structures. Furthermore staff within each service often lack the knowledge and skills for working with people from the 'other' group. There has been a tendency for people to be 'bounced' between services, each requiring the service user to deal with the 'other' problem first (serial model). In some areas service provision has been enhanced by mental health and substance misuse services working together, with the mental health services focusing on care and treatment of the person's psychosis, and the substance misuse service the substance misuse issues (parallel model). This is generally considered to be an improvement on the serial model but it still has weaknesses, for example: treatment in either system may be incomplete due to a lack of attention to the co-morbid condition; each system can continue to provide standard treatment and not modify it to accommodate the co-morbid condition; there is the potential for miscommunication and contradictory recommendations and it falls to the service user to integrate the two systems (Drake *et al.*, 1993, 1995). Moreover in the current UK drug treatment system the focus is on 'problem drug users' (heroin and crack cocaine) leaving gaps in provision for those using other substances.

The differing treatment philosophies for mental health and substance misuse services can also make it difficult for people to receive coherent treatment. If necessary mental health services can compel people to receive treatment under the provision of the Mental Health Act. Some services are also proactive in engaging and retaining vulnerable service users with psychosis in treatment (in particular assertive outreach teams). Substance misuse services usually expect some level of readiness to change and the service user to attend a team base to receive treatment. Many people with psychosis and coexisting substance misuse do not see their substance use as problematic so are unlikely to access substance misuse services. If mental health services do not view the treatment of substance misuse as an integral part of mental health treatment, this aspect of the service users' needs is likely to be overlooked.

Given the high prevalence of substance misuse in people with psychosis, the fact that many do not see their substance use as a problem, and the negative impact substance use can have on mental health, it is inevitable that many service users in both community and inpatient mental health services will have psychosis and coexisting substance misuse. Yet evidence suggests that substance misuse often goes undetected in people with mental illness (for example, Noordsky *et al.*, 2003; Barnby, 2003). Even when it has been identified, the lack of competence in working with substance misuse issues in general mental health settings, and the sometimes negative attitudes of staff

to this group, may result in substance misuse needs not being addressed at all or, if they are, interventions not being delivered in line with best practice.

In some areas dual diagnosis practitioners/teams have been developed to support the delivery of more integrated care. Models vary in different localities but typically their work includes delivering staff training and supervision, and engaging in joint work with mental health colleagues.

People with psychosis and coexisting substance misuse often have multiple needs related to their psychosis and substance use, for example, physical health problems, financial difficulties, housing problems, difficulty in caring for their children and being involved in illegal activity. As a consequence they are likely to have contact with a variety of services, only some of which will be provided by the NHS. Not all the public services necessary for this desperate group of people will therefore be covered by this guidance.

2.5.4 Forensic/justice system

Assessments for substance misuse history or problems in secure hospital units or prisons usually rely on good history taking rather than the use of research tools. Bloye and colleagues (2003) recommend a multi assessment approach to enable a more comprehensive assessment of substance use disorders within the forensic population.

In recently established personality disorder services funded by the Dangerous and Severe Personality Disorder (DSPD) programme the Violence Risk Scale (VRS; Wong, *et al.,* 2006, 2007) is routinely being used. This is designed to integrate the assessment of risk, need, responsivity and treatment change in a single tool. It assesses the client's risk of violence, identifies treatment targets linked to violence, and assesses the client's readiness for change and their post-treatment improvement on the treatment targets. The tool uses the stages of change model and integrates the presence of substance misuse histories and problems in the risk assessment and the formulation of treatment targets. It is important to note that some of the service users in these DSPD units have a history of comorbid psychosis and personality disorder, as well as substance misuse.

The treatment of prisoners identified as having mental illness with or without coexisting substance misuse problems takes place in NHS or other hospitals once a prisoner has been identified as having a psychiatric disorder and been diverted. Treatment with medication can be given in prison for those prisoners who can give informed consent. For those patients who are remitted back to prison following a period of treatment in hospital, there are difficulties in providing specific substance misuse treatment programmes because the mental health inreach teams are not adequately resourced (Sainsbury's Mental Health Centre, 2008).

Most hospital secure units have treatment programmes for substance misuse based on cognitive behavioural principles (Derry, 2008). Most of these programmes are offered on a group basis and incorporate elements of motivation to change work, understanding links between substance misuse, mental health and offending, relapse prevention and skills development. These treatment programmes are not specific to forensic settings and are similar to interventions offered for generic service users in inpatient and community services. There are no good controlled evaluations with large sample sizes of these treatments, however in a recent retrospective evaluation of a inpatient drug and alcohol treatment programme, Derry and Batson (2008) found some evidence to suggest that those who had completed a treatment programmes were less likely to use drugs or alcohol after discharge. In addition, those who had completed a treatment programme spent a greater proportion of time in the community compared with those who did not complete the programme. Suggestions for future research included more objective assessments of drug use, the need to control for treatment adherence, motivation to change, and incorporating a level of personal insight of mental health problems in studies using large sample sizes.

Within secure units, there is a common practice of considering discharge into the community after service users with a history of drug or alcohol misuse have remained abstinent whilst using significant amounts of unescorted community leave. This practice can lead to extended detention long after abnormal mental states have been treated. Despite the significant impact this may have on length of stay, there is no good research evaluation of the practice and the impact on substance misuse post discharge has not been described. The effect of banning service users from using illicit substances or alcohol as part of the conditions of discharge has also not been evaluated.

2.6 ECONOMIC COSTS

The available epidemiological data from within the UK suggests that a significant number of individuals with psychosis, have coexisting substance misuse (Menezes *et al.*, 1996; Sinclair *et al.*, 2008; Weaver *et al.*, 2003). However, evidence on the extent to which these individuals incur extra costs in terms of health care or lost productivity is very limited both within and outside the UK.

To date, only one UK study compared the service use and costs of individuals with a diagnosis of psychosis and coexisting substance misuse with those with a diagnosis of psychosis alone (McCrone *et al.*, 2000). Service use data, including core psychiatric services, general health care, social, education, employment and legal services, were collected over a six month period using the Client Service Receipt Interview (CSRI). Mean core health care costs

(including psychiatric inpatient episodes, contacts with mental health staff and emergency and day care attendances) were significantly higher in service users with psychosis and coexisting substance misuse (£2,626 vs. £1,060; p=0.038). However, the difference in total mean costs (including supported accommodation, social and legal services) did not reach statistical significance between the two groups (£3,913 vs. £2,903; p=0.271).

A US-based study examined the costs of psychiatric treatment for seriously mentally ill people (diagnosed with schizophrenia; major affective disorder or other psychoses) with coexisting substance misuse in comparison with mentally ill people without substance misuse (Dickey & Azeni, 1996). Paid claims for psychiatric care, including hospital admissions, residential treatment, medical treatments and case management were collected for adult Medicaid beneficiaries in the state of Massachusetts. In this study, total annual mean costs (1992) were substantially higher in service users with coexisting substance misuse ($22,917 vs. $13,930). Importantly, these cost differences were largely explained by greater inpatient psychiatric treatment whilst substance misuse treatment accounted for a small proportion of the extra cost.

Another US study compared the long-term patterns of service use and costs in service users with a dual diagnosis of psychiatric and substance misuse disorders, with those without a dual diagnosis. Of service users with psychosis and coexisting substance misuse, 46–48% had a primary diagnosis of schizophrenia or bipolar disorder (Hoff & Rosenbeck, 1998). Data was analysed from longitudinal services use files that recorded all hospital and outpatient services provided by the Department of Veterans Affairs mental health system from 1990 to 1996. Costs were calculated for five types of health care: inpatient and outpatient psychiatric services, substance misuse and medical/surgical care. Separate analyses were conducted for patients who were categorised either as inpatient or outpatient at the time of case identification. Overall, there was no significant difference in mean annual costs between those with psychiatric and combined substance misuse when compared to those with a psychiatric diagnosis alone in the hospital sample. However, in the outpatient sample, patients with coexisting psychiatric and substance misuse disorders incurred substantially higher mean annual costs between 1990 and 1996. Most of these extra costs incurred by people with psychosis and coexisting substance misuse in the outpatient sample were due to inpatient psychiatric and substance misuse care.

To date, no single UK study has attempted to estimate the combined total health care and societal costs of treating people with a diagnosis of psychosis and coexisting substance misuse. In 2007, the total health service costs of severe mental illness (Schizophrenia; Bipolar Disorder and related conditions) were estimated at £3.8 billion whilst the total costs of lost employment were estimated at £5.4 billion (McCrone *et al.*, 2008). Based on UK-based estimates

of prevalence rates of between 36–44% for people with comorbid substance misuse (Menezes *et al.,* 1996; Weaver *et al.,* 2003), it is possible that the total annual health service and productivity costs of psychosis and substance misuse could be between £3.3 and £4 billion. However, further empirical research is required to assess the true economic burden of severe mental illness and substance misuse in the UK.

3 METHOD USED TO DEVELOP THIS GUIDELINE

3.1 OVERVIEW

The development of this guideline drew upon methods outlined by NICE (further information is available in *The Guidelines Manual* [NICE, 2009b]). A team of health professionals, lay representatives and technical experts known as the Guideline Development Group (GDG), with support from the NCCMH staff, undertook the development of a patient centred, evidence-based guideline. There are six basic steps in the process of developing a guideline:

1. Define the scope, which sets the parameters of the guideline and provides a focus and steer for the development work.
2. Define review questions considered important for practitioners and service users.
3. Develop criteria for evidence searching and search for evidence.
4. Design validated protocols for systematic review and apply to evidence recovered by search.
5. Synthesise and (meta-) analyse data retrieved, guided by the review questions, and produce GRADE evidence profiles and summaries.
6. Answer review questions with evidence-based recommendations for clinical practice.

The clinical practice recommendations made by the GDG are therefore derived from the most up-to-date and robust evidence base for the clinical and cost effectiveness of the treatments and services used in the treatment and management of psychosis and coexisting substance misuse. In addition, to ensure a service user and carer focus, the concerns of service users and carers regarding health and social care have been highlighted and addressed by recommendations agreed by the whole GDG.

3.2 THE SCOPE

Guideline topics are selected by the Department of Health and the Welsh Assembly Government, which identify the main areas to be covered by the guideline in a specific remit (see *The Guidelines Manual* for further information). The NCCMH developed a scope for the guideline based on the remit. The purpose of the scope is to:

- provide an overview of what the guideline will include and exclude
- identify the key aspects of care that must be included

- set the boundaries of the development work and provide a clear framework to enable work to stay within the priorities agreed by NICE and the NCC and the remit from the Department of Health/Welsh Assembly Government
- inform the development of the review questions and search strategy
- inform professionals and the public about expected content of the guideline
- keep the guideline to a reasonable size to ensure that its development can be carried out within the allocated period.

The draft scope was subject to consultation with registered stakeholders over a 4-week period. During the consultation period, the scope was posted on the NICE website (www.nice.org.uk). Comments were invited from stakeholder organisations and the Guideline Review Panel (GRP). Further information about the GRP can also be found on the NICE website. The NCCMH and NICE reviewed the scope in light of comments received, and the revised scope was signed off by the GRP.

3.3 THE GUIDELINE DEVELOPMENT GROUP

The GDG consisted of: professionals in psychiatry, clinical psychology, nursing, social work, and general practice; academic experts in psychiatry and psychology; a service user, a representative from a service user organisation and a carer. The guideline development process was supported by staff from the NCCMH, who undertook the clinical and health economics literature searches, reviewed and presented the evidence to the GDG, managed the process, and contributed to drafting the guideline.

3.3.1 Guideline Development Group meetings

Ten GDG meetings were held between May 2009 and October 2010. During each day-long GDG meeting, in a plenary session, review questions and clinical and economic evidence were reviewed and assessed, and recommendations formulated. At each meeting, all GDG members declared any potential conflicts of interest, and service user and carer concerns were routinely discussed as part of a standing agenda.

3.3.2 Service users and carers

Individuals with direct experience of services gave an integral service-user focus to the GDG and the guideline. The GDG included a service user and a representative of a service user group. They contributed as full GDG members to writing the review questions, helping to ensure that the evidence addressed their views and preferences, highlighting sensitive issues and terminology relevant to the guideline, and bringing service-user research to

the attention of the GDG. In drafting the guideline, they contributed to writing the guideline's introduction and identified recommendations from the service user and carer perspective.

3.3.3 National and international experts

National and international experts in the area under review were identified through the literature search and through the experience of the GDG members. These experts were contacted to recommend unpublished or soon-to-be published studies in order to ensure up-to-date evidence was included in the development of the guideline. They informed the group about completed trials at the pre-publication stage, systematic reviews in the process of being published, studies relating to the cost effectiveness of treatment and trial data if the GDG could be provided with full access to the complete trial report. Appendix 5 lists researchers who were contacted.

3.4 REVIEW QUESTIONS

Review (clinical) questions were used to guide the identification and interrogation of the evidence base relevant to the topic of the guideline. Before the first GDG meeting, an analytic framework (see Appendix 6) was prepared by NCCMH staff based on the scope and an overview of existing guidelines, and discussed with the guideline Chair. The framework was used to provide a structure from which the review questions were drafted. Both the analytic framework and the draft review questions were then discussed by the GDG at the first few meetings and amended as necessary. Where appropriate, the framework and questions were refined once the evidence had been searched and, where necessary, sub-questions were generated. Questions submitted by stakeholders were also discussed by the GDG and the rationale for not including any questions was recorded in the minutes. The final list of review questions can be found in Appendix 6.

For questions about interventions, the PICO (Patient, Intervention, Comparison and Outcome) framework was used (see Table 4).

Table 4: Features of a well-formulated question on effectiveness intervention – the PICO guide

Patients/ population	Which patients or population of patients are we interested in? How can they be best described? Are there subgroups that need to be considered?
Intervention	Which intervention, treatment or approach should be used?
Comparison	What is/are the main alternative/s to compare with the intervention?
Outcome	What is really important for the patient? Which outcomes should be considered: intermediate or short-term measures; mortality; morbidity and treatment complications; rates of relapse; late morbidity and readmission; return to work, physical and social functioning and other measures such as quality of life; general health status; costs?

In some situations, the prognosis of a particular condition is of fundamental importance, over and above its general significance in relation to specific interventions. Areas where this is particularly likely to occur relate to assessment of risk, for example in terms of behaviour modification or screening and early intervention. In addition, review questions related to issues of service delivery are occasionally specified in the remit from the Department of Health/Welsh Assembly Government. In these cases, appropriate review questions were developed to be clear and concise.

To help facilitate the literature review, a note was made of the best study design type to answer each question. There are four main types of review question of relevance to NICE guidelines. These are listed in Table 5. For each type of question, the best primary study design varies, where 'best' is interpreted as 'least likely to give misleading answers to the question'.

However, in all cases, a well-conducted systematic review (of the appropriate type of study) is likely to always yield a better answer than a single study.

Deciding on the best design type to answer a specific review question does not mean that studies of different design types addressing the same question were discarded.

Table 5: Best study design to answer each type of question

Type of question	Best primary study design
Effectiveness or other impact of an intervention	Randomised controlled trial (RCT); other studies that may be considered in the absence of RCTs are the following: internally/externally controlled before and after trial, interrupted time-series
Accuracy of information (e.g. risk factor, test, prediction rule)	Comparing the information against a valid gold standard in a randomised trial or inception cohort study
Rates (of disease, patient experience, rare side effects)	Prospecitve cohort, registry, cross-sectional study
Costs	Naturalistic prospective cost study

3.5 SYSTEMATIC CLINICAL LITERATURE REVIEW

The aim of the clinical literature review was to systematically identify and synthesise relevant evidence from the literature in order to answer the specific review questions developed by the GDG. Thus, clinical practice recommendations are evidence-based, where possible, and, if evidence is not available, informal consensus methods are used (see Section 3.5.6) and the need for future research is specified.

3.5.1 Methodology

A stepwise, hierarchical approach was taken to locating and presenting evidence to the GDG. The NCCMH developed this process based on methods set out by NICE (*The Guidelines Manual* [NICE, 2009b]), and after considering recommendations from a range of other sources. These included:

- Clinical Policy and Practice Program of the New South Wales Department of Health (Australia)
- BMJ *Clinical Evidence*
- Grading of Recommendations: Assessment, Development and Evaluation (GRADE) Working Group
- New Zealand Guidelines Group
- NHS Centre for Reviews and Dissemination
- Oxford Centre for Evidence-Based Medicine
- Oxford Systematic Review Development Programme

- Scottish Intercollegiate Guidelines Network (SIGN)
- The Cochrane Collaboration
- United States Agency for Healthcare Research and Quality.

3.5.2 The review process

Scoping searches

A broad preliminary search of the literature was undertaken in January 2009 to obtain an overview of the issues likely to be covered by the scope, and to help define key areas. Searches were restricted to clinical guidelines, health technology assessment reports, key systematic reviews and randomised controlled trials, and conducted in the following databases and websites:

- BMJ Clinical Evidence
- Canadian Medical Association (CMA) Infobase [Canadian guidelines]
- Clinical Policy and Practice Program of the New South Wales Department of Health (Australia)
- Clinical Practice Guidelines [Australian Guidelines]
- Cochrane Central Register of Controlled Trials (CENTRAL)
- Cochrane Database of Abstracts of Reviews of Effects (DARE)
- Cochrane Database of Systematic Reviews (CDSR)
- EMBASE
- Guidelines International Network (G-I-N)
- Health Evidence Bulletin Wales
- Health Management Information Consortium [HMIC]
- Health Technology Assessment (HTA) database (technology assessments)
- MEDLINE / MEDLINE in Process
- National Health and Medical Research Council (NHMRC)
- National Library for Health (NLH) Guidelines Finder

- New Zealand Guidelines Group
- NHS Centre for Reviews and Dissemination (CRD)
- OMNI Medical Search
- Scottish Intercollegiate Guidelines Network (SIGN)
- Turning Research Into Practice (TRIP)
- United States Agency for Healthcare Research and Quality (AHRQ)
- Websites of NICE and the National Institute for Health Research (NIHR) HTA Programme for guidelines and HTAs in development.

Existing NICE guidelines were updated where necessary. Other relevant guidelines were assessed for quality using the AGREE instrument (AGREE Collaboration, 2003). The evidence base underlying high-quality existing guidelines was utilised and updated as appropriate. Further information about this process can be found in The Guidelines Manual (NICE, 2009b).

Systematic literature searches

After the scope was finalised, a systematic search strategy was developed to locate all the relevant evidence. The balance between sensitivity (the power to identify all studies on a particular topic) and specificity (the ability to exclude irrelevant studies from the results) was carefully considered, and a decision made to develop highly sensitive strategies to identify as complete a set as possible of clinically relevant studies.

Searches were conducted in the following databases:

- CINAHL
- EMBASE
- MEDLINE / MEDLINE In-Process
- PsycINFO
- Cochrane Central Register of Controlled Trials (CENTRAL)

The search strategies were initially developed for Medline before being translated for use in other databases/interfaces. Strategies were built up through a number of trial searches, and discussions of the results of the searches with the review team and GDG to ensure that all possible relevant

search terms were covered. In order to assure comprehensive coverage, search terms for psychosis with substance misuse were kept purposely broad to help counter dissimilarities in database indexing practices and thesaurus terms, and imprecise reporting of study populations by authors in the titles and abstracts of records. Search terms for substance misuse were limited to the main drugs associated with the term at the advice of the GDG. The search terms for each Medline search are set out in full in Appendix 7.

Reference Manager

Citations from each search were downloaded into Reference Manager (a software product for managing references and formatting bibliographies) and duplicates removed. Records were then screened against the inclusion criteria of the reviews before being quality appraised (see below). The unfiltered search results were saved and retained for future potential re-analysis to help keep the process both replicable and transparent.

Search filters

To aid retrieval of relevant and sound studies, filters were used to limit a number of searches to randomised controlled trials, observational studies and qualitative research. The randomised controlled trial filter is an adaptation of a filter designed by the Centre for Reviews and Dissemination (CRD) and the Health Information Research Unit of McMaster University, Ontario. The observational studies filter and qualitative research filter were developed in-house. Each filter comprises index terms relating to the study type(s) and associated text words for the methodological description of the design(s).

Date and language restrictions

Systematic database searches were initially conducted in July 2009 up to the most recent searchable date. Search updates were generated on a 6-monthly basis, with the final re-runs carried out in May 2010 ahead of the guideline consultation. After this point, studies were only included if they were judged to be exceptional by the GDG (for example, if the evidence was likely to change a recommendation).

Although no language restrictions were applied at the searching stage, foreign language papers were not requested or reviewed, unless they were of particular importance to a clinical question. Date restrictions were applied for searches for qualitative research for the period from 1995 onwards, and for updates of published reviews. No date restrictions were imposed for the remainder of the searches.

Other search methods

Other search methods involved: 1) scanning the reference lists of all eligible publications (systematic reviews, stakeholder evidence and included studies) for more published reports and citations of unpublished research; 2) sending

lists of studies meeting the inclusion criteria to subject experts (identified through searches and the GDG) and asking them to check the lists for completeness, and to provide information of any published or unpublished research for consideration (See Appendix 5); 3) checking the tables of contents of key journals for studies that might have been missed by the database and reference list searches; 4) tracking key papers in the Science Citation Index (prospectively) over time for further useful references.

Full details of the Medline search strategies/filters used for the systematic review of clinical evidence are provided in Appendix 7.

Study selection and quality assessment

All primary-level studies included after the first scan of citations were acquired in full and re-evaluated for eligibility at the time they were being entered into the study information database. More specific eligibility criteria were developed for each review question and are described in the relevant clinical evidence chapters. Eligible systematic reviews and primary-level studies were critically appraised for methodological quality (see Appendix 10 for methodology checklists). The eligibility of each study was confirmed by at least one member of the appropriate topic group.

For some review questions, it was necessary to prioritise the evidence with respect to the UK context (that is, external validity). To make this process explicit, the topic groups took into account the following factors when assessing the evidence:

- participant factors (for example, gender, age and ethnicity)
- provider factors (for example, model fidelity, the conditions under which the intervention was performed and the availability of experienced staff to undertake the procedure)
- cultural factors (for example, differences in standard care and differences in the welfare system).

It was the responsibility of each topic group to decide which prioritisation factors were relevant to each review question in light of the UK context and then decide how they should modify their recommendations.

Unpublished evidence

The GDG used a number of criteria when deciding whether or not to accept unpublished data. First, the evidence must have been accompanied by a trial report containing sufficient detail to properly assess the quality of the data. Second, the evidence must have been submitted with the understanding that data from the study and a summary of the study's characteristics would be

published in the full guideline. Therefore, the GDG did not accept evidence submitted as commercial in confidence. However, the GDG recognised that unpublished evidence submitted by investigators might later be retracted by those investigators if the inclusion of such data would jeopardise publication of their research.

3.5.3 Data extraction

Study characteristics and outcome data were extracted from all eligible studies, which met the minimum quality criteria, using Review Manager 5 (The Cochrane Collaboration, 2008).

In most circumstances, for a given outcome (continuous and dichotomous), where more than 50% of the number randomised to any group were lost to follow up, the data were excluded from the analysis (except for the outcome 'leaving the study early', in which case, the denominator was the number randomised). Where possible, dichotomous efficacy outcomes were calculated on an intention-to-treat basis (that is, a 'once-randomised-always-analyse' basis). Where there was good evidence that those participants who ceased to engage in the study were likely to have an unfavourable outcome, early withdrawals were included in both the numerator and denominator. Adverse effects were entered into Review Manager as reported by the study authors because it is usually not possible to determine whether early withdrawals had an unfavourable outcome. Where there was limited data for a particular review, the 50% rule was not applied. In these circumstances the evidence was downgraded due to the risk of bias.

Consultation with another reviewer or members of the GDG was used to overcome difficulties with coding. Data from studies included in existing systematic reviews were extracted independently by one reviewer and cross-checked with the existing data set. Where possible, two independent reviewers extracted data from new studies. Where double data extraction was not possible, data extracted by one reviewer was checked by the second reviewer. Disagreements were resolved through discussion. Where consensus could not be reached, a third reviewer or GDG members resolved the disagreement. Masked assessment (that is, blind to the journal from which the article comes, the authors, the institution and the magnitude of the effect) was not used since it is unclear that doing so reduces bias (Jadad *et al.*, 1996; Berlin, 2001).

3.5.4 Synthesising the evidence

Meta-analysis

Where possible, meta-analysis based on a random-effects model (DerSimonian & Laird, 1986) was used to synthesise the evidence using Review Manager. If necessary, reanalyses of the data or sub-analyses were

used to answer review questions not addressed in the original studies or reviews.

Dichotomous outcomes were analysed as relative risks (RR) with the associated 95% CI (for an example, see Figure 1). A relative risk (also called a risk ratio) is the ratio of the treatment event rate to the control event rate. An RR of 1 indicates no difference between treatment and control. In Figure 1, the overall RR of 0.73 indicates that the event rate (that is, non-remission rate) associated with intervention A is about three quarters of that with the control intervention or, in other words, the relative risk reduction is 27%.

The CI shows with 95% certainty the range within which the true treatment effect should lie and can be used to determine statistical significance. If the CI does not cross the 'line of no effect', the effect is statistically significant.

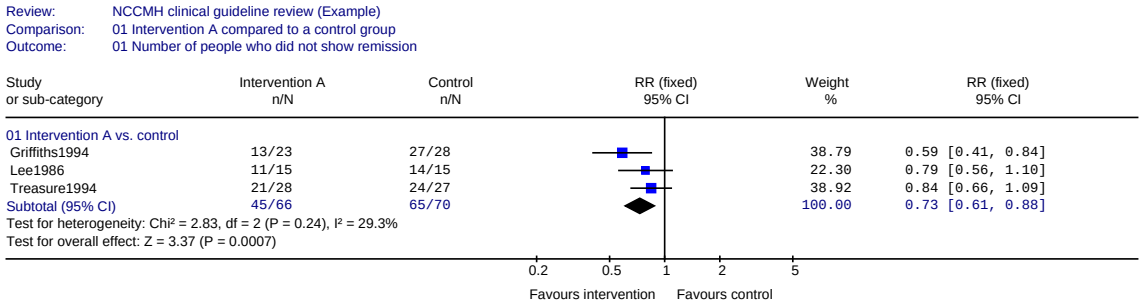

Figure 1: Example of a forest plot displaying dichotomous data

Continuous outcomes were analysed using the mean difference (MD), or standardised mean difference (SMD) when different measures were used in different studies to estimate the same underlying effect (for an example, see Figure 2). If reported by study authors, intention-to-treat data, using a valid method for imputation of missing data, were preferred over data only from people who completed the study.

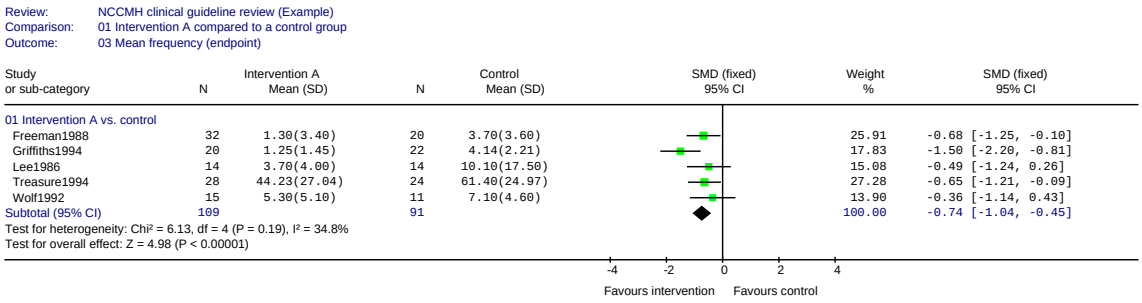

Figure 2: Example of a forest plot displaying continuous data

Heterogeneity

To check for consistency of effects among studies, both the I^2 statistic and the chi-squared test of heterogeneity, as well as a visual inspection of the forest plots were used. The I^2 statistic describes the proportion of total variation in study estimates that is due to heterogeneity (Higgins & Thompson, 2002). The I^2 statistic was interpreted in the following way:

- 50%: notable heterogeneity
- 30 to 50%: moderate heterogeneity
- 30%: mild heterogeneity.

Two factors were used to make a judgement about importance of the observed value of I^2: a) the magnitude and direction of effects, and b) the strength of evidence for heterogeneity (for example, P value from the chi-squared test, or a confidence interval for I^2). Where heterogeneity was judged to be important, an attempt was made to explain the variation by conducting sub-analyses to examine potential moderators.

Publication bias

To explore the possibility that the results entered into each meta-analysis suffered from publication bias, data from included studies were entered, where there was sufficient data, into a funnel plot. Asymmetry of the plot was taken to indicate possible publication bias and investigated further.

Where necessary, an estimate of the proportion of eligible data that were missing (because some studies did not include all relevant outcomes) was calculated for each analysis.

3.5.5 Presenting the data to the GDG

Study characteristics tables and, where appropriate, forest plots generated with Review Manager were presented to the GDG.

Where meta-analysis was not appropriate and/or possible, the reported results from each primary-level study were included in the study characteristics table (and where appropriate, in a narrative review).

Evidence profile tables

A GRADE[1] evidence profile was used to summarise both the quality of the evidence and the results of the evidence synthesis (seeTable 6

[1] For further information about GRADE, see www.gradeworkinggroup.org

for an example of an evidence profile). The GRADE approach is based on a sequential assessment of the quality of evidence, followed by judgment about the balance between desirable and undesirable effects, and subsequent decision about the strength of a recommendation.

For each outcome, quality may be reduced depending on the following factors:

- **study design** (randomised trial, observational study, or any other evidence)
- **limitations** (based on the quality of individual studies)
- **inconsistency** (see section 3.5.4 for how consistency was assessed)
- **indirectness** (that is, how closely the outcome measures, interventions and participants match those of interest)
- **imprecision** (based on the confidence interval around the effect size).

For observational studies, the quality may be increased if there is a large effect, plausible confounding would have changed the effect, or there is evidence of a dose-response gradient (details would be provided under the other considerations column). Each evidence profile also included a summary of the findings: number of patients included in each group, an estimate of the magnitude of the effect, and the overall quality of the evidence for each outcome.

Table 6: Example of GRADE evidence profile

Quality assessment							Summary of findings				
							No. of patients		Effect		Quality
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other	Intervention	Control	Relative (95% CI)	Absolute	
Outcome 1											
6	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1,2]	none	8/191	7/150	RR 0.94 (0.39 to 2.23)	0 fewer per 100 (from 3 fewer to 6 more)	⊕⊕OO LOW
Outcome 2											
3	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	120/600	220/450	RR 0.39 (0.23 to 0.65)	30 fewer per 100 (from 17 fewer to 38 fewer)	⊕⊕⊕⊕ HIGH
Outcome 3											
3	randomised trials	no serious limitations	serious inconsistency[3]	no serious indirectness	very serious[1,2]	none	83	81	-	MD -3.51 (-11.51 to 4.49)	⊕OOO VERY LOW
Outcome 4											
3	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	serious[1]	none	88	93	-	SMD -0.26 (-0.50 to -0.03)	⊕⊕⊕O MODERATE
Outcome 5											
4	randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious[1,2]	none	109	114	-	SMD -0.13 (-0.6 to 0.34)	⊕⊕OO LOW

[1] Optimal information size not met.
[2] The CI includes both 1) no effect and 2) appreciable benefit or appreciable harm.
[3] Considerable heterogeneity.

3.5.6 Method used to answer a review question in the absence of appropriately designed, high-quality research

In the absence of appropriately designed, high-quality research, or where the GDG were of the opinion (on the basis of previous searches or their knowledge of the literature) that there were unlikely to be such evidence, an informal consensus process was adopted. This process focused on those questions that the GDG considered a priority.

Informal consensus

The starting point for the process of informal consensus was that a member of the topic group identified, with help from the systematic reviewer, a narrative review that most directly addressed the review question. Where this was not possible, a brief review of the recent literature was initiated.

This existing narrative review or new review was used as a basis for beginning an iterative process to identify lower levels of evidence relevant to the review question and to lead to written statements for the guideline. The process involved a number of steps:

1. A description of what is known about the issues concerning the clinical question was written by one of the topic group members.
2. Evidence from the existing review or new review was then presented in narrative form to the GDG and further comments were sought about the evidence and its perceived relevance to the review question.
3. Based on the feedback from the GDG, additional information was sought and added to the information collected. This may include studies that did not directly address the review question but were thought to contain relevant data.
4. If, during the course of preparing the report, a significant body of primary-level studies (of appropriate design to answer the question) were identified, a full systematic review was done.
5. At this time, subject possibly to further reviews of the evidence, a series of statements that directly addressed the review question were developed.
6. Following this, on occasions and as deemed appropriate by the development group, the report was then sent to appointed experts outside of the GDG for peer review and comment. The information from this process was then fed back to the GDG for further discussion of the statements.
7. Recommendations were then developed and could also be sent for further external peer review [amend as appropriate].
8. After this final stage of comment, the statements and recommendations were again reviewed and agreed upon by the GDG.

3.5.7 Forming the clinical summaries and recommendations

Once the GRADE evidence profiles relating to a particular review question were completed, summary evidence tables were developed (these tables are presented in the evidence chapters). Finally, the systematic reviewer in conjunction with the topic group lead produced a clinical evidence summary.

Once the GRADE profiles and clinical summaries were finalised and agreed by the GDG, the associated recommendations were drafted. In making recommendations, the GDG took into account the trade-off between the benefits and downsides of treatment as well as other important factors, such as economic considerations, values of the development group and society, the requirements to prevent discrimination and to promote equality[2], and the group's awareness of practical issues (Eccles *et al.,* 1998; NICE, 2009b).

Finally, to show clearly how the GDG moved from the evidence to the recommendations, each chapter has a section called 'from evidence to recommendations'. Underpinning this section is the concept of the 'strength' of a recommendation (Schunemann *et al*., 2003). This takes into account the quality of the evidence but is conceptually different. Some recommendations are 'strong' in that the GDG believes that the vast majority of healthcare professionals and patients would choose a particular intervention if they considered the evidence in the same way that the GDG has. This is generally the case if the benefits clearly outweigh the harms for most people and the intervention is likely to be cost effective. However, there is often a closer balance between benefits and harms, and some patients would not choose an intervention whereas others would. This may happen, for example, if some patients are particularly averse to some side effect and others are not. In these circumstances the recommendation is generally weaker, although it may be possible to make stronger recommendations about specific groups of patients. The strength of each recommendation is reflected in the wording of the recommendation, rather than by using labels or symbols.

Where the GDG identified areas in which there are uncertainties or where robust evidence was lacking, they developed research recommendations. Those that were identified as 'high-priority' were included in the NICE version of the guideline, and in Appendix 12.

3.6 HEALTH ECONOMICS METHODS

The role of the health economist was to contribute to the guideline's development by providing evidence on the cost-effectiveness of interventions covered in this guideline. This was achieved by:

- Systematic literature review of existing economic evidence

[2] See NICE's equality scheme: www.nice.org.uk/aboutnice/howwework/NICEEqualityScheme.jsp

- Economic modelling, where economic evidence was lacking or was considered inadequate to inform decisions.

Systematic reviews of economic literature were conducted in all areas covered in the guideline. Economic modelling was planned in areas with potentially major resource implications, where the current extent of uncertainty over cost-effectiveness was significant and economic analysis was expected to reduce this uncertainty, in accordance with the NICE guidelines manual (NICE, 2009b). Prioritisation of areas for economic modelling was a joint decision between the Health Economist and the GDG. The rationale for prioritising clinical questions for economic modelling was set out in an economic plan agreed between NICE, the GDG, the Health Economist and other members of the technical team. The economic plan is presented in Appendix 19. The following clinical questions were selected as key issues that could potentially be addressed by further economic modelling:

- Cost-effectiveness of integrated models of care (usually involving the model of assertive community treatment) in people with psychosis and coexisting substance misuse

- Cost-effectiveness of specific psychological/psychosocial interventions (delivered within an integrated service model) in people with psychosis and coexisting substance misuse including:

    - individual interventions
    - group interventions
    - family interventions
    - contingency management
    - residential treatment (with/without recovery model)
    - combined interventions.

In addition, literature on the health-related quality of life of people with psychosis and coexisting substance misuse was systematically searched to identify studies reporting appropriate health state utility scores that could be used in potential cost-utility analysis.

The rest of this section describes the methods adopted in the systematic literature review of health economics studies. Methods employed in any economic modelling undertaken are described in the respective sections of the guideline.

3.6.1 Search strategy for economic evidence

Scoping searches

A broad preliminary search of the literature was undertaken in January 2009 to obtain an overview of the issues likely to be covered by the scope, and help define key areas. Searches were restricted to economic studies and health technology assessment reports, and conducted in the following databases:

- EMBASE
- MEDLINE / MEDLINE In-Process
- Health Technology Assessment (HTA) database (technology assessments)
- NHS Economic Evaluation Database (NHS EED).

* Any relevant economic evidence arising from the clinical scoping searches was also made available to the health economist during the same period.

Systematic literature searches

After the scope was finalised, a systematic search strategy was developed to locate all the relevant evidence. The balance between sensitivity (the power to identify all studies on a particular topic) and specificity (the ability to exclude irrelevant studies from the results) was carefully considered, and a decision made to utilise a broad approach to searching to maximise retrieval of evidence to all parts of the guideline. Searches were restricted to economic studies and health technology assessment reports, and conducted in the following databases:

- CINAHL
- EconLit
- EMBASE
- MEDLINE / MEDLINE In-Process
- PsycINFO
- Health Technology Assessment (HTA) database (technology assessments)
- NHS Economic Evaluation Database (NHS EED).

* Any relevant economic evidence arising from the clinical searches was also made available to the health economist during the same period.

The search strategies were initially developed for Medline before being translated for use in other databases/interfaces. Strategies were built up through a number of trial searches, and discussions of the results of the searches with the review team and GDG to ensure that all possible relevant search terms were covered. In order to assure comprehensive coverage, search terms for psychosis with substance misuse were kept purposely broad to help counter dissimilarities in database indexing practices and thesaurus terms, and imprecise reporting of study populations by authors in the titles and abstracts of records. Search terms for substance misuse were limited to the main drugs associated with the term at the advice of the GDG.

For standard mainstream bibliographic databases (CINAHL, EMBASE, MEDLINE and PsycINFO) search terms for psychosis and substance misuse were combined with a search filter for health economic studies. For searches generated in topic-specific databases (EconLit, HTA, NHS EED) search terms for psychosis and substance abuse were used without a filter. The sensitivity of this approach was aimed at minimising the risk of overlooking relevant publications, due to potential weaknesses resulting from more focused search strategies. The Medline search terms are set out in full in Appendix 9.

Reference Manager

Citations from each search were downloaded into Reference Manager (a software product for managing references and formatting bibliographies) and duplicates removed. Records were then screened against the inclusion criteria of the reviews before being quality appraised. The unfiltered search results were saved and retained for future potential re-analysis to help keep the process both replicable and transparent.

Search filters

The search filter for health economics is an adaptation of a filter designed by Centre for Reviews and Dissemination (CRD). The filter comprises a combination of controlled vocabulary and free-text retrieval methods.

Date and language restrictions

Systematic database searches were initially conducted in July 2009 up to the most recent searchable date. Search updates were generated on a 6-monthly basis, with the final re-runs carried out in May 2010 ahead of the guideline consultation. After this point, studies were included only if they were judged by the GDG to be exceptional (for example, the evidence was likely to change a recommendation).

Although no language restrictions were applied at the searching stage, foreign language papers were not requested or reviewed, unless they were of particular importance to an area under review. All the searches were restricted to research published from 1994 onwards in order to obtain data relevant to current healthcare settings and costs.

Other search methods

Other search methods involved scanning the reference lists of all eligible publications (systematic reviews, stakeholder evidence and included studies from the economic and clinical reviews) to identify further studies for consideration.

Full details of the Medline search strategies/filter used for the systematic review of health economic evidence are provided in Appendix 9.

3.6.2 Inclusion criteria for economic studies

The following inclusion criteria were applied to select studies identified by the economic searches for further consideration:

- No restriction was placed on language or publication status of the papers.
- Studies published from 1996 onwards were included. This date restriction was imposed in order to obtain data relevant to current healthcare settings and costs.
- Only studies from Organisation for Economic Co-operation and Development countries were included, as the aim of the review was to identify economic information transferable to the UK context.
- Selection criteria based on types of clinical conditions and patients as well as interventions assessed were identical to the clinical literature review.
- Studies were included provided that sufficient details regarding methods and results were available to enable the methodological quality of the study to be assessed, and provided that the study's data and results were extractable.
- Full economic evaluations that compared two or more relevant options and considered both costs and consequences (that is, cost–consequence analysis, cost-effectiveness analysis, cost–utility analysis or cost–benefit analysis), as well as costing analyses that compared only costs between two or more interventions, were included in the review.
- Economic studies were included if they used clinical effectiveness data from an RCT, a cohort study, or a systematic review and meta-analysis of clinical studies. Studies that had a mirror-image design were excluded from the review.
- Studies were included only if the examined interventions were clearly described. This involved the dosage and route of

administration and the duration of treatment in the case of pharmacological therapies; and the types of health professionals involved as well as the frequency and duration of treatment in the case of psychological interventions. Evaluations in which medications were treated as a class were excluded from further consideration.

3.6.3 Applicability and quality criteria for economic studies

All economic papers eligible for inclusion were appraised for their applicability and quality using the methodology checklist for economic evaluations recommended by NICE (NICE, 2009b), which is shown in Appendix 18 of this guideline. The methodology checklist for economic evaluations was also applied to the economic models developed specifically for this guideline. All studies that fully or partially met the applicability and quality criteria described in the methodology checklist were considered during the guideline development process, along with the results of the economic modelling conducted specifically for this guideline. The completed methodology checklists for all economic evaluations considered in the guideline are provided in Appendix 18.

3.6.4 Presentation of economic evidence

The economic evidence considered in the guideline is provided in the respective evidence chapters, following presentation of the relevant clinical evidence. The references to included studies as well as the evidence tables with the characteristics and results of economic studies included in the review, are provided in Appendix 17. Methods and results of any economic modelling undertaken alongside the guideline development process are presented in the relevant evidence chapters. Characteristics and results of all economic studies considered during the guideline development process are summarised in economic evidence profiles accompanying respective GRADE clinical evidence profiles in Appendix 17.

3.6.5 Results of the systematic search of economic literature

The titles of all studies identified by the systematic search of the literature were screened for their relevance to the topic (i.e. consideration of health economics issues and health-related quality of life in people with psychosis and coexisting substance misuse). References that were clearly not relevant were excluded first. The abstracts of all potentially relevant publications (82 references) were then assessed against the inclusion criteria for economic evaluations by the health economist. Full texts of the studies potentially meeting the inclusion criteria (including those for which eligibility was not clear from the abstract) were obtained. Studies that did not meet the inclusion criteria, were duplicates, secondary publications of one study, or had been updated in more recent publications were subsequently excluded. Overall, six economic evaluations were identified as being eligible for inclusion and were

appraised for their applicability and quality using the methodology checklist for economic evaluations. The findings of these studies were considered when formulating the guideline recommendations.

3.7 STAKEHOLDER CONTRIBUTIONS

Professionals, service users, and companies have contributed to and commented on the guideline at key stages in its development. Stakeholders for this guideline include:

- service user/carer stakeholders: the national service user and carer organisations that represent people whose care is described in this guideline
- professional stakeholders: the national organisations that represent health care professionals who are providing services to service users
- commercial stakeholders: the companies that manufacture medicines used in the treatment of psychosis and coexisting substance misuse
- Primary Care Trusts
- Department of Health and Welsh Assembly Government.

Stakeholders have been involved in the guideline's development at the following points:

- commenting on the initial scope of the guideline and attending a briefing meeting held by NICE
- contributing possible review questions and lists of evidence to the GDG
- commenting on the draft of the guideline
- highlighting factual errors in the pre-publication check.

3.8 VALIDATION OF THE GUIDELINE

Registered stakeholders had an opportunity to comment on the draft guideline, which was posted on the NICE website during the consultation period. Following the consultation, all comments from stakeholders and others were responded to, and the guideline updated as appropriate. The GRP also reviewed the guideline and checked that stakeholders' comments had been addressed.

Following the consultation period, the GDG finalised the recommendations and the NCCMH produced the final documents. These were then submitted to NICE for the pre-publication check where stakeholders are given the opportunity to highlight factual errors. Any errors are corrected by the NCCMH, then the guideline is formally approved by NICE and issued as guidance to the NHS in England and Wales.

4 EXPERIENCE OF CARE

4.1 INTRODUCTION

This chapter provides an overview of the experience of people with psychosis and coexisting substance misuse, and the experience of their families/carers. The first two sections present first-hand personal accounts written by people with psychosis and coexisting substance misuse, and their families and carers. This section provides some experiences of being diagnosed, accessing services, receiving treatment and caring for someone with psychosis and coexisting substance misuse. It should be noted that these accounts of the experience of people with psychosis and coexisting substance misuse are illustrative. This next section is a qualitative analysis of transcripts of people with psychosis and coexisting substance misuse from seven online websites and a review of the qualitative literature of the experience of people with psychosis and coexisting substance misuse. Following this is a summary of the themes emerging from the personal accounts, the online transcripts and the literature review which provides a basis for the recommendations in the final section of this chapter.

4.2 PERSONAL ACCOUNTS

4.2.1 Introduction

The writers of the personal accounts from people with psychosis and coexisting substance misuse were contacted through representatives on the GDG and through various agencies that had access to people with psychosis and coexisting substance misuse. The people who were approached to write the accounts were asked to consider a number of questions when composing their narratives. These included:

- When did you first seek help for your psychosis and coexisting substance misuse and whom did you contact? Please describe this first contact.
- What helped or did not help you gain access to services? Did a friend or family member help you gain access to these services?
- Do you think that any life experiences led to the onset of the problem? If so, please describe if you feel able to do so.
- In what ways has psychosis and substance misuse affected your everyday life (such as education, employment and making relationships) and the lives of those close to you?
- What possible treatments were discussed with you?

- What treatment(s) did you receive? Please describe any drug treatment and/or psychological therapy.
- Was the treatment(s) helpful? Please describe what worked for you and what didn't work for you.
- How would you describe your relationship with your practitioner(s) (for example, your GP, psychologist or other)
- Did you use any other approaches to help your psychosis and substance misuse in addition to those provided by NHS services, for example private treatment? If so please describe what was helpful and not helpful.
- Do you have any language support needs, including needing help with reading or speaking English? If so, did this have an impact on your understanding of the psychosis and substance misuse or on receiving treatment?
- Did you attend a support group and was this helpful? Did family and friends close to you or people in your community help and support you?
- How has the nature of the problem changed over time?
- How do you feel now?
- If your psychosis and coexisting substance misuse has improved, do you use any strategies to help you to stay well? If so, please describe these strategies.

Each author signed a consent form allowing the account to be reproduced in this guideline. Two personal accounts from people (both male) with psychosis and coexisting substance misuse were received in total. They offer different perspectives of their experience of illness and treatment, but despite the differences some common themes do emerge. Each person speaks of the isolation he felt at various stages of his illness and treatment and the challenges in finding employment after a long period out of work. In terms of treatment, the service users valued staff who were 'empathic', 'helpful', 'motivated' and 'keen', and understood mental health and substance misuse issues. Lack of planned care, gaps in their treatment and treatment being stopped abruptly (especially for the person being released from prison) were deemed unhelpful.

The service users identified a range of helpful and unhelpful treatments. Person A found that in prison CBT, group work, and creative and educative activities were helpful and, out of prison, his local alcohol service provided support better suited to him than Alcoholics Anonymous; self-help (delivered

in prison) was deemed to be unhelpful because the service user felt it was not properly explained to him. Person B was very positive about the treatment he received from his dual diagnosis practitioner which included writing a drug diary and a feelings notebook, and identifying and managing the risks and triggers.

Both men identified that support from assertive outreach teams and other workers to enable them to re-enter society and find employment (either paid or voluntary) was vital in building self-esteem and restoring confidence.

4.2.2 Personal account A

I was born in 1961 in London, and my parents came from Jamaica. I had a very successful career until 2003. At this time I would go days without sleep, having detailed nightmares, hallucinations and I wouldn't go out in the day time or answer my phone. As time went on my mood swings got worse and I had no control over them. I thought the world was against me and everyone wanted to do me harm.

I was drinking a lot and socially smoking weed. I lost my job, wife, family and home in 2004 and ended up in prison. In 2005, I was diagnosed with severe depression and personality disorder with agoraphobic, paranoid and psychotic features by a clinical psychiatrist.

In August 2005, I was arrested and remanded in custody. My lawyer had a good understanding of the prison system and talked me though the booking in process and what was best to say and do. At my booking in, I advised them of my mental health and all of my issues. I was interviewed the next day and I was told that the services I needed would be provided as soon as possible.

The doctor gave me four sleeping tablets (one per night) to keep me stable until I could see the CMHT. The staff that I met in the first 48 hours showed empathy and concern about my well-being, but the service provided didn't always live up to their promises. The action plan was good, and the full-time staff were helpful, motivated and keen, but the specialist team of a clinical psychologist, psychiatrist and counsellor didn't keep their appointments and this led to me having relapses in my mental health. On a couple of occasions, the staff forgot to open my cell door or were late in doing so and I missed my appointment. To address this problem, I was given stronger medication or larger doses. I never missed taking my medication because if you did you were escorted to the nurse and your mouth was checked after.

I tool olanzapine and diazepam daily, and if I was having a bad night I might get temazepam to help me sleep. I was offered lots of meaningful actives to do during the day, such as focus groups, arts and crafts, games and education. This did keep my mind occupied and help me feel better. I was also taught CBT and I started self-help treatment but it didn't entirely work

because it wasn't fully explained to me; however it did show me what I could do to help myself and how to handle my relationship with my family and friends, and my problems with drink and drugs .

One of the good things that came out of my prison stay was when we got the governor to change the day centre from being located in a mental health unit to a multicultural mental health day centre. This was my first taste that service user involvement works.

I was released on bail straight from court without any medication and ordered to stay with my family until my court date. My GP was in another town so to get treatment I had to lie and say I still lived there. The paperwork took a while to get to my GP and I was not given any antidepressants, only a referral to the CMHT and sleeping tablets.

On my return to court, the judge gave me probation as long as I followed the guidelines without fail. These included taking my medication and attending anger management, literacy and numeracy classes, in addition to attending all sessions recommended by the CMHT and my probation officer. The CMHT and my probation officer put together an action plan for me without my input. Six specialists were assigned to me. Again, the plan was good, but the services I needed were not available to start at the same time. At first this was not a problem but as time went by my mental health and drinking issues were not dealt with—the services looked at what they could provide and not what I needed. The clinical psychiatrist I saw was very good at her job, knowledgeable and showed lots of empathy and people skills. However, after seven sessions she advised me she was going on honeymoon for 6 weeks and my treatment would be put on hold until her return. Again, as I was making progress, my treatment was put on hold. I had to rely on the CBT I had been taught in prison, and on drink and pills to get though any crisis I may come across.

I had to use drink to get though the hard days; by the time, I got help for my drinking it had become a bigger problem. Alcoholics Anonymous did not work for me because it was not holistic and I was always very depressed after AA meetings. I was asked to leave because I wasn't engaging correctly.

My brother paid for me to have four private sessions with a clinical psychiatrist, but he was only willing to help develop my CBT and coping skills. I was referred to Mind for counselling by my GP but failed a risk assessment (my local Mind only had female staff, small interview rooms and no security). At this stage of my recovery journey, I got housed by an organisation for the homeless, and accessed their services. I was given a keyworker, who was very knowledgeable and showed a lot of empathy and a willingness to help me address all my issues and support me to reach my aims and goals. We drew up an action plan together with targets and rewards

for hitting them. We met with my GP and had my medication reduced and sorted out some meaningful actives for me to do. I had interviews with the mental health and substance abuse team at the homeless organisation and was put on their self-help programme; the service provided was excellent and empowered me to aim higher and believe I could recover. However, just as I was feeling the benefit and moving on leaps and bounds the service came to an end due to lack of money.

I attended my local alcohol counselling services for my drinking problems; this service suited me better than AA and sorted out my drinking. The counsellor asked me keep a diary, account for my drinking and look for the triggers that caused it.

Then we worked with my keyworker and clinical psychologist to find ways for me to cope.

The service provided by the CMHT came to an end because my probation was up and not because I was ready to rejoin the community or because I had fully recovered. Ultimately I found the service patchy; it was full of great intentions but they failed to deliver what they had promised.

I also attended a programme that helped me to prepare for the moving back into the community. The homeless organisation's resettlement officer helped me sort out my housing benefit, got my gas and electricity turned on, and hired a removal van, a bed, and cooker for me. She also gave me advice on paying my bills. The system would not give me a community or crisis loan because I was not on Jobseeker's Allowance or Income Support. I only had the bare minimum in my flat. This did not help my mental health or empower me to keep on going.

Now it was time to look for full-time work. Trying to get employment with a criminal record and mental health issues was near on impossible. I had a lot of interviews but even more excuses why people were not employing me. I was appointed a floating support worker to help me with my move on from supported housing back into the community. His caseload is large and the length of time his support will be available to me relies on funding; however, the service provided was good because he worked in an holistic way, always returned my calls within 2 hours, kept all of our appointments, treated me as a person at all times, and provided a professional, honest and reliable service.

All the services helped me in different ways but because the services provided didn't all start at the same time the process was slow and put a lot of pressure on me and my ability to cope. This led to relapse, binge drinking, and withdrawal from the community. I think my recovery journey is going well but I know my hardest tests are still to come.

4.2.3 Personal account B

I am 33 years old and have a history of paranoid schizophrenia and substance misuse.

In 1994 after I finished my A levels I started to hang out with the 'trendy guys' who lived in my town and spent many hours smoking cannabis spliffs (rolled tobacco cigarettes laced with cannabis resin) and bongs (water pipes which would cool down the cannabis smoke). In the following autumn, I went to university. I thought that students should spend most of their time getting stoned and living the life of a 1960s hippie. That was the plan and that's what I did. I not only continued to smoke cannabis but also became experienced with other substances: speed (amphetamine), ecstasy, LSD and magic mushrooms.

Initially, much of my university work was of a high quality. However, as the year progressed and I became more involved with drugs, I began to feel more self -conscious about my existence. I would feel uncomfortable walking to the campus and developed a dread about my course. A feeling of helplessness and a sort of isolation developed and my academic work began to suffer. I changed courses the following year—I didn't feel so anxious but I was smoking one to two ounces of cannabis resin a week – and taking a variety of other drugs.

I finished my degree (with a third class) and found an office job. However, I found the job tedious and in 1999 decided to do a master's degree. I continued to use drugs every weekend (ecstasy and cannabis and occasionally cocaine and magic mushrooms). The amount of cannabis I was using led to lung problems.

During the new year celebrations of 2000, I decided to take about 10 ecstasy tablets in about 45 minutes**.** That new year's party may have changed my whole life. During the next term my tutor was concerned that I had very dull eyes. I thought nothing of it. Then as the year went on I started thinking that a DJ was talking to me through the radio and the walls contained mini-microphones and cameras. My body felt more and more intense, and not in a good way. My behaviour became more angry and irrational. I accused people of ridiculous things (for example, I thought that my flatmate had broken into my room and removed a bit of my printer to stop it working). Nevertheless I continued to see my old university friends every weekend and my pattern of drug use continued.

I felt uncertain as to what was happening to me. My feelings became more and more intense. My friends kept telling me that instead of the smiles which I had initially met them with, I looked angry and depressed. My mood deteriorated and I became more isolated. I thought that I should get some

help, so I went to the university student services. I got to the front door, felt very self-conscious and walked away.

Despite my continued drug use and deteriorating mental health I completed my masters degree. I found an interesting job but as I walked through the factory and heard Radio 4 talking about me, that was it. How would I be able to do a job well if I thought that a national radio station was talking about me?

I wanted to get treatment but had heard (incorrectly) from a GP that the only way a doctor in the UK would treat me was if I posed a serious risk to myself or others and that would mean putting me on a section of the Mental Health Act.

My parents became worried about my mental health and accessed a neurologist in the United States (which is where we come from). We were concerned that I might have more than just mental health problems and there could be some underlying physiological problem. After seeing the neurologist I was referred on to a psychologist. By the end of it they had identified that I was psychotic and referred me to a psychiatrist who gave me drugs to stop those symptoms.

I returned to England and lived with my parents for about 10 months. My GP referred me to the local psychiatrist and I accessed a community psychiatric nurse (CPN) and mental health support worker. My CPN was very helpful and the support worker helped me get out of the house and do things like play badminton and have lunch at the seaside. I was in some form of recovery at this stage but still felt that I was functioning at a much lower level than I was capable of. I would describe my mental state as 'gormless'. I did not feel very sharp in my thinking. Looking back I'm not sure if this was a reflection of my mental state, the medication I was being prescribed, or a combination of both.

Eventually, I acquired some voluntary work, still feeling gormless, but better able to get things done. This was negotiated through an employment company for disadvantaged people who were able to persuade them that I would be an asset to the team. I was assigned a support worker, which worked out well. I was able to get out of the house and be a part of society at some level, which was better than staying in, watching telly and eating junk food on my own. Indeed, I was even provided with a reference, which helped me get work subsequently.

I decide to move to London and find paid work. I knew a guy who was renting out cheap rooms and I managed to get a job. Initially I was socially isolated but eventually my old friends from my university days contacted me. I was glad to have friends again but we were soon back smoking skunk—

about 20 to 30 joints over the weekend. I began to feel 'gormless' again and my behaviour became weird. I could no longer undertake simple tasks at work and this along with other things, such as being slightly smelly, being late to work, spending more time smoking cigarettes than doing the job, led to my dismissal.

Still getting stoned on skunk, I went from one job to the next, each being progressively worse than the former. I just wasn't able to do my job properly. Nevertheless, I continued to smoke weed. Soon, I got to the stage where I would sit at home all day, in my smelly unwashed clothes, eat biscuits for dinner and defer bill payments.

I needed to change my life. My main social contact was a middle-aged artist who would convince me that I should give him money to buy cannabis. Most of my friends had moved away and I did not get on very well with my family. I could not maintain any kind of employment and I had little or no money. I had lost control of my own life and the people who did have control of it were mostly dealers and 'friends'. I began to get scared just walking down my road. Every year I would watch my life go no further than the previous one. And most of all, I was very vulnerable and truly out of control. I wanted my life back. Desperately.

Throughout this period I saw my psychiatrist every 6 months and I would tell him how smoking weed ruined my chances of having a real life. After 2 or so years, he put me in touch with a dual diagnosis practitioner. For me, it was very important to stop using cannabis. I would probably not have been able do this on my own but by accessing the dual diagnosis service it was much easier.

I met with my dual diagnosis practitioner every 3 weeks. One area of work I did with her was identify the triggers that stimulated me to smoke spliffs. The triggers would range from spending time with the artist or my old friends to watching films alone on television (strong spliffs and funny movies go together like strawberries and cream for me). We identified that the artist posed a real danger to my recovery. Every time I stopped smoking weed I would go and see him and the habit would restart.

We also identified that the addiction to cannabis is strong and psychological, that my brain craves that 'lovely' THC (tetrahydrocannabinol - the chemical in cannabis which makes the feeling of using so pleasant) and that it would manipulate me to score by changing my thinking patterns. I would think, 'the artist has a book that I want back'; that is the THC addiction sending me to the artist to smoke that crafty spliff. A tool to combat this is to 'know your enemy'.

My dual diagnosis worker helped me to identify and overcome the triggers and armed me with tools to fight the cravings. One tool I use is to picture traffic lights. If I want a joint I look at a picture of a traffic light on my wall.. The traffic lights act like a reminder, or a prompt, challenging me to think about whether I really want this and/or how smoking cannabis affected me in the past. Red is the first warning. This alerts me to ask myself: Do I really want to get stoned? Remember your history. Do I want to be that smelly, unkempt, poor drug user again? Remember that it was hard enough coming off the weed and would be just as easy to get back onto the 'addiction wagon'. Yellow is 'well why not, life is pretty bad', like getting sacked from my job and my family disowning me. Yellow is considering the threat that using cannabis would have and the consequences which would come from smoking it. In this case, I may think that there is little else to lose and having a joint wouldn't hurt. This may be the case, but considering my history of cannabis addiction the threat would be significant. And the bottom line would be 'do I really want to go through that all over again?' This would refer me back to the red traffic light. Then there is the green light, which is 'nuclear holocaust'. Everything that could possibly go wrong has and is getting worse. In that case, going out, scoring a draw and getting obliterated might not be so bad. I haven't got to green yet!

For about 9 months, the THC addiction was still strong. I felt that by writing stories and feelings in a notebook, I could manage these very intense feelings, which included blaming everyone except me for the failures of my life (such as 'I was poor because my brother introduced me to smoking cannabis'). In real life, I could not blame anyone for my substance misuse. Often feelings of social isolation would come out in my notebook. Using cannabis had masked these feelings and would make me less lonely. Harbouring unpleasant thoughts and not being able to express them, especially during rehabilitation, could lead to mental anguish. By writing these thoughts on paper and being able to look back on them, I felt emotionally liberated. I could release the mental tension and feel better. It was like popping a blister.

I also found that smoking tobacco in 'rollies' was a great substitute for smoking joints, in terms of the process of preparing the rollies, the act of smoking, and doing something with my hands. Over time I reduced the rollies and, recognising the harms tobacco itself can cause, I now smoke one herbal cigarette a day.

I was spending long periods at home watching television and thinking about how much I would like to smoke a joint and feeling lonely and socially isolated, so my dual diagnosis practitioner and I identified that activity was the best way forward. I looked at every possible opportunity to get involved with as much as possible. I volunteered to do things that interested me. I considered working as a support worker with people with learning disabilities or in the office of my housing association, or befriending an old

lady. None of these activities came to much, but just the 'doing' helped to stop that lonely feeling which comes with social isolation. I felt that involvement with society would be the best way ahead in terms of recovery from substance misuse. It would also help me to regain my confidence by proving that I can do jobs successfully even though I have a history of mental health issues.

The changes I have made to my drug use and lifestyle have brought about wider benefits too. I have re-established good relationships with my family again and recently spent about a month with them. I am training to be a drugs worker through work I am involved in at a local substance misuse service. I have also taken part in delivering dual diagnosis training and been a service user link worker to an acute psychiatric ward.

I also run a social club, which is proving to be very successful. It provides hot meals to people who may have issues with substance misuse, mental health and/or learning disabilities. We aim to re integrate people with these issues back into society at their own pace, by providing opportunities such as fun classes, which may inspire them into mainstream education, or making new social networks or joining the management committee. From my own perspective, running this club has enabled me to regain a huge amount of confidence and I am keen to start these clubs more widely. My vision is for each club, under the umbrella of the wider social club organisation, to be run independently –they would choose their own activities and food (within reason). By providing this responsibility, it may help others in their recovery journeys.

My status has improved, as well as my mental health. Since I have accessed the dual diagnosis service my medication dose has dropped by 25%. Two years ago, I was frightened of a 30-minute bus ride to visit my friends but I am not scared on buses any longer or even walking the streets of London at night. I have made new friends and these friendships are blossoming. I have found a new kind of respect for myself and am truly looking forward to a future without limits.

From my point of view, de-stigmatising treatment for mental health is vital to promoting early diagnosis and recovery. An approachable practitioner who empathises and understands mental health and substance misuse issues is also vital. It's important for professionals to plan treatment in conjunction with the service user, taking account of the person's readiness to change. Mental health professionals need to maintain an open mind and sense of optimism about what the service user can achieve, rather than limiting options through low expectations. This can help to develop the person's self-esteem. Reducing or stopping substance misuse altogether may reduce medication doses. When a person is in recovery, social support from the NHS, family members and other social systems, is crucial. When addressing substance misuse, tools such as a drug diary, feelings notebook, and traffic

lights, can be useful to enable the person to identify and manage the risks/triggers. Distraction techniques (such as volunteering and fun classes) can help them to start rebuilding their lives and returning to work is important because that is part of the person's identity. Ideally the work should be something that is suited to the person's skills and/or wishes. It's important for the service user to feel a sense of achievement and involving others can help them develop important connections and make new friends.

4.3 PERSONAL ACCOUNTS—CARERS

4.3.1 Introduction

The methods used for obtaining the carers' accounts were the same as outlined in section 4.2.1, but the questions included:

- In what way do you care for someone with psychosis and substance misuse?
- How long have you been a carer of someone with psychosis and substance misuse??
- In what ways has being a carer affected your everyday life (such as schooling, employment and making relationships) and the lives of those close to you?
- How involved are/were you in the treatment plans of the person with psychosis and substance misuse??
- Were you offered support by the person's practitioners (for example, their GP, psychologist, or other)?
- How would you describe your relationship with the person's practitioner(s)?
- Have you and your family been offered help or received assessment/treatment by a healthcare professional?
- Did you attend a support group and was this helpful?
- Did any people close to you help and support you in your role as a carer?

Three accounts from carers of people with psychosis and coexisting substance misuse were received, which offer different perspectives of being a carer. Two of the carers are parents (one mother, one father) and one is a grandmother. Many of the common themes from the personal accounts are echoed in the carer accounts, including the lack of continuity of care, which may impact on carers as well, who have to fill in the gap. The accounts below reveal the difficulties of caring with someone who has psychosis and coexisting

substance misuse, such as challenging behaviour and, in the case of drug misuse, contending with the drugs world, including dealers and other users. All of the carers spoke of providing practical support to their family members, which ranges from helping them with their shopping, taking their medication, finding appropriate housing and employment, and managing money and benefits. For carer B a significant financial burden was placed on the family. As all of the accounts below demonstrate, carers value support from healthcare professionals and other workers, and appreciate it when they recognise that they, the carers, have valuable knowledge about their family member's illness and substance problem which can help adherence to treatment and prevent relapse. What is clear from the accounts is that carers have very different individual needs: some may require more support from healthcare professionals than others, who may prefer to cope within their family environment, rather than attending support groups. However during a crisis, all of the carers expressed that they would like to know whom to contact and to be able to access help quickly.

4.3.2 Carer account A

It is difficult to know where to begin to summarise what it has meant to see myself as the carer of my son Jack. Did it all begin 20 years ago when, aged 18, he had the first episode that could be deemed to be psychotic? Or was it much earlier when he was having difficulties at school and was labelled dyslexic, although one teacher said that she wondered whether he was a genius?

In some ways we were fortunate in being able to pay for him to see educational psychologists and Jack went through various tests and attended special schools that were supposed to meet his needs and help to prepare him for life in the world outside the safety of his family.

However, as I discovered much later, some of the boys at his specialist day school had access to marijuana and what began as a prank led to him self-medicating because of his worries about not 'fitting' in and not being able to keep up at school.

Jack is the youngest of three siblings and his older brother and sister were high achievers at school and university and are both married with children. This has highlighted Jack's feelings of inadequacy and fuelled his anger at what he feels to be an unfriendly world.

In his late teens Jack began experimenting with LSD, which led to his first admission to a private psychiatric hospital. It soon became apparent that we would not be able to afford long-term private treatment and he was transferred to an NHS hospital under the care of the same psychiatrist.

The nightmare began. There were times when he seemed quite mad—he grew his hair and a beard and my beautiful, funny and happy little boy turned into

a frightened and frightening stranger. We went through outpatients, then he was sectioned and spent a few weeks in one major teaching hospital. The psychiatrist said to me at the time that there was nothing they could do to stop people bringing in 'ganja', so while heavy medication (haloperidol, called the 'liquid cosh' by the patients) was being administered the patients were smoking dope on the patios! As I am a psychotherapist and had a lot of support, I battled the system at that time in which parents were not told which drugs were being prescribed. This meant that when one's child was sent home, the family had no idea of the possible side effects and what to do about them. We had one terrifying Sunday when Jack went into spasms and his face and jaw locked until we managed to get the antidote pill through a private doctor.

I became involved in what was then the National Schizophrenia Fellowship where there was some support and a bit of information for what were mostly the mothers of children with a similar diagnosis to Jack. By then he was labelled as schizophrenic, although this has now been removed and replaced by 'possible Asperger's'.

As Jack became more alienated from us, things got worse. He was picked up by the police, once while wandering along the underground railway line and once while climbing on a statue in a park. He broke things in the house, and although he never attacked me or stole money I was often frightened as he crashed about upstairs.

Things came to a head when he was sectioned for the second time and spent 10 weeks in a locked ward. Although dope was still available there his medication was changed and he gradually improved. We were lucky to have an excellent and understanding social worker and for the first time I felt supported to some degree by the system.

The next stroke of luck was that Jack was offered a place on a rehabilitation programme so that when he came out he was monitored by a team under an exceptional psychiatrist who was the first psychiatrist who appeared to see his patients as human beings. Although very overworked, this doctor took the time to consider each patient individually and agreed to gradually reduce Jack's medication. Jack also managed to stop using dope in order to be allowed to come home from his half-way house.

Fast forward about 10 years and Jack has been off neuroleptic drugs but still needs antidepressants and gets very bad headaches. He is not happy—he leads an isolated life and has had a couple of strange, seemingly psychotic episodes, over the last year. We need support, but the services are underfunded and understaffed; only last week Jack kept an appointment with his social worker (a different one sadly to our earlier helper) and no-one told him that they had been called out on an emergency. He felt let down and

angry that he was just left to wait rather than being told. Three close friends of ours have had sons of a similar age who have committed suicide, and this never leaves my mind especially when I hear Jack feeling let down and undervalued.

I struggle with my sadness, wondering what I could have done differently in Jack's early life. Sometimes it is unbearable. Jack's father and I separated 22 years ago—how much was this a factor?

The family and my relationship with Jack's very patient step-father is affected. The ache in my heart is always there due to living with a son who wishes that he was not alive. I suffer for him and I suffer for myself. I am lucky in many ways in that Jack has a decent small flat and is able to drive his car; he also studies a lot and practises martial arts when he has the energy. But there are days when he stays in bed all day, and he is sometimes angry and unapproachable and leaves a mess in the kitchen and fills our non-smoking household with his cigarette fumes. He has not used 'recreational' drugs for many years and hardly drinks alcohol, but he is very self-deprecating and bitter and very much into the occult as a way of escaping the reality of everyday life. This can lead to some dangerous practices.

My experience with the mental health services has been that there is no awareness of the need for continuity—the staff in our centre seem to change almost monthly. The one psychiatrist is overworked and so only crises are dealt with promptly. Most of the social workers are very friendly and well meaning, but don't seem to have much in the way of counselling or psychological training or support for themselves.

We have been offered a consultation for a diagnosis of Asperger's, but nothing has come of this. Basically Jack is not ill enough to get real help or well enough to lead a 'normal' life. We continue to do our best to manage in a kind of limbo, but it is not a comfortable place for Jack, or those who love him.

4.3.3 Carer account B

I am the carer of my son who is 32 years old and currently has a dual diagnosis. He has been ill for 12 years, originally with the diagnosis of schizoaffective disorder, but over the past few years this has changed to dual diagnosis, though his condition and substance misuse behaviour have been much the same throughout. His main drug is cannabis (skunk), but he has used most of the other commonly available recreational drugs. Initially, and before he was ill, these were mainly ecstasy, amphetamines and alcohol. He still uses these but crack, cocaine and heroin (smoked) have become regulars.

When my son was first ill he was 200 miles away at university. The first indication of problems was a call from a friend with whom he shared student

accommodation, who expressed some concern about his behaviour. I then received a call from my son about money problems. When I suggested I visit to help sort things out, my son readily agreed. I found him pleased to see me but quite agitated, and exhibiting some paranoia, but the most disturbing issue was his 'pressure of speech'. I assumed it was problems with his studies, though he denied it. I then managed to meet with his professor who said he was coping well, the only concern being a lack of actual work being submitted. He suggested I speak to student welfare. They felt that his behaviour suggested mental health problems and suggested talking to the university GP. She referred me to a visiting psychiatric nurse at the end of the week. The intervening few days convinced me that the problems were serious as my son's paranoia and pressured speech became more apparent. I also became aware of the heavy cannabis use of my son and his fellow students, almost at the level of ordinary tobacco use – my presence in the house only inhibited them slightly. The psychiatric nurse became quite alarmed and arranged an immediate meeting with a psychiatrist, who wanted to admit him to hospital but, given the distances involved for me, agreed to my request that we returned home. A consultation with our GP at home resulted in my son being admitted to hospital under a Section 3.

Over the next 4 years my son was in hospital several times, mainly under section. For the rest of that period he lived in the family home. He was then encouraged by the assertive outreach team to move into independent accommodation on the rather spurious grounds that a young man of 24 needed his independence. While he was able to live independently with only limited support, his drug use accelerated due to his lack of ability to control his social circumstances. The flat became the hangout for both his old friends, who were still living at home and therefore had their illegal activities restricted, together with, more unfortunately, members of the drug community (fellow users and suppliers), who in effect made use of him. This situation has persisted since, being relieved slightly by a period in a council hostel and other short periods when he effectively moved back home.

Approximately 7 years ago during another Section 3 enforced period in hospital he was put on depot injections of Clopixol, which has kept his illness under control but means he is quite debilitated for a few days after the fortnightly injections and generally claims that, in part, his drug use (particularly cannabis), is necessary to relieve side effects of the medication.

My life has been affected in several ways. There is the normal disruption suffered by all carers of somebody with a serious mental health condition such as daily visits when he was in hospital, urgent calls at any time of the day or night for support during periods of paranoia or stress, and highly charged, emotionally stressful situations dealing with illogical and delusional arguments and accusations. The drug misuse adds financial and safety concerns. Encounters with drug suppliers have not only been stressful, they

were also probably dangerous. In the early days I had to settle drug debts running to several hundred pounds. Currently we have a fairly stable relationship, with small loans usually being repaid the following week from benefits, though arguments still arise when it is obvious that all of the week's benefits have been spent within a few hours and I am expected to fund the whole week; it also stressful to be called in the early hours of the morning for money. I am not sure that my financial support is in my son's best interests - while it ensures he does not go without, it does not encourage him to be independent and I suspect drug suppliers have been happy to advance credit to him because he has me to bail him out when debts get too high.

Initially treatment for my son was only offered for his mental health problems, indeed, his first consultant said that his admitted use of cannabis was not a problem so long as it was not excessive. Times have changed. Various antipsychotic drugs were tried, including clozapine, but none was really very successful until the Clopixol depots. Very little other treatment has been offered. During the second detention in hospital an assessment was carried out by a clinical psychologist and although he felt sessions could be helpful, the consultant insisted that it was too early. I did not feel I was involved in any real sense in forming treatment plans at this time but anyway they amounted to little more than prescribing medication. Just as importantly I was not asked about my views on my son's history and therefore several things were recorded as delusions that were in fact true. Although he was definitely ill, the assumption that most of his stories were untrue still rankles with my son and means he distrusts the medical team. During the central period of his illness I had a good relationship with his key worker on the assertive outreach team and was invited to CPA reviews. My son was generally uncooperative at these due to the build up of stress at the situation causing problems, but the outcome was that little was offered apart from continuation of the medication; even variation of the dosage to reduce side effects was never seriously discussed. Since that particular key worker moved on 3 years ago I have had little contact with his care team, and only when initiated by me.

Initially his drug misuse was almost ignored. He was encouraged to go to the drug and alcohol service but having eventually got him there, they decided he was not ready for treatment as his mental state was not stabilised. The main reason for this attitude was his lack of interest in stopping his drug use (he still maintains his stance on cannabis though he does accept that other drugs , especially crack, cause him financial problems). Following a change in the structure of the drug and alcohol service and the emergence of dual diagnosis as a label, my son did start regular meetings with a counsellor. Although these went on for several months they appeared to have little effect, floundering again on the belief of my son that cannabis use is not a real problem. At the time of writing his only treatment is medication though he has been relatively stable and open to other possibilities.

My view is that the traditional approach to substance misuse is not really suitable for dual diagnosis sufferers since it relies heavily on the premise that there is a desire to stop using drugs that needs to be supported. My experience with my son and his peers is that they have little interest in stopping their drug use and their mental health problems mean they are not open to the normal logic. This is especially true of cannabis use where there is a strong belief in the general population that use is not a problem anymore than responsible drinking is.

At the start of my son's illness a family counsellor came to our home. She spent most of the time talking to my wife, although she did little to reassure her and offered little in the way of advice on dealing with our son's delusions. His drug use was ignored other than suggesting that we were over controlling in trying to stop it. I do not remember much about her visits, except that I was unimpressed, especially when she criticised me for putting pressure on my son to take his medication; shortly afterwards he was re-admitted after relapsing because of non-compliance. She completely ignored my daughter, who had great difficulty coming to terms with her 'big brother's' problems. My daughter still has reservations about contact with him but these are now largely over fears for her young family and his social situation.

In an attempt to understand more about the illness and the help available we became involved with Rethink (then National Schizophrenia Fellowship). This was helpful in a social sense but only to a limited extent since nobody else appeared to have drug misuse concerns. From this I became involved with the PCT advisory group, NIMHE and the National Forum for Assertive Outreach. From these I gained more insight into services but, unfortunately, what I learnt primarily was how little there was to offer someone like my son. Most interventions I have seen relate to injectors (for example, needle exchanges, substitution programmes) and are not relevant to cannabis and crack smokers. More structured activities would help as at least part of the problem is boredom and emptiness.

Generally people I was in contact with were sympathetic but were unable to offer much help. As a civil servant my managers were quite helpful in allowing time off for visiting, consultations and meetings. Over time most non-professional support fell away including my wife, who appeared to lose hope as time went on and things did not seem to be improving. Others, such as his neighbours, have had almost no sympathy for his situation. The council housing department were particularly lacking in understanding for his condition and how it affected his ability to obey their rules. Housing has been a particular problem and the caring team seemed unprepared to engage with the issue, despite the obvious effects it had on his illness (he reacts

particularly badly to stressful situations). However, the police were generally very helpful and understanding in their contact with him, largely as a victim.

4.3.4 Carer account C

I have been the main carer of my grandson for nearly 15 years. Jim is now 30 and has a diagnosis of schizophrenia and an alcohol problem. He started living with me when he was 15 after things became increasingly difficult for him while living with his stepfather and mother, who also has mental health problems.

When Jim started living with me he was taking drugs and drinking. At that time I had no idea about the drug use but did know that he was drinking with his friends at weekends. He was unhappy and quite isolated. He got some work with his father (my son), but his behaviour started becoming a bit strange and he would say odd things. We knew there was something wrong and his father paid for him to go to a private hospital; he did not receive a diagnosis at this time.

Not long after that first admission he was admitted to another hospital near to where his mother lived. Around 2000 Jim became increasingly unwell and we had our first contact with our local mental health services. A consultant psychiatrist and nurse came to see him at home. They thought he might have a drug-induced psychosis. They were both good: they listened, provided advice and gave us information. Jim was started on medication for the psychosis but it made little, if any, difference and he got worse. He would be agitated and suspicious and think things had special meanings for him. He was not offered any help for his drug use.

Sometimes he could be very scary and on one occasion he smashed up my house and attacked me. I had to call the police. Jim ended up being taken to hospital under a section of the Mental Health Act. As well as the police, there was an ambulance, doctor, social workers. I hadn't realised that was how it would be.

Jim has had several admissions to hospital, the longest of which was for 18 months. During that admission he spent a long time on the psychiatric intensive care unit as well as time on other wards. The hospital was a terrible place. Most of the staff – doctors and nurses - were awful. They were disrespectful and not interested in the patients. I wrote a letter of complaint about one of the wards but did not get any response. The one exception was the manager of the intensive care unit. He was gentle and calm and would always explain what was going on and the reason for things. Although Jim hated it there he did not want me to complain as he was afraid it would have negative consequences for him. He used to spend most of his time in his room so that he could keep out of the way of the other patients and staff.

When he was in hospital I visited Jim every day – including Christmas day. I took him food and cigarettes. After one of his admissions Jim was placed in a hostel. It was dirty and the staff were awful. It was just dreadful. I couldn't let him stay there.

Despite being tried on lots of different medications Jim didn't really get any better. When he was on the open wards he would abscond, often to go out drinking. I used to go out looking for him, but he would often end up back at my house.

It wasn't until one of his mental health review tribunals that a doctor asked why he had not been tried on clozapine. After that he was started on it and it made a difference straight away. Since being discharged from that admission he hasn't been re-admitted to hospital – that's about 6 years now. Clozapine has been a lifesaver for him.

After his discharge Jim was put under the care of the assertive outreach team. I've got nothing but praise for them. Over the years he has had a number of care co-ordinators and two support, time and recovery (STR) workers. The consultant psychiatrist responsible for his care is the one that we met during our first contact with local services. The dual diagnosis nurse specialist has also been involved over quite a few years now. Having continuity, where you can build up a strong relationship with someone, has been really helpful. All the assertive outreach staff have been very good and they're always reliable. I've been given their mobile phone numbers so I can contact them if I need to. They always take any concerns I have seriously and recognise that I know Jim really well and can spot when things aren't right at an early stage. When there have been times when Jim's mental health has deteriorated they have responded quickly and, when necessary, have visited him at home every day. The STR workers have bent over backwards to get Jim out and doing more social things. They'll phone, pick him up and do things like going to the gym, meeting up for coffee or going shopping. They've all been really flexible and helpful. I always attend the CPA meetings and these have been arranged at times that are convenient for me – I still work a few hours each week.

Over the years I've provided Jim with a lot of practical support, like doing his washing, ironing and shopping, making sure he's managing his money and not getting behind with his bills, liaising with his bank and the utility companies, and taking him up to the mental health team to have his blood taken, or to collect his medication. Although he's lived in his own flat for a long time now, he always comes to stay with me overnight once or twice a week – and sometimes has stays for longer periods. When he does that I know he's had a decent meal. I set limits on his drinking. I won't let him drink strong lagers in my house. He knows I don't like him drinking and am worried about the effect it has on him. I'm sure he would make more progress

if only he could stop. I phone him everyday to remind him to take his medication – even when I'm away on holiday.

I have been offered a carer's assessment and been given information about carers' groups but they're not my sort of thing. I get a lot of support from my partner, who gets on well with Jim, and other family members provide support too.

Over the years Jim has gradually made changes: he can live on his own, manage his money, take his medication (with reminders from me), do some shopping, travel on public transport on his own, and visit his brothers and Mum and stay over with them. He stopped taking drugs a long time ago and has had a few periods when he has stopped drinking but he keeps going back to it. Jim has often talked about courses or getting some voluntary or paid work but hasn't been able to follow through on his ideas yet. His assertive outreach team offered to do things with him but he always declines. Left to his own devices he will often stay in bed all morning. I think he lacks confidence. If only he had a bit more self-belief he could achieve more. I think it's difficult for him because his Dad and brother have been very successful. I think his Dad is a bit embarrassed and disappointed by him and he feels that.

I strongly believe that whatever happens to Jim it is up to me and my family to deal with it. I'll continue to keep supporting him as long as he needs me.

4.4 REVIEW OF THE QUALITATIVE LITERATURE

4.4.1 Introduction

A systematic search for qualitative studies, observational studies and reviews of qualitative studies of people with psychosis and coexisting substance misuse. The aim of the review was to explore the experience of care for people with psychosis and coexisting substance misuse and their families and carers in terms of the broad topics of receiving a diagnosis, accessing services and having treatment.

4.4.2 Evidence search

Reviews were sought of qualitative studies that used relevant first-hand experiences of people with psychosis and coexisting substance misuse and their families/carers. For more information about the databases searched see Table 7.

Table 7: Clinical review protocol for the review of qualitative studies

Component	Description
Electronic databases	CINAHL, EMBASE, MEDLINE, PSYCINFO, HMIC, PsycEXTRA, PsycBOOKS
Date searched	Database inception to 25.06.2010
Study design	Systematic reviews of qualitative studies, qualitative studies
Population	People with psychosis and coexisting substance misuse
Critical outcomes	None specified - any narrative description of service user experience of psychosis and coexisting substance misuse

4.4.3 Studies considered

Based on the advice of the GDG, this review was focused on qualitative research only as it was felt it was most appropriate to answer questions about the experience of care of those with psychosis and coexisting substance misuse. As good quality qualitative research exists within the literature, quantitative and survey studies were excluded.

The search found 21 qualitative studies which met the inclusion criteria (Alvidrez *et al.,* 2004; Bradizza & Stasiewicz, 2003; Carey *et al.,* 1999; Charles & Weaver, 2010; Costain, 2008; Dinos *et al.,* 2004; Hawkins & Abrams, 2007; Healey *et al.,* 2009; Johnson, 2000; Lobban *et al.,* 2010; Loneck & Way, 1997; Padgett *et al.,* 2008a, Padgett *et al.,* 2008b; Penn *et al.*, 2002; Pollack *et al.*,1998; Strickler *et al.,* 2009; Todd *et al.,* 2002; Turton *et al.,* 2009; Vogel *et al.,* 1998; Wagstaff, 2007; Warfa *et al.,* 2006;) and 28 were considered for the review but they did not meet the inclusion criteria. The most common reasons for exclusion were because quantitative or survey methodology had been used or because the people included in the research did not have psychosis and coexisting substance misuse. The characteristics of all the studies reviewed in this section, and references to excluded studies are summarised in Appendix 13.

Once qualitative studies were assessed for methodological quality, themes from each study were extracted and synthesized in a narrative synthesis to reflect overarching themes to capture the experience of people with psychosis and coexisting substance misuse, and their carers. The studies have been categorised under seven main headings: service user experience of psychosis and coexisting substance use, access and engagement, carers' perspective, service user experience of illness, social networks, employment, and treatment.

4.4.4 Experience of psychosis and coexisting substance misuse and reasons for substance use

Eight studies (Alvidrez *et al.,* 2004; Bradizza & Stasiewicz, 2003; Carey *et al.,* 1999; Charles & Weaver, 2010; Costain, 2008; Healey *et al.,*, 2009; Lobban *et al.,* 2010; Warfa *et al.*, 2006;), four of which were conducted in the UK, looked at

reasons for substance use in a population of participants with psychosis and coexisting substance misuse.

Carey and colleagues (1999) and Alvidrez and colleagues (2004) interviewed participants about positive and negative aspects and consequences of substance misuse and abstaining. Both studies identified interpersonal problems and alienation from social networks (especially substance using social networks) as a negative aspect of abstaining from substance use. Conversely, one positive aspect of substance use mentioned was improved social skills and less social inhibition. While some participants felt that their drug use was the driving force behind the development of mental disorders (*'It activates...it triggers the mental illness'*), the majority of participants expressed that drug use has both beneficial and negative effects on their psychiatric symptoms (Alvidrez *et al.,* 2004). In a more recent study by Charles and Weaver (2010), five of 14 participants perceived their substance use to directly influence development of their mental health problems, while five others felt that substance use made their psychiatric symptoms worse. Additionally, seven people acknowledged that substance use contributed to relapse and worsened their mental health after the onset of psychosis.

Seven studies found that substances were commonly used by people with psychosis for managing their symptoms. Charles & Weaver (2010) found that participants did not self-medicate, but did use substances to prevent the effects caused by their anti-psychotic medication (for example, drowsiness). Bradizza & Stasiewicz (2003) also found that experiencing symptoms of psychosis triggered alcohol and drug urges, as such substances helped people to cope with psychotic episodes:

'that's why I kept using heroin. I mean, my paranoia was bad. I thought everything and everyone was after me'.

For people with schizophrenia, substance use relieved negative symptoms (for example, lack of motivation and energy) but exacerbated psychotic symptoms (for example, paranoia). Participants described the cyclical nature of their mental illness and drug misuse. Psychiatric symptoms trigger substance use, which acts as a catalyst for additional symptoms that precipitate further substance use:

'..The worst problem in my life right now is this vicious cycle that I've been in for the past seven years, which is battling substance abuse and then how the substance abuse impacts my depression, my self-esteem and the paranoia...' (Alvidrez *et al.,* 2004)

'It's like you know something really isn't no good for you, but at the same time, you want the results of an escape from reality temporarily, so you go ahead and do it'. (Alvidrez *et al.,* 2004)

Positive aspects of abstaining consisted of improved living skills, better physical health, getting off the streets and away from crime, regaining trust from others and engaging in social activities. Fears and negative perceptions of abstaining from substance use included anticipating the physical effects of withdrawal, loss of relationships with substance-using friends, and the cycle of relapse.

Despite the perceived positive aspects of substance use, participants did have insight and awareness about the dangers of using substances to alleviate symptoms:

'[alcohol] has a tendency to make a person think that his problem is less severe than it might be. It kind of clouds an image of what's really going on and will cause continual problems.' (Alvidrez *et al.,* 2004)

Cannabis was most often mentioned for helping with delusions, controlling symptoms, and 'normalising behaviour' (Costain, 2008). Participants in Costain's (2008) study also perceived improvement in cognitive functioning from cannabis, as well as increased levels of energy and reduced psychological pain. The authors point out that this may influence adherence to treatment for patients with schizophrenia, and that clinicians must be aware of the phenomenological expressions and beliefs of patients with schizophrenia. They argue that ignoring this issue may have an impact on the development of a therapeutic relationship. Additionally, patients with bipolar disorder would often use substances because they had a desire to feel normal without the sedative effects of their medication, or to attempt to recapture how they felt pre-diagnosis (Healey *et al.,* 2009). Substances used to help people relax were most often alcohol or cannabis (Wagstaff, 2007). Warfa and colleagues (2006) also found cannabis was used by participants to have a 'good impact' or feeling of being strong.

Feelings of anger and loneliness were most often expressed as emotions leading to substance use. In relation to this, other participants with bipolar disorder felt that substance use was a way to control and manage mood states, particularly mania and depression (Healey *et al.,* 2009), though many realised that this was not a reliable method of controlling mania. Anxiety, depressive symptoms and relieving pressure were also cited as reasons for substance use (Carey *et al.*, 1999; Alvidrez *et al.*, 2004; Healey *et al.*, 2009). Most participants experimented with alcohol and drugs before receiving a diagnosis of psychosis or in the early course of their illness. The substance misuse then became out of control, either because they were unaware of their mental disorder, or did not understand the effects the substances had on their mood. In this experimental phase with substances, dependency is often established.

Additional triggers leading to substance misuse were feelings of being stressed or overwhelmed by life events. These issues could stem from poor housing, unemployment, family relationships and legal problems (Carey *et al.*, 1999; Bradizza & Stasiewicz, 2003). In some instances, previous traumatic life events served as a trigger for substance use (Charles & Weaver, 2010).

4.4.5 Access and engagement

Having a diagnosis of psychosis and coexisting substance misuse can significantly impact on a person's ability to access and engage in services and in treatment. This can be due to a myriad of factors including stigma, ethnicity, socioeconomic status, gender, and perception of services. Several themes emerged under the broad heading of 'access and engagement' to services for those with psychosis and coexisting substance misuse, including the factors that may act as barriers to accessing treatment services, such as external and internal stigma, ethnicity and gender. This review also identified 'reasons for seeking help' as a theme emerging from the included studies. There were six studies from which themes of access and engagement emerged (Dinos *et al.,* 2004; Johnson, 2000; Penn *et al.,* 2002; Loneck & Way, 1997; Todd *et al.,* 2002; Warfa *et al.,* 2006;).

Dinos and colleagues (2004) interviewed patients in community and day mental health services in London in an attempt to describe the relationship of stigma to mental illness and the consequences of stigma for the individual. One significant theme that emerged for participants with a dual diagnosis was anxiety surrounding managing information regarding both their illnesses, and issues of disclosure (whether to disclose to friends, family and prospective employers). Overt discrimination from others was experienced by most of the participants in this study, typically in the form of verbal or physical harassment, or through actions such as damage to property. Those with a comorbid mental illness and substance misuse reported having been verbally abused and patronised more frequently than those with other diagnoses. People with psychotic disorders experienced physical violence, as well as reduced contact with others. They also felt that they had been discriminated against in that they had not been selected by educational institutions or employers due to their diagnosis. As a result, most participants felt fearful, anxious, angry, and depressed, as well as isolated, guilty and embarrassed. These feelings resulting from stigma were a significant hindrance to recovery and a barrier to seeking help:

> *'It makes you feel bad.. it makes you feel even worse… when people don't trust you and think you're going to do something to someone.'*

On the other hand, many participants reported positive aspects to having a mental illness, expressing relief that they had a proper diagnosis and appreciating their treatment:

'I feel that if I survive it I've been through a very privileged experience and that I can actually make something of it…'

Interestingly, no participants who were drug dependent expressed this positive view of their illness. It is evident that for this study population, stigma was a pervasive concern for the majority.

- ***Black and minority ethnic groups and socioeconomic status***

One UK study (Warfa *et al.,* 2006) looked at drug use (specifically cannabis and khat[3]) in black and minority ethnic (BME) groups. Whereas East African communities showed that use of khat was linked to their culture, cannabis was seen as entangled with religious uses for black Caribbean populations. Participants in the study stated that the cultural context of their substance use was not taken into account by healthcare professionals. Some participants in the study mentioned that their clinics or clinicians exhibited cultural awareness, while others felt that there needed to be increased cultural and religious sensitivity within services in the UK (Warfa *et al.,* 2006).

Johnson (2000) interviewed families in the United States caring for a family member with psychosis and coexisting substance misuse. The marked differences in SES) and its connection with access and engagement in care emerged as significant themes. Upper-middle class European-American families felt a greater sense of individual and organised support compared with families of a lower SES. In contrast, upper middle class families from an ethnic minority were most difficult to identify as they did not access care as frequently. They were very rarely connected with an organised support group and therefore were less visible to services compared with other SES groups. The lower middle class families were found to have a more extensive family network although this did not seem to facilitate management of family members' illnesses.

Families of all ethnic and SES groups felt disregarded or dismissed by mental health professionals with whom they engaged, feeling that their knowledge and opinion was rarely taken into account by mental health professionals (especially staff at crisis centres, hospitals, and psychiatrists in all settings). The experience of stigma for middle-class families differed from the lower-class families, in that those in the upper-middle class were often embarrassed that a family member was ill and therefore not functioning to their own or their social network's standards, and consequently felt distanced from other families in their network. The low and lower-middle class families felt stigmatised mostly when dealing with professional mental health and legal systems. Surprisingly, only 25% of the families interviewed had been involved in an organised support network (for example, a family group or

[3] Khat is a plant native to East Africa and the Arabian Peninsula, and when chewed, acts as a stimulant.

self-help group). One suggestion the authors make is that there needs to be greater knowledge of other families struggling with an ill family member and information about community groups to go to for support.

Gender

Penn and colleagues (2002) examined treatment concerns for women with coexisting mental illness and substance misuse. The women interviewed emphasised how a client-centered approach facilitates treatment, especially when the clinician embodies traits such as empathy, honesty, and being encouraging and direct. All participants identified that negative staff attitudes or changes in the service significantly hindered their treatment progress (for example high staff turnover, lack of coordination between services, feeling judged). Childcare services were mentioned as necessary for women accessing treatment, as was support that specifically accounted for women's needs.

Reasons for seeking and accessing help

Many people with psychosis and coexisting substance misuse do not come to treatment until the pattern of illness is well established (Vogel *et al.,* 1998). Similarly, Padgett and colleagues (2008b) interviewed psychiatric patients with a dual diagnosis who used to be homeless and found that people typically entered treatment once symptoms of mental illness became overwhelming (for example, increased hallucinations):

> *'I got to a point.. I can't take it no more. I'm going to the hospital'.*

Another key reason for reducing or stopping substance misuse was a change in personal life goals, for example an increase in the perceived value of health, income, and social relationships (Lobban *et al.,* 2010). In addition, the desire to be accepted within a certain social milieu can play a part in both initiating drug use and in terminating it. A significant event can lead to a dramatic change in behaviour and lend support to wanting to become abstinent as well (Lobban *et al.,* 2010).

4.4.6 Importance of social networks

There were eight qualitative studies addressing the effect of social networks on people with psychosis and coexisting substance misuse (Bradizza & Stasiewicz, 2003; Carey *et al.,* 1998; Charles & Weaver, 2010; Hawkins, 2007; Lobban *et al.,* 2010; Padgett, 2008a; Turton *et al.,* 2009; Wagstaff, 2007). All the studies highlighted that individuals often feel isolated from their social networks and do not have many people with whom to socialise. Given the pervasiveness of their illness, many found it difficult to make new friends and often relied on substance-abusing friends for support (Bradizza & Stasiewicz, 2003). Other participants highlighted the need for support and having contact with others who have experienced similar mental health and substance problems (Turton *et al.,* 2009):

'most of the counsellors there were ex-addicts themselves and I could relate to them, and the things they said because they've been through it'.

Both Hawkins & Abrams (2007) and Padgett and colleagues (2008a) examined the social networks of those with a dual diagnosis who were homeless. Social networks were perceived to be smaller, primarily because many members of their social networks died prematurely (homeless patients with stressful environments were at a higher risk of mortality), or patients withdrew or pushed others away. Many participants had witnessed a death of a loved one; and death appeared prominently in all of the narratives in this study. When social networks diminished, some participants reacted by attempting to rebuild their network, even if this involved negative social interactions with strong substance use triggers, while others reacted by isolating themselves further to escape social pressures. Many participants adopted 'loner talk' and wanted privacy, which arose from negative life experiences or distrust of those around them.

Social benefits were also frequently cited as reasons for substance misuse. Lobban and colleagues (2010) differentiated between internal and external attributions for ongoing drug-taking behaviour. Participants who made internal attributions for substance use described seeking out information and weighing up advantages and disadvantages of taking drugs in order to make their decisions. This was also found in Carey and colleagues' (1999) study, where participants made a 'decisional balance' before using substances use. Substance use was found to have a positive effect on interpersonal relationships in helping people 'fit in' and facilitating connections with others. Furthermore, drugs were a way to reduce social anxieties.

Social networks were seen as a way to experiment with substances in order to gain experience, providing the person with 'social currency' which further encourages substance misuse (Charles & Weaver, 2010). A study by Vogel and colleagues (1998) and by Charles & Weaver (2010) also confirms this finding, in that participants felt that using drugs and/or alcohol elicited feelings of confidence and 'belonging', which often promoted even more substance use.

Many participants talked about how drug use in their community was the 'norm' (Lobban *et al.*, 2010) Participants who attributed their substance use to those around them found that their social networks grew around drug-using communities, and also increased their level of detachment from non-drug using networks. Socialising in drug-using communities reinforced not only shared experiences, but also facilitated drug accessibility and consumption (Lobban *et al.*, 2010; Charles & Weaver, 2010). Therefore, the social aspect of belonging and acceptance plays a part in both initiating and terminating drug use, and is fundamental in increasing motivation to use substances. When the

social networks are associated with drug-using behaviour or triggers, this is a hindrance to promoting and maintaining abstinence. Young people in particular identified that their social networks were very important to them, and much of their substance use was linked to social activities. Thus, they felt that they would require drastic changes to their social networks and surroundings in order to reduce their substance use.

In summary, social inclusion was important to this population in terms of building relationships (and re-building social capital post-treatment), gaining employment, and engaging in activities in the community.

4.4.7 Experience of treatment

The experience of treatment for people with psychosis and coexisting substance misuse varies widely, but seems to revolve around central themes such as ambivalence towards medication, ceasing medication, the importance of self-help and mutual support groups, having a key worker, and cultural sensitivity integrated within services. Eight studies highlighted the experience of treatment for people with psychosis and coexisting substance misuse (Costain, 2008; Johnson, 2000; Loneck & Way, 1997; Pollack *et al.,* 1998; Todd *et al.,* 2002; Vogel *et al.,* 1998; Wagstaff, 2007; Warfa *et al.,* 2006).

Experience of assessment and referral from the staff perspective

Loneck and Way (1997) and Todd and colleagues (2002) looked at how to assess patients with psychosis and coexisting substance misuse from a staff perspective, how to refer them to appropriate services, and keep them engaged in the care plan. In the study by Loneck and Way (1997), healthcare professionals working in an accident and emergency ward emphasise that for patients with schizophrenia, a more supportive approach to engagement must be employed, whereas those with substance use disorders are more receptive to a style that is more directive and if necessary, confrontational. The approach advocated by these healthcare professionals for patients with psychosis and coexisting substance misuse is a combination of supportive and directive styles, and is confrontational only when necessary. Support was characterised by listening and assessing needs, whereas a directive approach meant having a structure and steps in order to move patients into appropriate services. If patients were resistant to the supportive approach and unwilling to accept referrals, persuasion and motivational techniques could be adopted to motivate patients to accept more appropriate referrals to services. Lastly, healthcare professionals identified that the therapeutic alliance is crucial to successfully engaging with patients with psychosis and coexisting substance misuse. The most important factors to ensure a strong therapeutic alliance were: agreement about goals and tasks, and strengthening the patient-clinician bond. Todd and colleagues (2002) found that the essence of optimal care was the provision of a comprehensive assessment and a care plan that addresses both urgent and non-urgent issues related to both illnesses. The care plan should be integrated across services, and make sense to the patient

such that it encourages engagement and motivation to change, and is readily accessible. However, staff feared that this proposed treatment service consisting of an integrated assessment and care plan would further strain the system and increase workload.

Experience of therapeutic relationship

When participants were asked about their most positive experience of services in the UK, they highlighted having a key worker (for example, a social worker) with whom they have a good relationship, in addition to accessing local counselling services or alternative treatment options (for example, spiritual services or specific cultural support groups) (Warfa *et al.*, 2006). These services and options were seen as integral to their progress in treatment.

One limitation cited by many participants was the lack of cultural awareness and sensitivity in mental health services. They also mentioned that meetings with healthcare professionals were not long enough, and there not enough attention being paid to social activities (Warfa *et al.*, 2006). Participants emphasised that alcohol or drug dependence made service engagement extremely difficult.

Emotional support and time investment by service providers was important across all cultural groups with psychosis and coexisting substance misuse (Warfa *et al.*, 2006). This, therefore, highlights the importance of developing an active therapeutic relationship with a patient, fostering trust and confidence and addressing both of the person's diagnoses

Treatment options

Once patients were in treatment, many were frustrated at the lack of individual 'talk' therapy to help discuss and heal the trauma incurred from having a mental illness, having a substance problem, and living on the streets. Conversely, some participants were positive views about services, particularly the atmosphere and amenities, the sense of privacy, and staff who were warm and humane (Warfa *et al.*, 2006).

Medication adherence and effects

Patients in the study by Warfa and colleagues (2006) found that medication for their psychosis works for them and generally improved their mental health. However, antipsychotic medication typically is associated with negative perceptions and, consistent with this view, the Wagstaff (2007) study found that the most common reason for participants to cease taking their psychotropic medication was that they did not perceive themselves as requiring medication in the first place. Costain (2008) found that many participants had side effects from their antipsychotic medication, and when participants also had anxiety symptoms, they stopped taking their medication and increased their cannabis use. The reasons for non-adherence to

medication were varied. Many felt that adherence to medication would not enable them to have control over their symptoms (e.g. delusions). Others did not perceive they had a mental illness and therefore the medications were irrelevant (Costain, 2008).

Pollack and colleagues (1998) found that participants cited symptom improvement as the bigger driver for adhering to their meditation, however the side effects and potential to be stigmatised because of the need for medication were a concern:

'*So actually, when you say you're suffering because of your side effects, it's not only the physical part, but how you think you're perceived by other people*'.

Other service users suggested that therapists should address ambivalence towards medication (Warfa *et al*., 2006)

Relapse was also associated with discontinuing drug treatment because of wanting to avoid the stigma of 'needing medication'

> *'I've realised the medication is doing a lot for me, but at the same time, it's going back and grabbing that security blanket again and that feeling, or that high, that desire, that craving…'* (Pollack *et al*., 1998)

All of these factors highlight the notion that the relationship between adherence to medication and substance use is complex. In terms of improving medication adherence or aftercare attendance, participants highlighted family influences as the most positive, especially in providing support or initiative.

Self-help groups

Many participants interviewed by Vogel and colleagues (1998) mentioned that a mutual support programme was extremely beneficial in enabling people with psychosis and coexisting substance misuse to share similar experiences and providing a non-judgemental atmosphere in which they could discuss problems. The support group increased participants' optimism, brought them comfort and changed their attitudes towards taking their mediation (Vogel *et al*., 1998).

Pollack and colleagues (1998) interviewed inpatients with psychosis and coexisting substance misuse about the factors that affected their attendance in an aftercare programme. Self-help meetings (for example, Alcoholics Anonymous [AA]) were easier to attend because of the flexible timing and the fact that they facilitated social activities:

> *'Just being around the other people, you know, I've pretty much alienated everyone due to my drug addiction and alcohol…so it provides me the opportunity to…generate a new relationship'.*

> *'I found that it was a joy to go and share my daily achievements with a group of people that knew my condition because their own condition was so similar'.*

On the other hand, attending AA meetings that were not designed for those with a with psychosis and coexisting substance misuse was unhelpful and perceived as contributing to relapse. As the meetings were tailored to people with alcohol and drug misuse disorders, one participant felt that they were treated differently because of their other diagnosis, leading them to seek other meetings.

Experience of treatment from the carers' perspective

One prominent theme that emerged from the interviews conducted by Johnson (2000) with carers of people with psychosis and coexisting substance misuse was the benefits and marked differences due to person taking the medication. Most families had noticed a significant improvement in functioning when their family member was on medication. However, many patients replaced their prescribed medication with street drugs, leading to deterioration in functioning and to rehospitalisation. Family members who cared for people with psychosis and coexisting substance misuse felt excluded from mental health services and considered that their efforts were largely ignored by mental health practitioners.

It was emphasised that greater knowledge of and contact with other families struggling with the same problem would be beneficial, as would more emotional support from extended social networks. Support groups, led by professionals, that were specifically for people with psychosis and coexisting substance misuse and their families and carers were also mentioned by carers as beneficial.

4.4.8 Employment

Strickler and colleagues (2009) interviewed people with psychosis and coexisting substance misuse about their experience with employment. Having a dual diagnosis was perceived as a prominent barrier to gaining and maintaining employment; the most frequently cited barriers were the psychiatric symptoms themselves (such as manic episodes, delusions, anxiety and stress). Both Strickler and colleagues (2009) and Bradizza and Stasiewicz (2003) found that regular employment was difficult to obtain for those with psychosis and coexisting substance misuse. Furthermore, the longer the period of unemployment, the more the difficulty of finding and sustaining employment increased. As a result, there is often an extended period of unemployment with little money available to engage in additional activities. This in turn, can encourage substance use. Employment was conceptualised as a positive event which aids recovery, and adds therapeutic value to a patient's life:

' Work was really kind of helpful. I didn't have as many symptoms because I was too busy working'.

'It helps my mental illness. It gives me structure'.

Employment helped to reduce substance use and keep participants away from drugs or alcohol. It occupied the patient and kept their daily living skills intact (for example, maintaining daily hygiene at a level suitable to attend work). The regular use or dependence on substances made consistent employment significantly more difficult.

Employment, therefore, held a positive structural value to participants, providing them with an additional sense of belonging and contributing to society:

'When I am working I feel like I am contributing. I don't feel isolated.'

4.4.9 Summary

The evidence from the narrative synthesis of the qualitative studies provides some important insights into the experience of people with psychosis and coexisting substance misuse and their carers. Substance misuse appears to stem from a range of environmental and social factors including the management of psychiatric symptoms and/or social situations that encourage and exacerbate substance use.

Perhaps the most central theme of the reviewed literature was the importance of social networks. People with psychosis and coexisting substance misuse commonly identified interpersonal problems and alienation from social networks across all studies. This alienation and lack of a positive social support network seemed to influence their substance use, ability to seek treatment, maintain positive change, and increased vulnerability to relapse. Many negative social networks grew around drug-using communities and reinforced substance misuse.

The reasons for substance misuse were cited in nearly every qualitative study included in this review. For the most part, service users highlighted the positive and negative drawbacks to substance use and its direct effect on their psychosis.

People with psychosis and coexisting substance misuse were often stigmatised by others and faced discrimination. Many also felt internal stigma which made them hesitant to disclose their diagnosis or 'edit' it. Awareness of stigma can often be a hindrance to recovery and a barrier to seeking help in this population. People from a minority ethnic group also felt that the cultural context of their substance use was not taken into account by healthcare professionals. From the carers' perspective, families from ethnic groups and

groups of lower socioeconomic status felt disregarded by mental health professionals. As a group, women felt that they faced additional barriers to treatment in the form of more social stigma, and the need for childcare while seeking and undergoing treatment. In addition, women felt that they received less support from treatment providers, and would benefit from a more empathetic and therapeutic approach. The studies focusing on women emphasise that a patient-centred and non-judgemental atmosphere is necessary in order to foster openness and willingness to change. All participants highlighted that negative staff attitudes hindered their treatment progress.

An inability to access services easily, combined with negative interactions with healthcare professionals, highlights the importance of an appropriate assessment and referral process, which takes into account both the psychosis and the substance misuse. The literature indicated that a good assessment, which is direct in nature, should be employed for the substance use problem, whereas a non-judgemental, empathetic approach is preferred for assessment of psychosis. Staff however, found this comprehensive assessment problematic due to the increase in resource use and strain on time for healthcare professionals.

Regarding treatment, most participants found medication to be beneficial, but ambivalence about it was common often due to the regimen and side effects. Participants also spoke positively about having a good relationship with a key worker or participating in a self-help group. Employment was seen as providing positive structural value and a sense of belonging.

Family and friends can have an important role to play in supporting a person with psychosis and coexisting substance misuse. They can promote and maintain change, but in order to do this they require information and support from healthcare professionals. The strain on carers, however, can be challenging and they may require a carer's assessment.

From a staff perspective, the qualitative studies suggest that an improvement in staff training is required to facilitate access and engagement in treatment for people with psychosis and coexisting substance misuse. When interventions were successfully delivered, a thorough assessments, as well as coordination between mental health services and substance misuse services were two components of care perceived as crucial.

One interesting result emerging from all the studies was the realisation that it is possible to conduct qualitative research with this specific population and engage them in focus groups and interviews. This finding can hopefully facilitate further research in the future for people with psychosis and coexisting substance misuse.

4.5 QUALITATIVE ANALYSIS

4.5.1 Introduction

The following section includes a qualitative analysis of transcripts available on the internet from people with psychosis and coexisting substance misuse. These were accessed from the following websites: Healthtalkonline (http://www.healthtalkonline.org/), Dual Recovery Anonymous (http://draonline.org/), Meriden Family Programme (http://www.meridenfamilyprogramme.com/) , Talktofrank(http://www.healthtalkonline.org/) , Foundations Associates (http://dualdiagnosis.org/), Bipolarworld(http://www.bipolarworld.net/) , and Rethink (http://www.rethink.org/) . The websites all provided information and support to people with psychosis and coexisting substance misuse and include personal narratives from people with these conditions and their carers. The review team undertook their own thematic analysis of the narrative accounts to explore emergent themes that could be used to inform recommendations for the provision of care for psychosis and coexisting substance misuse. It should be noted that patients with diagnoses of bipolar disorder, schizophrenia, schizoaffective disorder, and psychotic disorder were all included in these transcripts, in addition to having problematic or dependent substance use.

4.5.2 Methods

Using all the personal experiences available from seven websites, the review team analysed the accounts of 48 patients. All accounts were published on the website in their original form. The majority are written by people from the UK but there are also some from the US. Poems and letters were excluded from the analysis. Each transcript was read and re-read and sections of the text were collected under different headings using a qualitative software programme (NVivo). Initially the text from the transcripts was divided into six broad headings emerging from the data: impact and experience of psychosis and coexisting substance misuse; access and engagement; experience of treatment; carers' perspectives; and support and services. Under these broad headings, specific emergent themes that were identified separately by two researchers were extracted and regrouped under the subsections below.

There are some limitations to the qualitative analysis for this guideline. Some of the accounts are written in retrospect, whereas others are written more recently, or in the present. This may have had an impact on the way in which the experiences were recalled; moreover, the accounts cover different time periods which may affect factors such as attitudes, and information and services available.

4.5.3 Impact and experience of psychosis and coexisting substance misuse

Given the debilitating impact of having a diagnosis of psychosis or a psychotic-related disorder with coexisting substance misuse, the main themes emerging from the online accounts regarding experience of illness described the symptomatology of their disorder(s), the emotions they felt in receiving an accurate diagnosis, the use of self-medication to control psychiatric symptoms, and, lastly, gaining insight into their mental illnesses.

Symptoms of psychosis and coexisting substance misuse

Many patients alluded to the cyclical nature of their mental health problems (especially those with bipolar disorder), and how these symptoms were or were not affected by their substance use:

> *'When I first got sober, the manic-depressive disorder appeared even more pronounced than it had before. It was no longer hidden by alcohol and drugs. The stress of withdrawal in my early recovery triggered wild mood swings for me.'*

> *'At times my moods were changing from depression to manic even without booze or drugs. Sometimes I got so depressed I would seclude myself for weeks at a time with out paying attention to whether I bathed or ate.'*

Participants also described how they would hide their symptoms from others:

> *'You can't lump everybody in together, you know, to say oh this is, these people are manic depressives, so their behaviour would be blah, blah, blah. Everybody is different…I might act different to the next manic depressive or whatever and, you know, perhaps I might not show my symptoms because there's one thing about manic depression, depressives you really are clever at hiding your symptoms and very good at manipulating people.'*

Self-medication as a reason to misuse substances

Self-medicating with drugs or alcohol as a way to manage symptoms emerged as a prominent theme in the online accounts. The most common reasons for self-medicating were to manage manic or depressive symptoms:

> *'The Army caught on to my problem, and tried to treat me with Lithium and Prozac. This helped for a little while, but I also started drinking. Eventually, I went off the meds and started self-medicating with the alcohol. '*

> *'I began to self medicate myself. Smoking weed drinking alcohol these help me come down from my intense moods '*

'I started to self-medicate. Alcohol and speed were my crutches. If I felt myself getting too high I would drink, if I felt I was getting two low then I would take a few grams of speed.'

Gaining understanding

Gaining an understanding of mental illness is an important step towards both engaging in treatment and promoting the recovery process. The themes that emerged centred on accepting both diagnoses of a psychotic and substance misuse disorder, and understanding how both illnesses could be treated and how their substance misuse had had an impact on their psychiatric symptoms. Understanding their conditions frequently led to positive thoughts about their illnesses and the future:

'Recovery from chemical dependency requires that I accept my addiction and abstain from mood-altering chemicals. It involves attending 12-Step meetings, working with my sponsor, working the 12-Steps and improving my physical health. Recovery from bipolar disorder..requires that I accept the disease. Attend dual disorder meetings; increase my activity when I'm depressed and decrease my activity when I'm manic, or slow down and think constructively.'

'Believing that my mind would return to rational thinking once time healed it from the years of drug abuse. The entire time ignorant of [bipolar disorder]. As if my mind completely blocked out those years of hospitals and knowledge. I'm beginning to believe it was shame, fear of stigma. But still, why I sabotage myself is a mystery, and I still have to fight it!'

' … drugs might not be responsible for all mental illness but where, where people with mental illness take drugs they greatly compound the problem and prevent recovery. And I think that other things being equal, people do recover more or less but the drugs stop them recovering.'

4.5.4 Access and engagement

Due to the additional burden of having both psychosis and a substance misuse problem, there are many barriers to accessing and/or engaging in treatment. This can stem from experience of stigma, cultural or ethnic factors, lack of coordination between services, and assessing and engaging the service user.

Stigma

There is a significant amount of stigma attached to a severe mental illness like psychosis, and coupled with a substance misuse problem there is additional risk of stigma. Many online accounts, from both service users and carers, highlighted the experience of interacting with others in the community and the stigma that their dual diagnoses carried. The experience of stigma often elicited feelings of shame, embarrassment, and frustration:

'When we go out there in the community people might know you have got a mental health problem, you might not look different to the, but they know you have got that. There is a stigma against it and a discrimination taboo..because of the label, and because of what it stands for. Which is people don't understand.'

'I found that a lot of people disbelieve me when I say I've had schizophrenia, … They don't believe it because my behaviour doesn't match their stereotype and if there's one thing that makes me upset more than anything else is.'

'So if we can get actually people on board to recognise that not all … mentally ill people are violent, psychopathic or whatever that which actually we're just normal people trying to live our lives every day with the added burden of having a mental health issue then perhaps… people would get on a lot better.'

'If anybody heard that you have a sick son, they don't want to know you. That's the worst part…I still hear people saying to me, "...he has two sons, they are sick". And when people hear that, they don't want their children to even come any nearer. Because they are afraid… that your son might do something… because they do not have enough knowledge that not all sick people are violent'.

'When he was sectioned, we told them he had been spiked, probably with LSD. Bizarrely that explanation is more socially acceptable than telling people your son has a mental health problem. That's how far this society is entrenched in stigma and prejudice about mental health, but tolerates drugs as part of the social structure.'

Access for BME groups and cultural factors

One theme that emerged in several testimonies was that access to care was more difficult for those coming from a BME group or a different cultural background. Factors that affected access to care for BME groups were a fear of accessing treatment due to the conceptualisation of mental illness in their home country or native culture, or fear of stigma:

'Well people look at you differently if you say you've got a mental health problem back home. They don't treat you the same. I think now it's changed but that, when I was there it was different…'

Many felt that they were or would be treated differently by mental health professionals as a result of their ethnicity or cultural background:

'…it wasn't so much racist it was more institutionalised racist. It's embedded within the system.'

'…within the mental health system it's their foreign-ness which is emphasised because it is their foreign-ness which is considered to, to shape their, their

diagnosis'.

'…it's very hard for minority to express their views, because any time a minority express their views… "if you don't like it, what are you doing here?"'

'But they don't know where to go to no one. They don't go to a doctor or no GP. They want to deal with it themselves.'

'You know, some Black folk they don't want to go to the GP, they don't want to go, then them's not treated, because the stories they hear about the system, so we've got to find a way to make it more attractive to help them to go and get treatment before it gets worse.'

Access to services

A significant number of factors affected accessing services, including fear of contacting a healthcare professional about substance misuse, and uncertainty about how to begin accessing treatment or who to contact:

'And I did ask somebody from my mental health team if it was possible to have like a social worker and she said no, she didn't know how I would access that. I asked my doctor the same thing she didn't know how I would access anything like that so it just leaves you vulnerable.'

Coordination between services

Another theme which emerged from the online accounts was the link between mental health services and the criminal justice system and the police. Several accounts compared how, in the UK, there needs to be more coordination between the police and mental health services in order to make the most effective referrals for people with psychosis and coexisting substance misuse. In addition, information regarding mental illness was mentioned as necessary to circulate to the police:

'…if you're struggling with a substance misuse problem you'd be better off in, in the criminal justice system. People say that their lives have been saved by being put in the criminal justice system being forced to come off the drugs and then given help to stay off. And I have to tell you that at the moment there's no, no plan to, to give that kind of care to, to people in my trust [NHS].'

'….if they realise that somebody is, you know, is not particularly a drunk, that there's something underlying with that person as well, mental health issues I think a mental health team should be available, a crisis team of some sort should be available to help that person while they're at in police custody, yeah. I never had any of that and so you can't, you haven't got access to your medication, you're off your medication, that's only going to make you worse. '

'Like my son, the policeman came, he was so rough on him, you know although he has mental problem. The police are not trained. The police don't know what

is mental health…if every community would work with the law enforcement, hand in hand, things might get better…'

4.5.5 Support and services for people with psychosis and coexisting substance misuse

In the online accounts, people with psychosis and coexisting substance misuse frequently highlighted the positive and negative aspects of their support networks, be it personal social networks, peers accessed through mutual support groups, or mental health services. Many participants described how their social networks facilitated or impinged on accessing care or treatment.

Positive and negative social support networks

One theme that emerged was how a lack of social support, or a social network that was based around substance misuse, hindered recovery:

'I had nobody there to help me with this '.

'I also remember having friends who really weren't my friends if I had booze or drugs they were always there, if I had nothing or tried to quit they were always gone. It really hurt to find out who were your real friends'.

However, having positive social support networks actively encouraged recovery:

'I have the encouragement and support of my wife even though we are planning to separate in the near future…I also have a very close...friend, and although he doesn't understand bi-polar disorder, he has been very supportive. He makes sure that I get out of the house at least three times a week.'

'The care and loving doesn't come from professionals. They haven't got time to hug me and kiss me and tell me how much they love me, and give me sweet things, chocolate to eat. That comes from a different source that comes from your friends, it comes from your family, it comes from the community. It comes from your spouse, your husband, your boyfriend and that happens after you've finished the day time treatment. So I think that is what the other thing is. The care and loving that we need.'

The impact of key workers

Another theme that emerged from the online accounts was the helpfulness of particular key workers in addressing both the psychosis and the substance misuse, acting as a positive role model and supporter, helping to encourage recovery, and referring the patient to useful community services. A key worker typically made the patient feel cared for and increased their motivation to get involved in social activities. Key workers were people to whom service users could go for help, who were separate from their personal support network and their clinicians:

'I have great help from [my key worker] who I see once a week and I know that if I have a problem I can just pick up the phone and, you know, as long as it's within working hours he's here.'

'Because he did say to me, "The first time I met you..you were seriously ill.. mentally," and he said, "The, the improvement over time has been great." And I said.. "[money adviser] that is partly because .. you've took a lot of my burden..and let me concentrate on getting better in myself.. putting apart that, the worry of all of that.'

'But just that small group it makes you feel like you're being cared about and cared for and [my key worker] does a great job with that I think.. He can be a pest at times making sure that you, I've got to go out with him, "Come on you're coming for a cup of coffee," that's only to get, make sure that I'm getting out.'

4.5.6 Experience of treatment

Due to the nature of treating both psychosis and substance misuse simultaneously, treatment for the dually diagnosed is complex and often managed across multiple services. Many online accounts highlighted experience of medication, the need for specific attributes in a therapist or mental health services, and the beneficial nature of mutual support groups addressing both of their illnesses. They also expressed the opinion that services and treatment were often disconnected.

Interactions with healthcare professionals

There were many reports within the online accounts of interactions with healthcare professionals. Some service users lacked confidence and trust in their healthcare professional:

'And the GP, oh they have no clue about mental illness. If you go to them about any major problem, they look into the book, any tablets they can give you.'

'I would get very frustrated with what I felt was incompetence and ineptitude by my doctors. I did not feel that they were listening to me nor were they willing to make medication changes when my current mix of medications did not seem to be stopping my cycling. I had three doctors within that year, until I found my current doctor, who I am finally comfortable with.'

'I've seen different psychiatrists but to me they always feel, they, it's always felt like they're sitting on a pedestal… and I'm just there as part of their job really'.

'So the important thing is they listen to what people are saying, especially the people who have the illness…But they don't listen to them. They just make presumptions. Because of the label of they have been given. They look at a label. "He's paranoid schizophrenic. So we put him in that category, he must be

saying this." Not necessarily. Things can change. Actually listen to what he's saying. Look at what he does. Look at his care plan. And listen … And now people are beginning to listen to me and that is what makes me feel good.'

There was a feeling among service users of having to conceal certain issues or disclose specific aspects of their illness in order to comply with their healthcare professional:

'….make it clear that you believe what they say, very clearly that you believe what they say because if you show or hint that you don't believe what they say then that's, then you've undermined your own authority in their eyes and therefore that makes the repair process a lot, a lot more difficult and a lot more long term.'

However some service users understood the pressures facing healthcare professionals:

'They've got loads to cope with. It's not their fault. Most of these things, people have a go about their consultant and the doctor. It's not their fault why these things are happening. It's the way the system is.'

Others highlighted the positive aspects of their healthcare professionals, such as how their doctor helped them achieve insight into their illnesses:

'I began to work with a new doctor, and when I told him about my continued marijuana smoking, he stated simply, "Do you know marijuana is bad for your mental health?" It was a non-judgmental statement. But, somehow it reverberated in me. I do not believe he judged me as good or bad for the choices I was making, but he just wanted to empower me by allowing me insight into what I was doing to myself. '

Self-help

Self-help groups, particularly in the online accounts from the US, emerged as a beneficial treatment option where people could openly discuss both their psychosis and substance misuse. Mutual support enabled patients to relate to someone with similar diagnoses and experiences, as well as to develop a positive social network outside of the formal group sessions. It was strongly emphasised that the support group should be focused on both illnesses, as one targeting only the substance misuse led to frustration for those who wished for their mental illness to be simultaneously addressed:

'I lost the zeal for AA several years ago because they didn't understand my bipolar condition. They felt meetings, a sponsor, and the big book along with a spiritual program were all you needed to obtain good sobriety. '

'Dual Recovery Anonymous helps keep my whole self together so I have a

chance to hope, cope and heal from the impact a dual disorder has had on my life'.

'The people at the meeting really made an impression on me. I could tell they were sincere and serious about what they were doing, and they said they used to be like me until they started working this honest program. They were practical and realistic, yet had uncommon sense, They were humble and unselfish, and I wanted to be as much like them as possible. I wanted what they had.'

'I was not compliant with good mental health practices...I refused psychiatric medication, assuring myself that increased effort to work the 12 Steps would restore me to sanity... Later I would learn that my sobriety program would restore me to sanity from addiction and not my total mental health, but it went a long way in improving my quality of life.'

'I met my third husband at my sponsor's house. He is also bipolar, and because we have worked through stabilizing his medication, then mine… we have learned why people in dual recovery need each other… '

'I think joining a group is a big help. You'll find that you make friends, you make the odd friend here and there and it's up to you if you want to continue the friendship outside which we have done with our, when we had our black and ethnic group going here we all made friends and we all had each other's telephone numbers and we'd go out independently as well.'

'My group has been a godsend... I get so much from my brothers and sisters in DRA [Dual Recovery Anonymous]... love, support, encouragement and finally, a sense of belonging. . . . I have DRA to treat my dual illnesses as a whole, rather than a part here, and a part there.

'People show up at our meeting that I have never seen at the social club where it's held. They say how happy they are that they have somewhere to go, and they share their experience, strength and hope without reserve. They ask questions, and they hang around for awhile to yak and drink coffee. And we don't feel alone anymore. They come back the next week.'

'So when you do start recognising your symptoms hopefully there will be somebody there, on the other end of a phone or perhaps a group you can go, even if it's just another mental health, mentally challenged person like yourself and sometimes they're better than the professionals I'm telling you, and give you better advice...'

Resistance or ambivalence towards medication

One of the most prominent themes that emerged from all the online accounts was a strong opinion about medication regimes for psychosis. Feelings towards medication were typically ambivalent, and side effects often

outweighed the positive aspects of medication in managing symptoms. In some cases, medication had a debilitating effect and was not allowing the service user to engage in other activities in their daily life (for example, holding down a job, staying awake).

Some online accounts highlighted the problematic nature of increasing and changing doses, and how this resulted in them stopping their medication altogether, or relapsing:

> *'I was seeing a psychiatrist once a week and slowly I felt like my life was getting better. However the medication did not continue to work. So my doctors just put the dose up each time they saw me. I was incredibly frustrated with this and decided that I would take myself off all the medication and do it my own way.'*

> *'Medications would only work for short periods of time, then we would have to increase dosages until we reached maximums, then we would have to search for something new. It was so frustrating for me, and I would often lose hope of ever feeling better.'*

> *'However, my dosage kept increasing…even at such a high dosage, the medication was not showing up in my system so the doctors dropped me off the medication out of concern. Again, I started drinking.'*

Others were concerned about the side effects of their medication:

> *'Well, lithium turned me into an emotionless zombie. I think they just had me on too high of a dose, but I wasn't about to live my life that way, so I stopped taking it. Of course, I went back on a manic high right away. '*

> *'I went back to the doctors and they started me on new meds. I was exhausted by fatigue as a side effect of meds. I couldn't hold a job.'*

> *'… most of the time you just try and dodge your medication anyway, everybody did it if they could.'*

> *'I was in a bit of a fog with all this sedating medications so I started reducing it with out telling the doctors.'*

> *'I soon stopped taking my prescribed medication preferring to self-medicate with substances that had euphoric side effects instead of the lethargy, dry mouth, impotence, and muscle spasms of the legitimate drugs.'*

However several online accounts expressed more positive views towards medication:

> *'Coming off my meds the second i felt better..then crashing...back on my meds again..then crashing lower..it was a vicious cycle. I met my disability counselor*

and she explained to me everytime I came off my meds and I dropped to a new low it was that much harder for the medication to bring me back to the original me...that scared me I didn't want to lose me forever..so I have been faithfully taking my meds for over a year!'

'Once I started taking medication for my bipolar disease, I became balanced; my mood swings were less severe. Medication management is critical for me, because any fluctuation of time or dosage can affect the purpose of the medication.'

Some patients, who were initially compliant with their medication regime, gradually stopped taking their medication without consulting anyone once they felt better, which led to relapse:

'For over a year I was taking my medication faithfully and feeling balanced and 'normal'. As with substance abuse, 'stinking thinking' started to set in, for my mental illness. I believed that I was 'well', so I slowly stopped taking my meds.'

'… however I started to believe that I did not need to continue taking my medication because I was feeling so much better. So I stopped it all together. Life retuned to the rollercoaster.'

4.5.7 Experience of recovery

Many online accounts were positive about the future in terms of recovery and learning how to cope with their mental illness as well as maintaining abstinence from substances. The majority of the accounts expressing feelings about their recovery mentioned the tumultuous journey and the need to recognise recovery as a constant yet manageable and rewarding struggle:

'Life does get better and it is an enabling disability…a sort of a perceptual thing that never leaves you. But it is actually a gift if you can learn about it and manage it and get the best out of yourself. I mean it's no different from what anybody else is trying to do is get the best out of ourselves aren't we so, you know, it's pretty good.'

'I still take each day as it comes. I'm always prepared for a relapse; even though I have five years 'under my belt' of being relatively 'episode free,' I'm always on alert.'

'I still experience peaks and valleys, but now the cycles aren't so great or frequent, and they are more manageable. I know that experience teaches expertise, help and hope replace helplessness and hopelessness, and weaknesses turn around to become strengths.'

'Now, after a few years.....some med changes and a lot of work. I AM getting better! I can see the light at the end of the tunnel! I know that I have to work

everyday to deal with my illness and I will always have to be diligent with my meds. But, I also know that I can feel better...'

'With thanks to the Doctor's I have seen since, my condition, though present, is understandable now. I have greatly controlled the symptoms I have experienced. Gone are the days of binge drinking and marital infidelity. I have settled into the life of being a simple person, who get's great pleasure out of all the little things in life, while coping with my disability at the same time.'

4.5.8 Carers' perspective of services

Many carers' held strong views on the efficacy of mental health services for people with psychosis and coexisting substance misuse. There were obvious differences between engagement in services in the US versus the UK. Carers perceived that US services outside of mental health care (e.g. the police), had a better understanding of mental health care than in the UK. Others drew on the lack of communication between services in the UK. Carers perceived mental health professionals as most effective when they spent a significant amount of time with not only the patient, but the carer as well, allowing for questions to be asked about treatment and medication regimes:

'I can go in there and the patient and the parent, and there will be a head nurse or a psychiatrist or somebody there to organise the meeting. And my son can say anything to me and I can give a good, -and I can answer him back. Then a psychiatrist will say, -will tell my son he is wrong or I am wrong or something like that, you know. A friendly, -this thing. And to me, that is very, very helpful, because sometimes -you don't say things in anger, things go better. My son has his view, I have my view, or my son wants something, I will say, "I will try my best to do it". And that is very helpful.'

Others expressed concern about the discontinuity of care, for example in the transition to adult services:

'…he was eighteen…and CAMHS needed to get rid of him, but he wasn't having any of it. We had no idea that such a schism existed within the services and had assumed there would be a thread of continuity…his CAMHS doctor is a saint. But he is an overworked and under-resourced saint and he hung on to him as long as he could.'

'The day after their eighteenth birthday they are adults and you are expected to be carers. But carers whose motives are suddenly viewed with suspicion. Carers whose agenda it is automatically opposed to theirs. You are part of the problem. You have to play by confidentiality rules and observe their conventions of procedure.'

Some carers felt neglected by services, feeling that they received inadequate information about their family member's illness:

'No-one told us what to expect or how to deal with anything...on a day-to-day basis; the services; medication; relapses; claiming our rightful benefits; Nothing!'

Carers emphasised the impact of coping with their family member's illness and substance use problems on their own. Many carers provided insight into experiences and offered advice on coping and caring for someone with both illnesses:

'Mental health needs to be handled with care and support. You have to put yourself into that person's shoes- if you are this person how would your family feel...'

'Learning all you can is a vital part. His mood swings have many times made me want to say I give up…this isn't worth it. After I learned, and still learning each day, all that I can about bipolar disorder I now know and have some idea of what I should expect and how to handle those things.'

Several online accounts highlighted the importance of having the right accommodation for people with psychosis and coexisting substance misuse:

'Along with non-compliance with medication regimes and continued substance abuse, inappropriate accommodation would seem to be one of the most common causes of relapse, including remaining too long with parent/carers.'

'Whilst there are some excellent models of supported accommodation, a huge percentage of options offer very little or no proper support, most especially if there are no family carers in the background. Service users are left vulnerable to a financially motivated system, overseen by under-resourced, underfunded and under-informed social workers, trained to feed them into what has become a multi-billion pound industry, regardless of consequences.'

4.5.9 Summary of the qualitative analysis of the online accounts

The online accounts highlighted the effect of substance use on psychiatric symptoms, and how many people hide their symptoms from others around them. Self-medication was frequently cited as a reason to use substances, as a way to manage or normalise psychiatric symptoms. The accounts illustrated the cycle of increased symptomatology and escalating substance use.

The theme of social networks also ran through all of the online accounts, especially in highlighting how influential positive support can be in promoting change and optimism in the life of someone who has psychosis and coexisting substance misuse. This social support could come in the form of a carer, a key worker or advocate, or formal support through a self-help group. A number of people commented that the relationship between patient and therapist is of prime importance.

Discontinuity of care and lack of coordination between services was also a prominent theme emerging from the accounts. A few highlighted how police and criminal justice systems could have increased awareness about mental health, and promote more coordination and integration between services.

Having a psychiatric diagnosis was often viewed as stigmatising and resulted in the service user concealing problems and symptoms from others. Many people expressed that they felt discriminated against because of their diagnosis.

When accessing services, those from BME groups emphasised that it was difficult for minorities to express their views, and many were reluctant to approach their GP for help. Lack of information from healthcare professionals is a barrier to coming to a full understanding of psychosis and its interaction with substance misuse, the range of treatments available and the role of services.

There were varied views about healthcare professionals emerging from the online accounts, and the main area of criticism concerned contact with the GP and maintaining a therapeutic relationship with a healthcare professional. A number expressed negative views, such as the healthcare professional being too brief and uninterested in the service user. Others felt that they had to conceal information from staff, and generally expressed a lack of confidence and trust in their healthcare practitioners. Conversely, positive interactions with healthcare professionals led to greater insight and facilitated readiness to change.

Another overarching theme emerging from the online accounts was a strong opinion about medication for psychiatric illness. There were mixed reports regarding medication; ambivalence and resistance towards medication were frequently cited due to side effects and other factors, and some people abruptly discontinued their medication once they felt better. Self-help groups (such as Dual Recovery Anonymous) were cited as beneficial in promoting change and ongoing support.

The impact of psychosis and coexisting substance misuse on carers was a prolific theme. Some people remarked on the change of roles that occurred as a result of one person having a diagnosis psychosis and coexisting substance misuse. Many people also commented on the supportive nature of family members and carers.

Lastly, several online accounts explained the process of recovery, and express optimism and hope for the future, stemming from ongoing support from their social networks, medication and treatment, and readiness to change.

4.6 OVERALL SUMMARY

Twenty-one studies were reviewed in the narrative synthesis of the qualitative literature and 48 testimonies from seven websites were analysed in the qualitative analysis (of the websites four were UK-based and three were US-based). Many of the same themes merged from both the qualitative literature and the online accounts. Table 8 provides a list of the themes emerging from both sources of evidence.

Table 8. List of themes emerging from the qualitative analysis and the narrative synthesis of the qualitative literature

	Qualitative (thematic) analysis of online accounts	Narrative synthesis of the qualitative literature
Reasons for substance use	✓	✓
Feelings of stigma	✓	✓
Socioeconomic status as a barrier to accessing treatment	x	✓
Culture or ethnicity as a barrier to accessing treatment	✓	✓
Gender-specific barriers to care	x	✓
The importance of a comprehensive assessment and referral	x	✓
Importance of social networks	✓	✓
Positive aspects of employment		✓
Difficulty accessing and engaging in services	✓	✓
Ambivalence towards medication	✓	✓
Medication compliance and effects	✓	✓
Utility of mutual help and self-help groups	✓	✓

The literature review of qualitative studies and the qualitative analysis of online accounts revealed that many people used substances (the most common of which were alcohol, cannabis and cocaine) in an effort to control their psychiatric symptoms, such as mania or depression, although substance use was often reported as exacerbating psychotic episodes. Additional reasons for substance use with coexisting psychosis included the social benefits. Being aware of the reasons for substance misuse is important in contributing to an understanding of the relationship between psychosis and substance misuse, and how staff can better identity and help maintain positive change.

Stigma was discussed in the qualitative analysis as well as in the literature review. Those with psychosis and coexisting substance misuse concealed their feelings and thoughts, which was a barrier to getting help or support. The literature showed that few people with psychosis and coexisting substance misuse seek help until they have had a serious psychotic episode or have hit

'rock bottom'. When people do present to services, typically one of their coexisting illnesses is treated while the other problem is left untreated. Furthermore, carers from BME groups of all socioeconomic statuses were difficult to engage in services, therefore more attention should be given to engaging this carer group and population in treatment (for example, through the provision of culturally-specific community groups). Families with a higher socioeconomic status had adequate support networks and did engage more frequently in treatment, but could benefit from more support groups with a focus on recovery for both psychosis and substance misuse.

Moreover, healthcare professionals in both mental health and substance misuse services could have benefitted from having more cultural sensitivity and awareness towards the linkages between culture and substance use, and provide culturally-specific services for BME groups presenting with psychosis and coexisting substance misuse. Evidence from the Warfa (2006) study showed that BME groups were heavily accessing culturally-tailored programmes in the UK.

Women felt additional internal stigma due to alcohol misuse being perceived largely as a male problem. They reacted positively to healthcare professionals who employed an empathic, non-judgemental approach, but were critical of a lack of childcare opportunities and rigid treatment programmes that did not allow for flexible timing to enable women to enter treatment and care for their family. Treatment could potentially be adjusted or more flexible treatment times could be provided in order to account for this.

Both the literature and the online accounts highlighted the perceived lack of coordination and communication between services (mental health and substance use). It is important to take these findings into account and ensure a better continuity of care. Having a key worker was frequently cited in both the literature and the online accounts as providing objective support to the service user and being beneficial for facilitating recovery and referring the person on to appropriate services.

One study highlighted the need for a comprehensive assessment to properly diagnose both the psychosis and coexisting substance misuse so that the person could be referred to appropriate services, and the need to provide a more integrated treatment where the coexisting disorders can be treated concurrently. A comprehensive assessment improves professionals' understanding of the role of substance misuse in a patient's life and provides insight into their lifestyle and social circumstances. This increases the possibility of providing effective, tailored treatment and support suited to the service user. Healthcare professionals should work collaboratively with people to agree a structured support plan and encourage and motivate patients with psychosis and coexisting substance misuse to engage in treatment. A non-judgmental attitude that will engender trust in their patients

is crucial. Integrating treatment and referrals are important in establishing a therapeutic relationship with the patient, together with continuity care. The positive aspects and benefits of a therapeutic relationship both in a treatment setting and in assessment procedures were cited frequently.

The need for more information about psychosis and substance misuse (as well as the relationship between the two) with regards to treatment modalities and options, and medication regimes were mentioned consistently in the literature and the online accounts. Lack of accessible information may be particular issue for people from BME groups, as well as for carers.

Social networks emerged as prominent theme in both the literature and the the online accounts. Positive social networks were seen as helping to promote long-term recovery and maintaining positive change, whereas negative social networks pressured people to use substances, exacerbated mental illness and encouraged relapse.

Employment and positive social activities in addition to standard treatment can help prevent relapse from substance use disorders occurring from boredom or re-engagement with substance using social networks. Employment promotes empowerment in this population, as do social activities that promote autonomy and independence.

Both reviews highlight the importance of mutual support and self-help groups so that people with psychosis and coexisting substance misuse can connect, communicate, and interact with those with similar complex needs and experiences. The literature and online accounts had a prominent theme of ambivalence and resistance towards medication regimens, due to side effects or the perceived irrelevance of drug treatment. Many cease taking their medication, leading them to relapse and causing their psychiatric symptoms to return. In order to control the onset of psychiatric symptoms, people self-medicate with more substance use, perpetuating the cycle. This results in more hospitalisations and treatment, therefore an effort should be made to promote adherence to medication, including providing as much information as possible about medication regimes to individuals and carers, and to ensure medication monitoring and follow-up.

In the literature as well as in the online accounts, one prominent issue which emerged for carers of people with psychosis and coexisting substance misuse was a feeling of being neglected by mental health services. More attention should be paid to carers in the care plan. There should be opportunities for carers to ask questions and information about medication and treatment should be provided. Where possible carers should be encouraged to participate in family support groups so that they can share their experiences.

Limitations

There are some limitations to the qualitative analysis and qualitative review of people's experience of psychosis and coexisting substance misuse in this guideline. First, the illustrative and retrospective nature of the online accounts must be taken into account. Furthermore a large proportion of these accounts were from the United States and treatment modalities or processes may differ or not be accessible in the UK. Second, treatments other than medication (for example, certain psychological interventions, alternative treatments) did not emerge as themes as expected. Thirdly, only certain substances were mentioned as substances of misuse in the literature and the online accounts (for example, cannabis and alcohol), whereas other substances were not mentioned frequently, or at all (for example, hallucinogens or heroin). Lastly, many of the sample sizes in the qualitative research studies were small, which limits the ability to generalise the results to a wider UK population. Despite these limitations, a number of themes were identified than ran through both sources of evidence.

4.7 FROM EVIDENCE TO RECOMMENDATIONS

Both the narrative synthesis of the qualitative literature and the qualitative analysis of the online accounts revealed overlapping and similar themes. Both forms of evidence highlight the value of gathering information about service user experience of psychosis and coexisting substance misuse. The qualitative evidence can therefore further inform the quantitative evidence in making stronger recommendations for improving the experience of service users and their carers. Though qualitative research is largely subjective due to its narrative nature and aimed at a specific population that may not generalise widely to the UK population, a number of themes were identified that ran through both sources of evidence.

Although highlighted in the website testimonies and the narrative synthesis of the qualitative studies, the GDG additionally discussed the importance of having an advocate or key worker to provide ongoing support and ensure coordination between services. It was also established within the group by consensus, that a positive therapeutic relationship between the healthcare practitioner and the service user is important in facilitating service user engagement in services and treatment and promoting change. The evidence reviewed here supports these discussions.

The evidence from both the narrative synthesis of the qualitative literature and the qualitative analysis of the online accounts suggests that those with psychosis and coexisting substance misuse should be provided information regarding comprehensive assessment, treatment decisions and options, and aftercare. This issue is important for carers as well, as many felt neglected by services and could benefit from more inclusion in the treatment progress and be provided with more information, if the service user agrees. Healthcare professionals could also provide information could about carer support groups and voluntary organisations, including those for psychosis and

substance misuse, and help families or carers to access these, as many carers felt that they would have benefited from support from other carers with similar circumstances.

Furthermore, the literature and the online accounts highlighted that healthcare professionals should be culturally competent and able to take account of the service user's cultural or ethnic background when providing information and treatment. Information about voluntary organisations and support groups in the community which may be culturally specific could benefit both service users and carers and facilitate treatment access and engagement.

4.8 CLINICAL PRACTICE RECOMMENDATIONS

4.8.1 Recommendations

Working with adults and young people with psychosis and coexisting substance misuse

4.8.1.1 When working with adults and young people with known or suspected psychosis and coexisting substance misuse, take time to engage the person from the start, and build a respectful, trusting, non-judgmental relationship in an atmosphere of hope and optimism. Be direct in your communications, use a flexible and motivational approach, and take into account that:

- stigma and discrimination are associated with both psychosis and substance misuse
- some people will try to conceal either one or both of their conditions
- many people with psychosis and coexisting substance misuse fear being detained or imprisoned, being given psychiatric medication forcibly or having their children taken into care, and some fear that they may be 'mad'.

4.8.1.2 When working with adults and young people with known or suspected psychosis and coexisting substance misuse:

- ensure that discussions take place in settings in which confidentiality, privacy and dignity can be maintained
- avoid clinical language without adequate explanation
- provide independent interpreters (who are not related to the person) if needed
- aim to preserve continuity of care and minimise changes of key workers in order to foster a therapeutic relationship.

Race and culture

4.8.1.3 Healthcare professionals working with adults and young people with psychosis and coexisting substance misuse should ensure that they are competent to engage, assess, and negotiate with service users and their carers from diverse cultural and ethnic backgrounds.

4.8.1.4 Work with local black and minority ethnic organisations and groups to help support and engage adults and young people with psychosis and coexisting substance misuse. Offer organisations and groups information and training about how to recognise psychosis with coexisting substance misuse and access treatment and care locally.

Providing information

4.8.1.5 Offer written and verbal information for adults and young people with psychosis and coexisting substance misuse appropriate to their level of understanding about the nature and treatment of both their psychosis and substance misuse. Written information should be available in the appropriate language or, for those who cannot understand written text, in an accessible format (audio or video).

4.8.1.6 All healthcare professionals in primary, secondary or specialist substance misuse services working with adults and young people with psychosis should offer information and advice about the risks associated with substance misuse and the negative impact that it can have on the experience and management of psychosis.

Working with and supporting families and carers

4.8.1.7 Encourage families, carers, significant others and advocates to be involved in the treatment of adults and young people with psychosis and coexisting substance misuse to help support treatment and care and promote recovery.

4.8.1.8 When families, carers or significant others live, or are in close contact, with the person with psychosis and coexisting substance misuse, offer family interventions as recommended in 'Schizophrenia: core interventions in the treatment and management of schizophrenia in adults in primary and secondary care' (NICE clinical guideline 82).

4.8.1.9 When families, carers or significant others are involved in supporting the person with psychosis and coexisting substance misuse, discuss any concerns about the impact of these conditions on them and other family members.

4.8.1.10 Offer families, carers or significant others a carer's assessment of their caring, physical, social, and mental health needs. Where needs are identified, develop a care plan for the carer.

4.8.1.11 Offer written and verbal information to the family member, carer or significant other appropriate to their level of understanding about the nature and treatment of psychosis and substance misuse, including how they can help to support the person. Written information should be available in the appropriate language or, for those who cannot understand written text, in an accessible format (audio or video).

4.8.1.12 Offer information to families, carers or significant others about local family or carer support groups and voluntary organisations, including those for psychosis and for substance misuse, and help families or carers to access these.

4.8.1.13 Negotiate confidentiality and sharing of information between the person with psychosis and coexisting substance misuse and their family, carer or significant other.

4.8.1.14 Ensure the needs of young carers or dependent adults of the person with psychosis and coexisting substance misuse are assessed. Initiate safeguarding procedures where appropriate (see recommendations 5.8.1.23 - 5.8.1.25).

Consent, capacity and treatment decisions

4.8.1.15 Before undertaking any investigations for substance misuse, and before each treatment decision is taken:

- provide service users and carers with full information appropriate to their needs about psychosis and substance misuse and the management of both conditions, to ensure informed consent
- understand and apply the principles underpinning the Mental Capacity Act (2005), and be aware that mental capacity is decision-specific (that is, if there is doubt about mental capacity, assessment of mental capacity should be made in relation to each decision)
- be able to assess mental capacity using the test set out in the Mental Capacity Act (2005).

These principles should apply whether or not people are being detained or treated under the Mental Health Act (2007).

Advance decisions and statements

4.8.1.16 Develop advance decisions and advance statements in collaboration with adults with psychosis and coexisting substance misuse, especially if their condition is severe and they have been treated under the Mental Health Act (2007). Record the decisions and statements and include copies in the care plan in primary and secondary care. Give copies to the person, their care coordinator, and their carer if the person agrees.

4.8.1.17 Take advance decisions and advance statements into account in accordance with the Mental Capacity Act (2005). Although decisions can be overridden using the Mental Health Act (2007), try to honour advance decisions and statements wherever possible.

5 ASSESSMENT AND CARE PATHWAYS

5.1 INTRODUCTION

During early stages of the development of this guideline, it was established that there is a paucity of evidence relating to the effectiveness of different service configurations and clinical pathways for delivering interventions specifically for people with psychosis and coexisting substance misuse. The GDG therefore developed, through expert consensus, a care pathway likely to complement coordinated, well managed treatment (for further information about the methods used in this chapter, please see Chapter 3, section 3.5.6). The pathway is summarised in Figure 3. Chapter 9 includes a companion care pathway for young people.

The traditional problem in dealing with this group of people has been the disparity between clinical models used in different parts of the care system, particularly between addiction/substance misuse specialities and the mainstream mental health services. This has been compounded by the two services being funded and commissioned separately, and variation and confusion over which service holds clinical responsibility for people with differing relative severities of each single condition. This has, at worst, led to the exclusion of individuals with a coexisting disorder from both treatment systems, or more often, led to variable access and then attempts at parallel or sequential treatment which may become disjointed and where accountability and governance is dispersed.

Models of care for treatment of adult drug misusers: update 2006 (National Treatment Agency for Substance Misuse, 2006), gives a workable definition of a care pathway and the required components to be articulated: 'An integrated care pathway (ICP) describes the nature and anticipated course of treatment for a particular client and a predetermined plan of treatment. A system of care should be dynamic and able to respond to changing individual needs over time. It should also be able to provide access to a range of services and interventions that meet an individual's needs in a comprehensive way.' The pathway therefore seeks to standardise the steps taken through access, assessment, treatment and discharge as well as provide guidance points for the thresholds and relationships between different treatment teams and services. Care pathways have been developed for drug misuse and for schizophrenia and bipolar disorder within the respective NICE guidelines (NCCMH, 2008a; NCCMH, 2008b; NCCMH, 2010; NCCMH, 2006).

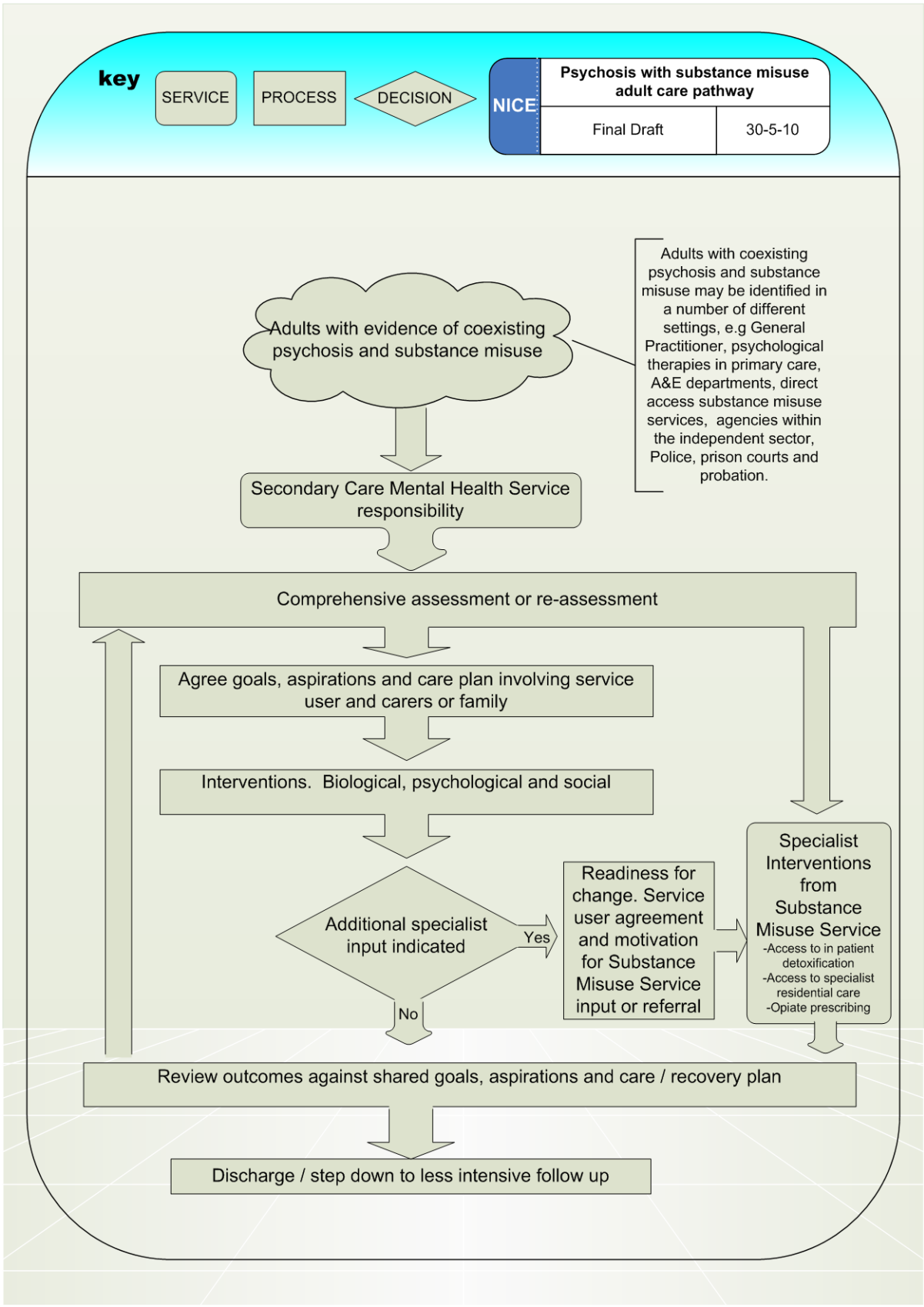

Figure 3: Care pathway for people with psychosis and coexisting substance misuse.

Both the text and Figure 3 are designed to be illustrative and offer some broad principles and direction, rather than to be prescriptive. They are sufficiently broad to take into account local context on the availability of services, individual need, and clinical discretion whilst providing a framework based on expert consensus.

5.2 PRINCIPLES UNDERPINNING CARE PATHWAYS

5.2.1 Access to mainstream services

People with a psychosis and coexisting substance misuse deserve access to good quality, patient focused, and coordinated care (Department of Health, 2002). The key message in the Department of Health guidance is that mainstream mental health services take responsibility for addressing the needs of people with a psychosis and substance misuse, drawing on support from substance misuse services. The rationale for this is that "substance misuse is usual rather than exceptional among people with severe mental health problems".

Locally agreed care pathways need to be explicit so that responsibilities are clear, and services for people with psychosis and coexisting substance misuse are delivered within mainstream mental health services with specialist support. In addition, mechanisms for resolving disagreements about team responsibility and specialist input for individuals need to be in place, such as regular care pathway meetings with executive powers.

5.2.2 Right care at the right intensity

Effective team working draws upon specialist skills and knowledge from within the team complemented by care pathways allowing access to further step up or step down resources ensuring that complexity is managed at the right intensity of care and that support for staff is maintained. The quadrant model (Department of Health, 2002) offers a tool for titrating the likely intensity of care and service involvement required based on the assessed relative severity of mental illness and substance misuse. Individuals who score high on both counts of need (for example, unstable schizophrenia with substance dependency) would therefore be candidates for coordinated specialist care for people with psychosis and coexisting substance misuse where available, or care from the mental health team with input from substance misuse services where required. Similarly a dependent drinker with moderate depressive symptoms would more likely be managed by substance misuse services and primary care services. The GDG decided however that we could not simply plot the service provision against the need identified by each quadrant as the provision of services varies by locality and the evidence for integrated services compared to shared care is not robust.

5.2.3 Skills and competencies

Skills and competencies for working with people with psychosis and coexisting substance misuse need to be developed through training and supervision to match demand. Suitable frameworks exist for developing skills at core, generalist and specialist levels depending on the type of staff and exposure to individuals with psychosis and coexisting substance misuse (Hughes, 2006). For example, staff working in psychiatric inpatient settings, early intervention for psychosis teams and assertive outreach teams are likely to have high exposure. The competencies encompass values and attitudes, knowledge and skills, and practice development. Chapter 6 (6.2.5) however reviews the gaps in evidence for the effectiveness of training staff in psychosis and coexisting substance misuse.

5.2.4 Choice

While at times people may struggle to make informed choices about their care and treatment options, it is good practice to promote shared decision making using the assumption of competency unless assessed otherwise. Even where capacity may be limited, the active involvement of family and carers can reinforce messages from services about personal responsibility and consideration of the impact the individual's choices have upon themselves and others. Motivation and stage of readiness for change concerning substance misuse behaviour are key points determining routes on the care pathway. Sustained change comes about from engaging in a constructive alliance with the individual where the individual is supported in working through the stages of change without losing their sense of capability and self-direction towards shared goals.

5.3 PRIMARY CARE

5.3.1 Identification and assessment

For this care pathway, primary care refers to general practice, accident and emergency departments and psychological therapy services in primary care. Services are generalist, office or department based, and offer limited intensity and frequency of contact. GPs are commonly the first resource that worried individuals or families will choose to consult and they often have a long-term perspective and relationship with people and families on their list. Frequent consultations with apparently minor ailments may signal underlying issues individuals are reluctant to disclose and the GP's task is to elicit these hidden concerns. GPs and other primary care services play a key role in early identification and appropriate referral with full assessment of psychosis and harmful substance misuse taking place in secondary care mental health or addictions services.

Initial assessment in primary care

Ziedonis and Brady (1997) suggested that primary care professionals should always maintain a high index of suspicion for either substance misuse in people with psychosis, or mental illness in people who misuse substances. These authors go on to suggest that when psychosis or substance misuse is detected, initial assessment for the other disorder should always take place and the findings included in referrals for secondary assessment. Alertness to and assessment for signs of current intoxication is particularly pertinent in presentations to accident and emergency departments.

It is important for primary care practitioners to suspect and exclude physical causes for presenting symptoms, including acute intoxication, withdrawal, and side effects from medications.

Primary care also plays a role in screening for physical co-morbidities which have a high rate of incidence in individuals with substance misuse and psychosis, including liver damage, blood borne viruses, cognitive changes, and nutritional deficiencies, particularly where dependent drinking and injecting drug use is suspected.

Further assessment in primary care

Primary care practitioners may see individuals over a period of time and may hear the concerns of family and friends. They are therefore in an ideal position to detect the insidious decline in functioning which may be the premonitory signs of a psychotic illness. Substance misuse may present with very similar symptoms, and it is the GP's task to establish the duration and extent of drug misuse in relation to the onset of symptoms. For example, a patient may describe increasing consumption of alcohol to the point where it takes priority over other activities and results in a shortage of money, self-neglect and social withdrawal. This may clearly be distinguished from an individual who describes hearing voices and withdraws from social contact due to paranoid beliefs about others, but has a few drinks in order to sleep.

It will usually be helpful to make an assessment of the individual's social support networks of family, friends, occupation and the degree to which the individual's networks are predicated around drinking or drug use activities. Carers may also need an assessment of their needs.

Where significant substance use is detected in primary care, the practitioner will usually need to assess the extent to which this substance use is problematic to the individual and those they come into contact with, including children, and whether there is physical or psychological dependency on the substance.

5.3.2 Management

GPs or other primary care practitioners will normally refer a person with a first presentation of suspected psychosis for secondary assessment and not

attempt to treat symptoms except to manage crisis situations until a secondary care appointment can be obtained.

While individuals with a diagnosis of psychosis and substance misuse will normally be managed in secondary care, they remain patients of primary care and GP's may play a key role as a source of background information and may be the first to be aware of changes in individuals' physical and mental health as well as their social situations. Therefore, liaise closely with the secondary care team will be necessary, and efforts should normally be made to include primary care practitioners in CPA reviews.

People with psychosis are known to have poorer physical health than the average patient and thus will benefit from annual health checks, including monitoring of weight, blood pressure, cardiovascular risk (if indicated), respiratory symptoms and smoking cessation intervention. Regular blood test monitoring is indicated for some medications, such as lithium. These individuals will also need to be counselled regarding contraception and may need information on the safety of their medications in pregnancy.

The Department of Health in England and Wales has drawn up Primary Care Quality Outcomes Frameworks (QOF) (BMA & NHS Employers, 2009)[4] including for psychosis which detail minimum standards general practices should strive to achieve regarding the monitoring and care of these patients. The QOF for schizophrenia, bipolar disorder and other psychosis asks practices to keep a register of these patients and to record how many of them have had a review within the previous 15 months. This should evidence that the patient has been offered routine health promotion and prevention advice appropriate to their age, gender and health status. In addition, there are further indicators for the percentage of patients on lithium who have had their renal and thyroid function measured in the past 15 months and a therapeutic lithium level recorded in the past 6 months.

Primary care physicians may also need to provide information and support to carers, families and friends, and in particular they play a vital role in monitoring and assessing the welfare of any children involved.

5.3.3 Discharge back to primary care

People with psychosis and coexisting substance misuse may be discharged back to primary care when their secondary care team is satisfied that their psychotic illness is stable and their substance use has stopped or is stable at a level at which it is unlikely to affect their mental health. Indicators of relapse need to be agreed prior to discharge including contingency plans in place to cope with a crisis.

[4] Further information about QOF: http://www.qof.ic.nhs.uk/

The GP may need to see these individuals at least for annual review and more often if indicated. They may need to ask questions to elicit symptoms of relapse of psychosis as well as gain an accurate picture of the type and quantity of substances the individual is using and the stability of their lifestyles. Prescribing records may give an indication of these patients' adherence with their prescribed medication, and individuals should normally be asked about their adherence with medication and any side effects or other problems they may be experiencing with medicines. Changes to medications would not normally be made within Primary Care but GPs may liaise with secondary care staff to gain advice about changes thought necessary and if indicated the patient may be seen for a secondary care review.

5.4 SECONDARY CARE (GENERAL MENTAL HEALTH SERVICES)

5.4.1 Assessment

NICE Schizophrenia Clinical Guidance 82 (NCCMH, 2010) section 2.4, NICE Bipolar Disorder Clinical Guidance 38, section 4.4.4 (NICE, 2006) and NICE Drug Misuse Clinical Guidance 51 and 52 (NICE, 2008) sections 3.7 and 6.2 respectively outline good practice core areas for comprehensive assessment and assessment questionnaires and tools. These tools have not been validated for this specific population with psychosis and coexisting substance misuse, but by consensus, the GDG considers them suitable. Assessment is also introduced in 2.4 of this guidance together with DSM-IV and ICD-10 criteria for substance misuse and harmful use and dependence syndrome.

Assessment of substance use will normally be an integral component of mental health assessments. Some substances can trigger psychotic episodes (in use and/or withdrawal) and some can trigger relapse in pre-existing psychotic disorders. Evidence suggests that substance use is often inadequately assessed and therefore under-detected (Barnby *et al*., 2003; Noordsky *et al*., 2003), resulting in potential misdiagnosis and inappropriate treatment (Carey & Corriea, 1998). Even low levels of substance use by people with psychosis can worsen symptoms.

Expert advice and assessment from substance misuse services will normally need to be sought where the patient is complex and high risk, for example injecting opiate use and dependency, or substances less commonly encountered in general mental health services. Referral thresholds for advice and subsequent interventions from substance misuse services are described in section 5.5.1.

5.4.2 Engagement and sources of information

Regardless of the circumstances at first presentation, engaging the person and working towards establishing a collaborative, respectful, trusting relationship

is essential. This may require considerable sensitivity, flexibility and persistence on the part of the healthcare professional. The healthcare professional and service user may have differing views on the 'main problem', working with the person on what they see as the priority can provide a basis for working more collaboratively in the short term, and building on the relationship over the longer term.

Some people will have family members, partners or friends involved in their care. A similar collaborative relationship is also required with this support system. They can provide helpful information to contribute to the assessment process and may subsequently provide support with treatment.

Given the multiple needs of people with psychosis and substance misuse problems a range of other service providers may be involved or have knowledge of the person (for example, GP, accident and emergency staff, housing providers, probation staff, drug/alcohol services). As well as contributing to assessment, maintaining constructive relationships and information sharing will be essential in developing effective coordinated plans.

Confidentiality may be a particular concern for this population and their family or carers. For example, whether information about use of substances will negatively impact on treatment received, whether information about illegal activity will be passed on to the police, whether information about illness will be passed on to employers, or concerns about parenting abilities to Children and Families social services. Wherever possible the organisations' confidentiality policy should be explained at the outset. It is important to highlight that the agreed care plan is likely to involve working with other agencies and as such information sharing is an integral part of providing appropriate care. Consent to obtain and share such information should be sought at an early stage. Under some circumstances it will be necessary to break confidentiality and pass on information to relevant agencies (for example, where there is a risk to children, vulnerable adults, or others). Where possible, it will be necessary to make service user aware of the action being taken.

Reliable systems and protocols for ensuring the safety of staff in both outpatient and community setting will normally include avoidance of attempting to assess or deliver interventions to people whilst they are severely intoxicated. A non-confrontational approach with the service user will need to be taken to agreeing to rearrange the assessment on a future occasion.

Most assessment information is likely to be obtained by asking the person themselves unless they are floridly psychotic. Supporting self-report with observation is an important aspect of assessment and can be particularly so

when people are reluctant to engage with services or to disclose feelings, what they are experiencing, or details of their substance use and funding behaviour.

The GDG was concerned about the routine use of biological testing because of its potential to work against a collaborative approach. In typical healthcare settings a case by case approach set against a clearly explained rationale for care and treatment is preferred. NICE Drug Misuse Psychosocial Interventions Clinical Guidance 51 (NICE, 2007) states that "urine testing for the absence or presence of drugs is an important part of assessment and monitoring". The guidance notes that "routine screening for drug misuse is largely restricted in the UK to criminal justice settings, including police custody and prisons (Matrix Research and Consultancy & National Association for the Care and Rehabilitation of Offenders [NACRO], 2004); it is sparsely applied in health and social care settings."

The NICE Drug Misuse Psychosocial Interventions Clinical Guideline 51, section 6.2.1. provides a thorough review of biological testing, and drug misuse clinician rated and self-report identification questionnaires and their potential for identifying drug misuse in high risk populations for both adults and adolescents.

5.4.3 Components of assessment

Table 9 provides an overview of the assessment components for people suspected of experiencing psychosis and substance misuse (column 1) and key factors to consider when obtaining such information (column 2). This table is consistent with related NICE guidance detailed in 5.4.1.

Having drawn together information from the assessment some consideration of the relationship between mental health and substance misuse will be possible. Knowing when the person last used particular substances may be important in determining whether their current presentation could be related to substance use alone, or whether it is a contributory factor to an underlying psychotic presentation. However, it can be difficult to distinguish symptoms and effects of mental illness from the effects of the misused substances.

There has been a tendency to try to identify primary and secondary diagnosis however, even with careful history taking it can be impossible to disentangle symptoms, and it is recommended that both are considered primary and treated at the same time.

It is important to obtain a picture of the person's reasons for using substances and their understanding of the relationship between their substance use and mental health. For example, some individuals will believe that drinking alcohol lifts their low moods, while others will have insight into the fact that crack cocaine makes them more paranoid.

When a diagnosis has been reached it will normally be fully explained and discussed with the person and their family or carers subject to consent. Information about substance use, medications being prescribed, the interaction between prescribed medication and illicit/non-prescribed substances should also be discussed and written information offered.

Table 9: Assessment - Components and considerations

Assessment component	Key considerations
Current/recent substance use	• Which substances is the person using? (polysubstance use is common) • How much they are using? (this may be expressed as weight or cost) • How often they are using? • Route(s) of administration (for example, oral, smoking, injecting) • When last used? (may help to explain current presentation) • How long they have been using at the current level? • Daily use: detail over past week • Patterns of use (for example, stable/chaotic, one substance to counteract effect of other, use following receipt of benefits followed by period of abstinence) • Evidence of physical dependence – past/recent experience of withdrawal symptoms in absence of substance use (may indicate need for pharmacological interventions (for example, for alcohol, opioids, benzodiazepines) • Whether meets diagnostic criteria DSM-IV/ICD 10 • Severity of dependence (? Use severity of dependence questionnaire) • Service users' understanding of effects of use on physical and mental health
Substance use history	• Identify substances that have been used • Build chronology: age of first use - 'first tried', weekend, weekly, daily – pattern of use over time, whether dependent • Reasons for use • Impact on physical health, mental health, relationships, education/ employment, involvement with criminal justice system, • Periods of abstinence – length, impact on mental health and other areas of life • Treatment episodes: dates, services interventions, what helped, triggers to relapse
Risks	• Consider risks associated with mental illness, substance use and inter-relationships between them • Consider risks to person themselves, family, carers, children, staff (on organisational premises and home visits) and wider community, for example, violence, self-harm, suicide, self-neglect, vulnerability to abuse and exploitation, accidental injury, withdrawal symptoms (for example, seizures, delirium tremens), injecting practices, blood borne viruses, accidental overdose, interactions between prescribed medication and illicit drugs and/or alcohol, unstable accommodation/homelessness, physical health problems, criminal activity • Risks to children • Risks to service users (are there vulnerable adult issues?)
Social circumstances	• Accommodation – situation and any identified needs • Family relationships – supportive or otherwise • Caring responsibilities: children, others – any safeguarding children or vulnerable adult issues? • Domestic violence • Friendships – supportive or otherwise (substance users?) • Education/employment (past and current) – vocational assessment required?
Finances	• Benefits/other income • Cost of current use • How substance use is being funded • Debts for example, rent arrears, utility arrears, to dealers
Legal/forensic	• Involvement in criminal activity to fund use (for example, shoplifting, burglary), as consequence of use (for example, drink/drug driving, violence) • Previous convictions, custodial sentences, any charges pending – were mental

	illness and/or substance use contributory factors?
Medication	• Current and past – for psychiatric, physical and substance use issues: prescribed, over the counter and homeopathic remedies – check whether prescribed medication is taken as indicated (consider non-adherence and/or abuse)
Personal and family history	• Family background • Early development – developmental milestones, schooling • Psychosocial history – physical or sexual abuse? • Family history of mental illness/psychological problems; substance misuse; physical health problems
Physical health/ medical history	• Physical illness(es) – past and current: consider those associated with mental illness and those associated with substance use for example, diabetes, cardiovascular disease, respiratory problems, blood borne viruses (hepatitis, HIV), liver disease, seizures, accidental injury, abscesses, bacterial endocarditis, DVT, tuberculosis, sexually transmitted diseases • If intravenous user, inspect injection sites • Hospital admissions, treatment and outcomes
Psychiatric/mental health history	• Diagnoses, treatment, hospital admissions • Review of previous acute episodes, relapse signatures (taking account of substance use issues) • Symptoms – during acute episodes – between episodes
Spiritual/cultural needs	• Beliefs, practices
Investigations	• Biological: Urine or saliva testing can be helpful to corroborate self-reports • Haematological: full blood count, liver function test, hepatitis B, C, HIV • ECG – important for people prescribed methadone who are also prescribed other medication that can cause QT-elongation
Reasons for and perceptions of use, motivation for change	• What are the reasons for use? (for example, block out auditory hallucinations, alleviate boredom, conform with a peers) • Does the person view their use as problematic? • Does s/he have want to make changes to current use (manner of use, stopping use)?
Strengths and supports	• What can the service user do well, what support do they have outside of statutory services?
Involvement of other agencies	• Identify all other agencies involved with the service user • Obtain collateral information • With consent of service user include them in future care/treatment planning and review
Family/carer needs	• Consider physical, mental health and social needs • Consider impact of mental illness/substance use on relationships, welfare of children, siblings, vulnerable adults • Assess knowledge/understanding regarding mental illness/substance use, inter-relationship, risks

1
2

5.4.4 Care planning

Care planning is normally a collaborative process involving the service user, and, where appropriate, his/her family/carers, and any other agencies.

Although any substance use is likely to have detrimental effects on health, and professionals will usually think the person should work towards abstinence, many people will be unwilling or unable to do so.

Understanding the person's perceptions of their use and motivation for change is essential for planning appropriate care/treatments. The transtheoretical model of change provides a helpful framework for informing decisions (Prochaska & Di Clemente, 1986; Prochaska *et al.,* 1992). It is important to note that the person's motivation to make changes may be different for different substances.

Working collaboratively and accepting the person's relative autonomy is essential in maintaining a therapeutic relationship. Being non-judgemental, avoiding confrontation and maintaining optimism are likely to be associated with better long term outcomes (Miller & Rollnick, 2002; Raistrick *et al*., 2006).

5.4.5 Safeguarding

Although it is essential to work collaboratively with people with psychosis and substance misuse, it is also important to recognise that those dependent upon them may also need help, and sometimes protection. When someone with psychosis and coexisting substance misuse looks after or has significant involvement with dependent children the needs and safeguarding of the child must be secured according to the Common Assessment Framework (see Chapter 9). The care co-ordinator may need to ensure that children's services are alerted to the need for assessment and possible help for the child. Similarly, when dependent or vulnerable adults are involved, the vulnerable adult may need to be assessed at home, the risks assessed and any necessary safeguarding procedures initiated.

5.5 SECONDARY MENTAL HEALTH CARE REFERRAL TO SPECIALIST SUBSTANCE MISUSE SERVICES

5.5.1 Referral threshold

Specialist drug and alcohol services whether hospital (inpatient units) or community-based (community drug and alcohol teams) are dedicated to providing assessment and treatment for problematic drug /alcohol users, for example, heroin and cocaine and patients with alcohol problems. There is no reason why people with psychosis and coexisting substance misuse should be

excluded from access to substance misuse services because of a diagnosis of psychosis.

Referral from mainstream mental health services to specialist substance misuse services for advice and management will occur where individuals with psychosis are known to be:

- an opiate user
- a severe alcohol user
- using alcohol and benzodiazepines.

Figure 3 shows this tertiary referral allowing access to more specialist skills and knowledge, resources for inpatient opiate detoxification and residential rehabilitation or support or treatment groups.

Because motivation is an important element of entry criteria to specialist addiction services secondary care staff may need to help individuals toward this readiness for change.

5.5.2 Assessment and recognition

The possible coexistence of a psychosis among people who come to specialist substance misuse services is often underestimated at least in part as a result of the complex clinical picture often presented when substance misuse is severe, involves the use of multiple substances and in people with evidence of personality disorder or other mental health problems. This is further complicated by that fact that substances may well be used to combat particular psychiatric symptoms or experiences such as anxiety, depression, intrusive thoughts, difficulties sleeping or more severe and troublesome experiences such as hallucinations. Moreover, significant life events, such as bereavement, divorce and trauma, are frequently associated with the emergence of mental health problems, including relapse for people with psychosis, are commonly also triggers for the beginning of, or a significant increase in substance misuse. Furthermore, substance misuse may alter the presentation of symptoms, improving some and worsening others; this is especially so when a person is either intoxicated or experiencing withdrawal. For these, and many other reasons, assessment of mental state for people with substance misuse problems can prove to be difficult and recognition of a coexisting psychosis delayed.

It is important that the assessment of people with a substance misuse problem is comprehensive, and may need to take place over several meetings over an extended period. It is also important to obtain additional information and history from friends, carers, significant others or indeed advocates, where this is permitted and feasible. Ideally assessment will cover not only all the information needed for a substance misuse assessment and that needed for a mental health assessment, but it also aim to examine how the individuals'

behaviour, mental state and experiences co-vary (or not) with changing patterns of substance misuse; and how patterns of substance misuse may co-vary (or not) with changes in mental state; and how both substance misuse and mental state change in the light of different life events. Understanding changes in mental state when someone misusing substances becomes either relatively or completely abstinent can be crucial in making the right diagnostic formulation, not least because communicative and cognitive functions can be greatly improved at these times. In any event, for some people where the index of suspicion for the coexistence of a psychosis with known substance misuse is high, use of the mental health act (for assessment) can be necessary and decisive.

5.5.3 Interfaces and coordination

Substance misuse services will normally need to work closely with secondary mental health services, to ensure that there are agreed local protocols derived from these guidelines that set out responsibilities and processes for assessment, referral, treatment and shared care across the whole care pathway for people with psychosis and coexisting substance misuse. This includes substance misuse professionals being available for care programme meetings for individuals receiving shared care with a secondary care mental health team. Secondary care community mental health services will usually need to continue to monitor and treat psychosis, and provide care co-ordination.

Referral and signposting options will always need to be discussed with and agreed by the service user. There may be choice of agencies and it is important that the service user is informed and involved in a shared decision. A range of Tier 2 and 3 drug and alcohol services will need to be considered in this respect (see section below), in line with the principle of the right care at the right intensity outlined in 5.2.2. Tier 2 examples would be information giving and signposting to mutual aid groups such as Alcoholics Anonymous or Narcotics Anonymous, and advice and linkage to needle exchanges provided by pharmacy services. Specialist liver clinics, probation services and homeless or housing agencies are also interfaces to be managed and fostered. Ensure there is clarity regarding the role of each service, clearly reflected in the care plan, with regular communication and appropriate information sharing between agencies.

5.5.4 Responsibility for prescribing

Where a treatment plan is agreed involving secondary care and specialist substance misuse services the responsibility for any opiate substitute prescribing will need to be clearly agreed between the consultants for the two teams, incorporated into the patient's written care plan, and implemented according to the prescribing guidelines. Any doctor prescribing for the service user will need to see the patient regularly.

Advice and guidelines on prescribing for service users with substance misuse problems, for example, on home alcohol detoxification programmes should be available from substance misuse services. Mental healthcare professionals working with people with psychosis and coexisting substance misuse may need to consider having supervision, advice, consultation and/or training from those with expertise in substance misuse specialist services to aid in developing and implementing treatment plans for substance misuse within secondary care mental health services.

5.5.5 Care Framework differences

Individuals with coexisting psychosis and significant substance misuse will need to remain under the care of secondary care, managed within the Care Programme Approach. The term Care Programme Approach describes the approach used in secondary adult mental health care to assess, plan, review and co-ordinate the range of treatment, care and support needs for people in contact with secondary mental health services who have complex characteristics

Specialist drug services operate under Models of Care for Treatment of Adult Drug Misusers: Update 2006 (National Treatment Agency for Substance Misuse, 2006), whereas specialist alcohol services operate under Models of Care for Alcohol Misuse (Department of Health / National Treatment Agency for Substance Misuse, 2006). Both models of care utilise a four-tier framework and these refer to the level of the interventions provided and not the provider organisations:

- Tier 1 interventions include provision of drug-related /alcohol-related information and advice, screening and referral. For alcohol tier 1 can also involve simple brief interventions.

- Tier 2 interventions include provision of drug-related information and advice, triage assessment, referral to structured drug treatment, brief psychosocial interventions, harm reduction interventions (including needle exchange) and aftercare. For alcohol interventions include provision of open access facilities and outreach that provide: alcohol-specific advice, information and support; extended brief interventions to help alcohol misusers reduce alcohol-related harm; and assessment and referral of those with more serious alcohol-related problems for care-planned treatment.

- Tier 3 interventions include provision of community-based specialised drug/ alcohol misuse assessment and co-ordinated care planned treatment and drug specialist liaison.

- Tier 4 interventions include provision of residential specialised drug / alcohol treatment, which is care planned and care coordinated to ensure continuity of care and aftercare.

5.6 INPATIENT AND RESIDENTIAL SERVICES

5.6.1 Adult mental health services

Substance misuse is a major problem within adult inpatient psychiatric settings. It is common amongst inpatients (Barnaby *et al*., 2003; Bonsack *et al*., 2006; Phillips & Johnson, 2003; Sinclair *et al*., 2008), with alcohol, cannabis and cocaine being the most commonly abused substances in inner urban settings. Patients with psychosis who abuse substances spend more time as inpatients and are admitted more frequently (Isaac *et al*., 2005; Menezes *et al*., 1996). Very high rates of cannabis use were found in a study of patients admitted to an inner urban Psychiatric Intensive Care Unit and those who continued to abuse cannabis (despite the best attempts of staff to restrict access to cannabis) spent longer in hospital (Isaac *et al*., 2005).

Violence is also a major cause of concern on acute inpatient wards (Healthcare Commission, 2007). Substance misuse has been identified by staff as an important contributor to violence on wards (Healthcare Commission, 2007). This is consistent with the epidemiological finding that most of the excess in serious offending behaviour seen in people with a diagnosis of schizophrenia occurs where there is co-morbid substance misuse disorder (Fazel *et al*., 2009). In the substance-abusing population as a whole, cocaine and alcohol are particularly associated with violence (Macdonald *et al*., 2008).

Individuals with psychosis are usually admitted to a general adult inpatient bed because of deterioration in their mental state and/or evidence of increased risk either to themselves or others. Substance misuse may be a co-incidental factor or play a causal role in the circumstances surrounding admission. In either case, assessment and management of the substance misuse will follow the general principles outlined above in other settings.

The Department of Health has issued specific guidance about the management of people with coexisting mental illness and substance misuse being cared for in day hospital and inpatient settings (Department of Health, 2006). Particular potential difficulties that face healthcare professionals in inpatient services include: the place and role of routine and occasional testing of biological samples (urine, blood, hair and, for alcohol, breath) as part of an agreed treatment plan; the requirement for policies on searching; and the practical management of episodes of substance misuse occurring in inpatients. This requires the development of local policies on the management of substances found on the premises, consideration of exclusion of visitors believed to be bringing-in illicit substances and good liaison with the police. For detained patients management of ongoing substance misuse may involve

a review of the leave status of the patient and the appropriate level of security for safe and effective care.

Admission of patients with coexisting opiate misuse and psychosis to an adult psychiatric inpatient unit is uncommon; but when it does it poses particular challenges. In this context it is imperative that an appropriate assessment by an expert in substance misuse and/or advice to the adult psychiatric team is available before developing a treatment plan for the opiate misuse. The treatment plan will often include prescription of substitute opiates (methadone or buprenorphine). Healthcare professionals working within adult mental health services generally, and in inpatient settings in particular, need to be aware of current guidelines on the management of substance misuse provided by the National Treatment Agency (Department of Health, 2007).

5.6.2 Secure mental health services

Although substance misuse is a very significant problem within general adult mental health services, both in the community and especially on in-patient units, a significant past history of substance misuse is even more common amongst patients in secure care (Department of Health, 2006; D'Silva & Ferriter, 2003; Isherwood & Brooke, 2001). Inpatients in medium secure units report high levels of previous substance misuse, which has commonly continued after admission (Wyte *et al*., 2004). Historically, dedicated substance misuse programmes were lacking within secure services despite the robust epidemiological evidence that links substance abuse and misuse with offending behaviour in people with a psychotic illness (Scott *et al*., 2004). Secure services now commonly provide structured substance misuse interventions: these are only in the early stages of evaluation (Miles *et al*., 2007).

5.6.3 Substance misuse inpatient services

There is evidence that a diagnosis of psychosis is much more prevalent in people in contact with community substance misuse services than in the general population (Weaver *et al*., 2003). There appears to be no data on the prevalence of psychosis that is not a consequence of substance misuse amongst inpatients in substance misuse services, who are admitted for detoxification. People who become or are recognised as being acutely psychotic whilst being treated in a substance misuse inpatient setting are often appropriately referred for treatment in general adult psychiatric inpatient services (an exception here is delirium tremens in the context of alcohol withdrawal, which is a medical emergency and would not occur in a competent inpatient setting providing alcohol withdrawal). There is no evidence that a diagnosis of a psychotic illness is a contra-indication for

admission for treatment of coexisting substance misuse where the psychotic illness has been effectively treated.

5.6.4 Residential and supported housing services

Residential and supported housing services for people with a diagnosis of a psychotic illness inevitably work with people who abuse substances. The general principles of assessment, treatment and care set out above are relevant to staff working in these settings; which will commonly be delivered through agencies other than the housing provider. There is a lack of evidence about how residential and supported housing services should work most effectively with people with psychosis and coexisting substance misuse although some practice guidance has been developed (Turning Point, 2007).

Residential and supported housing services for people with substance misuse have in the past commonly been reluctant to take in people with psychotic illness, despite the fact that psychosis is common amongst substance misusers (Weaver *et al.*, 2003). The National Treatment Agency has identified a need for residential programmes that take account of the specific needs of "drug misusers with severe and enduring mental health problems" (National Treatment Agency, 2006). There is no evidence that a diagnosis of a psychotic illness is a contra-indication for residential rehabilitative services for people with coexisting substance misuse where the psychotic illness has been effectively treated.

5.6.5 Prison mental health services and criminal justice

The Bradley Report (Department of Health 2009a) and the subsequent Government response and delivery plan (Department of Health 2009b) focuses on people with mental health and learning disabilities who become involved with the criminal justice system and makes wide ranging recommendations. The report recognizes the prevalence of psychosis with coexisting substance misuse in this population and makes a specific recommendation to develop improved services in prisons for these prisoners. Current problems within this system echo those outside:

> *"Mental health services and substance misuse services in prisons do not currently work well together; national policy is developed separately for mental health and for substance misuse, and this is reflected on the ground, where dual diagnosis is used as a reason for exclusion from services rather than supporting access" (p16 executive summary http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_098699.pdf).*

In terms of the care pathway the report calls for liaison and court diversion services to reduce the need for custodial interventions and allow access to appropriate treatment at an earlier stage in their offending behaviour. The Bradley Report also calls for better links into community mental health

provision when people are leaving prison with psychosis and coexisting substance misuse.

5.7 FROM EVIDENCE TO RECOMMENDATIONS

There is only a limited amount of empirical evidence about how healthcare professionals should work together to provide the most appropriate care and treatment for people with psychosis and coexisting substance misuse. And, what evidence we have, in this and other chapters, is often collected in different countries, such as the US, where the interventions, the training and competence of professionals, the configuration of the healthcare system, and in particular, what counts as 'standard care' may be very different. The GDG, nevertheless, extrapolated where this was possible and useful. The following recommendations are, therefore, developed through an iterative process, synthesising our collective experience to develop a framework of good practice recommendations that we hope will support healthcare professionals develop services in mental health, and substance misuse services in particular, so that people with psychosis and coexisting substance misuse can receive the care and treatment most likely to bring benefit and to improve their lives and those of their carers.

5.8 CLINICAL PRACTICE RECOMMENDATIONS

5.8.1 Recommendations

Recognition of psychosis with coexisting substance misuse

5.8.1.1 Healthcare professionals in all settings, including primary care, secondary care mental health services, CAMHS and accident and emergency departments, and those in prisons and criminal justice mental health liaison schemes, should routinely ask adults and young people with known or suspected psychosis about their use of alcohol and/or prescribed and non-prescribed (including illicit) drugs. If the person has used substances ask them about:

- the particular substance(s) used
- the quantity, frequency and pattern of use
- route of administration
- duration of current level of use.

In addition, conduct an assessment of dependency, and also seek corroborative evidence from family, friends, carers and/or significant others, where this is possible and permission is given.

5.8.1.2 Healthcare professionals in primary care, secondary care mental health services, CAMHS and specialist substance misuse services should routinely assess adults and young people with known or suspected substance use disorders for possible psychosis. Seek corroborative evidence from family, friends, carers and/or significant others, where this is possible and permission is given.

Primary care

Referral from primary care

5.8.1.3 Refer all adults and young people with psychosis and suspected psychosis, including those who are suspected of coexisting substance misuse, to either secondary care mental health services or CAMHS for assessment and further management.

5.8.1.4 Refer all adults and young people with substance misuse or suspected substance misuse who are suspected of having coexisting psychosis to secondary care mental health services or CAMHS for assessment and further management.

Physical healthcare

5.8.1.5 Monitor regularly the physical health of adults and young people with psychosis and coexisting substance misuse, as described in the guideline on schizophrenia (NICE clinical guideline 82). Pay particular attention to the impact of alcohol and drugs (prescribed and non-prescribed) on physical health.

Secondary care mental health services

Competence

5.8.1.6 Healthcare professionals working within mental health services should ensure they are competent in the treatment and care of adults and young people with psychosis and coexisting substance misuse.

5.8.1.7 Mental healthcare professionals working with adults and young people with psychosis and coexisting substance misuse should consider having supervision, advice, consultation and/or training from specialists in substance misuse services. This is to aid in the development and implementation of treatment plans for substance misuse within CAMHS or adult community mental health services.

Pathways into care

5.8.1.8 Do not exclude adults and young people with psychosis and coexisting substance misuse from age-appropriate mental healthcare because of their substance misuse.

5.8.1.9 Do not exclude adults and young people with psychosis and coexisting substance misuse from age-appropriate substance misuse services because of a diagnosis of psychosis.

Assessment

5.8.1.10 Adults and young people with psychosis and coexisting substance misuse attending secondary care mental health services should be offered a comprehensive, multidisciplinary assessment, including assessment of **all** of the following:

- mental, physical and sexual health
- social, family and economic situation
- current and past substance misuse and its impact upon their life, health and response to treatment
- criminal justice history and current status
- personal strengths and weaknesses and readiness for change.

The assessment may need to take place over several meetings to gain a full understanding of the person and the range of problems they experience, and to promote engagement.

5.8.1.11 When assessing adults and young people with psychosis and coexisting substance misuse, seek corroborative evidence from carers or advocates where this is possible and permission is given. Summarise the findings, share this with the person and record it in their care plan.

5.8.1.12 Review any changes in the person's use of substances. This should include changes in:

- the way the use of substances affects the person over time
- patterns of use
- mental and physical state
- circumstances and treatment.

Share the summary with the person and record it in their care plan.

5.8.1.13 When assessing adults and young people with psychosis and coexisting substance misuse, be aware that low levels of substance use that would not usually be considered harmful or problematic in people without psychosis, can have a significant impact on the mental health of people with psychosis.

5.8.1.14 Regularly assess and monitor risk of harm to self and/or others for adults and young people with psychosis and coexisting substance misuse. Specifically consider:

- physical health risks associated with substance use (for example, withdrawal seizures, delirium tremens, blood-borne viruses, accidental overdose, and interactions with prescribed medication) **and**
- the impact that substance use may have on other risks such as self-harm, suicide, self-neglect, violence, abuse of or by others, exploitation and accidental injury.

Biological/physical testing

5.8.1.15 Do not use biological or physical tests for substance use (such as blood and urine tests or hair analysis) in routine screening for drug and alcohol use for adults and young people with psychosis.

5.8.1.16 Consider using biological or physical tests for substance use as part of an agreed plan in the assessment, treatment and management of substance misuse for adults and young people with psychosis.

5.8.1.17 Biological or physical tests for substance use should only be considered in inpatient services as part of assessment and treatment planning for adults and young people with psychosis and coexisting substance misuse. Obtain consent for these tests and inform the person of the results as part of an agreed treatment plan. Where mental capacity is lacking, refer to the Mental Capacity Act (2005).

5.8.1.18 When developing a care plan for an adult or young person with psychosis and coexisting substance misuse, take account of the complex and individual relationships between substance misuse, psychotic symptoms, emotional state, behaviour and the person's social context.

Substance misuse services

Competence

5.8.1.19 Healthcare professionals in substance misuse services should be competent to:

- recognise the signs and symptoms of psychosis
- undertake a full mental health needs and risk assessment
- know how and when to refer to secondary care mental health services.

Joint working

5.8.1.20 Healthcare professionals in substance misuse services should be present at care programme meetings for adults and young people with psychosis and coexisting substance misuse within their service who are also receiving treatment and support in other health services.

5.8.1.21 Substance misuse services should provide advice, consultation, and training for healthcare professionals in adult mental health services and CAMHS regarding the assessment and treatment of substance misuse, and of substance misuse with coexisting psychosis.

5.8.1.22 Substance misuse services should work closely with secondary care mental health services to ensure that there are agreed local protocols derived from this NICE guideline for adults and young people with psychosis and coexisting substance misuse. The protocols should set out responsibilities and processes for assessment, referral, treatment and shared care across the whole care pathway.

Working with adults and young people with psychosis and coexisting substance misuse

Safeguarding issues

5.8.1.23 If people with psychosis and coexisting substance misuse are parents or carers of children or young people, ensure that the child's or young person's needs are assessed according to local safeguarding procedures[5].

5.8.1.24 If children or young people being cared for by people with psychosis and coexisting substance misuse are referred to CAMHS under local safeguarding procedures:

- use a multi-agency approach, including social care and education, to ensure various perspectives on the child's life are considered

[5] www.safeguardingchildren.org.uk

- consider using the Common Assessment Framework[6]; advice on this can be sought from the local named nurse for safeguarding.

Where concerns are identified, health or social care professionals working with the child or young person should develop a child protection plan.

5.8.1.25 When working with people with psychosis and coexisting substance misuse who are responsible for vulnerable adults, ensure that the home situation is risk assessed and that safeguarding procedures are in place for the vulnerable adult. Advice on safeguarding vulnerable adults can be sought from the local named nurse for safeguarding.

[6] www.dcsf.gov.uk/everychildmatters/strategy/deliveringservices1/caf/caframework

Working with the voluntary sector

5.8.1.26 Healthcare professionals in primary care and secondary care mental health services, and in specialist substance misuse services, should work collaboratively with voluntary sector organisations that provide help and support for adults and young people with psychosis and coexisting substance misuse. Ensure that advocates from such organisations are included in the care planning and care programming process wherever this is possible and agreed by the person.

5.8.2 Research recommendations

5.8.2.1 What is the prevalence, pattern and epidemiology of different combinations of coexisting psychosis and substance misuse (for example, schizophrenia with coexisting cannabis misuse; bipolar with coexisting alcohol misuse), and what patterns of use predict poor prognosis?

6 SERVICE DELIVERY MODELS FOR PEOPLE WITH PSYCHOSIS AND COEXISTING SUBSTANCE MISUSE

6.1 INTRODUCTION

This chapter looks at models of service delivery for people with psychosis and coexisting substance misuse. These models are means by which therapeutic interventions and supports are provided. Two broad questions are addressed in this chapter. First, is there evidence that providing therapeutic interventions and support relevant to both conditions in an integrated fashion (the same team addressing both issues), is superior to these interventions being provided separately? Second, is there evidence about the role of staffed accommodation and inpatient care in the management of coexisting substance misuse and psychosis?

In reviewing the evidence for the effectiveness of different service delivery models, the GDG decided to focus on RCTs. By using this type of study design to evaluate service-level interventions there are specific problems relating to defining such interventions precisely; for example, the 'intervention' and 'standard care' may vary between studies, between countries and over time; and experimental interventions have a tendency to overlap with standard care. Service-level interventions that claim superiority over other methods of care delivery must be able to characterise clearly what they do, how they do it, and how they differ from alternative types of service and from the standard care they hope to replace. For these reasons, it is essential for new services to be subjected to the rigour of evaluation through RCTs; services must be able to demonstrate their overall value in comparison with other interventions to remain a supportable component of care within the NHS. Other types of study design (that is, longer-term observational studies), might help to differentiate, evaluate and refine services and the ways in which they operate. For this reason, a narrative synthesis of observational studies was conducted after the review of RCTs.

6.2 INTEGRATED SERVICE MODELS

6.2.1 Introduction

Both in the UK, and elsewhere in the world, it has been proposed that effective treatment for people with psychosis and coexisting substance misuse usually requires an integrated treatment approach (Department of Health, 2002; Ziedonis *et al.*, 2005). An integrated approach combines elements of

mental health and substance misuse service models in one delivery system. This approach was originally pioneered in the US in the 1980s, and was developed in contrast with traditional treatment approaches that provided separate services either in parallel or sequentially (Mueser & Drake, 2003). Such services were felt unable to meet the needs of people with severe mental health and drug/alcohol problems; typically, service users perhaps got only one or the other component, or incompatible or inconsistent treatments from both, or worse still, fell somewhere between the two and received little care (Drake *et al.*, 2008). It was proposed that integrated care meant that both mental health and substance misuse treatments could be provided from the same team of clinicians at the same time and in an integrated manner. The potential advantages of such an integrated approach include ensuring that both elements of the dual problems are given attention, and that any interactions between mental health and substance use problems are formulated and addressed. Due to differences in service provision, organisation funding, and treatment philosophies in the UK, as compared with the US, it has been suggested that more shared care with drug and alcohol services is feasible in the UK (Graham *et al.,* 2003). Moreover, current Department of Health policy suggests that the main focus for service delivery should be within mental health services, and a key principle should be that both problems and the relationship between them are addressed simultaneously (Department of Health, 2002).

Integrated service delivery models that have been evaluated have involved changes in the health care systems to encompass intervention components delivered in a variety of service configurations. Services have included a number of different elements delivered in different combinations and with differing intensities, including motivational interventions and various forms of group, individual, and family counselling as well as housing interventions (Mueser *et al.*, 2005). Besides differing in the components of intervention offered, integrated service delivery models have also differed in structural form: varying from different case management models in community mental health teams, to more intensive, outreach oriented services, and there have also been evaluations of staffed accommodation (usually comparisons of residential integrated treatment with non-residential treatment).

Definition of intervention

Integrated service models

Integrated service models were defined as those that unify services at the provider level rather than requiring clients to negotiate separate mental health and substance abuse treatment programmes (Cleary *et al.*, 2008; Drake *et al.*, 1993).

Standard care

This was defined as the usual treatment received from a community mental health team (which will include a care coordinator) with the potential to access separate substance misuse services.

6.2.2 Clinical review protocol (integrated service models)

The review protocol, including the review question, information about the databases searched and the eligibility criteria used for this section of the guideline can be found in Table 10. During the early stages of guideline development, a recent Cochrane review (Cleary *et al.,* 2008) and related peer-reviewed publication (Cleary *et al.,* 2009) were identified that addressed the review question. These systematic reviews were used as a source of evidence, and only a new systematic search for more recent primary-level studies was conducted for the guideline (further information about the search strategy can be found in Appendix 7).

Where evidence allowed, the following two sub-questions were addressed: 1) What are the elements in an integrated service model that are most likely to be associated with better outcomes? 2) Are there any subgroups of people (for example, young people, BME groups) that benefit from some elements of the service model more than others?

Table 10: Clinical review protocol for the review of integrated service models

Component	Description
Review question	1.2.1 In people with psychosis and coexisting substance misuse, does an integrated service model (usually involving the model of assertive community treatment) when compared with an alternative management strategy lead to improved outcomes?
Electronic databases	CENTRAL, CINAHL, EMBASE, MEDLINE, PsycINFO
Date searched	01.01.2008 to 26.05.2010*
Study design	RCTs and observational studies
Population	People with psychosis and coexisting substance misuse
Intervention(s)	Integrated service model (usually involving the model of assertive community treatment)
Comparison	Alternative management strategies
Critical outcomes	• Reduced mortality (all causes) • Reduced relapse rates (measured by exacerbation of symptoms requiring change in health care management) • Reduced substance misuse (however measured) • Improved global and social functioning (e.g. employment, accommodation) • Improved subjective quality of life • Improved satisfaction with care • Reduced physical morbidity.
Note. RCT = Randomised controlled trial. *The search is an update to Cleary *et al*. (2008) and Cleary *et al*. (2009).	

6.2.3 Studies considered for review (integrated service models)[7]

Four RCTs, CHANDLER2006 (Chandler & Spicer, 2006), DRAKE1998 (Drake *et al*., 1998), ESSOCK2006 (Essock *et al*., 2006), MORSE2006 (Morse *et al*., 2006), that were included in the review by Cleary *et al*. (2008), met the eligibility criteria for this review. Of these, all were published in peer-reviewed journals between 1998 and 2006. In addition, one RCT identified during the search for new evidence, CRAIG2008 (Craig *et al*., 2008), was excluded from the meta-analysis because the GDG considered this to be a trial of training that was not comparable to other trials included in the analysis. Further information about this study can be found in section 6.2.5. Full study characteristics (and any associated references), as well as a list of excluded studies can be found in Appendix 13.

Of the four included RCTs, there were two involving a comparison of an integrated service model versus standard care (CHANDLER2006, MORSE2006). MORSE2006 also included an intervention group receiving non-integrated ACT, allowing a comparison between integrated and non-

[7] Here and elsewhere in the guideline, each RCT considered for review is referred to by a study ID (primary author and date of study publication, except where a study is in press or only submitted for publication, then a date is not used).

integrated ACT (see Table 11 for summary information). In addition, there were two trials involving a comparison of integrated ACT versus integrated clinical case management (DRAKE1998, ESSOCK2006) (see Table 12 for summary information).

In addition to the RCTs, three observational studies (Drake *et al*., 1997; Ho *et al*., 1999; Mangrum *et al*., 2006), that were included in the review by Cleary and colleagues (2008), met eligibility criteria for this review. All studies were published in peer-reviewed journals between 1997 and 2006.

Of the three observational studies, there was one involving a comparison of an integrated service model versus a parallel service model (Mangrum *et al*., 2006), one before-and-after study of a dual-diagnosis treatment program (Ho *et al*., 1999), and one comparing an integrated service model with standard care (Drake *et al*., 1997) (see section 6.2.5 for further information about each study and a narrative summary of results).

Table 11. Study information table for RCTs comparing an integrated service model with a non-integrated management strategy

	Integrated ACT/DDT versus standard care	Integrated ACT versus non-integrated ACT
Total no. of trials (N)	2 RCTs (277)	1 RCT (100)
Study ID	(1) CHANDLER2006 (2) MORSE2006	(1) MORSE2006
Number randomised	(1) 182 (2) 95	(1) 100
Diagnosis	(1) 66% DSM-IV schizophrenia, schizoaffective disorder, bipolar or psychotic disorder NOS and 100% current substance use disorder (34% alcohol dependence, 47% drug dependence)* (2) 89% DSM-IV schizophrenia, schizo-affective, atypical psychotic disorder or bipolar disorder; 9% major depression-recurrent disorder, 2% other. All had one or more substance use disorders; 46% substance dependence disorder for alcohol and/or drugs; 64% substance abuse disorder for alcohol and/or drugs, 40% an alcohol-only diagnosis, 18% drug-only diagnosis, 42% had both drug and alcohol disorders - cocaine most frequently used drug (34%) cannabis (19%)	(1) 89% DSM-IV schizophrenia, schizo-affective, atypical psychotic disorder or bipolar disorder; 9% major depression-recurrent disorder, 2% other. All had one or more substance use disorders; 46% substance dependence disorder for alcohol and/or drugs; 64% substance abuse disorder for alcohol and/or drugs, 40% an alcohol-only diagnosis, 18% drug-only diagnosis, 42% had both drug and alcohol disorders - cocaine most frequently used drug (34%) cannabis (19%)
Ethnicity	(1) 66% African American, 21% White (2) 73% African American, 25% White	(1) 73% African American, 25% White, 2% other
Treatment length	(1) 36 months (2) 24 months	(1) 24 months
Country	(1) USA (2) USA	(1) USA
Intervention (n)	(1) In-custody standard care + brief aftercare + IDDT (post-custody, participants received MI, substance abuse counselling, group treatment oriented to both disorder, family psychoeducation regarding dual disorders, multidisciplinary team, integrated substance abuse specialists, stagewise interventions, time unlimited services, outreach etc.) (n=103)** (2) Integrated ACT (n=46)	(1) Integrated ACT (n=46)
Control (n)	(1) In-custody standard care + usual post custody services + 60 days of post release case management and housing assistance (n=79) (2) Provided with a list of community agencies (mental health and substance abuse treatment) and staff provided linkage assistance to facilitate access	(1) Non-integrated ACT. Referred clients to other community providers for outpatient or individual substance abuse services and to 12-step groups (n=54)

	(n=49)	

Note. ACT = Assertive Community Treatment; DDT = Dual Disorders Treatment; MI = motivational interviewing; N = Total number of participants; n = number of participants in each group; RCT = Randomised controlled trial.
* Some participants had more than one dependence.
** Before release from custody, all participants received an intervention including intensive assessment, medications, treatment planning in preparation for discharge, consultation with jail staff, one-to-one counselling, and crisis intervention (for more details about the intervention, see Mercer-McFadden *et al*. 1998).

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Table 12. Study information table for RCTs comparing integrated ACT with integrated standard case management

	Integrated ACT versus integrated standard case management
Total no. of trials (N)	2 RCTs (421)
Study ID	(1) DRAKE1998 (2) ESSOCK2006
Number randomised	(1) 223 (2) 198
Diagnosis	(1) 53% DSM-III-R schizophrenia with active DSM-III-R substance use disorder (73% alcohol abuse, 42% drug abuse)* (2) 76% DSM-III-R schizophrenia, 17% mood disorder with co-occurring DSM-III-R substance use disorder (74% alcohol abuse, 81% other substances)*
Ethnicity	(1) 96% White (2) 55% African American, 27% White
Treatment length	(1) 36 months (2) 36 months
Country	(1) USA (2) USA
Intervention (n)	(1) Integrated ACT: community-based, high intensity, direct substance abuse treatment by team members, use of stage-wise dual-disorder model, dual-disorder treatment groups & exclusive team focus on patients for those with dual disorders. Caseload ~ 12 (n=109) (2) Integrated ACT with a direct substance use component (n=99)
Control (n)	(1) Standard case management: community-based, team working with client's support system & vigorously addressing co-occurring substance use. Caseload ~ 25 (n=114) (2) Standard case management: some services provided directly and teams had training from study authors in integrated treatment, including comprehensive assessment, individual motivational interviewing, group treatments, and stagewise interventions (n=99)

Note. ACT = Assertive Community Treatment; N = Total number of participants; n = number of participants in each group; RCT = Randomised controlled trial.
*Some participants had more than one dependence.

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4 6.2.4 Evidence from RCTs (integrated service models)

5 Meta-analysis was used to synthesise the evidence for each comparison. For
6 the comparison of an integrated service model with a non-integrated
7 management strategy, a GRADE summary of findings table is shown in Table

13. For the comparison of integrated ACT with integrated standard case management, a GRADE summary of findings table is shown in Table 14.

The forest plots and full GRADE evidence profiles can be found in Appendix 14 and 15, respectively.

Table 13. GRADE summary of findings table for RCTs comparing an integrated service model with a non-integrated management strategy

Outcomes	Effect size (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)
Substance use: 1. Substance use rating (high=poor) - by 6 months	SMD 0.14 (-0.26 to 0.54)	95 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 1. Substance use rating (high=poor) - by 12 months	SMD 0.18 (-0.22 to 0.58)	95 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 1. Substance use rating (high=poor) - by 18 months	SMD -0.15 (-0.55 to 0.25)	95 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 1. Substance use rating (high=poor) - by 24 months	SMD 0.05 (-0.35 to 0.45)	95 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 2. Days used substances - by 6 months	SMD 0.08 (-0.33 to 0.48)	95 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 2. Days used substances - by 12 months	SMD 0.11 (-0.3 to 0.51)	95 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 2. Days used substances - by 18 months	SMD 0.09 (-0.31 to 0.49)	95 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 2. Days used substances - by 24 months	SMD 0.13 (-0.28 to 0.53)	95 (1 study)	⊕⊕⊖⊖ low[1,2]
Service use: 1. Days in stable community residences (not in hospital) - by 6 months	MD 3.17 (-0.52 to 6.86)	95 (1 study)	⊕⊕⊖⊖ low[1,2]
Service use: 1. Days in stable community residences (not in hospital) - by 12 months	MD 2.84 (-2.07 to 7.75)	95 (1 study)	⊕⊕⊖⊖ low[1,2]
Service use: 1. Days in stable community residences (not in hospital) - by 18 months	MD 6.46 (1.36 to 11.56)	95 (1 study)	⊕⊕⊕⊖ moderate[1]
Service use: 1. Days in stable community residences (not in hospital) - by 24 months	MD 5.7 (0.59 to 10.81)	95 (1 study)	⊕⊕⊕⊖ moderate[1]

Note. Negative SMDs favour integrated service models, positive MDs favour integrated service models; CI = confident interval; MD = mean difference; RR = Relative Risk.

[1] Optimal information size not met.

[2] CI includes both 1) no effect and 2) appreciable benefit or appreciable harm.

Table 14. GRADE summary of findings table for RCTs comparing integrated ACT with integrated standard case management

Outcomes	Effect size (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)
Death - by 36 months	RR 1.18 (0.39 to 3.57)	421 (2 studies)	⊕⊕⊖⊖ low[1,2]
Substance use: 1. Not in remission - by 36 months - alcohol	RR 1.15 (0.84 to 1.56)	143 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 1. Not in remission - by 36 months - drugs	RR 0.89 (0.63 to 1.25)	85 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 2. Substance abuse (SATS, low=poor) - by 6 months	SMD 0.03 (-0.17 to 0.23)	379 (2 studies)	⊕⊕⊕⊖ moderate[1]
Substance use: 2. Substance abuse (SATS, low=poor) - by 12 months	SMD 0.08 (-0.23 to 0.39)	374 (2 studies)	⊕⊕⊕⊖ moderate[1]
Substance use: 2. Substance abuse (SATS, low=poor) - by 18 months	SMD -0.02 (-0.22 to 0.19)	375 (2 studies)	⊕⊕⊕⊖ moderate[1]
Substance use: 2. Substance abuse (SATS, low=poor) - by 24 months	SMD 0.11 (-0.14 to 0.37)	365 (2 studies)	⊕⊕⊕⊖ moderate[1]
Substance use: 2. Substance abuse (SATS, low=poor) - by 30 months	SMD 0.11 (-0.1 to 0.31)	358 (2 studies)	⊕⊕⊕⊖ moderate[1]
Substance use: 2. Substance abuse (SATS, low=poor) - by 36 months	SMD 0.05 (-0.15 to 0.26)	360 (2 studies)	⊕⊕⊕⊖ moderate[1]
Service use: 1. Days in stable community residences (not in hospital) - by 12 months	MD -10 (-38.61 to 18.6)	378 (2 studies)	⊕⊕⊖⊖ low[1,2]
Service use: 1. Days in stable community residences (not in hospital) - by 24 months	MD 8.54 (-4.46 to 21.55)	377 (2 studies)	⊕⊕⊖⊖ low[1,2]
Service use: 1. Days in stable community residences (not in hospital) - by 36 months	MD 5.17 (-9.2 to 19.55)	364 (2 studies)	⊕⊕⊖⊖ low[1,2]
Functioning: 1. Average general score (GAS, low=poor) - by 6 months	SMD 0.13 (-0.18 to 0.43)	162 (1 study)	⊕⊕⊖⊖ low[1,2]
Functioning: 1. Average general score (GAS, low=poor) - by 12 months	SMD 0.07 (-0.23 to 0.38)	171 (1 study)	⊕⊕⊖⊖ low[1,2]
Functioning: 1. Average general score (GAS, low=poor) - by 18 months	SMD 0.11 (-0.18 to 0.41)	176 (1 study)	⊕⊕⊖⊖ low[1,2]
Functioning: 1. Average general score (GAS, low=poor) - by 24 months	SMD 0.18 (-0.13 to 0.48)	166 (1 study)	⊕⊕⊖⊖ low[1,2]
Functioning: 1. Average general score (GAS, low=poor) - by 30 months	SMD -0.06 (-0.37 to 0.24)	164 (1 study)	⊕⊕⊖⊖ low[1,2]
Service use: 1. Days in stable community residences (not in hospital) - by 36 months	SMD 0.04 (-0.26 to 0.34)	170 (1 study)	⊕⊕⊖⊖ low[1,2]
Functioning: 1. Average general score (GAS, low=poor) - by 6 months	SMD -0.07 (-0.28 to 0.14)	361 (2 studies)	⊕⊕⊖⊖ low[1,2]
Functioning: 1. Average general score (GAS, low=poor) - by 36 months	SMD 0.01 (-0.19 to 0.22)	372 (2 studies)	⊕⊕⊖⊖ low[1,2]
Satisfaction: Average general score (QOLI, low=poor) - by 6 months	SMD 0.06 (-0.17 to 0.29)	377 (2 studies)	⊕⊕⊖⊖ low[1,2]
Satisfaction: Average general score (QOLI, low=poor) - by 12 months	SMD 0.01 (-0.2 to 0.23)	370 (2 studies)	⊕⊕⊖⊖ low[1,2]
Satisfaction: Average general score (QOLI, low=poor) - by 18 months	SMD 0.02 (-0.19 to 0.22)	366 (2 studies)	⊕⊕⊖⊖ low[1,2]
Satisfaction: Average general score (QOLI, low=poor) - by 24 months	SMD 0.07 (-0.13 to 0.27)	373 (2 studies)	⊕⊕⊖⊖ low[1,2]
Satisfaction: Average general score (QOLI,	SMD 0.03	379	⊕⊕⊕⊖

low=poor) - by 30 months	(-0.17 to 0.23)	(2 studies)	moderate[1]
Satisfaction: Average general score (QOLI, low=poor) - by 36 months	SMD 0.08 (-0.23 to 0.39)	374 (2 studies)	⊕⊕⊕⊖ moderate[1]
Note. Negative SMDs favour integrated ACT, positive MDs favour integrated ACT; CI = confident interval; MD = mean difference; RR = Relative Risk. [1] Optimal information size not met. [2] CI includes both 1) no effect and 2) appreciable benefit or appreciable harm.			

6.2.5 Training (integrated service models)

Craig and colleagues (Johnson *et al.*, 2007; Hughes *et al.*, 2008; Craig *et al.*, 2008) undertook a cluster-randomised trial involving brief (5 day) substance misuse training of care coordinators working within community mental health teams in South London (the COMO study). In addition to the training the care coordinators received supervision from the trainer during the follow-up period. Forty care coordinators received training and their patients with coexisting substance misuse and psychosis were followed up over eighteen months (127 patients). One hundred and five patients of thirty-nine care coordinators who did not receive the training were also followed up. There was no significance difference at follow-up between patients in terms of inpatient bed days, admissions and substance use at follow-up (Johnson *et al.*, 2007). Craig and colleagues (2008) reported that there were no significant differences in service costs but symptoms (as measured by the BPRS) and needs for care were significantly lower at follow-up in the intervention group. Hughes and colleagues (2008) reported that the training course in dual diagnosis interventions had a significant effect on secondary measures of staff knowledge and self-efficacy that was detectable at 18 months post-training. However improvements in attitudes towards working with drinkers and drug users in mental health settings failed to reach statistical significance. This study did not meet the eligibility criteria for the review of service delivery models but did provide some evidence that a training programme for staff in substance misuse combined with supervision may have an impact on symptoms. The brief training course had only a modest impact on staff knowledge and skills in working with substance misusers.

Health economic evidence of substance misuse training

The study by Craig and colleagues (2008) included an economic evaluation, comparing the costs and outcomes of a programme for case managers receiving substance misuse training with a waiting list control condition. A societal perspective was used for the cost analysis. The Client Service Receipt Inventory (CSRI) was used to collected resource use data over the 18 month follow-up period, including inpatient days, health care professional visits (Psychiatrist, Social worker, GP, Drug or Alcohol worker), medications and criminal justice (court, police, prison). An array of effectiveness measures were used in the study including psychiatric symptoms (BPRS), drug and alcohol consumption, quality of life (Manchester Short Assessment) and social functioning. Mean total 18-month costs were £26,449 in the intervention

group and £23,266 in the control group, resulting in a difference of £1,033 (95% CI: -£5,568 to £6,734). In terms of effectiveness, the intervention resulted in significant improvements in psychiatric symptoms, but no significant differences were detected in drug and alcohol consumption, quality of life scores or social functioning. The authors did not attempt to synthesise incremental costs and outcomes, therefore the economic evaluation took the form of a simple cost-analysis. Although the results of the analysis are applicable to the UK context, it is difficult to interpret whether the training programme was cost-effective, given the array of outcome measures used and the variability across the effectiveness measures of the training programme compared to the control group.

6.2.6 Evidence from observational studies (integrated service models)

Mangrum and colleagues (2006) investigated hospitalisation and arrest outcomes for people with psychosis and coexisting substance misuse allocated to integrated (n = 123) or parallel treatment (n = 93). Eighteen to twenty three percent of the sample had a principal diagnosis of schizophrenia, 19-22% with bipolar, 2-3% with an alcohol use disorder, and 5-11% had a substance use disorder. Service Users in the parallel treatment condition received substance abuse and mental health treatment by separate clinics; therefore services were not coordinated and lacked a centralised case management component. Results using weighted least squares methods revealed a significant effect favouring the integrated treatment group post-baseline on measures of any psychiatric hospitalisation, $F(1) = 21.17$, $p < 0.0001$ and hospital days, $F(1) = 4.28$, $p = 0.04$. Thus, a significant difference was found in number of days hospitalised favouring those in the integrated group.

Ho and colleagues (1999) prospectively looked at 6-month treatment engagement and outcome of four groups (n = 179) successively enrolled in a day hospital of a dual-diagnosis treatment program, monitoring effectiveness changes over a 2-year period. The entire sample met criteria for psychosis (schizophrenia, schizoaffective disorder, or psychotic disorder not otherwise specified) and substance dependence (with the primary drug of use being cocaine, followed by alcohol and marijuana). Results demonstrated that all groups made sequential improvements (from group 1 to 4). Participants in group 4 had the highest engagement, attendance and retention rates, as they received the fullest spectrum of treatment (and had access to more activities and therapeutic treatments) when compared with the other three groups. Furthermore, an increasing percentage of participants from group 1 to 4 maintained sobriety for at least 1 to 4 months in the first six months of treatment (Cochrane-Armitage trend test statistic: 1 month, 2.16, $p = 0.03$; 2 months, 4.26, $p = 0.01$; 3 months, 6.37, $p = 0.001$; 4 months, 2.02, $p = 0.04$).

Drake and colleagues (1997) conducted a quasi-experimental study comparing integrated treatment with standard treatment on outcomes of mental health, substance abuse and housing for homeless individuals with psychosis and coexisting substance misuse. The entire sample met criteria for alcohol or drug dependence, and most had a diagnosis of schizophrenia (range: 27.1 to 41.1% of sample), schizoaffective disorder (range: 6.8 to 13.9%) or bipolar disorder (range: 13.6 to 17.7%). At 18 month follow-up, patients in the integrated treatment group (n = 158) had significantly fewer days in an institution and more days in stable housing, made more progress in terms of substance abuse recovery (p = 0.002), and showed greater improvement of alcohol use disorders than those in standard treatment (n = 59) (p = 0.05). There were no significant differences between the two groups on treatment retention.

6.2.7 Clinical evidence summary (integrated service models)

There were two trials comparing an integrated service model (integrated ACT or integrated DDT) with standard care (N = 277); one of these trials also compared integrated ACT with non-integrated ACT (N = 100). However, no data from the critical outcomes could be combined using meta-analysis, so for each outcome the evidence comes from a single study. Based on these critical outcomes, the evidence (*GRADED* moderate to low quality) is inconclusive regarding the effectiveness of using an integrated approach for people with psychosis and coexisting substance misuse.

In addition, there were two trials compared integrated ACT with integrated standard case management (N = 421), but again the evidence (*GRADED* moderate to low quality) was inconclusive.

The three observational studies generally demonstrated support for integrated service models, but methodological issues and study setting make it difficult to generalise their results to the UK.

6.2.8 Health economic evidence (integrated service models)

The systematic search of the health economics literature identified two US-based studies (Clark *et al*., 1998; Morse *et al*., 2006) that considered the cost-effectiveness of integrated service models versus standard or non-integrated care. Details on the methods used for the systematic search of the economics literature are described in Appendix 9.

The study by Clark *et al.* (1998), assessing the cost-effectiveness of ACT versus standard case management (SCM), was based on the RCT described by Drake and colleagues (1998). The study sample consisted of 193 people recruited across multiple sites, diagnosed with schizophrenia, schizoaffective disorder or bipolar disorder alongside an active substance use disorder. The time horizon of the economic analysis was three years with participants

interviewed at six-month intervals. A societal perspective was adopted for the cost analysis. Therefore, resource use data including mental health and general health care, legal services, community services (e.g. homeless shelters) and informal care-giving, were all collected. The primary outcome measure used for the cost-effectiveness analysis was the QoL year which weighted participants' subjective quality of life (measured by the Quality of Life Interview on a 0-1 scale) over consecutive six-monthly intervals.

Overall, mean three-year costs were similar across both groups: $118,079 for ACT and $124,145 for SCM. Average QoL year ratios per $10,000 were 0.24 for integrated care participants and 0.20 for standard care participants. Overall, no significant differences in costs and effectiveness were detected between the two groups over the three-year period. There are several methodological issues with the study that limits the generalisability of the results to the UK context. First, estimates of quality of life were elicited directly from patients in the study rather than from national sample estimates. The latter approach is recommended by NICE for estimating QALYs for cost-utility analyses in the UK (NICE, 2009b). The authors did not attempt to combine total costs and outcomes by using incremental cost-effectiveness ratios, instead calculating ratios of cumulative quality of life years to total costs. No power calculations were provided in the determination of sample sizes and no formal consideration was given to study non-completers which may have biased the results.

The study by Morse and colleagues (2006) included a cost analysis, which compared costs over 24 months between three treatment programmes: integrated ACT, non-integrated ACT, and standard care. The study was based on an RCT of 149 individuals with coexisting severe mental illness and substance use disorders who were homeless at baseline. Again a societal perspective was adopted for the cost analysis. Resource use data associated with mental health care, substance abuse treatment, physical health care and emergency shelters were collected from Medicaid claims. Over 24-months, total average costs in integrated ACT ($48,764) and standard care ($41,726) were significantly lower than in the non-integrated ACT programme ($71,211), while no significant cost differences were detected between the integrated ACT and standard care programmes. Most of the cost differences were explained by higher outpatient care incurred by the non-integrated ACT group, while inpatient care was similar across all three programmes. The results of the study have limited applicability to the UK setting for a number of reasons. First, the study was US based and it is unlikely that treatment patterns and associated resource use is generalisable to the UK context. High attrition rates may have biased the results of the cost analysis, although the authors argue that this limited statistical power rather than internal validity of the study findings. Finally, the study was a cost analysis and no formal attempt was made to compare total costs across the two treatment pathways with any differences in effectiveness.

Health economics summary

The literature review identified only two US-based studies that considered the cost-effectiveness of integrated care models (Clark *et al*., 1998; Morse *et al*., 2006). Both studies suggest that integrated care models may be no more costly than non-integrated models, with no differences in health outcomes. However, both studies are of limited applicability to the NHS context and limited in terms of their methodological quality.

Given the uncertainty surrounding the cost-effectiveness of integrated models of care and the associated resource implications, it was anticipated that an economic model would be developed to address these issues. However, due to both the scarcity and the generally low quality of the clinical data that was identified in the guideline systematic review, the GDG agreed that it would not be possible to model the cost-effectiveness of integrated models of care.

6.2.9 From evidence to recommendations (integrated service models)

Early in the development process, the GDG distinguished between outcomes that were critical to decision making and those that were important but not critical. Critical outcomes included: mortality (all causes), relapse rates (measured by exacerbation of symptoms requiring change in health care management), substance misuse (however measured), global and social functioning (e.g., employment, accommodation), subjective quality of life, satisfaction with care, and physical morbidity. Only critical outcomes were included in the GRADE evidence profiles.

The review found only moderate to low quality evidence from randomised trials and this was inconclusive. Furthermore, all of the clinical evidence and the health economic evidence included in this review were from North America, and therefore, are of questionable relevance to clinical practice in the UK.

It was surprising that the RCT literature does not strongly support integrated service models over non-integrated service models. Policy suggests that the lead service in working with people who are misusing substances and have a diagnosis of psychosis should be the mental health service.

The literature does not address the needs of people with coexisting opiate misuse and psychosis: a small group amongst patients with psychosis. For reasons of safety in prescribing and the expertise required in monitoring the service user's requirements of substitute opiates a parallel model in which both substance misuse services and mental health services work with the patient in the overall context of the Care Programme Approach.

There are cogent reasons given the high prevalence of substance misuse amongst patients with a psychosis that staff working within psychosis services develop as part of their basic training and continuing professional development, skills and knowledge in substance misuse assessment and treatment interventions. More research is required on how this training is provided and the impact of ongoing supervision when working with people with psychosis and coexisting substance misuse.

6.2.10 Recommendations (integrated service models)

6.2.10.1 For most adults with psychosis and coexisting substance misuse, treatment for both conditions should be provided by healthcare professionals in community-based mental health teams, including early intervention in psychosis services.

Coordinating care

6.2.10.2 Consider seeking specialist advice and initiating joint working arrangements with specialist substance misuse services for adults and young people with psychosis being treated by community mental health teams, and known to be:

- severely dependent on alcohol **or**
- dependent on both alcohol and benzodiazepines **or**
- dependent on opioids.

Adult community mental health services or CAMHS should continue to provide care coordination and treatment for the psychosis within joint working arrangements.

6.2.10.3 Consider seeking specialist advice and, if necessary, initiate joint working arrangements with specialist substance misuse services if the person's substance misuse:

- is difficult to control
- leads to significant impairment of functioning, family breakdown or significant social disruption such as homelessness.

6.2.10.4 Delivery of care and transfer between services for adults and young people with psychosis and coexisting substance misuse should include a care coordinator and use the care programme approach.

6.3 STAFFED ACCOMMODATION

6.3.1 Introduction

People with severe mental health problems frequently live in staffed or supported accommodation, either as a step in a rehabilitation programme or more permanently (Macpherson *et al.,* 2004; Wolfson *et al.,* 2009). There is a wide range of accommodation providing varying degrees of support from 24-hour staffing to daytime staffing with out-of-hours telephone cover, to out-of-hours cover provided by the generic on-call service for emergencies only. The staffing can range from a full NHS multidisciplinary team to third-sector or private providers with unqualified staff. Registered care homes have to meet standards set by the Care Quality Commission in terms of the levels and experience of the care staff and will offer 24-hour staffing.

Projects funded through Supporting People programme[8] will have less staff who will not be expected to provide direct care: the numbers of staff hours will depend on the nature of the project and the presumed needs of the client group. At the lowest level people may live independently with "floating support". Additional direct care inputs may also be provided to people in Supporting People projects.

Other variations include housing scheme with a warden (Sheltered Housing or Special Sheltered Housing) generally for older people. In Core and Cluster housing: staff are based in the core setting that houses residents with the greatest support needs. Satellite (cluster) housing accommodates other residents grouped by needs for support.

In Family Placements, the service user becomes part of the family. This may particularly suit people with educational under-achievement or cognitive impairment. In Adult Placement (also known as supported lodgings) a private landlord provides support to tenants renting rooms in a house. Group homes, generally for older people, provide mutual support for those who value it. Finally, dispersed intensive supported housing (Howat *et al.*, 1988) offers a specialist form of supported housing with support provided over extended hours as an alternative to residential care.

Current practice

In the past, substance misuse was generally seen as a reason for exclusion from residential care, staffed and supported housing. Few units were prepared to tackle the challenges presented by people with coexisting mental illness and substance misuse, leading to very vulnerable individuals in housing need, being placed in extremely unsatisfactory bed and breakfast

[8] Further information is available here: http://www.communities.gov.uk

accommodation and to patients spending extended periods on acute inpatient wards in the absence of suitable alternative accommodation.

Residential care for people with substance misuse ("rehab") is seen as an important component in the management of people recovering from severe substance dependence. Traditionally such units were very reluctant to take in patients with a diagnosis of psychosis, even if this was effectively treated.

Definition of intervention

Any staffed accommodation or supported housing for people with a diagnosis of psychosis and coexisting substance misuse that may include an element of specific treatment for the substance misuse.

6.3.2 Clinical review protocol (staffed accommodation)

The review protocol, including the primary review question, information about the databases searched and the eligibility criteria used for this section of the guideline can be found in Table 15. During the early phase of guideline development, a recent peer-reviewed systematic review (Cleary *et al*., 2009) was identified that addressed the review question. This systematic review was used as a source of evidence, and only a new systematic search for more recent primary-level studies was conducted for the guideline (further information about the search strategy can be found in Appendix 7).

Table 15: Clinical review protocol for staffed accommodation

Component	Description
Review question	1.2.3 In people with psychosis and coexisting substance misuse, does staffed accommodation when compared to an alternative management strategy lead to improved outcomes?
Electronic databases	CENTRAL, CINAHL, EMBASE, MEDLINE, PsycINFO
Date searched	01.01.2008 to 26.05.2010*
Study design	RCTs and observational studies
Population	People with psychosis and coexisting substance misuse
Intervention(s)	Staffed accommodation
Comparison	Alternative management strategies
Critical outcomes	• Reduced mortality (all causes) • Reduced relapse rates (measured by exacerbation of symptoms requiring change in health care management) • Reduced substance misuse (however measured) • Improved global and social functioning (e.g. employment, accommodation) • Improved subjective quality of life • Improved satisfaction with care • Reduced physical morbidity.
Note. RCT = Randomised controlled trial. *The search is an update to Cleary *et al*. (2009).	

6.3.3 Studies considered for review (staffed accommodation)

One RCT (N = 132), BURNAM1995 (Burnam *et al*., 1995), included in the review by Cleary and colleagues (2008), met eligibility criteria for this review. BURNAM1995 involved a comparison of a residential integrated mental health and substance use treatment programme versus standard care (see Table 16 for summary information). Full study characteristics (and any associated references), as well as a list of excluded studies can be found in Appendix 13. Forest plots and a GRADE evidence profile can be found in Appendix 14 and 15, respectively).

In addition to the RCT, five observational studies (Anderson, 1999; Blankertz & Cnaan, 1994; Brunette *et al*., 2001; de Leon *et al*., 2000; Nuttbrock *et al*., 1998) met eligibility criteria for this review. Of these, all were published between 1994 and 2004. Further information about each observational study and a narrative summary of results can be found in section 6.3.5.

Table 16: Study information table for trials comparing staffed accommodation with standard care

	Staffed accommodation versus standard care
Total no. of trials (N)	1 RCT (132)
Study ID	(1) BURNAM1995
Number randomised	(1) 132
Diagnosis	(1) Schizophrenia and or major affective disorder with co-occurring substance disorder*
Ethnicity	(1) 58% White
Treatment length	(1) 9 months
Country	(1) USA
Intervention (n)	(1) Residential integrated mental health and substance use treatment: educational groups, 12-step programmes including AA or NA, discussion groups, individual counselling, case-management, psychiatric consultation, ongoing medication management, general community activities (n=67)
Control (n)	(1) Routine care with no special intervention but free to access other services (shelters, mental health clinics, AA groups) (n=65)
Note. AA = Alcoholics Anonymous; N = Total number of participants; n = number of participants in each group; NA = Narcotics Anonymous; RCT = Randomised controlled trial. *Participants paid $10 for each assessment interview.	

6.3.4 Evidence from RCTs (staffed accommodation)

For the comparison of staffed accommodation with standard care, a GRADE summary of findings table is shown in Table 17.

Table 17. GRADE summary of findings table for RCTs comparing staffed accommodation with standard care

Outcomes	Effect size (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)
Substance use: 1. Days used alcohol (low=poor) - 3 months	SMD -0.32 (-0.71 to 0.07)	104 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 1. Days used alcohol (low=poor) - 6 months	SMD 0 (-0.4 to 0.4)	97 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 1. Days used alcohol (low=poor) - 9 months	SMD -0.05 (-0.49 to 0.38)	82 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 2. Level of alcohol use (low=poor) - 3 months	SMD -0.21 (-0.6 to 0.18)	104 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 2. Level of alcohol use (low=poor) - 6 months	SMD -0.06 (-0.46 to 0.33)	97 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 2. Level of alcohol use (low=poor) - 9 months	SMD -0.21 (-0.65 to 0.23)	82 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 3. Days used drugs (low=poor) - 3 months	SMD -0.22 (-0.61 to 0.17)	104 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 3. Days used drugs (low=poor) - 6 months	SMD -0.11 (-0.51 to 0.28)	97 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 3. Days used drugs (low=poor) - 9 months	SMD -0.04 (-0.48 to 0.39)	82 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 4. Severity of drug use (low=poor) - 3 months	SMD -0.14 (-0.52 to 0.25)	104 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 4. Severity of drug use (low=poor) - 6 months	SMD -0.18 (-0.57 to 0.22)	97 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 4. Severity of drug use (low=poor) - 9 months	SMD -0.16 (-0.6 to 0.28)	82 (1 study)	⊕⊕⊖⊖ low[1,2]
Functioning: 1. % time on streets (low=poor) - 3 months	SMD 0.04 (-0.35 to 0.42)	104 (1 study)	⊕⊕⊖⊖ low[1,2]
Functioning: 1. % time on streets (low=poor) - 6 months	SMD -0.06 (-0.46 to 0.34)	97 (1 study)	⊕⊕⊖⊖ low[1,2]
Functioning: 1. % time on streets (low=poor) - 9 months	SMD 0.10 (-0.34 to 0.54)	82 (1 study)	⊕⊕⊖⊖ low[1,2]
Functioning: 2. % time in independent housing (low=poor) - 3 months	SMD -0.16 (-0.55 to 0.23)	104 (1 study)	⊕⊕⊖⊖ low[1,2]
Functioning: 2. % time in independent housing (low=poor) - 6 months	SMD -0.22 (-0.61 to 0.18)	97 (1 study)	⊕⊕⊖⊖ low[1,2]
Functioning: 2. % time in independent housing (low=poor) - 9 months	SMD 0.22 (-0.22 to 0.66)	82 (1 study)	⊕⊕⊖⊖ low[1,2]

Note. Negative SMDs favour staffed accommodation; CI = confident interval; MD = mean difference; RR = Relative Risk.
[1] Optimal information size not met.
[2] CI includes both 1) no effect and 2) appreciable benefit or appreciable harm.

6.3.5 Evidence from observational studies (staffed accommodation)

There were five studies (Anderson, 1999; Blankertz & Cnaan, 1994; Brunette *et al*., 2001; de Leon *et al*., 2000; Nuttbrock *et al*., 1998) which employed a non-

randomised approach and examined the efficacy of residential settings for people with psychosis and coexisting substance misuse.

Brunette and colleagues (2001) compared the effectiveness of long-term and short-term residential treatment programs. The sample consisted of participants diagnosed primarily with schizophrenia spectrum disorder (63% of the sample), in conjunction with an alcohol use disorder (32%), substance use disorder (12%) or polysubstance use (56%). Service Users in the long-term program had better engagement in treatment (Chi-square test, $\chi^2 = 11.4$, df = 1, $p < .001$) and were more likely to maintain abstinence from substance use post-discharge (Chi-square test, $\chi^2 = 10.4$, df = 1, $p < .001$). There were no significant differences between short and long term residential treatment on other measures, including psychiatric hospitalisation or incarceration. It is important to note that the groups were non-equivalent however; so the data may be biased.

Anderson (1999) explored the different impacts of an integrated approach for the treatment of dual diagnosis (n = 76) and a more restrictive and traditional substance abuse model based on a therapeutic community approach (n = 139). The sample consisted of homeless participants, of whom 68.4% had a psychotic spectrum disorder (Axis 1). Fifty percent of the sample had a polysubstance abuse diagnosis (Axis 1), 22.9% had crack/cocaine problems, and 29.8% alcohol dependent. Results indicated significant differences in only five of the 33 characteristics studied. Length of stay in the program was correlated to positive treatment outcomes. Furthermore, the restrictive program was associated with twice the number of medically unadvised dropouts. It should be noted that results from this study should be interpreted with caution and cause and effect cannot be assumed, as the data analysis was based on a bivariate correlational analysis as well as a patient satisfaction survey.

Blankertz and Cnaan (1992, 1994) compared the effectiveness of psychosocial rehabilitation versus a modified therapeutic community for homeless individuals with psychosis and coexisting substance misuse. Nearly eighty percent of the overall sample had schizophrenia, and 11% had bipolar disorder. Two thirds of the sample population had a concurrent Axis III personality disorder. Substance use included alcohol (66%) cocaine, (55%), amphetamine (27%), heroin (29%), marijuana (40%), and other drugs (30%). Of the sample, 57% of the clients were polysubstance users. Results demonstrated that those receiving two years of psychosocial rehabilitation had increased abstinence (based on the ASI, $p < 0.01$), improved mental state and increased treatment retention compared to the therapeutic community.

Nuttbrock and colleagues *(*1998) compared a community residential treatment programme (n = 87) with a therapeutic community (n=98). Of the total sample, 48.8% had a primary diagnosis of a nonaffective psychotic disorder,

and 53.5% had a secondary diagnosis of a substance use disorder (abuse or dependence). Of those with a substance use disorder, 87.6% reported polysubstance use, 43.9% reported crack, and 21.2% reported alcohol as their primary drug of use). Service users in both programs improved on substance abuse and psychopathology outcomes, however the reductions and improvements were even greater in the therapeutic community. These results were not statistically significant after a Bonferroni correction was applied. Service users in the therapeutic community were more drug free, had more improvement in psychiatric symptoms and had improved cognitive functioning. Regression analyses indicated that improvements on psychological symptoms at 2 month follow-up and level of functioning at 12 month follow-up were significantly greater among therapeutic community residents.

More recently, DeLeon and colleagues (2000) compared two types of therapeutic communities for dually diagnosed patients (medium intensity therapeutic community (n = 66) and low intensity therapeutic community (n = 93) versus treatment as usual (n = 183). Treatment as usual consisted of the general residential programs and support services (housing, case management, day treatment) available for those with mental illness and substance use problems. In order to meet inclusion criteria, participants had to have a primary mental illness Axis 1 referral diagnosis (usually schizophrenia or major depression), a secondary Axis 1 referral diagnosis of substance abuse/dependent disorder, and a history of homelessness. Results indicated that those in the more modified, higher intensity therapeutic community (TC_2) had significantly higher retention rates and did better on 12 month follow-up outcomes than did those in the lower intensity (TC_1) (Chi-square test, $\chi^2 = 12.05$, $p < 0.002$). Moreover, at two year follow-up, participants in the low intensity therapeutic community had significantly lower substance use as well as significant improved mental state (TC_1). There were no significant differences found on other measures, or favouring the high intensity modified therapeutic community. Those in the TC_2 improved statistically on 9 out of 12 outcome measures (including reduced frequency of alcohol and drug use, criminality, increased employment and improvements on the two measures of psychological functioning (SMAS and TSCS). Those in TC_1 and TAU improved on less outcome measures, 7 and 3 of 12, respectively.

6.3.6 Clinical evidence summary (staffed accommodation)

In one trial of residential accommodation (N = 132), the evidence (*GRADED* low quality) was inconclusive to reach a decision about the effectiveness of this approach when compared to standard care for people with psychosis and coexisting substance misuse.

Taken together, the observational studies suggest that substance use outcomes improved at follow-up, and the majority of these studies favoured longer duration integrated residential programs than shorter residential

programmes. However, the substantial methodological limitations of these studies make interpretation very difficult.

6.3.7 Health economic evidence (staffed accommodation)

The systematic search of the health economics literature identified one US-based study that considered the cost-effectiveness of a staffed accommodation intervention (French *et al.,* 1999). Details on the methods used for the systematic search of the economics literature are described in Appendix 9.

The study by French and colleagues (1999) assessed the costs and outcomes of a modified therapeutic community (TC) intervention over 12-months follow-up for homeless mentally ill chemical abusers (MICAs), compared with standard services in a treatment-as-usual (TAU) condition. This study was based on the same US patient cohort assessed by De Leon and colleagues (2000). An array of outcome measures were used in the economic analysis, including substance use, criminal activity, HIV-risk behaviour, psychological status and employment status. The perspective of the cost analysis was from the health service provider. Resource use data were collected for the modified TC intervention, hospital detoxification, A&E visits, inpatient days, residential days, non-residential day visits, outpatient visits and methadone maintenance. Over 12 months, the total mean cost per patient was $29,255 for the modified TC group and $29,638 for the TAU group. Overall, the higher initial cost of the modified TC intervention was offset by the higher health service utilisation in the TAU group, including residential and non-residential day visits. In terms of effectiveness, multivariate analysis showed that modified TC patients reported significantly greater reductions in criminal activity and psychological dysfunction whilst no significant differences in substance use or HIV-risk behaviour were detected. No formal synthesis of costs and outcomes was carried out by the authors.

The results of this study is of limited applicability to the UK, as it is based on a US cohort and does not attempt to synthesise costs and benefits of the two interventions being compared in the form of an incremental cost-effectiveness ratio (ICER). The authors used an array of effectiveness measures rather than a single measure such as the QALY which makes interpretation of the results difficult. Other methodological limitations relate to the cohort study design, specifically in terms of comparability between the two treatment groups in terms of subject demographic characteristics. No mention was made of how patients were allocated to both treatment groups, leading to possible selection bias, although the authors used multivariate statistical analyses to attempt to control for this. The sample sizes used for clinical outcomes and the cost analysis were different and no sensitivity analyses were performed to explore uncertainty around the base-case results.

6.3.8 From evidence to recommendations (staffed accommodation)

Early in the development process, the GDG distinguished between outcomes that were critical to decision making and those that were important but not critical. Critical outcomes included: mortality (all causes), relapse rates (measured by exacerbation of symptoms requiring change in health care management), substance misuse (however measured), global and social functioning (e.g., employment, accommodation), subjective quality of life, satisfaction with care, and physical morbidity. Only critical outcomes were included in the GRADE evidence profiles.

Service users with coexisting substance misuse and psychosis are not ideally treated in a general ward setting, but tend to spend long periods in hospital (Menezes *et al.*, 1996). This environment is often counter-productive, where they generate great concern over the restrictions that are often imposed on them with regard to their potential to acquire illicit drugs, and in the disruption that is often created in their relationships with non-addicted patients.

Many of the patients with combined diagnoses are too vulnerable to be discharged from hospital and yet gain little from staying in, so there have been moves to place such patients in supported staffed accommodation that may include an element of specific treatment for the substance misuse.

Nevertheless, the evidence from randomised evidence is currently inconclusive, and positive results from observational studies could be explained by other factors, and relates to studies from the United States, which make generalisation to the UK context problematic.

6.4 CLINICAL PRACTICE RECOMMENDATIONS

6.4.1 Recommendations (staffed accommodation)

Staffed accommodation

Exclusion from services

6.4.1.1 Do not exclude people with psychosis and coexisting substance misuse from staffed accommodation solely because of their substance misuse.

6.4.1.5 Do not exclude people with psychosis and coexisting substance misuse from staffed accommodation aimed at addressing substance misuse solely because of their diagnosis of psychosis.

Aims of treatment

6.4.1.6 Ensure that people with psychosis and coexisting substance misuse who live in staffed accommodation receive treatment for both their psychosis and their substance misuse with the explicit aim of helping the person remain in stable accommodation.

6.4.2 Research recommendations (staffed accommodation)

6.4.2.1 Is providing treatment for psychosis and substance misuse services within staffed accommodation more cost-effective than a combination of hospital and home treatment?

6.4.2.2 What service delivery models allow people with psychosis and coexisting substance misuse to remain living outside hospital?

6.5 INPATIENT CARE

6.5.1 Introduction

The issues surrounding the management of inpatients with coexisting substance misuse and psychosis have been discussed in some detail at Chapter 5 (section 5.6). In brief, substance misuse is a common problem amongst people with a psychotic illness admitted to inpatient services (including secure services). Coexisting substance misuse results in longer lengths of stay in hospital and contributes substantially to incidents of violence within inpatient settings (Isaac *et al.,* 2005; Healthcare Commission, 2007). Continuing substance misuse may be a reason for delay in discharge from hospital either because psychotic symptoms are exacerbated or because of concern over the future risks to themselves or others that the patient might present should they continue to abuse substances.

Current practice

Current practice within inpatient services is not well described in the literature, although the difficulties both staff and patients experience because of coexisting substance misuse have been very clearly documented (Healthcare Commission, 2007; Loubser *et al.,* 2009). The Department of Health has issued guidance for inpatient services about working with people with psychosis and coexisting substance misuse (Department of Health, 2006), which is focused on the need to develop policies and procedures surrounding the practicalities associated with substance misuse amongst inpatients.

Definition of service

Any hospital-based specialist mental health service.

6.5.2 Clinical review protocol (inpatient care)

The review protocol, including the review question(s), information about the databases searched and the eligibility criteria used for this section of the guideline can be found in Table 1. A new systematic search for systematic reviews published since 2000 was conducted in August 2009 (further information about the search strategy can be found in Appendix 7).

Table 18. Clinical review protocol for inpatient care

Component	Description
Review question	1.3.1 When a person with psychosis and coexisting substance misuse is admitted to an inpatient mental health setting (including forensic settings), should treatment follow the same principles as interventions delivered in a community setting?
Electronic databases	CENTRAL, CINAHL, EMBASE, MEDLINE, PsycINFO
Date searched	01.01.2008 to 26.05.2010
Study design	RCTs and observational studies
Population	People with psychosis and coexisting substance misuse
Intervention(s)	Inpatient care
Comparison	Community care
Critical outcomes	• Reduced mortality (all causes) • Reduced relapse rates (measured by exacerbation of symptoms requiring change in health care management) • Reduced substance misuse (however measured) • Improved global and social functioning (e.g. employment, accommodation) • Improved subjective quality of life • Improved satisfaction with care • Reduced physical morbidity.
Note. RCT = Randomised controlled trial. *The search is an update to Cleary *et al*. (2008) and Cleary *et al*. (2009).	

6.5.3 Studies considered for review (inpatient care)

Two studies included in the psychological interventions chapter were conducted in inpatient settings, KAVANAGH2004 (Kavanagh *et al*., 2004) and LYKKE2010 (Lykke *et al*., 2010).

Of the included studies, one was a RCTs examining motivational interviewing (MI) versus standard care (KAVANAGH2004), and one was an observational study of 'cognitive milieu therapy' (LYKKE2010).

A number of other studies were also conducted in inpatient settings, but these were excluded from the review because only a small proportion of the sample were diagnosed with psychosis (e.g., Moos *et al.,* 2000; Rosenheck & Fontana, 2001; Timko *et al*., 2006).

6.5.4 Clinical evidence summary (inpatient care)

Evidence from two studies included in the psychological interventions chapter was of low quality and difficult to interpret, but suggested possible benefit of using psychological interventions to reduce substance misuse.

6.5.5 Health economic evidence (inpatient care)

No studies assessing the cost-effectiveness of inpatient care for people with psychosis and coexisting substance misuse were identified by the systematic search of the economic literature undertaken for this guideline. Details on the methods used for the systematic search of the economics literature are described in Appendix 9.

6.5.6 From evidence to recommendations (inpatient care)

Early in the development process, the GDG distinguished between outcomes that were critical to decision making and those that were important but not critical. Critical outcomes included: mortality (all causes), relapse rates (measured by exacerbation of symptoms requiring change in health care management), substance misuse (however measured), global and social functioning (e.g., employment, accommodation), subjective quality of life, satisfaction with care, and physical morbidity. Only critical outcomes were included in the GRADE evidence profiles.

The empirical literature does not at present provide good evidence to support clinical practice in this field. There are very few examples of evaluations of approaches to the management of substance misuse or specific substance misuse programmes within inpatient settings. Two studies have evaluated psychological therapies delivered in the inpatient setting, but provide little evidence to reach conclusions about the effectiveness of treatment (in addition, Miles *et al.,* 2007 report the results of a non-controlled study evaluating an integrated treatment for inpatients). In the absence of good quality evidence, it seems appropriate to ensure that any interventions that have proven efficacy in community settings in working with this population be deployed when a person is in an inpatient setting, wherever this is practicable.

6.6 CLINICAL PRACTICE RECOMMENDATIONS

6.6.1 Recommendations (inpatient care)

Inpatient mental health services

Substance misuse

6.6.1.1 All inpatient mental health services should ensure that they have policies and procedures for promoting a therapeutic environment free from drugs and alcohol that have been developed together with service users and carers. These should include: search procedures, visiting arrangements, planning and reviewing leave, drug and alcohol testing, disposal of legal and illicit substances, and other security measures. Soon after admission, provide all service users, and their families, carers and significant others, with information about the policies and procedures.

6.6.1.2 When carrying out a comprehensive assessment for all adults and young people admitted to inpatient mental health services, ensure that they are assessed for current substance misuse and evidence of withdrawal symptoms at the point of admission.

6.6.1.3 Ensure that planned detoxification from either drugs or alcohol is undertaken only:

- with the involvement and advice of substance misuse services
- in an inpatient setting, preferably in specialist detoxification units, or designated detoxification beds within inpatient mental health services, **and**
- as part of an overall treatment plan.

For the further management of opioid detoxification see the guideline on drug misuse: opioid detoxification (NICE clinical guideline 52). For the further management of assisted alcohol withdrawal see the guideline on alcohol use disorders: diagnosis, assessment and management of harmful drinking and alcohol dependence.

Discharge

6.6.1.4 Do not discharge adults and young people with psychosis and coexisting substance misuse from an inpatient mental health service solely because of their substance misuse.

6.6.1.5 When adults and young people with psychosis and coexisting substance misuse are discharged from an inpatient mental health service, ensure that they have:

- an identified care coordinator and
- a care plan that includes a consideration of needs associated with both their psychosis and their substance misuse.

7 PSYCHOLOGICAL AND PSYCHOSOCIAL INTERVENTIONS FOR PEOPLE WITH PSYCHOSIS AND COEXISTING SUBSTANCE MISUSE

7.1 INTRODUCTION

7.1.1 Factors related to the development of psychological treatment approaches

There is limited understanding of just how the problems of psychosis and substance use tend to be linked together (Blanchard *et al.,* 2000). Whilst people with psychosis give many different reasons for substance use, the research consistently shows that drugs and alcohol are used by this group for many of the same reasons as those reported by the general population: to increase pleasure, to fit in with others and to alleviate negative affective states, including boredom and depression (Gregg *et al.,* 2009). However, compared with the rest of the population, these reasons may be more prominent for people with psychosis. Many people with psychosis experience negative affective (Blanchard *et al.,* 2000), and Gregg and colleagues (2009) found that reports of drug and alcohol use to cope with distressing emotions and symptoms were common, with more than half of the large sample of people with psychosis and substance use reporting they used to cope with or reduce hallucinations or feelings of suspiciousness. Some individuals with psychosis describe using substances to try and counteract the side effects of antipsychotic medication (for example, Spencer *et al.,* 2002; Gregg *et al.,* 2007); or as a preferred alternative to taking prescribed medications (Schneier & Siris, 1987). Restrictive lifestyles and limitations for obtaining pleasure in other ways may also play a part (Barrowclough *et al.,* 2006); along with a desire to fit in and be accepted by others, especially since psychosis is characterised by high levels of interpersonal difficulties (Penn *et al.,* 2004).

Alcohol is the substance most frequently used by people with psychosis. As regards illicit drugs, cannabis is most common, although rates of poly substance use are high. This pattern of use is seen in the UK (Weaver *et al.,* 2003), the US (see review by Blanchard *et al.,* 2000) and Australia (Kavanagh *et al.,* 2004a) and is associated with the same demographic correlates as for the general population (Teeson *et al.,* 2000). It would seem that the social context

and availability of substances most often influence substance choices in psychosis (Kavanagh *et al.,* 2004a; Patkar *et al.,* 1999) rather than any relationship to service users' symptomatology (Brunette *et al.,* 1997).

Since the patterns and key motives of substance use are shared with the general population, the indications are that the psychological processes determining and maintaining use in people with psychosis may be similar to those found in non psychosis populations (Barrowclough *et al.,* 2006). Therefore it would seem likely that people with psychosis may benefit from treatment approaches developed for non – psychosis clients, although treatment may need to be modified to take account of issues specific to their mental health problems and associated circumstances.

Some of these issues present considerable challenges to treatment programmes. The functional aspects of substance use in psychosis may in part explain why motivation for reduction of substance use in clients with psychosis is usually low (Baker *et al.,* 2002; Barrowclough *et al.,* 2001; Martino *et al.,* 2002), and for many of this client group, attempting to facilitate motivation to reduce or abstain from substances may need to be the primary focus of therapy. Importantly, people with psychosis often suffer from low self esteem (Barrowclough *et al.,* 2003); thus, self efficacy may be low, which may further decrease motivation since people may feel unable to make change. Additionally, psychosis is commonly associated with a range of complex problems, making the problematic aspects of drug and alcohol use less obvious to the individual. This may be especially so when others in the same peer group are using at the same level, so use is not seen as unusual or particularly harmful. Added to these motivational issues, the nature of the mental health problems may lead to further treatment challenges. Studies indicate that engagement in treatment is often difficult and attrition rates are high (Drake *et al.,* 2004). Reasons why this might be the case include suspiciousness or paranoid symptoms, exacerbated by substance use; chaotic lifestyles making appointment scheduling difficult; and medication issues such as poor adherence to anti-psychotics (Martino *et al.,* 2002) or the substances rendering the medications less effective.

7.1.2 Current Practice

In both the UK and the US there has been agreement by consensus that a key element of treatment approaches for coexisting substance use and psychosis is the need to take account of individuals' motivation to address or reduce their substance use (Department of Health, 2002; Ziedonis *et al.,* 2005). Since motivation to change is often low, motivational techniques including motivational interviewing (MI, Miller & Rollnick, 2002) have been emphasised. Motivational interviewing is "a client-centred, directive method for enhancing intrinsic motivation to change by exploring and resolving ambivalence" (Miller & Rollnick, 2002). It aims to build intrinsic motivation for change and involves engaging the service user, offering information and

feedback from assessments, where appropriate, and exploring and resolving ambivalence in an affirming and non judgemental way. It is reported that the approach can successfully be employed with people with psychosis, although the process is likely to be lengthier and some of the strategies may need adaptation to take account of issues such as thought disorder, psychotic symptoms and impaired cognitive ability (Handmaker *et al.,* 2002, Martino, 2002, Barrowclough *et al.,* 2005).

The additional element that has been used most commonly in recent treatment approaches for people with psychosis and coexisting substance misuse is cognitive behaviour therapy (CBT). CBT is one of the most commonly used therapeutic orientations in the field of substance use disorders (Stewart & Conrad, 2005). Moreover, CBT is recommended for all people with schizophrenia (NCCMH, 2010), and for depression in pregnant women with bipolar disorder (NCCMH, 2006). The CBT approach for individuals with psychosis and coexisting substance misuse is guided by individual formulations and by Marlatt and Gordon's (1985) model of relapse prevention. Components may include: identifying and increasing awareness of high risk situations/warning signs; developing new coping skills for handling such situations and signs, with particular attention to psychotic symptoms and mental health related problems identified as contributing to risk of use (for example, CBT strategies for dealing with distressing voices, paranoia or depressed mood); coping with cravings and urges; making lifestyle changes so as to decrease need/urges for drugs and/or alcohol or to increase healthy activities/alternative options to substance use; normalising lapses in substance use and developing strategies and plans for acting in the event of lapse/relapse so that adverse consequences may be minimised; cognitive restructuring around alcohol and drug expectancies.

7.2 EVIDENCE REVIEW

7.2.1 Introduction

A number of existing NICE guidelines have reviewed the evidence for psychological and psychosocial interventions, and provided recommendations, both for people with psychosis without substance misuse (that is, bipolar disorder; schizophrenia), and for people with substance misuse without psychosis (that is, alcohol; drug misuse: psychosocial interventions) (see Table 19).

For the purposes of the current guideline, two main issues were addressed. First, in people with psychosis and coexisting substance misuse, is there evidence that any psychological/ psychosocial intervention, or combination of interventions, improve outcomes such as substance misuse, global and social functioning, and quality of life? Second, should interventions

Table 19: Relevant interventions included in current NICE guidelines

Intervention name	Existing NICE guideline*
Opportunistic brief interventions	
Brief interventions for people not in contact with services	Substance misuse: DMP
Brief interventions for people in contact with services	Substance misuse: DMP
Self-help based interventions	
Self-help interventions (including guided self-help/bibliotherapy, 12-step based interventions)	Substance misuse: Alcohol** DMP
Behavioural therapies	
Cue exposure	Substance misuse: Alcohol**
Behavioural self-control training	Substance misuse: Alcohol**
Contingency management	Substance misuse: Alcohol** DMP
Cognitive and behavioural based therapies	
CBT	Substance misuse: Alcohol** DMD DMP Psychosis: Bipolar disorder Schizophrenia (update)
Coping and Social skills training	Substance misuse: Alcohol**
Relapse prevention	Substance misuse: Alcohol**
Family-based interventions	
Family intervention	Substance misuse: Alcohol** DMD DMP Psychosis: Bipolar disorder Schizophrenia (update)
Motivational techniques	
Motivational interviewing/ Motivational Enhancement Therapy	Substance misuse: Alcohol** DMP
Social Network and Environment Based Therapies	
Social Behaviour and Network Therapy	Substance misuse: Alcohol**
The Community Reinforcement Approach	Substance misuse: Alcohol**
Social-systems interventions	Substance misuse: DMD DMP
Other interventions	
Adherence therapy	Psychosis: Schizophrenia (update)

Arts therapies	Psychosis: Schizophrenia (update)
Cognitive remediation	Psychosis: Schizophrenia (update)
Counselling and supportive psychotherapy	Substance misuse: Alcohol** Psychosis: Schizophrenia (update)
Couples-based interventions (including behavioural couples therapy)	Substance misuse: Alcohol** DMD DMP
Individual drug counselling	Substance misuse: DMD
Interpersonal and social rhythm therapy (IPSRT)	Psychosis: Bipolar disorder
Interpersonal therapy	Substance misuse: DMD DMP
Multi-modal care programmes	Substance misuse: Alcohol** DMP
Psychoeducational interventions	Substance misuse: Alcohol** Psychosis: Bipolar disorder Schizophrenia (update)
Psychodynamic psychotherapy and psychoanalysis	Substance misuse: Alcohol** DMD DMP Psychosis: Schizophrenia (update)
Social skills training	Psychosis: Schizophrenia (update)
Vocational interventions	Substance misuse: DMP
Note. DMD = Drug misuse: opioid detoxification; DMP = Drug misuse: psychosocial interventions. * Available from www.nice.org.uk ** Management of alcohol dependence guideline.	

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recommended for a single diagnosis (either psychosis or substance misuse) be modified as a result of the presence of the coexisting diagnosis and treatment provided? For example, in people with psychosis and coexisting substance misuse, should family intervention for treatment of their psychosis be modified as a result of the substance misuse problem and the treatment provided (for example, methadone)? In addition to the main issues, the GDG were also interested in whether there was any evidence that sub-groups of people (for example, young people, people with a particular type of psychosis, people from BME groups) may benefit from alternative treatment strategies?

Where no evidence existed for a particular intervention in people with psychosis and coexisting substance misuse, the GDG used informal consensus to reach a conclusion about whether it was appropriate to use interventions recommended by existing NICE guidance.

7.2.2 Definitions

Brief interventions

In the NICE DMP guideline (NCCMH, 2008b), brief interventions were defined as interventions with a maximum duration of two sessions. The main aim of the intervention is to enhance the possibility of change in terms of abstinence or the reduction of harmful behaviours associated with drug misuse. The principles of brief interventions include expressing empathy with the service user, not opposing resistance and offering feedback, with a focus on reducing ambivalence about drug misuse and possible treatment. A number of brief interventions are based on principles drawn from motivational interviewing. Brief interventions can be conducted in a variety of settings, including non-medical settings, and can be given opportunistically to people not in formal drug treatment or as an adjunct to formal structured drug treatment (Ashton, 2005).

Self-help based interventions

Self-help intervention

In the NICE alcohol guideline (NCCMH, in press), a self-help intervention was defined as an intervention where a healthcare professional (or para-professional) would facilitate the use of the self-help material by introducing, monitoring and reviewing the outcome of such treatment. The intervention is limited in nature, usually no more than three to five sessions some of which may be delivered by telephone. Self-administered intervention are designed to modify drinking behaviour and makes use of a range of books, web pages, CD-ROMs or a self-help manual that is based on an evidence-based intervention and designed specifically for the purpose. An example is Guided Self Change (GSC) (Sobell & Sobell, 1993). This treatment is manual-based and uses the principles of cognitive behavioural therapy and motivational

enhancement therapy. The service user has an initial assessment followed by four treatment sessions and two follow-up telephone calls.

Self-help group

In the NICE DMP guideline (NCCMH, 2008b), a self-help group was defined as a group of people who misuse drugs who meet regularly to provide help and support for one another. The group is typically community based, peer led and non-professional.

12-step self-help group

In the NICE DMP guideline (NCCMH, 2008b), a 12-step self-help group was defined as a non-profit fellowship of people who meet regularly to help each other remain abstinent. The core of the 12-step programme is a series of 12 steps that include admitting to a drug problem, seeking help, self-appraisal, confidential self-disclosure, making amends – when possible – where harm has been done, achieving a spiritual awakening and supporting other drug-dependent people who want to recover.

Twelve-Step Facilitation (TSF)

In the NICE alcohol guideline (NCCMH, in press), Twelve-Step Facilitation was defined as an intervention based on the twelve-step or Alcoholics Anonymous (AA) concept that alcoholism is a spiritual and medical disease. As well as a goal of abstinence, this intervention aims to actively encourage commitment to and participation in AA meeting. Participants are asked to keep a journal of AA attendance and participation and are given AA literature relevant to the 'step' of the programme the service user has reached. Twelve-Step Facilitation is highly structured and manualised (Nowinski *et al*., 1992) and involves a weekly session in which the service user is asked about their drinking, AA attendance and participation, given an explanation of the themes of the current sessions, and goals for AA attendance are set.

Behavioural therapies

Cue exposure

In the NICE alcohol guideline (NCCMH, in press), cue exposure was defined as a treatment for alcohol misuse that is based on both learning theory models and social learning theory and suggests that environmental cues associated with drinking can elicit conditioned responses which can in turn lead to a relapse (Niaura *et al*. 1988). The first case study using cue exposure treatment for excessive alcohol consumption was reported by Hodgson & Rankin (1976). Treatment is designed to reduce craving for alcohol by repeatedly exposing the service user to alcohol related cues until the service user 'habituates' to the cues and can hence maintain self-control in a real-life situation where these cues are present.

Behavioural self-control training

In the NICE alcohol guideline (NCCMH, in press), behavioural self-control training (also referred to as 'behavioural self-management training') was defined as approach based on the techniques described by Miller and Muńoz (1976). Service users are taught to set limits for drinking, self-monitor drinking episodes, refusal skills training and training for coping behaviours in high-risk relapse situations. Behavioural self-control training is focused on a moderation goal rather than abstinence.

Contingency management

In the NICE DMP guideline (NCCMH, 2008b, contingency management was defined as an approach that considers drug use as an example of operant behaviour that is maintained partly by the pharmacological effects of the drug in combination with other social and non-drug reinforcement provided by the drug using lifestyle (Petry, 2006). In the Alcohol guideline, contingency management was described as a system of reinforcement designed to make continual alcohol use less attractive and abstinence more attractive.

Contingency management seeks to provide alternative incentives contingent on abstinence from a particular target drug. There are four primary methods of providing incentives:

- Voucher-based reinforcement: People who misuse drugs or alcohol receive vouchers with various monetary values (usually increasing in value after successive periods of abstinence) for providing biological samples (usually urine) that are negative for the tested substances. These vouchers are withheld when the biological sample indicates recent substance use. Once earned, vouchers are exchanged for goods or services that are compatible with a substance-free lifestyle.

- Prize-based reinforcement: This is more formally referred to as the 'variable magnitude of reinforcement procedure' (Prendergast *et al*., 2006). Participants receive draws, often from a number of slips of paper kept in a fishbowl, for providing a negative biological specimen. Provision of a specimen indicating recent substance use results in the withholding of draws. Each draw has a chance of winning a 'prize', the value of which varies. Typically, about half the draws say 'Good job!'. The other half results in the earning of a prize, which may range in value from £1 to £100 (Prendergast *et al*., 2006).

- Clinic privileges: Participants receive clinic privileges for performing the target behaviour, for example, providing a negative biological sample. But these privileges are withheld when the target behaviour is not performed. An example of a clinic privilege is a take-home methadone dose (for example, Stitzer *et al*., 1992).

- Cash incentives: People who misuse drugs receive cash (usually of a relatively low value, for example, £1.50–£10) for performing the target behaviour, such as submitting a urine sample negative for drugs or adherence with particular interventions. Cash incentives are withheld when the target behaviour is not performed.

Cognitive and behavioural based therapies

Standard Cognitive Behavioural Therapy (CBT)

In the NICE alcohol guideline (NCCMH, in press) and DMP guideline (NCCMH, 2008b), sstandard CBT was defined as a discrete, time-limited, structured psychological intervention, derived from a cognitive model of drug misuse (Beck *et al*., 1993). There is an emphasis on identifying and modifying irrational thoughts, managing negative mood and intervening after a lapse to prevent a full-blown relapse.

In the NICE guideline on schizophrenia (updated edition; NCCMH, 2010)[9], CBT was defined as a discrete psychological intervention where service users:

- establish links between their thoughts, feelings or actions with respect to the current or past symptoms, and/or functioning, and
- re-evaluate their perceptions, beliefs or reasoning in relation to the target symptoms.

In addition, a further component of the intervention should involve the following:

- service users monitoring their own thoughts, feelings or behaviours with respect to the symptom or recurrence of symptoms, and/or
- promotion of alternative ways of coping with the target symptom, and/or
- reduction of distress, and/or
- improvement of functioning.

Coping and Social Skills Training

In the NICE alcohol guideline (NCCMH, in press), coping and social skills training was defined as a variant of CBT that is based on social learning theory of addiction and the relationship between drinking behaviour and life problems (Marlatt & Gordon, 1985; Kadden *et al*., 1992). Treatment is manual-based (Marlatt & Gordon, 1985) and involves increasing the individual's ability to cope with high-risk social situations and inter-personal difficulties.

[9] A similar definition was provided in the NICE bipolar guideline.

Relapse-prevention

In the NICE alcohol guideline (NCCMH, in press), relapse prevention was defined as a CBT adaptation based on the work of Marlatt (Marlatt & Gordon, 1985), this incorporates a range of cognitive and behavioural therapeutic techniques to identify high risk situations, alter expectancies and increase self-efficacy. This differs from standard CBT in the emphasis on training people who misuse alcohol to develop skills to identify situations or states where they are most vulnerable to alcohol use, to avoid high-risk situations, and to use a range of cognitive and behavioural strategies to cope effectively with these situations (Annis, 1986; Marlatt & Gordon, 1985).

Family-based interventions

Family intervention

In the NICE guideline on schizophrenia (updated edition; NCCMH, 2010), family intervention was defined as discrete psychological interventions where:

- family sessions have a specific supportive, educational or treatment function and contain at least one of the following components:
    - problem solving/crisis management work, or
    - intervention with the identified service user.

Motivational techniques

Motivational interviewing

For the purposes of the current guideline, MI was defined as "a client-centred, directive method for enhancing intrinsic motivation to change by exploring and resolving ambivalence" (Miller & Rollnick, 2002). It aims to build intrinsic motivation for change and involves engaging the client, offering information and feedback from assessments, where appropriate, and exploring and resolving ambivalence in an affirming and non judgemental way. In people with psychosis, the process is likely to be lengthier and some of the strategies may need adaptation to take account of issues such as thought disorder, psychotic symptoms and impaired cognitive ability (Handmaker *et al.*, 2002, Martino, 2002, Barrowclough *et al.*, 2005).

Motivational Enhancement Therapy

In the NICE alcohol guideline (NCCMH, in press), Motivational Enhancement Therapy (MET) was defined as an approach based on the methods and principles of MI (Miller *et al.*, 1992). It is patient-centred and aims to result in rapid internally motivated changes by exploring and resolving ambivalence towards behaviour. The treatment strategy of motivational interviewing is not to guide the client through recovery step by step, but to use motivational methods and strategies to utilise the service user's resources. A more specific manualised and structured form of motivational interviewing based on the work of Project MATCH is usually utilised (Project Match Research Group, 1993).

Social Network and Environment Based Therapies

Social Behaviour and Network Therapy

In the NICE alcohol guideline (NCCMH, in press), Social Behaviour and Network Therapy (SBNT) was defined as comprising of a range of cognitive and behavioural strategies to help clients build social networks supportive of change which involve the service user and members of the service user's networks (for example, friends and family) (Copello, 2002). The integration of these strategies has the aim of helping the service user to build 'positive social support for a change in drinking'.

The Community Reinforcement Approach

In the NICE alcohol guideline (NCCMH, in press), the community reinforcement approach (Hunt & Azrin, 1973; Meyers & Miller, 2001; Sisson & Azrin, 1989), was defined as an approach where emphasis is placed on maintaining abstinence through the development of activities that do not promote alcohol use, for example, recreational and social activities, employment and family involvement.

Social-systems interventions

In the NICE DMP guideline (NCCMH, 2008b), it was suggested that social-systems interventions were developed primarily (but not exclusively) for young people. These interventions aim to address a range of risk and protective factors for drug misuse within the service user's wider social network. Family members, partners, close friends and other significant individuals (such as teachers or probation officers) may be involved in joint treatment sessions with the service user in a range of settings (for example, Henggeler *et al*., 1999).

Other interventions

Adherence therapy

In the NICE guideline on schizophrenia (updated edition; NCCMH, 2010), adherence therapy was defined as any programme involving interaction between service provider and service user, during which service users are provided with support, information and management strategies to improve their adherence to medication and/or with the specific aim of improving symptoms, quality of life and preventing relapse.

Arts therapies

In the NICE guideline on schizophrenia (updated edition; NCCMH, 2010), arts therapies were defined as complex interventions that combine psychotherapeutic techniques with activities aimed at promoting creative expression. In all arts therapies:

- the creative process is used to facilitate self-expression within a specific therapeutic framework

- the aesthetic form is used to 'contain' and give meaning to the service user's experience
- the artistic medium is used as a bridge to verbal dialogue and insight-based
- psychological development if appropriate
- the aim is to enable the service user to experience him/herself differently and develop new ways of relating to others.

Arts therapies currently provided in the UK comprise: art therapy or art psychotherapy, dance movement therapy, body psychotherapy, dramatherapy and music therapy.

Cognitive remediation

In the NICE guideline on schizophrenia (updated edition; NCCMH, 2010), cognitive remediation was defined as:

- an identified procedure that is specifically focused on basic cognitive processes, such as attention, working memory or executive functioning, and
- having the specific intention of bringing about an improvement in the level of performance on that specified cognitive function or other functions, including daily living, social or vocational skills.

Counselling and supportive psychotherapy

In the NICE guideline on schizophrenia (updated edition; NCCMH, 2010), counselling and supportive therapy were defined as discrete psychological interventions that:

- are facilitative, non-directive and/or relationship focused, with the content largely determined by the service user, and
- do not fulfil the criteria for any other psychological intervention.

Couples-based interventions

In the NICE alcohol guideline (NCCMH, in press), it is suggested that the content and definition of couples therapy can vary and reflect different approaches, for example, cognitive behavioural or psychodynamic. Couples-based interventions (including behavioural couple's therapy [BCT]) involve the spouse or partner expressing active support for the person who misuses alcohol in reducing alcohol use, including via the use of behavioural contracts. Couples are helped to improve their relationship through more effective communication skills, and encouraged to increase positive behavioural exchanges through acknowledgement of pleasing behaviours and engagement in shared recreational activities (Fals-Stewart *et al*., 2005).

Standard BCT is manual based and structured (Fals-Stewart *et al*., 2004) and combines cognitive-behaviour treatment strategies with methods that address relationship issues arising from alcohol misuse as well as more general relationship problems with the aim of reducing distress.

Individual drug counselling

In the NICE DMD guideline (NCCMH, 2008a), individual drug counselling was defined as the assessment of an individual's needs, provision of information and referral to services to meet these needs (including psychosocial interventions, methadone and residential rehabilitation). No attempt is made to engage in any specific formal psychological intervention. Sessions are normally weekly and last 15–20 minutes (Rawson *et al*., 1983). This to some extent resembles keyworking as used in the UK drug treatment field.

Interpersonal and social rhythm therapy (IPSRT)

In the NICE guideline on bipolar disorder (NCCMH, 2006), IPSRT was defined as discrete, time limited, structured psychological intervention derived from an interpersonal model of affective disorders that focuses on:

- working collaboratively with the therapist to identify the effects of key problematic areas related to interpersonal conflicts, role transitions, grief and loss, and social skills, and their effects on current symptoms, feelings states and/or problems
- seeking to reduce symptoms by learning to cope with or resolve these interpersonal problem areas
- seeking to improve the regularity of daily life in order to minimise relapse.

Interpersonal therapy

In the NICE DMP guideline (NCCMH, 2008b), interpersonal therapy (IPT) was defined as a discrete, time-limited, structured psychological intervention, originally developed for the treatment of depression, which focuses on interpersonal issues and where therapist and service user:

- work collaboratively to identify the effects of key problematic areas related to interpersonal conflicts, role transitions, grief and loss, and social skills, and their effects on current drug misuse, feelings states and/or problems; and
- seek to reduce drug misuse problems by learning to cope with or resolve interpersonal problem areas (Weissman *et al*., 2000).

Multi-modal care programmes

In the NICE DMP guideline (NCCMH, 2008b), multi-modal care programmes were defined as those including a combination of therapy activities delivered in intensive schedules of 10 hours per week or more. Content of these programmes varies but would usually include education, daily living skills and other psychologically based interventions (for example, CBT, relapse prevention and reinforcement-based approaches), mostly delivered in group format. Such programmes are not common in generic drug treatment services in the UK, although they are available in some areas. They are more commonly used within drug services linked to the criminal justice system as a way of providing more intensive programmes for those referred. The current use of these interventions in the UK is limited and their distribution is not well understood.

Psychoeducational interventions

In the NICE guideline on schizophrenia (updated edition; NCCMH, 2010), psychoeducational interventions were defined as:

- any programme involving interaction between an information provider and service users or their carers, which has the primary aim of offering information about the condition; and
- the provision of support and management strategies to service users and carers.

To be considered as well defined, the educational strategy should be tailored to the need of individuals or carers.

Psychodynamic and psychoanalytic therapies

In the NICE guideline on schizophrenia (updated edition; NCCMH, 2010), psychodynamic interventions were defined as having:

- regular therapy sessions based on a psychodynamic or psychoanalytic model; and
- sessions that could rely on a variety of strategies (including explorative insight-orientated, supportive or directive activity), applied flexibly.

To be considered as well-defined psychodynamic psychotherapy, the intervention needed to include working with transference and unconscious processes.

Psychoanalytic interventions were defined as having:

- regular individual sessions planned to continue for at least 1 year; and
- analysts required to adhere to a strict definition of psychoanalytic technique.

To be considered as well-defined psychoanalysis, the intervention needed to involve working with the unconscious and early child/adult relationships.

Social skills training

In the NICE guideline on schizophrenia (updated edition; NCCMH, 2010), social skills training was defined as a structured psychosocial intervention (group or individual) that aims to enhance social performance, and reduce distress and difficulty in social situations. The intervention must:

- include behaviourally-based assessments of a range of social and interpersonal skills, and
- place importance on both verbal and non-verbal communication, the individual's ability to perceive and process relevant social cues, and respond to and provide appropriate social reinforcement.

Vocational interventions

In the NICE DMP guideline (NCCMH, 2008b), pre-vocational training was defined as any approach to vocational rehabilitation in which participants are expected to undergo a period of preparation before being encouraged to seek competitive employment. This preparation could involve either work in a sheltered environment (such as a workshop or work unit), or some form of pre-employment training or transitional employment (Crowther *et al*., 2001). Supported employment was defined as any approach to vocational rehabilitation that attempts to place service users immediately in competitive employment. It is acceptable for supported employment to begin with a short period of preparation, but this has to be of less than one month's duration and not involve work placement in a sheltered setting, or training, or transitional employment (Crowther *et al*., 2001).

7.2.3 Clinical review protocol (psychological/ psychosocial interventions)

The review protocol, including the review questions, information about the databases searched, and the eligibility criteria used for this section of the guideline, can be found in Table 20. During the early stages of guideline development, a recent Cochrane review (Cleary *et al.,* 2008) and related peer-reviewed publication (Cleary *et al.,* 2009) were identified that addressed the review question. These systematic reviews were used as a source of evidence, and only a new systematic search for more recent primary-level studies was conducted for the guideline (further information about the search strategy can be found in Appendix 7).

If the evidence allowed, the following sub-question was asked for review question 2.2.1 and 2.4.1: Are there sub-groups of people (for example, adolescents, people with a particular type of psychosis, BME groups) that may benefit from alternative strategies? In addition, the following sub-

question was asked for review question 2.4.1: Should interventions be matched to stages of the treatment process (i.e. engagement, persuasion, active treatment, relapse prevention)?

Table 20: Clinical review protocol for the review of psychological/ psychosocial interventions

Component	Description
Review question	1.2.2 In people with psychosis and coexisting substance misuse, do psychological/psychosocial interventions when compared to an alternative management strategy lead to improved outcomes? 2.2.1 For people with psychosis and coexisting substance misuse, should the psychological/psychosocial (family interventions, CBT, arts therapies) treatment of their psychosis be modified as a result of the substance misuse problem and the treatment provided (for example, methadone, buprenorphine, psychological treatment etc)? A) During the acute phase B) During non-acute phase If so, how should treatment be modified? 2.4.1 For people with psychosis and coexisting substance misuse, should psychological/psychosocial treatment for substance misuse be modified as a result of the presence of psychosis and the treatment provided? A) During the acute phase B) During non-acute phase If so, how should treatment be modified?
Electronic databases	CENTRAL, CINAHL, EMBASE, MEDLINE, PsycINFO
Date searched	01.01.2008 to 26.05.2010*
Study design	RCTs and observational studies
Population	People with psychosis and coexisting substance misuse
Intervention(s)	Individual psychological/psychosocial interventions for people with psychosis and coexisting substance misuse
Comparison	An alternative management strategy
Critical outcomes	Reduced mortality (all causes) Reduced relapse rates (measured by exacerbation of symptoms requiring change in health care management) Reduced substance misuse (however measured) Improved global and social functioning (for example, employment, accommodation) Improved subjective quality of life Improved satisfaction with care Reduced physical morbidity.
*The search is an update to Cleary *et al.* (2008) and Cleary *et al.* (2009).	

7.2.4 Studies considered for review (psychological/psychosocial interventions)[10]

11 RCTs, BAKER2006 (Baker *et al*., 2006b), BARROWCLOUGH2001 (Barrowclough *et al*., 2001), EDWARDS2006 (Edwards *et al*., 2006), GRAEBER2003 (Graeber *et al*., 2003), HELLERSTEIN1995 (Hellerstein, Rosenthal & Miner, 1995), JERRELL1995 (Jerrell & Ridgely, 1995), KAVANAGH2004 (Kavanagh *et al*., 2004b), RIES2004 (Ries *et al*., 2004), SCHMITZ2002 (Schmitz *et al*., 2002), TRACY2007 (Tracy *et al*., 2007), WEISS2007 (Weiss *et al*., 2007), that were included in the review by Cleary and colleagues (2008), met the eligibility criteria for this review. In addition, one further trial was identified during the search for evidence, WEISS2009 (Weiss *et al*., 2009). Full study characteristics (and any associated references), as well as a list of excluded studies can be found in Appendix 13.

Of the 12 included RCTs, there were four involving a comparison of CBT versus standard care (EDWARDS2006, SCHMITZ2002, WEISS2007, WEISS2009), two of MI versus standard care (GRAEBER2003, KAVANAGH2004b), two of a group therapy (social skills training/ psychoeducation) versus standard care (HELLERSTEIN1995, JERRELL1995), two of contingency management versus standard care (RIES2004, TRACY2007), and two of CBT combined with MI versus standard care (BAKER2006b, BARROWCLOUGH2001) (see Table 21 and Table 22 for summary information about each trial).

In addition to the RCTs, three observational studies (James *et al*., 2004; Santa Ana *et al*., 2007; Weiss *et al*., 2000), that were included in the review by Cleary and colleagues (2008), met the eligibility criteria for review. A further three studies (Helmus *et al*., 2003; Lykke *et al*., 2010; Tyrer *et al*., in press) were found during the search for evidence.

Of the six observational studies, one involved a comparison of CBT versus standard care (Weiss *et al*., 2000), one of motivational interviewing versus therapist attention activity control (Santa Ana *et al*., 2007), one of group psychotherapy versus standard care (single educational session) (James *et al*., 2004), one of a contingency management program (Helmus *et al*., 2003), one of cognitive milieu therapy (Lykke *et al*., 2010), and one of nidotherapy (Tyrer *et al*., in press) (see section 7.2.6 for further information about each study and a narrative summary of results).

[10] Here and elsewhere in the guideline, each RCT considered for review is referred to by a study ID (primary author and date of study publication, except where a study is in press or only submitted for publication, then a date is not used).

Table 21: Study information table for trials comparing CBT, MI, or CBT plus MI with standard care

	CBT versus standard care	MI versus standard care	CBT + MI versus standard care
Total no. of trials (N)	4 RCTs (216)	2 RCTs (56)	2 RCTs (166)
Study ID	(1) EDWARDS2006 (2) SCHMITZ2002 (3) WEISS2007 (4) WEISS2009	(1) GRAEBER2003 (2) KAVANAGH2004b	(1) BAKER2006b (2) BARROWCLOUGH2001
Number randomised	(1) 47 (2) 46 (3) 62 (4) 61	(1) 30 (2) 25	(1) 130 (2) 36
Diagnosis	(1) 72% DSM-IV schizophrenia/schizophreniform, 11% affective psychosis, 17% NOS/ delusional /other and all actively using cannabis. (2) 100% DSM-IV bipolar disorder and substance use disorder (72% alcohol, 61% cocaine, 26% marijuana, 59% were dependent on more than 1 drug). (3) 100% DSM-IV bipolar disorder and substance dependence (most common; 27% alcohol, 26% marijuana). (4) 100% DSM-IV bipolar disorder with dependence (26.2% had alcohol dependence only, 8.2% had drug dependence only, and 65.6% had both).	(1) 100% DSM-IV schizophrenia and met criteria for an alcohol use disorder within the 3- month period prior to study enrolment; service users with additional non-alcohol substance use (except active intravenous drug abuse) were eligible for protocol enrolment. (2) 100% DSM-IV psychotic disorder with a current DSM-IV substance use disorder (88% alcohol, 76% cannabis, 12% inhalants, 8% cocaine or heroin).	(1) 75% ICD-10 schizophrenia or schizoaffective disorder with SCID-1 diagnosis of abuse or dependence past 12 months (alcohol 69%, cannabis 74%, amphetamine 42%)* (2) ICD-10 & DSM-IV schizophrenia or schizoaffective disorder with DSM-IV substance abuse or dependence.
Ethnicity	(1) NR (2) 80% White (3) 94% White (4) 92% White	(1) 40% White, 40% Hispanic, 20% African American (2) 84% White	(1) NR (2) White European
Treatment length	(1) 6 months (2) 3 months (3) 8 months (4) 6 months	(1) 6 months (2) 12 months	(1) 12 months (2) 18 months
Country	(1) Australia (2) USA (3) USA (4) USA	(1) USA (2) Australia	(1) Australia (2) UK
Intervention (n)	(1) Cannabis-focused CBT (weekly over 3	(1) Motivational interviewing (3 sessions)	(1) Motivational interviewing and CBT

	months) (n=23) (2) Medication monitoring and CBT (16 sessions) (n=25) (3) Integrated group CBT (20 weekly 1 hour sessions) (n=31) (4) Integrated group CBT (12 weekly 1 hour sessions) (n=31)	(n=15) (2) Brief motivational intervention (6–9 sessions) (n=13)	(10 weekly one hour sessions) + routine care (n=65 (2) Family support worker plus motivational interviewing, manualised individual CBT for the participant and CBT for family / caregiver (a total of 29 individual sessions) + routine care (n=18
Control (n)	(1) Psychoeducation + standard EPPIC care (n=24) (2) Standard care (includeds medication monitoring) (n=21) (3) Group drug counselling (n=31) (4) Group drug counselling (n=30)	(1) Three-session educational intervention (n=15) (2) Standard care (n=12)	(1) Routine care plus self-help books (n=65) (2) Routine care plus family support worker (n=18)
Note. CBT = cognitive behavioural therapy; MI = motivational interviewing; N = total number of participants; n = number of participants in each group.			

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Table 22: Study information table for trials comparing group approaches or contingency management with standard care

	Group psychotherapy (social skills training/ psychoeducation) versus standard care	Contingency management versus standard care
Total no. of trials (N)	2 RCTs (94)	2 RCTs (71)
Study ID	(1) HELLERSTEIN1995 (2) JERRELL1995	(1) RIES2004 (2) TRACY2007
Number randomised	(1) 47 (2) 47	(1) 41 (2) 30
Diagnosis	(1) RDC schizophrenia with 74% DSM-III-R psychoactive substance abuse/ dependence. (2) 62% DSM-III-R schizophrenia with coexisting substance disorder.	(1) 73% schizophrenia or schizoaffective disorder, 24% major recurrent depression or bipolar disorder, 2% other, and DSM-IV substance misuse disorder with active substance use in the previous 6 months. (2) 100% current or lifetime DSM-IV diagnosis of an Axis I psychiatric disorder and current diagnosis of cocaine or alcohol abuse or dependence.
Ethnicity	(1) 43% African American, 32% Hispanic (2) 64% White	(1) NR (2) NR
Treatment length	(1) 8 months (2) 18 months	(1) 6.5 months (2) 1 month
Country	(1) USA (2) USA	(1) USA (2) USA
Intervention (n)	(1) Group outpatient psychotherapy & psychoeducation plus drug treatment all at same site (twice weekly) (n=23) (2) Behavioural skills programme: psychoeducational approach with self-management skills, repeated practice & reinforcement (weekly group sessions with two licensed clinicians) (n=22)	(1) Contingency management of supplementary social security income/food vouchers and motivational message (n=22) (2) Petry's low-cost contingency management with variable ratio reinforcement (n=15)
Control (n)	(1) Comparable levels of psychiatric care and substance abuse treatment from separate sites without formal case-coordination (n=24) (2) Twelve step recovery programme: clinical staff (some 'recoverers') offered mock AA meetings within the Mental Health Centre, took or referred clients to community AA	(1) Non-contingency management of benefits (n=19) (2) Assessment-only treatment (n=15)

	meetings, facilitated a sponsor relationship & provided counselling (n=25)	

Note. N = total number of participants; n = number of participants in each group; NR = not reported; RCT = randomised controlled trial.
*Some participants were dependent on more than one of these.

7.2.5 Evidence from RCTs (psychological/psychosocial interventions)

Meta-analysis was used to synthesise the evidence for each comparison (GRADE summary of findings tables are shown in Table 13, Table 24, Table 25, Table 26, and Table 27).

The forest plots and full GRADE evidence profiles can be found in Appendix 14 and 15, respectively.

Table 23. GRADE summary of findings table for RCTs comparing CBT with standard care

Outcomes	Effect size (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)
Substance use: 1. Using substances - by 1 month - alcohol or drugs	RR 0.48 (0.26 to 0.9)	61 (1 study)	⊕⊕⊕⊖ moderate[1]
Substance use: 2. Using substances - by 3 months – alcohol	RR 5.88 (0.79 to 44.03)	46 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 2. Using substances - by 3 months – drugs	RR 2.02 (0.85 to 4.8)	46 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 2. Using substances - by 3 months - alcohol or drugs	RR 0.74 (0.55 to 1)	61 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 3. Any substance (skewed data) - average score (ASI) by 3 months	MD -0.07 (-0.16 to 0.02)	62 (1 study)	⊕⊕⊖⊖ low[1,3]
Substance use: 3. Any substance (skewed data) - average score (ASI) by 6–9 months	MD -0.06 (-0.16 to 0.04)	62 (1 study)	⊕⊕⊖⊖ low[1,3]
Substance use: 3. Any substance (skewed data) - days reporting any substance use (ASI) by 3 months	MD -2.1 (-5.9 to 1.7)	61 (1 study)	⊕⊕⊖⊖ low[1,2,3]
Substance use: 3. Any substance (skewed data) - days reporting any substance use (ASI) by 6 months	MD -2.7 (7.25 to 1.85)	61 (1 study)	⊕⊕⊖⊖ low[1,2,3]
Substance use: 4. Drugs use - by 3 months (skewed data)	MD 0.05 (-1.55 to 1.66)	103 (2 studies)	⊕⊕⊖⊖ low[1,3]
Substance use: 5. Drugs use - by 6 months (skewed data) - days reporting drug use (ASI) by 6 months	MD -3.7 (-7.99 to 0.59)	57 (1 study)	⊕⊕⊖⊖ low[1,2,3]
Substance use: 6. Alcohol use - by 3 months (skewed data)	MD -1.95 (-4.48 to 0.58)	103 (2 studies)	⊕⊕⊖⊖ low[1,2,3]
Substance use: 7. Alcohol use - by 6 months (skewed data) - days reporting alcohol use (ASI) by 6 months	MD 0 (-3.66 to 3.66)	57 (1 study)	⊕⊕⊖⊖ low[1,2,3]

Note. A RR of < 1 favours the intervention, negative MDs favour the intervention; CI = confidence interval; MD = mean difference; RR = Relative Risk.

[1] Optimal information size not met.

[2] CI includes both 1) no effect and 2) appreciable benefit or appreciable harm.

[3] Skewed data.

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Table 24. GRADE summary of findings table for RCTs comparing MI with standard care

Outcomes	Effect size (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)
Substance use: 1. Not abstinent or not improved on all substances - by 12 months	RR 0.51 (0.24 to 1.1)	25 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 2. Not abstaining from alcohol - by 3 months	RR 0.52 (0.26 to 1.03)	28 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 2. Not abstaining from alcohol - by 6 months	RR 0.36 (0.17 to 0.75)	28 (1 study)	⊕⊕⊕⊖ moderate[1]
Substance use: 3. Other measures of alcohol use (skewed data)	SMD -1.29 (-2.12 to -0.46)	28 (1 study)	⊕⊕⊕⊖ moderate[1]
Substance use: 3. Other measures of alcohol use (skewed data) - drinking days - by 6 months	SMD -1.29 (-2.12 to -0.46)	28 (1 study)	⊕⊕⊖⊖ low[1,3]

Note. A RR of < 1 favours the intervention, negative MDs favour the intervention; CI = confidence interval; MD = mean difference; MI = motivational interviewing; RCT = randomised controlled trial; RR = Relative Risk.

[1] Optimal information size not met.

[2] CI includes both 1) no effect and 2) appreciable benefit or appreciable harm.

[3] Skewed data.

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Table 25. GRADE summary of findings table for RCTs comparing CBT plus MI with standard care

Outcomes	Effect size (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)
Death - by about 1 year	RR 1.25 (0.22 to 7.28)	166 (2 studies)	⊕⊕⊖⊖ low[1,2]
Substance use: 1. Average number of different drugs used during the past month (OTI) - by 3 months	MD 0.37 (-0.01, 0.75)	119 (1 study)	⊕⊕⊕⊖ moderate[2]
Substance use: 1. Average number of different drugs used during the past month (OTI) - by 6 months	MD 0.19 (-0.22, 0.60)	119 (1 study)	⊕⊕⊕⊖ moderate[2]
Substance use: 2. Average score - alcohol (skewed data) - alcohol - estimated daily consumption - past month - 3 months	MD 1.57 (-0.90, 4.04)	52 (1 study)	⊕⊕⊕⊖ moderate[2]
Substance use: 2. Average score - alcohol (skewed data) - alcohol - estimated daily consumption - past month - 6 months	MD 1.21 (-1.07, 3.49)	52 (1 study)	⊕⊕⊕⊖ moderate[2]
Substance use: 2. Average score - alcohol (skewed data) - alcohol - estimated daily consumption - past month - 12 months	MD 1.39 (-1.10, 3.88)	46 (1 study)	⊕⊕⊕⊖ moderate[2]
Substance use: 3. Average score - amphetamine (skewed data) - amphetamine- estimated daily consumption - past month - 3 months	MD 0.09 (-0.40, 0.58)	20 (1 study)	⊕⊕⊕⊖ moderate[2]
Substance use: 3. Average score - amphetamine (skewed data) - amphetamine- estimated daily consumption - past month - 6 months	MD -1.28 (-2.79, 0.23)	20 (1 study)	⊕⊕⊕⊖ moderate[2]
Substance use: 3. Average score - amphetamine (skewed data) - amphetamine- estimated daily consumption - past month - 12 months	MD 0.13 (-0.11, 0.37)	17 (1 study)	⊕⊕⊕⊖ moderate[2]
Substance use: 4. Average score - cannabis (skewed data) - cannabis- estimated daily consumption - past month - 3 months	MD -0.57 (-4.27, 3.13)	73 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 4. Average score - cannabis (skewed data) - cannabis- estimated daily consumption - past month - 6 months	MD 0.70 (-4.00, 5.40)	73 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 4. Average score - cannabis (skewed data) - cannabis- estimated daily consumption - past month - 12 months	MD 4.41 (-1.40, 10.22)	58 (1 study)	⊕⊕⊖⊖ low[1,2]
Functioning: 1. Average global functioning score (GAF) - 3 months	MD -2.70 * (-7.05, 1.65)	119 (1 study)	⊕⊕⊖⊖ low[1,2]
Functioning: 1. Average global functioning score (GAF) - 6 months	MD -0.09 * (-3.70, 3.52)	119 (1 study)	⊕⊕⊕⊖ moderate[2]
Functioning: 1. Average global functioning score (GAF) - 9 months	MD 8.44 * (0.48, 16.40)	32 (1 study)	⊕⊕⊕⊖ moderate[2]
Functioning: 1. Average global functioning score (GAF) - 12 months	MD 4.89 * (-2.62, 12.39)	129 (2 studies)	⊕⊕⊖⊖ low[1,2]
Functioning: 1. Average global functioning score (GAF) - 18 months	MD 6.68 * (-5.24, 18.60)	28 (1 study)	⊕⊕⊖⊖ low[1,2]
Functioning: 2. Average social functioning score (SFS) - by end of 9 month treatment	MD 5.01 * (-0.55, 10.57)	32 (1 study)	⊕⊕⊖⊖ low[1,2]
Functioning: 2. Average social functioning score (SFS) - by 12 months (3 months following treatment	MD 7.27 * (0.86, 13.68)	32 (1 study)	⊕⊕⊕⊖ moderate[2]

end)			
Note. A RR of < 1 favours the intervention, negative MDs favour the intervention (except if marked with *, then postive MDs favour the intervention); CI = confidence interval; MD = mean difference; MI = motivational interviewing; RR = Relative Risk. [1] Optimal information size not met. [2] CI includes both 1) no effect and 2) appreciable benefit or appreciable harm.			

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Table 26. GRADE summary of findings table for RCTs comparing social skills training/ psychoeducation with standard care

Outcomes	Effect size (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)
Substance use: 1. Average score - C-DIS-R Drugs (skewed data) - C-DIS-R DRUGS by 6 months	MD -2.99 (-5.51 to -0.47)	46 (1 study)	⊕⊕⊕⊖ moderate[1]
Substance use: 1. Average score - C-DIS-R Drugs (skewed data) - C-DIS-R DRUGS by 12 months	MD -2.47 (-5.76 to 0.82)	46 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 1. Average score - C-DIS-R Drugs (skewed data) - C-DIS-R DRUGS by 18 months	MD -0.79 (-3.35 to 1.77)	25 (1 study)	⊕⊕⊕⊖ moderate[1]
Substance use: 2. Average score - C-DIS-R Alcohol (skewed data) - C-DIS-R Alcohol by 6 months	MD -1.81 (-3.41 to -0.21)	46 (1 study)	⊕⊕⊕⊖ moderate[1]
Substance use: 2. Average score - C-DIS-R Alcohol (skewed data) - C-DIS-R Alcohol by 12 months	MD -0.71 (-2.54 to 1.12)	46 (1 study)	⊕⊕⊕⊖ moderate[1]
Substance use: 2. Average score - C-DIS-R Alcohol (skewed data) - C-DIS-R Alcohol by 18 months	MD 0.04 (-2.27 to 2.35)	25 (1 study)	⊕⊕⊕⊖ moderate[1]
Functioning: 1. Average role functioning score (RFS) - by 6 months	MD 0.61 * (-1.63 to 2.85)	47 (1 study)	⊕⊕⊕⊖ moderate[1]
Functioning: 1. Average role functioning score (RFS) - by 12 months	MD 1.07 * (-1.15 to 3.29)	47 (1 study)	⊕⊕⊕⊖ moderate[1]
Functioning: 1. Average role functioning score (RFS) - by 18 months	MD -2.55 * (-6.24 to 1.14)	25 (1 study)	⊕⊕⊖⊖ low[1,2]
Functioning: 2. Average social adjustment score (SAS) - by 6 months	MD -0.92 * (-6.58 to 4.74)	47 (1 study)	⊕⊕⊖⊖ low[1,2]
Functioning: 2. Average social adjustment score (SAS) - by 12 months	MD 2.58 * (-3.39 to 8.55)	47 (1 study)	⊕⊕⊖⊖ low[1,2]
Functioning: 2. Average social adjustment score (SAS) - by 18 months	MD -4.66 * (-15.29 to 5.97)	25 (1 study)	⊕⊕⊖⊖ low[1,2]
Service use: Days in hospital (skewed data)	MD 1.80 (-4.46 to 8.06)	29 (1 study)	⊕⊕⊖⊖ low[1,2]
Note. Negative MDs favour the intervention (except if marked with *, then postive MDs favour the intervention); CI = confidence interval; MD = mean difference; RR = Relative Risk. [1] Optimal information size not met. [2] CI includes both 1) no effect and 2) appreciable benefit or appreciable harm.			

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Table 27. GRADE summary of findings table for RCTs comparing contingency management with standard care

Outcomes	Effect size (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)
Substance use: 1. No. of days/weeks of drug use (confirmation by urine drug screen) - Days of cocaine use	SMD -1.04 (-1.8 to -0.28)	30 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 2. No. of days/weeks of alcohol use (confirmation by breathalyzer)	SMD -1.16 (-1.83 to -0.49)	71 (2 studies)	⊕⊕⊖⊖ low[1,2]
Substance use: 3. No. of days/weeks using both drugs and alcohol (confirmation by urine or breathalyzer) – weeks	SMD -0.82 (-1.47 to -0.17)	41 (1 study)	⊕⊕⊖⊖ low[1,2]
Substance use: 4. Alcohol positive breathalyzer samples	SMD -0.82 (-1.47 to -0.17)	30 (1 study)	⊕⊕⊖⊖ low[1,2]
Note. Negative SMDs favour the intervention; CI = confidence interval; MD = mean difference; RR = Relative Risk. [1] Optimal information size not met. [2] CI includes both 1) no effect and 2) appreciable benefit or appreciable harm.			

7.2.6 Observational studies (psychological/ psychosocial interventions)

Cleary and colleagues (2009) included three observational studies that met the guideline eligibility criteria. Of the three, one US study (Weiss *et al*., 2000) of people with coexisting bipolar disorder and substance dependence was classified as examining integrated group sessions (12–20 weekly 1 hour) using a CBT relapse prevention model (n = 21) versus standard care (n = 24). After 6 months follow up, there were statistically significant treatment group differences favouring CBT on a number of substance misuse outcomes and a measure of mania. However, assessment was not blind, although the substance misuse outcomes were verified by urine toxicology screens and breath alcohol assessments.

One US study (Santa Ana *et al*., 2007), was described by Cleary and colleagues (2009) as a comparison of group motivational interviewing (two, 2-hour sessions; n = 50) versus a control group (group discussion, two, 2-hour sessions; n = 51). Participants were psychiatric inpatients with coexisting substance dependence. At 1- and 3-months follow-up there was a statistically significant difference between groups favouring the motivational interviewing group on rates of alcohol use and binge drinking, and drug use days. There were no significant differences between groups on measures of abstinence or on aftercare treatment attendance.

Cleary and colleagues (2009) included one Australian study (James *et al*., 2004), that compared the effectiveness of a 6 week manualised group-based intervention (incorporating both substance use and mental health

interventions; n = 32) versus standard care (consisting of a single educational session; n = 31). Participants were diagnosed with schizophrenia or bipolar disorder and coexisting substance dependence or harmful use. At 3-months follow-up, there were statistically significant differences between the two groups, favouring group therapy in terms of reduced drug use and symptoms of psychosis, but not severity of dependence or alcohol use.

One non-randomised study (Helmus *et al*., 2003), not included by Cleary and colleagues (2009), examined the effectiveness of a community based contingency management program. The sample consisted of 20 participants diagnosed with schizophrenia (15%), schizoaffective disorder (20%), bipolar disorder (30%), or MDD (35%) and a coexisting substance use disorder (alcohol dependence, 70%; cocaine abuse, 5%; polysubstance dependence, 5%). Using an A-B-A within-subjects reversal design, participants had a 4-week baseline phase, followed by 12 weeks of contingency management reinforcing their dual diagnosis group counselling attendance and alcohol abstinence (based on breath alcohol levels), and then a 4 week return to baseline phase. Group counselling was provided twice weekly with alcohol breath tests given before each session. The results demonstrated that contingency management attendance was significant higher than at baseline, and remained elevated in the return to baseline phase. There were no significant effects found on alcohol use, however, as the breath tests remained negative throughout the entire study.

Lykke and colleagues (2010) conducted a pragmatic clinical trial evaluating cognitive milieu therapy in a convenient sample of 136 inpatients in Denmark, using a pre-post intervention design. Of the 136 participants, 53 to 65% had an ICD-10 diagnosis of schizophrenia, with a coexisting diagnosis of substance abuse (29–41% alcohol only, 5–6% cannabis only, 50–59% polysubstance abuse). Cognitive milieu therapy is carried out within a structured inpatient environment, and incorporates both motivational and cognitive behavioural strategies in an effort to address both mental health and substance misuse problems simultaneously. Results revealed that the most significant changes post-treatment were in functioning (Global Assessment of Functioning scale, p=.0001), global symptomatology as assessed by the Global Assessment Scale (p=.0001), and levels of anxiety/depression on the Brief Psychiatric Rating Scale (BPRS) (p=.0001). In addition, participants displayed significant improvement on anxiety levels (Beck Anxiety Inventory, p=.0001), depressive symptoms (Beck Depression Inventory, p=.0001), and self-esteem (Robson Self-Concept Questionnaire, p=.0022) at post-treatment follow-up. A regression analysis did not identify any predictors associated with treatment completion, although reduced chance of completion of treatment was associated with a higher BPRS score. Regression analysis for achieving sustained abstinence was associated with the absence of a polysubstance abuse diagnosis (OR = 0.19; p=.018) and lower BPRS score (OR= 0.80, 1 per point, $p < .01$).

One further study (Tyrer *et al*., in press), was a secondary sub-group analysis of an RCT conducted in the UK, which looked at the impact of nidotherapy for people with psychosis, a significant proportion of whom had coexisting substance misuse problems (Ranger *et al*., 2009). Nidotherapy is a "collaborative treatment involving the systematic assessment and modification of the environment to minimise the impact of any form of mental disorder on the individual or on society" (Tyrer *et al.,* 2003). The sub-group analysis of the people with psychosis and coexisting substance misuse suggested that participants referred to nidotherapy had a 63% reduction in hospital bed use after one year compared to those referred to a standard assertive outreach team (p = .03). There was also some evidence that nidotherapy improved social functioning (MD -2.0, 95% CI -4.0 to -0.1), without any detrimental effect on psychiatric symptoms (MD -2.6, 95% CI -8.0 to 2.8) or engagement with services (MD .23, 95% CI -1.6 to 2.1).

7.2.7 Clinical evidence summary (psychological/ psychosocial interventions)

For the majority of interventions included in related NICE guidance, the current systematic review found no direct evidence for people with psychosis and coexisting substance misuse (Table 28). With regard to the evidence that was available, it should be interpreted with some caution because the research was not conducted in the UK and methodological issues limit the quality of the evidence.

There were three small RCTs (N = 149) of MI compared to standard care. However, data could not be combined using meta-analysis, so for each outcome, the evidence comes from a single study. Nevertheless, the evidence (*GRADED* moderate to low quality) suggests that for people with psychosis and coexisting substance misuse this approach may reduce substance misuse at up to 12 months follow-up. These results were supported by one observational study.

In two small RCTs (N = 71) of contingency management compared to standard care, there was evidence (*GRADED* low quality) suggesting benefit in terms of reduced substance misuse at up to 6 months follow-up. One small observational study demonstrated improved attendance after contingency management, but no effect on alcohol use.

In four small RCTs of CBT (N = 216), two small trials of CBT plus MI (N = 166), and two small trials of group psychotherapy (social skills training/ psychoeducation) (N = 94), the evidence (*GRADED* moderate to low quality) is inclusive with regard to the effectiveness of these approaches when compared to standard care for people with psychosis and coexisting substance misuse. Two small observational studies favoured CBT and group psychotherapy in terms of reduced substance misuse and improved symptoms of psychosis.

The study of nidotherapy, suggests that collaborative psychosocial interventions involving the systematic assessment and modification of the environment may be worth studying further.

Table 28: Relevant interventions included in current NICE guidelines and summary of evidence of effectiveness for people with psychosis and coexisting substance misuse

Intervention name	Existing NICE guideline*	Recommended	Evidence relevant to people with psychosis and substance misuse
Opportunistic brief interventions			
Brief interventions for people not in contact with services	Substance misuse: DMP	 Yes^	–
Brief interventions for people in contact with services	Substance misuse: DMP	 Yes^	–
Self-help based interventions			
Self-help intervention (including self-help groups, 12-step self-help groups)	Substance misuse: Alcohol** DMP Psychosis: Bipolar disorder	 Yes Yes Yes^	–
Twelve-step facilitation	Substance misuse: Alcohol**	 Yes†	
Behavioural therapies			
Cue exposure	Substance misuse: Alcohol**	 Yes (BT in general recommended)	–
Behavioural self-control training	Substance misuse: Alcohol**	 Yes (BT in general recommended)	–
Contingency management	Substance misuse: Alcohol** DMD DMP	 Research recommendation Yes Yes	Low quality evidence in favour of contingency management.
Cognitive and behavioural based therapies			
CBT	Substance misuse: Alcohol** DMD DMP Psychosis: Bipolar disorder Schizophrenia (update)	 Yes No Yes^ Yes^ Yes	Moderate to low quality evidence available, but insufficent to reach conclusion about direction of effect.
Coping and social skills training	Substance misuse: Alcohol**	 No	Moderate to low quality evidence available, but insufficent to reach conclusion about direction of effect.
Relapse prevention	Substance misuse: Alcohol** DMD Psychosis: Bipolar disorder	 Not specifically (but interventions that promote absinence and prevent relapse recommended)	–

		No Yes^	
Family-based interventions			
Family intervention	Substance misuse: Alcohol** DMD DMP Psychosis: Bipolar disorder Schizophrenia (update)	 Yes^ No Yes^ Yes^ Yes^	–
Motivational techniques			
Motivational interviewing/ Motivational Enhancement Therapy	Substance misuse: Alcohol** DMP	 Yes† No	Moderate to low quality evidence in favour of motivational interviewing.
Social Network and Environment Based Therapies			
Social Behaviour and Network Therapy	Substance misuse: Alcohol**	 Not specifically (but social network therapies recommended)	–
The Community Reinforcement Approach	Substance misuse: Alcohol** DMD	 Not specifically (but social network therapies recommended) No	–
Social-systems interventions	Substance misuse: DMD DMP	 No No	–
Other interventions			
Adherence therapy	Psychosis: Schizophrenia (update)	 No	–
Arts therapies	Psychosis: Schizophrenia (update)	 Yes	–
Cognitive remediation	Psychosis: Schizophrenia (update)	 No	–
Counselling and supportive psychotherapy	Substance misuse: Alcohol** Psychosis: Schizophrenia (update)	 No No	–
Couples-based interventions (including behavioural couples therapy)	Substance misuse: Alcohol** DMD DMP	 Yes Yes^	–
Individual drug counselling	Substance misuse: DMD	 No	–
Interpersonal and social rhythm therapy (IPSRT)	Psychosis: Bipolar disorder	 Yes^	–
Interpersonal therapy	Substance misuse: DMD DMP	 No No	–

Multi-modal care programmes	Substance misuse: Alcohol** DMP	 Yes^ No	–
Psychoeducational interventions	Substance misuse: Alcohol** DMP Psychosis: Bipolar disorder Schizophrenia (update)	 No No Yes^ No	–
Psychodynamic psychotherapy and psychoanalysis	Substance misuse: Alcohol** DMD DMP Psychosis: Schizophrenia (update)	 No No No No	–
Social skills training	Psychosis: Schizophrenia (update)	 No	–
Vocational interventions	Substance misuse: DMP	 No	–
Note. DMD = Drug misuse: opioid detoxification; DMP = Drug misuse: psychosocial interventions. * Available from www.nice.org.uk. ** Management of alcohol dependence guideline. ^ For specific groups and/or in certain circumstances (see relevant guideline for further information). †These interventions were seen as components of any effective psychosocial intervention delivered in alcohol services with the assessment and enhancing of motivation forming a key element of the assessment process.			

7.2.8 Health economic evidence (psychological/ psychosocial interventions)

The systematic search of the health economics literature identified two relevant papers: one comparing the cost-effectiveness of CBT combined with MI versus standard care (Haddock *et al.* 2003) and one comparing group psychotherapy with standard care (Jerrell & Ridgley, 1997). Details on the methods used for the systematic search of the economics literature are described in Appendix 9.

One UK study (Haddock *et al.* 2003), based on the RCT conducted by Barrowclough and colleagues (2001), evaluated the cost-effectiveness of an integrated programme of CBT combined with MI plus standard care versus standard care alone. The study sample consisted of 36 people diagnosed with psychosis and coexisting substance dependence or misuse along with their carers, recruited from the mental health units of three UK NHS hospital trusts. Resource use and outcome data were collected over 18 months follow-up. The study adopted a societal perspective, with data on hospital care, primary care, community and domiciliary services, medications, service user travel and out-of-pocket expenses and productivity losses all collected from the Client Service Receipt Inventory (CSRI). The primary measure of

effectiveness was change in the Global Assessment of Functioning Scale (GAF).

Over 18 months follow-up, the intervention group was on average £1,260 (p = 0.25) less costly, while experiencing an average of 22.5% improvement in GAF scores in comparison to routine care. Incremental cost-effectiveness ratios were calculated by the authors but not reported in the paper. Cost-effectiveness acceptability curves (CEACs) were used to measure uncertainty around the sample estimates of mean costs and outcomes. The probability of the intervention being less costly than standard care (at a willingness-to-pay of 0) was 69.3%. Overall, the authors concluded that the integrated programme of CBT combined with MI was no more costly than standard care, and there was a high probability of it being cost-effective. The results of the study are relevant to the UK setting, although the major limitations are the small sample size (which may not have been representative of the study population) and the measure of effectiveness used in the analysis (which limits comparability across health care interventions).

One US-based study was identified that assessed the cost-effectiveness of three primary-care programmes: 12-step recovery; case management and behavioural skills training in comparison to a 'do nothing' alternative (Jerrell *& Ridgely,* 1997). The study population included 132 people with an axis I DSM-III-R diagnosis of psychosis or major affective disorder with a coexisting substance disorder and previous psychiatric treatment. The primary measures of effectiveness in the study were psychological functioning, psychiatric and substance abuse symptoms. As no significant differences in clinical effectiveness were detected across the three treatment groups, the economic analysis was based on differences in costs only. A societal perspective was taken for the cost analysis, with data on mental health and general health care resource use, criminal justice and social services, family and caregiver resources and any other transfer payments, collected over an 18-month period. Total costs were reported separately for intensive mental health care (inpatient days, residential treatment, emergency visits) and supportive mental health care (outpatient visits, medication visits, supported housing visits).

For intensive mental health care costs, the total cost in the 12-step group was $10,275, in the behavioural skills group was $4,276 and in the case management group was $7,643. For supportive mental health care costs, the total cost in the 12-step group was $7,798, in the behavioural skills group was $6,112 and in the case management group was $5,970. No formal statistical tests were conducted to quantify the significance of any cost differences between the three treatment groups. Overall, the authors concluded that no differences in outcomes were detected between the three groups, but the 12-step group incurred the highest intensive and supportive costs over the 18-month period. The study is of limited relevance to the UK context as it was

based in the US and has a number of methodological limitations. The non-randomised study design and lack of information about the power of the study, in terms of detecting differences between the three treatment groups, limits the internal validity of the effectiveness results. Resource use components were not described separately from costs and it is not possible to ascertain whether the cost analysis was based on actual costs or service charges.

Health Economics Summary

In summary, there was limited evidence of the cost-effectiveness of specific psychological/psychosocial interventions for people with psychosis and coexisting substance misuse. The UK-based study by Haddock and colleagues (2003) suggested that a combination of CBT and MI plus standard care was cost-effective compared with standard care alone. The US based study by Jerrell and Ridgely (1997) showed that a behavioural skills training was more costly in terms of intensive and supportive mental health care, when compared with 12-step recovery or case management programmes.

Given the uncertainty surrounding the cost-effectiveness of psychological/psychosocial interventions and the associated resource implications, it was anticipated that further economic modelling would be developed to address these issues. However, due to both the scarcity and the generally low quality of the clinical data that was identified in the guideline systematic review, the GDG agreed that it would not be possible to model the cost-effectiveness of specific psychological/psychosocial interventions in people with psychosis and coexisting substance misuse.

7.2.9 From evidence to recommendations (psychological/ psychosocial interventions)

Early in the development process, the GDG distinguished between outcomes that were critical to decision making and those that were important but not critical. Critical outcomes included: mortality (all causes), relapse rates (measured by exacerbation of symptoms requiring change in health care management), substance misuse (however measured), global and social functioning (for example, employment and accommodation), subjective quality of life, satisfaction with care, and physical morbidity. Only critical outcomes were included in the GRADE evidence profiles and considered when making recommendations.

There was little direct evidence relating to most psychological interventions for people with psychosis and coexisting substance misuse. The evidence that was available was generally difficult to interpret because of the context the research was conducted in and/or methodological issues. As a result, the GDG decided that it was not possible to recommend any specific psychological or psychosocial intervention or combination of interventions to

people with psychosis and coexisting substance misuse. As no evidence was found relating to the modification of interventions recommended for people with a single diagnosis, the GDG concluded that people with psychosis and coexisting substance misuse should be offered the same range of evidence-based interventions recommended for people with a single diagnosis. However, the GDG felt it was important to emphasise that low levels of substance use that would not usually be considered harmful or problematic in people without psychosis, can have a significant impact on the mental health of people with psychosis.

7.3 CLINICAL PRACTICE RECOMMENDATIONS

7.3.1 Recommendations (psychological/ psychosocial interventions)

Secondary care mental health services

Treatment

7.3.1.1 Before starting treatment for adults and young people with psychosis and coexisting substance misuse, review:

- the diagnosis of psychosis and that of the coexisting substance misuse, especially if either diagnosis has been made during a crisis or emergency presentation
- the effectiveness of previous and current treatments and the person's tolerance of them; discontinue ineffective treatments. [11]

7.3.1.2 Ensure that adults and young people with psychosis and coexisting substance misuse are offered evidence-based treatments for both conditions.

- For the treatment of psychosis, see 'Bipolar disorder: the management of bipolar disorder in adults, children and adolescents, in primary and secondary care' (NICE clinical guideline 38) or the guideline on schizophrenia (NICE clinical guideline 82).
- For the treatment of substance misuse, see 'Alcohol-use disorders: diagnosis and clinical management of alcohol-related physical complications' (NICE clinical guideline 100 and CGXX) or 'Drug misuse: psychosocial interventions'

[11] This recommendation also appears in section 8.2.12 where the pharmacological data is presented.

(NICE clinical guideline 51) and 'Drug misuse: opioid detoxification' (NICE clinical guideline 52). [12]

7.3.1.3 When developing a treatment plan for a person with psychosis and coexisting substance misuse, tailor the plan and the sequencing of treatments to the person and take account of:

- the relative severity of both the psychosis and the substance misuse at different times
- the person's social and treatment context and
- the person's readiness for change.

7.3.1.4 Do not exclude adults and young people with psychosis and coexisting substance misuse from contingency management programmes because of their psychosis.

7.3.2 Research recommendations (psychological/ psychosocial interventions)

7.3.2.1 Are psychological/psychosocial interventions (such as motivational interventions) more clinically effective and cost-effective at reducing substance misuse in people with psychosis and coexisting substance misuse?

7.3.2.2 Are psychological/ psychosocial interventions that are effective in people with substance misuse alone (such as, motivational interventions and contingency management) clinically and cost-effective interventions in reducing substance misuse compared with standard care in people with psychosis and coexisting substance misuse?For people with psychosis and coexisting substance misuse, do interventions that involve the assessment and modification of their environment lead to greater clinical improvement and cost-effectiveness than standard care or other more established interventions, such as motivational interviewing and contingency management?

Are interventions which involve the assessment and modification of the environment clinically and cost-effectiven when compared to standard care in people with psychosis and coexisting substance misuse?

[13] Here and elsewhere in the guideline, each RCT considered for review is referred to by a study ID (primary author and date of study publication, except where a study is in press or only submitted for publication, then a date is not used).

8 PHARMACOLOGICAL AND PHYSICAL INTERVENTIONS FOR PEOPLE WITH PSYCHOSIS AND COEXISTING SUBSTANCE MISUSE

8.1 INTRODUCTION

There are many pharmacological treatments for both psychotic disorders and substance misuse, but there is very little overlap between the treatments for each group of disorders. The pharmacological treatments for each of the substance misuse disorders are generally specific ones for each substance of dependence (for example, disulfiram and acamprosate for alcohol dependence; methadone for opioid addiction) and, whereas the treatment of psychoses shows much greater overlap with lithium salts and other mood stabilisers, antipsychotic drugs of all types, and anticonvulsant drugs all being used at different times, these show little commonality with the treatments for substance misuse. It might be expected that with a large number of drugs being used to treat each group of disorders that there could also be important interactions between them, both pharmacodynamic and pharmacokinetic, but these appear to be rare and generally unimportant in clinical practice. It might also be expected that polypharmacy would be a problem for these dual disorders but the data here are conflicting with no clear evidence of greater use of drug treatment in dual disorders (Centorrino *et al*., 2008; Goldberg *et al*., 2009; Kreyenbuhl *et al*., 2007).

For this reason, there are few specific recommendations for pharmacological treatment of both groups of disorders that are not covered by previous published NICE guidelines for substance misuse and the psychoses separately. Those that have been suggested, such as the specific use of disulfiram and naltrexone in service users with these coexisting diagnoses, have not been supported by the evidence (Petrakis *et al*., 2006). There have also been suggestions that some antipsychotic drugs, particularly clozapine, may have anti-craving actions suitable for the management of people with substance misuse and psychosis (Green, 2008; Zimmet *et al*., 2000), but here again evidence of efficacy is sparse.

8.1.1 Current practice

The pharmacological management of service users with psychosis and substance misuse is primarily concerned with treating the individual disorders. Nevertheless, special attention needs to be paid to treatment

adherence in this group, not least as the risk of adverse outcomes, including significant societal violence, is so much greater in this population (Kooyman *et al*., 2007).

8.2 EVIDENCE REVIEW

8.2.1 Introduction

A number of existing NICE guidelines have reviewed the evidence for pharmacological and physical interventions used to treat people with psychosis without substance misuse (that is, bipolar disorder and schizophrenia), and for people with substance misuse without psychosis (that is, alcohol and drug misuse: opioid detoxification).

For the purposes of the current guideline, three main issues were addressed for people with psychosis and coexisting substance misuse. First, modification of the medical treatment of psychosis as a result of substance misuse and the treatment provided (for example, methadone, buprenorphine *etc.*). Second, modification of the medical/physical treatment of substance misuse as a result of the presence of psychosis and the treatment provided (for example, antipsychotic drugs, lithium). Third, management of drug interactions or adverse effects from pharmacological interventions.

Where no evidence existed for a particular intervention in people with psychosis and coexisting substance misuse, the GDG used informal consensus to reach a conclusion about whether it was appropriate to cross-reference to existing NICE guidance.

Interventions and licensing in the UK

Table 29 lists the interventions included in current NICE guidelines together with their licensed indications in the UK (those relevant to this guideline).

Table 29: Relevant interventions included in current NICE guidelines and current licence status of medication

Intervention type/use	Name	UK licence (only relevant indications listed)	Reviewed by existing NICE guideline
MEDICATION			
Alcohol dependence	Acamprosate calcium	Maintenance of abstinence in alcohol dependence (it should be combined with counseling)	Alcohol (management of alcohol dependence guideline)
Alcohol deterrent compounds	Disulfiram	Adjuvant in the treatment of carefully selected and co-operative patients with drinking problems (?15+) Its use must be accompanied by appropriate supportive treatment	Alcohol (management of alcohol dependence guideline)
Alpha-adrenergic agonists	Clonidine	Hypertension; migraine (13+)	DMD
Alpha-adrenergic agonists	Lofexidine	Management of symptoms of opioid withdrawal (18+)	DMD
Antiepileptic drugs	Phenytoin	All forms of epilepsy except absence seizures; status epilepticus	Alcohol (clinical management guideline)
Antiepileptic drugs	Topiramate	Generalised tonic-clonic seizures or partial seizures	Alcohol (management of alcohol dependence guideline)
Antimanic drugs	Lithium	Bipolar disorder (12+)	Bipolar
Antimanic drugs	Valproic acid	Manic episodes associated with bipolar disorder (18+) Treatment of generalised, partial or other epilepsy. No mention of manic episodes	Bipolar
Antimanic drugs/ Anxiolytics	Benzodiazepine: Diazepam	Adjunct in acute alcohol withdrawal; short-term use in anxiety or insomnia	Bipolar/ Alcohol*
Antimanic drugs/	Benzodiazepine: Lorazepam	Short-term use in anxiety or insomnia, acute excitement	Bipolar

Anxiolytics		and acute mania	
Antimanic drugs/ Hypnotics	Benzodiazepine: Chlordiazepoxide	Adjunct in acute alcohol withdrawal; Short-term treatment of severe anxiety that is severe with or without insomnia/short-term psychosomatic/organic or psychotic illness	Alcohol*
Antimanic drugs/ Hypnotics	Chlormethiazole	Alcohol withdrawal	Alcohol*
Antimanic/ Control of epilepsy	Carbamazepine	Prophylaxis of bipolar disorder unresponsive to lithium	Bipolar
Antipsychotic drugs (first-generation)	For example: Haloperidol	Schizophrenia; mania	Bipolar/Schizophrenia (update)
Antipsychotic drugs (second-generation)	For example: Olanzapine Clozapine	Schizophrenia; some individual drugs also indicated for mania. Note, clozapine only indicated for schizophrenia in patients unresponsive to, or intolerant of, first-generation antipsychotic drugs	Bipolar/Schizophrenia (update)
Opioid agonists & partial agonists	Buprenorphine	Treatment for opioid drug dependence (subutex) (16+)	DMD
Opioid agonists & partial agonists	Methadone	Treatment of opioid drug addictions (?15+)	DMD
Opioid antagonists	Nalmefene	Unlicensed	Alcohol* / DMD
Opioid antagonists	Naltrexone	Adjunctive prophylactic therapy in the maintenance of detoxified formerly opioid dependent patients (18+)	Alcohol* / DMD
Serotogenic agents	Ondansetron	Prevention and treatment of postoperative nausea and vomiting	Alcohol
Serotogenic agents	SSRIs	Depression	Alcohol* / Depression
Skeletal muscle relaxants	Baclofen	Chronic severe spasticity	Alcohol*
PHYSICAL AND COMPLEMENTARY INTERVENTIONS			
Physical	Acupuncture	–	DMD
Physical	Electrical transcranial stimulation	–	Alcohol*

Complementary	Kudzu root	–	Alcohol*
Complementary	Vipassana meditation	–	Alcohol*
Note. DMD = drug misuse: opioid detoxification. * Management of alcohol dependence guideline.			

8.2.2 Clinical review protocol (pharmacological/ physical interventions)

The review protocol, including the primary clinical question, information about the databases searched and the eligibility criteria used for this section of the guideline can be found in Table 30. Initially a search for systematic reviews and existing guidelines that addressed the clinical question was conducted. Good quality systematic reviews were then used as a source of evidence, and only a new systematic search for more recent primary-level studies was conducted for the guideline (further information about the search strategy can be found in Appendix 7). If the evidence allowed, the following sub-question was asked for review question 2.1.1 and 2.3.1: Are there sub-groups of people (for example, young people, people with a particular type of psychosis, people from BME groups) that may benefit from alternative strategies?

Table 30: Databases searched and eligibility criteria for clinical evidence

Component	Description
Review questions	2.1.1 For people with psychosis and coexisting substance misuse, should the medical treatment of their psychosis be modified as a result of substance misuse and the treatment provided (e.g. methadone, buprenorphine etc)? A) During the acute phase B) During non-acute phase If so, how should treatment be modified? 2.3.1 For people with psychosis and coexisting substance misuse, should the medical/physical treatment of substance misuse be modified as a result of the presence of psychosis and the treatment provided (e.g. antipsychotics, lithium)? A) During the acute phase? B) During non-acute phase? If so, how should treatment be modified? 2.5.1 In people with psychosis and substance misuse, is there any evidence that the management of drug interactions or adverse effects from pharmacological treatments should be different from those people without coexisting disorders? If so, how should management of drug interactions be modified?
Electronic databases	CENTRAL, CINAHL, EMBASE, MEDLINE, PsycINFO
Date searched	Inception to 26.05.2010
Study design	Reviews, clinical guidelines, primary-level studies
Population	People with psychosis and coexisting substance misuse
Intervention(s)	Pharmacological/physical interventions
Comparison	Any relevant treatment
Critical outcomes	Reduced mortality (all causes) Reduced relapse rates (measured by exacerbation of symptoms requiring change in health care management) Reduced substance misuse (however measured) Improved global and social functioning (e.g. employment, accommodation) Improved subjective quality of life Improved satisfaction with care Reduced physical morbidity.
Note. BME = Black and minority ethnic.	

8.2.3 Studies considered for review (pharmacological/ physical interventions)[13]

Thirteen clinical evidence reviews and guidelines met the eligibility criteria for this section of the guideline (Buchannan *et al*., 2009 [Schizophrenia Patient Outcomes Research Team, PORT); Casas *et al*., 2008; Center for Substance Abuse Treatment, 2005 [Treatment Improvement Protocol series 42]; Center for Substance Abuse Treatment, 2005 [Treatment Improvement Protocol series 43]; Center for Substance Abuse Treatment, 2006 [Treatment Improvement Protocol series 45]; Green *et al*., 2008; Hjorthoj *et al*., 2009; Mills *et al*., 2009 [Australian guideline]; San *et al*., 2007; Smelson *et al*., 2008; Tiet & Mausbach, 2007; Vornick & Brown, 2006; Wobrock & Soyka, 2008). All were published in peer-reviewed journals between 2006 and 2009. In addition, a number of reviews were excluded as they had either been superseded by more recent reviews (for example, Brunette *et al*., 2005; Goldstein *et al*., 2006; Green, 2005), or are currently under review (that is, Lingford-Hughes *et al*., 2004).

In addition, a search was conducted for RCT evidence that may have been published too recently to be included in existing reviews. From this, four RCTs were found: BROWN2009 (Brown *et al*., 2009), KEMP2009 (Kemp *et al*., 2009), NEJTEK2008 (Nejtek *et al*., 2008), VANNIMWEGEN2008 (Van Nimwegen *et al*., 2008). A summary of study characteristics is given in Table 11 and the results are described in the text below. Additionally, a secondary analysis from the Clinical Antipsychotic Trials of Intervention Effectiveness project was reviewed (CATIE2008; Swartz *et al*., 2008).

[13] Here and elsewhere in the guideline, each RCT considered for review is referred to by a study ID (primary author and date of study publication, except where a study is in press or only submitted for publication, then a date is not used).

Table 31: Study information table for RCTs of pharmacological interventions

	Pharmacological interventions versus any control
Total no. of trials (N)	4 RCTs (216)
Study ID	(1) BROWN2009 (2) KEMP2009 (3) NEJTEK2008 (4) VANNIMWEGEN2008
Number randomised	(1) 50 (2) 31 (3) 94 (4) 41
Diagnosis	(1) Bipolar disorder I or II and alcohol dependence (2) Rapid cycling bipolar disorder I or II and substance abuse and/or dependence (3) Bipolar disorder I or II with and without psychotic features and stimulant dependence, currently in manic or hypomanic episode (4) Schizophrenia or schizophrreniform disorder and cannabis misuse
Treatment (mean dose) (n)	(1) Naltrexone (50 mg/day) + CBT (n=23) (2) Lithium (1440 mg/day; range 900-2400 mg) (n=16) (3) Risperidone (3.1 mg/day +- 1.2 mg) (n=46) (4) Olanzapine (11.1mg) (n=20)
Control (mean dose) (n)	(1) Placebo + CBT (all with usual medication) (n=27) (2) Lithium (1400 mg/day; range 600-2100 mg) + divalproex (1583 mg/day; range 1000-3250 mg) (n=15) (3) Quetiapine (303.6 mg/day +- 151.9 mg) (n=48) (4) Risperidone (3mg) (n=21)
Treatment length/design	(1) 12 weeks, double-blind RCT (2) 25 weeks, double-blind RCT (3) 20 weeks, double-blind RCT (5) 6 weeks; double-blind RCT
Country	(1) US (2) US (3) US (5) Holland
Note. N = Total number of participants; n = number of participants in each group.	

8.2.4 Evidence from existing reviews and guidelines for the use of pharmacological interventions to treat people with coexisting schizophrenia and substance misuse (pharmacological interventions)

Eleven recent existing reviews and/or guidelines included evidence for the pharmacological treatment of people with coexisting schizophrenia (or related disorders) and substance misuse (Buchannan *et al.*, 2009 [Schizophrenia Patient Outcomes Research Team, PORT); Center for Substance Abuse Treatment, 2005 [Treatment Improvement Protocol series 42]; Center for Substance Abuse Treatment, 2005 [Treatment Improvement Protocol series 43]; Center for Substance Abuse Treatment, 2006 [Treatment Improvement

Protocol series 45]; Green *et al*., 2008; Hjorthoj *et al*., 2009; Mills *et al*., 2009 [Australian guideline]; San *et al*., 2007; Smelson *et al*., 2008; Tiet & Mausbach, 2007; Wobrock & Soyka, 2008). They review a range of evidence, from case studies to RCTs.

Buchannan and colleagues (2009) updated the PORT psychopharmacological treatment recommendations last published in 2004 (Lehman *et al*., 2004). The authors conducted a systematic review of evidence sourced from quarterly searches of MEDLINE (January 2002 to March 2008) to supplement searches undertaken for their previous guideline. No other electronic database was used. The guideline covers pharmacological treatments for schizophrenia, with a subsection on the treatment of coexisting substance misuse. It mostly focuses on double-blind RCTs. It included studies provided at least 50% of participants had a schizophrenia spectrum disorder diagnosis and where study drugs had US Food and Drug Administration (FDA) approval. Studies involving people with coexisting schizophrenia and cocaine abuse or dependence included two double-blind RCTs comparing olanzapine to haloperidol, and one double-blind RCT comparing olanzapine to risperidone. Also included was one double-blind RCT comparing naltrexone to placebo in people with coexisting schizophrenia and alcohol use disorders. Finally, the authors mention a sub-analysis of a larger RCT that examined naltrexone, disulfiram, and naltrexone plus disulfiram compared to placebo in people with psychosis and coexisting substance misuse. The guideline development group concluded that based on the research examined there was insufficient evidence to support a specific recommendation for a pharmacological intervention to treat people with coexisting schizophrenia and substance misuse.

Green and colleagues (2008) conducted a narrative review of evidence, but did not describe their methodology for identifying relevant research. The authors focus on antipsychotic drugs for the treatment of coexisting schizophrenia and substance misuse, but also cover medications for substance disorders. They report a range of evidence (mostly low level evidence such as case reports and open-label non-comparative studies) suggesting that "atypical" antipsychotics may be helpful in reducing substance misuse in people with coexisting schizophrenia and substance misuse. The evidence reviewed covered a range of drugs of abuse, including alcohol, cocaine and marijuana. They found the most consistent evidence (from non-randomised studies) suggesting that clozapine treatment may reduce substance use. There was 'less substantial' evidence for quetiapine and aripiprazole, while that for olanzapine and risperidone is unclear, with some studies showing a benefit and others not. Overall they concluded that RCT evidence is required before firmer conclusions can be drawn.

With regard to evidence for drugs specifically used to treat substance misuse, Green and colleagues found preliminary evidence to support the use of

naltrexone and disulfiram in people with coexisting schizophrenia and alcohol dependence. They found no relevant studies of acamprosate. They report case studies indicating the potential benefit of valproic acid in people with coexisting schizophrenia and alcohol abuse or dependence.

However, Green and colleagues conclude that "despite numerous suggestive reports, the questions of whether and to what degree antipsychotic medications and other medications for substance use disorders are effective in reducing substance use among people with [schizophrenia and] co-occurring disorders are not yet answered."

Hjorthoj and colleagues (2009) conducted a systematic review focusing on the treatment of cannabis use disorder in schizophrenia spectrum disorders, covering all types of intervention including psychosocial. The evidence was sourced from searches of four electronic databases searched to September 2008. The authors focused on studies which provided outcomes for cannabis use separately from outcomes for other substance misuse, although also looked at studies which reported cannabis use as part of a grouped outcome. With regard to pharmacological interventions for reducing cannabis use, they found evidence from non-randomised studies of benefit from using clozapine and quetiapine.

The Australian Government Department of Health and Ageing funded the National Drug and Alcohol Research Centre (Mills *et al*., 2009) to develop a guideline covering the management of people with mental health conditions with coexisting alcohol and other drug abuse. The guideline, designed for alcohol and other drug workers, was based on a comprehensive review of the available evidence together with the experience of an expert panel. However, no details of the methodology used to undertake the review work were provided. For people with psychosis, Mills and colleagues found evidence that clozapine may be useful, but that evidence of benefit for second-generation antipsychotics is not yet clear. The guideline authors also suggest that pharmacological interventions may be more effective than psychosocial interventions, because negative symptoms associated with psychosis may restrict involvement and outcomes from psychosocial interventions. In addition, this group of people may have greater tolerance to medication regimes.

Mills and colleagues conclude that treatments which work for mental health disorders without coexisting substance misuse will also work for those with a coexisting disorder. They raise the issue of adherence and also the importance of an awareness of possible interactions and side effects.

San and colleagues (2007) produced a systematic review of treatment with antipsychotic drugs for people with coexisting schizophrenia and substance misuse. The evidence was sourced from searches of three electronic databases

searched to November 2006. The authors found three RCTs comparing olanzapine with haloperidol, plus other non-RCT evidence. From this they concluded that there was preliminary evidence that compared with haloperidol, olanzapine is more effective in reducing cravings whilst retaining antipsychotic action, and that clozapine showed similar potential. They also concluded that older antipsychotics (first-generation) were not as appropriate in this population compared with newer drugs (second-generation) since they were more likely to increase EPS symptoms. Based on case reports, open and retrospective studies, they found that newer antipsychotics may be of use, although the evidence is generally weak. The authors point out the limitations of the evidence base, including small sample sizes, short follow-up periods, and high dropout rates, as well as the paucity of RCTs and blinded studies.

Smelson and colleagues (2008) conducted a review of FDA-approved medications for people with schizophrenia with coexisting substance misuse. There are no details of the methods used, including how evidence was sourced. However, they provide reasonably comprehensive tables of evidence found (compared with other reviews). They cover both medication for the treatment of schizophrenia (antipsychotics) and that for the treatment of substance misuse disorders. They conclude that there is very little evidence to support specific treatment recommendations and, therefore, that clinicians should base treatment decisions on what suits the service user in terms of efficacy and side effects. They found the most evidence suggesting benefit for clozapine, olanzapine and risperidone, although this evidence is not strong. They suggest that second-generation antipsychotics may be better for controlling drug craving in those with cocaine dependence. The authors make the point that non-adherence is a bigger threat to effective treatment rather than poor efficacy and, therefore, advocate clinicians should consider depot medication. The authors found evidence to support the use of disulfiram and naltrexone.

Tiet and Mausbach (2007) report a systematic review of studies of treatment for people with mental disorders, including schizophrenia and bipolar disorder, with coexisting substance abuse. Studies were sourced from a search of two electronic databases. The search date is unclear, but is probably no later than 2006. The authors estimated effect sizes using Cohen's *d* but they do not give confidence intervals. It is unclear whether, or how, they applied diagnostic criteria when assessing studies. The authors concluded that treatments which are effective in reducing psychiatric symptoms in those with mental disorder without coexisting substance abuse, also work with coexisting substance abuse, and those treatments that are effective for improving substance abuse also work in those with a mental disorder. Specifically, they found that naltrexone may reduce coexisting alcohol-related disorders. They found no evidence of enhanced efficacy with higher doses.

The Treatment Improvement Protocol (TIP) series 42, 43 and 45 published by the Center for Substance Abuse Treatment are based on systematic reviews and reviews of published meta-analyses together with the views of an expert consensus panel for the treatment of substance abuse in those with coexisting disorders (TIP series 42), medication treatment of opioid addiction – treatment of coexisting disorders (TIP series 43) and detoxification and substance misuse (TIP series 45). The methods for evidence review are not available, but the guidelines were drafted by expert panels.

Treatment Improvement Protocol series 42 (Center for Substance Abuse Treatment, 2005) does not focus on specific pharmacological treatments, but on general management and care by clinicians, and special considerations (such as for pregnant women). It is not considered further here.

Treatment Improvement Protocol series 43 (Center for Substance Abuse Treatment, 2005), which focuses specifically on opioid addiction, recommends stabilisation of addiction symptoms with methadone, and using newer antipsychotics as either initial or second-line treatment. This is based on the supposed lower side effect profile and increased effectiveness of many newer antipsychotics compared with older medications.

Treatment Improvement Protocol series 45 (Center for Substance Abuse Treatment, 2006), which focuses on detoxification, recommends avoiding abrupt withdrawal of existing medication because of the risk of withdrawal symptoms or precipitating a psychiatric episode. It recommends maintenance on existing medications, unless the person has been abusing the medication or the psychiatric symptoms were caused by the medication. It also recommends giving consideration to withdrawal of medications which lower seizure threshold during acute alcohol withdrawal, or at least using a loading dose or schedule taper of a benzodiazepine. The authors point out the importance of balancing risks and benefits of medication for people with mental disorder and coexisting substance misuse. These include the tension between the tendency for some medications to 'impair cognition and blunt feelings' which may hinder people from addressing problems in their lives which they need to change in order to abstain from misused substances successfully. However, untreated mental disorders "can be powerful relapse triggers, especially for people with a long-standing pattern of relying on alcohol or other drugs to manage their symptoms".

With regard to psychotic disorders, TIP series 45 has no specific recommendations for treatment in the presence of coexisting substance abuse apart from usual care.

Wobrock and Soyka (2008) conducted a systematic review of pharmacological treatment of people with schizophrenia or psychosis and coexisting substance misuse based on searches of five electronic databases searched to November

2007. They report a range of evidence including other reviews, RCTs and case studies. With regard to first-generation antipsychotics, Wobrock and Soyka found that 'most studies reported that patients with the dual diagnosis showed a generally poorer response to treatment'. Whether the authors are using studies with both substance abuse and substance non-abuse populations, or whether they are comparing studies with substance abuse populations with studies with non-abusing populations is unclear. They include a range of substances including alcohol. They found some evidence that switching to flupenthixol improves outcomes in alcohol or cocaine abuse.

With regard to second-generation antipsychotics, Wobrock and Soyka found little high quality evidence, but concluded a theoretical case for the use of second-generation antipsychotics based on limited evidence that second-generation antipsychotics, particularly aripiprazole, clozapine, olanzapine, quetipaine and risperidone may be more effective than older antipsychotics for both psychotic symptoms and for reducing craving and drug consumption. They found some evidence for the use of naltrexone in controlling alcohol abuse, as well as for the use of disulfiram, but did not consider this to be appropriate because of the risk of inducing psychosis.

Summary of evidence from reviews and guidelines

Although some of the reviews and guidelines described above, either did not search widely for relevant studies, or did not describe the source of the evidence reviewed, they all came to the conclusion that there is poor evidence for the effectiveness of pharmacological interventions for people with coexisting schizophrenia and substance misuse. Some authors concluded that no specific drugs can be recommended and that treatment should follow that used for schizophrenia alone, while others suggest that the limited evidence for several second-generation antipsychotics, including clozapine, quetiapine, risperidone and olanzapine should be interpreted as an indication for use of these drugs. All call for better quality research to be undertaken.

8.2.5 Evidence from new RCTs for the use of pharmacological interventions to treat people with coexisting schizophrenia and substance misuse (pharmacological interventions)

One additional RCT (VANNIMWEGEN2008) and a secondary analysis from an earlier RCT (CATIE2008) were found that were not included in the published reviews and guidelines.

The VANNIMWEGEN2008 trial was a 6-week double-blind RCT comparing olanzapine with risperidone in people with schizophrenia, schizoaffective disorder or schizophreniform disorder with coexisting cannabis use. Participants were a subsample (N = 41) of 138 inpatients or outpatients from four mental health centres aged 18 to 30. The authors report no differences between the study drugs in terms of cannabis use or cravings.

CATIE2008 was a secondary analysis of a large pragmatic trial that included 1432 participants (643 substance users and 789 non-users). People with schizophrenia were recruited at 57 US sites and randomly assigned to olanzapine, perphenazine, quetiapine, risperidone or ziprasidone for up to 18 months. Among the substance users, there were no significant differences between treatment groups in time to all-cause discontinuation. The authors also report that substance users and non-users were generally similar in terms of improvement of symptoms of psychosis and side-effects. An analysis of the effective of treatment on substance misuse outcomes has not yet been published.

Summary of evidence from new RCTs

There is no new evidence showing increased effectiveness of any particular antipsychotic in reducing substance misuse in people with coexisting schizophrenia and substance misuse.

8.2.6 Evidence from existing reviews and guidelines for the use of pharmacological interventions to treat people with coexisting bipolar disorder and substance misuse (pharmacological interventions)

Two reviews focus solely on the treatment of people with coexisting bipolar disorder and substance misuse (Casas *et al.*, 2008; Vornik & Brown, 2006). In addition, three reviews and guidelines discussed above also cover bipolar disorder (Mills *et al.*, 2009; Tiet & Mausbach, 2007; TIP series 45).

Casas *et al.*, (2008) developed a guideline based on a systematic review of published evidence together with expert consensus and surveys of expert practice. Evidence was sourced from a search of MEDLINE (to 2005). How the evidence was assessed, or what outcomes were used, is unclear. Similarly the diagnostic criteria used to include or exclude studies are unclear. Nevertheless, recommendations are made for the treatment of different episode types. With regard to mania, Casas and colleagues recommend that treatment for "concomitant substance use disorder ... should be initiated at the same time [as treatment for mania] without giving priority to one over the other. However, if substance abuse presents as an acute intoxication or abstinence syndrome, then the treatment of the manic episode must be adapted." They recommend second-generation antipsychotics, as well as, carbamazepine and valproate, but not antidepressants. For rapid cycling bipolar disorder, Casas and colleagues recommend that treatment should be adapted if substance abuse presents as acute intoxication or abstinence syndrome, using the same drugs as are recommended for use in a manic episode; otherwise treat as for mania. The authors found that lithium was shown to be effective in young people with coexisting substance abuse, and that valproate was helpful in reducing alcohol consumption. They found no

RCT evidence for carbamazepine, gabapentin, lamotrigine, or benzodiazepines.

With regard to bipolar disorder, Mills and colleagues (2009) found evidence to suggest that alcohol use outcomes improved with the use of valproate; that carbamazepine and lithium may help to reduce substance misuse; and that quetiapine and lamotrigine may also be of value in those with cocaine dependence.

In addition to the findings described above, Tiet and Mausbach (2007) found that the combination of valproate and lithium may reduce coexisting alcohol use in bipolar disorder.

With regard to TIP series 45 (Center for Substance Abuse Treatment, 2006), the general advice covered above, can also be applied to the treatment of bipolar disorder and coexisting substance abuse, the TIP series 45 guideline authors looked at drugs commonly prescribed for bipolar disorder. With regard to lithium, they concluded that "studies [...]have shown that lithium has no conclusively positive effect on rates of abstinence in either depressed or nondepressed patients." They also state that "anticonvulsant mood stabilizers, such as divalproex sodium and carbamazepine, can be effective in controlling mania and, some evidence suggests, in coexisting addictive conditions as well. Carbamazepine is known to be as effective as some benzodiazepines in inpatient treatment of alcohol withdrawal and, because of its anticonvulsant properties, it may be a good choice for treating those patients at high risk of withdrawal seizures."

Vornik and Brown (2006) reviewed pharmacological interventions for bipolar disorder and coexisting substance abuse. There is no description of how evidence was sourced or of any criteria by which evidence was assessed, which makes it difficult to assess the overall quality of the conclusions drawn. The authors report some evidence from RCTs for the effectiveness of mood stabilisers, including carbamazepine for reducing depressive symptoms in bipolar disorder (depressed phase) and coexisting cocaine abuse; major depressive disorder and coexisting substance use; and valproate in reducing alcohol use. They report non-randomised evidence for lamotrigine in reducing psychiatric symptoms and cocaine use. They also found evidence for the effectiveness of antipsychotics, including quetiapine (randomised open-label) and aripiprazole (open-label, non-randomised) for reducing psychiatric symptoms and drug craving.

Summary of evidence from reviews and guidelines

As with schizophrenia, not all the reviews searched more than one electronic database or gave full details of their methodology, which makes it hard to judge their quality. However, the reviews and guidelines largely came to similar conclusions, other than concerning the use of lithium. Some used the

Geller and colleagues (1998) trial in young people (see Chapter 9) as evidence for lithium's effectiveness (for example, Casas *et al.*, 2008), but others found no particular effect (for example, TIP series 45). With regard to other drugs used as mood stabilisers, most reviewers found evidence for the use of carbamazepine, valproate for improving alcohol-related outcomes, and antipsychotics. One found low-level evidence for the use of lamotrigine.

8.2.7 Evidence from new RCTs for the use of pharmacological interventions to treat people with coexisting bipolar disorder and substance misuse (pharmacological interventions)

Three relevant RCTs were found which were not included in the published reviews and guidelines (BROWN2009, KEMP2009, NEJTEK2008).

BROWN2009 reported results from a 12-week placebo-controlled double-blind RCT of naltrexone plus CBT in 50 people with bipolar disorder I or II (currently depressed or mixed phase) with coexisting alcohol dependence. All participants continued to take their usual medication throughout the trial. The authors report a trend towards a greater decrease in number of drinking days in the treatment group. However, baseline rates of drinking were higher in the treatment group, although the authors say this is not statistically significant.

KEMP2009 reported results from a 6-month, double-blind, maintenance trial of lithium monotherapy versus the combination of lithium and divalproex in people with coexisting rapid-cycling bipolar disorder and substance abuse and/or dependence. Of 149 participants enrolled into an open-label acute stabilisation phase, 31 were randomised to the maintenance phase. The results suggested there was advantage in using combination therapy in terms of the primary outcome measure (time to relapse; defined as treatment for a mood disorder), or secondary outcomes (time to discontinuation, psychiatric symptoms, and substance misuse).

NEJTEK2008 report results from a 20-week, double-blind, RCT comparing risperidone to quetiapine in people with coexisting bipolar disorder I or II and stimulant dependence. Of 96 participants who consented and were randomly assigned, 80 attended at least one follow up visit. The results suggested little difference between study medication in terms of drug use or craving, or mood.

Summary of evidence from new RCTs

When tested in an RCT, there was insufficient evidence to reach a conclusion about the effectiveness of using naltrexone to improve alcohol-related outcomes in people with coexisting bipolar disorder and alcohol dependence. Evidence from one trial suggests that for those with rapid-cycling bipolar

disorder and coexisting substance misuse, the combination of lithium with divalproex is more effective than lithium alone in preventing relapse of bipolar symptoms and in reducing substance misuse in those whose symptoms have stabilised. In terms of antipsychotic medication, evidence from one trial suggests little difference between risperidone and quetiapine, but a lack of placebo control makes it difficult to determine if these medications were effective.

8.2.8 Clinical evidence for the management of drug interactions or adverse events from pharmacological interventions in people with psychosis and coexisting substance misuse (pharmacological interventions)

None of the reviews focus substantially on interactions between treatment medication and substances of misuse, or on adverse events which are specific to, or especially elevated in, those with psychosis and coexisting substance misuse compared with those with psychosis alone.

Adverse events associated with most psychotropic drugs are well documented. For antipsychotics, these include extrapyramidal symptoms (notably with first-generation drugs), weight gain, and increased glucose and lipid levels, leading to increased risk of diabetes (notably with second-generation drugs). Clozapine, which is used in several of the trials discussed above, tends to be associated with more reports of side effects than other antipsychotic medication. However, as Green and colleagues (2008) state, interactions between psychotropic medications and drugs of abuse are rare. These authors also point out that some newer medication can be sedating which can be problematic with some drugs of abuse. In addition, Farren and colleagues (2000) reported near syncopal episode following cocaine use in a service user treated with clozapine.

Meanwhile, pharmacological treatments for alcohol abuse, such as naltrexone and acamprosate, are not contraindicated in schizophrenia, and disulfiram also seems to be well tolerated, although it has been suggested that symptoms of psychosis and liver toxicity should be closely monitored (Green *et al*, 2008).

Treatment Improvement Protocol series 43 covers problems with treatments for opioid dependence, such as methadone and buprenophine. These drugs can precipitate withdrawal in people also taking drugs to treat HIV infection, such as nelfinavir, efavirenx, and nevirapine. There is a similar problem with these opioid treatments and carbamazepine, phenytoin and phenobarbital.

With antidepressants, some SSRIs which inhibit the isoenzymes that metabolise methadone (particularly, CYP3A4, CYP1A and CYP2D6) could lead to increased serum methadone levels. Fluvoxamine is the most likely to cause excessive serum methadone levels due to inhibition of CYP1A2 and has

been implicated in over-sedation and respiratory depression when combined with methadone. Also, there is some indication that methadone increases serum levels of tricyclic antidepressants, so lower doses may be needed. Rifampin, carbamazepine, phenobarbital and some HIV infection medications may induce liver enzymes that alter the transformation of methadone. So clinicians may need to adjust the dose of methadone accordingly.

Treatment Improvement Protocol series 45 warns that benzodiazepines, which are known to be addictive, are particularly so in those already addicted to other substances. Because of their reduced side effect profile and lower risk of dangerous drug interactions, SSRIs may be considered as the antidepressants of choice for those with addiction and coexisting psychiatric conditions. However, the potential for different SSRIs to cause drug interactions should be considered in individual cases.

8.2.9 Clinical evidence summary (pharmacological interventions)

There is limited evidence from well conducted RCTs for the relative effectiveness of pharmacological treatments for people with psychosis and coexisting substance misuse, either of treatments for psychosis symptoms or of treatments aimed at improving substance misuse. There is also little data on interactions between drugs given as medication and drugs of abuse. See Table 32 for a summary for each medication.

Table 32: Relevant interventions included in current NICE guidelines and summary of evidence of effectiveness

Intervention type/use	Name	Recommended in existing NICE guideline? *	Evidence found from existing reviews and new RCTs	Notes from Summary of Product Characteristics
MEDICATION				
Alcohol dependence	Acamprosate calcium	Alcohol**: Yes^	No evidence, but no known contraindication in those with schizophrenia.	
Alcohol deterrent compounds	Disulfiram	Alcohol**: Yes^	At best, there is preliminary evidence of effectiveness in people with coexisting schizophrenia and alcohol dependence, but some reviewers consider that using this medication risks inducing psychosis.	Chlordiazepoxide and diazepam toxic effect may be enhanced. Very rare reports of potentiation of organic brain syndrome and choreoatphetosis with pimozide. The intensity of the Disulfiram-alcohol reaction may be increased by amitriptyline and chlorpromazine and decreased by diazepam. Avoid lithim liquid (contains 5% ethanol).
Alpha-adrenergic agonists	Clonidine	DMD: Not routinely	No evidence.	Anntipsychotics and tricyclic antidepressants may provoke orthostatic hypotension. CNS depressants may be potentiated and cause excessive drowsiness. Increased risk of rebound hypertension if clonidine is withdrawn in patients taking tricyclics antidepressants.
Alpha-adrenergic agonists	Lofexidine	DMD: Yes^	No evidence.	Efficacy may be reduced by tricyclic antidepressants. Concomitant use of drugs which prolong the QT interval should be avoided.
Antiepileptic drugs	Phenytoin	Alcohol**: No	No evidence.	Class warning for anticonvultants. A small increased risk of suicidal ideation and behaviour reported.

				Potential for drug interactions is complex and includes a range of psychotropic drugs
Antiepileptic drugs	Topiramate	Alcohol**: No	No evidence.	SPC Class warning for anticonvultants. A small increased risk of suicidal ideation and behaviour reported. Inhibits the enzyme CYP 2C19.
Antimanic drugs	Lithium	Bipolar: Yes	There is limited evidence of effectiveness in reducing substance misuse in those with bipolar disorder; of combined use with valoprate in reducing coexisting alcohol use.	Avoid lithium liquid with metronidazole or in patients with alcohol misuse.
Antimanic drugs	Valproic acid	Bipolar: Yes	Case study evidence of benefit in coexisting schizophrenia and alcohol dependence; recommended by one author for mania but evidence is unclear; evidence of usefulness in reducing alcohol consumption.	Class warning for anticonvultants. A small increased risk of suicidal ideation and behaviour reported. Combination with olanzapine may significantly increase the risk of certain olanzapine associated adverse events.
Antimanic drugs/ Anxiolytics	Benzodiazepine (for example, diazepam, lorazepam, chlordiazepoxide):	Bipolar: Yes^ Alcohol**: Yes	No evidence, but potentially addictive.	
Antimanic drugs/ Hypnotics	Clomethiazole (Chlormethiazole)	Alcohol**: No	No evidence, but potentially addictive.	Fatal cardiorespiratory collapse reported when combined with other CNS depressant drugs.
Antimanic/ Control of epilepsy	Carbamazepine	Bipolar: Not routinely	Evidence that it may reduce substance misuse in bipolar disorder, and control mania and depressive symptoms.	Class warning for anticonvultants. A small increased risk of suicidal ideation and behaviour reported. Avoid with MAOI's and individuals of Han Chinese and Thai origin

				with positive HLA-B*1502 allele, due to increased risk of developing carbamazepine-associated Stevens-Johnson syndrome. Principal iso enzyme responsible for metabolism is CYP 3A4, therefore use caution with inhibitors or inducers of this isoenzyme. Levels of carbamazepine and its principal active metabolite may be increased by concomitant use of a range of drugs including fluoxetine, fluvoxamine, paroxetine, trazodone and olanzapine, quetiapine and valproic acid.
Antipsychotic drugs	For example: Clozapine Haloperidol Olanzapine Risperidone	Bipolar: Yes Schizophrenia (update): Yes	Inconsistent findings on substance misuse outcomes. More frequent reports suggest clozapine may be of benefit.	Principal isoenzyme responsible for metabolism is CYP1A2. Clozapine is contraindicated in alcoholic and other toxic psychoses, drug intoxication and comatose conditions. Principal iso enzyme responsible for metabolism is CYP 1A2 . Sudden smoking cessation may significantly increase clozpaine plasma levels, concomitant benzodiazepine use may increase risk of circulatory collape. Consult the SPC of individual agents for information about other drugs.
Opioid agonists & partial agonists	Buprenorphine	DMD: Yes	No evidence.	Principal isoenzyme responsible for metabolism is CYP3A4.
Opioid agonists &	Methadone	DMD: Yes	No evidence. Some suggestion of	Principal isoenzyme responsible for

partial agonists			interacations with other medications.	metabolism is CYP3A4. Concomitant use with MAOI's and drugs which prolong the QT interval should be avoided
Opioid antagonists	Nalmefene	Alcohol**: No DMD: No	No evidence.	No UK licence.
Opioid antagonists	Naltrexone	Alcohol**: Yes^ DMD: Yes^	Some evidence of effectiveness in schizophrenia with coexisting alcohol dependence.	
Serotogenic agents	Ondansetron	Alcohol**: No	No evidence.	Metabolised by multiple hepatic isoenzymes: CYP3A4, CYP2D6 and CYP1A2. Therefore enzyme inhibition or reduced activity of one enzyme is normally compensated by other enzymes and should result in little or no significant change in overall ondansetron clearance or dose requirement.
Serotogenic agents	SSRIs	Alcohol**: Not routinely for alcohol misuse Depression: Yes^	No evidence in psychosis. Some suggestion of interactions with methadone, leading to increased serum methadone levels (SSRIs).	Individual SSRIs vary in their propencity to affect Cytochrome p450 isoenzymes. Consult current SPC for details.
Skeletal muscle relaxants	Baclofen	Alcohol**: No	No evidence.	Tricyclic antidepressants may potentiate effects, resulting in pronounced muscular hypotonia. Concomitant use of CNS drugs may lead to increased sedation.
PHYSICAL AND COMPLEMENTARY INTERVENTIONS				
Physical	Acupuncture	DMD: No	No evidence.	
Complementary	Mindfulness meditation	Alcohol*: No	No evidence.	

Note. DMD = Drug misuse: opioid detoxification; DMP = Drug misuse: psychosocial interventions.
* Available from www.nice.org.uk.
** Management of alcohol dependence guideline.
^ For specific groups and/or in certain circumstances (see relevant guideline for further information).

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8.2.10 Health economic evidence (pharmacological/ physical interventions)

No studies assessing the cost-effectiveness of pharmacological/physical interventions for people with psychosis and coexisting substance misuse were identified by the systematic search of the economic literature undertaken for this guideline. Details on the methods used for the systematic search of the economic literature are described in Appendix 9.

8.2.11 From evidence to recommendations (pharmacological/ physical interventions)

There is little robust evidence to guide the use of specific pharmacological treatments for people with psychosis and coexisting substance misuse in the UK. On the basis of the evidence reviewed, it is not possible to identify specific drugs which should be considered as agents of first choice.

The use of depot formulations may be expected to increase the opportunity to identify episodes of non-adherence to prescribed treatment. Whilst this may be an important consideration in individual cases there is, overall, insufficient evidence to recommend depot preparations as routine first line treatment.

Clozapine is frequently cited as having a particular role in this population, although there is no RCT evidence to support this view. In addition, its use may increase the risk of adverse effects, and due to the possibility of a syncopal episode, particular care should be exercised where the drug of misuse is cocaine.

8.3 CLINICAL PRACTICE RECOMMENDATIONS

8.3.1 Recommendations (pharmacological/ physical interventions)

Secondary care mental health services

Treatment

8.3.1.1 Before starting treatment for adults and young people with psychosis and coexisting substance misuse, review:

- the diagnosis of psychosis and that of the coexisting substance misuse, especially if either diagnosis has been made during a crisis or emergency presentation

- the effectiveness of previous and current treatments and the person's tolerance of them; discontinue ineffective treatments.[14]

8.3.1.2 Ensure that adults and young people with psychosis and coexisting substance misuse are offered evidence-based treatments for both conditions.

- For the treatment of psychosis, see 'Bipolar disorder: the management of bipolar disorder in adults, children and adolescents, in primary and secondary care' (NICE clinical guideline 38) or the guideline on schizophrenia (NICE clinical guideline 82).
- For the treatment of substance misuse, see 'Alcohol-use disorders: diagnosis and clinical management of alcohol-related physical complications' (NICE clinical guideline 100 and CGXX) or 'Drug misuse: psychosocial interventions' (NICE clinical guideline 51) and 'Drug misuse: opioid detoxification' (NICE clinical guideline 52). [15]

8.3.1.3 Use antipsychotics according to the guideline on schizophrenia (NICE clinical guideline 82) or bipolar disorder (NICE clinical guideline 38) because there is no evidence for any differential benefit for one antipsychotic over another for people with psychosis and coexisting substance misuse.

8.3.1.4 Use depot/long-acting injectable antipsychotics according to the guideline on schizophrenia (NICE clinical guideline 82) in managing covert non-adherence with treatment for psychosis and not as a specific treatment for psychosis and coexisting substance misuse.

8.3.1.5 When prescribing medication for adults and young people with psychosis and coexisting substance misuse:

- take into account the level and type of substance misuse, especially of alcohol, as this may alter the metabolism of prescribed medication, decrease its effectiveness and/or increase the risk of side effects
- warn the person about potential interactions between substances of misuse and prescribed medication
- discuss the problems and potential dangers of using non-prescribed substances and alcohol to counteract the effects or side effects of prescribed medication.

[14] This recommendation also appears in section 7.2.10 where the psychological data is presented.

[15] This recommendation also appears in section 7.2.10 where the psychological data is presented.

8.3.2 Research recommendations (pharmacological interventions)

8.3.2.1 Is clozapine clinically effective and cost-effective at reducing craving in people with psychosis and coexisting substance misuse?

8.3.2.2

9 YOUNG PEOPLE WITH PSYCHOSIS AND COEXISTING SUBSTANCE MISUSE

9.1 INTRODUCTION

As described in Chapter 5, there is a paucity of evidence relating to the effectiveness of different service configurations and clinical pathways for delivering interventions specifically for people with psychosis and coexisting substance misuse. The GDG therefore developed, through expert consensus, a care pathway likely to complement coordinated, well managed treatment. For young people, this is summarised in Figure 4.

Adolescence is a period of major developmental transitions - physically, psychologically and socially. During this period young people experience emotional distress, frequent interpersonal disruptions and challenges in establishing a sense of identity. These factors can act as both stressors for those vulnerable to a psychotic illness and as difficulties that can lead to substance misuse as a form of escape or self-treatment.

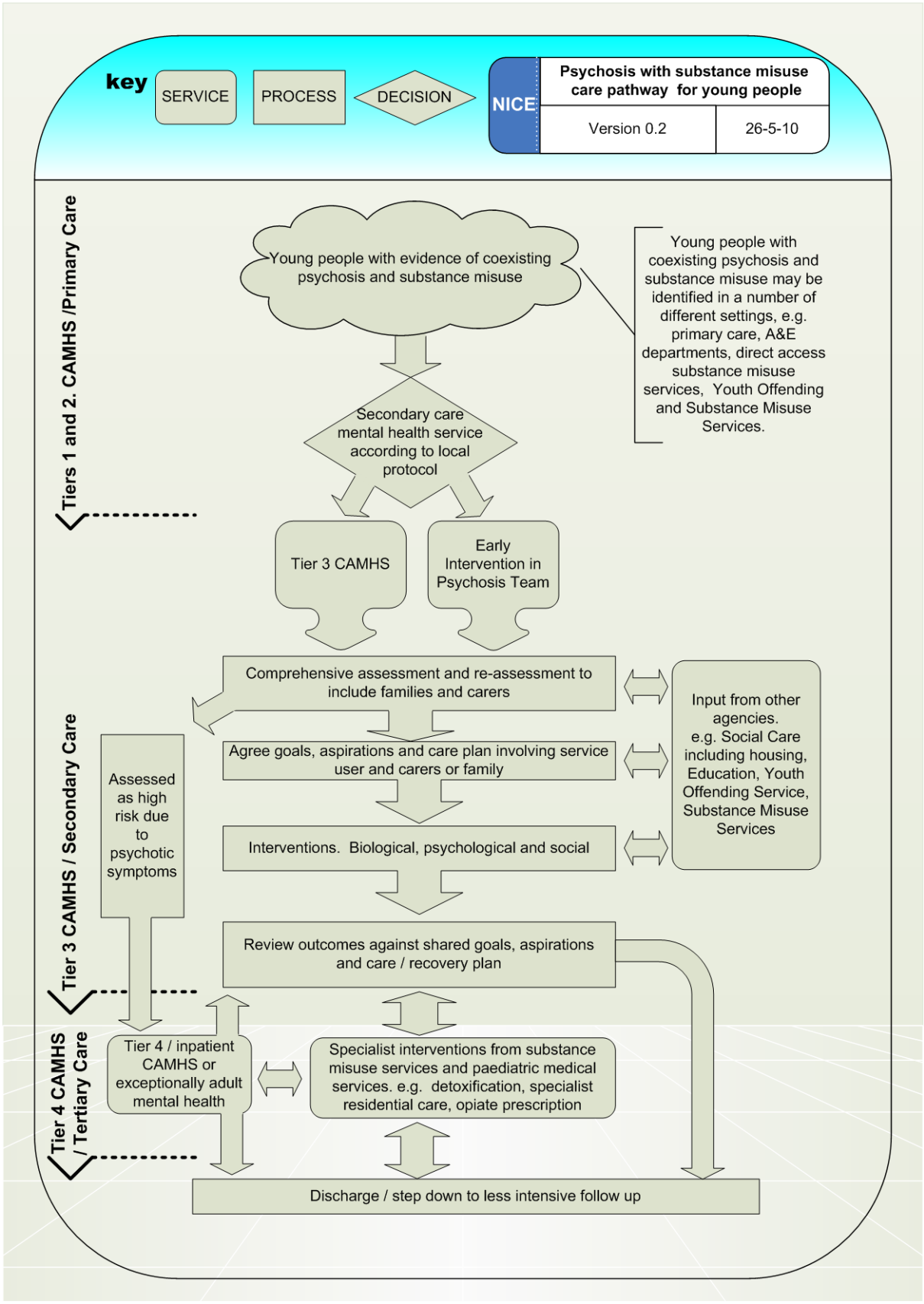
Little research has been carried out on the specific factors that lead young people to be vulnerable to both substance misuse and psychosis. Furthermore, little is known about the effectiveness of interventions specific to this age group. This chapter, therefore, covers what is known about prevalence, outcomes and service configuration for young people. In the absence of more specific evidence, the principles of intervention will be drawn from and adapted from the adult literature.

This guideline uses the term 'young people' to refer to people aged between their 14th and 18th birthdays, as people of this age generally prefer this descriptor to the term 'adolescent'.

9.2 PREVALENCE

It is not simple to identify the prevalence of substance misuse and psychosis in young people. Studies which explore the age range might include a discussion about each of the disorders, but rarely combine them. Studies which do investigate combined disorders usually do not focus on the under 18 year olds.

Figure 4: Care pathway for young people with psychosis and coexisting substance misuse.



A systematic review of coexisting substance use in people with psychosis carried out by Carra and Johnson (2009) pointed to wide variations in prevalence rates. Most recent UK studies reported rates of between 20 to 37% in mental health settings, and 6 to 15% in addiction settings (Carra & Johnson, 2009). Inpatient, crisis and forensic settings are, not surprisingly, higher, that is, 38 to 50% (Carra & Johnson, 2009). People from inner cities and some ethnic groups are over represented (Carra & Johnson, 2009). It should be emphasised that there are varying age ranges in these studies and few specifically focused on young people.

9.2.1 General practice

A study undertaken from 1993 to 1998 estimated that there were at least 195,000 comorbid service users and 3.5 million GP consultations involving comorbid service users of all ages in England and Wales (Frisher *et al.*, 2004). An unanticipated finding was that each year 80-90% of comorbid service users were newly diagnosed, although existing service users may continue to receive treatment. Thus, there is a significant problem in terms of primary care workload. The number of people newly developing comorbidity in primary care increased year-on-year. The impact on health services is far in excess of that for mono-morbid service users; comorbid individuals have an extra consultation frequency for all problems, estimated as an excess of 1,115,751 consultations in England and Wales in 1998.

During the six year study period, the annual comorbidity rate increased by 62%, but rates of comorbid schizophrenia, paranoia and psychoses increased by 128%, 144% and 147%, respectively (Frisher *et al.*, 2004). In this study, the level of comorbidity increased at a higher rate among younger service users, which indicates that comorbidity may increase, perhaps at a faster rate than observed in the study period, in future years. All comorbid diagnoses – including schizophrenia and psychosis - peaked at ages 16-24 or 25-34. In 1998, it was estimated that there were about 20,000 comorbid cases between ages 16 to 34 (7773 in age 16 to 24 and 12949 in 16 to 34 age range) in primary care.

The data reported by Frisher and colleagues indicate that substance abuse may be precipitating more serious forms of comorbidity, although it is by no means clear that this is the case. For example, nearly all diagnoses of comorbid schizophrenia precede substance abuse. In this study (Frisher *et al.*, 2004), the majority (54%) of service users had a psychiatric diagnosis first, and half become comorbid within 6 months of the first diagnosis.

The findings on transition from mono to comorbidity have major implications for understanding and preventing comorbidity. Perhaps individuals with comorbidity may be qualitatively different in the form of their mono-morbidity than those who remain mono-morbid. Early development of comorbidity suggests that there may be characteristics already present at the

mono-morbid stage which may predict the likelihood of developing comorbidity. Identifying such characteristics in future research might contribute to the early management or prevention of comorbidity in primary care.

9.2.2 Community substance misuse and mental health services

Weaver and colleagues (2003) conducted a multicentre study that derived estimates of psychosis and coexisting substance misuse (of whom, 76% were diagnosed with schizophrenia), in the age range of 16 to 30 years old. They found that one third of their sample was misusing substances. Although the age range looked at in this study exceeds the range considered for young people, it is helpful in providing a figure on substance misuse in the community.

9.2.3 First-episode psychosis

Donoghue and colleagues (2009) utilised data from two epidemiological studies of first-episode psychosis (the Schizophrenia in Nottingham study and the Aetiology and Ethnicity of Schizophrenia and Other Psychoses study), demonstrating that for 16 to 29 year olds, there was a significant increase from 14.9% to 30.1% in all substance use disorders between 1992-1994 and 1997-1999 (Donoghue *et al.,* 2009). Similarly, for cannabis-specific substance use disorder, there was a significant increase from 3.2% to 10.6%. These increases were seen in both males and females.

9.3 IMPACT OF SUBSTANCE MISUSE ON OUTCOME IN PSYCHOSIS

In a group of first episode patients treated with psychological therapy, 33% of the under 21 year olds had self reported substance misuse (Haddock *et al.,* 2006). Of relevance is the finding that young people may have differing needs with regard to engagement. Counselling appeared to be more beneficial for the younger age group.

An Australian study (Wade *et al.,* 2006), in a 15-30 year old age group (mean age 21.6 years), reported that substance misuse (53% at follow up) was an independent risk factor for problematic recovery in first-episode psychosis (for example, increased risk of admission, relapse of positive symptoms and shorter time to relapse). However, substance misuse was not associated with longer time to remission.

Hides and colleagues (2006) has pointed to a bidirectional relationship between substance misuse and cannabis relapse in that a higher frequency of cannabis use was predictive of psychotic relapse (if medication adherence, other substance use and duration of untreated psychosis were controlled for), while an increase in psychotic symptoms was predictive of relapse to

cannabis use. In this study, only 15% of service users had not used any illicit substance in the previous 12 months.

9.4 ASSESSMENT AND DIAGNOSIS

Many aspects of the assessment and diagnosis of young people with psychosis and coexisting substance misuse will be the same or similar as for adults. This is covered in detail in Chapter 5.

As is the case for adults, healthcare professionals in all settings should routinely ask young people with known or suspected psychosis about their use of substances. This may include questions about type and method of administration, quantities and frequency. It is important for healthcare professionals in all settings to routinely assess young people with known or suspected substance misuse for possible psychosis.

For young people with psychosis and coexisting substance misuse presenting to mental health services, a comprehensive assessment of a young person's psychosis and substance misuse is crucial. This includes an assessment of psychiatric, psychological and physical health, home and family environment, educational or employment status, medication, risk to self and others, relationships and social networks, forensic and criminal justice history, strengths, and aspirations. Assessing the relationship between substance use, emotional state and reasons for substance use is also important. In addition, gaining corroborative evidence where possible is helpful in order to assess the impact of substance misuse on mental state and behaviour.

The assessment of young people may take time and involve multiple sessions due to difficulty with concentration, ambivalence, lack of clarity about the purpose of the assessment(s), and the need to gradually gain trust and confidence in the practitioners and service. There are three crucial goals of an assessment. The first is to conduct the assessment in such a manner that fosters and promotes continuing engagement. The second is to ensure safety of the young person, and the third is to determine which substance(s) the young person is dependent on in order to determine whether administration of a pharmacological agent – possibly for detoxification – is appropriate. It is important to note that even if the young person is not dependent on a substance, serious harm may result from drug misuse.

The comprehensive assessment of a young person presenting with psychosis and coexisting substance misuse is similar to what is described for adults in Chapter 5. The issues brought up for adults however, apply even more strongly for young people, as they are more complex to engage, are more vulnerable, and can suffer from serious problems as a result of substance misuse, without having substance dependence. Additional differences between adults and young people relate to service delivery, as services for young people are usually provided separately from those for adults.

9.5 SERVICE CONFIGURATION AND CARE PATHWAYS

9.5.1 Configuration of CAMHS Services

Interventions for young people with psychosis and coexisting substance misuse may be provided by a range of agencies and services within each agency. Agencies will include Children's Services, which may be involved around social care/housing issues, education or safeguarding. Youth Offending Services may be involved. However, once a diagnosis of psychosis with substance misuse has been made, mental health services will usually be provided by specialist CAMHS or Early Intervention in Psychosis Services (EIS). Specialist substance misuse interventions for young people may be available from within core mental health services or from specialist substance misuse services.

In order to recognise the different levels of interventions for many child mental health problems, CAMHS has been organised into four main levels, or tiers, of delivery (Health Advisory Service, 1995; Department of Health, 2004) (see Text Box 1).

9.5.2 CAMH Services

Tier 1 CAMHS

Professionals at Tier 1 are most likely to encounter young people with psychosis and coexisting substance misuse when a change in their behaviour is noticed. This could be unusual behaviour or otherwise out-of-character behaviour, a decline in academic performance or increasing social isolation. Tier 1 professionals are unlikely to be involved in diagnosing psychosis, but may become aware of substance misuse difficulties. They could also become involved in providing for the young person's physical healthcare, social and educational needs when the young persons mental health needs are being met. Awareness of psychosis and substance misuse in young people may prevent inappropriate dismissal of the difficulties presented by the young person and encourage them to refer on to appropriate services. For Tier 1 professionals to be able to fulfil these roles for young people with psychosis and coexisting substance misuse they will need appropriate training. Training programmes for Tier 1 staff may require modification to cover psychosis with substance misuse or behaviours suggestive of the diagnosis. This training may be most effectively targeted at services that have young people with higher rates of mental health concerns for example Key Stage 4 Pupil Referral Units. Following appropriate training Tier 1 professionals may be involved in the sensitive detection of psychosis and substance misuse difficulties. When identified such concerns should lead to referral to or consultation with Tier 2 professionals.

Tier 2 CAMHS

Tier 2 professionals provide consultation and training to Tier 1 professionals in regard to all mental health problems. Tier 2 professionals therefore require an awareness of the problems of young people with psychosis and coexisting substance misuse and competence to detect psychotic symptoms in young people or the early features of psychosis. If a diagnosis of psychosis or early features of psychosis is suspected, a referral to Tier 3 CAMHS or EIS teams can be made according to local protocols.

Tier 3 CAMHS

Tier 3 services can provide a comprehensive assessment of the young person with psychosis and coexisting substance misuse. When a diagnosis of psychosis is made, it is important for Tier 3 professionals to consider the possibility of substance misuse.

1

Text Box 1: Child and adolescent mental health services (CAMHS) tiers structure	
Tier 1	• Provide primary or direct contact with young people, primarily for reasons other than mental health, including primary care/general practice, counselling and psychotherapy, general paediatrics, social services, health visitors and schools • First point of contact with the child/family with mental health problems • Draw on specialist CAMHS personnel who can consult and advise them about working with children and young people in their care who either have, or are at risk of developing, a mental health problem
Tier 2	• Specialist CAMHS professionals working in a community-based setting alongside Tier 1 workers, working in primary care, schools and other relevant community settings such as social services • Work as a part of a team, with Tier 1 staff, built around the individual child • Able to provide fairly rapid assessment and treatment to children within Tier 1 settings, as well as consultation/support to Tier 1 workers • Able to help identify those children needing referral to more specialist services • Ideally organised into multidisciplinary teams, with good links to Tier 3 services, thereby facilitating a more seamless transition acoss tiers • Sometimes, Tier 2 services are provided by the voluntary sector (for example, some but not all adolescent counselling and psychotherapy services)
Tier 3	• Comprise multidisciplinary teams of specialist CAMHS professionals working in (secondary care) specialist CAMHS facilities (e.g. Child and Family Consultation Services or Hospital Liaison Teams) • The National Service Framework for Children's Services states that all PCT / LHB areas should have at least one (or access to one) comprehensive Tier 3 multidisciplinary CAMHS team providing specialist co-ordinated assessments and interventions, and offering the full range of appropriate psychological and pharmacological treatments • Offer outreach services to those young people who are housebound or otherwise unable to access Tier 3 services based in secondary care facilities, or to work in conjunction with outpatient treatment plans (e.g. monitoring of medication). Emergency services, with 24-hour availability should also be in place in all localities • Provide consultation and training to Tier 1 workers and refer when necessary to Tier 4 services
Tier 4	• Highly specialised tertiary CAMHS that provide multidisciplinary services for very severe mental health problems, or for those who need very intensive treatment or supervision. These services vary in how they are organised. • Includes highly specialist outpatient treatment, crisis intervention and intensive home-based therapies. • Referrals to Tier 4 services usually come from Tier 3 CAMHS professionals, and service users are usually discharged back to Tier 3 services or outreach services after the Tier 4 intervention

2

When a diagnosis of psychosis and coexisting substance misuse has been made, priority should be given to both treatment of the psychosis and substance misuse. Constant review of risk is of key importance, and if the young person presents with a high risk to themselves or others due to their psychosis, then inpatient admission is important to consider.

All the mainstays of treatment, including prescribing medication, monitoring mental state and providing psychosocial intervention can be offered in Tier 3 CAMHS, by EIS teams or by a collaboration between the two.

Given that most young people with psychosis and coexisting substance misuse live with their families, with foster parents, or in social services residential placements, involving carers in treatment is helpful. Carers can be involved in relapse prevention work as well working with professionals in supporting the young person with their substance misuse. Supporting parents, including family therapy, should be offered to all families and include a focus on high levels of criticism and intrusiveness (expressed emotion) when identified.

As many young people with psychosis and coexisting substance misuse require a multi-agency response, clarity about the responsibilities of each agency facilitates the delivery of care. As well as their mental health and substance misuse needs, young people with psychosis and coexisting substance misuse will often have housing, employment or educational needs. Agencies must strive to collaborate to provide coordinated care. Different thresholds for entry into services can compromise this objective. For example, Tier 3 professionals may have concerns about a young person's social care that may not meet social service thresholds for intervention. This can reduce the effectiveness of therapeutic interventions as Tier 3 staff become involved in trying to coordinate or meet social care needs. Likewise social services may find accessing specialist therapy services for some of the young people they care for difficult because, for example, despite on-going substance misuse, Tier 3 staff may consider that the young person's mental health difficulties are in remission and therefore sub-threshold for active involvement. Failure to engage at all with the young person in these circumstances may prevent the success of social services interventions to improve the young person's social care and increase likelihood of relapse. Professionals need to work flexibly and creatively around these tensions over service thresholds. Respecting the validity of the principles leading to the development of thresholds whilst trying to meet the needs of the young person is required in these circumstances.

It is important for Tier 3 teams to develop sub-teams of professionals with expertise in the management of young people with psychosis and coexisting substance misuse either separately or in collaboration with EIP teams. One model of collaboration widely adopted is for CAMHS to provide psychiatric

input whilst EIS provide care co-ordination and psychosocial interventions. In some areas, stand alone CAMHS psychosis services have been set up. Tier 3 CAMHS professionals must also have the capacity to provide consultation and training to Tier 2 staff.

Healthcare professionals working in Tier 3 can also follow the recommendation for adults in other chapters.

Tier 4 CAMHS

For young people with psychosis and coexisting substance misuse, Tier 4 CAMH services principally comprise inpatient services. There is usually a limited role for other Tier 4 CAMH services such as specialist outpatient services and home-based treatment teams, as most non-bed based treatments can be picked up by other services such as Tier 3 CAMHS or EIS teams.

Inpatient services – Admission to an inpatient unit will usually be indicated due to the level of risk identified in managing the young person in the community. This can often present in an acute crisis. Admissions for the management of acute risk should be clearly linked to an acute exacerbation of risk, time-limited, and with clear goals in mind. Such admissions may also be required when risk is high and the motivation of the client to collaborate in community treatment is very low or non-existent. The aim of such admissions is usually to ensure that the client is 'just community ready'. Transfer back to the community is clearly facilitated in circumstances where the young person is effectively engaged in a structured outpatient programme.

Other factors warranting consideration for admission by a Tier 4 team for treatment of psychosis and coexisting substance misuse include other Axis I difficulties combined with a significant deterioration in functioning and a reduced capacity of either the family or community team to manage the young person.

Exceptionally, if a young persons' needs are thought to be best met by and adult ward and they choose this (for example if they are almost 18 years and adult services are much closer to home), then it is acceptable for them to be admitted to an adult mental health ward. It is also acceptable for a young person aged 16 or 17 years to spend a short time on an adult ward if an age appropriate bed is not available. In both these examples safeguarding measures need to be in place whilst the young person is on the adult ward. It is never acceptable for a young person under the age of 16 years to be admitted to an adult ward (See MHA 1983 revision 2007, section 31 and MHA Code of Practice [DH, 2008]).

Specialist home-based treatment teams for young people are in the early stages of development in the UK and consequently their place in the treatment of psychosis and coexisting substance misuse has yet to be established. Like

inpatient services, existing teams frequently manage acute risk and attempt to address chronic risk and/or low functioning patients.

Services are likely to take different forms dependent on their focus on acute or chronic issues. When focused on acute risk, services usually combine characteristics of assertive outreach and crisis intervention with intensive case management. These services have proved effective both when Tier 3 treatment has been disrupted and as a mechanism for organising an effective outpatient intervention plan. Typically services have a capacity for rapid and intensive engagement lasting no more than a few weeks, followed by patient/family centred intensive case management.

Services focused on chronic risk and/or low functioning are characterised by a stronger psychotherapy focus, a longer duration of treatment and an active engagement phase pre-treatment. These services have also been used as step-down from inpatient, when inpatient stays have become ineffective or for community rehabilitation. This type of intervention might be considered when parenting has become distorted by the patient's presentation and family relationships are undermining individually focused treatment plans.
In most cases, psychoeducational work with parents is required prior to implementing more intensive interventions that may often be experienced as intrusive. These forms of home-based treatment are best avoided where there are longstanding concerns about parental capacity.

Home-based treatment services, regardless of whether they focus on the treatment of acute or chronic issues, share a number of characteristics: they require experienced staff with expertise in psychosis and coexisting substance misuse and a team structure that allows a high level of supervision and the effective management of risk in the community; each is likely to offer time-limited treatment but of different durations; and each is likely to balance limit setting with developing autonomy. Services need to effectively differentiate young person, parents, family, and wider system interventions and to focus primarily on the management of risk and the promotion of functioning.

9.6 EARLY INTERVENTION IN PSYCHOSIS SERVICES

Early intervention services are assertive community-based multidisciplinary teams that provide care for people aged between 14 and 35 years with a first presentation of psychotic symptoms during the first 3 years of psychotic illness (Department of Health, 2001) and are primarily concerned with the early identification and treatment of the early phase of psychotic illness. For young people (aged 14 to 18), EIS often work according to locally agreed protocols with Tier 3 and 4 CAMHs.

Often, the initial focus of the EIS is on engagement in order to develop a shared, individualised recovery focussed treatment plan that incorporates a range of interventions including antipsychotic drugs, CBT, family intervention, vocational activity and substance misuse. As substance use and misuse is so common in people presenting with a first episode of psychotic illness, EIS staff may consider the possibility of substance misuse in a young person presenting with psychotic symptoms and if a diagnosis of psychosis and coexisting substance misuse is made ensure that treatment for both conditions is offered.

Interventions for substance misuse may be complicated if the young persons peer group are also using substances and so staff in EIS need to develop strategies to help enable the young person to recognise the impact of their own substance use on their psychotic symptoms. In order to do this, EIS staff will need to fully assess substance use including type, amount and frequency of use of each substance used as well as understanding the context in which the young person uses each substance and its function.

9.7 SPECIALIST SUBSTANCE MISUSE SERVICES FOR YOUNG PEOPLE

The Health Advisory Service reports (1996; 2001) identified a four-tier framework similar to that described above for CAMHS. The functions of each tier, rather than the professional discipline involved, are the focus. Different models and configurations have developed in different regions due to a variety of factors including the prevalence of substance misuse, the general level of affluence or deprivation, existing services, and leadership in service development and innovation. A key issue is that interventions for those young people whose substance misuse is serious enough to require specialist help is not isolated, but integrated with other medical and social services so that continuity is established and maintained.

Tier 1 Universal, generic and primary services

This tier is aimed at all young people. It provides information and advice, health promotion and support to all young people, parents, families and carers. At this level, vulnerable individuals with risk factors including child protection issues may be identified. It is important for staff in such generic and mainstream services to be aware of the need for a destigmatising non-confrontational empathic approach to substance issue and be equipped to identify where more complex interventions may be required.

Tier 2 Specialist services

This tier is directed at vulnerable children who are in contact with children's services such as CAMHS, YOT, paediatrics, child psychology and voluntary services and who are potentially vulnerable to the use of substances. Staff should be skilled in the comprehensive assessment of children and young

people and appreciate the context of developmental issues. Implementation of advice and counselling, crisis management, outreach, interventions with family, as well as competence in 'brief interventions' or motivational enhancement treatments for substance misuse is part of the role. Collaboration with agencies in the formulation of care planning so that interventions are integrated – and substance misuse interventions are not delivered in isolation – is a key component.

Tier 3 Specialist addiction services

This tier comprises a multidisciplinary team to deliver a complex range of interventions for young people who have harmful and potentially serious substance misuse problems and dependence on substances. Close collaboration with CAMHS, youth justice, voluntary agencies and medical services is needed in the delivery of these complex care plans. These services should be integrated with children's services and should cater for the needs of young people and not be based on adult models. Staff should be competent in the delivery of the range of pharmacological and individual, group and family psychological treatments that are available for the treatment of dependent substance use. Training can be provided to staff to understand the intricacies of the relationship between mental, physical and social problems and substance misuse in this age group so that appropriate links can be forged between the diverse agencies in the locality or region.

Tier 4 Very specialised services

These are intensely focused interventions of a pharmacological and psychological nature that require implementation in a residential or inpatient setting or in a structured day programme, due to the severity of the problems. Since there are no residential units for adolescent substance misusers at present, units such as inpatient CAMHS, forensic or paediatric units might be appropriate for different stages of the care plan. Inpatient detoxification for alcohol dependence or titration of opiate substitution treatment are examples of medical interventions requiring inpatient treatment. Intense daily psychological support may only be achieved in an inpatient CAMHS unit or a structured day programme. Coordination of support for accommodation, education and other social needs may also require crisis and fostering placements in order to achieve stability and safety in critical situations, rather than the professional groups involved in provision of care.

Children and young people may need a range of services from a number of tiers at different times. Tiers 3 and 4 should not be involved without support from Tiers 1 and 2. Tiers 1 and 2 are key to the development of a broader base, a more comprehensive approach and the establishment of credibility and trust. Continuity of care from Tier 1, particularly in health and education is crucial. Where possible, coordination and management of the intervention can be done within Tier 1. This would reduce the stigmatisation and attempt to 'normalise' the child and his/her family. For those young people not

connected with Tier 1, any other services involved may want to ensure re-integration and provision of services at Tier 1. Tiers 3 and 4 act as a base for specialist opinion and focussed interventions.

9.7.1 Transition to adult services

The transition to adult services for young people is often marked by a series of discontinuities in terms of personnel, frequency of treatment (often less intense in adult services) and treatment approach, and often a failure to recognise and adapt treatment to developmental stage. Parents who are used to being intensively involved with CAMH services may feel disengaged with adult services. In such circumstances the Care Programme Approach (CPA) and joint working between adult mental health services and CAMHS may facilitate the transition. A period of engagement with adult services before handover is preferable. Flexible working around age-limit cut-offs is also likely to be helpful in promoting smooth transitions.

If the young person is primarily being managed in CAMHS, protocols with adult mental health services need to be in place to ensure the smooth transition of young people to adult services when they turn 18 years old (or in some localities 16 years). It is preferable that such protocols ensure that access criteria to adult services are consistent with young people who have been previously treated by CAMHS, and involve EIS in this process.

In exceptional circumstances where no age appropriate services are available for young people, establishing protocols in place for adult services for young people admitted to adult wards is important. These protocols should include liaison with and involvement of CAMHS.

9.8 INTERVENTIONS

9.8.1 Clinical evidence review

A number of existing NICE guidelines have reviewed the evidence for interventions used to treat young people with psychosis without substance misuse (that is, bipolar disorder), and interventions used to treat young people with substance misuse without psychosis (that is, alcohol; drug misuse: opioid detoxification; drug misuse: psychosocial interventions).

For the purposes of the guideline, the review questions relating to young people with psychosis and coexisting substance misuse were sub-questions of those for adults and, therefore, the review protocols are not repeated here (see Chapter 6, 7 and 8).

Where no evidence existed for a particular intervention in young people with psychosis and coexisting substance misuse, the GDG used informal consensus

to reach a conclusion about whether it was appropriate to cross-reference to existing NICE guidance.

9.8.2 Studies considered for review

Based on the searches conducted for Chapters 6, 7 and 8, only one RCT (Geller *et al*., 1998) focusing specifically on young people with psychosis and coexisting substance misuse, met eligibility criteria. Several further RCTs (Edwards *et al*., 2006; Green *et al*., 2004; Kemp *et al*., 2007) included young people, but interpretation of the evidence is difficult as the majority of participants were over 17 years old. One review (Crome & Bloor, 2005), which examined interventions for "substance misuse and psychiatric comorbidity in adolescents," included the study by Green and colleagues, but no other research specifically about psychosis. In addition, one review (Bender, *et al.*, 2006) systematically searched for studies of interventions for "dually diagnosed adolescents". However, all of the evidence reviewed was for young people with common mental health disorders, not psychosis.

9.8.3 Evidence for the use of pharmacological interventions

One RCT (Geller *et al*., 1998) randomised 25 young people aged 12 to 18 years old who had coexisting bipolar and substance dependency disorder to treatment with lithium or placebo. The results suggested that lithium may be effective in terms of numbers of participants screening positive for drug use after 6 weeks of treatment. This study was also reviewed for the NICE bipolar guideline (NICE, 2006), in which the evidence for psychiatric outcomes was judged to be inconclusive and of overall low quality. Substance misuse outcomes were not examined. The participants had less than two months' history of substance misuse, and the lithium serum levels achieved were high (0.9 to 1.3 meq/l – the guideline recommended 0.6 to 0.8 meq/l).

9.8.4 Guiding principles of treatment

Given the paucity of evidence relating to interventions for young people with psychosis and coexisting substance misuse, the GDG developed a set of guiding principles of treatment.

First, mental health services are the preferred service to lead the treatment of a young person with psychosis and coexisting substance misuse. At the same time, it is necessary for specialist substance misuse services to be involved in the management of young people with opiate misuse and may advise or offer a service to those with cannabis misuse, stimulant misuse, or severe alcohol misuse or dependence. A collaborative coordinated approach is likely to be the most helpful.

Engagement

Engagement is an essential precursor to treatment. Without it, treatments, especially psychosocial and environmental, are less likely to be effective. It is

important to take time to engage the young person by adopting a straightforward, non-confrontational, non-judgemental and optimistic approach. Assessing readiness to change can help inform care planning and treatment options.

Risk Management

Young people with psychosis and substance misuse can at times present with high risk to either themselves or others due to their psychosis, their substance misuse or a combination of the two. Careful and thorough risk assessments are needed at initial presentation and whilst ill, with risk management plans put in place to address any risks identified.

Medication for psychosis

Medication for the treatment of bipolar disorder should follow the NICE Bipolar Guideline (NICE, 2006). There is currently no NICE guideline for the treatment of young people with schizophrenia, but guiding principles can be adopted from the adult schizophrenia guideline (NICE, 2009a).

In the UK, licensing of antipsychotic drugs for the treatment of schizophrenia and bipolar disorder in under 18 year olds is variable, with some manufacturers not recommending these drugs in those under the age of 18 years and the drugs themselves not licensed for this use in this age group. However despite this, considerable clinical experience of their use in young people has been developed from open trials and from some controlled evaluations of drug treatments.

In 2000, the Royal College of Paediatrics and Child Health issued a policy statement on the use of unlicensed medicines or the use of licensed medicines for unlicensed applications, in children and young people. This states clearly that such use is necessary in paediatric practice and that doctors are legally allowed to prescribe unlicensed medicines where there are no suitable alternatives and where the use is justified by a responsible body of professional opinion (Joint Royal College of Paediatrics and Child Health/Neonatal and Paediatric Pharmacists Group Standing Committee on Medicines, 2000).

Caution should be taken with possible drug interactions with substances of misuse. Dosage should be adjusted according to age and weight/body mass index.

Psychological/ Psychosocial interventions

As for adults, the following psychosocial interventions are used with young people either on their own or in combination:

- Motivational interviewing
- CBT

- Relapse prevention work
- Psychoeducation
- Family work/therapy
- Contingency management.

The choice of intervention depends on the nature of the problem and which approach may appear more appropriate and suitable for a particularly substance misuse. Motivational enhancement therapy has becoming increasingly used and evidence is accumulating about its benefits and cost-effectiveness. Some young people may feel more comfortable concentrating on behavioural methods rather than treatments that use abstract forms of reasoning. The 'treatment' needs to focus not only on the substance misuse but also the psychiatric disorders such as depression, anxiety, ADHD, and conduct disorders (Chan *et al.,* 2008; Rowe *et al.,* 2004).

In the UK, there is also emphasis on harm reduction, including needle exchange, prevention of drug-related deaths, and treatment for physical illness and injury. Active support for families, and developing social skills and competence in parents and children is a recent focus. The Iowa Strengthening Families Program (Molgaard *et al.,* 1994) and Preparing for the Drug Free Years (Spoth *et al.*, 2004) and Community Reinforcement and Family Training (CRAFT) (Waldron *et al*., 2007) are examples.

Treatment of substance misuse

Where available, relevant NICE guidelines can be used to inform treatment of substance misuse. In addition, it should be noted that young substance misusers who are referred to Tier 3/4 services are likely to have some psychological and physical comorbidities as well as be polysubstance misusers. Thus, treatment of substance misuse should take account of these possibilities. Constant and consistent review of a young person's clinical state is crucial, as unpredictability is a feature of young substance misusers.

For relevant pharmacological treatments, section 9.8.3 can be consulted in addition to relevant NICE guidelines. It is crucial that dependence is diagnosed if medications for withdrawal or substitution are going to be prescribed. Medications should be prescribed by experienced practitioners who are aware of the risks in young people. Medications - apart from buprenorphine - are not licensed for use for under 18 year olds. For detoxification of alcohol dependence and management of opiate dependence by detoxification or substitution specialist substance misuse services should be involved.

Input from other agencies

Young people with psychosis and substance misuse often have a range of social needs. These should be fully assessed and the following services may need to be involved to address these needs:

- Housing
- Education
- Employment
- Youth Offending Services (YOS).

There are several key elements which contribute to the quality and effectiveness of young people's substance misuse services. These include having a comprehensive assessment, an integrated approach, family involvement, developmental appropriateness, engagement and retention, qualified staff, gender and cultural competence and evaluation of outcomes (Knudsen, 2009). Of note was the finding that treatment quality was significantly greater in programs offering intensive levels of care.

9.8.5 Issues of consent to treatment for young people

It is desirable to gain informed consent from both the young person and their parents, not least because the success of any treatment approach significantly depends upon the development of a positive therapeutic alliance between the young person, the family and the professionals. In most outpatient settings, consent is usually straight forward, as the young person will generally have a choice to, at least, accept or decline treatment. Nevertheless, it is important to provide information about the potential risks and benefits of the intervention being offered, and where appropriate, a choice given between different treatment options.

There may be times when professionals consider inpatient admission to be necessary, but either the young person or the family do not consent. Under the Mental Health Act 1983 (HMSO, 2007 amendment), there have been some changes to the law regarding young people under the age of 18 years.

If a young person aged 16 or 17 years old has capacity to give or refuse consent for treatment, it is no longer possible for the person with parental authority to over-rule the young person's wishes. However, for those under the age of 16 years a 'Gillick-competent' young person can still be admitted against his or her wishes with the consent of someone with parental authority. Whilst the use of parental consent is legal, the Code of Practice for the Mental Health Act (HMSO, 2007) advises against this, suggesting it is good practice to consider the use of other appropriate legislation, usually the Mental Health Act (HMSO, 2007). This includes safeguards such as the

involvement of other professionals, a time limit and a straightforward procedure for appeals and regular reviews. It also avoids a possible conflict with the Human Rights Act, 1998 (HMSO, 1998).

On the other hand, a 'Gillick competent' young person below the age of 16 years has the right to consent to treatment. If the person with parental authority objects, these objections must be considered but will not necessarily prevail.

Alternative legislation includes using a care order (Section 31) under the Children Act 1989 (HMSO, 1989) or a specific issue order (Section 8). Both of these options normally involve social services and can be time consuming. Another, more rapid alternative to the Children Act (HMSO, 1989), is to apply for a Wardship Order, which in an emergency can be organised by telephone.

9.8.6 Clinical evidence summary

In one small trial (N=25) assessing pharmacological interventions for young people, lithium was compared with placebo. Based on this evidence (*GRADED* low quality), it was not possible to reach a decision about the effectiveness of pharmacological interventions for young people with psychosis and coexisting substance misuse.

There was no evidence for psychological or psychosocial interventions for young people with psychosis and coexisting substance misuse.

9.8.7 From evidence to recommendations

Based on the limited evidence base, the GDG were required to extrapolate from data which may not accurately address treatment effectiveness for young people with psychosis and coexisting substance misuse. The GDG therefore developed guiding principles of treatment and recommendations based on consensus. The GDG recognises that as new evidence emerges on treatment for young people with psychosis and coexisting substance misuse, the recommendations in this guideline will be revised and updated accordingly.

9.9 CLINICAL PRACTICE RECOMMENDATIONS

9.9.1 Recommendations (Specific issues for young people with psychosis and coexisting substance misuse)

Competence

9.9.1.1 Professionals in Tier 1 (primary care and educational settings) should be competent to recognise early signs of psychosis and substance misuse in young people.

9.9.1.2 All healthcare professionals in Tier 3 (community mental health teams) and Tier 4 (specialist inpatient and regional services) CAMHS, and in early intervention in psychosis services, should be competent in the management of psychosis and substance misuse in young people.

Identification and referral

9.9.1.3 Professionals in Tier 1 (primary care and educational settings) should seek advice or consultation from Tier 2 CAMHS (primary care) when signs of psychosis are detected in young people. If healthcare professionals in Tier 2 CAMHS detect signs of psychosis in young people, a referral to Tier 3 CAMHS or early intervention in psychosis services for young people should be made according to local protocols.

9.9.1.4 Ask all young people seen in Tier 3 and Tier 4 CAMHS and in early intervention in psychosis services who have psychosis or suspected psychosis about substance misuse (see 5.8.1.1).

Assessment and treatment

9.9.1.5 Healthcare professionals working with young people with psychosis and coexisting substance misuse should ensure they are familiar with the legal framework that applies to young people including the Mental Health Act (2007), the Mental Capacity Act (2005), and the Children Act (2004).

9.9.1.6 For psychological, psychosocial, family and medical interventions for young people, follow the recommendations for adults in this guideline; they may need to be adapted according to the young person's circumstances and age. In addition, other agencies, including children's services, should be involved to ensure that the young person's educational, employment, family and housing needs are met.

9.9.1.7 When prescribing medication, take into account the young person's age and weight when determining the dose. If it is appropriate to prescribe unlicensed medication, explain to the young person and/or their parents or carers the reasons for doing this.

9.9.1.8 Those providing and commissioning services should ensure that:

- age-appropriate mental health services are available for young people with psychosis and coexisting substance misuse, **and**
- transition arrangements to adult mental health services are in place where appropriate.

9.9.2 Research Recommendactions

9.9.2.1 What risk factors predict the onset of substance misuse in young people with psychosis?

Appendices

APPENDIX 1: SCOPE FOR THE DEVELOPMENT OF THE CLINICAL GUIDELINE

1 Guideline title

Psychosis in conjunction with substance misuse: the assessment and management of psychosis with substance misuse

1.1 Short title

Psychosis with substance misuse

2 The remit

The Department of Health has asked NICE: "To develop a clinical guideline for the assessment and management of severe mental illness in conjunction with problematic substance misuse."

3 Clinical need for the guideline

3.1 Epidemiology

a) The term psychosis is used to describe a major group of severe disorders of mental health characterised by the presence of delusions and hallucinations that disrupt a person's perception, thoughts, emotions and behaviour. The two main forms of this are schizophrenia and bipolar disorder. Substance misuse is a broad term encompassing the use of any psychotropic medication or substance, whether illicit or not, or taken for pleasure or not, if the use is considered hazardous or harmful. It includes, for example, alcohol, and prescribed medications used for purposes other than those prescribed. Such use is usually, but not always, regarded as a problem if there is evidence of dependence, characterised by psychological reinforcement of repeated drug-taking behaviour and, in some cases, a withdrawal syndrome.

b) In the UK, the annual prevalence for probable psychotic disorder among adults living in private households is about 5 per 1000.This figure is 9 per 1000 in adults aged 30–44 years and 18 per 1000 in adults with an African-Caribbean family background. Among those diagnosed with a psychotic disorder, studies show that prevalence for any substance misuse ranges from 24–36% (7–20% for alcohol misuse only, 5–9% for drug misuse only, 8% for drug and alcohol misuse). In one study of people with a psychotic disorder, 35% of the sample had a lifetime history of any illicit drug use. Prevalence rates for substance misuse are even higher in forensic (50–70%) and inpatient (30–49%)

mental health services. In addition, patients with comorbid drug misuse spend twice as long in hospital, on average, and have higher levels of unmet needs, compared with other inpatients with psychosis.

c) Substance misuse among individuals with psychiatric disorders is associated with significantly poorer outcomes than for individuals with a single disorder. These outcomes include worsening psychiatric symptoms, poorer physical health, increased use of institutional services, poor medication adherence, homelessness and increased risk of HIV infection, as well as poor social outcomes including impact on carers and family and contact with the criminal justice system.

d) There is a substantial link between substance misuse and crime. Hence the provision in the Crime and Disorder Act 1998 for drug treatment and testing orders and in the Criminal Justice and Court Services Act 2000 drug abstinence orders and drug abstinence requirements.

e) Compared to people with psychosis only, people with psychosis and substance misuse have greater levels of inpatient mental health service use, higher overall treatment costs, and lower concordance with community care and medication.

3.2 Current practice

a) The National Service Framework for Mental Health, published in 1999, sets out how services will be planned, delivered and monitored. Several areas are relevant to this guideline including mental health promotion, primary care and specialist services. The following are also relevant:

- The Care Programme Approach (CPA). This is a framework for interagency working. It seeks to ensure that clients have a proper assessment and that services are coordinated in line with client need.

- Assertive outreach and crisis resolution services. These are proactive approaches to engaging with clients and managing problems.

b) Less than a fifth of people who have co-existing psychosis and substance misuse receive substance misuse interventions, and there is clearly uneven distribution of services with regard to ethnicity. In substance misuse services those with a severe mental illness and co-existing substance misuse are generally white; assertive outreach teams have a much higher proportion of clients classified as African-Caribbean than all other teams.

c) There are no uniformly agreed screening or assessment tools.

d) The following three treatment models have been described in the literature, but there is currently little guidance about which is the most effective or cost effective:

- Serial treatment – one treatment, either psychiatric or substance misuse is followed by the other
- Parallel treatment – the concurrent but separate treatment of both the psychiatric disorder and the substance misuse disorder
- Integrated treatment – substance misuse and psychiatric treatment are provided concurrently by the same personnel.

4 The guideline

The guideline development process is described in detail on the NICE website (see section 6, 'Further information').

This scope defines what the guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered

a) Adults and young people (14 and older) who have a clinical working diagnosis of schizophrenia[16], bipolar or other affective psychosis, in conjunction with substance misuse.

b) This will include specific consideration of the needs of people with coexisting learning difficulties or significant physical or sensory difficulties, and the needs of people from black and minority ethnic groups.

4.1.2 Groups that will not be covered

a) People with very late onset psychosis (onset after age 60) and coexisting substance misuse.

4.2 Healthcare setting

[16] This includes schizoaffective disorder and delusional disorder.

a) Care that is received from healthcare professionals in primary and secondary care, including standard inpatient and forensic settings, who have direct contact with, and make decisions concerning, the care of people with severe mental illness and substance misuse.

b) Whilst the guideline will not provide specific recommendations for accident and emergency departments, paramedic services, prison medical services, the police and those who work in the criminal justice and education sectors, the guideline will be relevant to their work. The evidence considered in this guideline will not be derived from these settings.

4.3 Clinical management

4.3.1 Key clinical issues that will be covered

a) Identification and assessment.

b) Sequencing of treatment, and integrated versus non-integrated models of care.

c) The use of antipsychotic medication and/or psychological or psychosocial interventions (for example, family intervention) for the treatment of people with co-existing psychosis, and substance misuse.

d) Psychosocial interventions for the management of substance misuse (for example, cognitive behavioural therapy [CBT], motivational interviewing and contingency management) in people with coexisting psychosis.

e) Pharmacological (for example, opioid antagonists) and physical interventions for the management of substance misuse in people with coexisting psychosis.

f) Residential rehabilitation and inpatient mental health care of people with coexisting psychosis and substance misuse (including in a forensic setting).

g) Working with non-NHS services (for example, the police and those who work in the criminal justice and education sectors).

h) Ways to improve access to mental health services for people from black and minority ethnic communities (this will include issues concerned with engagement with services).

i) Interactions between prescribed medication and substances misused.

j) Ways to improve insight (that is, an individual's awareness of mental disorder and substance misuse, awareness of the social consequences of disorder/substance misuse, awareness of the need for treatment, awareness of symptoms and attribution of symptoms to disorder/substance misuse).

k) Ways to improve and manage non-adherence to treatment. This guideline will cross refer to the NICE clinical guideline on medicines adherence where appropriate.

l) Note that guideline recommendations for pharmacological interventions will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use a drug's summary of product characteristics to support joint clinical decision-making between service users and prescribers.

4.3.2 Clinical issues that will not be covered

a) Primary prevention.

b) Diagnosis.

c) Management of violence in people with severe mental illness.

4.4 Economic aspects

Developers will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative interventions. A review of the economic evidence will be conducted and analyses will be carried out as appropriate. The preferred unit of effectiveness is the quality-adjusted life year (QALY), and the costs considered will usually only be from an NHS and personal social services (PSS) perspective. Further detail on the methods can be found in 'The guidelines manual' (see 'Further information').

4.5 Status

4.5.1 Scope

This is the final scope.

4.5.2 Timing

The development of the guideline recommendations will begin in May 2009.

5 *Related NICE guidance*

5.1 Published guidance

- Schizophrenia. NICE clinical guideline 82 (2009). Available from www.nice.org.uk/CG82
- Medicines adherence. NICE clinical guideline 76 (2009). Available from www.nice.org.uk/CG76
- Drug misuse: opioid detoxification. NICE clinical guideline 52 (2007). Available from www.nice.org.uk/CG52
- Drug misuse: psychosocial interventions. NICE clinical guideline 51 (2007). Available from www.nice.org.uk/CG51
- Interventions to reduce substance misuse among vulnerable young people. NICE public health guidance 4 (2007). Available from www.nice.org.uk/PH4
- Naltrexone for the management of opioid dependence. NICE technology appraisal guidance 115 (2007). Available from www.nice.org.uk/TA115
- Methadone and buprenorphine for managing opioid dependence. NICE technology appraisal guidance 114 (2007). Available from www.nice.org.uk/TA114
- Bipolar disorder. NICE clinical guideline 38 (2006). Available from www.nice.org.uk/CG38
- Violence. NICE clinical guideline 25 (2005). Available from www.nice.org.uk/CG25
- Schizophrenia. NICE clinical guideline 1 (2002). Available from www.nice.org.uk/CG1

5.2 Guidance under development

- NICE is currently developing the following related guidance (details available from the NICE website).
- Alcohol use disorders (prevention). NICE public health guidance. Publication expected March 2010.
- Alcohol use disorders (clinical management). NICE clinical guideline. Publication expected May 2010.

- Alcohol dependence and harmful alcohol use. NICE clinical guideline. Publication expected January 2011.

6 Further information

Information on the guideline development process is provided in:

- 'How NICE clinical guidelines are developed: an overview for stakeholders' the public and the NHS'
- 'The guidelines manual'.

These are available from the NICE website (www.nice.org.uk/guidelinesmanual). Information on the progress of the guideline will also be available from the NICE website (www.nice.org.uk).

APPENDIX 2: DECLARATIONS OF INTERESTS BY GDG MEMBERS

With a range of practical experience relevant to the treatment and management of psychosis in conjunction with substance misuse in the GDG, members were appointed because of their understanding and expertise in healthcare for people with psychosis and substance misuse and support for their families/carers, including: scientific issues; health research; the delivery and receipt of healthcare, along with the work of the healthcare industry; and the role of professional organisations and organisations for people with psychosis and substance misuse and their families/carers.

To minimise and manage any potential conflicts of interest, and to avoid any public concern that commercial or other financial interests have affected the work of the GDG and influenced guidance, members of the GDG must declare as a matter of public record any interests held by themselves or their families which fall under specified categories (see below). These categories include any relationships they have with the healthcare industries, professional organisations and organisations for people with psychosis and substance misuse and their families/carers.

Individuals invited to join the GDG were asked to declare their interests before being appointed. To allow the management of any potential conflicts of interest that might arise during the development of the guideline, GDG members were also asked to declare their interests at each GDG meeting throughout the guideline development process. The interests of all the members of the GDG are listed below, including interests declared prior to appointment and during the guideline development process.

Categories of interest

Paid employment

Personal pecuniary interest: financial payments or other benefits from either the manufacturer or the owner of the product or service under consideration in this guideline, or the industry or sector from which the product or service comes. This includes holding a directorship, or other paid position; carrying out consultancy or fee paid work; having shareholdings or other beneficial interests; receiving expenses and hospitality over and above what would be reasonably expected to attend meetings and conferences.

Personal family interest: financial payments or other benefits from the healthcare industry that were received by a member of your family.

Non-personal pecuniary interest: financial payments or other benefits received by the GDG member's organisation or department, but where the GDG member has not personally received payment, including fellowships and other support provided by the healthcare industry. This includes a grant or fellowship or other payment to sponsor a post, or contribute to the running costs of the department; commissioning of research or other work; contracts with, or grants from, NICE.

Personal non-pecuniary interest: these include, but are not limited to, clear opinions or public statements you have made about individuals with psychosis and substance misuse problems, holding office in a professional organisation or advocacy group with a direct interest in psychosis and substance misuse, other reputational risks relevant to psychosis and substance misuse.

Guideline Development Group - Declarations of interest	
Professor Peter Tyrer - Chair, Guideline Development Group	
Employment	Professor of Community Psychiatry Department of Psychological Medicine, Imperial College
Personal pecuniary interest	The originator of the treatment called nidotherapy which may be used in the population considered in this guideline, and conducted a study looking at Nidotherapy.
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	Published books and articles on Nidotherapy
Non-personal non-pecuniary interest	A contingency management study is being conducted within my department.
Action Taken	Nidotherapy was discussed by the GDG on 2 March 2010. It was decided that it was not appropriate for the Chair to be present and Peter Tyrer left the room for this discussion. All members were asked individually if they felt this approach was acceptable and all agreed.
Professor Mohammed T. Abou-Saleh	
Employment	Professor of Psychiatry, St George's, University of London and Honorary Consultant in Addiction Psychiatry, South West London and St George's Mental Health NHS Trust, London
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Non-personal non-pecuniary interest	Asked to chair a presentation at an event sponsored by a pharmaceutical company, although he did not receive any money for this.
Action Taken	None

Professor Christine Barrowclough	
Employment	Prof of Clinical Psychology, University of Manchester
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	Currently Chief Investigator for two major studies evaluating psychological therapy for people with psychosis with substance misuse.
Action Taken	None
Ms. Tina Braithwaite	
Employment	Service User/Carer Representative. Director of Service User Involvement, Revolving Doors Agency. Also I'm a Member of the lived experience advisory panel, REFOCUS Recovery Research Project.
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action Taken	None
Dr Andy Cotgrove	
Employment	Young people (CAMHS level 4), Pine Lodge Young People's Centre
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action Taken	None
Dr. Mike Crawford	
Employment	Reader in Mental Health Services Research, Imperial College London / CNWL Mental Health NHS Trust
Personal pecuniary interest	Involved in a study on Nidotherapy.
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action Taken	Nidotherapy was discussed by the GDG on 2 March 2010. It was decided that Mike Crawford could be present to answer any queries, but not be involved in the discussion. All members were asked individually if they felt this approach was acceptable and all agreed.
Professor Ilana Crome	
Employment	Professor of Addiction Psychiatry, Keele University November 2009 – ongoing Honorary Consultant Addiction Psychiatrist, South Staffordshire and Shropshire Foundation Trust. Prior to November 2009 – Honorary Consultant Addiction Psychiatrist, North Staffordshire Combined Healthcare NHS Trust.
Personal pecuniary interest	None

Personal family interest	None
Non-personal pecuniary interest	The Academic Psychiatry Unit, Keele University receives funding from pharmaceutical companies which covers speakers' expenses for regular departmental seminar series. Keele University has received funding from DH, Home Office, SCIE (Social Care Institute for Excellence, for research on drug misuse and mental illness. Policy roles for DH, Scottish Executive and Welsh Assembly
Personal non-pecuniary interest	Member, Advisory Council on the Misuse of Drugs. Specific roles in Cannabis and Schizophrenia research which informed recommendation on Cannabis re-classification; Pathways to Problems report. ACMD, Chair Working Group on Treatment Effectiveness Member, Faculty of Academic Psychiatry, Royal College of Psychiatrists Member, Young People's Working Group, Royal College of Psychiatrists Honorary Secretary, Professors of Psychiatry Club Chair, WG Older people and substance misuse, Royal College of Psychiatrists Member, British Association of Psychopharmacology, Consensus group on Addiction and Comorbidity Trustee, Society for the Study of Addiction Chair, Steering Committee Assertive Community Treatment of Alcohol Dependence Trial, MRC funded trial led by Institute of Psychiatry Member, Young people and drugs and alcohol study DIPEx Research Group (Youthtalk) Member, Young people and depression study DIPEx Research Group (Youthtalk) Consultant, PaRticipation of the ElDerly In Clinical Trials(PREDICT) 2007-2009 European Union Project developed and recently launched a charter for evaluation of medicines in older people. Steering Group Advisory Panel, National Undergraduate Substance Misuse Curriculum Implementation Group Advisor, Turning Point Editorial responsibilities for several journals eg

	International editor, American Journal of Addiction Editor, Drugs Education Prevention and Policy International Advisory Board: British Journal of Psychiatry. British Journal of Psychiatry, Addiction, Journal of Mental Illness and Substance, Misuse, J of Psychopharmacology Member, International Society of Addiction Journal Editors
Action Taken	None
Mr. Mike Firn	
Employment	Clinical Service Development Lead
Personal pecuniary interest	Non-guideline specific interest: specifically I am Chair of a mutual trading organisation (National Forum for Assertive Outreach) that has educational grants from Janssen-Cilag pharmaceuticals covering venue and catering costs of 2 regional network events in Manchester within the last year. There has been no product information or talks given at either of these events beyond acknowledgement of the room and catering costs.
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action Taken	None
Dr. Frank Holloway	
Employment	Consultant Psychiatrist and Clinical Director, Bethlem Royal Hospital
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action Taken	None
Dr. Cheryl Kipping	
Employment	Nurse Consultant, South London And Maudsley NHS Foundation Trust
Personal pecuniary interest	Member of independent review team into SUIs in a PCT area.
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	• Member of PROGRESS (dual diagnosis nurse consultant group). Co-ordinated group's response to consultation on scope of PSM guideline. • Member of DH steering group that developed DH (2002) Mental Health Policy Implementation Guide: Dual Diagnosis Good Practice Guide • Co-editor of Advances in Dual Diagnosis journal • Provide specialist dual diagnosis advice to National Mental Health Development Unit (NMHDU) dual diagnosis and acute programmes. Involved in

	development of dual diagnosis elearning packages for NMHDU Dual Diagnosis programme and National Acute Project Board.
Action Taken	None
Dr. Kate McKinnell	
Employment	Senior Medical Officer (Addictions) Sefton Integrated Recovery Team (CRI)
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action Taken	None
Dr. Jonathan Mitchell	
Employment	Consultant Psychiatrist – Early Intervention, East Glade Centre
Personal pecuniary interest	In 2006 I chaired an educational meeting sponsored by Eli Lilly for which I received a payment of £250. In 2007 I chaired an educational meeting sponsored by Jansen for which I was offered, but did not accept payment. I have no current or ongoing personal pecuniary interests.
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action Taken	None
Dr. David Ndegwa	
Employment	Consultant Forensic Psychiatrist / Clinical Director South London & Maudsley NHS Foundation Trust
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action Taken	None
Mr. Peter Pratt	
Employment	Chief Pharmacist, Sheffield Health & Social Care Trust And Rotherham Doncaster & South Humber NHS Trust
Personal pecuniary interest	Gave a presentation regarding payment by results in mental health at an event sponsored by Janssen-Cilag. Executive member of NAPICU committee (National Association of Psychiatric Intensive Care Units) Received payment for market research about schizophrenia.
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action Taken	None

Ms Theresa Renwick	
Employment	Social care lead for mental health, Royal Borough of Kensington and Chelsea
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action Taken	None
Mr. Leroy Simpson	
Employment	Service User/Carer Representative. Board Member, Salvation Army Housing Association.
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action Taken	None
Mrs. Penelope Wigram	
Employment	Service User/Carer Representative
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action Taken	None
Dr. Tim Kendall	
Employment	Director, NCCMH Medical Director, Sheffield Health and Social Care Trust Consultant Adult Psychiatrist
Personal pecuniary interest	Grant holder for £1.44 million per year (approx) from NICE for guidelines work. Work with NICE International. Undertake some research into mental health, and the mental health workforce for DH, Royal College of Psychiatrists and the academy of medical royal colleges.
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action Taken	None
Dr. Craig Whitttington	
Employment	Senior Systematic Reviewer, NCCMH
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	Conducted a sub-analysis on the nidotherapy study for publication and subsequent use by GDG
Mr. Matthew Dyer	
Employment	Health Economist, NCCMH

Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action Taken	None
Ms. Sarah Stockton	
Employment	Senior Information Scientist, NCCMH
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action Taken	None
Ms. Laura Shields	
Employment	Research Assistant, NCCMH
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action Taken	None
Ms. Katherine Leggett	
Employment	Guideline Development Manager
Personal pecuniary interest	None
Personal family interest	None
Non-personal pecuniary interest	None
Personal non-pecuniary interest	None
Action Taken	None

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APPENDIX 3: EXPERT REVIEWERS TO THE GUIDELINE DEVELOPMENT GROUP

Dr Michelle Cleary, Research Unit, Rozelle Hospital, Sydney South West Area Health Service

APPENDIX 4: STAKEHOLDERS AND EXPERTS WHO SUBMITTED COMMENTS IN RESPONSE TO THE CONSULTATION DRAFT OF THE GUIDELINE

Stakeholders
Experts

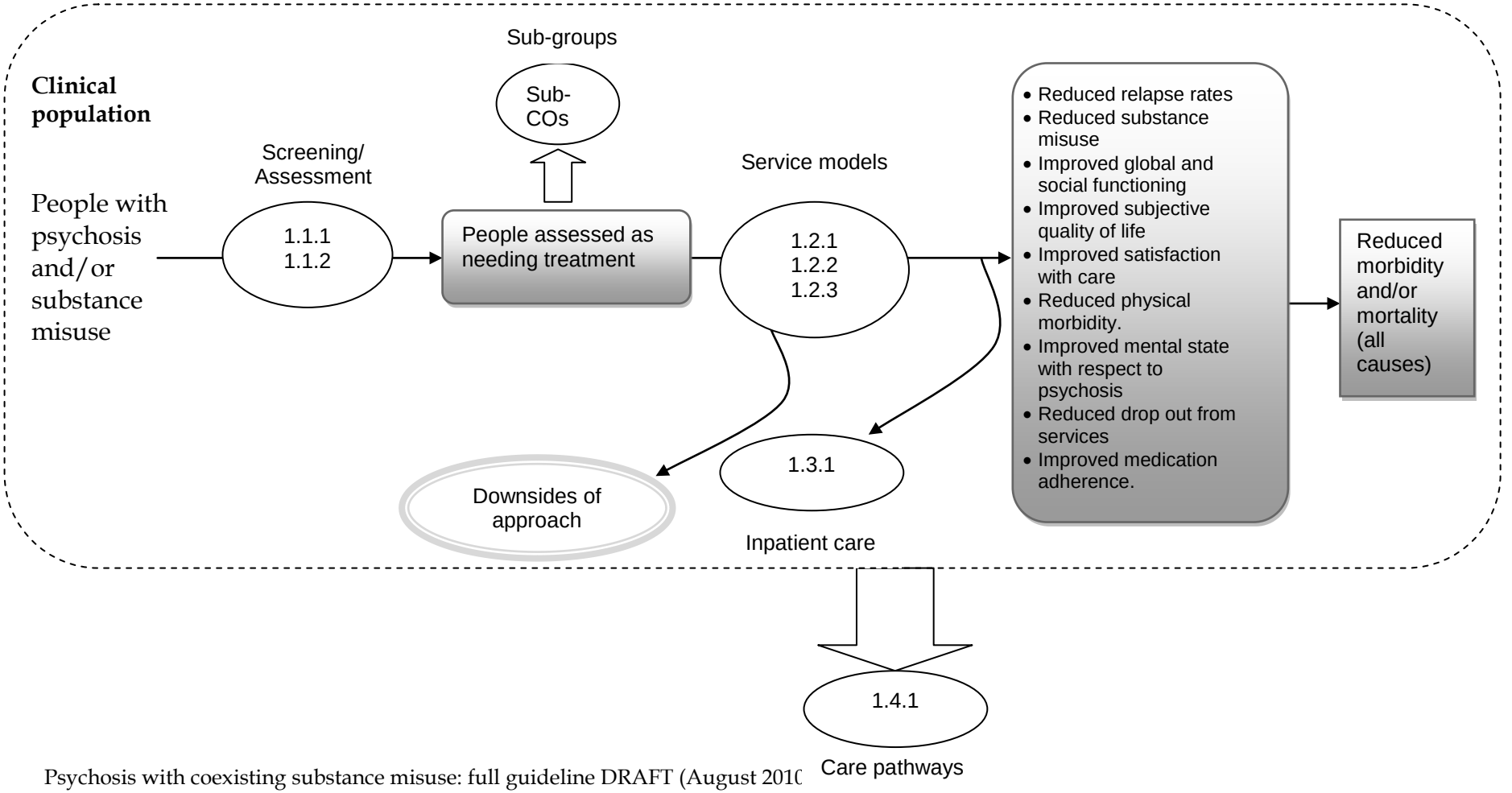
APPENDIX 5: RESEARCHERS CONTACTED TO REQUEST FURTHER INFORMATION ABOUT PUBLISHED OR UNPUBLISHED EVIDENCE

Dr. Alan Bellack, University of Maryland School of Medicine

Dr Maloney,

APPENDIX 6: ANALYTIC FRAMEWORK AND CLINICAL QUESTIONS

Assessment/service models/ inpatient care/care pathways



Assessment

No.	Primary clinical questions
1.1.1	In people with psychosis and coexisting substance misuse, what are the key elements for a comprehensive assessment (of needs and risks)? Sub-question 1: should the assessment be the same in primary and secondary care? Sub-question 2: should the assessment be modified for sub-groups of people (e.g., young people, women, people from BME groups, homeless people, offenders, type of psychosis, type of substance misuse)? Sub-question 3: what factors should trigger a reassessment?

Service models

No.	Primary clinical questions
1.2.1	In people with psychosis and coexisting substance misuse, does an integrated service model (usually involving the model of assertive community treatment) when compared with an alternative management strategy lead to: Critical outcomes: • Reduced mortality (all causes) • Reduced relapse rates (measured by exacerbation of symptoms requiring change in health care management) • Reduced substance misuse (however measured) • Improved global and social functioning (e.g. employment, accommodation) • Improved subjective quality of life • Improved satisfaction with care • Reduced physical morbidity. ondary outcomes: • Insight • Improved medication adherence • Improved access to services (reduced drop out) • Reduced relapse rates (measured by admission to hospital; number of bed days)

	• Improved mental state with respect to psychosis (e.g. PANSS) • Reduced offending behavior. Sub-question 1: What are the elements in an integrated service model that are most likely to be associated with better outcomes? Sub-question 2: Are there any subgroups of people (e.g. adolescents, BME groups) that benefit from some elements of the service model more than others? Sub-question 3: Are there subgroups of people (e.g. based on severity of substance misuse and severity of psychosis; adolescents, BME groups) that may benefit from alternatives strategies (non-integrated service models – serial treatment, for example)
1.2.2	In people with psychosis and coexisting substance misuse, do the psychological/psychosocial interventions listed below (delivered within an integrated service model) when compared to an alternative management strategy lead to improved outcomes? (for outcomes see 1.2.1) • Individual interventions • Group interventions • Family intervention • Contingency management • Combined interventions
1.2.3	In people with psychosis and coexisting substance misuse, does staffed accommodation when compared to an alternative management strategy lead to improved outcomes? (for outcomes see 1.2.1)

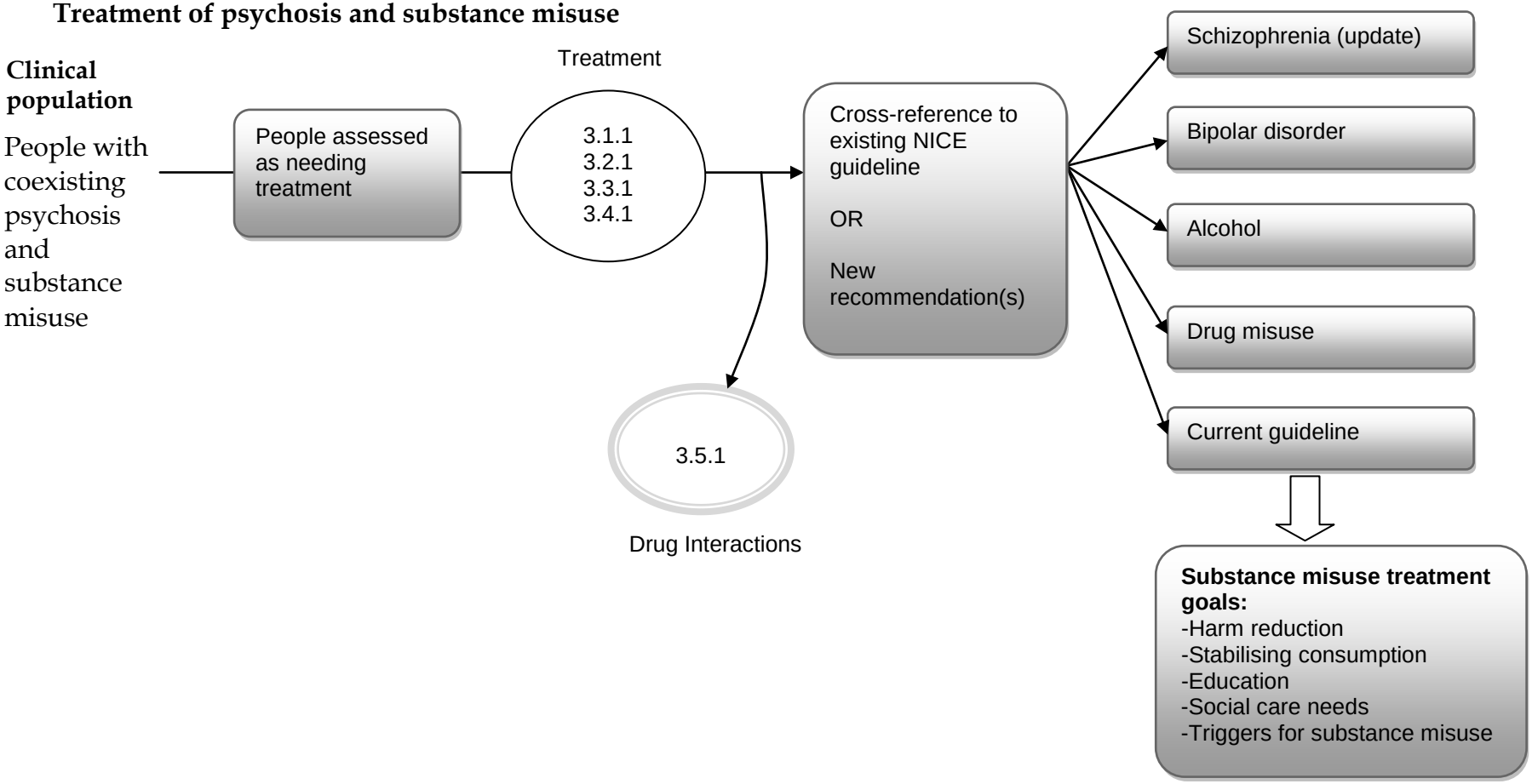
Inpatient care

No.	Primary clinical questions
1.3.1	When a person with psychosis and coexisting substance misuse is admitted to an inpatient mental health setting (including forensic settings), should treatment follow the same principles as interventions delivered in a community setting? Sub-question: Are there subgroups of people for whom we would alter our approach to treatment?

Care pathways

No.	Primary clinical questions
1.4.1	In people with psychosis and coexisting substance misuse, what is the most appropriate care pathway (involving all NHS and non-NHS providers) and referral guidance at each transition?

Treatment of psychosis and substance misuse



Medication for psychosis

No.	Primary clinical question
2.1.1	For people with psychosis and coexisting substance misuse, should the medical treatment of their psychosis be modified as a result of substance misuse and the treatment provided (e.g. methadone, buprenorphine etc)? A) During the acute phase B) During non-acute phase If so, how should treatment be modified? Sub-question 1: Are there sub-groups of people (e.g. adolescents, people with a particular type of psychosis, BME groups) that may benefit from alternative strategies?

Psychological/ psychosocial interventions for psychosis

No.	Primary clinical question
2.2.1	For people with psychosis and coexisting substance misuse, should the psychological/psychosocial (family interventions, CBT, arts therapies) treatment of their psychosis be modified as a result of the substance misuse problem and the treatment provided (e.g. methadone, Buprenorphine, psychological treatment etc)? A) During the acute phase B) During non-acute phase If so, how should treatment be modified? Sub-question 1: Are there sub-groups of people (e.g. adolescents, people with a particular type of psychosis, BME groups) that may benefit from alternative strategies?

Medication/physical interventions for substance misuse

No.	Primary clinical question
2.3.1	For people with psychosis and coexisting substance misuse, should the medical/physical treatment of substance misuse be modified as a result of the presence of psychosis and the treatment provided (e.g. antipsychotics, lithium)? A) During the acute phase B) During non-acute phase If so, how should treatment be modified? Sub-question 1: Are there sub-groups of people (e.g. adolescents, people with a particular type of psychosis, BME groups) that may benefit from alternative strategies?

Psychological/ psychosocial interventions for substance misuse

No.	Primary clinical question
2.4.1	For people with psychosis and coexisting substance misuse, should psychological/psychosocial treatment for substance misuse be modified as a result of the presence of psychosis and the treatment provided? A) During the acute phase B) During non-acute phase If so, how should treatment be modified? Sub-question 1: Are there sub-groups of people (e.g. adolescents, people with a particular type of psychosis, BME groups) that may benefit from alternative strategies? Sub-question 2: Should interventions be matched to stages of the treatment process (i.e. engagement, persuasion, active treatment, relapse prevention)?

Drug interactions

No.	Primary clinical question

2.5.1	In people with psychosis and substance misuse, is there any evidence that the management of drug interactions or adverse effects from pharmacological treatments should be different from those people without coexisting disorders? If so, how should management of drug interactions be modified?

APPENDIX 7: SEARCH STRATEGIES FOR THE IDENTIFICATION OF CLINICAL STUDIES

7.1 Search strategies

The search strategies should be referred to in conjunction with information set out in Section 3.5.2. Each search was constructed using the groups of terms as set out in Table 33. The full set of search terms is documented in sections 7.1.1 to 7.1.3. Each search was initially developed for Medline before being translated for use in other databases/interfaces.

Table 33: Summary of systematic search strategies

Search strategy construction
Psychological/psychosocial interventions Updates to Cleary *et al.* (2008) and Cleary *et al*. (2009). Searches were limited to updating the reviews, covering the time period since the searches for the published reviews were last conducted. *Search dates: 2008 onwards* i) (Psychosis with substance misuse terms) AND (RCT filter OR Observational study filter) Service delivery models [As above] Pharmacological/physical interventions Search results covering comprising all the above (psychological, service delivery and pharmacological) were merged into one dataset for the period from 2008 onwards to cut back on unnecessary duplication of effort at the sifting stage. *Search dates: inception of database onwards* i) (Psychosis with substance misuse terms) AND (pharmacological terms) Experience of care *Search dates: 1995 onwards* i) (Psychosis with substance misuse terms) AND (experience of care terms) AND (qualitative filter) ii) (Psychosis with substance misuse terms) AND (experience of care terms - modified to be more precise)

7.1.1 Population Search terms

MEDLINE – Ovid SP interface

** Search terms for substance misuse were limited to the main drugs associated with the term at the advice of the GDG.*

1. exp psychotic disorders/ or exp affective disorders, psychotic/
2. exp schizophrenia/or "schizophrenia and disorders with psychotic features"/or schizophrenic psychology/
3. ((mental disorders or mentally ill persons) and chronic disease).sh.
4. exp movement disorders/ or (dyskinesias or psychomotor agitation or neuroleptic malignant syndrome).sh.
5. (((acute or chronic$ or serious$ or sever$) adj3 (mental$ or psych$) adj3 (disease$ or disorder$ or disturbanc$ or ill$)) or smi$1).ti,ab.
6. (bipolar$ or ((cyclothymi$ or rapid or ultradian) adj5 cycl$) or rcbd or hebephreni$ or mania$ or manic$ or oligophreni$ or psychose$ or psychosi$ or psychotic$ or schizo$).ti,ab.
7. (((tardiv$ and dyskine$) or akathisi$ or acathisi$ or (neuroleptic$ and malignant and syndrome) or (neuroleptic and movement and disorder) or parkinsoni$ or neuroleptic-induc$) not (parkinson$ and disease)).ti,ab.
8. (emergency services, psychiatric or hospitals, psychiatric or psychiatric department, hospital or (mentally ill persons and (inpatients or hospitalization))).sh. or (psychiatric adj2 (admission$ or admitted or emerg$ or hospitali$ or inpatient$ or in patient$)).ti,ab.
9. or/1-8
10. comorbidity/ or "diagnosis, dual (psychiatry)"/
11. (comorbid$ or co morbid$ or ((dual$ or tripl$) adj2 (diagnos$ or disease$ or disorder$ or illness$ or mental or problem$ or psych$ or syndrome$)) or coexist$ or co exist$ or concur$ or con cur$ or cooccur$ or co occur$).ti,ab.
12. or/10-11
13. (designer drugs or needle exchange programs or needle sharing or overdose or street drugs or substance abuse detection or substance abuse, intravenous or substance abuse treatment centers or substance-related disorders or substance withdrawal syndrome).sh.
14. (((drug$1 or polydrug$ or psychotropic$ or substance$) adj3 (abstain$ or abstinen$ or abus$ or addict$ or excessive use$ or criminal or depend$ or habit$ or illegal$ or illicit$ or intoxicat$ or misus$ or nonprescri$ or non prescri$ or over dos$ or overdos$ or recreation$ or unlawful$ or withdraw$)) or ((drug$1 or polydrug$ or recreation$ or

substance$) adj use$1) or ((drug$1 or polydrug$ or substance$) adj rehab$) or abusable product$ or (crave$ adj2 inject$) or hard drug$ or needle fixation or soft drug$ or vsa$1).ti,ab.
15. ((club or designer or street) adj2 (drug$ or substance$)).ti,ab.
16. or/13-15
17. (amphetamine or amphetamine-related disorders).sh.
18. (dextroamphetamine or methamphetamine).sh.
19. (((amphetamin$ or crystal meth$ or desoxyn or dexamfetamin$ or dexedrine or dextroamphetamin$ or methamphetamin$ or psychostimulant$ or stimulant$ or uppers) adj5 (abstain$ or abstinen$ or abus$ or addict$ or banned or excessive use$ or criminal or depend$ or habit$ or illegal$ or illicit$ or intoxica$ or misus$ or nonprescri$ or non prescri$ or over dos$ or overdos$ or recreation$ or rehab$ or unlawful$ or using or utilis$ or utiliz$ or withdraw$)) or ((amphetamin$ or crystal meth$ or desoxyn or dexamfetamin$ or dexedrine or dextroamphetamin$ or methamphetamin$ or psychostimulant$ or stimulant$ or uppers) adj2 use$1)).ti,ab.
20. (amphetamin$ or crystal meth$ or desoxyn or dexamfetamin$ or dexedrine or dextroamphetamin$ or methamphetamin$ or psychostimulant$ or stimulant$ or uppers).ti,ab.
21. or/17-19
22. 20
23. exp cocaine/ or cocaine-related disorders.sh.
24. (((benzoylmethyl ecgonine or cocain$ or crack$1 or codrenine or ecgonine methyl ester benzoate or erythroxylin or locosthetic or neurocaine or sterilocaine) adj5 (abstain$ or abstinen$ or abus$ or addict$ or banned or excessive use$ or criminal or depend$ or habit$ or illegal$ or illicit$ or intoxica$ or misus$ or nonprescri$ or non prescri$ or over dos$ or overdos$ or recreation$ or rehab$ or unlawful$ or using or utilis$ or utiliz$ or withdraw$)) or ((benzoylmethyl ecgonine or cocain$ or crack$1 or codrenine or ecgonine methyl ester benzoate or erythroxylin or locosthetic or neurocaine or sterilocaine) adj2 use$1)).ti,ab.
25. (benzoylmethyl ecgonine or cocain$ or crack$1 or codrenine or ecgonine methyl ester benzoate or erythroxylin or locosthetic or neurocaine or sterilocaine).ti,ab.
26. or/23-24
27. 25
28. (heroin or heroin dependence or opioid-related disorders).sh.
29. (((heroin or diacetylmorphin$ or diagesil or diamorf or diamorphin$) adj5 (abstain$ or abstinen$ or abus$ or addict$ or banned or excessive use$ or criminal or depend$ or habit$ or illegal$ or illicit$ or intoxica$ or misus$ or nonprescri$ or non prescri$ or over dos$ or overdos$ or recreation$ or rehab$ or unlawful$ or using or utilis$ or utiliz$ or

withdraw$)) or ((diamorphin$ or acetomorphine or anpec or diacephine or diacetylmorphine$ or diagesil or diamorf or diaphorin or duromorph or epimorph or heroin or morfin$ or morphacetin or morphia or morphian$ or morphin$ or morphium or opso$1 or skenan) adj2 use$1)).ti,ab.

30. (heroin or diacetylmorphin$ or diagesil or diamorf or diamorphin$).ti,ab.
31. or/28-29
32. 30
33. (cannabis or marijuana abuse or marijuana smoking).sh.
34. (((bhang or cannador or cannabis or ganja or ganjah or hashish or hemp or marihuana or marijuana or sativex or skunk) adj5 (abstain$ or abstinen$ or abus$ or addict$ or banned or excessive use$ or criminal or depend$ or habit$ or illegal$ or illicit$ or intoxica$ or misus$ or nonprescri$ or non prescri$ or over dos$ or overdos$ or recreation$ or rehab$ or unlawful$ or using or utilis$ or utiliz$ or withdraw$)) or ((bhang or cannador or cannabis or ganja or ganjah or hashish or hemp or marihuana or marijuana or sativex or skunk) adj2 use$1)).ti,ab.
35. (bhang or cannador or cannabis or ganja or ganjah or hashish or hemp or marihuana or marijuana or sativex or skunk).ti,ab.
36. or/33-34
37. 35
38. 9 and 12 and (or/22,27,32,37)
39. 9 and (or/16,21,26,31,36)
40. or/38-39

7.1.2 Question specific search strategies

a) Psychological/psychosocial interventions

See Table 33 for information for the strategy used to identify psychological/psychosocial evidence.

b) Service delivery models

See Table 33for information for the strategy used to identify evidence for service delivery models.

c) Pharmacological/physical interventions

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1. exp antipsychotic agents/

2. (antipsychotic$ or anti psychotic$ or (major adj2 (butyrophenon$ or phenothiazin$ or tranquil$)) or neuroleptic$).ti,ab.
3. (amisulprid$1 or aminosultoprid$1 or amisulpirid$1 or sertol$1 or socian or solian).ti,ab.
4. (aripiprazol$1 or abilify or abilitat).ti,ab.
5. (benperidol$1 or anquil or benperidon$1 or benzoperidol$1 or benzperidol$1 or frenactil$1 or frenactyl or glianimon$1 or phenactil$1).ti,ab.
6. chlorpromazine.sh. or (chlorpromazin$1 or aminazin$1 or chlorazin$1 or chlordelazin$1 or contomin$1 or fenactil$1 or largactil$1 or propaphenin$1 or thorazin$1).ti,ab.
7. chlorprothixene.sh. or (chlorprothixen$1 or aminasin$1 or aminasin$1 or aminazin$1 or aminazin$1 or ampliactil$1 or amplictil$1 or ancholactil$1 or chlopromazin$1 or chlor pz or chlorbromasin$1 or chlordelazin$1 or chlorderazin$1 or chloropromazin$1 or chlorpromanyl or chlorpromazin$1 or chlorprotixen$1 or clordelazin$1 or clorpromazin$1 or cloxan or contomin$1 or elmarin$1 or fenactil$1 or hibanil$1 or hibernal$1 or hibernol$1 or klorpromex or largactil$1 or largactyl or megaphen$1 or neurazin$1 or novomazin$1 or phenathyl or plegomazin$1 or plegomazin$1 or proma or promacid$1 or promactil$1 or promapar or promazil$1 or propaphen$1 or propaphenin$1 or prozil or psychozin$1 or sanopron$1 or solidon$1 or sonazin$1 or taractan$1 or taroctil$1 or thor prom or thorazen$1 or thorazin$1 or torazin$1 or truxal or vegetamin a or vegetamin b or wintamin$1 or wintermin$1 or zuledin$1).ti,ab.
8. clozapine.sh. or (clozapin$1 or alemoxan$1 or azaleptin$1 or clopine or clozaril$1 or denzapin$1 or dorval or dozapin$1 or fazaclo or froidir or klozapol or lapenax or leponex or wander compound or zaponex).ti,ab.
9. flupenthixol.sh. or (flupentixol$1 or flupenthixol$1 or depixol$1 or emergil$1 or fluanxol$1 or flupentixol$1 or emergil$1 or fluanxol$1 or piperazineethanol$1 or viscoleo).ti,ab.
10. fluphenazine.sh. or (anatensil or anatensol or antasol or dapotum or elinol or flufenazin$ or flumezin or fluorfenazine or fluphenacin or fluphenazin or fluphenazin$ or fluphenzine or ftorphenazine or luogen depot or lyogen or lyorodin or moditen or moditin or omca or pacinol or permitil or phthorphenazine or prolixan 300 or prolixene or prolixin$ or sevinal or sevinol or siqualine or siqualon$ or siquoline or tensofin or trancin or valamina or vespazin$).ti,ab.
11. fluspirilene.sh. or (fluspirilen$1 or fluspi or imap or kivat or redeptin$1 or spirodiflamin$1).ti,ab.
12. haloperidol.sh. or (haloperidol$1 or aloperidin$1 or bioperidolo or brotopon or celenase or cerenace or dozic or duraperidol or einalon s or eukystol or fortunan$1 or haldol or halidol or haloneural$1 or

haloperitol$1 or halosten or keselan or linton or peluces or serenace or serenase or siegoperidol$1 or sigaperidol$1).ti,ab.

13. methotrimeprazine.sh. or (levomepromazin$1 or 2 methoxytrimeprazin$1 or hirnamin$1 or levo promazin$1 or levomeprazin$1 or levopromazin$1 or levoprom$1 or mepromazin$1 or methotrimeprazin$1 or methotrimperazin$1 or milezin$1 or minozinan$1 or neozin$1 or neuractil$1 or neurocil$1 or nirvan or nosinan$1 or nozinan$1 or sinogan or tisercin$1 or tizercin$1 or tizertsin$1 or veractil$1).ti,ab.
14. (olanzapin$1 or lanzac or midax or olansek or olzapin or rexapin or zalasta or zolafren or zydis or zypadhera or zyprex$1).ti,ab.
15. (paliperidon$1 or 9 hydroxyrisperidon$1 or invega).ti,ab.
16. paroxetine.sh. or (paroxetin$1 or aropax or deroxat or motivan or paxil$1 or pexeva or seroxat or tagonis).ti,ab.
17. (pericyazin$1 or aolept or neulactil$1 or neuleptil$1 or periciazin$1 or properciazin$1 or propericiazin$1).ti,ab.
18. perphenazine.sh. or (perphenazin$1 or chlorperphenazin$1 or chlorpiprazin$1 or chlorpiprozin$1 or decentan$1 or etaperazin$1 or ethaperazin$1 or etrafon or fentazin$1 or perfenazin$1 or perfenazin$1 or perferazin$1 or perphenan$1 or perphenezin$1 or thilatazin$1 or tranquisan$1 or triavail or trifalon$1 or trilafan$1 or trilafon$1 or trilifan$1 or triliphan$1).ti,ab.
19. pimozide.sh. or (pimozid$1 or antalon$1 or opiran$1 or orap or pimocid$1 or pimorid$1 or pinozid$1).ti,ab.
20. prochlorperazine.sh. or (prochlorperazin$1 or buccastem or capazin$1 or chlormeprazin$1 or chlorpeazin$1 or chlorperazin$1 or compazin$1 or dicopal$1 or emelent or kronocin$1 or meterazin$1 or metherazin$1 or nipodal$1 or phenotil or prochlor perazin$1 or prochlorpemazin$1 or prochlorperacin$1 or prochlorperzin$1 or prochlorpromazin$1 or proclorperazin$1 or stemetil or stemzine or tementil$1 or temetil$1).ti,ab.
21. promazine.sh. or (promazin$1 or alofen$1 or alophen$1 or ampazin$1 or amprazim$1 or centractyl or delazin$1 or esparin$1 or lete or liranol$1 or neo hibernex or neuroplegil$1 or piarin$1 or prazin$1 or pro tan or promantin$1 or promanyl$1 or promilen$1 or promwill or protactil$1 or protactyl$1 or romthiazin$1 or romtiazin$1 or sediston$1 or sinophenin$1 or sparin$1 or tomil or varophen$1 or verophen$1).ti,ab.
22. (quetiapin$1 or ketipinor or quepin or seroquel or tienapin$1).ti,ab.
23. risperidone.sh. or (risperidon$1 or belivon$1 or ridal or riscalin or risolept or rispen or risperdal$1 or sizodon).ti,ab.
24. (sertindol$1 or indole or serdolect or serlect).ti,ab.
25. sulpiride.sh. or (sulpirid$1 or abilit or aiglonyl$1 or arminol$1 or bosnyl or deponerton$1 or desisulpid$1 or digton or dobren or

dogmatil$1 or dogmatyl or dolmatil$1 or eglonyl or ekilid or equilid or guastil$1 or isnamid$1 or leboprid$1 or levopraid or levosulpirid$1 or meresa or miradol$1 or modal or neogama or pontirid$1 or psicocen$1 or sulfirid$1 or sulp$1 or sulperid$1 or sulpitil$1 or sulpivert or sulpor or sulpyride or synedil$1 or tepavil$1 or vertigo meresa or vertigo neogama or vipral).ti,ab.

26. trifluoperazine.sh. or (trifluoperazin$1 or apotrifluoperazine$1 or calmazin$1 or dihydrochlorid$1 or eskazin$1 or eskazin$1 or eskazinyl or fluoperazin$1 or flupazin$1 or jatroneural$1 or modalina or stelazin$1 or terfluzin$1 or terfluzin$1 or trifluoperazid$1 or trifluoperazin$1 or trifluoperzin$1 or trifluoroperazin$1 or trifluorperacin$1 or trifluperazin$1 or triflurin$1 or triftazin$1 or triftazinum or triphtazin$1 or triphthasin$1 or triphthazin$1).ti,ab.
27. (zotepin$1 or lodopin$1 or losizopilon or nipolept or setous or zoleptil).ti,ab.
28. clopenthixol.sh. or (zuclopenthixol$1 or acuphase or clopenthixol$1 or clopixol or cisordinol$1 or sedanxol$1).ti,ab.
29. or/1-28
30. exp serotonin uptake inhibitors/
31. (ssri$ or ((serotonin or 5 ht or 5 hydroxytryptamine) adj (uptake or reuptake or re uptake) adj inhibit$)).ti,ab.
32. citalopram.sh. or (celexa or cipramil$1 or cytalopram or elopram or escitalopram or lexapro or nitalapram or sepram or seropram).ti,ab.
33. (escitalopram or cipralex or lexapro or seroplex).ti,ab.
34. fluoxetine.sh. or (fluoxetin$1 or fluctin$1 or flunirin$1 or fluoxifar or prosac or prozac or prozamin$1 or sarafem or symbyax).ti,ab.
35. fluvoxamine.sh. or (fluvoxamin$1 or depromel$1 or desiflu or dumirox or faverin$1 or fevarin$1 or floxyfral$1 or fluoxamin$1 or fluroxamin$1 or fluvoxadura or luvox).ti,ab.
36. (nefazadon$1 or dutonin$1 or nefadar or reseril$1 or serzon$1).ti,ab.
37. paroxetine.sh. or (paroxetin$1 or aropax or deroxat or motivan$1 or paxil or pexeva or seroxat or tagonis).ti,ab.
38. sertraline.sh. or (sertralin$1 or altrulin$1 or aremis or besitran$1 or gladem or lustral$1 or naphthylamin$1 or sealdin$1 or serad or serlain$1 or tresleen or zoloft).ti,ab.
39. or/30-38
40. benzodiazepines.sh.
41. (benzo$1 or benzodiazepin$).ti,ab.
42. diazepam.sh. or (diazepam or alupram or ansiolin$1 or antenex or apaurin$1 or apaurin$1 or apozepam or assival$1 or audium$1 or bialzepam or bialzepan$1 or calmpos$1 or cercin$1 or cersin$1 or chlordiazepam or dialar or diastat or diazelium or diazemuls or diazidem or ducen$1 or duxen$1 or eridan or eurosan$1 or evacalm$1 or fanstan$1 or faustan$1 or gewacalm$1 or lamra or lembrol$1 or

lipodiazepam or lorinon$1 or methyldiazepinon$1 or methyldiazepinon$1 or morosan$1 or neocalm$1 or neurolytril$1 or noan or novazam or paceum or plidan or psychopax or relanium or rimapam or sedapam or seduxen$1 or serendin$1 or setonil$1 or sibazon$1 or sonacon$1 or stesolid$1 or stesolin$1 or tanquo tablinen$1 or tensium or tranimul$1 or tranquo puren or umbrium$1 or valaxon$1 or valclair or valiquid$1 or valium or valpam or valreleas$1 or vatran$1 or vival$1 or vivol4 or zetran$1).ti,ab.

43. lorazepam.sh. or (lorazepam or almazin$1 or alzapam or apolorazepam or ativan or bonatranquan$1 or donix or duralozam or durazolam or idalprem or kendol$1 or laubeel or lorabenz or loranas$1 or loranaz$1 or lorans or lorax or lorazep von ct or loridem$1 or lorivan$1 or mesmerin$1 or novo lorazem$1 or novolorazem$1 or novo lorazem$1 or nu loraz or nuloraz or orfidal or orifadal$1 or pro dorm or quait or securit or sedicepan$1 or sinestron$1 or somagerol$1 or tavor or temesta or tolid or wypax).ti,ab.
44. narcotic antagonists.sh.
45. ((narcotic$ or opiate$ or opioid$) adj antagonist$).ti,ab.
46. naltrexone.sh. or (antaxone or celupan or depade or nalorex or naltrel or naltrexone$ or nemexin or opizone or revia or trexan or vivitrex or vivitrol).ti,ab.
47. (arthene or cervene or cessalor incystene or nalmefene or nalmetrene or revex or soberal).ti,ab.
48. or/40-47
49. (analgesics, opioid or opiate agonist or partial agonist).sh.
50. ((narcotic$ or opiate$ or opioid$ or partial$) adj2 (agonist$ or analg?esi$)).ti,ab.
51. exp methadone/ or (adanon or algidon or algolysin or algoxale or althose or amidon or amidone or amidosan or anadon or biodone or butalgin or deamin or depridol or diaminon or dianone or dolafin or dolamid or dolesone or dolophine or dorex or dorexol or fenadon or heptadon or heptanon or ketalgin or linctus or mecodin or mepecton or mephenon or metadol or metasedin or methaddict or methadon or methadone or methadose or methex or miadone or moheptan or phenadon or phenadone or phymet or physepton or physeptone or physeptone or pinadone or polamidon or polamivet or polamivit or sinalgin or symoron).ti,ab.
52. buprenorphine.sh. or (buprenex or buprenorphin$ or buprex or finibron or lepetan or prefin or suboxone or subutex or temgesic or transtec).ti,ab.
53. or/49-52
54. adrenergic alpha-agonists.sh.
55. ((adrenergic alpha or alpha adrenergic) adj2 agonist$).ti,ab.
56. (lofexidin$ or britlofex or lofetensin or loxacor).ti,ab.

57. clonidine.sh. or (arkamin$1 or caprysin$1 or catapres or catapresan$1 or catapressan or catapressant or catasan$1 or chlofazolin$1 or chlophazolin$1 or chlophelin$1 or clinidin$1 or clofelin$1 or clofelin$1 or clofenil$1 or clomidin$1 or clondin$1 or clonidin$1 or clonistada or clonnirit or clophelin$1 or clopheline or dcai or dichlorophenylaminoimidazoline or dixarit or duraclon or gemiton or haemiton or hemiton or isoglaucon or klofelin or klofenil or normopresan or paracefan or tenso timelets).ti,ab.
58. or/54-57
59. disulfiram.sh. or (abstensil$1 or abstinyl or alcophobin$1 or antabus or antabuse or antadix or antaethan$1 or antaethyl or antiaethan$1 or anticol$1 or antietanol$1 or aversan or contralin$1 or contrapot or cronetal$1 or dicupral or disulfid$1 or disulfiram or disulfizam or disulphiram or espenal or esperal or etabus or ethyl thiurad or exhorran or hoca or stopethyl or stopetyl or teraetil or tetra ethyl thiuramdisulfide or tetradin$1 or tetraethylthiuram or tetraetil$1 or teturam or teturamin or thiuram or thiuranide or tiuram or ttd).ti,ab.
60. (acamprosate or aotal or calcium acetylhomotaurinate or campral or n acetylhomotaurine calcium).ti,ab.
61. chlormethiazole.sh. or (chlomethiazol$ or chlorethiazol$ or chlormethiazol$ or clomethiazol$ or distraneurin or distraneurin$ or hemineurin$1 or heminevrin$1 or hemithiamin$ or zendra).ti,ab.
62. chlordiazepoxide.sh. or (a poxide or ansiacal or benzodiapin$1 or cebrum or chlordiazepoxid$ or chlordiazepoxyd$1 or chlorodiazepoxid$1 or chlozepid$1 or clopoxid$1 or contol or decacil$1 or defobin$1 or disarim or dizepin$1 or dopoxid$1 or droxol$1 or eden psich or elenium or elenum or equibral or kalmocaps or labican or librelease or libritabs or librium or lipoxide or mesural or metaminodiazepoxide or methaminodiazepoxide or mildmen or mitran or multum or murcil or napoton$1 or novosed or o c m or ocm 505 or psichial or psicosan or psicoterina or radepur or reliberan or reposans 10 or risolid or seren vita or servium or silibrin or sk lygen or sonimen or timosin or tropium or viansin or viopsicol).ti,ab.
63. or/59-62
64. anticonvulsants.sh.
65. (anticonvuls$ or anti convuls$ or antiepilep$ or anti epilep$).ti,ab.
66. (epitomax or topamax or topamax or sprinkle or topamax or topimax or topirimate or topiramate).ti,ab.
67. valproic acid.sh. or (2 propylpentanoate or 2 propylpentanoic acidor 2 propylvalerate sodium or 2 propylvaleric acid or alpha propylvalerate or alpha propylvaleric acid or apilepsin$1 or convulex or convulsofin$1 or depacon$1 or depaken$1 or depakin$1 or depakot$1 or deprakin$1 or di n propylacetate or di n propylacetate sodium or di n propylacetic acid or dipropyl acetic acid or dipropylacetate or

dipropylacetatic acid or dipropylacetic acid or diprosin$1 or divalproex or epilim or ergenyl or everiden$1 or goilim or labazen$1 or leptilan$1 or leptilanil or mylproin or myproic acid or n dipropylacetic acid or orfiril or orlept or propymal or sodium 2 propylpentanoate or sodium 2 propylvalerate or sodium di n propyl acetate or sodium di n propylacetate or sodium dipropyl acetate or sodium dipropylacetate or sodium n dipropylacetate or stavzor or valerin$1 or valparin$1 or valpro or valproate or valproic acid or vupral$1).ti,ab.

68. carbamazepine.sh. or (amizepin$1 or atretol$1 or biston or calepsin$1 or carbagen$1 or carbama or carbamaze or carbamazepin$1 or carbategral or carbatrol or convuline or degranol or epimaz or epimax or epitol or equetro or finlepsin$1 or hermolepsin$1 or lexin or mazepin$1 or neurotol or neurotop or servimazepin$1 or sirtal or stazepin$1 or tegral or tegretal or tegretol or tegrital or telesmin$1 or teril or timonil or trimonil).ti,ab.
69. or/64-68
70. neuromuscular agents.sh.
71. ((neuromuscular or skeletal muscle) adj (agent$ or drug$ or relaxant$)).ti,ab.
72. baclofen.sh. or (apobaclofen$1 or atrofen$1 or baclofen$ or baclofeneirex or baclofene-irex or baclophen or baclospas or beta 4 chlorophenyl 4 aminobutanoic acid or beta amino methyl chlorohydrocinnamic acid or beta aminomethyl para chlorohydrocinnamic acid or beta para chlorophenyl gamma aminobutyric acid or chlorophenyl gaba or clofen or genbaclofen or genpharm or kemstro or lioresal or intralcal or lebic or lioresal or lioresal or lioresyl or lyflex or nu baclo or nubaclo or pcp-gaba or pmsbaclofen).ti,ab.
73. or/70-72
74. lithium$.sh. or (lithium or camcolit or candamid$1 or carbolith or carbolitium or cibalith s or contemnol$1 or dilithium or eskalith or hypnorex or li salt or limas or linthane or liskonium or liskonum or litarex or lithane or lithiofor or lithionit or lithiophor or lithobid or lithocarb or lithonate or lithotabs or maniprex or mesin or micalith or neurolepsin or neurolithium or plenur or priadel or quilinormretard or quilonorm or quilonum or teralithe or theralite or theralithe).ti,ab.
75. or/1-74

d) Experience of care

Due to the difficulties of identifying qualitative research with precision from bibliographic databases, search request #15 was generated without the use of a qualitative filter.

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1. (consumer participation or consumer satisfaction or health behavior or hospital patient relations or medication adherence or nurse patient relations or patient acceptance of health care or patient advocacy or patient compliance or patient participation or patient preference or physician patient relations or professional patient relations or public opinion or treatment refusal).sh.
2. (attitude or attitude to health or knowledge, attitudes, practice or patient satisfaction).sh.
3. ((((acute or chronic$ or serious$ or sever$) adj3 (mental$ or psych$) adj3 (disease$ or disorder$ or disturbanc$ or ill$)) or smi$1 or bipolar$ or ((cyclothymi$ or rapid or ultradian) adj5 cycl$) or rcbd or hebephreni$ or mania$ or manic$ or oligophreni$ or psychose$ or psychosi$ or psychotic$ or schizo$ or (tardiv$ and dyskine$) or akathisi$ or acathisi$ or (neuroleptic$ and malignant and syndrome) or (neuroleptic and movement and disorder) or parkinsoni$ or neuroleptic-induc$ or (psychiatric adj2 (admission or admitted or emerg$ or hospitali$ or inpatient$ or in patient$)) or ((mental$ or psych$) adj (disease$ or disorder$ or illness$)) or comorbid$ or co morbid$ or ((dual$ or tripl$) adj2 (diagnos$ or disease$ or disorder$ or illness$ or mental or problem$ or psych$ or syndrome$)) or coexist$ or co exist$ or concur$ or con cur$ or cooccur$ or co occur$ or ((drug$1 or polydrug$ or substance$) adj3 (abstain$ or abstinen$ or abus$ or addict$ or excessive use$ or criminal or depend$ or habit$ or illegal$ or illicit$ or intoxicat$ or misus$ or nonprescri$ or non prescri$ or over dos$ or overdos$ or recreation$ or unlawful$ or withdraw$)) or ((drug$1 or polydrug$ or recreation$ or substance$) adj use$1) or ((drug$1 or polydrug$ or substance$) adj rehab$) or abusable product$ or (crave$ adj2 inject$) or hard drug$ or needle fixation or soft drug$ or vsa$1 or ((club or designer or street) adj2 (drug$ or substance$)) or amphetamin$ or crystal meth$ or desoxyn or dexamfetamin$ or dexedrine or dextroamphetamin$ or methamphetamin$ or psychostimulant$ or stimulant$ or uppers or benzoylmethyl ecgonine or cocain$ or crack$1 or codrenine or ecgonine methyl ester benzoate or erythroxylin or locosthetic or neurocaine or sterilocaine or diacetylmorphin$ or diamorphin$ or diagesil or diamorf or heroin or acetomorphine or anpec or diacephine or diacetylmorphine$ or diagesil or diamorf or diaphorin or duromorph or epimorph or heroin or morfin$ or morphacetin or morphia or morphian$ or morphin$ or

morphium or opso$1 or skenan or bhang or cannador or cannabis or ganja or ganjah or hashish or hemp or marihuana or marijuana or sativex or skunk or polydrug$) adj8 (acceptance or account$1 or adher$ or aspiration$ or attitude$ or aversion$ or awareness or barrier$ or belief$ or centredness or choice$ or cognitions or complianc$ or conception$1 or concern$1 or confus$ or content$ or diary or diaries or demand$ or disatisf$ or disclos$ or discontent$ or disgruntle$ or engaging or engage$1 or experienc$ or feeling or happy or help$ or incentive$ or involv$ or knowledge or literacy or narrat$ or need or needs or nonadher$ or obstacle$ or opinion$ or participa$ or perception$ or perceived or perspective$ or position$ or prefer or preferred or preference$ or persistence or refus$ or satisf$ or scepticism or selfobservat$ or self observat$ or (service$ adj2 use$) or stigma$ or story or stories or support$ or tolerance or understand$ or unhappy or utili?ation or view$ or willing$ or voice$) adj8 (adult$1 or attender$ or client$ or consumer$ or individuals or inpatient$ or men or minorities or outpatient$ or participant$ or patient$ or people or population or public or subjects or survivor$ or women or user$ or care giver$ or caregiver$ or carer$ or (care adj (manager$ or worker$)) or family or families)).ti,ab.

4. ((((acute or chronic$ or serious$ or sever$) adj3 (mental$ or psych$) adj3 (disease$ or disorder$ or disturbanc$ or ill$)) or smi$1 or bipolar$ or ((cyclothymi$ or rapid or ultradian) adj5 cycl$) or rcbd or hebephreni$ or mania$ or manic$ or oligophreni$ or psychose$ or psychosi$ or psychotic$ or schizo$ or (tardiv$ and dyskine$) or akathisi$ or acathisi$ or (neuroleptic$ and malignant and syndrome) or (neuroleptic and movement and disorder) or parkinsoni$ or neuroleptic-induc$ or (psychiatric adj2 (admission or admitted or emerg$ or hospitali$ or inpatient$ or in patient$)) or ((mental$ or psych$) adj (disease$ or disorder$ or illness$)) or comorbid$ or co morbid$ or ((dual$ or tripl$) adj2 (diagnos$ or disease$ or disorder$ or illness$ or mental or problem$ or psych$ or syndrome$)) or coexist$ or co exist$ or concur$ or con cur$ or cooccur$ or co occur$ or ((drug$1 or polydrug$ or substance$) adj3 (abstain$ or abstinen$ or abus$ or addict$ or excessive use$ or criminal or depend$ or habit$ or illegal$ or illicit$ or intoxicat$ or misus$ or nonprescri$ or non prescri$ or over dos$ or overdos$ or recreation$ or unlawful$ or withdraw$)) or ((drug$1 or polydrug$ or recreation$ or substance$) adj use$1) or ((drug$1 or polydrug$ or substance$) adj rehab$) or abusable product$ or (crave$ adj2 inject$) or hard drug$ or needle fixation or soft drug$ or vsa$1 or ((club or designer or street) adj2 (drug$ or substance$)) or amphetamin$ or crystal meth$ or desoxyn or dexamfetamin$ or dexedrine or dextroamphetamin$ or methamphetamin$ or psychostimulant$ or stimulant$ or uppers or benzoylmethyl ecgonine

or cocain$ or crack$1 or codrenine or ecgonine methyl ester benzoate or erythroxylin or locosthetic or neurocaine or sterilocaine or diacetylmorphin$ or diamorphin$ or diagesil or diamorf or heroin or acetomorphine or anpec or diacephine or diacetylmorphine$ or diagesil or diamorf or diaphorin or duromorph or epimorph or heroin or morfin$ or morphacetin or morphia or morphian$ or morphin$ or morphium or opso$1 or skenan or bhang or cannador or cannabis or ganja or ganjah or hashish or hemp or marihuana or marijuana or sativex or skunk or polydrug$) and (acceptance or account$1 or adher$ or aspiration$ or attitude$ or aversion$ or awareness or barrier$ or belief$ or centredness or choice$ or cognitions or complianc$ or conception$1 or concern$1 or confus$ or content$ or diary or diaries or demand$ or disatisf$ or disclos$ or discontent$ or disgruntle$ or engaging or engage$1 or experienc$ or feeling or happy or help$ or incentive$ or involv$ or literacy or narrat$ or knowledge or need or needs or nonadher$ or obstacle$ or opinion$ or participa$ or perception$ or perceived or perspective$ or position$ or prefer or preferred or preference$ or persistence or refus$ or satisf$ or scepticism or selfobservat$ or self observat$ or (service$ adj2 use$) or stigma$ or story or stories or support$ or tolerance or understand$ or unhappy or utili?ation or view$ or willing$ or voice$) and (adult$1 or attender$ or client$ or consumer$ or individuals or inpatient$ or men or minorities or outpatient$ or participant$ or patient$ or people or population or public or subjects or survivor$ or women or user$ or care giver$ or caregiver$ or carer$ or (care adj (manager$ or worker$)) or family or families)).ti.

5. (((mental$ or psych$ or psychiatric) adj2 (disease$ or disorder$ or distress or health or ill or problem$)) and (acceptance or account$1 or adher$ or aspiration$ or attitude$ or aversion$ or awareness or barrier$ or belief$ or centredness or choice$ or cognitions or complianc$ or conception$1 or concern$1 or confus$ or content$ or diary or diaries or demand$ or disatisf$ or disclos$ or discontent$ or disgruntle$ or engaging or engage$1 or experienc$ or feeling or happy or help$ or incentive$ or involv$ or knowledge or literacy or narrat$ or need or needs or nonadher$ or obstacle$ or opinion$ or participa$ or perception$ or perceived or perspective$ or position$ or prefer or preferred or preference$ or persistence or refus$ or satisf$ or scepticism or selfobservat$ or self observat$ or (service$ adj2 use$) or stigma$ or story or stories or support$ or tolerance or understand$ or unhappy or utili?ation or view$ or willing$ or voice$) and (adult$1 or attender$ or client$ or consumer$ or individuals or inpatient$ or men or minorities or outpatient$ or participant$ or patient$ or people or population or public or subjects or survivor$ or women or user$ or care giver$ or

caregiver$ or carer$ or (care adj (manager$ or worker$)) or family or families)).ti.

6. (((mental$ or psych$ or psychiatric) adj2 (disease$ or disorder$ or distress or health or ill or problem$)) and (acceptance or account$1 or adher$ or aspiration$ or attitude$ or aversion$ or awareness or barrier$ or belief$ or centredness or choice$ or cognitions or complianc$ or conception$1 or concern$1 or confus$ or content$ or diary or diaries or demand$ or disatisf$ or disclos$ or discontent$ or disgruntle$ or engaging or engage$1 or experienc$ or feeling or happy or help$ or incentive$ or involv$ or knowledge or literacy or narrat$ or need or needs or nonadher$ or obstacle$ or opinion$ or participa$ or perception$ or perceived or perspective$ or position$ or prefer or preferred or preference$ or persistence or refus$ or satisf$ or scepticism or selfobservat$ or self observat$ or (service$ adj2 use$) or stigma$ or story or stories or support$ or tolerance or understand$ or unhappy or utili?ation or view$ or willing$ or voice$) and (care or healthcare or health care or medication or service$ or therap$ or treatment$)).ti.
7. ((acceptance or account$1 or adher$ or aspiration$ or attitude$ or aversion$ or awareness or barrier$ or belief$ or centredness or choice$ or cognitions or complianc$ or conception$1 or concern$1 or confus$ or content$ or diary or diaries or demand$ or disatisf$ or disclos$ or discontent$ or disgruntle$ or engaging or engage$1 or experienc$ or feeling or happy or help$ or incentive$ or involv$ or knowledge or literacy or narrat$ or need or needs or nonadher$ or obstacle$ or opinion$ or participa$ or perception$ or perceived or perspective$ or position$ or prefer or preferred or preference$ or persistence or refus$ or satisf$ or scepticism or selfobservat$ or self observat$ or (service$ adj2 use$) or stigma$ or story or stories or support$ or tolerance or understand$ or unhappy or utili?ation or view$ or willing$ or voice$) adj3 (adult$1 or attender$ or client$ or consumer$ or individuals or inpatient$ or men or minorities or outpatient$ or participant$ or patient$ or people or population or public or subjects or survivor$ or women or user$ or care giver$ or caregiver$ or carer$ or (care adj (manager$ or worker$)) or family or families)).ti.
8. ((acceptance or account$1 or adher$ or aspiration$ or attitude$ or aversion$ or barrier$ or belief$ or centredness or communicat$ or complianc$ or conception$ or concern$1 or content$ or demand$ or disatisf$ or disclos$ or discontent$ or disgruntle$ or experience$1 or engaging or engage$1 or happy or help$ or idea$1 or incentive$ or interview$ or involv$ or knowledge or literacy or narrat$ or need or needs or nonadher$ or obstacle$ or opinion$ or participa$ or perception$ or perceived or perspective$ or position$ or preference$ or refus$ or research or satisf$ or scepticism or service$ use$ or stigma or story or stories or understand$ or unhappy or utili?ation or view$ or

willing$ or voice$) adj2 (client$ or consumer$ or inpatient$ or minorities or outpatient$ or patient$ or people or public or survivor$ or user$)).ti,ab.

9. ((acceptance or account$1 or adher$ or aspiration$ or attitude$ or aversion$ or awareness or barrier$ or belief$ or centredness or choice$ or cognitions or complianc$ or conception$1 or concern$1 or confus$ or content$ or diary or diaries or demand$ or disatisf$ or disclos$ or discontent$ or disgruntle$ or engaging or engage$1 or experienc$ or feeling or happy or help$ or incentive$ or involv$ or knowledge or literacy or narrat$ or need or needs or nonadher$ or obstacle$ or opinion$ or participa$ or perception$ or perceived or perspective$ or position$ or prefer or preferred or preference$ or persistence or refus$ or satisf$ or scepticism or selfobservat$ or self observat$ or (service$ adj2 use$) or stigma$ or story or stories or support$ or tolerance or understand$ or unhappy or utili?ation or view$ or willing$ or voice$) adj4 (((acute or chronic$ or serious$ or sever$) adj3 (mental$ or psych$) adj3 (disease$ or disorder$ or disturbanc$ or ill$)) or smi$1 or bipolar$ or ((cyclothymi$ or rapid or ultradian) adj5 cycl$) or rcbd or hebephreni$ or mania$ or manic$ or oligophreni$ or psychose$ or psychosi$ or psychotic$ or schizo$ or (tardiv$ and dyskine$) or akathisi$ or acathisi$ or (neuroleptic$ and malignant and syndrome) or (neuroleptic and movement and disorder) or parkinsoni$ or neuroleptic-induc$ or (psychiatric adj2 (admission or admitted or emerg$ or hospitali$ or inpatient$ or in patient$)) or ((mental$ or psych$) adj (disease$ or disorder$ or illness$)) or comorbid$ or co morbid$ or ((dual$ or tripl$) adj2 (diagnos$ or disease$ or disorder$ or illness$ or mental or problem$ or psych$ or syndrome$)) or coexist$ or co exist$ or concur$ or con cur$ or cooccur$ or co occur$ or ((drug$1 or polydrug$ or substance$) adj3 (abstain$ or abstinen$ or abus$ or addict$ or excessive use$ or criminal or depend$ or habit$ or illegal$ or illicit$ or intoxicat$ or misus$ or nonprescri$ or non prescri$ or over dos$ or overdos$ or recreation$ or unlawful$ or withdraw$)) or ((drug$1 or polydrug$ or recreation$ or substance$) adj use$1) or ((drug$1 or polydrug$ or substance$) adj rehab$) or abusable product$ or (crave$ adj2 inject$) or hard drug$ or needle fixation or soft drug$ or vsa$1 or ((club or designer or street) adj2 (drug$ or substance$)) or amphetamin$ or crystal meth$ or desoxyn or dexamfetamin$ or dexedrine or dextroamphetamin$ or methamphetamin$ or psychostimulant$ or stimulant$ or uppers or benzoylmethyl ecgonine or cocain$ or crack$1 or codrenine or ecgonine methyl ester benzoate or erythroxylin or locosthetic or neurocaine or sterilocaine or diacetylmorphin$ or diamorphin$ or diagesil or diamorf or heroin or acetomorphine or anpec or diacephine or diacetylmorphine$ or diagesil or diamorf or diaphorin or duromorph or epimorph or heroin

or morfin$ or morphacetin or morphia or morphian$ or morphin$ or morphium or opso$1 or skenan or bhang or cannador or cannabis or ganja or ganjah or hashish or hemp or marihuana or marijuana or sativex or skunk or polydrug$)).ti.

10. ((((acute or chronic$ or serious$ or sever$) adj3 (mental$ or psych$) adj3 (disease$ or disorder$ or disturbanc$ or ill$)) or smi$1 or bipolar$ or ((cyclothymi$ or rapid or ultradian) adj5 cycl$) or rcbd or hebephreni$ or mania$ or manic$ or oligophreni$ or psychose$ or psychosi$ or psychotic$ or schizo$ or (tardiv$ and dyskine$) or akathisi$ or acathisi$ or (neuroleptic$ and malignant and syndrome) or (neuroleptic and movement and disorder) or parkinsoni$ or neuroleptic-induc$ or (psychiatric adj2 (admission or admitted or emerg$ or hospitali$ or inpatient$ or in patient$)) or ((mental$ or psych$) adj (disease$ or disorder$ or illness$)) or comorbid$ or co morbid$ or ((dual$ or tripl$) adj2 (diagnos$ or disease$ or disorder$ or illness$ or mental or problem$ or psych$ or syndrome$)) or coexist$ or co exist$ or concur$ or con cur$ or cooccur$ or co occur$ or ((drug$1 or polydrug$ or substance$) adj3 (abstain$ or abstinen$ or abus$ or addict$ or excessive use$ or criminal or depend$ or habit$ or illegal$ or illicit$ or intoxicat$ or misus$ or nonprescri$ or non prescri$ or over dos$ or overdos$ or recreation$ or unlawful$ or withdraw$)) or ((drug$1 or polydrug$ or recreation$ or substance$) adj use$1) or ((drug$1 or polydrug$ or substance$) adj rehab$) or abusable product$ or (crave$ adj2 inject$) or hard drug$ or needle fixation or soft drug$ or vsa$1 or ((club or designer or street) adj2 (drug$ or substance$)) or amphetamin$ or crystal meth$ or desoxyn or dexamfetamin$ or dexedrine or dextroamphetamin$ or methamphetamin$ or psychostimulant$ or stimulant$ or uppers or benzoylmethyl ecgonine or cocain$ or crack$1 or codrenine or ecgonine methyl ester benzoate or erythroxylin or locosthetic or neurocaine or sterilocaine or diacetylmorphin$ or diamorphin$ or diagesil or diamorf or heroin or acetomorphine or anpec or diacephine or diacetylmorphine$ or diagesil or diamorf or diaphorin or duromorph or epimorph or heroin or morfin$ or morphacetin or morphia or morphian$ or morphin$ or morphium or opso$1 or skenan or bhang or cannador or cannabis or ganja or ganjah or hashish or hemp or marihuana or marijuana or sativex or skunk or polydrug$) and (acceptance or account$1 or adher$ or aspiration$ or attitude$ or aversion$ or awareness or barrier$ or belief$ or centredness or choice$ or cognitions or complianc$ or conception$1 or concern$1 or confus$ or content$ or diary or diaries or demand$ or disatisf$ or disclos$ or discontent$ or disgruntle$ or engaging or engage$1 or experienc$ or feeling or happy or help$ or incentive$ or involv$ or knowledge or literacy or narrat$ or need or needs or nonadher$ or obstacle$ or opinion$ or participa$ or

perception$ or perceived or perspective$ or position$ or prefer or preferred or preference$ or persistence or refus$ or satisf$ or scepticism or selfobservat$ or self observat$ or (service$ adj2 use$) or stigma$ or story or stories or support$ or tolerance or understand$ or unhappy or utili?ation or view$ or willing$ or voice$) and (care or healthcare or health care or medication or service$ or therap$ or treatment$)).ti.

11. ((acceptance or account$1 or adher$ or aspiration$ or attitude$ or aversion$ or awareness or barrier$ or belief$ or centredness or choice$ or cognitions or complianc$ or conception$1 or concern$1 or confus$ or content$ or diary or diaries or demand$ or disatisf$ or disclos$ or discontent$ or disgruntle$ or engaging or engage$1 or experienc$ or feeling or happy or help$ or incentive$ or involv$ or knowledge or literacy or narrat$ or need or needs or nonadher$ or obstacle$ or opinion$ or participa$ or perception$ or perceived or perspective$ or position$ or prefer or preferred or preference$ or persistence or refus$ or satisf$ or scepticism or selfobservat$ or self observat$ or (service$ adj2 use$) or stigma$ or story or stories or support$ or tolerance or understand$ or unhappy or utili?ation or view$ or willing$ or voice$) adj4 (care or healthcare or medication$ or psychotherapy$ or service$ or therap$ or treatment$ or ((perceived or perception$ or unmet$) adj need$))) .ti,ab.
12. caregivers/or exp disabled persons/or mentally ill persons/ or inpatients/or outpatients/or survivors/or (consumer$ or patient$).hw.
13. (adult$1 or attender$ or client$ or consumer$ or individuals or inpatient$ or men or minorities or outpatient$ or participant$ or patient$ or people or public or subjects or survivor$ or women or user$ or care giver$ or caregiver$ or carer$ or (care adj (manager$ or worker$)) or family or families).ti,ab. or (population or sample).ti.
14. or/12-13
15. or/2,4,5,7 or (or/6,9,10 and 14)
16. or/1,3,8 or (11 and 14)

7.1.3 Search filters

a) Randomised controlled trial search filter – this is an adaptation of a filter designed by the Health Information Research Unit of the McMaster University, Ontario.

MEDLINE – Ovid SP interface

1. exp clinical trial/ or cross over studies/ or double blind method/ or random allocation/ or randomized controlled trials as topic/ or single blind method/
2. (clinical adj2 trial$).ti,ab.

3. (crossover or cross over).ti,ab.
4. (((single$ or doubl$ or trebl$ or tripl$) adj5 blind$) or mask$ or dummy or doubleblind$ or singleblind$ or trebleblind$ or tripleblind$).ti,ab.
5. (placebo$ or random$).mp.
6. (clinical trial$ or controlled clinical trial$ or random$).pt.
7. animals/ not (humans/or human$.ti,ab.)
8. (or/1-6) not 7

b) Observational studies filter – developed in-house

MEDLINE – Ovid SP interface

1. exp case control studies/ or exp cohort studies/ or cross sectional studies/ or epidemiologic study characteristic as topic/ or epidemiologic studies/
2. case reports.pt.
3. ((cross sectional or epidemiologic$ or observational) adj (study or studies)).ti,ab.
4. (case control$ or cohort$1 or cross sectional or followup$ or follow up$ or followed or longitudinal or prospective$ or retrospective$).ti,ab.
5. or/1-4

c) Qualitative filter – this is an adaptation of filters designed by the Health Information Research Unit of McMaster University, Ontario, and the University of Alberta.

MEDLINE – Ovid SP interface

1. qualitative research/
2. interview/ or personal narratives/ or exp interviews as topic/ or interview, psychological/
3. narration/
4. exp tape recording/ or videodisc recording/
5. sampling studies/ or cluster analysis/
6. anthropology, cultural/
7. nursing methodology research/
8. observation/
9. (qualitative or ethno$ or emic or etic or heuristic or semiotics or phenomenolog$).ti,ab.
10. interview$.ti,ab.
11. (((audio or tape or video$) adj5 record$) or audiorecord$ or taperecord$ or videorecord$ or videotap$).ti,ab.

12. (story or stories or storytell$ or story tell$).ti,ab.
13. testimon$.ti,ab.
14. ((focus adj4 (group$ or sampl$)) or narrat$ or ((life or lived) adj experience$)).ti,ab.
15. ((participant$ or nonparticipant$) adj3 observ$).ti,ab.
16. (constant adj (comparative or comparison)).ti,ab.
17. (content analy$ or (field adj (note$ or record$ or stud$ or research)) or fieldnote$).ti,ab.
18. (data adj1 saturat$).ti,ab.
19. discourse analys?s.ti,ab.
20. (grounded adj (theor$ or study or studies or research)).ti,ab.
21. (hermeneutic$ or heidegger$ or husserl$ or colaizzi$ or giorgi$ or glaser or spiegelberg$ or strauss).ti,ab.
22. (maximum variation or snowball).ti,ab.
23. (cross case analys$ or metaethno$ or meta ethno$ or metanarrative$ or meta narrative$ or metasynthes$ or meta synthes$ or metasummar$ or meta summar$ or metastud$ or meta stud$ or qualitative synthes$ or qualitative overview or metaoverview or meta overview).ti,ab.
24. purpos$ sampl$.ti,ab.
25. ((structured or unstructured) adj1 categor$).ti,ab.
26. ((thematic$ adj3 analys$) or themes).ti,ab.
27. (theoretical sampl$ or ricoeur or spiegelberg$ or merleau).ti,ab.
28. (van kaam$ or van manen or constant compar$).ti,ab.
29. action research.ti,ab.
30. human science.ti,ab.
31. (critical social$ or ethical enquiry or (pilot testing and survey) or shadowing or ((philosophical or social) adj research$)).ti,ab.
32. or/1-31

APPENDIX 8: QUALITY CHECKLISTS FOR CLINICAL STUDIES AND REVIEWS

The methodological quality of each study was evaluated using NICE checklists (NICE, 2009). The checklists for systematic reviews and for RCTs are reproduced below (for other checklists and further information about how to complete each checklist, see *The Guidelines Manual* [NICE, 2009]).

Methodology checklist: systematic reviews and meta-analyses

Study identification *Include author, title, reference, year of publication*			
Guideline topic:	Review question no:		
Checklist completed by:			
SCREENING QUESTIONS			
In a well-conducted, relevant systematic review:	*Circle one option for each question*		
The review addresses an appropriate and clearly focused question that is relevant to the guideline review question	Yes	No	Unclear
The review collects the type of studies you consider relevant to the guideline review question	Yes	No	Unclear
The literature search is sufficiently rigorous to identify all the relevant studies	Yes	No	Unclear
Study quality is assessed and reported	Yes	No	Unclear
An adequate description of the methodology used is included, and the methods used are appropriate to the question	Yes	No	Unclear

Methodology checklist: randomised controlled trials

Study identification Include author, title, reference, year of publication		
Guideline topic:		Review question no:
Checklist completed by:		
		Circle one option for each question
A. Selection bias (systematic differences between the comparison groups)		
A1	An appropriate method of randomisation was used to allocate participants to treatment groups (which would have balanced any confounding factors equally across groups)	Yes No Unclear N/A
A2	There was adequate concealment of allocation (such that investigators, clinicians and participants cannot influence enrolment or treatment allocation)	Yes No Unclear N/A
A3	The groups were comparable at baseline, including all major confounding and prognostic factors	Yes No Unclear N/A
Based on your answers to the above, in your opinion was selection bias present? If so, what is the likely direction of its effect?		
Low risk of bias Unclear/unknown risk High risk of bias		
Likely direction of effect:		
B. Performance bias (systematic differences between groups in the care provided, apart from the intervention under investigation)		
B1	The comparison groups received the same care apart from the intervention(s) studied	Yes No Unclear N/A
B2	Participants receiving care were kept 'blind' to treatment allocation	Yes No Unclear N/A
B3	Individuals administering care were kept 'blind' to treatment allocation	Yes No Unclear N/A
Based on your answers to the above, in your opinion was performance bias present? If so, what is the likely direction of its effect?		
Low risk of bias Unclear/unknown risk High risk of bias		

Likely direction of effect:		
C. Attrition bias (systematic differences between the comparison groups with respect to loss of participants)		
C1	All groups were followed up for an equal length of time (or analysis was adjusted to allow for differences in length of follow-up)	Yes No Unclear N/A
C2	a. How many participants did not complete treatment in each group?	
	b. The groups were comparable for treatment completion (that is, there were no important or systematic differences between groups in terms of those who did not complete treatment)	Yes No Unclear N/A
C3	a. For how many participants in each group were no outcome data available?	
	b. The groups were comparable with respect to the availability of outcome data (that is, there were no important or systematic differences between groups in terms of those for whom outcome data were not available).	Yes No Unclear N/A
Based on your answers to the above, in your opinion was attrition bias present? If so, what is the likely direction of its effect?		
Low risk of bias	Unclear/unknown risk	High risk of bias
Likely direction of effect:		
D. Detection bias (bias in how outcomes are ascertained, diagnosed or verified)		
D1	The study had an appropriate length of follow-up	Yes No Unclear N/A
D2	The study used a precise definition of outcome	Yes No Unclear N/A
D3	A valid and reliable method was used to determine the outcome	Yes No Unclear N/A
D4	Investigators were kept 'blind' to participants' exposure to the intervention	Yes No Unclear N/A
D5	Investigators were kept 'blind' to other important confounding and prognostic factors	Yes No Unclear N/A
Based on your answers to the above, in your opinion was detection bias present? If so, what is the likely direction of its effect?		

Low risk of bias	Unclear/unknown risk	High risk of bias
Likely direction of effect:		

APPENDIX 9: SEARCH STRATEGIES FOR THE IDENTIFICATION OF HEALTH ECONOMICS EVIDENCE

10.1 Search strategies

The search strategies should be referred to in conjunction with information set out in Section 3.6.1.

For standard mainstream bibliographic databases (CINAHL, EMBASE, MEDLINE and PsycINFO) search terms for psychosis with substance abuse were combined with a search filter for health economic studies. For searches generated in topic-specific databases (HTA, NHS EED) search terms on psychosis with substance abuse were used without a filter. The search strategies were initially developed for Medline before being translated for use in other databases/interfaces.

10.1.1 Population Search terms

MEDLINE – Ovid SP interface

** Search terms for substance misuse were limited to the main drugs associated with the term at the advice of the GDG.*

1. exp psychotic disorders/ or exp affective disorders, psychotic/
2. exp schizophrenia/or "schizophrenia and disorders with psychotic features"/or schizophrenic psychology/
3. ((mental disorders or mentally ill persons) and chronic disease).sh.
4. exp movement disorders/ or (dyskinesias or psychomotor agitation or neuroleptic malignant syndrome).sh.
5. (((acute or chronic$ or serious$ or sever$) adj3 (mental$ or psych$) adj3 (disease$ or disorder$ or disturbanc$ or ill$)) or smi$1).ti,ab.
6. (bipolar$ or ((cyclothymi$ or rapid or ultradian) adj5 cycl$) or rcbd or hebephreni$ or mania$ or manic$ or oligophreni$ or psychose$ or psychosi$ or psychotic$ or schizo$).ti,ab.
7. (((tardiv$ and dyskine$) or akathisi$ or acathisi$ or (neuroleptic$ and malignant and syndrome) or (neuroleptic and movement and disorder) or parkinsoni$ or neuroleptic-induc$) not (parkinson$ and disease)).ti,ab.
8. (emergency services, psychiatric or hospitals, psychiatric or psychiatric department, hospital or (mentally ill persons and (inpatients or hospitalization))).sh. or (psychiatric adj2 (admission$ or admitted or emerg$ or hospitali$ or inpatient$ or in patient$)).ti,ab.
9. or/1-8

10. comorbidity/ or "diagnosis, dual (psychiatry)"/
11. (comorbid$ or co morbid$ or ((dual$ or tripl$) adj2 (diagnos$ or disease$ or disorder$ or illness$ or mental or problem$ or psych$ or syndrome$)) or coexist$ or co exist$ or concur$ or con cur$ or cooccur$ or co occur$).ti,ab.
12. or/10-11
13. (designer drugs or needle exchange programs or needle sharing or overdose or street drugs or substance abuse detection or substance abuse, intravenous or substance abuse treatment centers or substance-related disorders or substance withdrawal syndrome).sh.
14. (((drug$1 or polydrug$ or psychotropic$ or substance$) adj3 (abstain$ or abstinen$ or abus$ or addict$ or excessive use$ or criminal or depend$ or habit$ or illegal$ or illicit$ or intoxicat$ or misus$ or nonprescri$ or non prescri$ or over dos$ or overdos$ or recreation$ or unlawful$ or withdraw$)) or ((drug$1 or polydrug$ or recreation$ or substance$) adj use$1) or ((drug$1 or polydrug$ or substance$) adj rehab$) or abusable product$ or (crave$ adj2 inject$) or hard drug$ or needle fixation or soft drug$ or vsa$1).ti,ab.
15. ((club or designer or street) adj2 (drug$ or substance$)).ti,ab.
16. or/13-15
17. (amphetamine or amphetamine-related disorders).sh.
18. (dextroamphetamine or methamphetamine).sh.
19. (((amphetamin$ or crystal meth$ or desoxyn or dexamfetamin$ or dexedrine or dextroamphetamin$ or methamphetamin$ or psychostimulant$ or stimulant$ or uppers) adj5 (abstain$ or abstinen$ or abus$ or addict$ or banned or excessive use$ or criminal or depend$ or habit$ or illegal$ or illicit$ or intoxica$ or misus$ or nonprescri$ or non prescri$ or over dos$ or overdos$ or recreation$ or rehab$ or unlawful$ or using or utilis$ or utiliz$ or withdraw$)) or ((amphetamin$ or crystal meth$ or desoxyn or dexamfetamin$ or dexedrine or dextroamphetamin$ or methamphetamin$ or psychostimulant$ or stimulant$ or uppers) adj2 use$1)).ti,ab.
20. (amphetamin$ or crystal meth$ or desoxyn or dexamfetamin$ or dexedrine or dextroamphetamin$ or methamphetamin$ or psychostimulant$ or stimulant$ or uppers).ti,ab.
21. or/17-19
22. 20
23. exp cocaine/ or cocaine-related disorders.sh.
24. (((benzoylmethyl ecgonine or cocain$ or crack$1 or codrenine or ecgonine methyl ester benzoate or erythroxylin or locosthetic or neurocaine or sterilocaine) adj5 (abstain$ or abstinen$ or abus$ or addict$ or banned or excessive use$ or criminal or depend$ or habit$ or illegal$ or illicit$ or intoxica$ or misus$ or nonprescri$ or non prescri$ or over dos$ or overdos$ or recreation$ or rehab$ or unlawful$

or using or utilis$ or utiliz$ or withdraw$)) or ((benzoylmethyl ecgonine or cocain$ or crack$1 or codrenine or ecgonine methyl ester benzoate or erythroxylin or locosthetic or neurocaine or sterilocaine) adj2 use$1)).ti,ab.

25. (benzoylmethyl ecgonine or cocain$ or crack$1 or codrenine or ecgonine methyl ester benzoate or erythroxylin or locosthetic or neurocaine or sterilocaine).ti,ab.
26. or/23-24
27. 25
28. (heroin or heroin dependence or opioid-related disorders).sh.
29. (((heroin or diacetylmorphin$ or diagesil or diamorf or diamorphin$) adj5 (abstain$ or abstinen$ or abus$ or addict$ or banned or excessive use$ or criminal or depend$ or habit$ or illegal$ or illicit$ or intoxica$ or misus$ or nonprescri$ or non prescri$ or over dos$ or overdos$ or recreation$ or rehab$ or unlawful$ or using or utilis$ or utiliz$ or withdraw$)) or ((diamorphin$ or acetomorphine or anpec or diacephine or diacetylmorphine$ or diagesil or diamorf or diaphorin or duromorph or epimorph or heroin or morfin$ or morphacetin or morphia or morphian$ or morphin$ or morphium or opso$1 or skenan) adj2 use$1)).ti,ab.
30. (heroin or diacetylmorphin$ or diagesil or diamorf or diamorphin$).ti,ab.
31. or/28-29
32. 30
33. (cannabis or marijuana abuse or marijuana smoking).sh.
34. (((bhang or cannador or cannabis or ganja or ganjah or hashish or hemp or marihuana or marijuana or sativex or skunk) adj5 (abstain$ or abstinen$ or abus$ or addict$ or banned or excessive use$ or criminal or depend$ or habit$ or illegal$ or illicit$ or intoxica$ or misus$ or nonprescri$ or non prescri$ or over dos$ or overdos$ or recreation$ or rehab$ or unlawful$ or using or utilis$ or utiliz$ or withdraw$)) or ((bhang or cannador or cannabis or ganja or ganjah or hashish or hemp or marihuana or marijuana or sativex or skunk) adj2 use$1)).ti,ab.
35. (bhang or cannador or cannabis or ganja or ganjah or hashish or hemp or marihuana or marijuana or sativex or skunk).ti,ab.
36. or/33-34
37. 35
38. 9 and 12 and (or/22,27,32,37)
39. 9 and (or/16,21,26,31,36)
40. or/38-39

10.1.2 Search filters

Health economics and quality of life search filter – this is an adaptation of a filter designed by the NHS Centre for Reviews and Dissemination at the University of York.

MEDLINE - Ovid SP interface

1. exp "costs and cost analysis"/ or health priorities/ or health resources/ or exp resource allocation/
2. budgets/ or socioeconomic factors/ or (economi$ or fee or fees or financ$).hw.
3. quality adjusted life years/ or "quality of life"/ or "value of life"/
4. exp models, economic/ or models, statistical/ or monte carlo method/
5. health status indicators/
6. decision trees/
7. (budget$ or cost$ or econom$ or expenditure$ or financ$ or fiscal or funding or pharmacoeconomic$ or socioeconomic$ or price or prices or pricing or (value adj3 money) or (burden adj3 (disease$ or illness$))).ti,ab.
8. (daly or qol or hql or hqol or hrqol or hr ql or hrql or (quality adj2 life) or (adjusted adj2 life) or qaly$ or (health adj2 stat$) or well being or wellbeing or qald$ or qale$ or qtime$ or eq5d or eq 5d or qwb or ((quality or value$) adj3 (life or survival or well$)) or hui$1 or (utilit$ adj1 (health or score$ or weigh$)) or (life adj2 year$) or health year equivalent$ or ((disability or quality) adj adjusted) or utility value$ or (weight$ adj3 preference$) or euroqol or euro qol or visual analog$ or standard gamble or time trade or qtwist or q twist or (valu$ adj2 quality)).ti,ab.
9 decision tree/ or decision trees/
10 (decision analy$ or monte carlo or markov or simulation model$ or rosser or disutili$ or willingness to pay or tto or hye or hyes or (resource adj (allocat$ or use$ or utilit$))).ti,ab.
11 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).ti,ab.
12 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).ti,ab.
13 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).ti,ab.
14 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).ti,ab.
15 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).ti,ab.
16 ec.fs. *[ANDed with subject heading searches for the main population/topic]*
17 or/1-16

APPENDIX 10: METHODOLOGY CHECKLISTS FOR ECONOMIC STUDIES

The methodological quality of each study was evaluated using the NICE checklists for economic evaluations, reproduced below (for information about how to complete the checklist, see *The Guidelines Manual* [NICE, 2009]).

Section 2: Study limitations (the level of methodological quality) This checklist should be used once it has been decided that the study is sufficiently applicable to the context of the clinical guideline.	**Yes/ Partly /No/ Unclear/ NA**	**Comments**

Study identification *Including author, title, reference, year of publication*			
Guideline topic:			Question no:
Checklist completed by:			
Section 1: Applicability (relevance to specific guideline review question(s) and the NICE reference case). This checklist should be used first to filter out irrelevant studies.		**Yes/ Partly/ No/Unclear /NA**	**Comments**
1.1	Is the study population appropriate for the guideline?		
1.2	Are the interventions appropriate for the guideline?		
1.3	Is the healthcare system in which the study was conducted sufficiently similar to the current UK NHS context?		
1.4	Are costs measured from the NHS and personal social services (PSS) perspective?		
1.5	Are all direct health effects on individuals included?		
1.6	Are both costs and health effects discounted at an annual rate of 3.5%?		
1.7	Is the value of health effects expressed in terms of quality-adjusted life years (QALYs)?		
1.8	Are changes in health-related quality of life (HRQoL) reported directly from patients and/or carers?		
1.9	Is the valuation of changes in HRQoL (utilities) obtained from a representative sample of the general public?		
1.10	Overall judgement: Directly applicable/Partially applicable/Not applicable There is no need to use section 2 of the checklist if the study is considered 'not applicable'.		
Other comments:			

2.1	Does the model structure adequately reflect the nature of the health condition under evaluation?		
2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?		
2.3	Are all important and relevant health outcomes included?		
2.4	Are the estimates of baseline health outcomes from the best available source?		
2.5	Are the estimates of relative treatment effects from the best available source?		
2.6	Are all important and relevant costs included?		
2.7	Are the estimates of resource use from the best available source?		
2.8	Are the unit costs of resources from the best available source?		
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?		
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?		
2.11	Is there no potential conflict of interest?		
2.12	Overall assessment: Minor limitations/Potentially serious limitations/Very serious limitations		
Other comments:			

APPENDIX 11: EVIDENCE TABLES FOR ECONOMIC STUDIES

Study ID **Country** **Study type**	**Intervention details**	**Study population** **Study design** **Data sources**	**Costs: description and values** **Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments**
Clark et al. 1998 USA Cost-effectiveness analysis (CEA)	Compared assertive community treatment (ACT) and standard case management (SCM) for patient with severe mental illness and substance misuse disorders	Study population: Patients with DSM-III-R diagnosis of schizophrenia, schizoaffective disorder, or bipolar disorder and; an active substance use disorder. Patients randomised to ACT (n=100) or PSM (n=93) Ave age: 34 Years; 74% Male Time-frame: 3 Years Study design: RCT (multi-centre) Data source(s): 7 mental health catchment areas in the US	**Costs** Resource use: Mental health treatment; General health care; legal system; community services (homeless shelters/soup kitchens); administration; informal care (family members' input) **Outcomes** Subjective QoL year details provided from patients' perspective using Quality of Life Interview instrument. A modified range from 0 (terrible) to 1 (delighted) was used and weighted (cumulative) scores were derived based on the time spent on each rating	**Costs** ACT: $118,078 per patient SCM: $124,145 per patient **Outcomes (QoL improvement from baseline)** ACT: 0.10 SCM: 0.04 **Cost-effectiveness** Ratios of cumulative quality of life years to total societal costs rather than of incremental cost-effectiveness were computed. Average QoL ratios per $10,000 in societal costs were 0.24 (ACT) and 0.20 (SCM).	Perspective: Societal Currency: US $ Cost Year: 1995 Time horizon: 3 years Discounting: Yes (3% costs; 5% outcomes) Funded by: National Institute of Mental Health, National Institute on Alcohol Abuse and Alcoholism/ New Hampshire Division of Mental Health and Developmental Services

Study ID **Country** **Study type**	**Intervention details**	**Study population** **Study design** **Data sources**	**Costs: description and values** **Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments**
Craig et al. 2008 UK Cost-Analysis (CA)	Programme for case managers that trained them to manage substance use disorders among persons with severe mental illness compared with waiting list control	Study population: Patients with clinical diagnosis of schizophrenia, schizoaffective disorder, or other non-affective psychotic illnesses or bipolar disorder with psychotic symptoms plus abuse or dependence on at least one substance Intervention (n=124) Control (n=104) Time-frame: 18 months Study Design: RCT (Cluster) Data source(s): Community mental health services in four London boroughs	**Costs** Resource use: Hospital inpatient days; Day Care; Medication; HC professional appointments (Psychiatrist, Community Nurse, Social Worker, Psychologist, Drug or Alcohol worker, Counsellor, GP); Criminal Justice (Court/ Police/Prison)	**Total Mean Costs** Intervention: 18,672 Control: 17,639	Perspective: Societal Currency: UK £ Cost Year: 2003/04 Time horizon: 18 months Discounting: No Funded by: Bethlem and Maudsley NHS Trust

Study ID **Country** **Study type**	**Intervention details**	**Study population** **Study design** **Data sources**	**Costs: description and values** **Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments**
French et al., 1999 USA Cost-Consequences Analysis (CCA)	Modified therapeutic community (TC) intervention compared with standard services in a treatment-as-usual (TAU) condition	Study population: Homeless mentally ill chemical abusers (MICAs) – axis I diagnoses of schizophrenia, major depression, mania and who also use drugs or alcohol Modified TC (n=228); TAU (n=53) Study Design: Cohort Study Data source(s): Homeless facilities and psychiatric hospitals located in New York City	**Costs** Perspective: Health service Intervention, hospital detox, emergency room visits, short-term residential stays, non-residential stays, outpatient visits, methadone maintenance, inpatient days **Outcomes** Substance use, criminal activity, HIV-risk behaviour, psychological status, employment status	**Costs** Modified TC: $29,255 TAU: $29,638 **Outcomes** Modified TC patients reported significantly greater reductions in criminal activity and psychological dysfunction; no significant differences in substance use or HIV-risk behaviour No formal synthesis of costs and outcomes	Perspective: Health service Currency: US $ Cost Year: 1994 Time horizon: 12 months Discounting: NA Funded by: National Institute on Drug Abuse, Public Health Service, US Department of Health and Human Services

Study ID **Country** **Study type**	**Intervention details**	**Study population** **Study design** **Data sources**	**Costs: description and values** **Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments**
Haddock et al. 2003 UK CEA	Integrated programme of cognitive-behavioural (CBT) combined with motivational intervention (MI) plus routine care (RC) versus RC alone	Study population: Patients (entered as patient and carer pairs) with ICD-10 diagnosis of schizophrenia, schizoaffective disorder or delusional disorder and DSM-IV diagnosis of substance dependence or misuse. Intervention (n=18) Control (n=18) Study Design: RCT Data source(s): Mental health units of 3 UK NHS hospital trusts	**Costs** Resource use: Intervention; hospital services; primary care services (GPs/practice nurses); community or domiciliary services (social workers/occupational therapists); day services; medication; patient costs (travel/out-of-pocket payments); productivity losses **Outcomes** Change in the Global Assessment of Functioning Scale (GAF) over 18 months	**Costs** Intervention: 8,753 (SD 4,804) Control: 10,013 (SD 10,717) **Outcomes** Intervention: 60.12 (SD 18.96) Control: 53.44 (SD 13.00) **Cost-effectiveness** Not reported Probability of intervention being less costly than routine care (at WTP of 0) was 69.3%	Perspective: Societal Currency: UK £ Cost Year: 1998/99 Time horizon: 18 months Discounting: No Funded by: West Pennine, Manchester and Stockport Health Authorities, Tameside and Glossop NHS Trust R&D support

Study ID Country Study type	Intervention details	Study population Study design Data sources	Costs: description and values Outcomes: description and values	Results: Cost-effectiveness	Comments
Jerrell et al. 1997 USA CEA	Comparison of three primary interventions (with emphasis on any ethnic differences): 12-Step recovery, case management and behavioural skills training	Study population: Patients with Axis I DSM-III-R diagnosis of psychosis or major depression with a co-occurring substance disorder 12-Step (n=39) Behavioural skills (n=48) Case Management (n=45) Study Design: RCT Data source (s): 5 community mental health centres in the US	**Costs** Perspective: Societal Resource use: 2 categories: Intensive mental health (inpatient days, nursing days, residential treatment, emergency days); Supportive mental health (case management hours, outpatient visits, supporting housing days, service days) **Outcomes** Psychological functioning (Social Adjustment Scale-II; Role Functioning Scale), mental health and substance abuse (Diagnosis Interview Schedule used by C-DIS_R programme)	**Total Costs** **Intensive mental health costs** 12-Step: $10,275 Behavioural skills: $4,276 Case Management: $7,643 **Supportive mental health costs** 12-Step: $7,798 Behavioural skills: $6,112 Case Management: $5,970 No differences between three treatment approaches in psychological functioning or psychiatric or substance abuse symptoms. Analysis was therefore based on cost differences	Perspective: US Health service Currency: US $ Cost Year: Not reported Time horizon: 18 months Discounting: No Funded by: National Institute of Mental Health

Study ID Country Study type	Intervention details	Study population Study design Data sources	Costs: description and values Outcomes: description and values	Results: Cost-effectiveness	Comments
Morse et al. 2006 USA CA	Three treatments: Integrated Assertive Community Treatment (IACT); Assertive Community Treatment Only (ACTO) and Standard Care (Control)	Study Population: Individuals (homeless at baseline) with co-occurring SMI and substance use disorders IACT (n=54); ACTO (n=54); Control (n=49) Mean Age: 40 yrs; 80% Male Study design: RCT Data source(s): US-based community mental health agencies	**Costs** Perspective: Societal Outpatient care (Direct treatments for IACT and ACTO; other mental health, other substance abuse treatment, physical health care, psychosocial rehabilitation); Inpatient care; Emergency Shelter; Social security; Transfer payments and maintenance benefits **Outcomes** Client Satisfaction; BPRS scale; Substance use (Interviewer rating)	**Costs** IACT: $48,764 ACTO: $71,211 Control: $41,726 IACT and Control groups had significantly lower total mean costs than ACTO but no significant differences between IACT and Control **Outcomes** IACT and ACTO participants significantly more satisfied with their treatment than control; no significant differences between IACT and ACTO. There was no significant effect of treatment group on BPRS scale (p=0.1) or substance use levels (p=0.72)	Perspective: Societal Currency: US $ Cost Year: 2001 Time horizon: 24 months Discounting: No Funded by: National Institute of Mental Health

APPENDIX 12: HIGH PRIORITY RESEARCH RECOMMENDATIONS

Research Recommendation 1

What is the prevalence, pattern and epidemiology of different combinations of coexisting psychosis and substance misuse (for example, schizophrenia with coexisting cannabis misuse; bipolar with coexisting alcohol misuse), and what patterns of use predict poor prognosis?

Why this is important

Many studies report that rates of substance use are considerably higher in people with psychosis than in the general population, and that the co-morbidity of substance use and psychosis is associated with poorer outcomes. However, the definitions and methods of assessment of both substance use and psychosis vary from study to study, which makes it difficult to draw conclusions about patterns and prevalence in patient groups differentiated by diagnosis, race and other demographics. Additionally, studies tend to be cross-sectional, so little is known about how substance use might change over time. Moreover, although there are some indications that relatively low levels of substance use can be associated with adverse outcomes for people with psychosis, the research provides little guidance about what levels and patterns of substance use in which patient groups are associated with the worst clinical and social outcomes. Such information is necessary to target resources at groups most at risk of very poor outcomes, to determine whether early intervention efforts might be more effective than interventions for long-standing comorbidity and to investigate whether different interventions are required for different diagnostic groups and types of substance. A cross-sectional study is required using a representative sample large enough to reliably establish the prevalence, pattern, and epidemiology of different combinations of psychosis and coexisting substance misuse (for example, schizophrenia with coexisting cannabis misuse; bipolar disorder with coexisting alcohol misuse).

Criteria for selecting high-priority research recommendations

Criterion	Explanation	Answer
Importance to patients or the population	What would be the impact on the population of any new or altered guidance (for example, acceptability to patients, quality of life, morbidity or disease prevalence, severity of disease or mortality)?	Improved quality of life, less time in inpatient services, improved morbidity and mortality rates.
Relevance to NICE guidance	How would the answer to this question change future NICE guidance (that is, generate new knowledge and/or evidence)? How important is the question to the overall guideline? The research recommendation should be categorised into one of the following categories of importance: • High: the research is essential to inform future updates of key recommendations in the guideline • Medium: the research is relevant to the recommendations in the guideline, but the research recommendations are not key to future updates • Low: the research is of interest and will fill existing evidence gaps.	Such information is necessary for a number of reasons, including: to target resources at groups most at risk of very poor outcomes; to determine whether early intervention efforts might be more efficacious than interventions for long standing co-morbidity; to investigate whether different interventions are required for different diagnostic groups and types of substance. This is of high importance.
Relevance to the NHS	What would be the impact on the NHS and (where relevant) the public sector of any new or altered guidance (for example, financial advantage, effect on staff, impact on strategic planning or service delivery)?	More efficient use of resources, and targeting of effective treatments to the right people.
National priorities	Is the question relevant to a national priority area (such as a national service framework or white paper)? The relevant document should be specified.	The DH document "The National Service Framework for Mental Health – Five Years On" (2004) identified that for "dual diagnosis", one fundamental problem is a lack of research evidence on which to base service development. As part of the Darzi review we should expect patients to have "access to the most effective treatments" – On the basis of our current

		knowledge the most effect psychological/psychosocial treatment in this population remains unknown.
Current evidence base	What are the problems with the current evidence base? (that is, why is further research required?) Reference should be made to the section of the full guideline that describes the current evidence base, including details of trials and systematic reviews.	It is difficult to interpret the current evidence base regarding prevalence and epidemiology of psychosis and coexisting substance misuse. And little is known about whether different interventions are needed for different combinations of psychosis and substance misuse. See Chapter 2, 5, 6, 7, 8, 9.
Equality	Does the research recommendation address equality issues? For example, does it focus on groups that need special consideration, or focus on an intervention that is not available for use by people with certain disabilities?	People with psychosis and coexisting substance misuse are often excluded from services and have poorer prognosis than people without both diagnoses.
Feasibility	Can the proposed research be carried out within a realistic timescale and at an acceptable cost? Are there any ethical or technical issues?	It should be possible to conduct this type of research in realistic timescale and at an acceptable cost.
Other comments	Any other important issues should be mentioned, such as potential funders or outcomes of previous attempts to address this issue, or methodological problems. However, this is not a research protocol.	

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Research Recommendation 2

What risk factors predict the onset of substance misuse in young people with psychosis?

Why this is important

The timing of onset of substance misuse in relation to the onset of psychotic symptoms is variable, with some young people starting to use substances before the onset of their psychosis, some as their psychosis develops and others soon after the onset of their psychosis. The course of psychosis is known to be adversely affected by substance misuse, and people with psychosis and coexisting substance misuse have a more prolonged and serious condition than those with psychosis alone. People with psychosis and substance misuse are more likely to be non-adherent to prescribed medication, have poor engagement with treatment programmes, increased risk of suicide, more and longer inpatient stays, increased risk of violence and time spent in the criminal justice system, and poorer overall prognosis. Because onset of psychosis at a younger age is also an indicator of poor prognosis, people with a combination of younger age of onset and coexisting substance misuse may have a particularly poor prognosis. A clearer understanding of the risk factors for substance misuse in young people with psychosis, and the interrelationship of the two conditions over time, may facilitate the development of treatment approaches for the coexisting conditions in this group. This may then improve the longer term outcome for a group of people who tend to have a poor prognosis. A prospective cohort study is required to establish what risk factors predict the onset of substance misuse in young people with psychosis.

Criteria for selecting high-priority research recommendations

Criterion	Explanation	Answer
Importance to patients or the population	What would be the impact on the population of any new or altered guidance (for example, acceptability to patients, quality of life, morbidity or disease prevalence, severity of disease or mortality)?	Improved quality of life, less time inpatient services, improved morbidity and mortality rates.
Relevance to NICE guidance	How would the answer to this question change future NICE guidance (that is, generate new knowledge and/or evidence)? How important is the question to the overall guideline? The research recommendation should be categorised into one of the following categories of importance: • High: the research is essential to inform future updates of key recommendations in the guideline • Medium: the research is relevant to the recommendations in the guideline, but the research recommendations are not key to future updates • Low: the research is of interest and will fill existing evidence gaps.	Before interventions can be developed for young people to prevent or reduce substance misuse, it is important to understand risk factors. This is of high importance.
Relevance to the NHS	What would be the impact on the NHS and (where relevant) the public sector of any new or altered guidance (for example, financial advantage, effect on staff, impact on strategic planning or service delivery)?	Effective treatments would lead to cost-savings and less pressure on inpatient services.
National priorities	Is the question relevant to a national priority area (such as a national service framework or white paper)? The relevant document should be specified.	The DH document "The National Service Framework for Mental Health – Five Years On" (2004) identified that for "dual diagnosis", one fundamental problem is a lack of research evidence on which to base service development.
Current evidence base	What are the problems with the current evidence base? (that is, why is further research required?) Reference should be made to the section of the full guideline that describes the current evidence base, including details of trials and systematic reviews.	Little is known about risk factors for substance misuse in young people with psychosis. See Chapter 9.

Equality	Does the research recommendation address equality issues? For example, does it focus on groups that need special consideration, or focus on an intervention that is not available for use by people with certain disabilities?	Younger age of onset is an indicator for poor prognosis. This recommendation focuses on young people.
Feasibility	Can the proposed research be carried out within a realistic timescale and at an acceptable cost? Are there any ethical or technical issues?	It should be possible to conduct this type of research in realistic timescale and at an acceptable cost.
Other comments	Any other important issues should be mentioned, such as potential funders or outcomes of previous attempts to address this issue, or methodological problems. However, this is not a research protocol.	

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Research Recommendation 3

Are psychological/psychosocial interventions (such as motivational interventions) more clinically effective and cost-effective at reducing substance misuse in people with psychosis and coexisting substance misuse?

Why this is important

Psychological/psychosocial interventions are recommended for the treatment of substance misuse: see the guidance 'Drug misuse: psychosocial interventions' (NICE clinical guideline 52). Among these psychosocial interventions, motivational interviewing has a strong evidence base with regard to improving clinical and social outcomes. In general, a non-judgmental style of engagement is considered appropriate as a prelude to enhancing engagement. During such a motivational approach, the person's appreciation and attitude to their illness can be gained and further, more intensive psychosocial interventions started. These may include supportive counselling, behavioural and cognitive techniques with an individual, group or family, as well as contingency management and skills training. However, there has been limited evidence for the effectiveness of treatments for substance misuse in people with psychosis, especially in the UK. All trials to date have been methodologically inadequate and underpowered. Therefore, sufficient studies are not available to allow the reporting of any robust conclusions about what works. Studies to date have included samples that are too heterogeneous in terms of types of substance, diagnostic groups and duration of conditions to give definitive outcomes. A randomised controlled trial in which participants are stratified for presenting condition is required. It should report short- and longer-term outcomes (including cost-effectiveness outcomes) of at least 12 months' duration.

Criteria for selecting high-priority research recommendations

Criterion	Explanation	Answer
Importance to patients or the population	What would be the impact on the population of any new or altered guidance (for example, acceptability to patients, quality of life, morbidity or disease prevalence, severity of disease or mortality)?	Improved quality of life, less time inpatient services, improved morbidity and mortality rates.
Relevance to NICE guidance	How would the answer to this question change future NICE guidance (that is, generate new knowledge and/or evidence)? How important is the question to the overall guideline? The research recommendation should be categorised into one of the following categories of importance: • High: the research is essential to inform future updates of key recommendations in the guideline • Medium: the research is relevant to the recommendations in the guideline, but the research recommendations are not key to future updates • Low: the research is of interest and will fill existing evidence gaps.	This type of research would provide a more robust evidence base on which to make treatment recommendations. This is of high importance.
Relevance to the NHS	What would be the impact on the NHS and (where relevant) the public sector of any new or altered guidance (for example, financial advantage, effect on staff, impact on strategic planning or service delivery)?	Effective treatments would lead to cost-savings and less pressure on inpatient services.
National priorities	Is the question relevant to a national priority area (such as a national service framework or white paper)? The relevant document should be specified.	The DH document "The National Service Framework for Mental Health – Five Years On" (2004) identified that for "dual diagnosis", one fundamental problem is a lack of research evidence on which to base service development. As part of the Darzi review we

		should expect patients to have "access to the most effective treatments" – On the basis of our current knowledge the most effect psychological/psychosocial treatment in this population remains unknown.
Current evidence base	What are the problems with the current evidence base? (that is, why is further research required?) Reference should be made to the section of the full guideline that describes the current evidence base, including details of trials and systematic reviews.	There are few well conducted RCTs and none in the UK on which to base treatment recommendations. See Chapter 7.
Equality	Does the research recommendation address equality issues? For example, does it focus on groups that need special consideration, or focus on an intervention that is not available for use by people with certain disabilities?	People with psychosis and coexisting substance misuse are often excluded from services and have poorer prognosis than people without both diagnoses.
Feasibility	Can the proposed research be carried out within a realistic timescale and at an acceptable cost? Are there any ethical or technical issues?	It should be possible to conduct this type of research in realistic timescale and at an acceptable cost.
Other comments	Any other important issues should be mentioned, such as potential funders or outcomes of previous attempts to address this issue, or methodological problems. However, this is not a research protocol.	

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Research Recommendation 4

For people with psychosis and coexisting substance misuse, do interventions that involve the assessment and modification of their environment lead to greater clinical improvement and cost-effectiveness than standard care or other more established interventions, such as motivational interviewing and contingency management?

Why is this important?

People with psychosis and coexisting substance misuse are often locked into adverse environmental circumstances that seem to reinforce both pathologies and prevent resolution and progress. There is currently some evidence that when the primary focus of management becomes the improvement of the environment with decisions made in consensus with the service user, both substance misuse and psychotic symptoms improve. The service user can then be more successfully treated outside hospital, with savings on costs. As so many people with this dual pathology spend long periods in hospital, such gains would be important for both patients and NHS services. The answer to this question assumes added importance when one considers the very limited efficacy of current treatment approaches. A randomised controlled trial in which participants are stratified for presenting problem is required. It should report short- and longer-term outcomes (including cost-effectiveness outcomes) of at least 12 months' duration.

Criteria for selecting high-priority research recommendations

Criterion	Explanation	Answer
Importance to patients or the population	What would be the impact on the population of any new or altered guidance (for example, acceptability to patients, quality of life, morbidity or disease prevalence, severity of disease or mortality)?	Improved quality of life, less time inpatient services, improved morbidity and mortality rates.
Relevance to NICE guidance	How would the answer to this question change future NICE guidance (that is, generate new knowledge and/or evidence)? How important is the question to the overall guideline? The research recommendation should be categorised into one of the following categories of importance: • High: the research is essential to	It would allow recommendations to be made about the use of interventions which involve the assessment and modification of the environment.

	inform future updates of key recommendations in the guideline • Medium: the research is relevant to the recommendations in the guideline, but the research recommendations are not key to future updates • Low: the research is of interest and will fill existing evidence gaps.	This is of high importance.
Relevance to the NHS	What would be the impact on the NHS and (where relevant) the public sector of any new or altered guidance (for example, financial advantage, effect on staff, impact on strategic planning or service delivery)?	Effective treatments would lead to cost-savings and less pressure on inpatient services.
National priorities	Is the question relevant to a national priority area (such as a national service framework or white paper)? The relevant document should be specified.	The DH document "The National Service Framework for Mental Health – Five Years On" (2004) identified that for "dual diagnosis", one fundamental problem is a lack of research evidence on which to base service development. As part of the Darzi review we should expect patients to have "access to the most effective treatments" – On the basis of our current knowledge the most effect psychological/psychosocial treatment in this population remains unknown.
Current evidence base	What are the problems with the current evidence base? (that is, why is further research required?) Reference should be made to the section of the full guideline that describes the current evidence base, including	No prospective randomised trials have not been conducted that have examined interventions which involve the assessment and modification of the

	details of trials and systematic reviews.	environment. See Chapter 7.
Equality	Does the research recommendation address equality issues? For example, does it focus on groups that need special consideration, or focus on an intervention that is not available for use by people with certain disabilities?	People with psychosis and coexisting substance misuse are often locked into adverse environmental circumstances that seem to reinforce both pathologies and prevent resolution and progress. Furthermore, they are often excluded from services and have poorer prognosis than people without both diagnoses.
Feasibility	Can the proposed research be carried out within a realistic timescale and at an acceptable cost? Are there any ethical or technical issues?	A secondary analysis of an existing RCT (see Chapter 7) suggests that environmental type interventions can be carried out within a realistic timescale and at an acceptable cost.
Other comments	Any other important issues should be mentioned, such as potential funders or outcomes of previous attempts to address this issue, or methodological problems. However, this is not a research protocol.	

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Research Recommendation 5

Is clozapine clinically effective and cost-effective at reducing craving in people with psychosis and coexisting substance misuse?

Why is this important?

Guidance on schizophrenia (NICE clinical guideline 82) states that clozapine should be offered to people with schizophrenia whose illness has not responded adequately to treatment despite the sequential use of adequate doses of at least two different antipsychotic drugs. However, there is insufficient evidence to guide healthcare professionals about the use of clozapine in people with psychosis and coexisting substance misuse. Expert opinion often advocates clozapine as having a particular role with this population, but the evidence to support such statements is lacking. Clozapine is expensive and has a wide range of side effects, some of which may be life-threatening if not monitored correctly. A randomised controlled trial in which participants are stratified for presenting problem is required. It should report short- and longer-term outcomes (including cost-effectiveness outcomes) of at least 12 months' duration.

Criteria for selecting high-priority research recommendations

Criterion	Explanation	Answer
Importance to patients or the population	What would be the impact on the population of any new or altered guidance (for example, acceptability to patients, quality of life, morbidity or disease prevalence, severity of disease or mortality)?	Pharmacological treatment that reduces substance misuse would likely lead to substantial improvements in morbidity and mortality rates.
Relevance to NICE guidance	How would the answer to this question change future NICE guidance (that is, generate new knowledge and/or evidence)? How important is the question to the overall guideline? The research recommendation should be categorised into one of the following categories of importance: • High: the research is essential to inform future updates of key recommendations in the guideline • Medium: the research is relevant to the recommendations in the guideline, but the research recommendations are not key to future updates • Low: the research is of interest and will fill existing evidence gaps.	The evidence base which supports the use of clozapine in treatment-resistant schizophrenia commonly excludes people with coexisting substance misuse. Future guidance could be given about the use of clozapine in people with psychosis and coexisting substance misuse. This is of high importance.
Relevance to the NHS	What would be the impact on the NHS and (where relevant) the public sector of any new or altered guidance (for example, financial advantage, effect on staff, impact on strategic planning or service delivery)?	Clozapine is already widely used within the NHS, but the clinical risk/benefit and financial impact is not yet know for this population. Extending the evidence-base for clozapine use will assist clinicians to make clinical and cost effective judgements on the use of this drug.
National priorities	Is the question relevant to a national priority area (such as a national service framework or white paper)? The relevant document should be specified.	The DH document "The National Service Framework for Mental Health – Five Years On" (2004) identified that for "dual diagnosis", one fundamental problem is a lack of research evidence on which to base service development. As part of the Darzi review we should expect patients to have

		"access to the most effective treatments" – On the basis of our current knowledge the most effect pharmacological treatment in this population remains unknown.
Current evidence base	What are the problems with the current evidence base? (that is, why is further research required?) Reference should be made to the section of the full guideline that describes the current evidence base, including details of trials and systematic reviews.	As stated above, the evidence base for clozapine is with treatment-resistant schizophrenia without coexisting substance misuse. Little is known about the use of clozapine for people with other psychoses.
Equality	Does the research recommendation address equality issues? For example, does it focus on groups that need special consideration, or focus on an intervention that is not available for use by people with certain disabilities?	There may be certain physical conditions or concurrent treatments that may prevent some people being included, but that would be a feature of most clinical trials involving pharmacotherapy.
Feasibility	Can the proposed research be carried out within a realistic timescale and at an acceptable cost? Are there any ethical or technical issues?	As a general principal, people with coexisting substance misuse should not be excluded from clinical trials involving clozapine. Special precautions may be needed to ensure the safety of patients taking concurrent substance which may interact with clozapine (for example smoking tobacco can lead to a reduction in clozapine levels, with corresponding increase in patients who stop smoking).
Other comments	Any other important issues should be mentioned, such as potential funders or outcomes of previous attempts to address this issue, or methodological problems. However, this is not a research protocol.	

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