NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Centre for Clinical Practice – Surveillance Programme

Surveillance review consultation document

4-year surveillance review of CG120: Psychosis with coexisting substance misuse: Assessment and management in adults and young people

Background information

Guideline issue date: March 2011
4 year review: 2015

Surveillance review recommendation

Surveillance review proposal for consultation:

The Psychosis with coexisting substance misuse guideline should not be considered for an update at this time.

Main findings of the current 4 year surveillance review

An Evidence Update was produced for the guideline in 2012 and was used as a source of evidence for the review proposal. The Evidence Update indicated that there is currently insufficient new evidence to generate change to the current guidance recommendations.
A literature search was conducted for randomised controlled trials and systematic reviews between 31st July 2011 (the end of the search period for the Evidence Update) and 4th November 2014 and relevant abstracts were assessed. Clinical feedback was also obtained from members of the guideline development group (GDG) through a questionnaire survey. Overall, 60% of questionnaire responders were not aware of any evidence that would change the current guideline recommendations and felt that CG120: Psychosis with coexisting substance misuse did not require an update at this time.

New evidence was identified for the current 4 year surveillance review relating to the following clinical areas within the Psychosis with coexisting substance misuse guideline.

Clinical area: Assessment		
Q: In people with psychosis and coexisting substance misuse, what are the key elements for a comprehensive assessment (of needs and risks)?		
Evidence summary	**GDG/clinical perspective**	**Impact**
<u>Evidence Update (2012)</u> No new evidence identified. <u>4-year surveillance review (2015)</u> A systematic review[1] (29 studies) examined risk factors for relapse in first episode psychosis. Persistent substance use disorder was found to increase the risk of relapse 3-fold in this sub population. Clinical variables and general demographic variables were found to have little impact on relapse rates. **Self-Rated Assessment** A secondary analysis[2] of an RCT (n=1042) sought to examine the degree to which individuals with schizophrenia disclose their use of drugs on self-rated assessments. The findings showed high rates of under-reported drug use among individuals with schizophrenia when compared to laboratory assays, and indicated that self-rated assessments alone should be used with caution. **Self-Harm** A meta-analysis[3] (222 studies, n=31,294) showed that comorbid bipolar disorder and substance misuse was significantly associated with suicide attempts and that this population should be targeted for suicide prevention efforts. A systematic review and meta-analysis[4] (18 studies) examined risk factors for deliberate self-harm before and after treatment for first episode psychosis. Alcohol	None identified through GDG questionnaire.	The new evidence on risk factors for relapse is consistent with CG120, which recommends (1.2.1) assessment of substance usage frequency and duration within a comprehensive assessment. The new evidence on self-rated assessment is consistent with CG120, which states (in the section on engagement and sources of information) that supplementing self-report with observation is important in the assessment, especially when people are reluctant to reveal their experience or details of their substance use or financial status. The new evidence reinforces recommendation 1.2.1, which states that when conducting an assessment of dependency, corroborative evidence should be sought from families, carers or significant others, where this is possible and permission is given. The new evidence on self-harm is consistent with CG120 1.4.14 which recommends regular assessment and monitoring of risk of harm to self and development of a risk management plan to be reviewed when service users' circumstances or levels of risk change. The evidence partially addresses research recommendation 1 for patients with first episode psychosis and alcohol or other substance misuse, although further research is required on specific sub-populations.

and other substance misuse were associated with an increased risk of deliberate self-harm in addition to duration of untreated psychosis. **Cognitive Function** A systematic review and meta-analysis[5] examined the effect of substance misuse on cognitive function in psychosis. Results showed that substance users performed significantly better than nonusers in the cognitive domains of attention and psychomotor speed and verbal memory, but were limited by methodological limitations. A systematic review and meta-analysis[6] (22 studies) compared the symptoms and social function of patients with psychosis and current substance use to those with psychosis and no history of substance use. Current substance users were found to have more severe positive symptoms than patients who had never used substances, but the findings were limited by demographic differences. **Disengagement** A systematic review[7] (10 studies) examined rates and definitions of disengagement among services for first-episode psychosis (FEP) and identified the most relevant demographic and clinical predictors of disengagement. Substance misuse and dependence was found to be a risk factor for disengagement, indicating that approaches to reduce risk of service disengagement in this population could increase service effectiveness. A secondary analysis[8] (n=198) of an RCT explored factors predictive of incarceration among people with coexisting severe mental illness and substance use disorder. Positive social relationships and substance use treatment engagement were associated with a reduced likelihood of incarceration.		The new systematic review evidence on cognitive and social function is consistent with recommendation 1.2.1 to assess dependency and duration of current level of use. Finally, the new evidence on service disengagement is consistent with CG120 1.4.10 which recommends promoting engagement through a comprehensive multidisciplinary assessment.

Clinical area: Assessment		
Q: Should the assessment be modified for subgroups of people (for example, young people, women, people from BME groups, homeless people, offenders, type of psychosis, type of substance misuse)?		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence Update (2012) No new evidence identified. 4-year surveillance review (2015) A post-hoc analysis[9] of an RCT (n=323) investigated the effects of comorbid substance abuse in first-episode schizophrenia on cognition and psychopathology. Substance use and non-substance use disorder patients showed similar psychopathology and neuropsychological performances at baseline and during the first 6 months of antipsychotic treatment. A correlation between longer duration of cannabis use and higher cognitive performance as well as reduced symptom improvement and more extrapyramidal motor symptoms in patients with higher frequency of cannabis consumption.	None identified through GDG questionnaire.	No relevant evidence was identified through the evidence update. The new evidence identified in the four year surveillance reinforces CG120 recommendation 1.4.10 to offer a comprehensive multidisciplinary assessment to include an assessment of current and past substance misuse and its impact upon their life, health and response to treatment.
Clinical area: Service models		
Q: 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 healthcare 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 Secondary outcomes: • Insight • Improved medication adherence • Improved access to services (reduced dropout) • Reduced relapse rates (measured by admission to hospital; number of bed days)		

• Improved mental state with respect to psychosis (for example, Positive and Negative Syndrome Schedule [PANSS]) • Reduced offending behaviour.		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence Update (2012) No new evidence identified. 4-year surveillance review (2015) A systematic review[10] (66 studies) found that community-based strategies for integrated treatment from the first outbreak of schizophrenia significantly reduced negative and psychotic symptoms, days of hospitalisation, and comorbidity with substance abuse and improved global functioning and adherence to treatment. A meta-analysis[11] (13 studies n=2824) found that integrated treatment of co-occurring substance use and mental health disorders resulted in modest, non-statistically significant improvements in psychiatric outcomes and alcohol use when compared to treatment as usual. Further examination of the effectiveness of integrated treatment in outpatient versus residential treatment settings revealed that the effectiveness of integrated care varies by setting. The impact of the evidence is weakened by the inclusion of small heterogeneous studies and geographical specificity to the USA. A secondary analysis[12] (n=383) of an RCT examined quality of life among patients with bipolar disorder in primary care versus community mental health settings**.** The effect of treatment setting on quality of life was adjusted for hazardous drinking and substance abuse. Participants reported similar impairments in mental and physical health related quality of life across both treatment settings, indicating the need for integrated care regardless of the setting they present at. The limitations of the study, including reliance on self-report	None identified through GDG questionnaire.	The systematic review evidence on community based strategies for integrated treatment is consistent with CG120 recommendation 1.4.5 which states that for most adults with psychosis and coexisting substance misuse, treatment for both conditions should be provided by healthcare professionals in secondary care mental health services such as community-based mental health teams. The evidence on outpatient versus residential care setting for integrated care is unlikely to impact on CG120 recommendations for staffed accommodation and reinforces the recommendation for further research to decide if staffed accommodation is more cost effective than a combination of hospital and home treatment.

without formal diagnostic interview, weaken its impact on CG120.		
Clinical area: Service models		
Q: What are the elements in an integrated service model that are most likely to be associated with better outcomes?		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence Update (2012) No new evidence identified. 4-year surveillance review (2015) A systematic review[13] (280 studies) and consensus building technique identified essential evidence based components of first episode psychosis services. In total, 32 components were established, including acceptance of referrals with potential comorbid psychosis and substance misuse, a comprehensive assessment upon admission, and integrated mental health and addictions treatment. A systematic review[14] (14 studies) assessed the evidence of component interventions in effective outpatient integrated treatment for patients with comorbid schizophrenia and substance use disorders. The findings suggested that behavioural treatment and specific interventions (e.g. motivational interviewing, family interventions) were effective. Programs integrating multiple interventions were also found to be more effective. The impact of the review is weakened by the heterogeneous study designs, and further research is needed to corroborate the findings. **Service delivery** A systematic review[15] (8 studies) of evidence supporting the efficacy of mental health apps for mobile devices found significant reductions in substance use. However, it should be noted that although trials on psychotic disorders were included,	Clinical feedback indicated that psychiatric and addiction services have changed greatly in the last 5 years and this group of patients is likely to be affected by the changes e.g. in commissioning for substance misuse services. However, no evidence was cited that may impact on CG120. Clinical feedback stated that there are some advances in online computer aided substance misuse programmes not considered in the original guideline and not tested in those with a dual diagnosis of psychosis and substance misuse, but only in depression and anxiety. This was stated as an area for future research, with two references cited that were outside the scope of the surveillance review.	The new evidence on components of first episode psychosis services is consistent with CG120 recommendation 1.5.2 for patients with psychosis and coexisting substance misuse attending substance misuse services to be offered a comprehensive, multidisciplinary mental health assessment in addition to an assessment of their substance misuse. Further research is required on technological innovations for service delivery, such as computer aided programmes and mental health applications for mobile devices, before these can be incorporated into CG120.

coexisting substance misuse was not reported in the abstract. The evidence was of low quality and is unlikely to impact on CG120.		
Clinical area: Service models		
Q: Are there subgroups of people (for example, based on severity of substance misuse and severity of psychosis; young people, BME groups) who may benefit from alternatives strategies (non-integrated service models, serial treatment, for example)?		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence Update (2012) No new evidence identified. 4-year surveillance review (2015) No new evidence identified.	Clinical feedback indicated that people older than 60 years' were excluded from the scope of CG120 and suggested that this exclusion may no longer be justified. The scope of CG120 incorporated a cut-off age of 60 because people with very late onset psychosis were considered to have different needs and a different evidence base for treatment. Feedback highlighted that this might have greater relevance in services which are not age stratified i.e. older peoples services that are not separated from adult services. No evidence was cited or retrieved in the surveillance review to support this feedback. Clinical feedback indicated that there are emerging novel psychoactive substances (NPS) that may have relevance for people who may be susceptible because of serious mental illnesses. Feedback also indicated that the variability and unpredictability of these substances adds an extra level of concern for this sub-group of patients and creates a need for enhanced competence. No evidence was cited or retrieved in the surveillance review on this sub-topic.	No evidence was cited or retrieved in the surveillance review to support the clinical feedback indicating that people over the age of 60 were incorrectly excluded from the scope of CG120. Any emerging research in this area will be considered at the next surveillance review. No evidence was cited or retrieved in the surveillance review relating to the clinical feedback about the implications of novel psychoactive substance dependence. Any emerging research in this area will be considered at the next surveillance review.
Clinical area: Service models		
Q: In people with psychosis and coexisting substance misuse, do the psychological/psychosocial interventions listed below (delivered within an integrated service model) when compared with an alternative management strategy lead to improved outcomes? • Individual interventions • Group interventions		

• Family intervention • Contingency management • Combined interventions		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence Update (2012) No new evidence identified. 4-year surveillance review (2015) **Behavioural and Contingency Management** A secondary analysis[16] (n=96) of an RCT investigated predictors of treatment response of individuals receiving contingency management treatments for addictions who suffer from co-occurring severe mental illness. The findings suggested that individuals with low levels of stimulant use and psychiatric severity, as well as those actively engaged in services, are most likely to succeed in a typical contingency management intervention. For other sub-groups, modifications to contingency management may be required. A systematic review[14] (14 studies) assessed the evidence of component interventions in effective outpatient integrated treatment for patients with comorbid schizophrenia and substance use disorders. The findings suggested that behavioural treatment and specific interventions (e.g. motivational interviewing, family interventions) were effective. Programs integrating multiple interventions were also found to be more effective. The impact of the review is weakened by the heterogeneous study designs, and further research is needed to corroborate the findings. **Family Intervention** An RCT[17] (n=108) found that both brief (2-3 months) and longer term (9-18 months) family education programs for co-occurring severe mental illness and substance misuse led to improved psychiatric, substance abuse and functional outcomes. The longer	None identified from GDG questionnaire.	**Behavioural and Contingency Management** The evidence from the 4 year surveillance review was insufficiently robust to impact on CG120, which does not recommend any specific psychological or psychosocial intervention or combination of interventions to people with psychosis and coexisting substance misuse. Recommendations 1.4.18-1.4.20 make general cross referrals to related guidelines CG38, CG82, CG100, CG115, CG51 and CG52 to ensure that evidence-based treatments are offered for both conditions. Recommendation 1.4.22 states that adults and young people with psychosis and coexisting substance misuse should not be excluded from contingency management programmes because of their psychosis, based on weak evidence in favour of this intervention. The new evidence is consistent with this recommendation. **Family Intervention** The new evidence supports the utility of family intervention for the CG120 population, but also indicates the need to modify programs to retain more families in treatment. This evidence is consistent with CG120 recommendation 1.1.8 which cross refers to CG82 schizophrenia recommendation 1.3.7 on family intervention. This recommends a specific supportive, educational or treatment function and inclusion of negotiated problem solving or crisis management work. Further evidence is required on the specific longer term program (Family Intervention for Dual Disorders) to

term program, which also incorporated communication and problem solving training, had significantly less severe overall psychiatric and psychotic symptoms and improved more in functioning. Substance abuse severity and family burden were not significantly different.		justify incorporating it into the recommendations.
Clinical area: Service models		
Q: In people with psychosis and coexisting substance misuse, does staffed accommodation when compared with an alternative management strategy lead to improved outcomes?		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence Update (2012) No new evidence identified. 4-year surveillance review (2015) A meta-analysis[11] (13 studies n=2824) found that integrated treatment of co-occurring substance use and mental health disorders resulted in modest, non-statistically significant improvements in psychiatric outcomes and alcohol use when compared to treatment as usual. Further examination of the effectiveness of integrated treatment in outpatient versus residential treatment settings revealed that the effectiveness of integrated care varies by setting. The limitations of small heterogeneous studies and geographical specificity to the USA should be noted.	None identified through GDG questionnaire.	The new evidence identified in the 4 year surveillance is unlikely to impact on CG120 recommendations for staffed accommodation. It reinforces the recommendation for further research to decide if staffed accommodation is more cost effective than a combination of hospital and home treatment.
Clinical area: Care Pathways		
Q: 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?		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence Update (2012) An 8-week study[18] of 102 veterans in the USA comparing a time-limited care coordination intervention (n=55) compared with a matched attention control (n=47) to evaluate the effects on engagement with outpatient treatment following discharge from a psychiatric unit. Participants had a schizophrenia spectrum or bipolar I disorder and a substance misuse	Clinical feedback advocated a review of current inpatient discharge policy, in order to reduce the length of inpatient stays. The current national practice is to retain patients in inpatient care for testing with the use of gradual exposure into the community. This was stated as incurring a high cost to the NHS, and having no evidence base. However, no new evidence was cited and no	The limitations of the evidence identified in the Evidence Update mean it is unlikely to impact on CG120 recommendation 1.6.6. This recommends that when adults and young people are discharged from an inpatient health service, they should have an identified care coordinator and a care plan considering their needs associated with both their psychosis and their substance misuse.

or dependence disorder and had used drugs or alcohol within the past 3 months. The study began in an inpatient facility and continued in the community after the patient's discharge from hospital. The results of this study provide limited evidence that an intervention with a specific focus on promoting engagement across the transition from inpatient to community care that includes assertive outreach and peer support components may increase engagement with outpatient treatment in people with psychosis with coexisting substance misuse who are discharged from inpatient psychiatric care. However, the Evidence Update concluded that this study was unlikely to impact on CG120 due to the limitations of the evidence. 4-year surveillance review (2015) No relevant evidence identified	further evidence was identified in the surveillance review.	No evidence was cited or retrieved in the surveillance review relating to the clinical feedback about inpatient discharge policy and inpatient length of stay. Any emerging research in this area will be considered at the next surveillance review.
Clinical area: Experience of care		
Q: For people with psychosis and coexisting substance misuse, what are their experiences of having problems with psychosis and substance misuse, of access to services, and of treatment?		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence Update (2012) No new evidence identified. 4-year surveillance review (2015) A secondary analysis[19] of an RCT aimed to validate a three factor model of perceived empowerment in patients with and schizophrenia with coexisting drug and alcohol misuse. The findings showed some evidence of associations between empowerment and both symptoms and global functioning, suggesting that empowerment should be assessed in treatments in addition to traditional outcome measures.	None identified through GDG questionnaire.	The new evidence on perceived empowerment is unlikely to impact on CG120. Further evidence and a standardised definition of empowerment is required before it can be considered for inclusion in CG120, which lists the following critical outcomes: •Reduced mortality (all causes) •Reduced relapse rates •symptoms requiring change in healthcare 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
Clinical area: Pharmacological interventions for psychosis		
Q: Are there sub-groups of people (for example, young people, people with a particular type of psychosis, BME groups) who may benefit from alternative strategies?		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence Update (2012) No new evidence identified. 4-year surveillance review (2015) A subgroup analysis[20] of an RCT of unstable patients with schizophrenia showed no superiority of long acting injectable risperidone to psychiatrist's choice of oral antipsychotic in most clinically defined subgroups, although the white patients benefited more than the other groups on substance abuse outcomes.	None identified through GDG questionnaire.	Further evidence is required on long acting injectable risperidone in various subgroups before updating the recommendations on pharmacological interventions.
Clinical area: Psychological and psychosocial interventions for psychosis		
Q: For people with psychosis and coexisting substance misuse, should the psychological and psychosocial treatment (family intervention, CBT, arts therapies) of their psychosis be modified as a result of the substance misuse problem and the treatment provided (for example, methadone, buprenorphine, psychological treatment)? (a) During the acute phase (b) During non-acute phase If so, how should treatment be modified?		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence Update (2012) No new evidence identified. 4-year surveillance review (2015) An RCT[21] (n=103) of patients with cannabis use disorder and psychosis found that specialised psychosocial treatment plus treatment as usual did not reduce the frequency of cannabis use, but produced a non-significant reduction in the amount of cannabis used.	None identified through GDG questionnaire.	Further research is necessary to demonstrate effectiveness of specialised psychosocial treatment plus treatment as usual before it can be incorporated into CG120, which currently cross refers to CG178 Schizophrenia guideline for the psychosocial treatment of the schizophrenia population.
Clinical area: Psychological and psychosocial interventions for psychosis		
Q: Are there sub-groups of people (for example, young people, people with a particular type of psychosis, BME groups) who may benefit from alternative strategies?		

Evidence summary	GDG/clinical perspective	Impact
Evidence Update (2012) No new evidence identified. 4-year surveillance review (2015) A secondary analysis[22] (n=506) of an RCT of middle aged versus younger adults receiving web-delivered psychosocial treatment for substance use disorders identified unique features of middle aged substance abusers to inform age-specific substance abuse treatment planning.	None identified through GDG questionnaire.	The new evidence identifying unique features of middle aged substance abusers to inform age-specific substance abuse treatment planning is insufficient to impact on CG120. Currently CG120 only makes recommendations for adapting adult recommendations for young people (1.8.7) but does not differentiate between adult age groups. Further evidence is required before adult age sub-group treatment planning can be incorporated into CG120.
Clinical area: Pharmacological and physical interventions for substance misuse		
Q: 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 (for example, 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 (for example, young people, people with a particular type of psychosis, BME groups) who may benefit from alternative strategies?		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence Update (2012) No new evidence identified. 4-year surveillance review (2015) A pilot RCT[23] (n=55) found that varenicline treatment of concurrent alcohol and nicotine dependence in schizophrenia may be problematic because of safety concerns limiting recruitment and poor tolerability. Although there were no serious neuropsychiatric adverse events in the varenicline group, gastrointestinal adverse effects limited study completion.	None identified through GDG questionnaire.	The new evidence is unlikely to impact on CG120. CG120 cross refers to CG100 and CG115 for alcohol misuse treatment, which do not recommend varenicline for off label use. Varenicline is covered by TA123 and is licensed for smoking cessation but not alcohol dependence. Further research on off label use of varenicline is required before it could be considered for the CG120 population. CG120 also cross refers to CG178 Schizophrenia, which states that there is reasonable evidence of a benefit of varenicline for smoking cessation for people with schizophrenia. However, there are concerns about possible neuropsychiatric adverse effects as stated in the Summary of Product Characteristics, and found in the evidence review. The GDG considered that varenicline should be prescribed cautiously for smoking

		cessation for an adult with psychosis and schizophrenia. The new evidence is consistent with this recommendation.
Clinical area: Pharmacological and physical interventions for substance misuse		
Q: For people with psychosis and coexisting substance misuse, should psychological and 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 (for example, young people, people with a particular type of psychosis, BME groups) who may benefit from alternative strategies? Sub-question 2: Should interventions be matched to stages of the treatment process (that is, engagement, persuasion, active treatment, relapse prevention)?		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence Update (2012) No new evidence identified. 4-year surveillance review (2015) A secondary analysis[16] (n=96) of an RCT investigated predictors of treatment response of individuals receiving contingency management treatments for addictions who suffer from co-occurring severe mental illness. The findings suggested that individuals with low levels of stimulant use and psychiatric severity, as well as those actively engaged in services are most likely to succeed in a typical contingency management intervention. For other sub-groups, modifications to contingency management may be required. It should be noted that the proportion of patient with psychosis was not specified in the abstract.	None identified through GDG questionnaire.	The new evidence identified in the 4 year surveillance review is insufficient to impact on CG120, which cross refers to related guidelines' recommendations on psychological and psychosocial treatment. Further research is needed on specific sub groups specifically with psychosis and coexisting substance misuse to justify alternative strategies.
Clinical area: Research recommendation		
Q: What are the prevalence, risk and protective factors, and course of illness for different combinations of psychosis and coexisting substance misuse (for example, schizophrenia and cannabis misuse or bipolar disorder and alcohol misuse)?		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence Update (2012) No new evidence identified. 4-year surveillance review (2015)	None identified through GDG questionnaire.	**Prevalence** New systematic review evidence showed alcohol use disorders to be highly prevalent in bipolar disorder, indicating that patients with bipolar disorder should be

A systematic review and meta-analysis[24] (9 studies) investigated the potential impact of cannabis use on duration of untreated psychosis (DUP). Although in most studies DUP was shorter in cannabis using patients, meta-analysis did not detect a significant relationship between DUP and cannabis use. A systematic review[25] assessed comorbidity rates of alcohol use disorders (AUDs) in bipolar disorder and found that AUDs are highly prevalent in bipolar disorder, indicating that patients with bipolar disorder should be assessed for current and previous AUDs. A systematic review[26] (20 studies) found no significant differences between former substance users with psychosis and non-substance users with psychosis in ratings of positive symptoms, negative symptoms, depression or global function. The findings indicated that a history of substance use is not a poor prognostic indicator for patients who are able to stop using substances. A secondary analysis[27] (n=61) of an RCT of adults with co-occurring alcohol use disorders and severe mental illness found a 54% prevalence of cannabis use during the study, some of which was obtained via medical prescription. Among those who used cannabis, most used it frequently. Cannabis use prevalence was considerably higher than in non-severely mentally ill adults with alcohol use disorders. A systematic review[28] found some evidence that chronic cannabis abuse could alter brain morphology in schizophrenia in patients continuing their cannabis consumption, but that there is no convincing evidence that this alteration takes place before the onset of schizophrenia when looking at first-episode patients.		assessed for current and previous alcohol use disorders. New primary research evidence indicated a high prevalence of cannabis use among patients with co-occurring alcohol use disorders and severe mental illness. **Risk and protective factors** Systematic review evidence suggested that chronic cannabis abuse could alter brain morphology in schizophrenia. The systematic review evidence of cannabis impact on duration of untreated psychosis was inconclusive. Systematic review evidence indicated that opiates are the only sedative drugs that possess an anti-psychotic effect, despite possessing a similar addictive process. Further research is warranted on the value of opiate agonism in psychosis treatment. **Course of Illness** New systematic review evidence on current versus former substance misuse in psychosis patients indicated that a history of substance misuse among former users has potential value as a prognostic indicator. The research recommendation has not been fully addressed and remains ongoing.

A systematic review[29] investigated the distinction between pro-psychotic and anti-psychotic substances found opiates to be the only sedative drugs that possess an anti-psychotic effect, despite possessing a similar addictive process.		
Clinical area: Research recommendation		
Q: Are interventions for psychosis or substance misuse clinically and cost effective when compared with standard care for people with psychosis and coexisting substance misuse?		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence Update (2012) A study[30] of a subset (n=141) sample taken from a larger cohort study examined patients who were taking a single antipsychotic drug (risperidone, olanzapine or clozapine) and who had a diagnosis of cannabis dependence. People with cannabis dependence were more likely than those in a comparator group on risperidone, olanzapine and clozapine who did not have cannabis dependence (n=363) to have used nicotine, alcohol or other illicit drugs in the past year. The group taking clozapine had significantly lower nicotine use in the previous 12 months compared with those taking risperidone or olanzapine. People taking risperidone had significantly higher scores than those on clozapine or olanzapine for OCDUS total score, thoughts subscale and craving subscale. No significant differences were seen between clozapine and olanzapine. Nicotine use was significantly lower in the clozapine group, which could have been a factor contributing to the lower craving for cannabis in this group. A secondary analysis[31] of an RCT (n=120) compared risperidone and olanzapine in people with first-episode schizophrenia. This new analysis looked at data only for the first 16 weeks of treatment in 49 people meeting (DSM) - IV criteria for a lifetime history of cannabis misuse or dependence. No significant differences were seen between the rates of treatment completion	None identified through GDG questionnaire.	No conclusive evidence was found for the following interventions, due to small sample sizes or inconclusive results: • Interventions for residual insomnia in schizophrenia secondary to substance misuse • Adjunctive benzodiazepine for bipolar disorder with comorbid substance misuse. • Olanzapine and risperidone for schizophrenia and coexisting cannabis use. • Specific treatments for reducing cannabis use in people with schizophrenia • Citicoline for methamphetamine dependence in bipolar disorder • Aripiprazole or risperidone for amphetamine-induced psychotic disorder • Quetiapine as monotherapy or adjunctive treatment to lithium or valproate semisodium in people bipolar I disorder and alcohol dependence For other interventions, the research recommendation also remains ongoing for the specific CG120 comorbid

or treatment response for either drug. Rates of cannabis use at the end of the study were also not significantly different between people on olanzapine and people on risperidone. The new evidence shows conflicting results for comparisons of olanzapine and risperidone, and the small sample size for clozapine (n=23) may prevent any firm conclusions about its effects. The Evidence Update concluded that these studies reinforce the need for an adequately powered RCT to determine whether differences in the effects of antipsychotic drugs exist in this population. As such, the evidence was considered unlikely to affect CG120. An RCT[32] compared quetiapine with placebo as an add-on treatment to lithium (n=185) or valproate semisodium (n=177) in people with DSM-IV diagnosed bipolar I disorder and alcohol dependence assessed by the Structured Clinical Interview for DSM. The results of this study provide limited evidence that quetiapine has no effect on alcohol use in people with bipolar I disorder who drink heavily, and may not have additive effects on mania, depression or anxiety in people taking lithium or valproate semisodium. This evidence was considered unlikely to affect CG120, which recommends that people should have treatment according to the underlying psychotic disorder. <u>4-year surveillance review (2015)</u> A systematic review[33] investigated the evidence base for the different treatment options in residual insomnia in schizophrenia, which may be secondary to coexisting substance misuse. No conclusive evidence was found for specific interventions. A secondary analysis[34] of an RCT of lithium- or quetiapine-treated patients with bipolar disorder found that there was no significant effect of adjunctive benzodiazepine use on any outcome measure in patients with comorbid substance use disorders.		population. The totality of new evidence is unlikely to affect CG120, which defers to the related NICE guidelines for the treatment of specific psychosis and substance misuse conditions.

An RCT[35] (n=60) of patients with bipolar depression or major depressive disorder and methamphetamine dependence treated with citicoline found that there was a significant improvement in depressive symptoms but no significant differences in memory or methamphetamine use. An RCT[36] (n=45) of patients with amphetamine-induced psychotic disorder found that both aripiprazole and risperidone were effective in reducing positive and negative symptoms. Risperidone had a statistically significantly greater effect on positive psychotic symptoms while aripiprazole had a non-significantly greater effect on negative symptoms. A systematic review[37] (8 trials) investigated specific psychological treatments, antipsychotics and cannabinoids for cannabis reduction in people with schizophrenia. Results were inconclusive due to the small number and size of trials and indicated that further research is required. A systematic review[38] on aripiprazole for bipolar disorder in adults found that data does not support its use as a first choice maintenance monotherapy but it may be useful as a combination therapy for bipolar disorder patients with comorbidities such as drug abuse. A systematic review[39] (11 studies) examined the cost effectiveness of interventions to promote the physical health of people with mental health problems. Although most studies suggested that that value for money actions in specific contexts and settings are available, none were reported for psychosis and coexisting substance misuse which weakens the impact on CG120.		

A systematic review[40] investigated the effectiveness of antipsychotic treatments for cocaine dependence in schizophrenic patients. The results were inconclusive and reinforced the CG120 research recommendation for further research. An RCT[41] (n=90) of quetiapine in patients with bipolar disorder and alcohol dependence found no significant between-group differences on the primary outcome measure of drinks per day or other alcohol-related or mood measures. An RCT[42] (N=37) of methamphetamine dependent patients with a history of psychosis found that aripiprazole significantly decreased psychotic symptoms without serious adverse events. No statistically significance was found between the two groups in maintaining abstinence.		
Clinical area: Research recommendation		
Q: Are psychosocial interventions clinically and cost effective when compared with standard care for people with psychosis and coexisting substance misuse?		
Evidence summary	**GDG/clinical perspective**	**Impact**
<u>Evidence Update (2012)</u> A single-centre RCT[43] studied a motivational intervention to reduce cannabis use compared with treatment as usual over 12 months (n= 62) for psychosis and coexisting cannabis use. Participants were aged 18–35 years and smoked at least 3 cannabis joints per week in the month before joining the study. This evidence suggests that a specifically designed motivational intervention may reduce cannabis use in people with psychosis to a greater extent than usual care in the 6 months in which the intervention is delivered, but this difference may not be sustained at 12 months. The intervention is more time-intensive and	None identified through GDG questionnaire.	The totality of new evidence on psychosocial interventions is inconclusive and is unlikely to affect CG120, which defers to the related NICE guidelines for the treatment of specific psychosis or substance misuse conditions. The research recommendation remains ongoing.

resource-intensive than the general brief motivational intervention recommended in CG51, therefore the Evidence Update concluded that this new evidence is not likely to affect current recommendations. <u>4-year surveillance review (2015)</u> An RCT[44] (n=110) of phase-specific psychological therapy for people with problematic cannabis use following a first episode of psychosis was identified. Results showed that neither extended nor brief psychological therapy (motivational interviewing and with CBT) conferred benefit over standard care in terms of reductions in frequency or amount of cannabis use. A secondary analysis[45] (n=103) of an RCT of patients with cannabis use disorder and psychosis found that specialised psychosocial treatment (motivational interviewing and cognitive behaviour therapy) plus treatment as usual resulted in a higher risk of psychiatric emergency room contact and admission, but fewer days admitted to psychiatric hospitals. An updated systematic review[46] (32 studies) of psychosocial interventions for people with both severe mental illness and substance misuse found no compelling evidence to support any one psychosocial treatment over another for people to remain in treatment or to reduce substance use or improve mental state. A systematic review[37] (8 trials) investigated specific psychological treatments, antipsychotics and cannabinoids for cannabis reduction in people with schizophrenia. Results were inconclusive due to the small number and size of trials and indicated that further research is required. A secondary analysis[47] (n=121) of an RCT of adult		

inpatients with a psychiatric disorder or dual diagnosis found that gender, dual diagnosis status, age and education may be important predictors of aftercare treatment adherence and that gender may be a moderator of motivational interviewing. An RCT[48] (n=176) found that contingency management plus treatment as usual was associated with increased abstinence from stimulant drug use in stimulant-dependent patients with serious mental illness. It should be noted that the serious mental illnesses were not specified in the abstract, which weakens the impact on CG120. A systematic review of meta-analyses[49] (61 meta-analyses) showed that effect sizes of psychotherapies vs placebo for major psychiatric disorders tended to be higher than those of medication, but direct comparisons did not reveal consistent differences. It should be noted that the number of meta-analyses covering psychosis with coexisting substance misuse was not specified in the abstract, which weakens the impact on CG120. An RCT[50] of patients with psychosis and comorbid cannabis dependence found that a group psychological intervention, based on cognitive behavioural therapy and motivational interviewing, improved quality of life but did not improve cannabis use, symptoms, global functioning insight or attitude to treatment. An RCT[51] (n=121) of individuals with serious mental illness and alcohol or drug dependence found that a 12-session 12-step facilitation therapy resulted in greater participation but not did not demonstrate greater improvement in alcohol and drug use.		
Clinical area: Research recommendation		

Q: Is clozapine clinically and cost effective when compared with other pharmacological interventions for people with psychosis and coexisting substance misuse?		
Evidence summary	**GDG/clinical perspective**	**Impact**
Evidence Update (2012) A study[30] of a subset (n=141) sample taken from a larger cohort study examined patients who were taking a single antipsychotic drug (risperidone, olanzapine or clozapine) and who had a diagnosis of cannabis dependence. People with cannabis dependence were more likely than those in a comparator group on risperidone, olanzapine and clozapine who did not have cannabis dependence (n=363) to have used nicotine, alcohol or other illicit drugs in the past year. The group taking clozapine had significantly lower nicotine use in the previous 12 months compared with those taking risperidone or olanzapine. People taking risperidone had significantly higher scores than those on clozapine or olanzapine for OCDUS total score, thoughts subscale and craving subscale. No significant differences were seen between clozapine and olanzapine. Nicotine use was significantly lower in the clozapine group, which could have been a factor contributing to the lower craving for cannabis in this group. The Evidence Update concluded that the small sample size for clozapine (n=23) may prevent any firm conclusions about its effects. Therefore, these studies reinforce the need for an adequately powered randomised controlled trial to determine whether differences in the effects of antipsychotic drugs exist in this population. The Evidence Update concluded that the identified evidence is unlikely to affect CG120. 4-year surveillance review (2015) A pilot RCT[52] (n=30) of dually diagnosed (DD) patients with schizophrenia and cannabis use disorders found that both clozapine and ziprasidone reduced cannabis use. Clozapine treatment was associated with less positive symptoms of schizophrenia, more side effects	None identified through GDG questionnaire.	The small sample sizes of the new studies identified reinforces the need for an adequately powered randomised controlled trial to determine whether differences in the effects of antipsychotic drugs exist in this population. The current evidence is unlikely to affect CG120.

and poorer compliance with treatment.		

For the following areas of the guideline no new evidence was identified:

- Should the assessment be the same in primary and secondary care?
- What factors should trigger a reassessment?
- Are there any subgroups of people (for example, young people, BME groups) that benefit from some elements of the service model more than others?
- Are there subgroups of people for whom we would alter our approach to treatment?
- 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?
- For families, carers or significant others of people who have psychosis and coexisting substance misuse, what are their experiences of caring for people with psychosis and coexisting substance misuse, and what support is available for families, carers or significant others?
- 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 (for example, methadone, buprenorphine, and so on)?
    - During the acute phase
    - During non-acute phase

  If so, how should treatment be modified?
- Are there sub-groups of people (for example, young people, people with a particular type of psychosis, BME groups) who may benefit from alternative strategies?
- Should interventions be matched to stages of the treatment process (that is, engagement, persuasion, active treatment, relapse prevention)?
- In people with psychosis and coexisting 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?
- What and how should training be provided to healthcare professionals working with people with psychosis and substance misuse?
- Is providing treatment for psychosis and substance misuse services within staffed accommodation more cost effective than a combination of hospital and home treatment?
- What service delivery models allow people with psychosis and coexisting substance misuse to remain living outside hospital?
- Are environmental interventions clinically and cost effective when compared with standard care for people with psychosis and coexisting substance misuse?
- What risk factors predict the onset of substance misuse in young people with psychosis?

Ongoing research

An ongoing randomised controlled trial (publication date not known) on improving physical health and reducing substance use in psychosis (ISRCTN58667926) was identified which is relevant to the following review question:

- For people with psychosis and coexisting substance misuse, should the psychological and psychosocial treatment (family intervention, CBT, arts therapies) of their psychosis be modified as a result of the substance misuse problem and the treatment provided (for example, methadone, buprenorphine, psychological treatment)?
    a) During the acute phase
    b) During non-acute phase

  If so, how should treatment be modified?

The trial will evaluate the effectiveness and cost-effectiveness of a health promotion intervention, based on motivational interviewing and CBT, versus treatment as usual in improving health and quality of life.

Anti-discrimination and equalities considerations

None identified.

Conclusion

Through the 4 year surveillance review of CG120 no new evidence which may potentially change the direction of guideline recommendations was identified. The proposal is not to update the guideline at this time.

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